Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

Atrial Action Potential Heterogeneity Measured by Unipolar Electrograms

Edward J. Vigmond and Vincent Tsoi
Department of Electrical and Computer Engineering
University of Calgary
2500 University Drive NW
Calgary, Alberta, Canada T2N 1N4

Pierre Pagé
University of Montreal
Hôpital Sacré-Coeur Research Center
5400 Gouin Boulevard West
Montreal, PQ, Canada H4J 1C5

***Abstract*— Vagally-induced action potential duration (APD) heterogeneity can lead to the breakdown of atrial flutter into fibrillation. The exact distribution of vagal mediated effects in the atria is unknown, however. This study analyzed canine electrograms in order to determine changes in APD. Electrograms were recorded under control, and left and right vagal nerve stimulation. Simulations in a computer model were first performed in order to determine how local acetylcholine concentrations affect electrograms. Two measures were investigated to assess APD changes. Results indicate that APD is reduced nonuniformly, and contralateral effects were seen.**

I. Introduction

Atrial action potential duration (APD) heterogeneity is recognized as a condition promoting breakdown of flutter into fibrillation. Vagal innervation leads to spatially nonuniformity in APD due to both nonuniform innervation, and differences in acetylcholine (ACh) channel distribution. While modeling studies have demonstrated how nonuniform [ACh] can lead to atrial fibrillation[1], the exact distribution remains unknown.

Electrograms record extracellular potentials and can reliably measure activation times. They have the advantage of high temporal resolution without toxic side effects. Using them to determine APD has been performed for ventricles[2] although their suitability for quantifying the same in atria has not fully addressed[3]. Atrial myocytes can exhibit action potentials which vary considerably in morphology, ranging from a clear spike-and-dome to triangular. Thus, repolarization may not be abrupt and confound interpretation.

This study analyzed atrial unipolar canine electrograms in order to determine vagally-induced APD effects. Two measures were used to assess APD changes, one based on the end of the Ta wave, and the other based on the integral of the Ta wave. A computer atrial model was first used to determine ACh effects on these metrics by using known ACh distributions. The recorded electrograms were then examined based on computer results.

II. Methods

A. Experimental Recordings

Four plaque comprising 192 electrodes were sewn to the epicardial surface of the canine atria (see Fig. 1). Unipolar electrograms were recorded at 1 kHz with the right atrial appendage being paced. Each data set contained three sequences of data: a control, a left and a right vagal stimulation sequences. The left/right vagal stimulation sequences were recorded during stimulation of the left/right cervical vagosympathetic complexes for 1.5 ms at 15 Hz with a current of 1-2 mA. No vagal stimulation was applied during control.

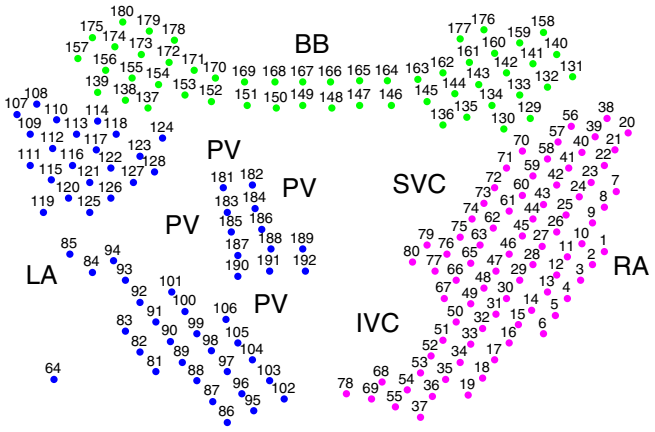

Fig. 1. Electrode plaques placed around the Pulmonary Veins (PV) in the left atrium (LA), across Bachmann's Bundle (BB), and the Inferior and Superior Vena Cava (IVC and SVC) in the Right Atrium (RA).

B. Computer Model

A morphologically realistic computer model of the atria was constructed based on the interconnected cable model[1]. To reconstruct electrograms from the monodomain simulation, the following equation was employed:

$$\Phi_e(\mathbf{r},t) = \frac{1}{4\pi\sigma_e}\int \frac{I_m(\mathbf{r}',t)}{|\mathbf{r}-\mathbf{r}'|}dr' \qquad (1)$$

where Φ_e is the extracellular potential, $\mathbf{r}$ is the electrode location, $\mathbf{r}'$ is the source location, I_m is the transmembrane current, and σ_e is the extracellular conductivity. The calculation was computed every 0.5 ms for electrodes uniformly allocated on the endocardial surfaces of the LA and RA. Due to the discrete nature and sparsity of connections between cables, a spatial filter was applied to remove noise contributed by the saltatory nature of AP conduction between cables.

Membrane dynamics were modeled using the Ramirez-Courtemanche-Nattel model of the canine atrial action potential with an ACh-dependent potassium channel added[1]. Discrete islands of ACh release were introduced into the model to mimic vagal ACh release.

C. Data Analysis

Two metrics were used to assess the changes in APD: the area under the Ta wave, TWA, and the interval between depolarization and the end of the Ta wave, $\overline{APD}$. Depolarization was defined by the first positive peak in the electrogram. The end of the Ta wave was defined as return to rest from the peak. If the Ta wave was positive, the potential had to recover to 30% of the peak, while for a negative wave, 70% recovery was used, based on empirical observations.

III. Results

Experimental electrograms displayed a great variety in Ta wave over the atria, even under control (see Fig. 2). The polarity of the wave could be positive or negative, and varied considerably in relative amplitude compared to the depolarization wave.

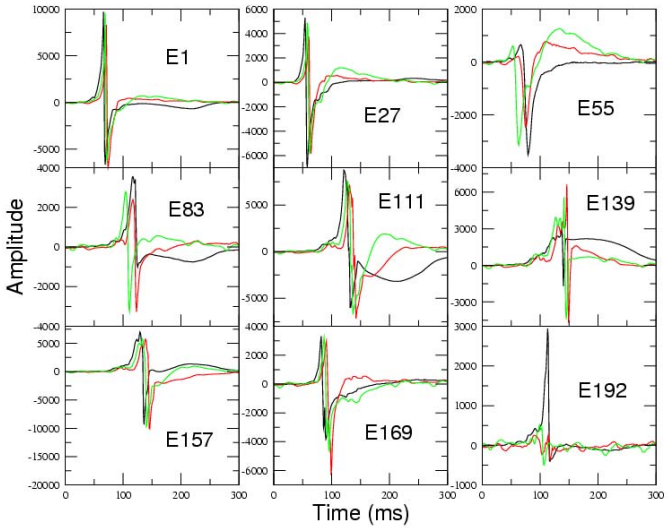

Fig. 2. Electrograms recorded at various electrodes (indicated in graphs) under control (black), left vagal stimulation (red) and right vagal stimulation (green).

The difference between control and left vagal stimulation is shown in Fig. 3. Note how both sides are the atria are affected, and how the changes are nonuniform.

IV. Discussion

Both metrics, TWA and $\overline{APD}$, changed under vagal stimulation. There was a certain degree of similarity between the two methods, with similar areas being identified as regions of great or little ACh-induced APD change. There were also large regions where the two methods disagreed. The $\overline{APD}$ was reported to reliably detect relative changes in APD, although not absolute APD[3]. However, it is still unknown how accurate this measure is when the action potential morphology changes. The TWA assumed islands of constant ACh release.

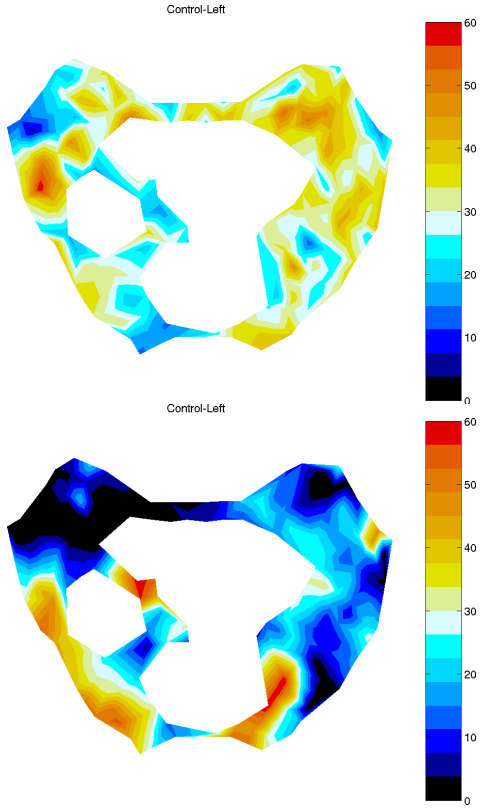

Fig. 3. Average effect over all dogs of left vagal stimulation measured by TWA (top) and $\overline{APD}$ (bottom).

Again, the actual [ACh] distribution is unknown. By looking at the Ta wave, one can determine if an electrode is above an island of ACh release, or just outside of one. Determining the atrial APD distribution is further complicated by pre-existing gradients. In the computer model, there were no visible Ta waves without ACh, which was not the case in the experimental control.

In conclusion, the electrograms confirm that atrial APD changes considerably under vagal stimulation. Contralateral effects are evident although ipsolatersal effects are predominant. The $\overline{APD}$ measure suggests an intrinsiclly shorter APD in the left atrium.

Acknowledgment

This work was supported by the Natural Sciences and Engineering Research Council of Canada and MITACS.

References

[1] E. J. Vigmond, V. Tsoi, S. Kuo, H. Arevalo, J. Kneller, S. Nattel, and N. Trayanova, "The effect of vagally induced dispersion of action potential duration on atrial arrhythmogenesis." *Heart Rhythm*, vol. 1, no. 3, pp. 334–44, 2004.

[2] C. K. Millar, F. A. Kralios, and R. L. Lux, "Correlation between refractory periods and activation-recovery intervals from electrograms: effects of rate and adrenergic interventions." *Circulation*, vol. 72, no. 6, pp. 1372–9, 1985.

[3] M. Halbach, U. Egert, J. Hescheler, and K. Banach, "Estimation of action potential changes from field potential recordings in multicellular mouse cardiac myocyte cultures." *Cell Physiol Biochem*, vol. 13, no. 5, pp. 271–84, 2003.