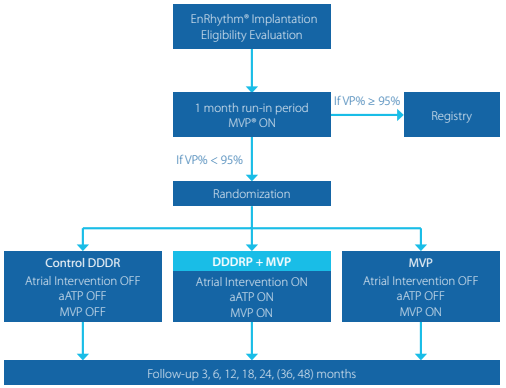
MINERVA[1] Results Summary

Evaluated whether DDDRP + MVP® 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



Composite End Point	Permanent AF
26%	**61%**
Death, CV Hospitalizations, Permanent AF Relative reduction between DDDRP + MVP and Control DDDR arms at 2 years	Relative reduction between DDDRP + MVP and Control DDDR arms at 2 years

Legend:
Control DDDR = standard dual chamber pacemaker
DDDRP + MVP = standard dual chamber pacemaker + MVP + atrial antitachycardia pacing + enhanced pacing modalities

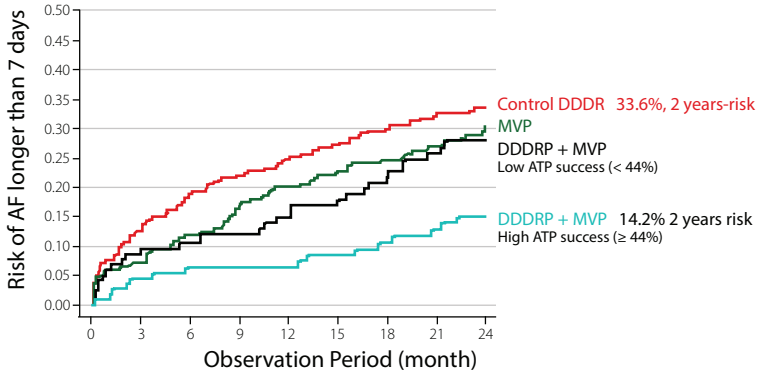
49% relative reduction (p = 0.001) in cardioversions for atrial arrhythmias between DDDRP + MVP and Control DDDR

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]

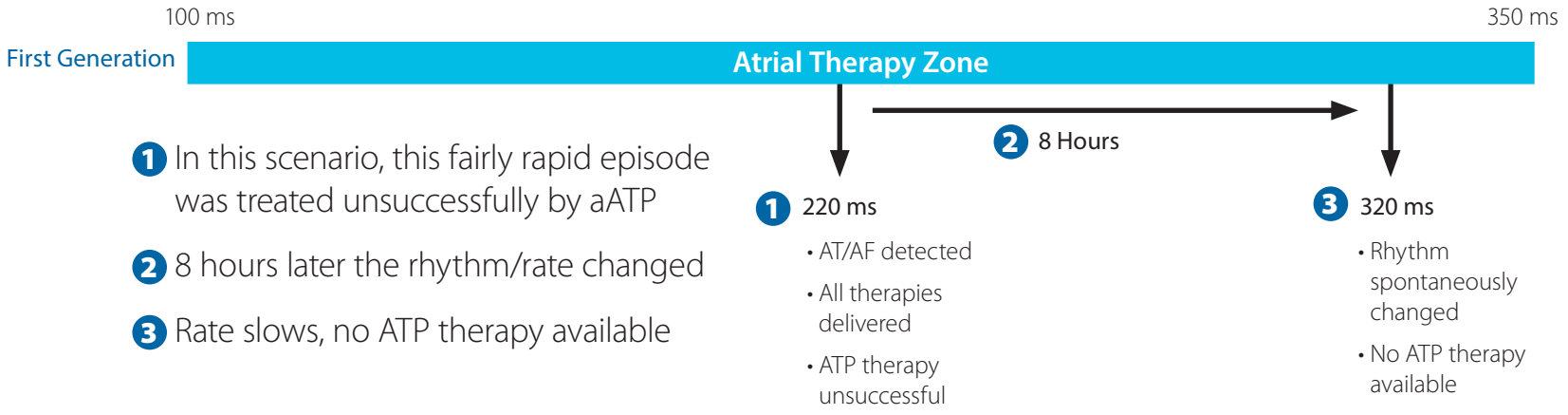
Potential Contribution of Reactive ATP®

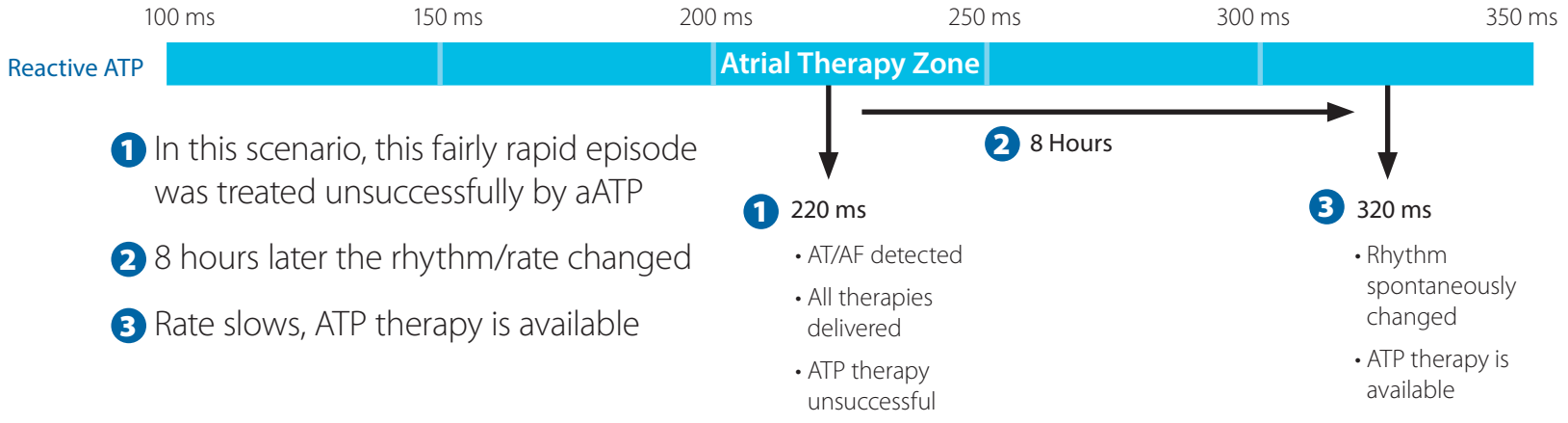
Risk of AF > 7 days and aATP efficacy[3]



- 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

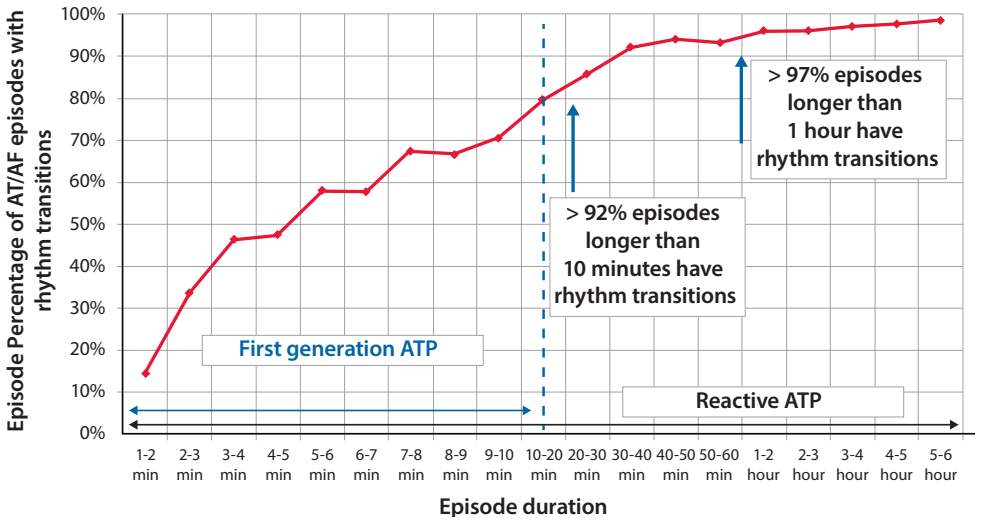




AT/AF Rhythm Transitions[3]

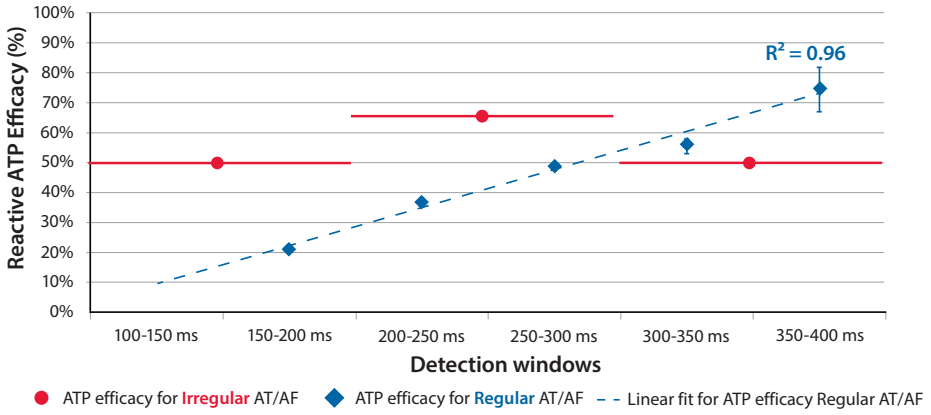
The percentage of episodes with rate or regularity transitions increases rapidly as a function of AT/AF episode duration.

- First generation: ~ 10 minutes to treat episodes
- Reactive ATP: can treat long lasting episodes



Results: Reactive ATP Efficacy[3]

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%



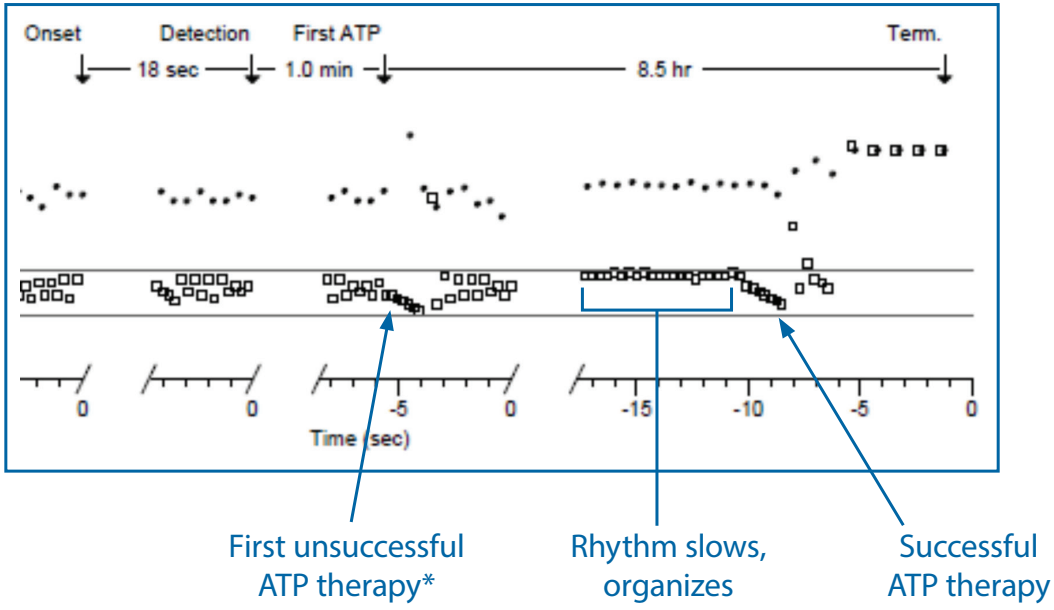
Reactive ATP in a MINERVA Patient

Episode Summary

Initial Type	AT/AF (spontaneous)
Duration	8.5 hr
A/V Max Rate	333 bpm/120 bpm
A. Median	200 bpm (300 ms)
Activity at onset	Rest, Sensor = 60 bpm
First Therapy	AT/AF Rx1: Ramp Seq. 1
Last Therapy	AT/AF Rx1: Ramp Seq. 2, Successful

Event Sequence	Date/Time	
Onset	30-Nov-2007	17:40:59
| 18 sec		
Detection	|	17:41:17
| 1.0 min		
First Rx: Ramp	|	17:42:17
| 8.5 hr		
Last Rx: Ramp	01-Dec-2007	02:13:20
| 10 sec		
Termination	|	02:13:30

Note: Therapy details not included in table above.



* All additional therapies in this 50 ms zone also delivered unsuccessfully.

Definitions

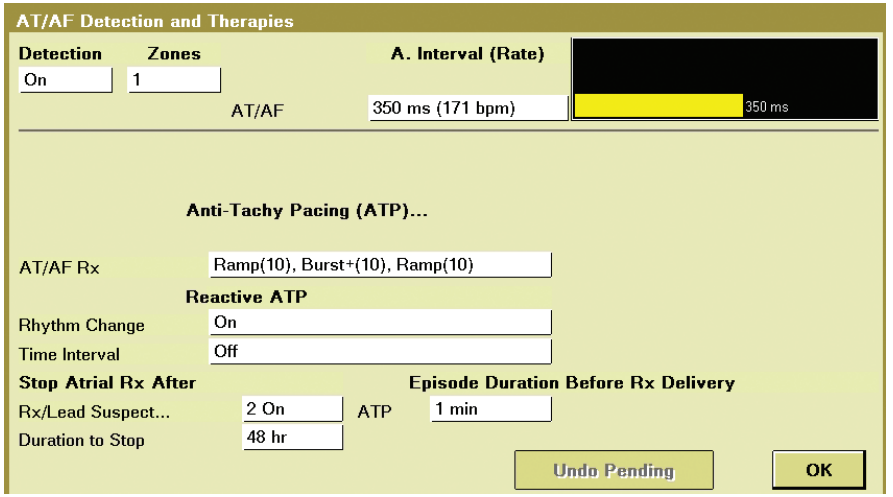
DDDRP: Atrial ATP + combination of three atrial intervention pacing algorithms

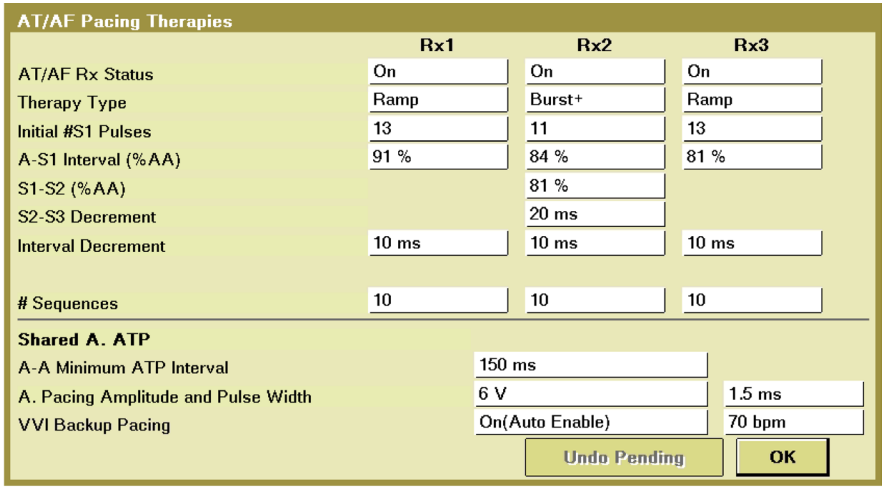
- Atrial Preference Pacing
- Atrial Rate Stabilization
- Post Mode Switch Overdrive Pacing

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

Programming Recommendations from MINERVA

Mode	AAIR ↔ DDDR nominal or AAI ↔ DDD
SAV	Investigator discretion or Optimized AV delay
PAV	Investigator discretion or Optimized AV delay
MVP Mode	ON
Rate Adaptive AV	Off (nominal)
Mode Switch	On (nominal)
PVAB Method	Partial (nominal)
Atrial tachyarrhythmias Detection	On
aATP therapies	On See programmer screens for programming recommendations
Atrial Rate Stabilization (ARS)	On (max 95 bpm)
Atrial Preference Pacing (APP)	On (max 95 bpm)
APP and ARS Maximum Rate	On
Post Mode Switch Overdrive	On (≤ 5 minutes)
Ventricular Rate Stabilization	Off





References

[1] Boriani G, et al. Atrial Antitachycardia Pacing and Managed Ventricular Pacing Reduce the End Point Composed by Death, Cardiovascular Hospitalizations, and Permanent Atrial Fibrillation compared to Conventional Dual Chamber Pacing in Bradycardia Patients: Results of the MINERVA Randomized study. AHA Late Breaking Clinical Trial, November 18, 2013.

[2] Boriani G, et al. Effects of Atrial Fibrillation Pacing Therapies on Healthcare Utilization in Bradycardia: Secondary results of the randomized MINERVA trial. Presented at HRS 2014 (AB08-42).

[3] Padeletti L, Mont L, Pürerfellner H, et al. The Effects of Reactive Atrial Antitachycardia Pacing on the Progression of Atrial Tachyarrhythmias: Results of he MINERVA Randomized Study. Late Breaking Clinical Trial. Presented at HRS 2014.

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 antegrade 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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(24-hour technical support for
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