The precise timing of tachycardia entrainment is determined by the postpacing interval, the tachycardia cycle length, and the pacing rate: Theoretical insights and practical applications

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BACKGROUND Previous observations have reported that the number of pacing stimuli required to entrain a tachycardia varies on the basis of arrhythmia type and location, but a quantitative formulation of the number needed to entrain (NNE) that unifies these observations has not been characterized.

OBJECTIVE We sought to investigate the relationship between the number of pacing stimulations, the tachycardia cycle length (TCL), the overdrive pacing cycle length (PCL), and the postpacing interval (PPI) on the timing of tachycardia entrainment.

METHODS First, we detailed a mathematical derivation unifying electrophysiological parameters with empirical confirmation in 2 patients undergoing catheter ablation of typical atrial flutter. Second, we validated our formula in 44 patients who underwent various catheter ablation procedures. For accuracy, we corrected for rate-related changes in conduction velocity.

RESULTS We derived the equations NNE = I(PPI − TCL)/(TCL − PCL)I + 1 and Tachycardia advancement = (NNE − 1) × (TCL − PCL) − (PPI − TCL), which state that the NNE and the amount of tachycardia advancement on the first resetting stimulation are determined using regularly measured intracardiac parameters. In the retrospective cohort, the observed PPI − TCL highly correlated with the predicted PPI − TCL (mean difference 5.8 ms; $r = 0.97$; $P < .001$), calculated as PPI − TCL = (NNE − 1) × (TCL − PCL) − tachycardia advancement.

CONCLUSION The number of pacing stimulations required to entrain a reentrant tachycardia is predictable at any PCL after correcting for cycle length–dependent changes in conduction velocity. This relationship unifies established empirically derived diagnostic and mapping criteria for supraventricular tachycardia and ventricular tachycardia. This relationship may help elucidate when antitachycardia pacing episodes are ineffective or proarrhythmic and could potentially serve as a theoretical basis to customize antitachycardia pacing settings for improved safety and effectiveness.

KEYWORDS Arrhythmia; Right ventricular overdrive pacing; Entrainment; Catheter ablation; Antitachycardia pacing; Number needed to entrain

ABBREVIATIONS **ATP** = antitachycardia pacing; **AV** = atrioventricular; **AVNRT** = atrioventricular nodal reentrant tachycardia; **AVRT** = atrioventricular reentrant tachycardia; **NNE** = number needed to entrain; **PCL** = pacing cycle length; **PPI** = postpacing interval; **RV** = right ventricular; **SVT** = supraventricular tachycardia; **TCL** = tachycardia cycle length; **VT** = ventricular tachycardia

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Introduction

As elegantly described by Waldo et al in 1977,[1] persistent overdrive pacing at a rate faster than that of the native tachycardia will first advance a reentrant tachycardia (tachycardia reset) followed by continuous resetting (tachycardia entrainment), which accelerates the tachycardia to the pacing rate. Since the initial description, various aspects of overdrive pacing have been described in order to identify critical components of the reentrant circuit, elucidate accessory pathways, and rule out automatic rhythms.[2–11] Overdrive

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pacing algorithms have also been developed and incorporated into implantable cardiac devices to painlessly terminate malignant arrhythmias.[12]

In order to accurately interpret entrainment maneuvers and/or to successfully pace-terminate a tachycardia, the number of pacing stimulations must be sufficient to reach the reentrant circuit. The initial paced wavefronts may not reach the tachycardia circuit, since these wavefronts often collide with wavefronts exiting the circuit. Although the number of pacing stimulations required to entrain a tachycardia is dependent on the pacing rate and the distance to the reentrant circuit,[13,14] a quantitative relationship that determines the precise number of pacing stimulations needed to entrain has not been described. We sought to mathematically describe the timing of tachycardia entrainment using regularly measured intracardiac parameters.

Methods

Study population

This study consisted of 2 parts. The first part is a mathematical derivation to express the number needed to entrain (NNE) as a function of the tachycardia cycle length (TCL), the pacing cycle length (PCL), and the postpacing interval (PPI). For the "proof of concept," we analyzed the intracardiac electrogram intervals and characterized the mathematical function in 2 patients undergoing ablation of typical (counterclockwise, cavotricuspid isthmus dependent) atrial flutter. We used this population because the reentrant circuit of typical atrial flutter is anatomically well defined and less susceptible to decremental conduction.

In the second part, we empirically validated our mathematical formula by retrospectively examining the intracardiac electrograms of consecutive 44 patients who had clinical electrophysiology studies and ablation of atrioventricular reentrant tachycardia (AVRT), atrioventricular nodal reentrant tachycardia (AVNRT), and monomorphic ventricular tachycardia (VT) at Stanford Hospital & Clinics from March 2012 to March 2015. All intracardiac measurements were performed by a single interpreter (D.W.K.). A second interpreter (M.P.T.) adjudicated caliper position for measurements when the timing of local activation was difficult to ascertain. The study was approved by the local institutional review board with a waiver of consent.

Overdrive pacing maneuvers

In patients with atrial flutter (the first part of the study), overdrive pacing was performed from within the coronary sinus by a standard multipolar electrode catheter. In the first patient, 4 overdrive pacing maneuvers were performed from the same location with an increasing number of extrastimuli (all at the same pacing rate). In the second patient, entrainment was obtained from within the coronary sinus at 3 progressively faster pacing rates.

In the second part of the study, we reviewed the intracardiac recordings from various catheter ablation procedures. Each case was reviewed in entirety, and the first entrainment maneuver meeting study criteria were included. Only cases where a sustained tachycardia was induced and the entrainment maneuver did not terminate the tachycardia were included. The PCL was required to be within 30 ms of the TCL. Cases demonstrating spontaneous beat-to-beat variability in the TCL of greater than 30 ms were excluded from the study.

Overdrive pacing was typically performed from the right ventricular (RV) apex. For VT cases, entrainment maneuvers from the ablation catheter, usually in the left ventricle, were included. The PPI was measured from the last pacing stimulus to the bipolar electrogram in the first return beat on the pacing catheter. The TCL was measured immediately before overdrive pacing ensued. During programmed overdrive pacing, the prematurity of the first captured beat was measured and used to calculate the total pacing prematurity. Tachycardia reset was determined when overdrive pacing first advanced the tachycardia circuit, as evidenced by a premature sensed event. Tachycardia entrainment was determined when overdrive pacing first advanced the tachycardia to the PCL (which occurred after the first reset stimulation). In AVRT and AVNRT cases, a high right atrial catheter was used. For cases involving VT, the pacing catheter and the reference/sensing catheter were in opposite chambers (such as an ablation catheter in the left ventricle and a bipolar pacing catheter in the RV apex).

We determined the number of pacing stimulations needed to entrain the tachycardia and the amount of tachycardia advancement on the first pacing stimulation that reset the tachycardia. In order to correct for atrioventricular (AV) nodal decremental conduction, we calculated the corrected PPI by subtracting AH prolongation associated with the shorter PCL, as described previously.[4] Bipolar electrograms were filtered between 30 and 500 kHz. For supraventricular tachycardia (SVT), the pacing output was typically twice the diastolic pacing threshold at 20-ms pulse width. For VT, the pacing output was set at minimal outputs to ensure consistent capture. All data were recorded on a digital acquisition system (CardioLab, Prucka Engineering, Inc., Houston, TX).

Statistical analysis

Continuous variables are presented as mean ± standard deviation, and categorical variables are presented as counts and percentages. Analysis of variance between the 3 groups of patients (AVRT, AVNRT, and VT) was evaluated with the 1-way analysis of variance test. The correlation between the observed PPI − TCL and the predicted PPI − TCL (calculated as [(NNE − 1) × (TCL − PCL) − tachycardia advancement]) was examined using a Spearman rank test. *P* values of .05 or less were considered statistically significant. The data were analyzed using SPSS Statistics version 22.0 (SPSS Inc., Chicago, IL).

Results

Part I results: Mathematical reasoning

We hypothesized that overdrive pacing would begin to advance a reentrant tachycardia precisely when the total