

In-Silico Investigation of the Right and Left Atrial Contributions to the P-Wave Morphology in ECG of Healthy and Atrial Fibrillation Patients

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Abstract

Atrial fibrillation (AF), the most common arrhythmia, can be diagnosed from altered morphology of P-waves in patient's ECG. This study aims to evaluate contributions of electrical activity in the right (RA) and left atria (LA) to the P-wave in both control and AF patients. Two 3D torso computational models generated from high-resolution CT patient scans were used for in-silico simulations of bi-atrial, RA-only and LA-only electrical activity and resulting 12-lead ECG. Body surface potentials were recorded in standard 12-lead ECG positions using pseudo-bidomain equations and finite element methods. We demonstrate that RA contributes nearly twice as much to P-wave morphology as LA and has a significantly greater impact on other indices.

1. Introduction

The ECG P-wave is generated during atrial depolarization, reflecting the underlying atrial structure and electrical activity. Most P-wave derived biomarkers are particularly valuable for diagnosing atrial fibrillation (AF). Prolonged P-wave duration, advanced interatrial block, abnormal P-wave axis, abnormal PtfV1, and low P-wave amplitude in lead I are all associated with an increased risk of AF [1]. As AF is the most common cardiac arrhythmia globally, affecting 2-3% of the European and North American populations, and with its prevalence expected to rise in the coming decades [2], there is a pressing need for a non-invasive, cost-effective, easily accessible, and widely available tool for assessing atrial anatomy and function. ECG offers these advantages comparing to other techniques like magnetic resonance imaging, ECG imaging or electroanatomical mapping. However, the low reliability of individual P-wave changes in detecting pathologies [3] highlights the need for a better mechanistic understanding of the right (RA) and left atrial (LA) contributions to P-wave morphology in order to improve clinical outcomes.

Loewe et al. [4] investigated the distinct contributions LA and RA to the P-wave using computational models of

two healthy patients, revealing that LA contributions are limited to 30% of the morphology. Krueger et al. [5] examined the ECG Ta-wave, which represents atrial repolarization, in models of both healthy and AF patients. However, Ta-wave is rarely observed in ECG due to its weak signal and partial overlap with the QRS complex.

The present study builds on Loewe's work by conducting in-silico experiments to explore how the contributions of RA and LA to the P-wave are altered under AF conditions. Using patient-specific anatomies, we performed simulations of atrial activations with and without AF ionic remodelling to generate 12-lead ECG P-waves. We then calculated absolute integrals and analysed P-wave parameters recommended by the electrocardiology societies [1] to examine the contributions of each atrium individually.

2. Methods

2.1. Anatomical models

Two detailed whole torso anatomical models were derived from CT scans with additional higher resolution contrast cardiac scans [6]. Both patients (P1 and P2) tetrahedral mesh models included the four-chamber heart, bones, kidneys, liver, stomach, spleen, lungs, blood pools with cardiac valves and skin (Figure 1A). Since these models were originally developed for simulations of defibrillators and ventricular electrophysiology, we removed defibrillator coils, and processed the atria using Paraview [7] and Meshtool [8] software.

Specifically, the atrial mesh was refined by removing and smoothing any outliers and irregular elements caused by segmentation artifacts. Unfortunately, both original atrial models had partially clipped left appendages, which we were unable to restore. Additionally, the pulmonary veins and inferior vena cava were not segmented, so we clipped the orifices at their locations. Any non-anatomical holes in the atrial walls were filled in. The atrial models were divided into regions: bulk tissue (RA/LA), crista terminalis (CT), pectinate muscles (PMs), Bachmann's bundle (BB) and appendages (RAA, LAA); rule-based

fibre orientations were added using the atrialmtk pipeline [9]. We also extended the pipeline's codebase to process atrial appendages in meshes. Finally, the atrial meshes were resampled to an average resolution of 370 μ m for the electrophysiological simulations (Figure 1B).

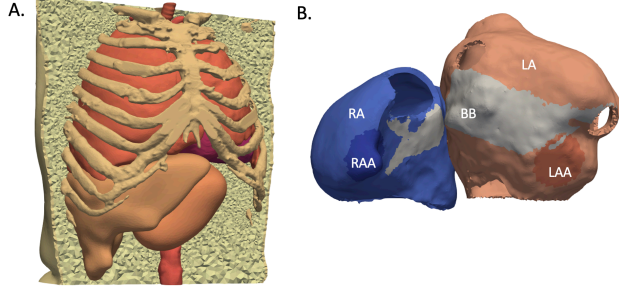


Figure 1. Human torso and atria. (A) Detailed anatomical model with all organs. (B) Processed atrial model with annotated regions.

2.2. Electrophysiological modeling

Human atrial myocytes membrane kinetics were simulated using the Courtemanche cell model [10]. To account for regional heterogeneity and variations in human atrial action potential, the maximum conductivities of selected ionic channels (g) were adjusted relatively to the default Courtemanche model. In the control case, these adjustments were based on work by Krueger et al. [5]. For RAA: $g_{CaL} \times 1.06$, $g_{to} \times 0.68$; for CT, BB: $g_{CaL} \times 1.67$; for LA: $g_{Kr} \times 1.6$; for LAA: $g_{CaL} \times 1.06$, $g_{to} \times 0.68$, $g_{Kr} \times 1.6$. For the AF ionic remodelling scenario, conductivities were adjusted relative to the control case as proposed by Loewe [11], who thoroughly referenced clinical experimental data. For all regions: $g_{K1} \times 2$, $g_{Ks} \times 2$, $g_{CaL} \times 0.45$, $g_{to} \times 0.35$, $g_{Kur} \times 0.5$, $g_{NaCa} \times 1.6$, $g_{leak} \times 1.5$. Lastly, in both control and AF cases, the mesh elements in the atrial septum were set to be non-conductive by setting I_{Na} current to 0, ensuring a complete separation of the RA and LA in the simulations.

We used a pseudo-bidomain propagation model [12] and finite element method to calculate 12-lead ECGs. Longitudinal intra- (σ_i) and extracellular (σ_e) conductivities were optimized using tuneCV [13] until conduction velocities (CVs) matched control ranges reported in the literature for each atrial region [14-17]. CVs in AF were derived by dividing control CVs by 1.4 following the ratio used in previous canine studies [18]. Conductivities were further linearly scaled in both control and AF cases to achieve physiological P-wave durations. The anisotropy ratios (AR) for AF were set as in [4] and scaled down by 1.6 for controls due to lower anisotropy in healthy tissue [18]. The final values, shown in Table 1, indicate faster conduction in the CT, PMs and BB.

Table 1. Intra- and extracellular longitudinal conductivities and anisotropy ratios in control and AF.

Region	Control			AF		
	$\sigma_{i\parallel}$	$\sigma_{e\parallel}$	AR	$\sigma_{i\parallel}$	$\sigma_{e\parallel}$	AR
RA	1.000	3.594	2.34	0.360	1.292	3.75
RAA	1.000	3.592	2.34	0.360	1.292	3.75
PM	1.181	4.241	6.57	0.421	1.511	10.52
CT	1.766	6.343	4.10	0.613	2.203	6.56
BB	1.766	6.343	5.62	0.613	2.201	9.00
LA	1.001	3.594	2.34	0.360	1.292	3.75
LAA	1.000	3.592	2.34	0.360	1.292	3.75

2.3. Simulations

The described set up gives us a total of six simulations per patient (RA only, LA only and bi-atrial scenarios for both control and AF cases). Single atrium simulations were performed by disabling depolarization of the other atrium. RA and LA were fully disconnected due to a non-conductive septum and a lack of mesh connection between RA and LA parts of the BB. For bi-atrial simulations we found the closest two points on RA and LA parts of the BB, so that the point of LA starts depolarizing when the point on RA activates. We also record the time of these activations so that 12-lead ECGs generated by LA-only could be time matched for analysis.

Simulations were run with openCARP software [19]. Single cell pacing for 50 cycles was used to establish steady state conditions with basic cycle length of 1000ms. Constant time stepping was set to 20 μ s. The simulations took 2-4h on a 16 core CPU machine (AMD Ryzen 9 7950X).

3. Results

For simulated bi-atrial ECGs of patients P1 and P2 in control and AF, the results meet the typical P-wave characteristics: largest amplitude in lead II, biphasic V1, and expected polarities (negative aVR, positive leads II, aVF, V5, and V6). The biphasic waves in precordial leads, due to interatrial block [3], were introduced in simulations by allowing RA to LA depolarization only through the BB. Maximum P-wave durations are 113ms and 207ms for P1, and 111ms and 203ms for P2 in control and AF conditions, respectively. These durations fall within clinically reported ranges, including instances of AF prolongation [1]. Additionally, leads II and V1 show signs of left atrial enlargement for P1 and right atrial enlargement for P2, contributing to P-wave extension. Nevertheless, the AF P-waves are longer and have lower amplitude compared to controls, consistent with clinical observations [20] (Figure 2).

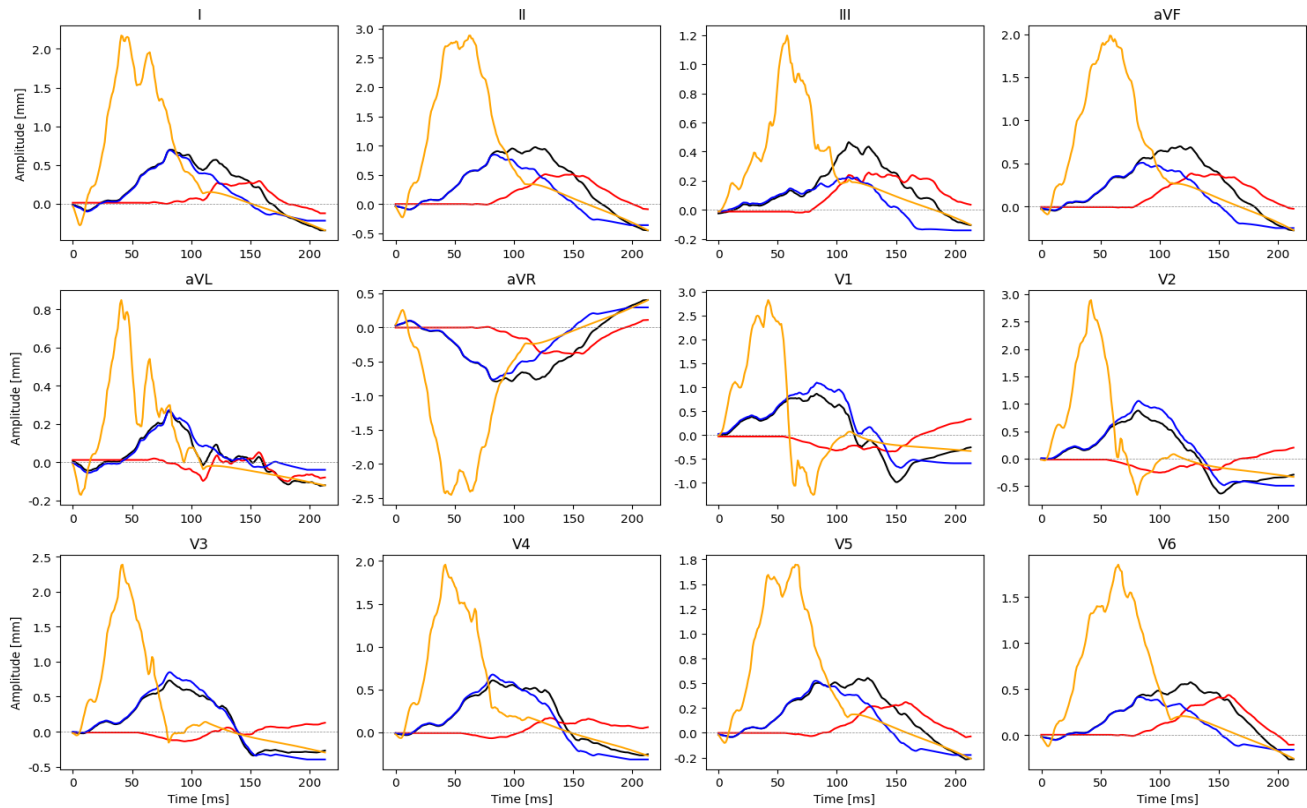


Figure 2. Simulated 12-lead ECG P-waves for patient 2. The four P-waves in each panel are for: AF RA-only (blue), AF LA-only (red), AF bi-atrial (black), control bi-atrial (orange).

We compared simulated P-waves from RA-only and LA-only models with bi-atrial simulations (Figure 2). To analyse the percentage contributions of RA and LA to P-wave morphology, we calculated the integrals of absolute values. We also assessed P-wave indices recommended by electrocardiologists [1], including duration (PWd in ms), dispersion (ms), PtfV1 (mm x ms), lead I voltage (μ V), lead II area (ms x mV), and spatial axis ($^{\circ}$), as detailed in Tables 2 and 3. The contributions of each atrium to the bi-atrial signal are presented for the absolute integer and lead I voltage, while the remaining metrics were reported for each individual atrium's P-wave.

Table 2. P-wave properties for patient 1 with maximum absolute integer %-age and duration across ECG leads.

Property	Control			AF		
	RA	LA	Biatria	RA	LA	Biatria
Abs. Int. %	80	46	-	84	46	-
PWd	80	87	113	152	155	207
Dispersion	10	7	13	10	37	30
Vol. L-I	91	19	110	28	7	35
Spat. Axis	66	73	68	68	75	67
L-II Area	8.8	6.1	15.9	5.5	3.5	8.7
PtfV1	106	123	273	74	78	186

For patient P1, the average LA contribution to the P-wave integral is 36% (range: 19%-46%) in control and 34% (range: 15%-46%) in AF. For patient P2, the average LA contribution decreased to 29% (range: 11%-49%) in control and 27% (range: 11%-50%) in AF. These contributions are close to the 30% limit reported by Loewe et al. [4]. Notably, LA contributions appear to decrease in AF, which may indicate that the LA signal exhibits smoother fluctuations and decreases in amplitude more than the RA signal. This effect is not fully offset by the simultaneous increase in P-wave duration (PWd) in AF.

Table 3. P-wave properties for patient 2 with maximum absolute integer %-age and duration across ECG leads.

Property	Control			AF		
	RA	LA	Biatria	RA	LA	Biatria
Abs. Int. %	89	49	-	88	50	-
PWd	84	83	111	158	155	203
Dispersion	10	13	10	6	29	11
Vol. L-I	214	3	217	68	1	69
Spat. Axis	40	52	46	40	56	49
L-II Area	10.6	5.3	14.8	6.7	3.3	9.6
PtfV1	18	86	65	26	53	81

LA contributions to the P-wave integral are highest in leads III and V6 for both patients, reflecting the LA's stronger signal relative to the RA, given its anatomical positioning relative to left arm, left leg and V6 electrodes.

Signals from leads II and V1, commonly used to assess sinus rhythm, show a dominant RA contribution (59-77%) in both AF and control simulations, which may bias LA function assessment. While RA and LA dispersions show somewhat conflicting results among patients, both increase with pathology, suggesting greater PWD variations between ECG leads. Lead I voltage is primarily influenced by RA, indicating that the peak value occurs during RA depolarization. RA also significantly contributes to the lead II area, likely due to a larger recorded RA peak. The spatial axis is larger for LA than RA, but balanced when comparing control to AF. PtfV1 values for RA and LA are generally lower in AF compared to controls, supporting the hypothesis that in AF the reduction in amplitude is not offset by the increase in duration in metrics dependent on amplitude and duration such as absolute integer, lead II area or PtfV1.

4. Conclusions

Our findings indicate that RA significantly influences P-wave morphology across the twelve ECG leads on average. To improve the assessment of LA function, leads III and V6 should be given particular consideration. However, for some P-wave indices, the contributions vary or even conflict among patients. This highlights the need to consider a larger number of patients in mechanistic studies and the challenges in assessing patient-specific atrial activity from ECG readings in the clinic.

Acknowledgments

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