LEADLESS CARDIAC PACEMAKERS: WHEN AND HOW TO IMPLANT

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ONCE UPON A TIME...

ADVANCES in PM SYSTEM
Lead: A simple system?

COMPONENTS
- Electrodes
- Conductors
- Insulation
- Fixation
- Connectors

ISSUES
- Mechanical failure
- Infection, extractions
- Mobility restrictions
- MRI incompatibility
Device & Lead Issues

• Infection ≈ 1 %
  • 2-7% infection rate for replacement/upgrades\(^1\)
  • ≤ 0.5% infection rate for new implants\(^1\)


• Malfunction ≈ 2.5 %
  • 1.65-20% annual ICD lead failure based on age\(^2,3\)


• Occlusion ≈ 0.5 %
  • 9-12% of device replacement or upgrade\(^4\)

• Redundant leads\(^4\) ≈ 1 %


Estimated annual complication rate ≈ 5%
IDEAS.....INNOVATIONS
Technical Challenges:

Integration of Multiple Elements

Physician training / comfort with new implant procedure

- Novel Delivery systems
- Unproven Fixation technology
  - Holding force, with repositioning/retrieval capability
  - Low, stable pacing thresholds

Novel power sources and ultra-low power circuitry

Increased electronic packaging density

Communication systems:

- External (telemetry; wireless)
- Inter-device (intrabody)

Biocompatible device packaging

- Lifetime hermeticity
BENEFIT OF LEADLESS APPROACH

Reduced invasiveness
- Percutaneous procedure
- Reduced hardware
- “Invisible to the patient”

Improved Efficiency
- No pocket
- No system connection
- Reduced procedure time

Improved Outcomes
- Fewer complications
History of Leadless Pacing

J. ELECTROCARDIOLOGY, 3 (3-4) 325-331, 1970

Special Article

Totally Self-Contained Intracardiac Pacemaker*

J. WILLIAM SPICKLER, PH.D., NED S. RASOR, PH.D.; PAUL KEZDI, M.D.; S. N. MISRA, M.D.; K. E. ROBINS, P.E., AND CHARLES LEBOEUF, P.E.
BUT..was it still too early...
LEADLESS INTRACARDIAC devices

- PM Devices
- ICD Devices
- LV Leads

Nanostim (CE) (St Jude Medical) December 2012
Micra (Medtronic) December 2013
S-ICD (C.H. → Boston Sc.) (CE & FDA) September 2009
WiCS (EBR) May 2011
When to Consider Leadless PPM Implant

• Standard VVI pacemaker indication:
  Permanent AF with pacing indication
  Sinus node dysfunction (intermittent pacing indication)
  Complete heart block (>70 years old, limited function)

• Unique indication:
  Prior device infection
  Vascular access issue (dialysis, Porta-cath)
Leadless Pacemakers

- Single-chamber, programmable VVIR device
- Capsule contains battery and electronics
- Inserted into right ventricle via femoral vein catheter

Nanostim – SJM-Abott
The Nanostim TM Leadless Pacemaker Delivery System

Delivery catheter
- Soft, flexible, deflectable catheter tip designed to minimize complications
- Tethered feature
- Integrated protective sleeve
- 18 F

Handle with four functions:
- Steering the deflectable tip
- Docking/Undocking
- Rotating the device
- Releasing tether

18 F introducer
Micra with Delivery System
I love you to the Moon and back. {477,710 miles to be exact.}
Retrieval Tools

1. The snare loop is placed around the device.
2. The snare loop is tightened to hold the device firmly.
Contraindications

• LPs are contraindicated for patients who have the following types of medical devices implanted:
  • an implanted device that would interfere with the implant of the Micra device in the judgment of the implanting physician,
  • an implanted inferior vena cava filter,
  • a mechanical tricuspid valve, or
  • an implanted cardiac device providing active cardiac therapy that may interfere with the sensing performance of the Micra device.

• The devices are contraindicated for patients who have the following conditions:
  • femoral venous anatomy unable to accommodate a 7.8 mm (23 French) introducer sheath or implant on the right side of the heart (for example, due to obstructions or severe tortuosity),
  • morbid obesity that prevents the implanted device from obtaining telemetry communication within ≤12.5 cm (4.9 in), or
  • known intolerance to the materials listed in the Instruction for Use, or to heparin, or sensitivity to contrast media that cannot be adequately premedicated.

• Steroid use — Do not use in patients for whom a single dose of 1.0 mg of dexamethasone acetate cannot be tolerated.
HOW DOES IT COMPARE?
The Two Landmark Trials

Percutaneous Implantation of an Entirely Intracardiac Leadless Pacemaker

Reddy V, NEJM 2015

A Leadless Intracardiac Transcatheter Pacing System

Reynolds D, NEJM 2016
## Comparison Between current LPs

### Nanostim LCP

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimensions (mm)</td>
<td>42.0 x 5.99</td>
</tr>
<tr>
<td>Volume (cc), weight (g)</td>
<td>1.2</td>
</tr>
<tr>
<td>Sheath size (French)</td>
<td>18 (id)/ 21 (od)</td>
</tr>
<tr>
<td>Fixation mechanism</td>
<td>Screw-in helix</td>
</tr>
<tr>
<td>Pacing mode</td>
<td>VVI(R)</td>
</tr>
<tr>
<td>Rate Response Sensor</td>
<td>Temperature</td>
</tr>
<tr>
<td>Communication</td>
<td>Conductive (250kHz)</td>
</tr>
<tr>
<td>Battery longevity (yrs)</td>
<td>8.5 - 9.8</td>
</tr>
</tbody>
</table>

### Micra TPS

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimensions (mm)</td>
<td>25.9 x 6.7</td>
</tr>
<tr>
<td>Volume (cc), weight (g)</td>
<td>0.8, 2</td>
</tr>
<tr>
<td>Sheath size (French)</td>
<td>23 (id)/ 27 (od)</td>
</tr>
<tr>
<td>Fixation mechanism</td>
<td>Nitinol tines</td>
</tr>
<tr>
<td>Pacing mode</td>
<td>VVI(R)</td>
</tr>
<tr>
<td>Rate Response Sensor</td>
<td>3-axis accelerometer</td>
</tr>
<tr>
<td>Communication</td>
<td>Radio-frequency</td>
</tr>
<tr>
<td>Battery longevity (yrs)</td>
<td>4.7 - 9.6</td>
</tr>
</tbody>
</table>

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Comparison Between current LPs

Retrieval of LCP
- Single-loop retrieval snare
- Capture of LCP
- Protective sleeve advanced over LCP

Retrieval of TPS
- 6Fr sheath within 8.5Fr sheath advanced through introducer
- TPS captured by snare
- TPS removed by pulling device back into introducer
## Comparison with Conventional System

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Lead-based Pacemaker</th>
<th>Leadless Pacemaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant procedure</td>
<td>Surgical pocket + lead (7 F)</td>
<td>Percutaneous femoral based delivery (18 F)</td>
</tr>
<tr>
<td>Implant time</td>
<td>30 – 40 minutes</td>
<td>15-20 minutes (shorter patient recovery)</td>
</tr>
<tr>
<td>X-ray exposure</td>
<td>For implanter: Next to the X-ray tube</td>
<td>For implanter: Further away from the source</td>
</tr>
<tr>
<td>Connections</td>
<td>Lead-can connectors</td>
<td>None</td>
</tr>
<tr>
<td>Apparatus in vascular system (chronic)</td>
<td>Yes (lead)</td>
<td>No (leadless)</td>
</tr>
<tr>
<td>Apparatus through tricuspid valve (chronic)</td>
<td>Yes (lead)</td>
<td>No (leadless)</td>
</tr>
<tr>
<td>System removal</td>
<td>Specialization required</td>
<td>Removal tools available</td>
</tr>
</tbody>
</table>
| Longevity (2.5V, 0.4ms, 60 bpm) AccentTM SR Inductive for lead-based (500 Ω for Accent, 600 Ω for leadless) | 100% pacing – 11.2 years  
75% pacing – 11.8 years  
50% pacing – 12.5 years  
25% pacing – 13.3 years | 100% pacing – 9.8 years  
75% pacing – 11.7 years  
50% pacing – 14.5 years  
25% pacing – 18.9 years |
| Battery Replacement                           | Pocket access                                                                       | Femoral access: removal+ new implant  
Option for another adjacent implant                                                   |
| MRI compatibility                              | Conditional – image impact MRI conditional status not yet determined                 |                                                                                   |
IDE PACING INDICATIONS:

MICRA TPS N 725
- Sinus node dysfunction: 17%
- Chronic AF with bradycardia: 64%
- AV block: 15%
- Other: 4%

LEADLESS II N526
- Sinus node dysfunction: 35%
- Chronic AF with bradycardia: 56%
- AV block: 9%
Leadless II Clinical Trial Primary Endpoints

**Safety (Intent-to-Treat Analysis)**
- 280 of the 300 patients achieved endpoint (93.3%; 95% CI = 89.9 to 95.9)
- This exceeded the performance goal of 86% (P<0.001)

**Efficacy (Intent-to-Treat Analysis)**
- 270 of the 300 patients achieved endpoint (90.0%; 95% CI = 86.0 to 93.2)
- This exceeded the performance goal of 85% (P = 0.007)

**Efficacy (Successful implants)**
- 289 patients with successful device implant
- 270 of the 289 patients achieved endpoint (93.4%; 95% CI = 89.9 to 96.0)
- This exceeded the performance goal of 85% (P <0.001)

Thus, all endpoints were achieved

# Leadless II Clinical Trial

## Device-Related SAEs

<table>
<thead>
<tr>
<th>Event</th>
<th>Primary Cohort (N = 300)</th>
<th>Total Cohort (N = 526)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Events</td>
<td>No. of Patients</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td>Cardiac perforation</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Cardiac tamponade with intervention</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac perforation requiring intervention</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pericardial effusion with no intervention</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Vascular complication</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Arrhythmia during device implantation</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Cardiopulmonary arrest during implantation procedure</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Device dislodgement</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Device migration during implantation owing to inadequate fixation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pacing threshold elevation with retrieval and implantation of new device</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Other*</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

* Includes: ischemic stroke, angina pectoris, pericarditis, acute confusion & expressive aphasia, dysarthria & lethargy post implant, contrast induced nephropathy, orthostatic hypotension with weakness, left leg weakness during implant, probable pulmonary embolism, ischemic stroke

Micra Clinical Evidence

Clinical Data of 725 Patients published in NEJM

• Shows safety and efficacy
• 94 physicians, 56 different centres, 19 countries
• Trial continues until 600 patients are followed up at 12 months

<table>
<thead>
<tr>
<th>Micra complication rate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>4%</td>
</tr>
<tr>
<td>Device infection rate</td>
<td>0%</td>
</tr>
<tr>
<td>Dislodgement</td>
<td>0%</td>
</tr>
<tr>
<td>System Revision</td>
<td>0.4%</td>
</tr>
<tr>
<td>Related Death</td>
<td>0.1%</td>
</tr>
<tr>
<td>Prolonged hospitalization</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

1 Reynolds et al, NEJM, November 9, 2015, DOI: 10.1056/NEJMoa1511643 ·
The 1 death was adjudicated as procedure related, not device related.
MICRA Trial: RESULTS

Low and stable thresholds at the 6-month visit

Primary efficacy end point 98.3%

Battery longevity estimation 12.5 y

Assumed performance of 89%

MICRA Trial: comparison with standard PM

Control cohort of 2667 pts with transvenous PM from 6 previously published studies

- 51% Fewer major complications
- 54% Fewer Hospitalizations
- 87% Fewer System Revisions

The HOW
Training For Leadless Pacemaker Implantation

- It probably matters less the type (electrophysiologist, non-electrophysiologist pacemaker-implanting cardiologist, or cardiac surgeon),
- BUT it is important for the physician to have the necessary skills:
  1. Technical, particularly catheter experience including vascular access/management, and catheter manipulation within the heart, and
  2. Cognitive, such as pacemaker indications, programming, and troubleshooting.
- Given that the skills for acute device retrieval overlap with those for device implantation, it is less necessary to have experience with lead extraction, a somewhat specialized skill.
### Product Specifications

<table>
<thead>
<tr>
<th>Volume</th>
<th>0.8 cc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length</td>
<td>25.9 mm</td>
</tr>
<tr>
<td>Outer diameter</td>
<td>6.7 mm (20.1 Fr)</td>
</tr>
<tr>
<td>Mass</td>
<td>1.75 g</td>
</tr>
</tbody>
</table>

**Materials in chronic contact with human tissue**
- Titanium, titanium nitride, parylene C, primer for parylene C, PEEK, siloxane, nitinol, platinum, iridium, liquid silicone rubber, and silicone medical adhesive

**Steroid**
- Dexamethasone acetate, < 1 mg, MCRD release mechanism

**Fixation mechanism**
- Nitinol FlexFix™ Tines

**Battery**
- Lithium-hybrid CFx silver vanadium oxide

**Nominal pacing cathode**
- 2.5 mm², Pt sintered, TiN coated

**Minimum pacing anode**
- 2.2 mm², TiN coated

**Cathode to anode spacing**
- 18 mm

---

### Longevity

**Projected service life in years**

<table>
<thead>
<tr>
<th>VVIR or VVI pacing %</th>
<th>Amplitude</th>
<th>Pacing Rate</th>
<th>Impedance</th>
<th>Longevity in Years (Pulse width 0.24 ms)</th>
<th>Longevity in Years (Pulse width 0.4 ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>1.5 V</td>
<td>60 min⁻¹</td>
<td>500 Ω</td>
<td>14.6</td>
<td>14.5</td>
</tr>
<tr>
<td>50%</td>
<td>1.0 V</td>
<td>60 min⁻¹</td>
<td>500 Ω</td>
<td>13.3</td>
<td>12.5</td>
</tr>
<tr>
<td></td>
<td>1.5 V</td>
<td>60 min⁻¹</td>
<td>500 Ω</td>
<td>11.7</td>
<td>10.4</td>
</tr>
<tr>
<td></td>
<td>2.0 V</td>
<td>60 min⁻¹</td>
<td>500 Ω</td>
<td>9.6</td>
<td>8.1</td>
</tr>
<tr>
<td><strong>100%</strong></td>
<td><strong>1.0 V</strong></td>
<td><strong>60 min⁻¹</strong></td>
<td><strong>500 Ω</strong></td>
<td><strong>11.8</strong></td>
<td><strong>10.5</strong></td>
</tr>
<tr>
<td>100%</td>
<td>1.5 V</td>
<td>60 min⁻¹</td>
<td>400 Ω</td>
<td>9.0</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>1.5 V</td>
<td>60 min⁻¹</td>
<td>600 Ω</td>
<td>10.0</td>
<td>8.4</td>
</tr>
<tr>
<td>100%</td>
<td>1.5 V</td>
<td>70 min⁻¹</td>
<td>500 Ω</td>
<td>9.1</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>1.5 V</td>
<td>100 min⁻¹</td>
<td>500 Ω</td>
<td>8.0</td>
<td>6.4</td>
</tr>
<tr>
<td>100%</td>
<td>2.5 V</td>
<td>60 min⁻¹</td>
<td>600 Ω</td>
<td>6.3</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>2.5 V</td>
<td>60 min⁻¹</td>
<td>500 Ω</td>
<td>5.6</td>
<td>2.4</td>
</tr>
<tr>
<td><strong>5.0 V</strong></td>
<td><strong>60 min⁻¹</strong></td>
<td><strong>500 Ω</strong></td>
<td></td>
<td><strong>1.8</strong></td>
<td><strong>1.2</strong></td>
</tr>
</tbody>
</table>

*Projected service life estimates are based on accelerated battery discharge data and device modeling as specified. Do not interpret these values as precise numbers.*
INTRODUCER REMOVAL AND HAEMOSTASIS
Management of Leadless Devices at End of Battery Life

CONCLUSIONS

• Leadless pacemakers represent new leap forward in technology
• May address the “Achilles’ heel” of traditional pacemaker device
• Appropriate patients include those currently indication for single-chamber device
• May see “creep” in single chamber implants for other indications until technology catches up
• The devices of the future could be largely devoid of intravascular leads
THE FUTURE IS BUILT HERE
Adenovirus Tbox 18 gene transduction (a gene coding a transcription factor responsible for the sinus node development)

Conversion of cardiomyocytes into pacemaker cells

Gene therapy: Biological pacemaker created by gene transfer

Potassium channel Lk1 inhibition in the cardiomyocytes of a guinea pig

Conversion of cardiomyocytes into pacemaker cells
PACEMAKERS POWERED BY HEARTBEAT

- piezoelectrical effect - high-efficiency mechanical-to-electrical energy conversion
- piezoelectric material - lead citrate titanate nanoribbons
- generates 0.2 µW/cm² energy
- the material was affixed to heart, lungs and diaphragm
- organ movement was not disturbed
- the material generated enough voltage by opened and also by closed chest
“Today you don’t think of a pacemaker implantation as something sensational. Well, ladies and gentlemen, then you are all wrong. It is still a sensation—for the patient”

Arne Larsson
Leadless Pacemakers Complication Rate Compares Favorably to Transeptal Pacemakers Published Data

Complication Rate

<table>
<thead>
<tr>
<th>Device</th>
<th>Complication Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micra</td>
<td>4.0%</td>
</tr>
<tr>
<td>Historical Control</td>
<td>7.6%</td>
</tr>
<tr>
<td>Danish Registry</td>
<td>7.5%</td>
</tr>
<tr>
<td>FOLLOWPACE</td>
<td>12.4%</td>
</tr>
<tr>
<td>Nanostim</td>
<td>6.5%</td>
</tr>
</tbody>
</table>

6 Medtronic Pacemaker Studies (2000-2012)
Single Chamber Only (2014)
Dual + Single Chamber (2012)

El-Chami, MF. AJC 2016
Figure 1. Micra Transcatheter Pacing System Positioned in the Right Ventricle.
23Fr introducer + dilator over the wire

Introduction of delivery catheter into RA

Introduction of delivery catheter into RV

Deployment
Figure: Diagrams of the four classifications of SVC obstruction based on contrast venography as originally defined by Stanford and Doty in 1986.
Leadless pacing: Going for the jugular.

Saleem-Tailo S1, van Driel VJ1, Chaldoupi SM1, Nikolic T1, van Wessel H1, Borieffs CJW1, Ramanna H1.

Author information
1 Department of Cardiology, Haga Teaching Hospital, The Hague, The Netherlands.

Abstract
BACKGROUND: Leadless pacing is generally performed from a femoral approach. However, the femoral route is not always available. Until now, data regarding implantation using a jugular approach other than a single-case report were lacking.

METHODS: The case records of all patients who underwent internal jugular venous (IJV) leadless pacemaker implantation (Micra, Medtronic, Dublin, Ireland) at our center were analyzed retrospectively.

RESULTS: Nineteen patients underwent IJV leadless pacemaker implantation, nine females, mean age of 77.5 ± 9.6 years; permanent atrial fibrillation in all patients with normal left ventricular ejection fraction. Implant indication was atrioventricular conduction disturbance in 10, pre-AV nodal ablation in seven, and replacement of a conventional VVI pacemaker in two (infection in one and lead malfunction in the other). The device was positioned at the coronary sinus in seven patients, apico-septal in seven patients, and mid-septal in five patients. In 12 patients, a sufficient device position was obtained at the first attempt, in three at the second, in one at the third, in one at the fourth, and in two at the sixth attempt. The mean pacing threshold was 0.56 ± 0.39V at 0.24-ms pulse width, sensed amplitude was 9.1 ± 3.2 mV, mean fluoroscopy duration was 3.1 ± 1.6 min. There were no vascular or other complications. At follow-up, electrical parameters remained stable in 15 of 19 patients.

CONCLUSION: Although experience is minimal, we suggest that the IJV approach is safe and may be considered in patients where the femoral approach is contraindicated.

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KEYWORDS: jugular vein; leadless pacing; pacemaker

PMID: 30553690 DOI: 10.1111/pace.13607
Implantation of a MICRA Leadless Pacemaker Via Right Internal Jugular Vein