Minneapolis Heart Institute Foundation®

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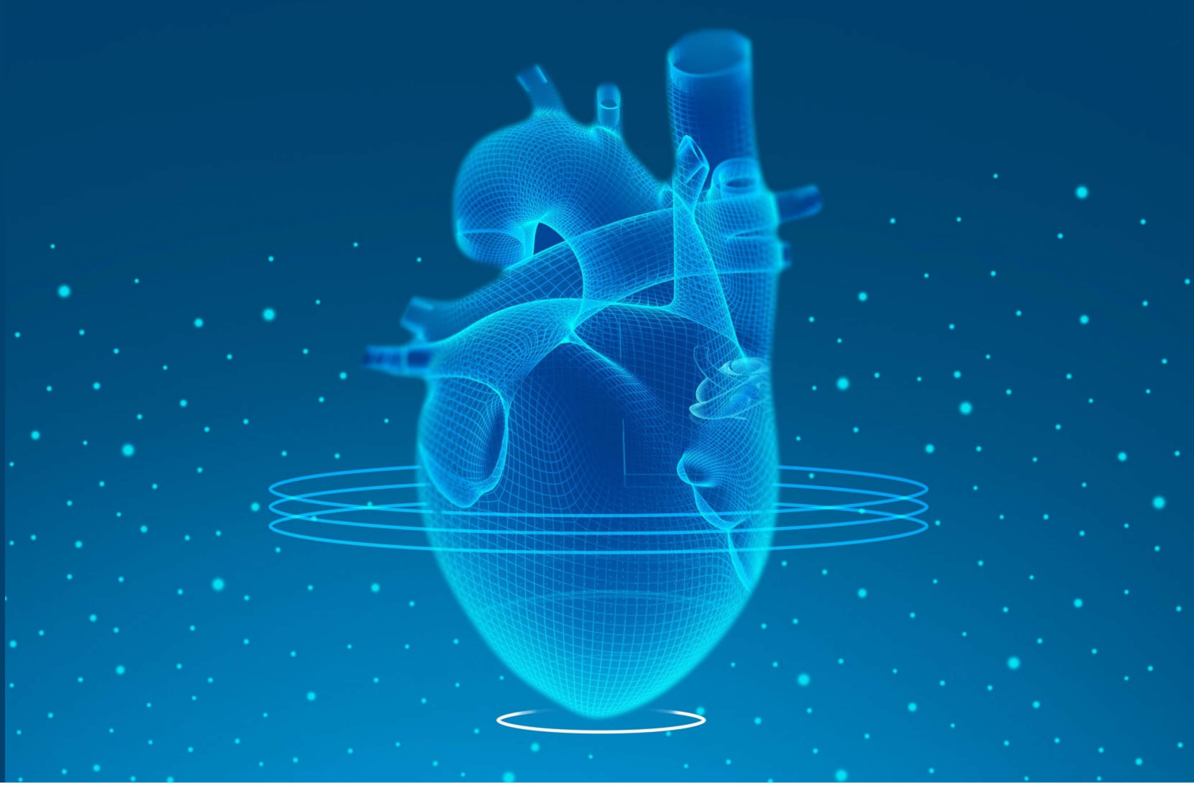

Heart Rhythm Science Center

February 21, 2022

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1

NO DISCLOSURES

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Introduction

- Introduce development and design of Heart Rhythm Science Center
- Highlight recent studies and publications in Device Safety and Innovation Pillar
- Demonstrate collaboration with industry in a manner that focuses on optimizing patient safety

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Vision

Advance the diagnosis and treatment of heart rhythm disorders worldwide

What is possible?

Leverage internal expertise and strengths to create an environment and partnership that accelerates heart rhythm science and thinks "BIG"

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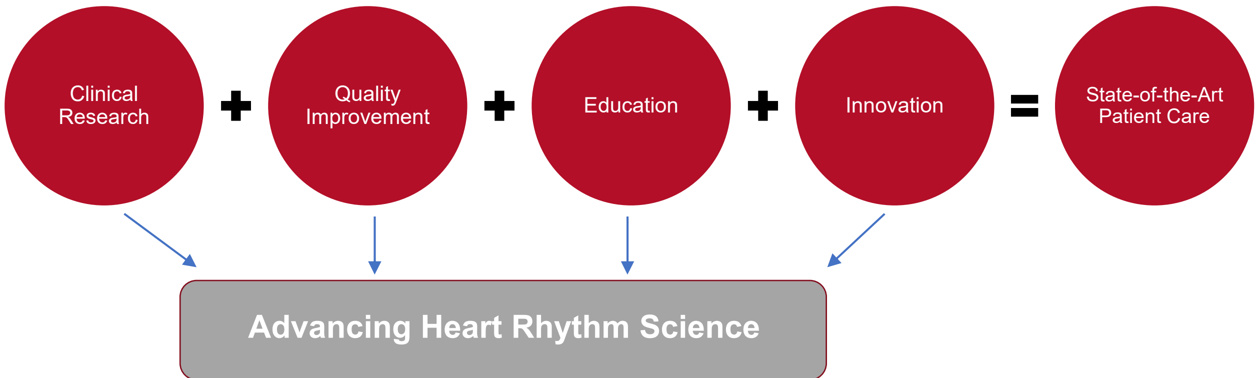
Integration within the Heart Rhythm Science Center
The Success Equation



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Goals

- Create more efficient and effective research process
  - Scale clinical questions into executable studies with reproducible processes for data collection and analysis
  - Identify and apply funding to support internal investigator-initiated studies
- Increase collaboration
  - Expands partnerships with HDI, Cardiovascular Imaging, MHI at United, Advanced heart failure and Valve science center
- Build on MHI clinical electrophysiology and MHIF research reputations
  - Accelerates partnership with industry and attracts multicenter studies
- Grow enrollment in studies
  - Enables research into novel and alternative treatment strategies and attracts industry and start-ups

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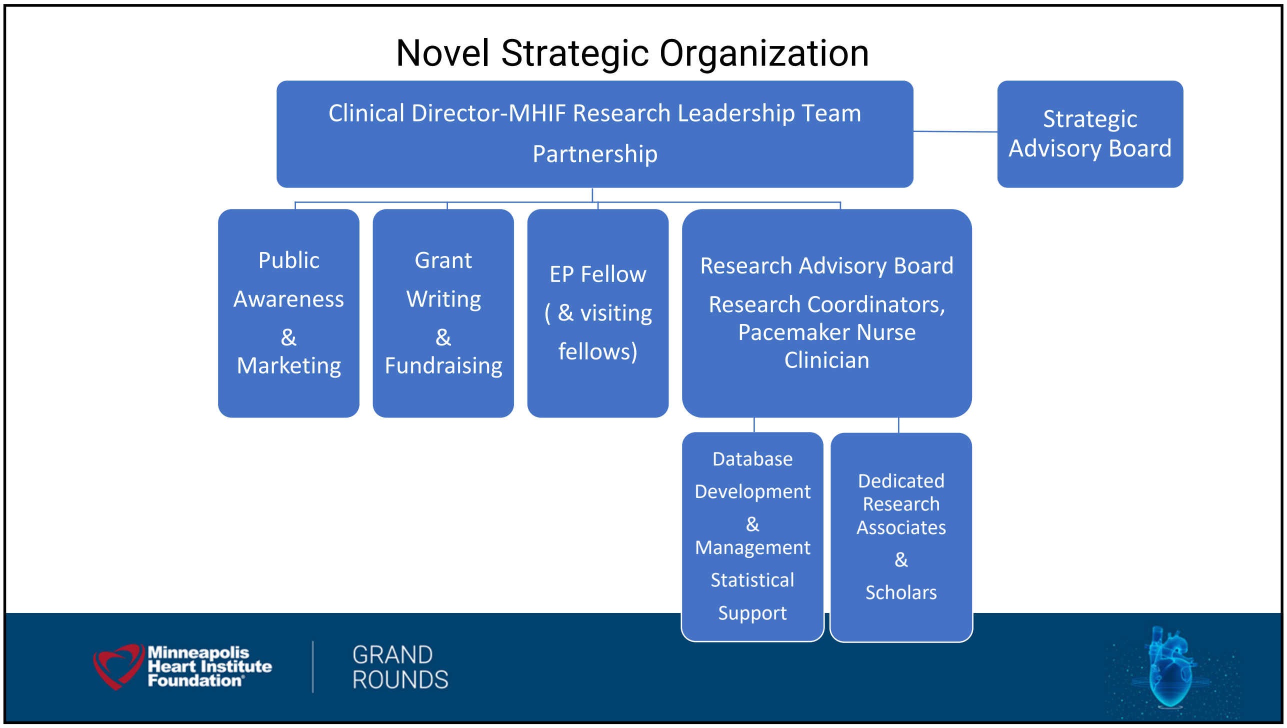
Novel Strategic Organization
Clinical Director-MHIF Research Leadership Team Partnership
Strategic Advisory Board
Public Awareness & Marketing
Grant Writing & Fundraising
EP Fellow (& visiting fellows)
Research Advisory Board
Research Coordinators, Pacemaker Nurse Clinician
Database Development & Management Statistical Support
Dedicated Research Associates & Scholars
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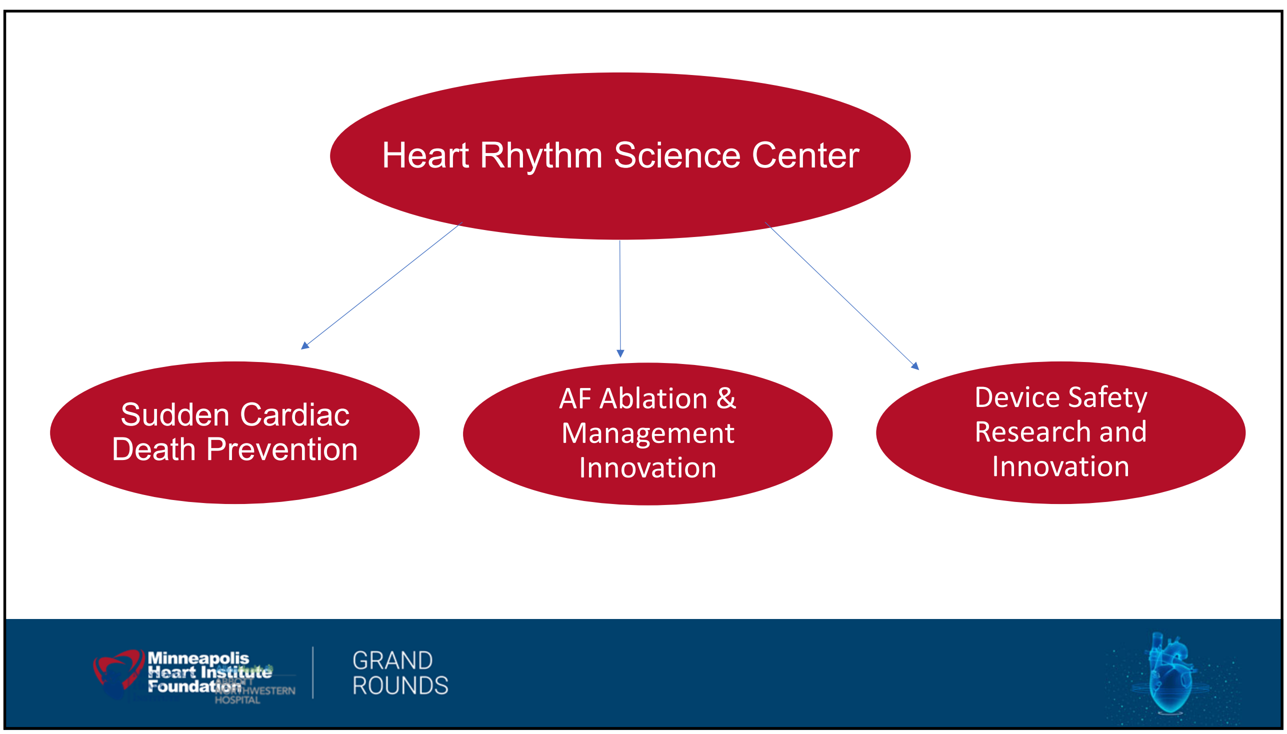
Heart Rhythm Science Center
Sudden Cardiac Death Prevention
AF Ablation & Management Innovation
Device Safety Research and Innovation
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Strategic Investments

Research

- Increase enrollment and attract latest studies and trials with cutting-edge technology
- Upgrading Dashboards, Databases, Software
- Funding and Resources for Investigator-Initiated Projects
- Publications, Presentations, Intellectual Property Development & Consulting
- Cardiac Device Clinic, EP Lab and Clinical Outcomes Data & Staff Coordination

Education

- Continuing Medical Education Seminars Fellowship
- Conference Attendance Professional organization representation Guideline and CPT committees

Outreach

- Marketing Material Community education and awareness events
- Conference & Seminar Hosting and Workshops and Live Case Studies

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ACKNOWLEDGEMENTS

Idea-Inspiration + Mentorship-Support

Catalyst

Collaboration-Growth + Innovation-Publication

Robert Hauser, Charles Gornick
Scott Sharkey, Kris Fortman, Ross Garberich
Alan Bank, Pierce Vatterott
Raed Abdelhadi, William Katsiyiannis
Dan Melby, JoEllyn Moore

Dawn Witt, Sue Casey, Pam Morley
Larissa Stanberry
Melanie Kapphahn-Bergs
Elizabeth Steele
Jessie Whelan, Jake Cohen

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Pillar: Device Safety Research and Innovation

- Monitor FDA databases and advisories
- Decades of work identifying device safety issues
  - Fidelis lead fracture, Riata lead malfunction, Boston Scientific generator failures, Leadless pacemaker safety issues, Battery malfunctions
- Develop and maintain registries tracking patient outcomes and safety over time
  - Large patient population with high percentage of follow-up
  - Build on current CIED and leadless pacemaker registries
- Surveillance and analysis of publicly available device safety data
  - Novel data analysis with other sources to produce vital patient safety research

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Pillar: Device Safety Research and Innovation

- Create patient education, support and awareness strategies, campaigns and materials
- Device Lead Management and Extraction
  - Dr. Gornick and Dr. Vatterott with years of ground-breaking expertise and research on lead management
  - Dr. Zakaib involvement in conduction system pacing and next generation leads with Medtronic sponsored LEADR trial
  - Drs. Moore, Olson, Peterson, Sengupta involvement in leadless left ventricular pacing
- Device Optimization and Heart Failure Management
  - Dr. Bank pioneering ground-breaking and proprietary research on device optimization
  - Collaboration with Dr. Samara with novel devices in cardiac contractility modulation

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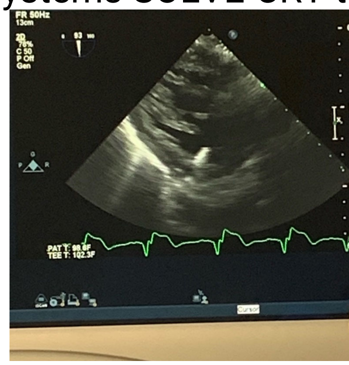
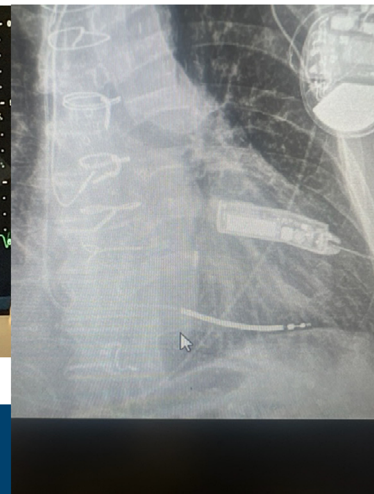
Pillar: Device Safety Research and Innovation

- EBR Systems SOLVE-CRT trial





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Pillar: Device Safety Research and Innovation

- Cardiac Implantable Electronic Device (CIED) interaction with common portable electronics
- Revolution in leadless pacing and what this means for providers and patients

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MHIF Summer Intern: Kathryn Xu

- Cardiovascular Implantable Electronic Devices (CIEDs) such as pacemakers and defibrillators contain an internal magnetic switch that functions to turn the CIED into magnet mode when triggered
- Magnet mode puts pacemakers into a fixed magnet rate and suspends shock therapy in defibrillators

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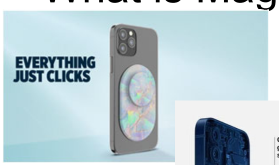
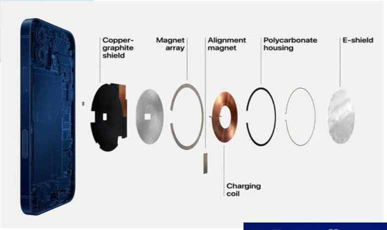
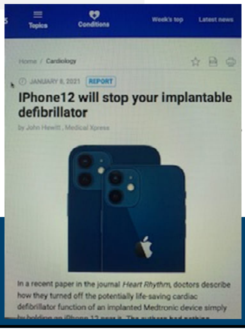
What is MagSafe?







- MagSafe is a magnetic technology from Apple in the iPhone 12 that facilitates easy attachment of accessories and accelerates wireless charging
- The iPhone 12 has been shown to potentially affect cardiac device programming resulting in magnet mode activation

IS MagSafe NOT SAFE or is 6 inches (15 cm) adequate?

1. Iphone 12 internal components courtesy of Apple, Inc
2. Greenberg JC, Attawil MR, Singh G. Letter to the editor---
Lifesaving therapy inhibition by phones containing magnets. Heart Rhythm 2021; 18: P1040-1041.

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Our Experiment Goals

1. To establish the maximum static magnetic field of common electronic gadgets
2. To confirm static magnetic field interference between various electronic gadgets and CIEDs
   - Focused on the iPhone 12 Pro, Apple Watch Series 6, and Airpods 2nd Generation
   - Tested 12 total CIEDs from Medtronic and Boston Scientific
3. To determine efficacy of current guidelines surrounding magnetic field interference

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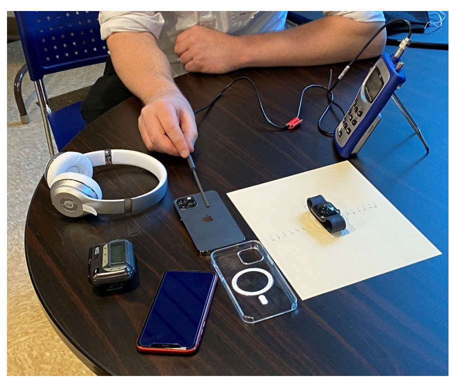
Methods - Measuring Maximum Static Magnetic Field



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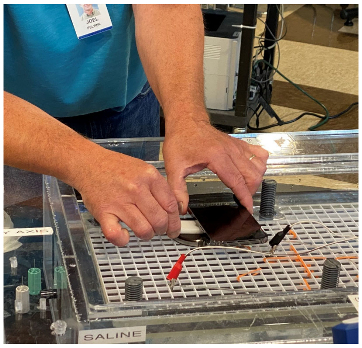
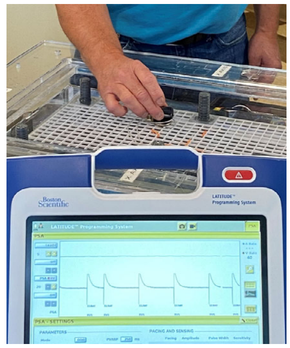
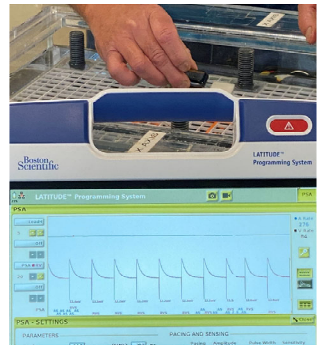
Methods – Testing



Placing electronic gadget over device


Normal pacing (40 bpm)


Magnet mode (84 bpm)

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Results – Electronic Gadget (EG) Interaction with CIEDs

- The iPhone 12 Pro, Apple Watch Series 6, and Airpods 2nd Generation initiated magnet mode in all of the devices when placed at the surface.
- 26 out of 37 CIED and EG combinations reached their maximum interaction distance at 1.0 cm
- There was one EG and device combination that resulted in interaction 1.5 cm
- The iPhone XR did not initiate magnet mode at any distance in the CIED tested

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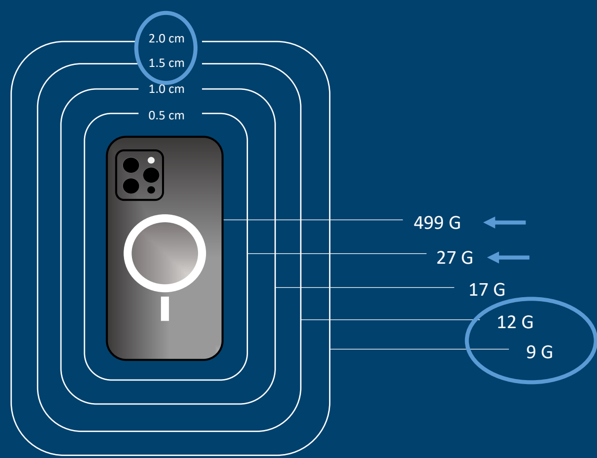
Results – iPhone 12 Pro Magnetic Field Distribution



10G = 1mT

Industry standard states that any magnetic field less than 10 G should be safe from cardiac device interactions

Magnetic field density and thus orientation also plays a role

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Conclusions

- The iPhone 12 Pro has a stronger magnet than previous iPhones
- Interference distance is consistent with the boundaries set by industry standards on electromagnetic compatibility (no interaction past distance where magnetic field <10 G)
- No device-device interaction would be anticipated at 6 inches (Apple advisory) given the magnetic field decreases based on the inverse square of the distance.
- Electronic products should not be worn on the same side as a CIED (e.g., coat pocket), and direct contact with the skin over an implanted device should be avoided.

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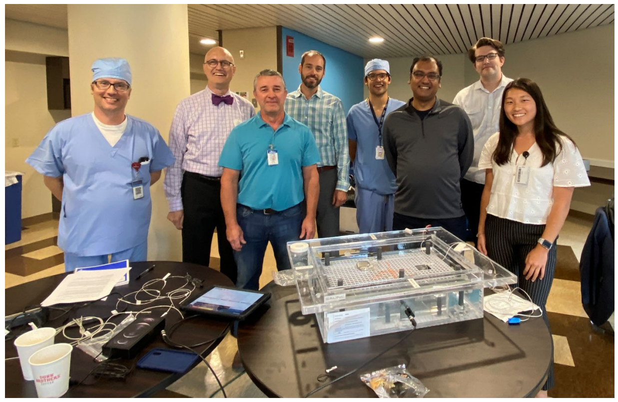
An example of the potential of HRSC
Special thanks to MHIF Summer Research Internship Program, and Industry partners: Boston Scientific and Medtronic, Inc!



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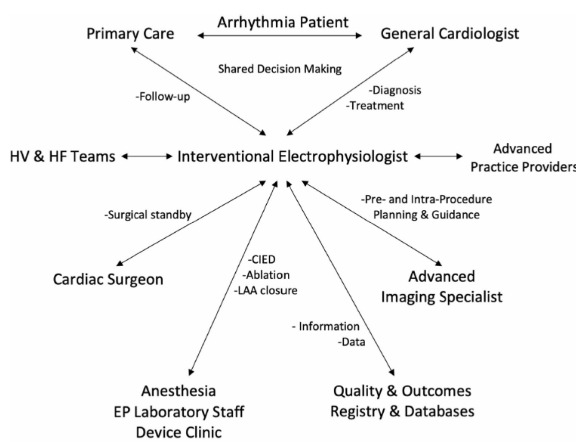
Interventional electrophysiology at a crossroads

Robert G. Hauser[1] · William T. Katsiyiannis[1] · Charles C. Gornick[1] · Jay D. Sengupta[1] · Raed H. Abdelhadi[1]
Journal of Interventional Cardiac Electrophysiology
https://doi.org/10.1007/s10840-021-01103-x
Heart Rhythm Science Center, Minneapolis Heart Institute Foundation, 920 East 28th, Street, Minneapolis, MN 55407, USA



HV=heart valve; HF=heart failure; CIED=cardiac implantable electronic device; LAA=left atrial appendage; EP=electrophysiology

Fig. 1 Multi-disciplinary Heart Rhythm Team

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Dr. Robert Hauser, MD

- Past President of HRS
- MHI Cardiologist
- Revolutionized device safety monitoring
- Mentor, Researcher, Teacher

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Leadless Pacemaker Perforations: Underappreciated and Lethal

Robert G. Hauser MD FACC FHRS

February 21, 2022

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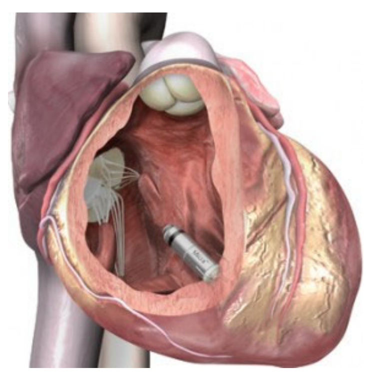
Potential Benefits of Leadless Pacemakers

- No transvenous lead complications
  - conductor fractures
  - insulation defects
  - venous occlusion
  - tricuspid regurgitation
- No pocket complications
  - hematoma
  - infection
  - discomfort
- No interference with transcatheter valve therapies



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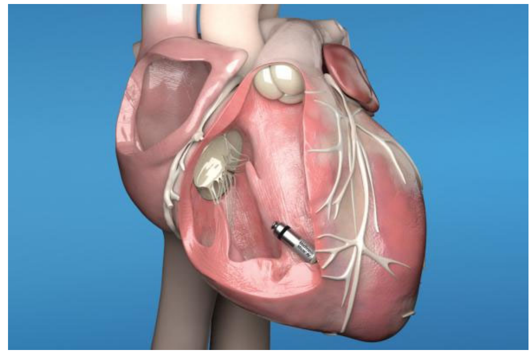
Leadless Intracardiac Pacemakers

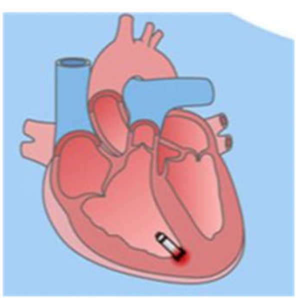


Single Chamber and AV Synchronous

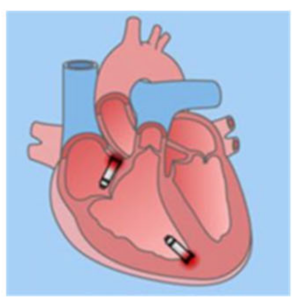
Dual Chamber

3

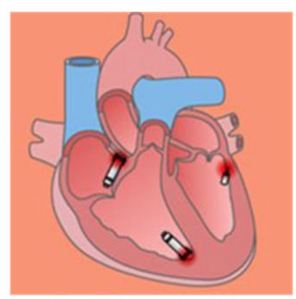
VVIR

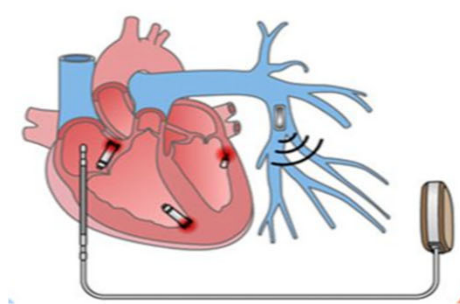


DDDR



CRT





CRT-D + Network

4

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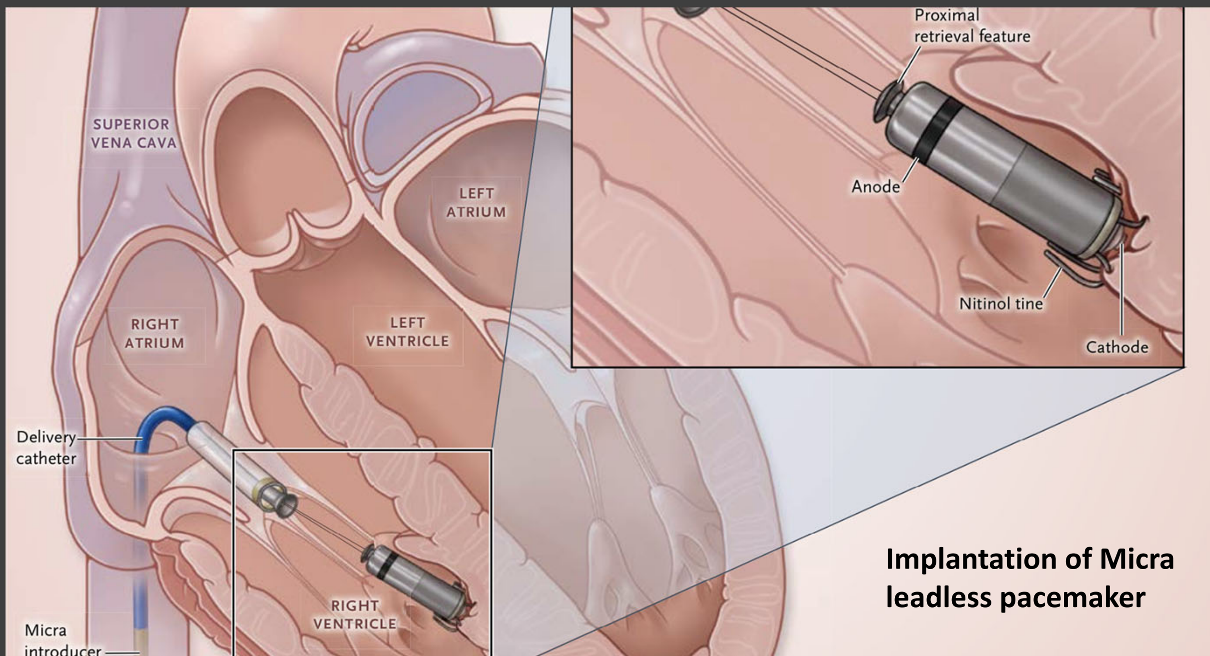

Implantation of Micra leadless pacemaker

5

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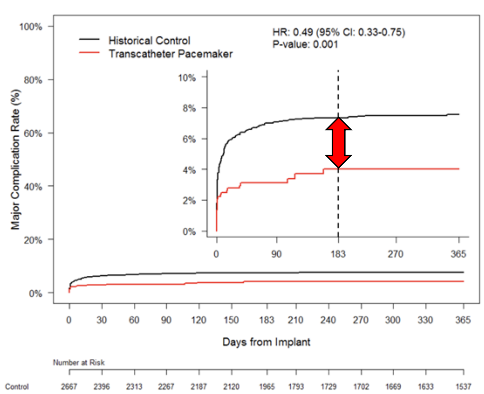
Micra™ vs Transvenous Pacemakers

- Reynolds, Ritter: **Micra TPS IDE Study** *in NEJM* 2016
- **725** Micra patients implanted at 56 centers vs **2,667** patients in the transvenous historical control group
- **99.2%** Micra implant success; **66%** implanted in RV apex, **33%** in septum.
- Of the 6 patients <u>not</u> implanted, **3** had cardiac perforations, and **1** had a pericardial effusion.



Adverse Event	No. of Events Associated with Major Complication Criterion*						No. of Patients (%)†
	Death	Loss of Device Function	Hospitalization	Prolonged Hospitalization‡	System Revision	Total Events	
Embolism and thrombosis	0	0	1	1	0	2	2 (0.3)
Deep vein thrombosis	0	0	0	1	0	1	1 (0.1)
Pulmonary thromboembolism	0	0	[illegible]	0	0	1	1 (0.1)
Events at groin puncture site: atrioventricular fistula or pseudoaneurysm	0	0	[illegible]	3	0	5	5 (0.7)
Traumatic cardiac injury: cardiac perforation or effusion	0	0	3	9	0	11	11 (1.6)
Pacing issues: elevated thresholds	0	1	[illegible]	1	2	2	2 (0.3)
Other events	1	0	[illegible]	4	1	8	8 (1.7)
Acute myocardial infarction	0	0	[illegible]	1	0	1	1 (0.1)
Cardiac failure	0	0	3	2	0	3	3 (0.9)
Metabolic acidosis	1	0	0	0	0	1	1 (0.1)
Pacemaker syndrome	0	0	1	0	1	1	1 (0.2)
Presyncope	0	0	0	1	0	1	1 (0.1)
Total	1	1	13	18	3	28	25 (4.0)

39%

1.6%

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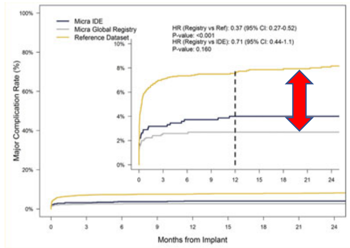
Micra "Real World" Performance

- El-Chami, Roberts: **Micra Post-Approval Registry** in *Heart Rhythm* 2018
- **1,817** Micra patients followed for 6.8±6.9 months.
- **99.1%** implant success, **64%** implanted in septum, **84%** required ≤3 deployments.



<u>14</u> Total Perforation/Effusion Events (0.77%)
- 8 patients required pericardiocentesis
- 2 patients required surgery and died
- 4 patients needed no intervention

Major complication criterion	Micra (n = 1817) No. of events (no. of patients, percentage)	Micra (n = 1817) 12-mo KM estimates (95% CI) (%)	Transvenous historical control (n = 2667) No. of events (no. of patients, percentage)	Transvenous historical control (n = 2667) 12-mo KM estimates (95% CI) (%)	Relative risk reduction (95% CI) (%)	*P*
Total major complications	46 (41, 2.26)	2.7 (2.0 to 3.7)	230 (196, 7.35)	7.6 (6.6 to 8.7)	63 (48 to 73)	<.0001
Death	5 (5, 0.28)	0.3 (0.1 to 0.8)	0 (0, 0.00)	0.0	NE	.0109
Hospitalization	17 (16, 0.88)	1.3 (0.8 to 2.1)	124 (106, 3.97)	4.1 (3.4 to 5.0)	71 (51 to 83)	<.0001
Prolonged hospitalization	33 (29, 1.60)	1.9 (1.3 to 2.7)	68 (64, 2.40)	2.4 (1.9 to 3.1)	24 (−18 to 51)	.2278
System revision	15 (13, 0.72)	0.9 (0.5 to 1.6)	102 (95, 3.56)	3.8 (3.1 to 4.6)	74 (54 to 85)	<.0001
Loss of device function	9 (9, 0.50)	0.7 (0.4 to 1.3)	0 (0, 0.00)	0.0	NE	.0003

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Mayo Clinic Experience 2014-2017

- Vaidya, Cha: *PACE* 2019.
- **<u>90</u>** leadless pacemakers (81% **Micra**, 19% **Nanostim**) vs **<u>90</u>** age and sex-matched transvenous pacemaker patients

Procedural characteristics	Leadless pacemaker (*N* = 90)	Transvenous pacemaker (*N* = 90)	*P*-value	Micra (*N* = 73)	Nanostim (*N* = 17)	*P*-value
Implant success rate	90 (100%)	90 (100%)		73 (100%)	17 (100%)	
Procedure time: median minutes (IQR)	111 (96-139)	85 (75-98)	<0.0001	109 (93-139)	113 (99-140)	0.005
Fluoroscopy time: median minutes (IQR)	8.9 (5.8-15.9)	2.9 (1.8-5.0)	<0.0001	6.9 (3.7-14.8)	14 (8.7-22.2)	0.66
Procedural complications						
Procedure-related major complications	0	1 (1%)	0.24	0	0	NA
Procedure-related minor complications	7 (8%)	3 (3%)	0.19	6 (8%)	1 (6%)	0.74
Pericardial effusion	2 (2%)	0	0.50	2 (3%)	0	1.00
Any infection	2 (2%)	3 (3%)	0.69	2 (3%)	0	1.00
Device endocarditis	0	3 (3%)	0.04*	0	0	NA
Device malfunction	1 (1%)	1 (1%)	0.24	0	1 (6%)	0.19
Device-related revision/extraction[a]	3 (3%)	4 (4%)	0.70	0	3 (18%)	0.0012*

[a] Device-related revision/extraction is defined as current or expected device malfunction or confirmed infection resulting in device extraction.
* *P*-value < 0.05. IQR = interquartile range.

- **100%** implant success
- Leadless implants took <u>longer</u>
- Leadless averaged **<2** deployments
- <u>Only</u> major complication was a pocket hematoma requiring evacuation
- <u>No</u> acute perforation, tamponade, or pericardial effusion
- **2** late pericardial effusions in leadless patients not requiring drainage
- <u>No</u> difference in procedure-related major or minor complications between leadless and transvenous pacemakers

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Micra Experience in a High-Volume Center

Single Center Study

- Bhatia, El-Chami: *J of Cardiovascular Electrophysiology* 2020
- **302** patients implanted at Emory Healthcare 2014-2019
- Mean follow-up: **3.0±1.4 years**.
- One tamponade (**0.3%**) treated with pericardiocentesis
- **23 Micras** were abandoned or extracted

	Abandoned	Extracted	Total
Pacing induced cardiomyopathy	6	3	9 (3.0%)
Increased threshold/failure to capture	3	3	6 (2.0%)
Bacteremia/endocarditis	0	2	2 (0.7%)
Premature battery depletion	2	0	2 (0.7%)
Pacemaker syndrome	1	0	1 (0.3%)
Bridge following extraction of infected lead	0	3	3 (1.0%)

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While gathering data for another study in December 2020, we found what appeared to be an unusual number of Micra implant deaths in the FDA MAUDE database

We used the online MAUDE key word search tool:
"death" "tamponade" "perforation"

Compared Micra to CaptureFix transvenous leads

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MACE in MAUDE: Micra vs CaptureFix TV leads

	Micra LICP	CapSureFix	*P* value
No. of major adverse events*	363	960	—
Major adverse event			
Death	96 (26.4)	23 (2.4)	<.001
Tamponade	287 (79.1)	225 (23.4)	<.001
Perforation without tamponade	61 (16.8)	731 (76.1)	<.001
Rescue thoracotomy	99 (27.3)	50 (5.2)	<.001
Repair RV tear	75 (20.7)	15 (1.6)	<.001
Repair PA tear	2 (0.5)	—	.075
Drainage only	24 (6.6)	35 (3.6)	.029
Pericardiocentesis without thoracotomy	190 (52.3)	195 (20.3)	<.001
Cardiopulmonary resuscitation	79 (21.8)	11 (1.1)	<.001
Shock/hypotension	80 (22.0)	56 (5.8)	<.001

Hauser, Sengupta: *Heart Rhythm* 2021; 18:1132-1139

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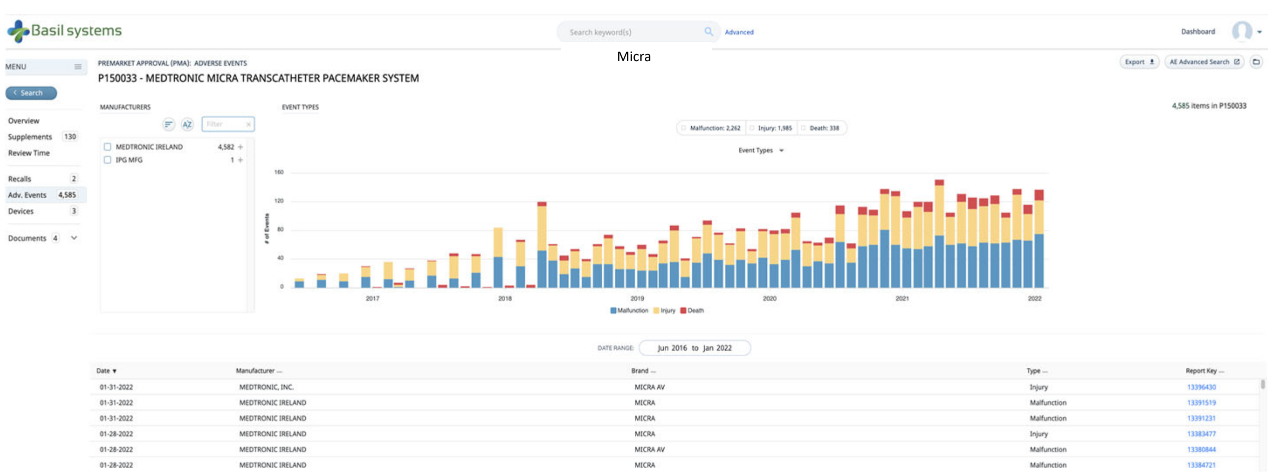
Basil Systems Software



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MACE According to Search Engine

	MAUDE Search Engine	Basil Search Engine	Difference
	No.	No.	No. (%)
Patients with one or more adverse event	363	488	125 (34)
Death	96	145	49 (51)
Tamponade	287	337	50 (17)
Perforation	348	398	50 (13)
Rescue thoracotomy	99	122	23 (23)
Pericardiocentesis without thoracotomy	190	239	49 (26)
Cardiopulmonary resuscitation	79	123	44 (56)
Shock/Hypotension	80	128	48 (60)

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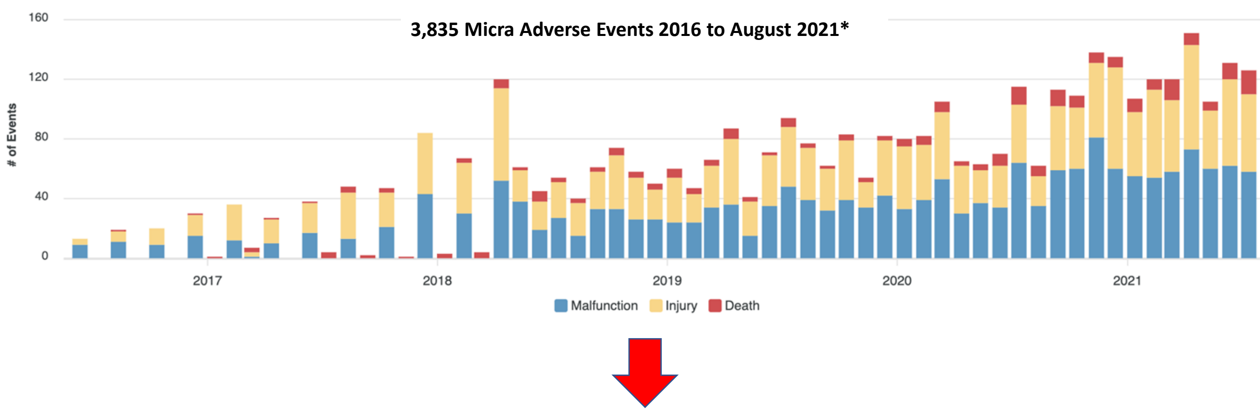
Basil Systems Search

FDA Manufacturers and User Device Experience Database



<u>563 Micra Perforations (30 day)</u>

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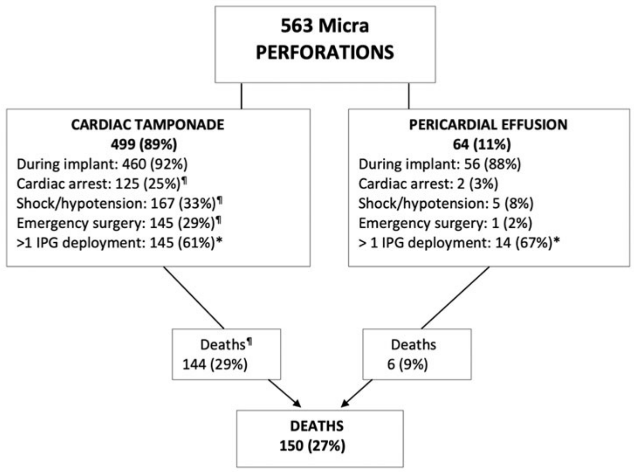
Micra MAUDE Data: Cardiac Perforation



¶ p<0.001 vs pericardial effusion. Other differences not significant.
* Percent of 237 tamponade and 21 pericardial effusion events whose number of deployments were reported.

Hauser, Sengupta *J Cardiovasc Electrophysiol* 2022 — Heart Rhythm Science Center

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Factors associated with perforation

- <u>Frail</u> (BMI < 20 kg/m^2), <u>elderly</u> (≥ 85 yrs), <u>female</u>, <u>COPD</u>
- <u>IPG</u> recapture, redeployment, repositioning, refixation
  - unacceptable electrical parameters
  - incomplete fixation, dislodgement
  - arrhythmias, interference with valve function
- <u>Operator error</u>
  - free wall implant
  - introducer or delivery system perforation
- <u>?Implanting center</u>
  - operator training & experience, CV surgery back-up, facilities

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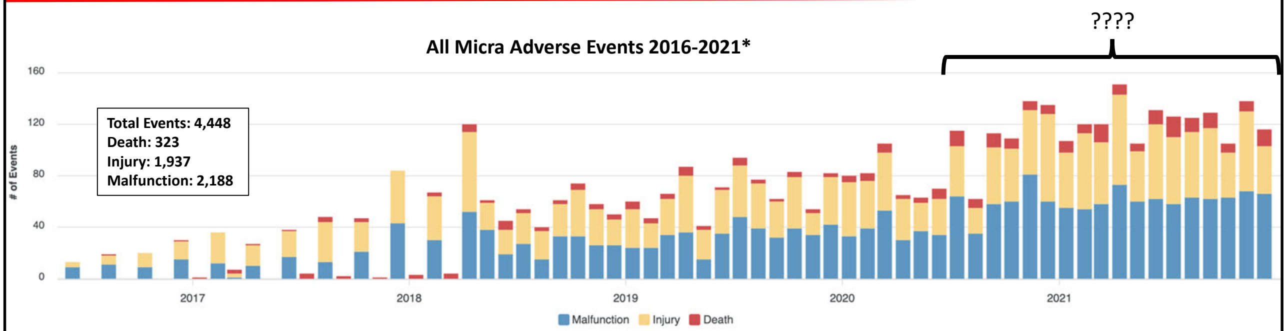
Updated Micra MAUDE Data 2016-2021

FDA Manufacturers and User Device Experience Database



784 Micra perforations, and 185 perforation-related deaths (24%)

64% (119/185) of deaths were in the USA

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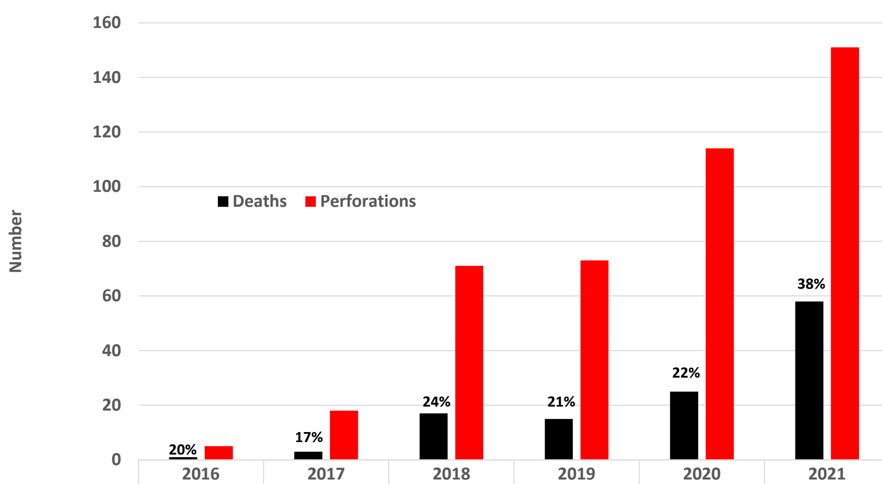
U.S. Micra Perforations & Deaths



	2016	2017	2018	2019	2020	2021
Deaths	1	3	17	15	25	58
Perforations	5	18	71	73	114	151

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Abbott Aveir™ Leadless Pacemaker*

- Successor to Nanostim LICP
- 200 patient study in 2021-22
- 98% implant success (196 of 200)
  - 17% (33/196) required repositioning
- Complications
  - 3 cardiac tamponades due to perforation (**1.5%**); all apical PG positioning
    2 of these required sternotomy (1%)
  - 2 premature deployments with device migration
- Satisfactory thresholds and rate-response
- Conclusion: "These results support the use of the novel LP for right ventricular pacing as an alternative to trans- venous pacemakers."

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Summary

1. Historical and contemporaneous but non-randomized data suggest that leadless pacemakers have fewer chronic complications than transvenous pacemakers.
2. Studies from experienced centers, including ours, show that the vast majority of Micra leadless pacemakers can be implanted without major complications.
3. The incidence of leadless cardiac perforation appears to be ≈1%. However, unlike transvenous lead perforation, leadless pacemaker perforations may be large and result in acute cardiac tamponade and death. Leadless pacemaker insertion should be confined to centers capable of managing implant complications.
4. Perforation mortality is increasing in the U.S., possibly due to the dispersion of implants to less qualified centers.

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Thank you

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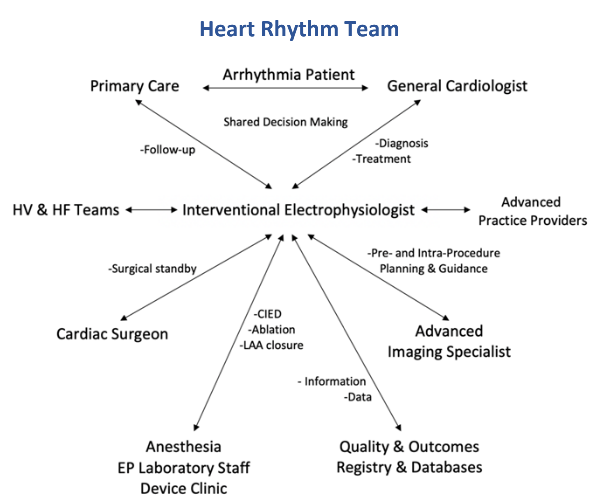
Implications of Leadless Pacemaker Experience*

<u>Level One EP Center</u>

- High volume & high complexity
- Broad institutional resources
- Focused on quality & safety
- Participation in clinical trials
- Heart Rhythm Team

<u>Open Access Device Registries</u>

- Performance
- Complications
- Outcomes



***Interventional electrophysiology at a crossroads**
Hauser, Katsiyiannis, Gornick, Sengupta, Abdelhadi
Journal Interventional Electrophysiology 2022

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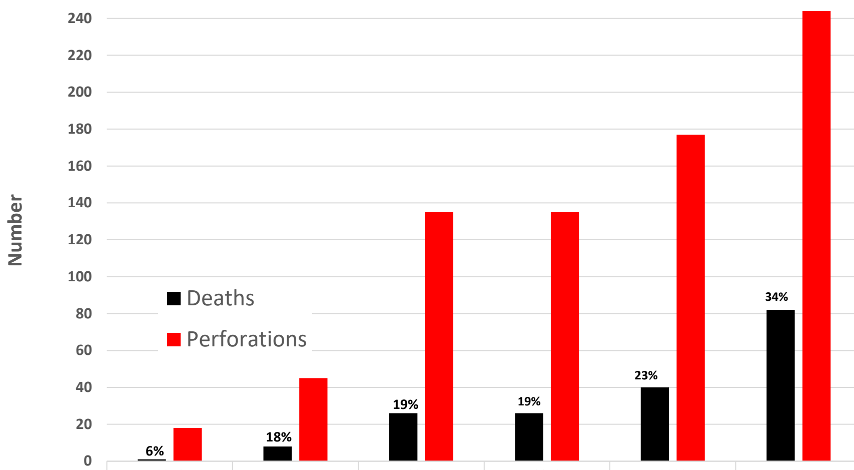
Increasing Number of Micra Perforations and Mortality



	2016	2017	2018	2019	2020	2021
Deaths	1	8	26	26	40	82
Perforations	18	45	135	135	177	244

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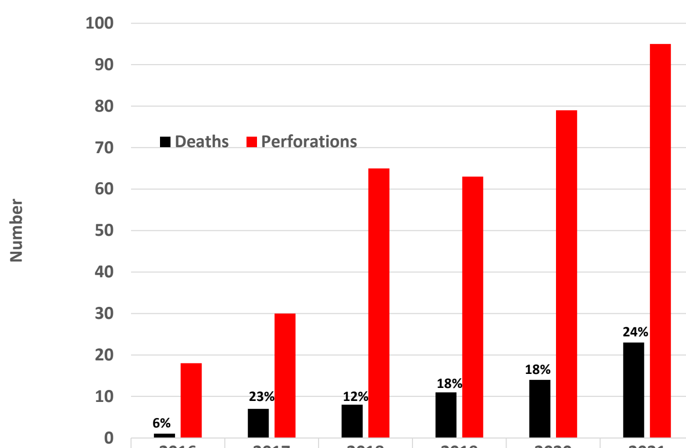
Non-U.S. Perforations & Deaths



	2016	2017	2018	2019	2020	2021
Deaths	1	7	8	11	14	23
Perforations	18	30	65	63	79	95

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