Correlation Between P-Wave Morphology and Origin of Atrial Focal Tachycardia—Insights From Realistic Models of the Human Atria and Torso

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Abstract—Atrial arrhythmias resulting from abnormally rapid focal activity in the atria may be reflected in an altered P-wave morphology (PWM) in the ECG. Although clinically important, detailed relationships between PWM and origins of atrial focal excitation have not been established. To study such relationships, we developed computational models of the human atria and torso. The model simulation results were used to evaluate an extant clinical algorithm for locating the origin of atrial focal points from the ECG. The simulations showed that the algorithm was practical and could predict the atrial focal locations with 85% accuracy. We proposed a further refinement of the algorithm to distinguish between focal locations within the large atrial bundles.

Index Terms—Atrial arrhythmias, body surface ECG, human atria model, P-wave morphology (PWM).

I. INTRODUCTION

Atrial arrhythmias, such as atrial fibrillation (AF), are characterized by rapid and irregular cardiac excitation waves, which are reflected in abnormal P-wave morphologies (PWM) in the ECG [1], [2]. Experimental evidence suggests that AF can result from reentrant excitation waves breaking up to form unsynchronized wavelets in the atria [2]. This may occur due to interactions of wavefronts originating from different regions within the atria. Thus, focal excitations originating from atrial regions other than the natural pacemaker site may predispose the development of AF. For successful treatment of AF by ablation procedures, it is crucial to locate the origins of atrial foci. However, due to the complexities of atrial anatomical structure and electrical heterogeneity, such focal origins are difficult to establish without using invasive diagnostic modalities.

The ECG is the most common noninvasive method for monitoring the activity of the heart by measuring the body surface potential (BSP) distribution. Correlations between the BSP and underlying electrical activity on the surface of the heart can be established by solving the inverse problem [3]. However, this method has some limitations, as it may not be able to locate the precise origins of atrial focal activity within the myocardium rather than on the heart surface. Besides, its implementation requires large multiple lead arrays (>200 leads) to map the BSP in detail not provided by the standard 12-lead ECG used in clinical studies.

Alternatively, computational models can be used to solve the forward problem in order to establish links between the origin of focal activity and the BSP. In this study, biophysically detailed computer models of the human atria and torso were developed to explore such links. The models were used to evaluate an existing clinical algorithm [1] for locating the origin of atrial excitation from the 12-lead ECG. An improvement to the algorithm was proposed in order to increase its predictive ability for focal origins within the large atrial bundles.

II. METHODS

A. Heterogeneous 3-D Model of the Human Atria

The Courtemanche–Ramirez–Nattel (CRN) model [4] for the action potential (AP) of a human atrial myocyte was modified to incorporate electrical heterogeneity in the atria [see Fig. 1(a)]. Heterogeneity in the conductance of the transient outward current $I_o$, L-type calcium current $I_{Ca,L}$, and the rapidly activated potassium current $I_{Kr}$ between cells of the crista terminalis (CT), atrial appendages (APG), and the atrio-ventricular ring (AVR) was based on experimental data from the canine right atrium (RA) [5]. Conductance of these ionic currents in the CRN model were, respectively, modified to produce AP morphologies for the CT, APG, and AVR cells, as described previously [6], [7]. Briefly, in the standard CRN model [4], the conductances of $I_o$, $I_{Ca,L}$, and $I_{Kr}$ were 0.1652, 0.1294, and 0.0294 nS/pF, respectively. In the CT model, the conductance of $I_o$ and $I_{Ca,L}$ were set to 0.2115 and 0.2067 nS/pF. In the APG model, the conductance of $I_o$ and $I_{Ca,L}$ were set to 0.1123 and 0.1312 nS/pF. In the AVR model, the conductance of $I_{Ca,L}$ and $I_{Kr}$ were 0.0829 and 0.0449 nS/pF.

The 3-D anatomical structure of the human atria [see Fig. 1(b)] was based on the Visible Female dataset with a spatial resolution of 0.33 mm × 0.33 mm × 0.33 mm [6]. The anatomical model was segmented into distinct regions of the RA, PM,
CT, AVR, as well as the left atrium (LA) and Bachmann’s bundle (BB). A region at the superior CT (SCT) was allocated as the sinoatrial node (SAN). Fiber orientation was manually introduced using principal component analysis [6] for the major conduction pathways in the bundles of the CT, PM, and BB.

The well-known monodomain partial differential equation [6]–[9] was used to describe the electrical excitation dynamics in the 3-D tissue. It was solved using the finite difference approach based on the forward Euler method with a time step of 0.005 ms and a spatial step of 0.33 mm. The same time step was used to solve the respective ordinary differential equations describing the CRN [4] single cell models.

B. Torso Model and BSPs

The propagation of electrical activity from the myocardium of the atria to the surface of the body was simulated, and the forward problem was solved using the boundary element method (BEM), derived from Green’s theorem [8]–[10]. A previously created torso mesh model [11] with considerations of geometric representations for the lungs and the blood masses of the atria and the ventricles [see Fig. 1(c)] was used. The mesh consisted of 820 elements; note that increasing the mesh resolution along with the proposed improvement to the algorithm in order to locate focal origins (superior or inferior) within the CT bundle.

C. Simulation of the PWM

An external current stimulus (2 nA during 2 ms to a region of ~5 mm³) was applied to the atrial model to initiate the AP excitation. To initiate sinus rhythm conduction, the stimulus was applied to the SAN region. To initiate ectopic foci, several well-known focal locations in the atria were selected as areas of interest: the superior and inferior CT (SCT and ICT), left and right pulmonary veins (LPV and RPV), left and right atrial appendages, and left septum/coronary sinus. Various points within these locations, spread out around the vicinity of each location, were randomly selected as stimulation points to initiate excitation. Such selections enabled simulations of a variety of foci as seen clinically [1]. After the initiation, the APs were conducted through the whole atria. From the resultant excitation patterns, BSP distributions and P-waves were determined. The previously developed algorithm [1] was applied to predict the excitation origin from the P-waves, and the predicted origins were compared with the actual origins (tissue stimulation points). The algorithm was based on a simple decision tree and is illustrated in Fig. 2, along with the proposed improvement to the algorithm.

In further test simulations, two areas of the atrium (the SAN and PV) were stimulated at various timings (simultaneously, and the PV stimulated 25, 50, and 75 ms before the SAN), and the resultant atrial activation patterns and BSP were studied.

III. RESULTS

A. Sinus Rhythm Conduction in the Atria

Fig. 3a(i) shows the atrial activation pattern simulated by the 3-D model under sinus rhythm conditions. Excitation is initiated
in the SAN region at the superior CT. It is then conducted rapidly down the CT and along the PM, through the fibers aligned along these bundles. The BB acts as the primary pathway for conduction between the two atria, with the first activation of the BB region at 26 ms. The total activation times for the RA and LA were 95 and 120 ms, respectively. These values were in good agreement with experimental data from human at body temperature [14], where the respective BB, RA, and LA activation times were 31 ± 13, 93 ± 17, and 116 ± 18 ms. Conduction velocities estimated from surface activation times were \( \sim 1.30 \text{ m/s}^{-1} \) in the CT and \( \sim 0.75 \text{ m/s}^{-1} \) in the atrial wall, also in agreement with experimental data [15].

### B. Simulated BSP and P-Waves

Fig. 3b(i) shows a snapshot (50 ms after the initiation) of the BSP under normal sinus rhythm conditions. The atrial conduction from the superior to ICT results in a BSP wave that propagates down toward the left leg, leaving a large positive region in the lower left torso and a negative region over the right shoulder. Such a BSP distribution is in agreement with experimental data [16]. Computed P-waves from some leads of the 12-lead ECG are shown in Fig. 3c(i). The P-wave is upright in the inferior limb leads (Leads II, III, and aVF) due to the superior–inferior conduction in the atria.

#### C. Ectopic Foci Conduction

Study of the P-waves produced by excitation originating from different locations along the CT shows that PWM is dependent on the precise foci location within this long bundle. When excitation is initiated near the SCT [see Fig. 3a(i)], a positive P-wave is seen in leads II and III [see Fig. 3c(ii)]—but when excitation is initiated at the ICT [see Fig. 3a(ii)], the P-wave in leads II and III is inverted [see Fig. 3c(ii)]. The latter is due to the effect of the inferior–superior atrial conduction on the BSP distribution [see Fig. 3b(ii)]. Such an inversion can be quantified by comparing the amplitude of the positive peak in lead \( V_1 \) with the peak amplitude in lead III. Thus, if the peak in lead III is positive with the amplitude greater than that in \( V_1 \), excitation was initiated in the SCT—the larger the difference, the more superior the excitation. If the peak in lead III is negative, or has smaller amplitude than the positive peak of \( V_1 \), then the excitation origin is in the inferior CT.

#### D. Focal Origin Prediction Algorithm

As illustrated in Fig. 3, P-waves produced due to atrial excitations originating from different “ectopic foci” locations demonstrate markedly different PWM. Table I summarizes results of analyzing the P-waves due to various atrial focal excitations (see Section II-C) with the algorithm shown in Fig. 2. The algorithm correctly predicted the location of excitation origins in 59 of 77 simulations. Averaging the success ratio for each location gave the accuracy of the algorithm of 78%. One of the major inaccuracies of the algorithm was in determining the LPV and RPV. However, if these are considered simply as PV, the algorithm predicted the correct excitation origin in 68 out of 77 simulations, with an averaged accuracy of 85%.

Note that the original algorithm [1] considers the CT as a single location, which results in 100% accuracy in determining the focal origins in this long bundle (see Table I). The proposed improvement of the algorithm (see Fig. 2 and Section III-C) enabled determining various focal locations along the CT without affecting the overall accuracy of the algorithm.

### IV. DISCUSSION

#### A. Model of the Human Atria

A realistic 3-D model of the human atria that incorporates cell heterogeneity and fiber anisotropy has been developed. Limitations of the model are either inherited from the single-cell model used (previously discussed in [4]), or due to a lack of experimental data for human (cell heterogeneity and tissue anisotropy are based on animal data [6], [7]). However, the model reproduces conduction velocities and overall atrial activation patterns seen in experiments [14], as well as PWMs seen in clinical recordings [1]. Experimental data [14] were taken...
from patients with previous AF—however, the model was primarily designed for studies of arrhythmic atria.

Test simulations were also run with the resolution of the model increased to 0.25 mm × 0.25 mm × 0.25 mm. The simulations produced activation patterns qualitatively similar to those obtained with the original resolution of 0.33 mm × 0.33 mm × 0.33 mm, with a small numerical difference (<3%) in the conduction velocities.

B. Torso Model and BSP

The 3-D model of the atria was incorporated into a torso model to simulate the BSP. The BSP patterns and resultant PWMs were in agreement with experimental data [1], [16]. The model is capable of producing complex PWMs associated with AF [7]. Note that computed P-waves in some leads had “notched” morphologies, as opposed to smoother P-waves seen in clinical records. This may be due to the simplified torso geometry and omission of several inhomogeneities within the torso. Inclusion of such structures as the skeletal muscle (which is electrically excitable) may contribute to a smoothing of the P-waves produced. However, this would require the use of a finite element method, which is more computationally costly than BEM [9], [12].

C. Multifocal Excitations

Simulations presented in this study consider only atrial electrical excitations from a single focus, whereas complex excitations during AF may originate from multiple foci [2]. Our test simulations showed that in the case of two foci in the SAN and PV, the resultant P-wave was clearly distinct from P-waves in either of the SAN or PV only cases when the PV was stimulated 50 ms before the SAN. In this case, the algorithm [1] correctly identified the ectopic focal point in the PV despite the obscuring presence of the normal excitation wave from the SAN. This gives validation of the algorithm itself, as well as the model. With any other timing tested (0, 25, or 75 ms), the wavefront initiated in one of the regions overrides the wavefront initiated in the other. The resultant “overridden” wavefront may propagate for a short time, but this time is not sufficient for it to produce a significant effect on the BSP and the resultant P-wave.

D. Algorithm for Locating Focal Origin

The accuracy of an existing algorithm for locating the origin of focal atrial excitation from the 12-lead ECG was evaluated. With the simulation results, an average of 85% of prediction accuracy was achieved, close to 93% reported previously [1]. Such a discrepancy may be due to either limitations of the model, or the algorithm. Notched P-waves seen in simulations and discussed earlier make some of the P-waves appear bifid even in the sinus rhythm conditions. In this case, the algorithm is less effective, as it can distinguish between focal origins in the LPV and RPV only based on bifidity in lead II or V1.

The algorithm [1] has been improved to distinguish between various focal origins within the long bundle of the CT. This may have important implications, as clinically observed shifts of the leading pacemaker site along the CT have been linked to arrhythmic conditions [17]. The proposed improvement can help primarily to monitor such pacemaker shifts from ECG.

REFERENCES