MINERVA\(^1\) Results Summary

**Evaluated whether DDDRP + MVP\(^{\circledast}\) reduces mortality, morbidity, or permanent AF compared with standard dual chamber pacing.**

Multicenter (63 centers) international, randomized single blind study with 3 arms enrolling 1,166 patients with:

- Class I or Class II indications for dual chamber pacing
- Previous atrial tachyarrhythmias
- No history of permanent AF or third-degree AV block

49% relative reduction (\(p = 0.001\)) in cardioversions for atrial arrhythmias between DDDRP + MVP and Control DDDR

52% relative reduction (\(p < 0.0001\)) in AF-related hospitalizations and ER visits between DDDRP + MVP and Control DDDR

- Resulting in an estimated healthcare utilization savings of $1,218 over a 10-year period.\(^2\)

**Potential Contribution of Reactive ATP\(^{\circledast}\)**

Risk of AF > 7 days and aATP efficacy\(^3\)

- 58% relative reduction in persistent AF between the control and high efficacy ATP (> 44%) study arms
- Episodes ≥ 2 minutes
- When Reactive ATP is successful, significantly fewer patients have AF episodes > 7 days
- Reactive ATP is a key contributor to these results
**Evolution of Reactive ATP**

1. In this scenario, this fairly rapid episode was treated unsuccessfully by aATP
2. 8 hours later the rhythm/rate changed
3. Rate slows, no ATP therapy available

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**First Generation**

1. 220 ms
   - AT/AF detected
   - All therapies delivered
   - ATP therapy unsuccessful

2. 8 Hours

3. 320 ms
   - Rhythm spontaneously changed
   - No ATP therapy available

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**Reactive ATP**

1. In this scenario, this fairly rapid episode was treated unsuccessfully by aATP
2. 8 hours later the rhythm/rate changed
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1. 220 ms
   - AT/AF detected
   - All therapies delivered
   - ATP therapy unsuccessful

2. 8 Hours

3. 320 ms
   - Rhythm spontaneously changed
   - ATP therapy is available
**AT/AF Rhythm Transitions**

The percentage of episodes with rate or regularity transitions increases rapidly as a function of AT/AF episode duration.
- First generation: ~10 minutes to treat episodes
- Reactive ATP: can treat long lasting episodes

**Results: Reactive ATP Efficacy**

1) GEE adjusted Reactive ATP efficacy was 44.4% (95% CI 41.3% – 47.6%)
2) In regular AT/AF, Reactive ATP efficacy is linearly associated with AT/AF cycle length at last ATP therapy
3) In irregular AT/AF, Reactive ATP efficacy is ≥ 50%
Reactive ATP in a MINERVA Patient

<table>
<thead>
<tr>
<th>Episode Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Type</td>
</tr>
<tr>
<td>Duration</td>
</tr>
<tr>
<td>A/V Max Rate</td>
</tr>
<tr>
<td>A. Median</td>
</tr>
<tr>
<td>Activity at onset</td>
</tr>
<tr>
<td>First Therapy</td>
</tr>
<tr>
<td>Last Therapy</td>
</tr>
</tbody>
</table>

**Event Sequence**

- **Onset**: 30-Nov-2007 17:40:59
- **Detection**: 18 sec
- **First Rx**: Ramp
- **Last Rx**: Ramp
- **Termination**: 02:13:30

Note: Therapy details not included in table above.

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**Definitions**

**DDDRP**: Atrial ATP + combination of three atrial intervention pacing algorithms
- Atrial Preference Pacing
- Atrial Rate Stabilization
- Post Mode Switch Overdrive Pacing

**Permanent AF**: Patient in AF at two consecutive follow-up visits and physician determination not to cardiovert

* All additional therapies in this 50 ms zone also delivered unsuccessfully.
## Programming Recommendations from MINERVA

<table>
<thead>
<tr>
<th>Mode</th>
<th>AAIR ↔ DDDR nominal or AAI ↔ DDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAV</td>
<td>Investigator discretion or Optimized AV delay</td>
</tr>
<tr>
<td>PAV</td>
<td>Investigator discretion or Optimized AV delay</td>
</tr>
<tr>
<td>MVP Mode</td>
<td>ON</td>
</tr>
<tr>
<td>Rate Adaptive AV</td>
<td>Off (nominal)</td>
</tr>
<tr>
<td>Mode Switch</td>
<td>On (nominal)</td>
</tr>
<tr>
<td>PVAB Method</td>
<td>Partial (nominal)</td>
</tr>
<tr>
<td>Atrial tachyarrhythmias Detection</td>
<td>On</td>
</tr>
<tr>
<td>aATP therapies</td>
<td>On</td>
</tr>
<tr>
<td>Atrial Rate Stabilization (ARS)</td>
<td>On (max 95 bpm)</td>
</tr>
<tr>
<td>Atrial Preference Pacing (APP)</td>
<td>On (max 95 bpm)</td>
</tr>
<tr>
<td>APP and ARS Maximum Rate</td>
<td>On</td>
</tr>
<tr>
<td>Post Mode Switch Overdrive</td>
<td>On (≤ 5 minutes)</td>
</tr>
<tr>
<td>Ventricular Rate Stabilization</td>
<td>Off</td>
</tr>
</tbody>
</table>

### AT/AF Detection and Therapies

<table>
<thead>
<tr>
<th>Detection Zones</th>
<th>A. Interval (Rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>On</td>
<td>350 ms (171 bpm)</td>
</tr>
</tbody>
</table>

#### Anti-Tachy Pacing (ATP)...

**AT/AF Rx**

- Ramp(10), Burst+(10), Ramp(10)

**Reactive ATP**

<table>
<thead>
<tr>
<th>Rhythm Change</th>
<th>On</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Interval</td>
<td>Off</td>
</tr>
</tbody>
</table>

#### Stop Atrial Rx After

- Rx/Lead Suspect... 2 On
- Duration to Stop 48 hr
- Episode Duration Before Rx Delivery 1 min

### AT/AF Pacing Therapies

#### Rx1

- AT/AF Rx Status On
- Therapy Type Ramp
- Initial #S1 Pulses 13
- A-S1 Interval (%AA) 91%
- S1-S2 (%AA) 81%
- S2-S3 Decrement 20 ms
- Interval Decrement 10 ms
- # Sequences 10

#### Rx2

- AT/AF Rx Status On
- Therapy Type Burst+
- Initial #S1 Pulses 11
- A-S1 Interval (%AA) 84%
- S1-S2 (%AA) 81%
- S2-S3 Decrement 20 ms
- Interval Decrement 10 ms
- # Sequences 10

#### Rx3

- AT/AF Rx Status On
- Therapy Type Ramp
- Initial #S1 Pulses 13
- A-S1 Interval (%AA) 81%
- S1-S2 (%AA) 81%
- S2-S3 Decrement 10 ms
- Interval Decrement 10 ms
- # Sequences 10

### Shared A. ATP

- A- A Minimum ATP Interval 150 ms
- A. Pacing Amplitude and Pulse Width 6 V
- VVI Backup Pacing On (Auto Enable) 70 bpm

**Undo Pending** OK
References

Brief Statement: IPGs
Indications
Implantable Pulse Generators (IPGs) are indicated for rate adaptive pacing in patients who may benefit from increased pacing rates concurrent with increases in activity. Pacemakers are also indicated for dual chamber and atrial tracking modes in patients who may benefit from maintenance of AV synchrony. Dual chamber modes are specifically indicated for treatment of conduction disorders that require restoration of both rate and AV synchrony, which include various degrees of AV block to maintain the atrial contribution to cardiac output and VVI intolerance (e.g., pacemaker syndrome) in the presence of persistent sinus rhythm. See device manuals for the accepted patient conditions warranting chronic cardiac pacing. Antitachycardia pacing (ATP) is indicated for termination of atrial tachyarrythmias in patients with one or more of the above pacing indications. For the MR Conditional IPG, a complete SureScan® pacing system consisting of a SureScan IPG and 2 SureScan leads is required for use in the MR environment.

Contraindications
IPGs are contraindicated for concomitant implant with another bradycardia device and concomitant implant with an implantable cardioverter defibrillator. There are no known contraindications for the use of pacing as a therapeutic modality to control heart rate. The patient's age and medical condition, however, may dictate the particular pacing system, mode of operation, and implant procedure used by the physician. Rate-responsive modes may be contraindicated in those patients who cannot tolerate pacing rates above the programmed Lower Rate. Dual chamber sequential pacing is contraindicated in patients with chronic or persistent supraventricular tachycardias, including atrial fibrillation or flutter. Asynchronous pacing is contraindicated in the presence (or likelihood) of competition between paced and intrinsic rhythms. Single chamber atrial pacing is contraindicated in patients with an AV conduction disturbance. Antitachycardia pacing (ATP) therapy is contraindicated in patients with an accessory anetragrade pathway.

Warnings and Precautions
Changes in a patient's disease and/or medications may alter the efficacy of the device's programmed parameters. Patients should avoid sources of magnetic and electromagnetic radiation to avoid possible underdetection, inappropriate sensing and/or therapy delivery, tissue damage, induction of an arrhythmia, device electrical reset, or device damage. Do not place transthoracic defibrillation paddles directly over the device.

For MR Conditional IPG Systems, before performing an MRI scan, refer to the SureScan pacing system technical manual for additional information; patients and their implanted systems must be screened to meet the MRI Conditions of Use. Do not scan patients who do not have a complete SureScan pacing system consisting of a SureScan IPG and two SureScan leads; patients who have broken, abandoned, or intermittent leads; or patients who have a lead impedance value of < 200 Ω or > 1,500 Ω.

Potential Complications
Potential complications include, but are not limited to, rejection phenomena, erosion through the skin, muscle or nerve stimulation, oversensing, failure to detect and/or terminate arrhythmia episodes, and surgical complications such as hematoma, infection, inflammation, and thrombosis.

SureScan systems have been designed to minimize potential complications in the MRI environment. Potential MRI complications include, but are not limited to, lead electrode heating and tissue damage resulting in loss of sensing or capture or both, or induced currents on leads resulting in continuous capture, VT/VF, and/or hemodynamic collapse.

See the device manuals before performing an MRI Scan for detailed information regarding the implant procedure, indications, MRI conditions of use, contraindications, warnings, precautions, and potential complications/adverse events. For further information, call Medtronic at 1 (800) 328-2518 and/or consult Medtronic’s website at www.medtronic.com.

Caution: Federal law (USA) restricts these devices to sale by or on the order of a physician.

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