

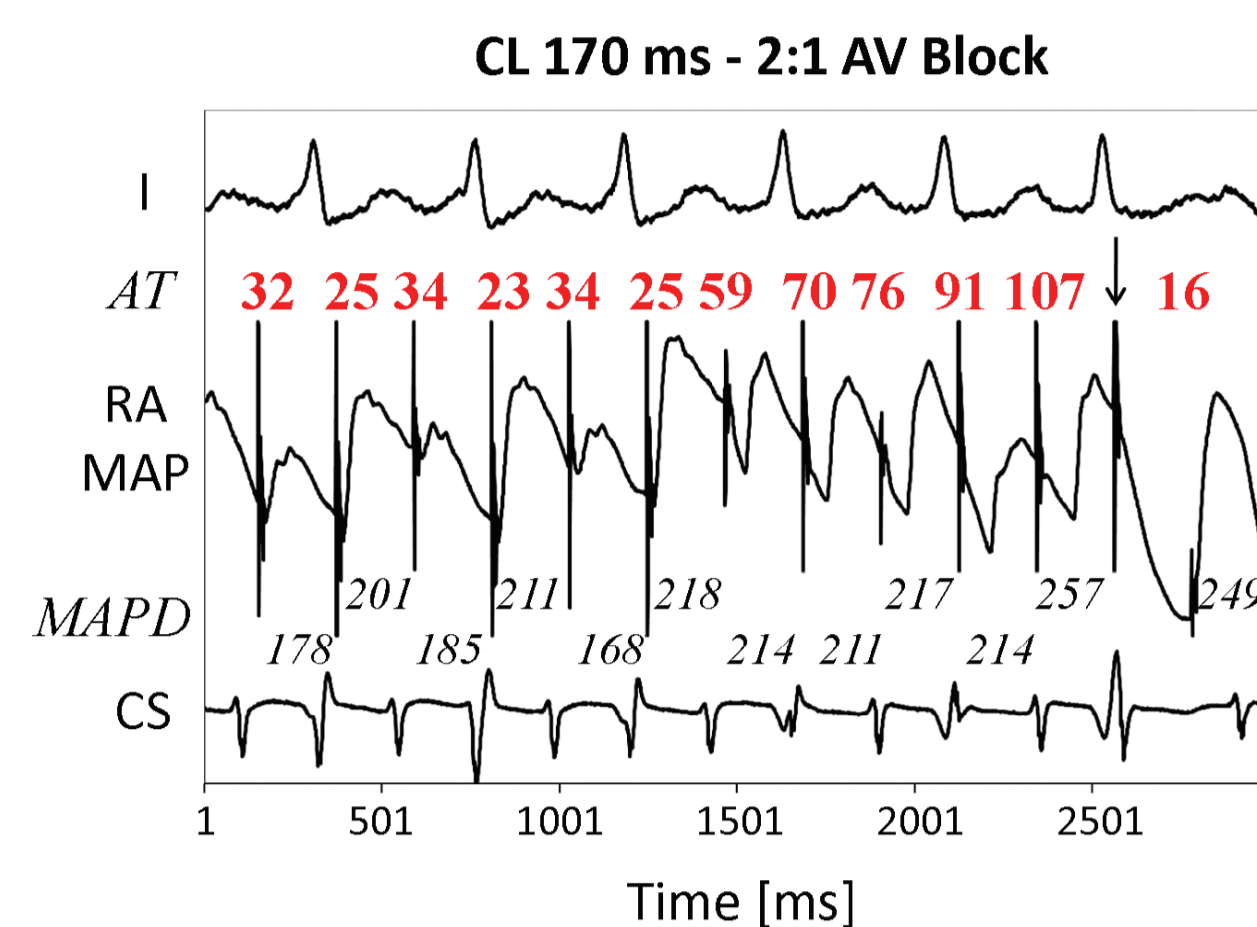
# Decreased Excitability as A Protective Mechanism Against Repolarization Alternans-Induced Atrial Reentry

## Introduction

It has been well established that repolarization alternans (Re-ALT), a beat-to-beat alternation of action potential duration, is a mechanism facilitating dispersion of repolarization, wavebreaks and reentry (Pastore et al., Circ 99).

We recently observed in human left atrium (Fig 1) periods of intermittent 1:1 and 2:1 atrial capture preceded by atrial Re-ALT and decreased excitability (i.e. prolongation of activation time, AT) during rapid pacing.

This observation suggests that decreased excitability may play a protective role against rapid pacing-induced Re-ALT and atrial reentry.



**Figure 1. Intermittent left atrial capture.** ECG (top), monophasic action potential (middle) and coronary sinus EGM (bottom) in a patient referred for pulmonary vein isolation (Courtesy of S. Narayan, UCLA, San Diego, CA).

## Hypothesis

We hypothesized that decreased excitability plays a protective role against Re-ALT induced arrhythmias by facilitating periods of intermittent capture during tachycardia.

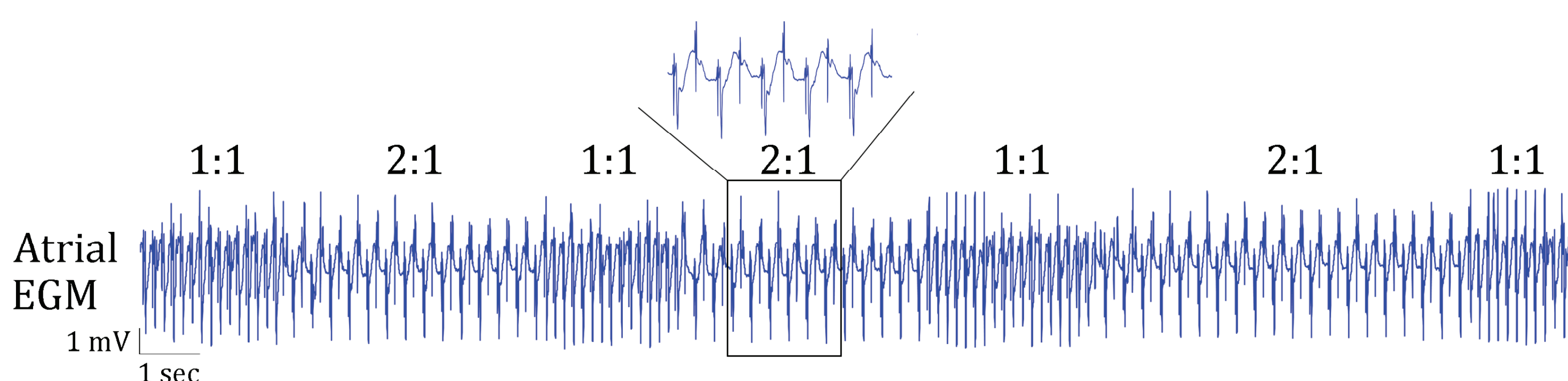
## Methods

- Two pacemakers (PM), each with a lead screwed into the right atrium, were implanted in 13 sheep:
  - 1<sup>st</sup> PM: recording of single broadband (800 Hz, 0.4 Hz high pass filter) unipolar atrial electrogram (EGM).
  - 2<sup>nd</sup> PM for delivery of customized electrophysiology protocols including atrial pacing for 400 beats ( $S_1S_1$ ) starting at a cycle length (CL) of 400 ms with 10 ms decrement until loss of 1:1 atrial capture.
- Parameters analyzed from EGM until the 1<sup>st</sup> beat of 2:1 atrial capture:
  - Activation time (AT) - time interval from the pacemaker stimulus to the atrial R peak
  - Activation recovery interval (ARI) - time interval from the atrial R-wave peak to the apex of the T-wave
  - Re-ALT ( $\Delta Ta$ ) - beat-to-beat differences in atrial T-wave apex amplitude

## Results - 1

### 1. Intermittence of atrial capture

Similarly to human findings, intermittent 2:1 atrial capture (Fig 2) was observed in all sheep (n=9) at a mean pacing CL of  $156 \pm 26$  ms, but no periodicity was noticed.

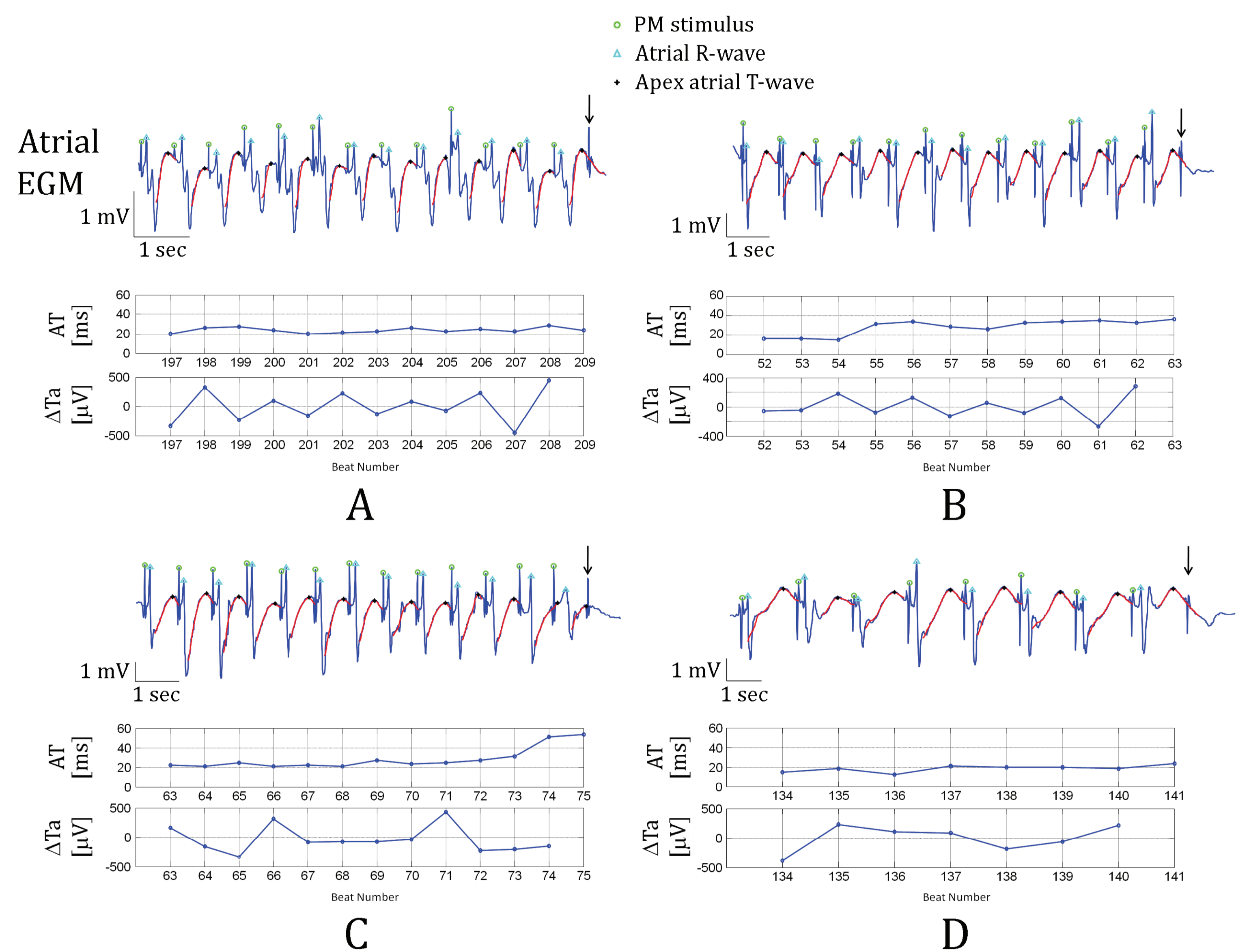


**Figure 2. Intermittency of right atrial capture.** Representative example of atrial unipolar EGM showing intermittent 1:1 and 2:1 atrial capture of variable duration at a pacing CL of 160 ms. The inset shows the EGM during 2:1 capture.

## Results - 2

### 2. Activation and repolarization dynamics prior to 2:1 capture

179 transitions from 1:1 to 2:1 capture were analyzed from 11 sheep. Figure 3 shows representative recordings prior to 2:1 atrial capture exhibiting the four different patterns with their unipolar EGM and corresponding AT and  $\Delta Ta$  time series. Atrial EGMs display 1:1 atrial capture until the first non captured beat (arrow).



**Figure 3. Depolarization and repolarization dynamics prior to 2:1 capture.** Representative recordings exhibiting the four different patterns of AT and  $\Delta Ta$ . From top to bottom of each panel are shown atrial unipolar EGM and its corresponding time series of AT and  $\Delta Ta$ . Atrial EGM shows 1:1 atrial capture until the first beat (black arrow) of 2:1 capture as shown in figures 1 and 2.

**Panel A** shows Re-ALT with a progressive increase in magnitude (maximum  $450 \mu V$ ) and no AT change preceding 2:1 capture. **Panel B** shows the 2<sup>nd</sup> pattern characterized by a similar increase in Re-ALT (maximum  $280 \mu V$ ) but associated to a gradual increase in AT (from 26 to 36 ms). **Panel C** shows the 3<sup>rd</sup> pattern characterized by the lack of any significant Re-ALT. AT, however, markedly increased four beats prior to capture failure (from 28 to 54 ms) in this example. **Panel D** shows the last pattern characterized by the absence of any Re-ALT and AT changes preceding 2:1 capture.

### 3. Summary data

34% of the episodes were of type A and 39% of type B. Importantly, Re-ALT was observed in 73% and AT prolongation in 56% of the episodes. Only 10% showed neither changes in AT nor Re-ALT (type D).

## Conclusions

- Using an ovine model of rapid atrial pacing mimicking pulmonary veins tachycardia, Re-ALT and decreased excitability (as assessed by AT prolongation) are frequently observed before intermittent atrial capture.
- These findings suggest that decreased excitability may play a protective role against pro-arrhythmogenic effect of rapid pacing-induced Re-ALT.
- Because rapid atrial tachycardia slows propagation velocity and promotes fibrillatory conduction, transitions to 2:1 capture may reduce susceptibility to atrial fibrillation.