Heart Rhythm Science Center
February 21, 2022

NO DISCLOSURES
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

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”
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
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

Heart Rhythm Science Center

- Sudden Cardiac Death Prevention
- AF Ablation & Management Innovation
- Device Safety Research and Innovation
Strategic Investments

Research
- Increase enrollment and attract latest studies and fields 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 Critical Outcomes Data & Staff Coordination

Education
- Continuing Medical Education Seminars Fellowship
- Conference Attendance Professional Organization representation Guideline and CPT committees
- Marketing Material Community education and awareness events
- Conference & Seminar Hosting and Workshops and Live Case Studies

Outreach
- Idea-Inspiration + Mentorship-Support
- Collaboration-Growth + Innovation-Publication

ACKNOWLEDGEMENTS

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

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

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
Pillar: Device Safety Research and Innovation

- EBR Systems SOLVE-CRT trial

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
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

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?
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

Methods - Measuring Maximum Static Magnetic Field
Methods – Testing

- Placing electronic gadget over device
- Normal pacing (40 bpm)
- Magnet mode (84 bpm)

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
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.
An example of the potential of HRSC
Special thanks to MHIF Summer Research Internship Program, and Industry partners: Boston ScIntific and Medtronic, Inc!
Dr. Robert Hauser, MD

- Past President of HRS
- MHI Cardiologist
- Revolutionized device safety monitoring
- Mentor, Researcher, Teacher
Leadless Pacemaker Perforations: Underappreciated and Lethal

Robert G. Hauser MD FACC FHRS

February 21, 2022

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
Leadless Intracardiac Pacemakers

- VVIR
- Single Chamber and AV Synchronous
- Dual Chamber

- VVIR
- DDDR
- CRT
- CRT-D + Network
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 not implanted, 3 had cardiac perforations, and 1 had a pericardial effusion.
### 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.

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

<table>
<thead>
<tr>
<th>Major complication criterion</th>
<th>Micra (n = 1817)</th>
<th>Transvenous historical control (n = 2667)</th>
<th>Relative risk reduction (95% CI) (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of events (no. of patients, percentage)</td>
<td>No. of events (no. of patients, percentage)</td>
<td>12-mo KM estimates (95% CI) (%)</td>
<td>12-mo KM estimates (95% CI) (%)</td>
<td>12-mo KM estimates (95% CI) (%)</td>
</tr>
<tr>
<td>Total major complications</td>
<td>46 (41, 2.26)</td>
<td>2.7 (2.0 to 3.7)</td>
<td>230 (196, 7.35)</td>
<td>7.6 (6.9 to 8.7)</td>
</tr>
<tr>
<td>Death</td>
<td>9 (4, 0.28)</td>
<td>0.3 (0.1 to 0.8)</td>
<td>2 (0, 0.00)</td>
<td>0.0</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>17 (16, 0.88)</td>
<td>1.3 (0.8 to 2.1)</td>
<td>124 (100, 3.97)</td>
<td>4.1 (3.4 to 5.0)</td>
</tr>
<tr>
<td>Prolonged hospitalization</td>
<td>33 (29, 1.60)</td>
<td>1.9 (1.3 to 2.7)</td>
<td>68 (64, 2.40)</td>
<td>2.4 (1.9 to 3.1)</td>
</tr>
<tr>
<td>System revision</td>
<td>15 (13, 0.72)</td>
<td>0.9 (0.5 to 1.6)</td>
<td>102 (95, 3.56)</td>
<td>3.8 (3.1 to 4.6)</td>
</tr>
<tr>
<td>Loss of device function</td>
<td>9 (9, 0.50)</td>
<td>0.7 (0.4 to 1.3)</td>
<td>0 (0, 0.00)</td>
<td>0.0</td>
</tr>
</tbody>
</table>

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### Mayo Clinic Experience 2014-2017

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

#### Procedural characteristics

<table>
<thead>
<tr>
<th>Procedural characteristics</th>
<th>Micra (n = 70)</th>
<th>Nanostim (n = 70)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant success rate</td>
<td>95 (100%)</td>
<td>95 (100%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Procedural function median (median)</td>
<td>89 (93.13)</td>
<td>89 (93.13)</td>
<td>.99</td>
</tr>
<tr>
<td>Procedural function median (median)</td>
<td>4.9 (3.9)</td>
<td>4.9 (3.9)</td>
<td>.99</td>
</tr>
</tbody>
</table>

#### Procedural complications

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<thead>
<tr>
<th>Procedural complications</th>
<th>Micra (n = 70)</th>
<th>Nanostim (n = 70)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pocket hematoma</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Postoperative infection</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Device-related complications</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>.25</td>
</tr>
<tr>
<td>Device-related infection</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>.99</td>
</tr>
<tr>
<td>Device-related hospitalization</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>

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- 100% implant success
- Leadless implants took longer
- Leadless averaged <2 deployments
- Only major complication was a pocket hematoma requiring evacuation
- No acute perforation, tamponade, or pericardial effusion
- 2 late pericardial effusions in leadless patients not requiring drainage
- No difference in procedure-related major or minor complications between leadless and transvenous pacemakers
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.
MACE in MAUDE: Micra vs CaptureFix TV leads

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

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

Basil Systems Software

Heart Rhythm Science Center
MACE According to Search Engine

<table>
<thead>
<tr>
<th>Event</th>
<th>MAUDE Search Engine</th>
<th>Basil Search Engine</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with one or more adverse event</td>
<td>363</td>
<td>488</td>
<td>125 (34%)</td>
</tr>
<tr>
<td>Death</td>
<td>96</td>
<td>145</td>
<td>49 (51%)</td>
</tr>
<tr>
<td>Tamponade</td>
<td>287</td>
<td>337</td>
<td>50 (17%)</td>
</tr>
<tr>
<td>Perforation</td>
<td>348</td>
<td>398</td>
<td>50 (13%)</td>
</tr>
<tr>
<td>Rescue thoracotomy</td>
<td>99</td>
<td>122</td>
<td>23 (23%)</td>
</tr>
<tr>
<td>Pericardiocentesis without thoracotomy</td>
<td>190</td>
<td>239</td>
<td>49 (26%)</td>
</tr>
<tr>
<td>Cardiopulmonary resuscitation</td>
<td>79</td>
<td>123</td>
<td>44 (56%)</td>
</tr>
<tr>
<td>Shock/Hypotension</td>
<td>80</td>
<td>128</td>
<td>48 (60%)</td>
</tr>
</tbody>
</table>

Basil Systems Search

FDA Manufacturers and User Device Experience Database

3,835 Micra Adverse Events 2016 to August 2021*

563 Micra Perforations (30 day)
Factors associated with perforation

- Frail (BMI < 20 kg/m²), elderly (≥ 85 yrs), female, COPD
- IPG recapture, redeployment, repositioning, refixation
  - unacceptable electrical parameters
  - incomplete fixation, dislodgement
  - arrhythmias, interference with valve function
- Operator error
  - free wall implant
  - introducer or delivery system perforation
- Implanting center
  - operator training & experience, CV surgery back-up, facilities
**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

**U.S. Micra Perforations & Deaths**
Abbott Aveir™ Leadless Pacemaker*

- Successor to Nanostim LCP
- 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.”

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.
Thank you

Implications of Leadless Pacemaker Experience*

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

Open Access Device Registries
- Performance
- Complications
- Outcomes

*Interventional electrophysiology at a crossroads
Hauser, Katsiyiannis, Gornick, Sengupta, Abdelhadi
Journal Interventional Electrophysiology 2022
Increasing Number of Micra Perforations and Mortality

Non-U.S. Perforations & Deaths