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Acute Changes in P-Wave Morphology by Pulmonary Vein Isolation in Atrial Fibrillation Patients

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Abstract

Pulmonary vein (PV) plays an important role in atrial fibrillation (AF) initiation, progression, and stability. Successful PV isolation (PVI), either by radiofrequency catheter or Cryoballoon ablation, may terminate AF and prevent its recurrence. Whereas, incomplete PV isolation or reconnection of isolated PVs underlies mechanisms of AF recurrence. Hence, defining parameters able to predict a successful PVI and detect reconnections can assist clinicians in treatment of AF patients. Here, we developed a highly detailed human atrial model to simulate PVI and its acute effect on the P-wave morphology. Afterwards, the simulation results were compared and validated by recorded ECGs from patients before and after PVI procedure. In both simulation data and clinical recordings, we observed morphological changes in P-wave after PVI. More importantly our simulation helped us to find electrode positions, in which the differences in P-wave morphology before and after PVI were more pronounced.

1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia with a very high prevalence and associated with severe complications such as stroke [1, 2]. The progression of AF from short-lived “paroxysmal” episodes to longer-lasting forms is a hallmark feature of this chronic disease with important clinical implications. Indeed, the longer a patient has been in AF, the more difficult it becomes to restore normal sinus rhythm, and treatment options extremely limited.[3] Therefore, making efficient AF prevention and therapy is a major clinical challenge.

Although mechanisms underlying AF initiation and perpetuation is not well understood, atrial muscle sleeves surrounding the pulmonary veins (PVs) are known to be the most frequent source of focal activities initiating atrial fibrillation (AF).[4] As a consequence, pulmonary veins

(PVs) play a significant role in atrial fibrillation initiation, progression, and stability. Therefore, PV isolation (PVI) is the therapy choice for patients with paroxysmal AF stubborn to antiarrhythmic therapies and patients with persistent AF.[5]

Despite the acute success of PVI in AF termination, specifically in paroxysmal AF patients, AF recurrences are not rare.[6, 7] More than 40% of patients experience AF recurrence one year after their PVI procedure[8], and in nearly all cases, with AF recurrence, one or more of the PVs is found to have re-established electrical connection to the atria. As a consequence, these patients may require additional catheter ablation[5, 9-11]. This influences patient’s quality of life and risk for stroke.

Even though the mechanism underlying PV reconnections is not well understood, it is assumed to be caused by remained gaps in the line of blocks during PVI procedure or failure to generate a complete transmural block line. Therefore, finding non-invasive approach capable of detecting complete PVI and predicting PV reconnections during follow up, is highly desirable in clinical routines.[12]

Due to the presence of discontinuity in the left atria and PV connections there might be conduction delay between left atria and PV [13, 14]. Therefore, it is possible that the final portion of P-wave reflects electrical activation of the PVs[14]. As a consequence, a successful PVI might be associated with a reduction in P-wave duration. Whereas, unsuccessful PVI might cause little or no changes in the P-wave durations.

In figure 1 an example of recorded ECG of a patient in three consecutive time points (pre PVI, acute post PVI and 3 months after) is illustrated. As it is shown in this figure, there were acute morphological changes in the second half of the P-wave. These morphological changes were stable after three months, and in this period the patient had neither an AF recurrence nor any symptoms related to AF.

Therefore, we hypothesized that morphological changes in the final part of the P-wave could serve as a predictor for a successful PV isolation or presence of reconnections. To test this hypothesis, we developed a highly detailed human

atrial model and simulated circumferential PV isolation line. Afterwards, we compared the P-wave in the control simulations (without ablation lines) and PVI simulations.

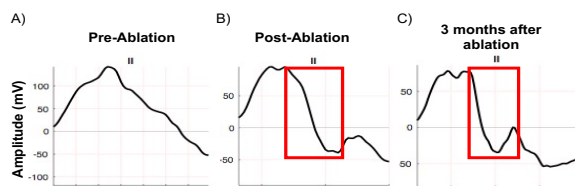


Figure 1. An example of Lead II ECG of a patient A) Pre-ablation. B) Acute post ablation (the area with a morphological change indicate by a red box). C) 3 months after ablation without AF recurrence after ablation

2. Method

2.1 Human atria computer model

We have developed a highly detailed human atrial model including epicardial layer and all major endocardial bundle structures. One to three layers of realistic fiber orientations were incorporated into the model, corresponding to their location in the atrium. The model consisted of approximately 5 million nodes spaced at $200\mu\text{m}$. Ionic currents for each node were described by the Courtemanche-Ramirez-Nattel human atrial cell model. [15] To simulate the ECG from the simulated atrial electrical activity, we embedded the atrial model in an inhomogeneous torso model. The torso model included lungs and interactivity blood masses. 256 body surface potentials were simulated using a bi-domain equation solved at 1-mm resolution.[16]

Two transmural ablation lines surrounding PVs positioned on the atrial model based on the documented method and localization of clinical ablation points (see figure 2). Virtual ablation lesions consisted of the tissue volumes within 0.35 cm (i.e., the ablation lesion radius for standard irrigated-tip catheters). [17] Along the ablation line intercellular coupling will be set to zero to avoid any conduction toward the PVs.[18, 19]. In both control (no ablation lines) and post ablation the normal propagation was initiated by injecting intracellular current in the region of the sino-atrial node.

2.1 Analysis

For all 256 electrograms, P-wave duration, P-wave amplitude and P-wave area were calculated. P-wave duration was defined as the interval between the stimulus time and the moment that all model elements became repolarized. P-wave amplitude was defined as the maximal vertical peak to peak distance. P-wave area was defined as

the time integral of the unfiltered signal between the onset and the end of the P wave.

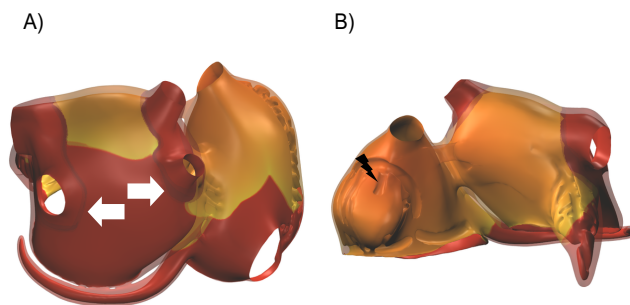


Figure 2. A) Position of ablation lines (white arrows). B) Anterior view of the human atrial model and the pacing location (black flash).

3. Result

In the simulated standard 12 lead ECG signals, there were slight morphological changes in the simulated P-waves in PVI simulation compared with the P-waves in control simulation. These changes occurred at the second half of the P-wave. In figure 3, ECG leads with the largest differences between P-waves in control and PVI simulations is depicted.

For all 256 body surface electrograms in control and PVI simulations, P-wave area and amplitude were calculated. Averaged P-wave area for all 256 leads decreased from 1.3517 ± 0.7193 in control to 1.0832 ± 0.5796 in PVI simulations. The averaged P-wave amplitude decreased as well from $0.0309\text{mV} \pm 0.0114$ in control to $0.0284\text{mV} \pm 0.0104$ in PVI simulations.

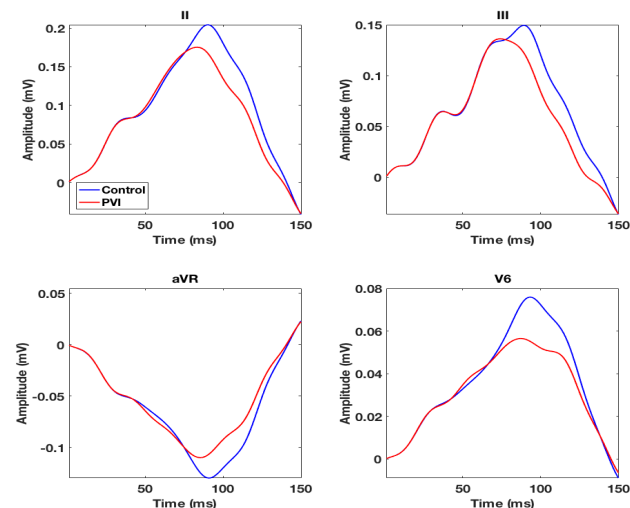


Figure 3. P-wave before (blue) and after (red) PVI in lead II, III, aVR, and V6.

In order to quantify morphological differences between P-waves in control and PVI simulations, Euclidean distances between P-waves pre and post ablations were calculated. In figure 4 projected color coded differences on the torso and simulated electrograms on the electrodes with largest differences illustrated. Highest differences were observed in the posterior side of the torso.

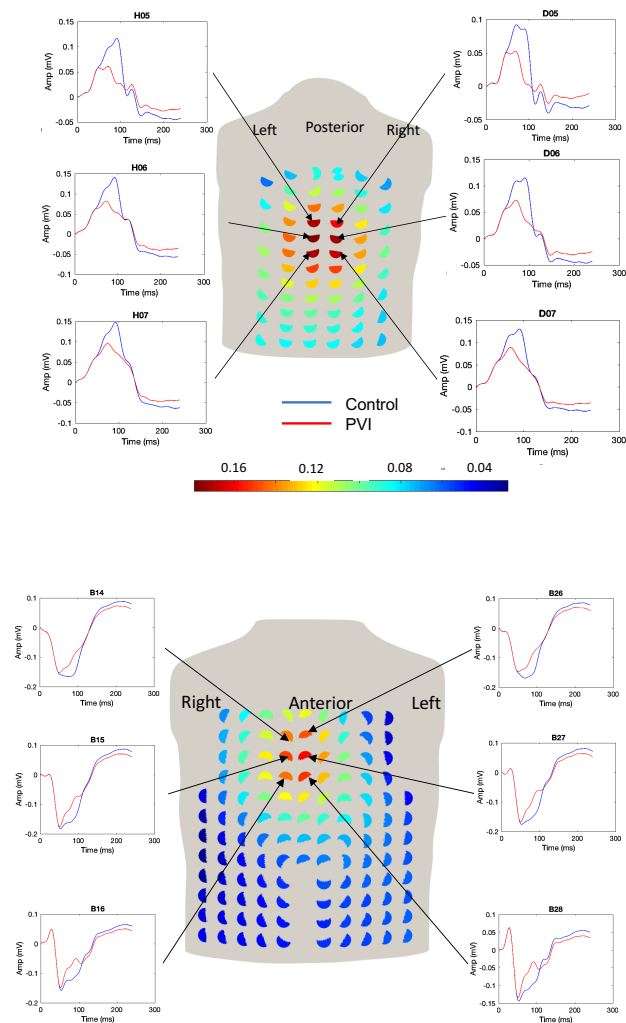


Figure 4. The Euclidean distance between pre- and post-simulated P-wave, color coded. Red shows the highest differences and blue shows the lowest difference. Top: Anterior view. Bottom: Posterior view.

4. Discussion

We have developed a highly detailed computer model of a human atria and torso to simulate PVI. The simulation results showed that a complete PVI led to a decrease in both the amplitude and the area of the P-wave. Notably, differences between P-waves in control and PVI

simulations were pronounced more in the posterior side of the torso rather than the anterior side. Recording electrograms from those locations are not considered in the clinical routines. Hence, analyzing those electrograms might be a great tool for clinicians to be sure that the PVI procedure is complete and to detect possible PV reconnections during the follow-up.

5. Limitations

Although the atrial model contains many details of atrial electrophysiology, the simulated activation sequence of our atrial model may not exactly reflect that of the patients in this study. The simulations were performed only on a generic computer model of the atria and torso, and anatomical variations were not included in this study. Thus, the simulated atrial electrogram morphology may not match the surface ECG of all patients. Finally, presence of fibrosis and slow conduction areas in the atria may cause changes in the atrial activation sequence. Therefore, PVs may not be the latest sites of activation.

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