Entrainment Response in a Model of Reentrant Tachycardia

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Abstract

Studies suggest that entrainment response (ER) of reentrant tachycardia to overdrive pacing can be estimated using signals from sites other than the paced site. A cellular automaton model of reentry was developed to validate a formula for estimation of ER using remote sites against the difference between the post-pacing interval (PPI) and tachycardia cycle length determined solely from paced site signals. The model was also used to study resetting of tachycardia phase by single premature paced stimuli, and the general behavior and features of entrained surfaces.

From simulation results, ER at the paced site was accurately estimated from >99.8% of 20,764 remote sites during pacing at 24 sites and 3 paced cycle lengths. Modeling of the ER predicts complex perturbations of the activation sequence in the neighborhood of the overdrive pacing site. For single premature stimuli that penetrated the tachycardia circuit, phase reset of the tachycardia was linearly related to distance between the central obstacle and the paced site.

1. Introduction

Cardiac electrophysiologists measure the entrainment response (ER) of reentrant tachycardia to overdrive pacing in order to help locate arrhythmia circuits during catheter ablation procedures. Overdrive pacing continuously resets the phase of the tachycardia circuit [1]. The time delay measured at the pacing electrode between the last paced beat and the first following tachycardia beat is called the postpacing interval (PPI_P). It is a measure of the distortion of the tachycardia activation pattern needed to reset the tachycardia, and it can be used as an index of the proximity of the pacing site to the tachycardia circuit. The ER is typically quantified as PPI_P minus the tachycardia cycle length (TCL).

Information related to PPI_P is also available from locations spatially [2,3] and temporally [4] distant from the pacing site. It has been proposed that entrainment response can be estimated using signals measured from these remote sites [3]. Specifically, ER can be estimated as pacing delay (PD) minus tachycardia delay (TD),

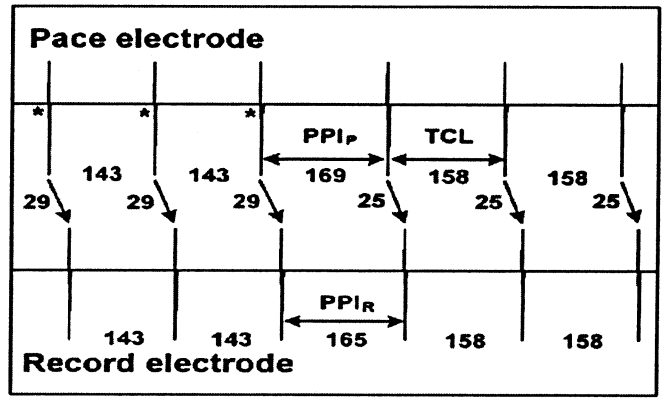

Fig. 1. Electrograms synthesized from activation times at the pacing site (top) and a remote recording site (bottom) during entrainment pacing. Paced beats are marked with asterisks. Inter-beat intervals are labeled in milliseconds. Diagonal arrows associate pacing site beats with corresponding beats at the remote site, and the time delay between them (ms) appears to the left of the arrows. Substituting PD (29ms), TD (25ms), PPI_R (165ms), and TCL (158ms) into (1) gives 11ms, which is equal to PPI_P - TCL.

where PD is the time between a pacing stimulus at the pacing site and its arrival at the remote electrode, and TD is the time between a tachycardia beat at the pacing site and the next tachycardia beat arriving at the remote electrode. This difference provides an accurate estimate of the standard ER measure (PPI_P - TCL) in those parts of the tachycardia circuit where the remote site is activated orthodromically (in the same direction and pattern as the native tachycardia) during pacing. However, in regions not activated orthodromically during pacing [3,5,6], the ER estimate must be adjusted by adding the difference between the PPI at the remote site (PPI_R) and TCL (see [3]):

$$ER = (PD - TD) + (PPI_R - TCL) \quad (1)$$

See example in Fig. 1.

We developed a numerical, cellular automaton model of reentrant tachycardia to test (1) and to explore the

distortion of activation surfaces containing a reentrant circuit caused by entrainment pacing at varied prematurities and pacing sites. Rules used to compute ER were based only on measurable activation times, and not from *a priori* knowledge of the activation sequence determined from the model. Thus, this method could be used to estimate entrainment response from intracardiac catheters in a clinical setting.

2. Methods

2.1. Cellular automaton model

For the purposes of this study, a computer model of a ~6 x 6 cm patch of cardiac tissue was developed using the Matlab programming language to simulate the basic macroscopic properties of activation propagation in cardiac muscle. Tissue was represented as a 2 dimensional rectangular array of elements each assigned to one of four states: active, excitable, refractory (temporarily inexcitable), or fixed inexcitable. The array contains a circular, fixed inexcitable region and several narrow corridors for conduction. See Table 1 for model parameters and subsequent figures for geometry. Activated elements influenced neighboring elements according to an inverse square relation. Excitable elements became active at the next time step if the sum of the influence of elements in their vicinities exceeded a threshold. After activation, an element was refractory for a fixed period.

Table 1. Model parameters

Array dimensions	160 x 160 elements
Element size	0.4 mm/element
Conduction velocity	400 mm/second
Tachycardia cycle length	158 milliseconds
Refractory period	120 milliseconds
Time step	1 millisecond

Circus movement was initiated from preset initializing conditions and would continue indefinitely as a stable pattern of activation of the model. The model could be paced to assess ER by activating cells in the transiently excitable region between the trailing edge of refractoriness and the approaching activation wave front. A record of activation times of each element in the array was compiled during simulations so that each element in the array could be treated as a remote electrode.

2.2. Model response to entrainment

In stable reentry, simulations of entrainment pacing were run for three pacing cycle lengths (133, 143, and 152 ms) at each of 24 pacing sites distributed throughout the array. Pacing stimuli were continued until a stable paced rhythm was achieved (determined by repetition of the pattern of activated elements). Pacing was then terminated and the simulation continued until stable tachycardia resumed. Sets of activation times were acquired for all potentially excitable elements in the array.

For a given simulation, activation times of each potentially excitable element were analyzed to calculate estimated ER at each site, and this estimate was compared to the standard ER determined at the pacing site, PPI_P - TCL.

The array of activation times for a given simulation was also used to map the perturbation of the tachycardia activation pattern by overdrive pacing. Isochronal maps were generated for periods of both stable pacing and stable tachycardia, and the normalized dot products (Fig. 2a) and activation time differences (PPI_R – TCL, see (1) and Fig. 2b) of the two maps were computed. Regions of the array were classified by activation type:

Activation type	Dot product		PPI_R – TCL
Orthodromic	> 0.95	*and*	≈ 0 ms
Antidromic	< 0	*and*	Any
Pseudoorthodromic	≥ 0	*and*	≠ 0 ms

By these definitions, the antidromic area was that where the difference between wavefront angle during pacing and tachycardia was >90°. The orthodromic area was the intersection of the set of elements with dot product greater than 0.95 with the set of elements where

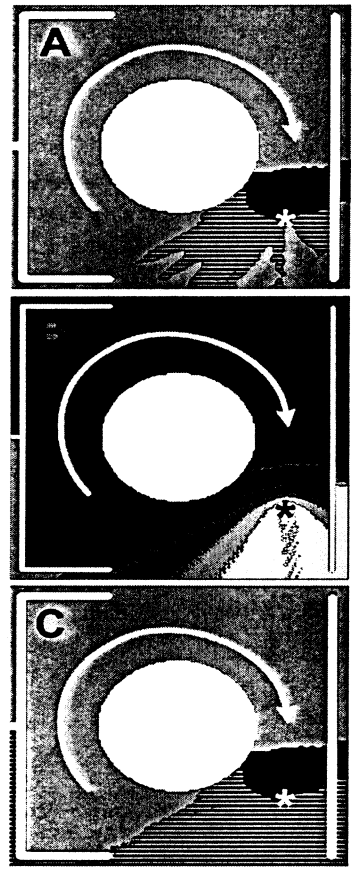

Fig. 2. Example maps of calculated values from entrainment model. Pacing site indicated by stars, direction of tachycardia circuit by white arrow.

(a) **Dot product** of isochronal maps generated during stable pacing and stable tachycardia. Black: dot product < 0, hatched: dot product 0 – 0.95, gray: dot product > 0.95.
(b) **PPI_R – TCL.** In this example, grayscale extends from –12 ms (black, at edge of wavefront collision) to +12 ms (white), with most of surface 0 ms (dk. gray)
(c) **Classification** of paced activation as antidromic (black), orthodromic (dark gray), or pseudoorthodromic (hatched) – see text.

the numerical adjustment for (PPI_R – TCL) was ~0 ms. The pseudo-orthodromic area consisted of those remaining elements not classified as either antidromic or orthodromic. A map showing classification of the same simulation results into these three regions appears in Fig. 2c. The percentage of the surface in each classification was correlated to prematurity and to distance from pacing site to central obstacle.

2.3. Model response to single beat reset

The model was also used to assess the response to single beat reset, the time by which a single premature stimulus at a given site will advance the phase of the tachycardia circuit. The tachycardia was considered to be advanced by the premature stimulus if the phase of the entire circuit following the stimulus was advanced in relation to that expected in the absence of the premature stimulus. Again, the model was run until stable tachycardia was reached, after which a single pacing stimulus was applied at 100 randomly chosen pacing sites and at 2 prematurities (20 and 30 ms). Resulting activation patterns were analyzed to determine which pacing sites advanced tachycardia and by how much, and the relation of tachycardia phase shift to prematurity and distance from pacing site to central obstacle were examined.

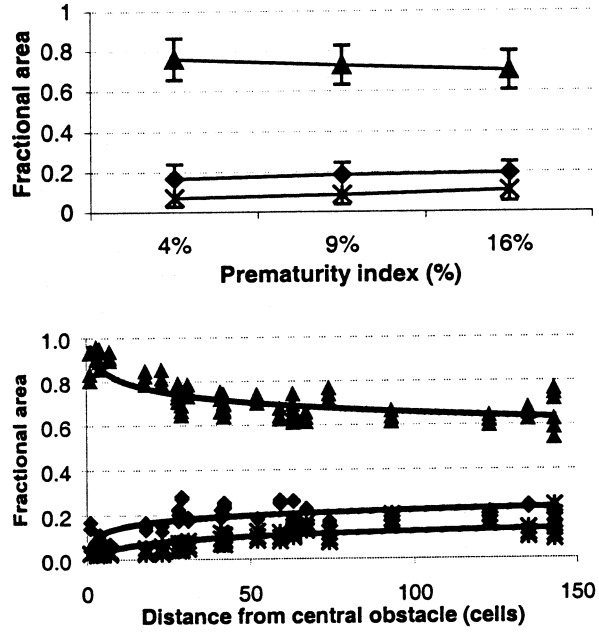

Fig. 3. Fractional areas of model categorized as orthodromic (▲), pseudoorthodromic (♦) and antidromic (✳) during pacing (top) for each of the pacing prematurities, and (bottom) as a function of distance from the pacing site to the nearest point on the central obstacle.

3. Results

3.1. Model response to entrainment

For entrainment simulations at 24 pacing sites at each of the three paced cycle lengths (133, 143, and 152ms), ER estimates based on remote sites were within one millisecond of PPI_P - TCL for more than 99.8% of 20,763 remote sites. The ~40 sites that failed to meet this criterion were apparently accounted for by temporal and spatial granularities of the model. Thus, the relation proposed in (1) appeared to be uniformly true in this model of reentrant tachycardia, inclusive of measurements and paced sites located in blind-ended tracts distant from the central obstacle.

Relative areas of regions of orthodromic and antidromic activation during pacing are plotted for each of the pacing prematurities in Fig. 3. Also in Fig. 3 is a plot of the relative areas of orthodromic, antidromic, and pseudoorthodromic regions versus the functional distance from the pacing site to the nearest point on the central obstacle. As expected, increasing prematurity and increasing distance of the pacing site from the central obstacle increased the area of myocardium that was "nonorthodromically" activated during overdrive pacing. Qualitative examination of maps exemplified by Fig. 2 also reveals that fixed, continuous resetting of the activation pattern during overdrive pacing was only possible after the development of a continuous band of antidromic activation that extended from the central obstacle across the entire width of the tachycardia circuit.

3.2. Model response to single beat reset

For simulations in which a single premature stimulus was delivered, the time by which the premature beat advanced the next beat at each model element was calculated. A map of these times is plotted in Fig. 4 for a 20ms premature stimulus. It is similar to Fig. 2b, but in this case the antidromically-activated area did not reach the central obstacle, and no resetting of the tachycardia occurred.

In Fig. 5, the time by which a 20ms premature stimulus advanced the entire tachycardia circuit is plotted

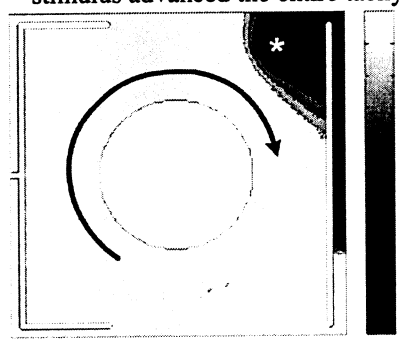

Fig. 4. Time by which each array element is advanced by a 20ms premature stimulus at the site marked with a star. Lt gray = 0 ms, black = 20 ms. Black arrow – direction of circuit

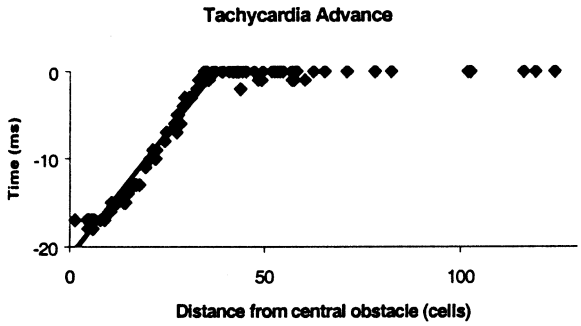

Fig. 5. Time by which a 20ms premature stimulus advanced the tachycardia as a function of distance from pacing site to nearest point on the central obstacle at each of the 100 pacing sites. The solid line represents the best linear fit to the advance times corresponding to sites within 35 cells of the central obstacle.

versus distance from pacing site to the nearest point on the tachycardia circuit for each of the 100 pacing sites. Only those pacing sites close enough to the central obstacle to cause antidromic activation on the tachycardia circuit caused a change in the phase of the circuit. Within this limit, advance of the tachycardia increases linearly with decreasing distance to the obstacle. This result suggests that the entrainment response could be estimated simply and accurately by proper analysis of tachycardia phase after placement of single premature beats.

4. Discussion

Several clinical studies have examined the region within a reentrant tachycardia circuit that conducts antidromically (or, more generally, nonorthodromically) during entrainment pacing [2,3,6], but theoretical determination of the size and shape of this region has not been presented. Our model of reentrant tachycardia provides a tool to delineate the manner by which overdrive pacing of a reentrant circuit on an excitable surface distorts the activation pattern of the surface. Examination of this distortion allows several significant conclusions.

First, by quantifying the distortion of the tachycardia pattern during entrainment pacing, the method for estimating ER from remote sites is numerically validated. This suggests that it might be possible to develop a system to automatically and rapidly compute ER from remote recording sites, avoiding difficulties associated with making signal measurements close to large amplitude pacing stimuli.

Second, common features of the distortion patterns can give insight into mechanisms of entrainment on a surface. Simulations illustrated that the area of perturbed activation patterns necessarily grows during entrainment pacing until the antidromic region invades circuit and extends across entire span of advancing wavefront.

Results of single beat reset simulations show that the ability of a single beat to advance the phase of a tachycardia circuit may be used as a measure of proximity of the pacing site to the central obstacle. During tachycardia, activation propagates radially from the circuit surrounding the central obstacle, and single premature beats that are not sufficiently early and/or close to the central obstacle do not propagate a sufficient distance antidromically to enter and reset the circuit (see above, and Fig. 4). This suggests the possible use of single beat reset of tachycardia phase as a technique for determining proximity to the tachycardia circuit that involves much less time and calculation than measuring entrainment response.

The limitations of this study are those inherent to all modeling studies. The model used in this case was chosen for simplicity, and no efforts were made to model such phenomena as anisotropy, heterogeneity of conduction and refractoriness, and other aspects of cardiac electrophysiology, because they were not deemed necessary in this application. Validation of the predictions and observations made will clearly require additional study in experimental and clinical models.

References

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