Biophysical Modelling of Bundle Branch Reentry Initiation and Maintenance

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Abstract

Bundle branch reentry (BBR) is a complex triggering mechanism of ventricular tachycardia, which initiation and maintenance are not well understood. We present a multi-scale functional model of the His bundle and bundle branches coupled to a simplified representation of the septum to study initiation and maintenance of BBR in-silico. The model includes a pathological region in the base of the left bundle branch characterized by a lower IKr current and a lower conductivity. The effect of the size of the pathological region and the percentage of IKr block have been studied to determine their potential role in BBR initiation and maintenance. Both characteristics together with sudden changes in pacing frequency affected the triggering and perpetuation of a BBR. We conclude that a pathological basal region in a bundle branch, characterized by larger APD and refractory periods can induce and perpetuate BBR when a short-to-long BCL change occurs after the conduction block.

1. Introduction

Bundle branch reentrant ventricular tachycardia (BBR-VT) is a typical form of monomorphic VT [1] resulting from macroreentry involving both bundle branches [2]. Macroreentry initiated from the His-Purkinje system in human hearts was first reported by Akhtar et al. [3,4]. Initiation of BBR depends on cycle length and can be facilitated by a slow drive train or a short-long-short sequence [5,6]. Sustained BBR was identified as a mechanism of clinical tachycardia by Caceres et al. [6]. The most common form of BBR-VT shows a typical left bundle branch block (LBBB) pattern, in which the reentrant circuit is formed by anterograde propagation in the right bundle branch (RBB), followed by transseptal propagation into the LBB, and retrograde propagation to the LBB (see Fig. 1). Generally, the formation of this kind of reentrant circuit requires an unidirectional conduction block in one bundle, and a slow conduction in the other. While transient BBR can be induced by a normal electrophysiologic response, it can result in sustained BBR when there is a conduction delay within the cardiac conduction system (CCS).

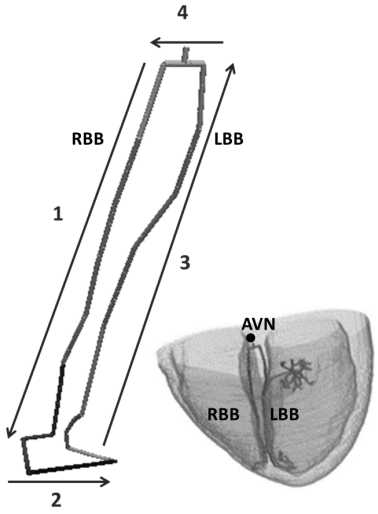

Figure 1. Schematic representation of the reentrant circuit for LBBB BBR-VT. The electrical impulse propagates anterogradely by the RBB (1), travels through the septum to the LBB (2), entries to the LBB, and propagates retrogradely by this branch (3). The reentrant circuit is closed in the junction between left and right bundle branches (4).

BBR-VT usually occurs in patients with underlying structural heart disease and significant His-Purkinje system impairment. It has been observed in patients with ischaemic and non-ischaemic dilated cardiomyopathy [7,8], and less common in patients showing valvular heart disease after surgery [9, 10], coronary artery disease [11, 12] or myotonic dystrophy [13]. However, this disease has also been observed in patients with no apparent structural heart disease [14,15]. CCS impairment is considered a substrate for BBR-VT, manifested as a His-Ventricle (HV) interval prolongation and/or bundle branch block QRS configuration. Although a prolonged HV interval during sinus rhythm has been considered a prerequisite for BBR-VT, Li et al. [2] demonstrated that it was not necessary, pointing out func-

tional transient conduction abnormalities in the CCS as a substrate for BBR-VT.
Recognition of BBR-VT is important because pharmacology antiarrhythmic therapy is usually ineffective [16] and it requires personalized catheter ablation patterns, e.g. the RBB which is the most common target of ablation [17,18].

Some authors have developed computer models of BBR. Ten-Tusscher & Panfilov [19] did not analyzed on the initiation mechanism, but they studied the final BBR pattern after it was triggered. Deo et al. [20] studied the generation of arrhythmias by artificially produced single ectopic beats originating in the Purkinje system. Both models needed to increase the effective path length of the reentrant circuit by decreasing the conduction velocity in the CCS and in the ventricles.

The aim of this paper is to present a 1D computational model of the bundle branches and a simplified transseptal propagation, to study if a pathological region in the base of a bundle branch can induce and perpetuate a BBR when a short-to-long BCL change occurs after the conduction block.

2. Material and methods

2.1. Biophysical model

We have developed a biophysical anatomically based model of the main branches of the bundle of His (HB), coupled to a ventricular cable mode to represent transseptal propagation between the ventricles. The Stewart Purkinje cell model [21] has been used to characterized the HB and the Ten-Tusscher and Panfilov model for ventricular cells [22]. Conduction velocity in the non-impaired HB region has been reduced to $0.52m/s$ to increase the effective path length of the reentrant circuit, while conduction velocity in the myocardium has been fixed to the physiological value of $0.50m/s$. A pathological region, characterized by larger action potential durations (APD) and refractory periods (RP) has been included in the basal third of the LBB. A transitional region is used to couple normal and pathological tissue, which smoothly adapts I_{Kr} current and tissue conductivity between both regions. To check under which conditions there is a conduction block in the CCS we also developed a reduced 1D cable model of Purkinje cells (from now on "strand model") of $5cm$ in length (312 elements) and included the pathological region.

Tissue electrical propagation is modelled by the monodomain equation. The problem is solved using operator splitting with adaptive time step and a minimum time increment of $0.02ms$. A high-order finite-element method is used, as described in [23], in order to improve numerical efficiency without jeopardizing the accuracy of the solution.

Table 1. APD_{90} and conduction velocity for each scenario

I_{Kr} Block (%)	$\sigma(cm^2/ms)$	$APD_{90}(ms)$	$v_{cond}(cm/s)$
0 (no block)	0.00125	311.3	52.3
20	0.00065	327.5	28.0
40	0.00065	356.4	25.7/59.4
60	0.00065	387.5	57.9

3. Results

Different scenarios were studied varying the percentage of I_{Kr} blockage (20, 40 and 60 %) and the length of the pathological region (1 or 2 cm).
APD_{90} and conduction velocities were measured for each scenario on a homogeneous strand model (of either healthy or pathological cells) at all their nodes (see Table 1) to have a better knowledge of fiber properties in each scenario. For the healthy strand model, the diffusion coefficient (σ) was set to $0.00125cm^2/ms$. For the pathological model σ was set to $0.00065cm^2/ms$ and I_{Kr} was blocked at different percentages. The electrical propagation blocked in alternate pulses for 40% and 60% I_{Kr} blockage and showed an influence on the conduction velocity. In these cases, measured velocities were of $0.59m/s$ and $0.58m/s$, respectively, because the excitability of the cell increased due to the higher resting potential of the Purkinje cells.

Following, we used a strand cable model that combined healthy and pathological regions to study at which time the block was obtained for each scenario. The simulation shows a natural conduction block after a few pulses using a BCL of 400ms. A 20% I_{Kr} blockage does not produce an anterograde block, while a 40% and 60% I_{Kr} blockage produces an anterograde block at different time pulses. As expected, the propagation was earlier blocked for higher I_{Kr} blockage and larger pathological regions (see Table 2). APD_{90} heterogeneity between the healthy and the pathological region was clearly differentiated (see Fig. 2).

Finally, we used the 1D anatomical model that includes the HB and septum to study BBR. We stimulated the atrioventricular node (AVN) with a BCL of $400ms$ until a block was produced in the pathological region in the expected pulse. We left the AVN unpaced to observe the natural frequency of the reentrant circuit (see Fig.1 and Table 2). Results showed that the frequency of the BBR circuit was higher for shorter pathological regions, i.e., the total time of a complete circuit round was shorter. For a higher I_{Kr} block, the total time of a complete circuit round increased. With a 60% I_{Kr} block in a pathological region of $2cm$, the reentrant circuit was not completed because a bidirectional block was produced within the pathological region.

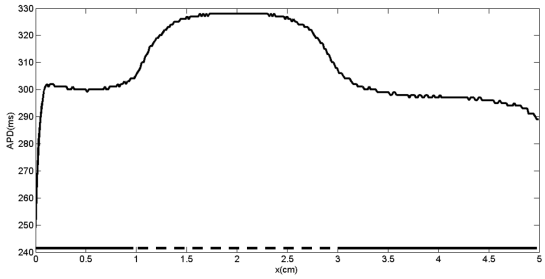

Figure 2. APD_{90} heterogeneity between healthy and pathological cells before the first block ($40\%I_{Kr}$ blockage in a pathological region of $2cm$). Dashed line indicates the pathological region.

Table 2. BBR dependency on I_{Kr} blockage for a pathological region of 1 and 2cm length and BCL=400ms. NB: no block within the pathological region; BB: bidirectional block within the pathological region.

I_{Kr} Block (%)	Time of first unidirectional block (number of pulse)		Steady state BBR frequency	
	1cm	2cm	1cm	2cm
20	NB	NB	NB	NB
40	13600 ms (35)	8400 ms (22)	2.47 Hz	2.40 Hz
60	5200 ms (14)	3600 ms (10)	2.27 Hz	BB

We study the effect of a short-to-long BCL change, particularly in the case of 40% I_{Kr} block and a pathological region of $2cm$. When a change from 400 to $550ms$ occurred right after the anterograde block, the BBR was perpetuated over time with a frequency that increased from 1.92 up to its stabilization value of $2.57Hz$.

4. Discussion

Results obtained showed that the existence of a pathological region characterized by a larger RP in one of the bundle branches can lead to a conduction block that, under certain conditions, e.g. short-to-long cycle length changes, can derive in a sustained BBR-VT. A unidirectional block can be obtained as a natural response of a pathological region, characterized by long APD and RP and by a low conduction velocity, for a BCL of $400ms$. The transitional region included in the model between healthy and pathological regions was very important because it partly uncoupled the electrical properties between them. Results obtained in the strand model were completely extrapolated to the anatomical His-Purkinje model. Characteristics of the pathological region, such as RP and length had a high influence in the unidirectional blockage, the initiation and the sustainability of the BBR and its frequency. Despite the transitional region, the electrotonic current smoothed the effect of the pathological regions, delaying the time of the first effective blockage. The block was sooner obtained for a pathological region of $2cm$. Greater I_{Kr} blocks facilitated the induction of the anterograde blockage because they increased the APD and the RP. The total time at which a complete BBR is completed decreased for shorter pathological regions, because time needed for the retrograde pulse to travel through a shorter pathological region was shorter. For a pathological region of $1cm$, after unidirectional block was produced the BBR circuit propagated faster for a lower I_{Kr} blockage due to its higher conduction velocity. 60% I_{Kr} block did not produce a BBR for a $2cm$ length pathological region, because it was prevented by the larger RP that generates a bidirectional conduction block in the pathological region.

This model presents some limitations. We present a 1D model of simplified bundle branches and transseptal propagation which is not yet included in a complete 3D model of the ventricles. The absence of a ventricular model simplifies the problem, because we did not have to take into account the effects produced by coupling Purkinje fibers with ventricular myocytes through Purkinje-Muscle junctions. The properties of the pathological region are not related to a particular pathology, although the assumption could be explained considering genetic level impairment. Nevertheless, we have characterized a well defined pathological region in the basal third of the LBB, presenting a possible mechanism underlying the BBR initiation and maintenance as Deo et al. did [20]. Frequencies obtained for each BBR complete circuit are slightly lower than the minimum clinical measurements which ranges from 2.8Hz to 3.2 Hz for BBR [6]. These values match closely with the ones obtained by Ten-Tusscher & Panfilov [19].

5. Conclusions

Our results point out that a pathological basal region in one of the bundle branches, characterized by a larger APD and RP, can lead to an unidirectional conduction block in the affected bundle. This conduction block could derive in a sustained BBR if a short-to-long BCL change takes place when the block is produced. This hypothesis supposes a contribution to the understanding of the mechanisms of the initiation and maintenance of BBR-VT, which for the moment are not well understood.

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