Atrial Arrhythmia Detection, Prevention and Therapy Algorithm
How Do They Work?

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• Why atrial arrhythmia (AF) is important in pacemaker patients
• Atrial arrhythmias (AF) supression work
• Clinical trials
Why atrial fibrillation is important in pacemaker patient

- AF increase morbidity
  - Stroke
  - Heart failure
  - Tachycardia induced cardiomyopathy
- AF increase mortality
Risks of Atrial Fibrillation

• Stroke
  • Patients with AF are 5 times more likely to have a stroke than the general population
• Cause of 75,000 cases of stroke annually
• 23% of all strokes in the U.S.
Risks of Atrial Fibrillation

- Long-term Mortality Rates Framingham Study

Atrial arrhythmias (AF) suppression work
Hypothesis

• Suppression of paroxysmal and possibly persistent AF can be achieved by stimulation at one or more sites using a variety of overdrive or PAC responsive algorithms.

• Proposed mechanism(s)
  • Reduced dispersion of refractoriness
  • Improved atrial homogeneity
  • Reduction in triggers
Options to Stabilize or Suppress AF

- Alternate sites of stimulation
  - Bi-atrial stimulation
  - Dual-site atrial stimulation
  - Bachmann’s bundle or interatrial septum
  - Low septal pacing
  - Coronary sinus

- Overdrive algorithms
  - Elevated base rate
  - PAC responsive algorithm (ELA)
  - Consistent Atrial Pacing (Medtronic)
  - AF Suppression™ (St. Jude Medical)
Mechanism of AF/AT Suppression

1. Pace conditioning
2. PAC suppression
3. Post-PAC response
4. Post-exercise response
5. Post-AF response
6. Rate soothing

Mitchell ARJ, Sulke N. Europace 2004; 6: 351
Pace conditioning

- Adjusts the atrial pacing rate to just above the underlying intrinsic rhythm in such a way that the atrium is paced for at least 95% of the time
Pace conditioning
PAC Suppression

- aims to reduce the incidence of PACs by increasing the heart rate upon detection of a PAC
Post-PAC response

- prevents pauses after PACs by controlling the atrial rate in the two beats after a PAC
**Post-exercise response**

- Aims to prevent the rapid heart-rate drop that can occur after exercise by enabling a post-exercise rate.
Post-exercise Response
Rate soothing

- Aims to prevent ATs by overdrive pacing the atrium at a rate that is only just above the sinus rate
Post AF response
AF Suppression Starts
AF Suppression Continues
Atrial Rhythm Classification (ARC)

ARC differentiates atrial flutter (AFL Region) from atrial fibrillation (AF Region) using Rate, Range, and Standard Deviation.

- AFL Region arrhythmias receive SVT zone therapy
- AF Region arrhythmias receive AFib zone therapy
Clinical trials
**ADOPT-A Clinical Trial**

**Study Design**

**Pacemaker Implant**
- Trilogy DR DAO Integrity AFx DR

- **Prospective**
- **Patient Blinded**
- **Randomized**

- **DDDR Pacing AF Suppression-ON**
  - Follow-up Baseline, 30, 90, 180 days
  - Device Assessment QOL
  - Symptomatic AF Episodes via Event Recorder

- **DDDR Pacing AF Suppression-OFF**
  - Follow-up Baseline, 30, 90, 180 days
  - Device Assessment QOL
  - Symptomatic AF Episodes via Event Recorder
# ADOPT-A Clinical Trial

## Atrial Pacing

<table>
<thead>
<tr>
<th>AF Suppression</th>
<th>% Atrial Beats Paced</th>
<th><em>p</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>OFF</td>
<td>67.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ON</td>
<td>92.9</td>
<td></td>
</tr>
</tbody>
</table>
ADOPT-A Clinical Trial

Symptomatic AF Burden

AF Burden (%)

1-Month 3-Month 6-Month

AFs OFF AFs ON

4.44% 3.19% 2.63% 1.93% 1.73% 1.37%

(n = 288)

p < 0.05

Follow up
## ADOPT-A Clinical Trial

### AF Burden Reduction

<table>
<thead>
<tr>
<th></th>
<th>AFs OFF</th>
<th>AFs ON</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Patients</td>
<td>158</td>
<td>130</td>
</tr>
<tr>
<td>Patients with AF Days</td>
<td>81</td>
<td>73</td>
</tr>
<tr>
<td>Total AF Days</td>
<td>682</td>
<td>421</td>
</tr>
<tr>
<td>Total Follow-up Duration (Days)</td>
<td>27,359</td>
<td>22,526</td>
</tr>
<tr>
<td>AF Burden</td>
<td>2.493%</td>
<td>1.869%</td>
</tr>
<tr>
<td>AF Burden Reduction</td>
<td>25.03%</td>
<td></td>
</tr>
</tbody>
</table>
AF Episode Reduction

<table>
<thead>
<tr>
<th></th>
<th>AFs OFF</th>
<th>AFs ON</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Months Prior to Implant</td>
<td>8.1 ± 4.2</td>
<td>8.3 ± 4.1</td>
</tr>
<tr>
<td>Implant to 6 Months</td>
<td>3.2 ± 8.5</td>
<td>4.3 ± 11.5</td>
</tr>
</tbody>
</table>

p = < 0.0001
Freedom to first hospitalization (n = 288)

6% Reduction in Hospitalizations

AFs OFF
p= NS

AFs ON
ADOPT-A Clinical Trial

Freedom from First Cardioversion (n=288)

63% reduction in Cardioversions

AFs OFF
p = 0.0925
AFs ON
ADOPT-A Clinical Trial

• Conclusion
  • AF Suppression pacing appears to be safe and to reduce AF burden in sinus node dysfunction patients with paroxysmal or persistent AF.
  • AF Suppression pacing offers incremental benefit to DDDR pacing alone.
Two Large US Trials:

- **ASPECT**¹
  - n=298 implanted, 277 intention-to-treat analysis (138 septal),
    35 centers, 6 month follow-up (crossover at 3 months);
  - Single-blind study,
  - Lead site randomized to RA septal or non-septal
  - Intervention pacing algorithms ON vs. OFF

  Primary endpoint: AT/AF frequency

- **ATTEST**²
  - n=368 implanted, 324 in efficacy cohort,
    28 centers, 3 month follow-up; Single-blind study
  - All therapies ON vs. OFF (Intervention and ATP)
  - Primary endpoint: AT/AF burden and frequency

¹ AT500 FDA P980035/S13/A3; Data on file, Medtronic, Inc.
**AT500™ Pacing System**  
**ASPECT Trial Design**

**Enrollment (n=298)**

- **Non-Septal Atrial Lead**  
  - N = 150
  - Randomization (1 month)

- **Septal Atrial Lead**  
  - N = 148
  - Randomization (1 month)

**Crossover:**
- 1 month run-in
- 3 month periods for each phase

**Clinical Follow-up Programming at discretion of Physician**

*AT500 FDA P980035/S13/A3; Data on file, Medtronic, Inc.*
AT500™ Pacing System

ASPECT Trial Results

(No changes in device-recorded AT/AF Burden or frequency with specialized algorithms ON vs. OFF)

Patients with septal leads had 47% fewer symptomatic AT/AF episodes ON vs. OFF.

Symptomatic frequency reduction in Septal Arm:

**OFF**

**ON**

\[ p = 0.01 \]

\[ p = 0.89 \]
AT500™ Pacing System
Clinical Results

• ASPECT\(^1,2,3\)
  • No change in frequency or burden of AT/AF episodes when prevention algorithms were enabled
  • Significant reduction in frequency of symptomatic AT/AF episodes when the atrial lead was placed in the septum
  • Significant reduction in frequency of premature atrial contractions (PACs) in both septal and non-septal lead placement groups
  • Patients with non-septal lead placement and high frequency PACs may represent a responder group for intervention algorithms

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\(^1\) AT500 FDA P980035/S13/A3; Data on file, Medtronic, Inc.
\(^3\) Harvey M, Holbrook R, Young M, et al. JACC 2003; 41:Abstract #1017-5
Class I / II Indications for Dual Chamber Pacing
+ At least 1 episode of paroxysmal or persistent AT/AF documented by ECG in last year and 1 symptomatic episode in past 3 months

Enrollment
Brady + AT/AF (n=368)

Randomization (at 1 month)

ON 3 mos
OFF 3 mos

Prevention & ATP Therapies ON vs. OFF

Clinical Follow-up Programming at discretion of physician

AT500™ Pacing System
ATTEST Trial Design

AT500 FDA P980035/S13/A3; Data on file, Medtronic, Inc.
AT500™ Pacing System
ATTEST Trial Results
(ATP Did Not Significantly Alter Episode Duration)

AT500 FDA P980035/S13/A3; Data on file, Medtronic, Inc.
AT500™ Pacing System
Clinical Results

• ATTEST\textsuperscript{1}
  • 99.9% (99.7% GEE) Positive Predictive Value for detection of AT/AF episode (based upon Investigator review)
  • 54% (41% GEE) ATP therapy success rate for device-defined AT
  • Median % of atrial pacing was 98% ON vs. 75% OFF group
  • No incidence of ventricular pro-arrhythmia
  • No significant reduction in AT/AF burden, total frequency or symptomatic AT/AF frequency ON vs. OFF

Note: Median % of ventricular pacing was 97% in the ON group while only 30% of patients were diagnosed with AVB, suggesting high level of RV-pacing may have minimized affect of the atrial therapies.

\textsuperscript{1} Lee M, Weachter R, Pollak S, et al. For the ATTEST Investigators. JACC 41:In Press 2003
SAFE Study Design

Prospective, parallel, randomized, multi-center study
The problem of successful of AF suppression

- Anti-arrhythmias to be used
- The sites of atrial pacing
- Progression of computer technology
- Choosing appropriate patients
- Maybe DDD pacemaker for bradycardia has little effect for AT/AF supression
  - Detrimental effect of apex RV ventricular pacing (‘ventricular pro-arrhythmic pacing’)
Conclusion

- The AF suppression technology in pacemaker patient is still being progress
- There are clearly groups of patients who benefit from AF suppression algorithm but there are also many who do not
- Reduced ventricular pacing is also very important