In Vivo Analysis of Conduction Pattern Dynamics: System Development and Application Using OpenEP

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Abstract

Atrial low voltage, measured during electroanatomic mapping, may indicate the presence of atrial fibrosis, has been implicated in atrial fibrillation perpetuation and shows useful associations with clinical outcomes. Low voltage is however a marker of the underlying substrate, but it is the electrophysiological properties of this substrate which are critical to arrhythmogenesis. Nevertheless, the influence of low voltage on in vivo conduction pattern dynamics is uncertain. Here, we develop a novel method for dynamic conduction velocity assessment. A central electrode pair of a multi-spline, multi-electrode catheter was used to apply a series of pacing trains (S1) followed by coupled premature extra stimulus (S2). For each S1S2 interval, two perpendicular electrodes were selected to calculate conduction velocities in longitudinal and transverse directions. Conduction velocity restitution curves were generated by plotting conduction velocity at each S1S2 interval. The slope of the line fitted to the descending part of the conduction velocity restitution curve showed a very good correlation with the percentage of low voltage area underlying the geodesic path connecting electrodes on which conduction velocity was calculated. (R^2 = 0.64). Using this novel method, we could achieve intraprocedural assessment of the effect of low voltage regions on conduction pattern dynamics.

1. Introduction

Atrial fibrillation, an abnormal uncoordinated rhythm in the upper chambers of the heart, is the most common cardiac rhythm disorder [1,2]. The progression of atrial fibrillation is mediated by ion-channel remodelling and structural alterations including fibrosis [2]. Low atrial endocardial voltage measured during electro-anatomic mapping, which may indicate the presence of atrial fibrosis, is a marker of atrial fibrillation perpetuation and maintenance [3-5]. Moreover, it has been shown that the presence of low voltage areas and their extent predict atrial fibrillation recurrences after catheter ablation [5]. However, low voltage is only a marker of the underlying electrophysiolocal substrate, but it is the electrophysiological properties of this substrate which are responsible for arrhythmogenesis [2]. Nevertheless, the influence of low voltage on *in vivo* conduction pattern dynamics is uncertain. Here, we therefore develop a novel method for dynamic conduction velocity and conduction velocity restitution assessment and apply this method to investigate the electrophysiological basis for pro-arrhythmia associated with low voltage areas.

2. Method

All analyses and visualisations were performed using OpenEP, an open-source toolkit for electrophysiology data analysis (*https://openep.io*)[6].

2.1. Analysis of voltage data

Bi-atrial voltage maps were created using a multi-spline, multi-electrode catheter (PentaRay, Biosense Webster, Diamond Bar, California) with the Carto3 electroanatomic mapping system (Biosense Webster, Diamond Bar, California). In Figure 1, examples of voltage maps generated from acquired data using OpenEP are shown. The extent of low voltage area was quantified as a percentage of total atrial surface area for each chamber using a bipolar voltage threshold of 0.5 mV (Figure 1).

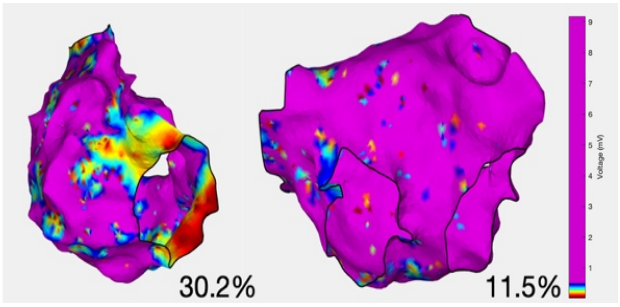

Figure 1: Examples of voltage maps calculated using OpenEP. Percentage values show the extent of atrial surface area with bipolar voltages < 0.5mV.

For each S1S2 interval, two perpendicular electrodes were selected to calculate conduction velocities in longitudinal and transverse directions. Using the location points assigned to each electrode in the Carto3 system, the distance between the pacing electrode and the electrode selected for the analysis was calculated (d) (Figure 2).

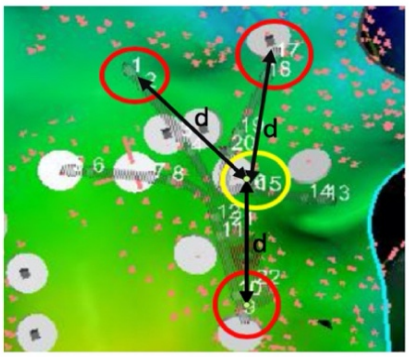

Figure 2: Position of the Pentaray catheter on the posterior left atrial wall with the pacing electrode highlighted in yellow and the recording electrodes highlighted in red.

For each selected electrode, local activation times were automatically calculated using OpenEP via a non-linear energy operator [7] (red) calculated from the recorded bipolar signal (black) (Figure 3).

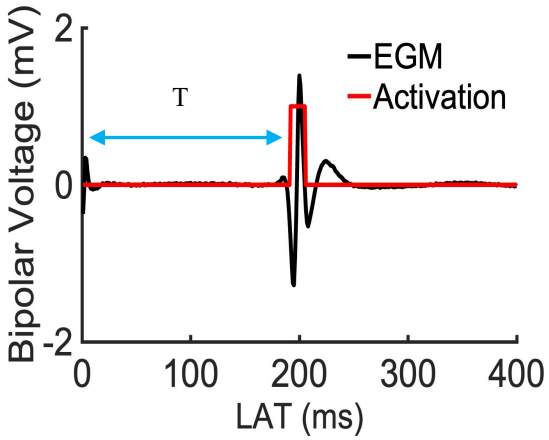

Figure 3. An example of bipolar recorded electrogram (Black). Red shows the non-linear energy operator calculated to detect the local activation time (LAT). The time difference between the pacing stimulus and the first sharp deflection (T).

For each S1S2 interval local conduction velocity was calculated as the distance between the pacing and the selected recording electrodes (d) divided by the time difference from pacing spike to the first sharp deflection (T) in the recording electrode.

2.2. Low voltage area quantification

To quantify the percentage of low voltage area underlying the pacing and the recording electrode, the geodesic paths between electrodes was calculated (Figure 4). Low voltage area percentage was calculated as the proportion of mesh elements within the geodesic path and its 3mm corridor (white dashed lines in Figure 4) with bipolar voltages below 0.5mV.

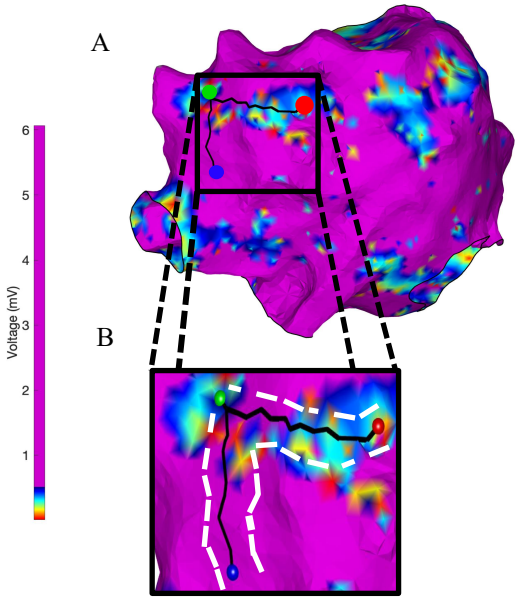

Figure 4: Quantifying low voltage area. (A) Voltage map with the location of pacing electrode (Green) and recording electrodes used to calculate conduction velocity (Blue and Red). (B) Magnified recording area (Black: geodesic path, White: area in which low voltage area was quantified).

2.3. Calculation of conduction velocity restitution curves

Conduction velocity restitution curves were generated by plotting calculated conduction velocities at each S1S2 interval. Two lines were fitted to the plateau and the descending part of the curve. The slope of the descending line was used to quantify conduction velocity restitution.

3. Results

In total, 22 paroxysmal atrial fibrillation patients undergoing first time atrial fibrillation ablation were included in this study.

3.1 Conduction velocity restitution curves

An example of conduction velocity restitution curves in regions with and without low voltage areas are shown in Figure 5.

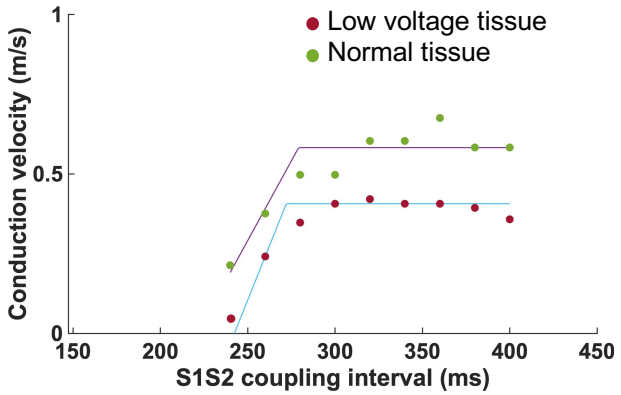

Figure 5: Conduction velocity restitution curves in normal and low voltage areas.

The averaged conduction velocities in the plateau of conduction velocity restitution curves were significantly higher in the normal tissue (0.58 m/s ± 0.05) compared to the low voltage tissues (0.41 m/s ± 0.02) (Figure 6A). The slopes of the fitted lines in the descending parts of conduction velocities restitution curves were significantly higher in the low voltage (0.03m/s ± 0.002) tissue compared to normal tissue (0.01 m/s ± 0.001) (Figure 6B).

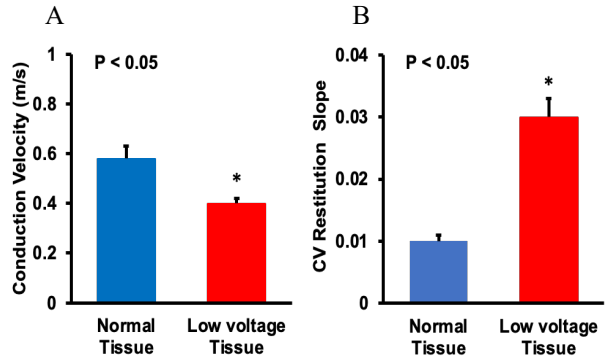

Figure 6: A) The averaged conduction velocities in the plateau of conduction velocity restitution curves. B) The slopes of the fitted lines in the descending parts of conduction velocities restitution curves.

3.2 Conduction velocity restitution curves

To investigate further the effect of low voltages areas on conduction patterns dynamics, conduction velocity restitution slopes were plotted against percentage of low voltage area (Figure 7). We observed a very good correlation between conduction velocity restitution slope showed with the low voltage underlying the geodesic path ($R^2 = 0.64$).

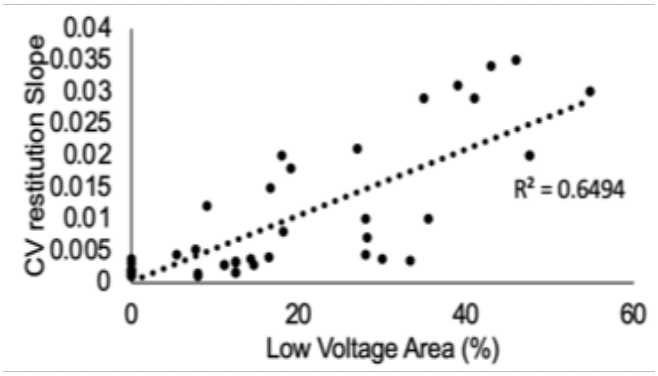

Figure 7: Slope of fitted line to the descendent part of conduction velocity restitution curve versus low voltage area percentage.

4. Discussion

It has been shown in several studies that low voltage area in the atria is a surrogate marker for the presence of atrial fibrosis and plays an important role in atrial fibrillation maintenance [4,8,9]. Moreover, it has been proposed in clinical studies that isolating low voltage areas improved atrial fibrillation recurrences after catheter ablations [9-13]. However, identifying low voltage areas as ablation targets remained challenging due to the absence of standardized method defining them [4] and lack of understanding of their effect on conduction pattern dynamic. In the present study, we proposed a novel method to assess the effect of low voltage areas on conduction pattern dynamic by calculating conduction velocity restitution.

We hypothesized that changes in the low voltage atrial tissue conductivity dynamic, potentially due to the presence of atrial fibrosis, provide a substrate for atrial fibrillation initiation and perpetuation. Hence, measuring these changes in the conduction pattern dynamic may provide a more sensitive parameter to detect arrhythmogenic substrates and identify them as ablation targets. In this study, we observed a steeper decline in conduction velocity restitution curve in low voltage area compared to normal tissue and the slopes of conduction velocities restitution curves correlated well with the percentage of low voltage area.

5. Conclusion

This observation provides an electrophysiological basis for the pro-arrhythmic nature of low voltage areas in atrial fibrillation patients. In addition, this study provides a

methodology which may be used to gain further insight in the in vivo electropathophysiology of atrial fibrillation.

6. Acknowledgement

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