Advances in Pacing…
Transcatheter Pacing Technology

Michael Kutayli MD

Agenda

- Background and historical perspective
- Unmet clinical needs in cardiac pacing
- Transcatheter Pacing System (TPS)
- Micra™ TPS procedure
- Clinical evidence

Pacing Evolution
Cardiac Pacing Milestones

- External Pacemaker: 1958
- Implantable Pacemaker: 1960
- Rate Responsive Pacemaker: 1986
- MRI Conditional Pacemaker: 2011
- Intracardiac Pacemaker: Today

Early Intracardiac Pacemaker Concepts

- Totally Self-Contained Intracardiac Pacemaker
- Transcatheter Pacing System (TPS)
- Micra™ TPS procedure
- Clinical evidence

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New Opportunities To: Redefine The Patient Experience

- Potential to increase pacemaker patient satisfaction
- No chest scar, bump, and no visible or physical reminder
- Minimally-invasive procedure
- Potential for fewer post-implant activity restrictions

Pocket Related Complications
- 8% at 5 years with traditional technology\textsuperscript{1,2}
- Infection
- Hematoma
- Erosion

Lead Related Complications
- 11% at 5 years with traditional technology\textsuperscript{1,2}
  - Fractures
  - Insulation breaches
  - Venous thrombosis and obstruction
  - Tricuspid regurgitation

Agenda
- Background and historical perspective
- Unmet clinical needs in cardiac pacing
  - Transcatheter Pacing System (TPS)
Technical Challenges To Consider

- Deep miniaturization (>90% size reduction)
- New battery and electronics
- Percutaneous procedure/delivery
  - 23 Fr femoral delivery
  - New deflectable delivery system
  - New fixation
- Without compromising traditional features and functionality
- Longevity
- Patient access to MRI
- Intracardiac rate adaptive pacing
- External communication systems
- End of service considerations

Micra™ Transcather Pacing System (TPS)

Micra Pacing Capsule
Micra Delivery Catheter
Micra Introducer

Micra™ Transcatheter Pacing System

- Micra Pacing Capsule
- Micra Delivery Catheter
- Micra Introducer

Size
- Volume: 0.8 cc
- Length: 25.9 mm
- Width: 20 Fr

Battery
- 12+ years estimated average longevity

Capabilities
- Pacing Mode: VVIR
- Bipolar sensing
- MRI SureScan™, allowing 1.5 T or 3 T full body MRI scans
- Capture Management™
- Rate Response
- Diagnostic: battery status, threshold, impedance, % paced
- Device can be manually deactivated and automatically deactivates at EOS
Comparison To Traditional Pacing Technology

<table>
<thead>
<tr>
<th></th>
<th>Conventional</th>
<th>Micra TPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total volume</td>
<td>10.6 cc</td>
<td>0.8 cc</td>
</tr>
<tr>
<td>Rate Response</td>
<td>Subcutaneous Accelerometer</td>
<td>Intracardiac Accelerometer</td>
</tr>
<tr>
<td>Communication</td>
<td>Model 2000 Programmer</td>
<td>Model 2000 Programmer</td>
</tr>
<tr>
<td>Battery</td>
<td>Lead or Radiofreq. on Area</td>
<td>FlexFix™ Nitinol Tines</td>
</tr>
<tr>
<td>MR conditional</td>
<td>1.5T</td>
<td>1.5T + 3T</td>
</tr>
<tr>
<td>Battery Service Life</td>
<td>10.3 years</td>
<td>12.5 years</td>
</tr>
</tbody>
</table>

*Medtronic model ADSR01 with 30 cm by 6 Fr lead †Projected based on ADSR01 use conditions of 100% pacing at 60 bpm, 1.5 V at 0.24 ms, and 500 Ω

Deep Miniaturization

Completely self-contained within the heart, no lead required

Low Power Circuit Design Yields A 12+ Year Estimated Average Longevity

- **Fixation**: Stable fixation separated from electrode interface enables low and stable thresholds
- **Capture management**: Hourly safety margin confirmation optimizes pacing output
- **Efficient Electronics**: Extra low-power, highly integrated CMOS
- **Proprietary Li/SVO CFx battery**: Chemistry has high energy density
**Delivery Catheter And Micra Introducer**

**Delivery Catheter**
- 105 cm long catheter system with a handle that controls deflection and deployment of the Micra Pacing Capsule

**Micra Introducer**
- 56 cm working length, with extended distal taper
- 23 Fr inner diameter (27 Fr outer diameter)
- Hydrophilic coated sheath

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**Fixation Mechanism**

**FlexFix™ Tines**
- Atraumatic, nitinol tines provide secure capsule placement
- Four, active tines gently self expand to ensure consistent deployment
- 2 tines have 15x the holding force necessary to hold the device in place
- No dislodgements in 725 patient clinical trial

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Fixation Mechanism
Fixation separated from electrode interface enables low and stable thresholds

Rate Response Overview
Due to the intracardiac location of Micra, rate response presents two key challenges:

**Challenge 1:** Sensing activity during cardiac motion
**Solution:** Micra incorporates filtering of accelerometer signal to minimize impact of cardiac motion

**Challenge 2:** Device orientation will change with implant location
**Solution:** Micra incorporates 3-axis accelerometer to allow individual selection of best vector

Rate response function confirmed via treadmill testing in clinical trial

Rate Response Function Confirmed Via Treadmill Testing
Capture Management Overview

In order to maximize battery life in Micra while maintaining adequate patient safety margins, the following changes have been made to Capture Management:

Hourly Threshold Confirmation Test
Safety Margins
  - Acute: 1.5V over highest threshold in past 2 weeks
  - Chronic: 0.5V over highest threshold in past 2 weeks
Nominal pulse width = 0.24 ms

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Micra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threshold Measurement Frequency</td>
<td>1/day</td>
</tr>
<tr>
<td>Threshold Confirmation Test</td>
<td>Hourly at threshold + 0.125V; triggers new test if 0.5V exceeded</td>
</tr>
<tr>
<td>Threshold for Adjusting Output</td>
<td>Highest threshold measured in last 2 weeks</td>
</tr>
<tr>
<td>Acute Phase Pacing Output (Threshold)</td>
<td>Threshold + 1.25V</td>
</tr>
<tr>
<td>Chronic Phase Pacing Output (Nominal)</td>
<td>Threshold + 0.5V</td>
</tr>
<tr>
<td>Nominal Pulse Width</td>
<td>0.24 ms (to minimize T wave oversensing)</td>
</tr>
</tbody>
</table>

Titanium Nitrite electrodes with low polarization facilitate evoked response detection

Micra Projected Longevity Comparable To Existing Single Chamber Devices

*Micra longevity projected from 300 patient 6-month data, all others from Product Performance Data as of Sept 16, 2015

8/31/2016
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**Procedure Design And Challenges To Consider**

- Mitigate dislodgement risk
- Mitigate perforation risk
- Enable atraumatic repositioning at implant
- Achieve low and stable thresholds
- Provide end of service options

**Minimally Invasive Procedure**

- [Image of a procedure]

Femoral Access
- 23 Fr inner diameter (27 Fr outer diameter)
- Hydrophilic coated sheath

Navigation To Target Location
Integrated delivery system facilitates implant procedure

Confirm Positioning
Inject contrast medium to ensure septal orientation
**Device Deployment**

Femoral approach and flexible distal catheter design result in an 11% push efficiency\(^1\)

**Device Deployment**

Delivery system provides visual feedback when adequate tip pressure is achieved and retracts during device deployment\(^1\)

**Testing Fixation**

"Pull and hold" test

- 2 tines have 15x the holding force necessary to hold the device in place\(^1,2\)
Testing Fixation

“Pull and hold” test

- 2 tines have 15x the holding force necessary to hold the device in place\(^1\,\,\,\,^2\)

Testing Electricals

Electrode tissue interface allows for low and stable chronic thresholds\(^2\)

Fixation Enables Repositioning
Device Lifecycle Management

**Designed for Options:**

- Micra can be turned OFF and an additional Micra can be added:
  - Micra takes up <1% of the volume of a normal right ventricle
- Micra can be turned OFF and a traditional system or upgrade can be implanted
- The Micra design incorporates a proximal retrieval feature to enable acute retrieval

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Multiple Micra Can Be Implanted in the RV

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Device Lifecycle Management

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2. Fluoroscopy image courtesy of Bert Hansky, MD.
Device Lifecycle Management

Clinical Trial Experience (n=725)

- 2 patients experienced increased thresholds and 1 patient required a CRT upgrade
- In all cases, it was possible to successfully either turn Micra OFF or retrieve the device

One Micra device was retrieved (17 days post implant) and replaced; two devices were turned off and successfully replaced with transvenous systems


Background and historical perspective

Unmet clinical needs in cardiac pacing

Transcatheter Pacing System (TPS)

Micra™ TPS procedure

- Clinical evidence

The Micra TPS Global Clinical Trial

Study Design:

- Prospective, non-randomized, single-arm, multi-site, FDA IDE study
- Pre-defined historical control group for comparison
- 2667 patients from 6 trials of commercially available technology
- 725 patients, 94 implanters, 56 centers, 19 countries, 5 continents
- North America, Europe, Asia, Australia, Africa
- VVIR patients: Class I or II guideline indication for de novo ventricular pacing with no restriction by comorbidity (e.g. COPD)
The Micra TPS Global Clinical Trial

Primary Objectives (6 months):

- **Safety:** Freedom from device or procedure-related major complications
  - Death, permanent loss of therapy, hospitalization, prolonged hospitalization, or system revision
  - Target performance >90%, lower CI >83%

- **Efficacy:** Demonstrate low and stable pacing thresholds
  - ≤ 2V and no increase of >1.5V (relative to implant)
  - Target performance >89%, lower CI >80%

Patient Flow Diagram

Baseline Characteristics

<table>
<thead>
<tr>
<th>Micra (N=725)</th>
<th>Historical Control (N=2667)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>75.9 ± 10.9</td>
<td>71.1 ± 12.1</td>
</tr>
<tr>
<td>Male gender</td>
<td>58.8%</td>
<td>55.1%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>78.6%</td>
<td>67.2%</td>
</tr>
<tr>
<td>AF</td>
<td>72.6%</td>
<td>36.6%</td>
</tr>
<tr>
<td>Vascular Disease</td>
<td>42.2%</td>
<td>19.2%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>28.6%</td>
<td>21.9%*</td>
</tr>
<tr>
<td>CAD</td>
<td>28.0%</td>
<td>38.4%</td>
</tr>
<tr>
<td>CHF</td>
<td>17.0%</td>
<td>15.0%</td>
</tr>
<tr>
<td>COPD</td>
<td>12.4%</td>
<td>7.2%*</td>
</tr>
<tr>
<td>Vascular Disease</td>
<td>7.3%</td>
<td>10.1%</td>
</tr>
</tbody>
</table>
## Baseline Characteristics

**Micra Patients Older, More Comorbidities**

<table>
<thead>
<tr>
<th></th>
<th>Micra (n=725)</th>
<th>Historical Control (n=2667)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>75.9 ± 10.9</td>
<td>71.4 ± 12.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>58.8%</td>
<td>55.1%</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypertension</td>
<td>78.6%</td>
<td>67.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AF</td>
<td>72.6%</td>
<td>36.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Valvular Disease</td>
<td>42.2%</td>
<td>19.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>28.6%</td>
<td>21.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAD</td>
<td>28.0%</td>
<td>38.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHF</td>
<td>17.0%</td>
<td>15.0%</td>
<td>0.20</td>
</tr>
<tr>
<td>COPD</td>
<td>17.4%</td>
<td>7.2%</td>
<td>0.001</td>
</tr>
<tr>
<td>Vascular Disease</td>
<td>7.3%</td>
<td>10.1%</td>
<td>0.032</td>
</tr>
</tbody>
</table>


### Primary Objectives Met

**Safety (n=725):**
- 96.0% freedom from device or procedure-related major complications at 6 months (95% CI, 93.9 to 97.3; P<0.0001)
  - No dislodgements
  - No systemic infections

**Efficacy (n=297):**
- 98.3% with adequate 6-month pacing capture threshold (95% CI, 96.1 to 99.5; P<0.0001)

### Micra Major Complications (N=725)

<table>
<thead>
<tr>
<th>Major Complication</th>
<th>Death</th>
<th>Loss of Pacing Function</th>
<th>Hospitalization</th>
<th>Prolonged Hospitalization</th>
<th>Nontraumatic Revision</th>
<th>Total Events</th>
<th>No. Patients Requiring Surgical Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep vein thrombosis</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1 (0.1%)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1 (0.1%)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>AF/atrial fibrillation</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>5</td>
<td>5 (0.7%)</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Cardiac perforation / effusion</td>
<td>3</td>
<td>0</td>
<td>11</td>
<td>11</td>
<td>11 (1.4%)</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Elevated thresholds</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2 (0.3%)</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Atrial myxomatous fibrosis</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1 (0.1%)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3 (0.4%)</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1 (0.1%)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Pacemaker syndrome</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1 (0.1%)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Freygasin</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1 (0.1%)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Syncope</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1 (0.1%)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total major complications</td>
<td>1</td>
<td>1</td>
<td>13</td>
<td>13</td>
<td>13 (4.4%)</td>
<td>42</td>
<td></td>
</tr>
</tbody>
</table>

*Not mutually exclusive as a single event may meet more than one major complication criterion.*

51% Fewer Major Complications With Micra Vs Transvenous Pacemakers

To adjust for differences in patient populations, propensity matching to a subset of the historical control confirmed a reduction in major complications with Micra (HR: 0.46; 95% CI: 0.28 to 0.74).


Micra Complication Rate Compares Favorably to Recent Published Data

Please note: major complications and all complications definition vary between the above cohorts.


Most Major Complications Reduced With Micra Vs Transvenous Pacemakers Within Subgroups
High Implant Success Rate

- 99.2% implant success (719 of 725 attempts) with 94 implanters
- Median implant time was 28 minutes introducer in to introducer out
  22 min after 1st 10 implants

Physicians Consistent With Guidelines
Indications for Pacing (N=725)

Consistent with Guideline Recommendations for VVI Pacing®

Physicians Consistent With Guidelines
Indications for Pacing (N=725)

Healthcare Utilization:
Overall, 51% Fewer Major Complications With Micra Vs Transvenous Pacemakers1

<table>
<thead>
<tr>
<th>E-Month Kaplan-Meier Estimates</th>
<th>Micra (n=725)</th>
<th>Historical Control (n=2667)</th>
<th>Relative Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Major Complications</td>
<td>4.0%</td>
<td>7.4%</td>
<td>51%</td>
</tr>
<tr>
<td>Death</td>
<td>0.1%</td>
<td>0%</td>
<td>NS</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>2.3%</td>
<td>3.5%</td>
<td>54%</td>
</tr>
<tr>
<td>Prolonged Hospitalization</td>
<td>2.6%</td>
<td>4.4%</td>
<td>NS</td>
</tr>
<tr>
<td>System Revision</td>
<td>0.4%</td>
<td>3.5%</td>
<td>87%</td>
</tr>
<tr>
<td>Loss of Device Function</td>
<td>0.1%</td>
<td>0%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Not mutually exclusive as a single event may meet more than one major complication criteria. NS = Not significant.
Micra Pacing Thresholds Low And Stable

Battery Longevity Estimate:
- Based on use conditions of the 300 patients with 6-month data, median battery longevity estimate is 12.5 years.
- Use conditions included: median pacing 49%, median pacing threshold 0.50V, median impedance 573Ω; estimated longevity range of 6.0–14.6 years.

Micra Electrical Performance

Summary
Largest Transcatheter Pacing Dataset (n=725)

Micra Transcatheter Pacing Study
- Single-arm, global multi-center clinical trial
- 94 implanters, 56 centers, 19 countries, 5 continents

Met performance and safety objectives with wide margins
- 96% of patients experienced no major complications at 6 months
- 51% lower complication rate than traditional pacing systems
- 0 dislodgements
- 0 system infections
Summary
Largest Transcatheter Pacing Dataset (n=725)

Successfully implanted in a wide variety of patients
• 99.2% implant success rate – highest implant success rate in the industry

98.3% of patients had low and stable pacing thresholds at 6 months, yielding estimated longevity on average of 12.5 years

Thank you