MICRA and the Future of Leadless Pacing

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Staff Clinical Cardiac Electrophysiologist
Piedmont Heart Institute
2019 Atlanta Cardio Conference
Disclosures

• None
Objectives

• Understand the concept of leadless pacing - benefits and limitations compared to traditional pacemakers

• Identify ideal candidates for this therapy

• AV synchrony with leadless pacemakers

• Review future devices in this arena
  • LV pacing – CRT
  • Subcutaneous ICD (Anti-tachycardia pacing)
Pre-Question

• Which of the following leadless pacemaker is currently commercially available?

  • MICRA
  • Nanostim
  • Bullet (Nutri-powered)
  • WiSE-CRT
Pre-Question

• Manatee is a/an,
  • Mammal
  • Reptile
  • Amphibian
  • Fish
Pacing brief history

<table>
<thead>
<tr>
<th>Paradigm Shifts in Cardiac Pacemakers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1950s</strong></td>
</tr>
<tr>
<td>AC-powered pacemakers tethered to an extension cord (Furman)</td>
</tr>
</tbody>
</table>

Pacemaker brief history

1958

Pocket complications
Transvenous lead complications

Medtronic Website
Special Article

Totally Self-Contained Intracardiac Pacemaker*


SUMMARY

Recent developments in miniature long-life power sources and electronics, such as nuclear circuits have been improved substantially. In addition, the development of the endocardial catheter electrode has broadened the choice of operating procedures to include transcatheter.

Fig. 4. Intracardiac pacemaker with catheter for transvenous insertion.

Fig. 8. Nuclear-powered intracardiac pacemaker.
Leadless pacemaker deployment
Leadless pacemakers

NANOSTIM – LEADLESS II (NEJM 2015)

Micra Transcatheter Pacing Study (NEJM 2016)
### Leadless Pacemaker Implantation

#### Efficacy Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Nanostim (LCP)</th>
<th>Micra (TPS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Implant success (%)</strong></td>
<td>95.8</td>
<td>99.2</td>
</tr>
<tr>
<td><strong>Pacing capture threshold</strong></td>
<td>90.0 (≤2.0 V at pulse width of 0.24 msec and an increase of ≤1.5 V from time of implantation)</td>
<td>98.3 (≤2.0 V at 0.4 msec and sensing amplitude ≥5.0 mV or a value ≥ value at implantation)</td>
</tr>
<tr>
<td><strong>Threshold at implant</strong></td>
<td>0.82 V @ 0.4</td>
<td>0.63 V @ 0.24</td>
</tr>
<tr>
<td><strong>Threshold at 6 mo</strong></td>
<td>0.4 V @ 0.4</td>
<td>0.54 V @ 0.24</td>
</tr>
</tbody>
</table>

Deshmukh, Friedman et al: JAFIB 10:1, 2017
### Leadless Pacemaker Implantation

#### Safety Outcomes

<table>
<thead>
<tr>
<th>Event</th>
<th>Nanostim (%)</th>
<th>Micra (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total events (Leadless)</strong></td>
<td>6.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Cardiac perforation</td>
<td>1.6</td>
<td>1.6</td>
</tr>
<tr>
<td>Vascular complication</td>
<td>1.2</td>
<td>0.7</td>
</tr>
<tr>
<td>Arrhythmia during device implantation</td>
<td>0.6</td>
<td>0.0</td>
</tr>
<tr>
<td>Cardiopulmonary arrest during implantation procedure</td>
<td>0.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Device dislodgement</td>
<td>1.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Device migration during implantation owing to inadequate fixation</td>
<td>0.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Pacing threshold elevation with retrieval and implantation of new device</td>
<td>0.8</td>
<td>0.3</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0.2</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Deshmukh, Friedman et al: JAFIB 10:1, 2017
MICRA historical control

Ideal Candidates for Leadless pacemaker

• Single chamber – ventricular pacing only. Patients who do not need AV synchrony
  • Chronic Atrial Fibrillation with slow ventricular rates
  • Atrial Fibrillation with planned AVN ablation
  • Infrequent pacing
  • High risk for infection/recurrent infections (ESRD?)
Atrial Fibrillation and AVN ablation
### Micra Major Complications

<table>
<thead>
<tr>
<th></th>
<th>Global Trial (n=726) no. (%)</th>
<th>US continued access study + EU post-approval study + Commercial experience (n=1,420) no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perforation</td>
<td>11 (1.5)</td>
<td>10 (0.7)</td>
</tr>
<tr>
<td>Dislodgement</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Groin (AV fistula, pseudoaneurysm, etc.)</td>
<td>5 (0.7)</td>
<td>3 (0.2)</td>
</tr>
<tr>
<td>Infection</td>
<td>0 (0.0)</td>
<td>1 (0.1)</td>
</tr>
</tbody>
</table>
Micra Pacing Thresholds at 12-month

Pacing Capture Threshold

Battery Longevity Estimate
Based on use conditions of the 300 patients with 6-month data, median battery longevity estimate is 12.5 years.*

MICRA and AV node ablation

• 21 patients MICRA followed by AV node ablation

• 2 deaths – non cardiac

• 1 pacing induced cardiomyopathy

• 67% f/u at 1 year and stable thresholds
Comparison of Device Performance at a Median Follow-up of 12 Months - Nanostim

Nanostim Yarlagadda et al: Heart Rhythm 15:994, 2018

- **Capture Threshold at Follow-up**
  - Voltage in V
  - Follow-up times: Implant, 2 wks, 3 mos, 6 mos, 12 mos
  - Graph showing a comparison between Leadless and Single chamber groups, with the Leadless group having a statistically significant lower threshold (P=0.009).

- **R Wave amplitude at Follow-up**
  - Voltage in mv
  - Follow-up times: Implant, 2 wks, 3 mos, 6 mos, 12 mos
  - Graph showing the comparison between Leadless and Single chamber groups, with the Leadless group having a lower amplitude (P=0.446). The Single chamber group showed a slight decrease over time.

- **Impedance at Follow-up**
  - Impedance in Ohms
  - Follow-up times: Implant, 2 wks, 3 mos, 6 mos, 12 mos
  - Graph showing a comparison between Leadless and Single chamber groups, with the Leadless group having a lower impedance (P=0.003). The Single chamber group showed an increase in impedance.

1. MAE (loss of pacing and sensing) LP group
2. (lead dislodgement) in the CTP group

Yarlagadda et al: Heart Rhythm 15:994, 2018
Mismatch between 27F Sheath and 8F ablation catheter

• Serial sheaths to allow for hemostatic seal
Figure of eight stitch for hemostasis
AV synchrony?

Courtesy: Ashish Bhimani, MD
Atrial Contraction Detection Via Accelerometer

MASS/MASS2 studies collected open-loop data
N=75 patients
MARVEL tested the closed loop performance

A1 – Isovolumic contraction and mitral/tricuspid valve closings
A2 – Aortic/pulmonic valve closing
A3 – Early passive ventricular filling
A4 – Atrial contraction generating active filling
The Micra - FUTURE

Bradyarrhythmia with AF

Micra VR
• Approved
• >36,000 pts.

Micra AV
• Atrial synchronous ventricular pacing
• Mechanical sensing accelerometer

Micra AR
• Atrial pacing
• Modified fixation

Micra DDD
• Dual chamber pacing & sensing

AV Block

Sinus Node Dysfunction

AV Block + Sinus Node Dysfunction

HRS 2019 Lucas Boersma, MD
A worldwide experience of the management of battery failures and chronic device retrieval of the Nanostim leadless pacemaker

Dhanunjaya Lakkireddy, MD, FACC, FHRS,* Reinoud Knops, MD,† Brett Atwater, MD,‡ Petr Neuzil, MD,§ John Ip, MD,‖ Elkin Gonzalez, MD,¶ Paul Friedman, MD, FHRS,** Pascal Defaye, MD,†† Derek Exner, MD,‡‡ Kazutaka Aonuma, MD,§§ Rahul Doshi, MD, FHRS,¶¶ Johannes Sperzel, MD,‖‖ Vivek Reddy, MD†††

From the *Kansas University Medical Center, Kansas City, Kansas, †Amsterdam Medical Center, Amsterdam, The Netherlands, §Duke University Medical Center, Durham, North Carolina, ¶Na Homolce Hospital, Prague, Czech Republic, ¶¶Sparrow Clinical Research Institute, Lansing, Michigan, *Hospital Universitario de la Paz, Madrid, Spain, **Mayo Clinic, Rochester, Minnesota, ††CHRU Albert Michallon, Grenoble, France, ‡‡Libin Cardiovascular Institute of Alberta, Calgary, Canada, §§University of Tsukuba Hospital, Ibaraki, Japan, †‖USC University Hospital, Los Angeles, California, †¶¶Kerckhoff Klinik, Bad Nauheim, Germany, and †††Mount Sinai Medical Center, New York, New York.
No statistically significant difference ($p > 0.05$) in retrieval success rates over time.

<table>
<thead>
<tr>
<th>Duration from Implant</th>
<th>% Retrieval Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 year (n = 22)</td>
<td>86%</td>
</tr>
<tr>
<td>&gt;1-2 years (n = 30)</td>
<td>93%</td>
</tr>
<tr>
<td>&gt;2 years (n = 21)</td>
<td>90%</td>
</tr>
</tbody>
</table>
Techniques for successful early retrieval of the Micra transcatheter pacing system: A worldwide experience

Muhammad R. Afzal, MD, * Emile G. Daoud, MD, FHRS, * Ryan Cunnane, MD, †
Shiva K. Mulpuru, MD, ‡ Alan Koay, MD, § Azlan Hussain, MD, § Razali Omar, MD, FHRS, §
Koh Kok Wei, MD, § Anish Amin, MD, § Gregory Kidwell, MD, § Nirav Patel, MS, ||
Charles Love, MD, FHRS, ** Michael Lloyd, MD, FHRS, †† Maciej Sterliński, MD, ††
Seth Goldbarg, MD, FHRS, §§ Miguel A. Leal, MD, FHRS, §§ James Gabriels, MD, |||
Apoor Patel, MD, ||| Ram Jadonath, MD, ||| Eric Grubman, MD, FHRS, ***
George Crossley, MD, FHRS, ††† Chris Pepper, MD, ††† Dhanunjaya Lakkdirddy, MD, FHRS, §§§

From the *Division of Cardiovascular Medicine, Department of Internal Medicine, Electrophysiology Section, Ross Heart Hospital, The Ohio State University Wexner Medical Center, Columbus, Ohio, †University of Michigan, Ann Arbor, Michigan, §Mayo Clinic, Rochester, Minnesota, §National Heart Institute, Kuala Lumpur, Malaysia, §OhioHealth Heart and Vascular Physicians, Section of Electrophysiology, Riverside Methodist Hospital, Columbus, Ohio, ||Medtronic Inc, Minneapolis, Minnesota, **Johns Hopkins University, Baltimore, Maryland, ††Emory University, Atlanta, Georgia, †††Institute of Cardiology, Warsaw, Poland, §§Weill Cornell Medical College, New York, New York, §§University of Wisconsin, Madison, Wisconsin, |||North Shore University Hospital, New York, Manhasset, ***Yale University, New Haven, Connecticut, †††Vanderbilt University, Nashville, Tennessee, †††University of Leeds, West Yorkshire, England, and §§§University of Kansas Medical Center, Kansas City, Kansas.
<table>
<thead>
<tr>
<th>Indication for retrieval</th>
<th>n</th>
<th>Days since implant</th>
<th>Postextraction management</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bridge to PPM</td>
<td>2</td>
<td>58.5 ± 43</td>
<td>TV system</td>
<td>2</td>
</tr>
<tr>
<td>Need for upgrade to CRT</td>
<td>1</td>
<td>61</td>
<td>Successful CRT upgrade</td>
<td>1</td>
</tr>
<tr>
<td>High capture threshold</td>
<td>11</td>
<td>17 ± 22</td>
<td>New TPS</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>53</td>
<td>Transitioned to TV system</td>
<td>3</td>
</tr>
<tr>
<td>Need for upgrade to ICD</td>
<td>1</td>
<td></td>
<td>Successful ICD implantation for cardiac arrest</td>
<td>1</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1</td>
<td>17</td>
<td>TV system after infection resolution</td>
<td>1</td>
</tr>
<tr>
<td>Vegetation on TPS</td>
<td>1</td>
<td>46</td>
<td>TV after infection resolution</td>
<td>1</td>
</tr>
<tr>
<td>Incessant VT attributed to TPS</td>
<td>1</td>
<td>3</td>
<td>New TPS</td>
<td>1</td>
</tr>
</tbody>
</table>
### 11.1. Subcutaneous Implantable Cardioverter-Defibrillator

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-NR</td>
<td>1. In patients who meet criteria for an ICD who have inadequate vascular access or are at high risk for infection, and in whom pacing for bradycardia or VT termination or as part of CRT is neither needed nor anticipated, a subcutaneous implantable cardioverter-defibrillator is recommended (1-5).</td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR</td>
<td>2. In patients who meet indication for an ICD, implantation of a subcutaneous implantable cardioverter-defibrillator is reasonable if pacing for bradycardia or VT termination or as part of CRT is neither needed nor anticipated (1-4).</td>
</tr>
<tr>
<td>III: Harm</td>
<td>B-NR</td>
<td>3. In patients with an indication for bradycardia pacing or CRT, or for whom antitachycardia pacing for VT termination is required, a subcutaneous implantable cardioverter-defibrillator should not be implanted (1-4, 6-8).</td>
</tr>
</tbody>
</table>

**EFORTLESS REGISTRY 3 year f/u 1000 pts – 50% VT not VF**

Markus Bettin et al. JACEP 2017;3:1499-1506
Implantable Devices

EMPOWER™ Modular Pacing System
EMBLEM™ Family of S-ICDs

Programmers
Model 3200 S-ICD Programmer
Next Generation BSC 3300 LATITUDE Programming System

EMPOWER™ Delivery and Retrieval
Preloaded delivery catheter with extendable inner catheter
Dedicated retrieval system with single & tri-loop snares

EMPOWER™ Details
32.1 mm x 6 mm
0.8 cc
Active fixation talons
Tether / Snare port

HRS 2019 Petr Neuzil, MD,PhD,FESC
Heart Failure and Cardiac dyssynchrony
Cardiac Resynchronization
Cardiac Resynchronization

- MUSTIC SR
- MIRACLE
- MUSTIC AF
- PATH CHF
- MIRACLE-ICD
- CONTAK-ICD
- MIRACLE-ICD II
- COMPANION
- CARE-HF
- REVERSE
- MADIT-CRT
- RAFT
- DANISH

- Reduced mortality (24% to 36% benefit)
- Reduced hospitalizations (30% decrease)
- Improved 6 minute walk test (50 to 70 meter increase)
- Improved 105 -point Minnesota scale (greater than or equal to 10 point reduction of HF symptoms)
- Improved NYHA class
- Increase in peak oxygen consumption
CRT – Benefit and pitfalls

• ~5% **failure** rate

• ~Up to 10% **complication** rate (including dislodgement and phrenic stimulation)

• ~1/3\(^{rd}\) of patients are **non-responders**

• **Upgrades** – higher risk and high non-responder rate
How about we go inside the LV?
WiSE-CRT, EBR Systems, Sunnyvale, California
DETECT Co-implant RV pacing
Locates and transmits WiSE-CRT; EBR system
Receive and Pace

WiSE-CRT; EBR system
Alternate to Transvenous LV lead
WiSE-CRT; EBR system

SELECT-LV ↑HF clinical composite score in 85% (n=35)
SELECT-LV results n=35

- 97% successful implantation (34 patients)
- 62.5% pts ≥ 5% increase in LVEF (N=32)
- 52% pts ≥ 15% improvement in LVESV (N=25)
- Mean QRS decrease of 36 ms (165 to 129 ms or 22% reduction. (N=20)
- 66.7% pts ≥ 1 class improvement in functional capacity (N=33)
Complications n=35

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;24 h</td>
<td>VF during catheter contact with LV endocardium</td>
<td>3</td>
<td>8.6%</td>
</tr>
<tr>
<td></td>
<td>Electrode embolization to lower extremity</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Femoral artery fistula (required surgical repair)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>24 h to 1 month</td>
<td>Acute CVA (AF noncompliant with anticoagulation)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Femoral pseudoaneurysm</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pocket hematoma (generator)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Suspected infection (generator site)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Death (following VF during initial implant procedure)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1 to 6 months</td>
<td>Defective transmitter circuitry</td>
<td>3</td>
<td>8.6%</td>
</tr>
</tbody>
</table>

Values are n (%) or n.
AF = atrial fibrillation; CVA = cerebrovascular accident; LV = left ventricular; VF = ventricular fibrillation.
Next Step….

• SOLVE CRT clinical study. (Stimulation of the Left Ventricular Endocardium for Cardiac Resynchronization Therapy)
  • Prospective **randomized, double blinded pivotal trial**

• Safety and Efficacy – FDA Approval

• Randomize **350** heart failure patients in the United States, Europe, and Australia who have failed to respond to, or are otherwise unable to receive, conventional CRT

• Piedmont participation
## Possibilities with Leadless Technology

<table>
<thead>
<tr>
<th>Applications of leadless technology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dual Chamber Nanostim</strong></td>
</tr>
<tr>
<td>▪ 2 Discrete devices: Right Atrium and Right Ventricle</td>
</tr>
<tr>
<td>▪ Beat to Beat Communication</td>
</tr>
<tr>
<td>▪ Chronically retrievable</td>
</tr>
<tr>
<td><strong>Leadless ICD/PM</strong></td>
</tr>
<tr>
<td>▪ Leadless ICD system with device-to-device communication to Nanostim</td>
</tr>
<tr>
<td>▪ Nanostim device paces, senses, and delivers ATP therapy</td>
</tr>
<tr>
<td><strong>Leadless CRT</strong></td>
</tr>
<tr>
<td>▪ Evaluate leadless options for CRT therapy delivery</td>
</tr>
<tr>
<td>▪ Applicable to low and high voltage</td>
</tr>
<tr>
<td><strong>Pediatric Leadless</strong></td>
</tr>
<tr>
<td>▪ Miniaturize present leadless pacemaker</td>
</tr>
<tr>
<td>▪ Fully retrievable</td>
</tr>
<tr>
<td>▪ Reduce complications from venous adhesions</td>
</tr>
</tbody>
</table>

HRS 2019 Lucas Boersma, MD; Abbott/ St Jude Medical
Future – the Swiss

Zurbuchen et al. Heart Rhythm 2017

Zurbuchen et al. Ann of Biomed Engineer 2017
Future

Summary

• Single ventricular pacemaker available commercially
  • Retrieval - ?
  • Niche indications – needs further development for more widespread use
  • AV synchrony soon
  • Multi-chamber – in future

• LV pacing – trial in future

• Sub Q ICD – leadless pacemaker; work in progress
Post-Question

• Which of the following leadless pacemaker is currently commercially available?
  
  • MICRA
  
  • Nanostim
  
  • Bullet (Nutri)
  
  • WiSE-CRT
Post-Question

• Which of the following leadless pacemaker is currently commercially available?
  
  • MICRA
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I'll be back
Pre-Question

• Manatee is a/an,
  • Mammal
  • Reptile
  • Amphibian
  • Fish
Acknowledgements

• Dr. Abhishek Deshmukh – Mayo Clinic

• Sponsors

• Alliance of Cardiovascular Professionals

• Michael Cavness
Thank you for your attention

Questions

danesh.kella@piedmont.org
Leadless pacing – MICRA Trial

- N=725 patients
- 719 with successful implantation
- Complications n=25 (4%)
  - Cardiac Injury=11 (1.6%)

NEJM Feb 2016
Other leading device companies

- St. Jude Medical (Abbott)
  Nanostim Pacemaker.

- Boston Scientific