Effects of Biventricular Pacing Locations on Anti-Tachycardia Pacing Success in a Patient-Specific Model

Eric N Paccione[1,2,3], Matthias Lange[2], Benjamin A Orkild[1,2,3], Jake A Bergquist [1,2,3], Eugene Kwan[1,2], Bram Hunt[1,2], Derek Dosdall[1,2], Rob S Macleod[1,2,3], Ravi Ranjan[1,2]

[1] University of Utah Department of Biomedical Engineering, Salt Lake City, USA
[2] Cardiovascular Research and Training Institute, Salt Lake City, USA
[3] Scientific Computing and Imaging Institute, Salt Lake City, USA

Abstract

Patients with drug-refractory ventricular tachycardia (VT) often undergo implantation of a cardiac defibrillator (ICD). While life-saving, shock from an ICD can be traumatic. To combat the need for defibrillation, ICDs come equipped with low-energy pacing protocols. These anti-tachycardia pacing (ATP) methods are conventionally delivered from a lead inserted at the apex of the right ventricle (RV) with limited success. Recent studies have shown the promise of biventricular leads placed in the left ventricle (LV) for ATP delivery. This study tested the hypothesis that stimulating ATP from multiple biventricular locations will improve termination rates in a patient-specific computational model. VT was first induced in the model, followed by ATP delivery from 1-4 biventricular stimulus sites. We found that combining stimulation sites does not alter termination success so long as a critical stimulus site is included. Combining the RV stimulus site with any combination of LV sites did not affect ATP success except for one case. Including the RV site may allow biventricular ATP to be a robust approach across different scar distributions without affecting the efficacy of other stimulation sites. Combining sites may increase the likelihood of including a critical stimulus site when such information cannot be ascertained.

1. Introduction

Ventricular tachycardia (VT) affects over 300,000 Americans annually and is the leading cause of sudden cardiac death [1]. VT is characterized by episodes of rapid activation in the ventricular myocardium, resulting in decreased quality of life and increased risk of complications. Patients with drug-refractory VT often undergo implantation of a cardiac defibrillator (ICD), which can automatically deliver shocks during a VT episode. When shocks occur, a high burst of energy is delivered to disrupt arrhythmia and return the patient to sinus rhythm. While life-saving, shock from an ICD can be traumatic, and recipients often experience an increased incidence of depression and anxiety [2]. To combat the need for defibrillation, ICDs come equipped with low-energy pacing protocols. These anti-tachycardia pacing (ATP) methods act as a first line of defense to pace the heart out of VT without the need for a full ICD shock. Conventional ATP is delivered from a single lead inserted at the apex of the right ventricle (RV), but its limited success has inspired alternate pacing locations [3–5].

Previous studies have investigated biventricular pacing (BiVP), which differs from traditional RV pacing in that both the right ventricular apex and the left ventricular (LV) free wall are paced. Patients with heart failure or LV dysfunction may have BiVP leads implanted to help synchronize ventricular contractions [6]. This patient population has been shown to have a high risk of developing ventricular arrhythmias, yet, few studies have investigated using BiVP leads to eliminate VT episodes [3, 7, 8]. Clinically, BiVP as an ATP delivery method has been shown only to benefit patients with ischemic heart disease and with VT cycle lengths (CL) less than 320 ms, which has limited BiVP as a standard ATP delivery method [4]. Computational studies have shown that ATP success depends on the distance from the pacing site to the scar-dependent VT exit site, the VT CL, and stimulus positions on the LV free wall [9]. These studies have provided support for the LV freewall as viable ATP delivery sites in a broader range of VT morphologies. Neither study demonstrated efficacy in human heart models nor investigated simultaneous pacing protocols from combined stimulus sites. Furthermore, ICD implantation often lacks knowledge of scar distribution or VT exit sites. Therefore, implantation of a lead at the critical site for VT termination would be difficult without information from a computational model or invasive mapping procedures. Thus, a generalizable and clinically feasible approach to biventricular ICD ATP delivery is needed.

In this study, we tested the hypothesis that simultaneously stimulating ATP from multiple BiVP points may improve termination rates over the conventional RV apex approach by increasing the likelihood of stimulating from a site critical to VT termination. We examined the effect of clinically relevant biventricular pacing locations on the ability to deliver ATP and terminate VT in a patient-specific computational model of the ventricles.

2. Methods

Model Generation: Late-Gadolinium Enhanced Magnetic Resonance Images (LGE-MRI) were collected from a single patient at the University of Utah health systems and used to segment both ventricles. These ventricular wall segmentations were used to generate a patient-specific volumetric mesh using TetGen with average edge length of 0.928 mm [10]. LGE-MRI signal intensity (SI) greater than 70% of the maximum was defined as scar, while SI greater than 40% of maximum was defined as fibrotic regions.[11, 12] LV and RV blood pool segmentations were used to identify the endocardial surface. A rule-based algorithm was used to assign cardiac fiber angle throughout the myocardium [13].

Electrophysiological Properties: The open-source electrophysiology (EP) modeling software OpenCARP was used for all simulations [14]. The monodomain formulation was used to link individual cellular models defined throughout the myocardium and solve the resulting reaction-diffusion equations. The ion exchange at the cell membrane was modeled according to Ten Tusscher and Panfilov (TTP) [15]. Tissue-slab simulations of the TTP model were used to tune transverse and longitudinal conductivities for each region (Table 1) with healthy cells set to a value of 0.8 m/s in the longitudinal direction while fibrotic cells conducted at 0.4 m/s longitudinally. Transverse conduction velocity were set at half of the longitudinal for each region, respectively. Healthy regions were assigned anisotropic conductivities, while fibrotic regions were more isotropic to replicate the electrophysiology of diseased myocardium. Epicardial, endocardial, and midmyocardial regions were defined as healthy, with no changes to the membrane kinetics of their respective regions as defined in the TTP model. Fibrotic regions were assigned modified membrane kinetics based on data from previous literature, resulting in a longer action potential duration and decreased excitability compared to normal myocardium (Table 2) [16]. Scar regions were defined as having zero conductivity.

Simulation Protocol: The patient-specific model underwent VT induction protocols according to clinical conventions, stimulated at four induction sites: RV apex, LV apex, LV free wall, and ventricular septum. At each stimulus site, a train of eight S1 pulses was independently applied at a pacing interval of 600 ms. Following the S1 train, the simulation was continued with a single S2 pulse. The simulation was repeated for several S2 pacing intervals ranging from 280 ms (the refractory period of the cell model) to 350 ms. S2 simulations that initiated a VT circuit continued until a total simulation time of 10 seconds. If electrical activity persisted at 10 seconds, the VT circuit was visualized and confirmed to have stable reentry. Local activation time maps of the VT were generated and used to identify VT cycle length (CL) (Figure 2). The resultant simulated VT reentry site and cycle length matched clinical recordings of this patient as determined by a trained electrophysiologist.

Table 1. Region Conductivities.

Region	$CV(m/s)$	$G_L(S/m)$	$G_T(S/m)$
Healthy	0.8	0.1274	0.0669
Border Zone	0.4	0.033	0.035
Scar	0.0	0.0	0.0

Table 2. Membrane Kinetic Changes in Border Zone.

Ion Channel	Percent of Normal Conductivity
Na	38
Ca_L	31
Kr	30
Ks	20

A single site at the RV apex and three sites along the lateral LV free wall in the apicobasal direction were defined as possible ATP delivery sites, representing feasible BiVP ICD lead implantation sites (Figure 1). Of these sites, 1 to 4 were chosen for ATP delivery in subsequent simulations. A single ATP train of 8 pulses at 88% of the VT CL was applied from each ATP site combination. ATP was applied when the ATP stimulus sites were excitable following the first cycle of the clinically-matched VT circuit. The simulation continued for an additional 8 seconds following the onset of ATP. The absence of any active mesh elements ($>$-40mV) at the final simulation time point following ATP delivery determined the successful termination of VT.

3. Results

Termination of VT varied depending on the stimulus sites utilized for delivery; these results are summarized in Table 4.

When the lower LV free wall site was included (LowFW), all ATP site combinations resulted in the termination of the VT circuit. When LV LowFW was not a pacing site, only one other site resulted in termination. Without the RV apex stimulation, the upper LV free wall

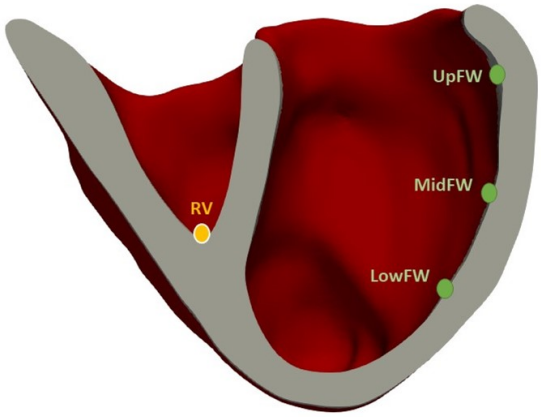

Figure 1. AP cross-section of biventricular model with ATP stimulus site definitions. Red is the mesh surface and gray is the cross-section cut plane. (LowFW: Lower LV Free Wall, MidFW: Mid LV Free Wall, UpFW: Upper LV Free Wall)

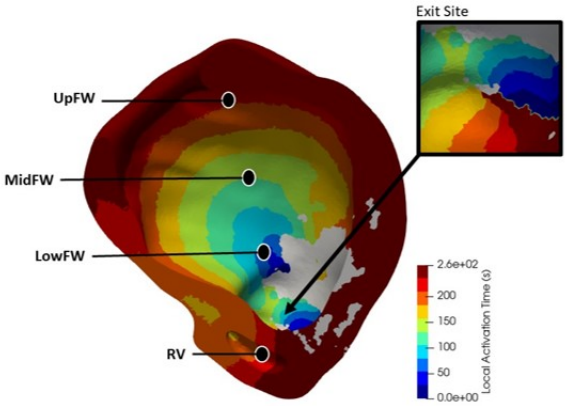

Figure 2. Right lateral cross-section of local activation time map with stimulus site definitions and exit site. Blue represents the earliest sites of activation in the analyzed VT beat. White areas are scar (no activation).

site could terminate the VT. Other pacing locations and combinations on the LV free wall with RV pacing did not change termination outcomes.

4. Discussion and Conclusions

Previous research demonstrated the ability of proximal ATP locations to terminate fast VTs (<320ms) [4]. The most proximal location to our exit site (LowFW, Table 4) successfully terminated VT in all cases where that site was included for ATP pacing. Interestingly, the second most proximal site (RV apex) did not follow this trend. This suggests that the critical distance for a single-point stimulation to terminate VT may be highly sensitive and directional. Here we demonstrated that combining stimulation sites does not alter termination success when the critical point is included. Combining the RV apical stimulus site with any combination of LV sites did not affect ATP success except for one case. Thus, including the RV as a stimulus site may not affect the efficacy of other stimulation sites. Combining sites may increase the likelihood of including a critical stimulus site when such information cannot be ascertained. Further studies will be needed to assess the robustness and feasibility of such an approach.

We suspect these observations largely depend on the patient-specific infarct, its location, and the VT beat analyzed. Clinically, these factors are rarely known at the time of ICD implantation. To generalize ATP delivery methods, comparing against other patient-specific models is critical. In subsequent studies, we will add additional patient-specific models and VT beats of varying CL to this analysis and assess if the trends we observe in this case persist.

The ATP method we applied in this study was a standard 8-beat train at 88% of the VT CL; however, this may not be the ideal ATP protocol in the context of biventricular ATP pacing. Further studies should compare other methods of ATP delivery, such as ramped pacing or other ATP

Table 3. VT Termination by ATP. A check mark signifies successful termination and an X unsuccessful.

Site(s)	Termination
RV	✗
RV + LowFW	✓
RV + MidFW	✗
RV + UpFW	✗
RV + LowFW + MidFW + UpFW	✓
RV + MidFW + UpFW	✗
RV + LowFW + MidFW	✓
RV + LowFW + UpFW	✓
LowFW	✓
MidFW	✗
UpFW	✓
LowFW + MidFW + UpFW	✓
MidFW + UpFW	✗
LowFW + MidFW	✓
LowFW + UpFW	✓

Table 4. Euclidean distance from pacing locations to VT exit site.

Site	Distance (mm)
LowFW	20.61
RV	30.22
MidFW	55.44
UpFW	82.32

CLs. Additionally, we only delivered ATP simultaneously in combined cases. Future research should explore delaying ATP delivery between combined sites, which may improve the robustness of this approach across different patients and VT morphologies.

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Address for correspondence:

Eric Paccione
The Nora Eccles Harrison CVRTI
Salt Lake City, UT 84112
eric.paccione@utah.edu