Optimal Regional Voltage Thresholds for Identifying Ablation Targets in Patients with Atrial Fibrillation

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Abstract

Pulmonary vein isolation plus ablation of additional arrhythmic substrate is used to treat persistent atrial fibrillation (AF) patients. Atrial arrhythmogenic substrate contains increased myocardial fibrosis and displays low bipolar voltage $< 0.5\,mV$ during SR or < 0.3-$0.5\,mV$ during AF. However, discrepancies were reported in the extent and location of low voltage areas (LVA) between SR and AF maps. This paper studies these differences and identifies if regional thresholds can improve the correlation.

Twenty-eight patients with AF underwent high-density voltage mapping during both SR and AF. Each patient's voltage information was projected onto a mean geometry to analyse the spatial accordance of LVA identified during AF at various thresholds with those during SR at $0.5\,mV$ threshold. The model was split into six regions to identify which regions have the lowest agreement between SR and AF and if regional thresholds could improve this.

Areas of high and low voltage were similar in both mapping modalities. However, differences of $> 0.7\,mV$ occurred on the lateral and posterior wall. When using one threshold for the entire atria, agreement at the posterior wall was $< 70\%$. This improved by 10% when using a regional AF threshold. Therefore, substrate targeted for ablation during AF mapping can be more accurately identified on the posterior wall using a lower threshold.

1. Introduction

Atrial fibrillation (AF) is a common cardiac arrhythmia affecting over 43.6 million people worldwide and causing a significant burden to the patients and the healthcare system [1]. In patients with paroxysmal AF, isolating the pulmonary veins yields success rates of up to 75-90% after a single procedure [2]. However, for persistent AF patients, the success rate drops to around 30-50% [3]. One potential reason is additional arrhythmic substrate in the atrial body, which is maintaining the arrhythmia. Techniques such as LGE-MRI and electroanatomical mapping are current approaches to identify the substrate. Specifically, arrhythmogenic atrial regions have been identified to display low bipolar voltages $<0.5\,mV$ during sinus rhythm (SR) [4, 5]. Additionally targeting these areas for ablation in combination with pulmonary vein isolation increased the success rate up to 69% [4–6]. Mapping the atria during AF can additionally be beneficial to avoid performing multiple cardioversions during the procedure and to map native rather than induced AF, especially in patient who cannot be cardioverted to or maintained in SR during mapping and ablation [4]. However recently, discrepancies in the extent and distribution of the LVA were identified between SR and AF mapping.

Recently, it was found that using a threshold of around $0.3\,mV$ during AF mapping revealed a high spatial concordance between the mapping modalities [7], with regions such as the anterior, lateral wall and left atrial appendage (LAA) showing high concordances. However, significant discordance in LVA were found at the posterior wall. Therefore, further analysis is required on the relationship between SR and AF voltage mapping, identifying if regional voltage thresholds can result in improved substrate agreement between AF and SR maps.

In this paper, we sought to understand the discrepancies between SR and AF mapping, explicitly looking at region-based differences. We hypothesised that regional thresholds can reduce dissimilarity and sought to identify optimal thresholds.

2. Methods

2.1. Dataset

For this study, a total of 28 patients with persistent AF underwent high-density mapping acquired during both SR and AF prior to pulmonary vein isolation. Bipolar voltage

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mapping was performed using a 20-pole Lasso mapping catheter and the CARTO-3 software. To prevent analysis with poor wall contact, electrograms recorded >7 mm from the geometry were excluded. Additionally, points containing only noise or pacing artifacts were removed based on manual assessment.

2.2. LA Shape Model

A mean left atria (LA) geometry was built using Scalismo, a statistical shape modelling software [8,9]. The first step was to align all the geometries, to prevent variations caused by spatial displacement; this was performed automatically using the iterative closest point algorithm [10]. Following, dense correspondence between all the geometries was established so that each geometry had the same number of surface points representing the same anatomical landmarks. This was done using the Gaussian process morphable models [11]. The mean shape was then created by calculating the mean across all point coordinates that are in correspondence.

Since the mean shape was constructed from the patient geometries, alignment and correspondence between each patient's geometry and the mean shape were already established. From this information, each patient's voltages values could be obtained for every point of the mean geometry. The mean voltage value for each node across all patients was then calculated for the maps during SR and during AF, allowing a visual comparison between maps in different rhythms without the influence of outliers obtained from patient specific differences. Additionally, a new map was constructed indicating the difference between SR and AF voltage.

2.3. Atria Regions

Recently, it has been identified that there are regional differences in the voltage, with the most extensive LVA being located on the antero-septal wall and the roof [12, 13]. To further examine the difference between SR and AF voltage mapping and identify the optimal threshold for different atria regions, the LA mean shape was split into six anatomical regions, shown in Figure 1: the left atrial appendage (LAA), the anterior, posterior, and lateral wall, the roof, and the septum.

To obtain the six regions, rings around the pulmonary veins, the mitral valve and the LAA were drawn manually using Blender, a 3D computer graphics software [14]. After, the Eikonal equation was solved to obtain the shortest path from each ring to the others. These paths were then used to split the atria into the six regions.

The SR and AF voltage values were then compared for each region of the atria, along with calculating the optimal threshold for each region during AF to obtain the best

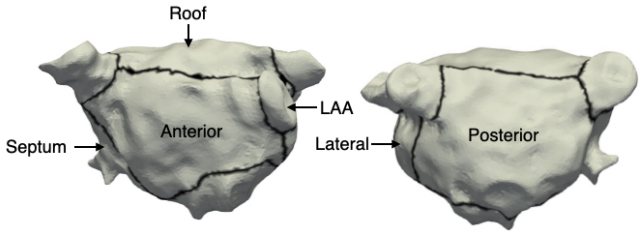

Figure 1. Mean shape showing the six atria regions.

correlation with SR (threshold < 0.5 mV) for identifying LVA. This was performed by calculating the sensitivity and specificity for each region over the data of all patients. The threshold and accuracy were then obtained by choosing the point closest to the top left hand corner of the ROC curve.

3. Results

Figure 2 shows the mean shape constructed from all patients with the mean voltages during SR and AF.

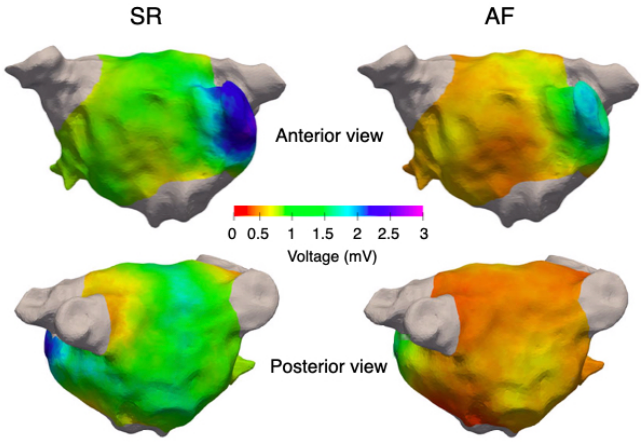

Figure 2. Mean voltage map across all the patients during SR (left) and during AF (right) visualised on the mean shape. The top row shows the anterior view and the bottom row the posterior view.

The voltage across the entire map was lower in AF than in SR. However, both maps show that the highest voltage values are located in the LAA and the lowest around the pulmonary veins and the mitral valve.

The difference in voltage between SR and AF can then be seen in Figure 3.

Figure 3, shows that a difference of up to 1.2 mV can occur between the SR and AF maps, with the greatest difference of > 1 mV occurring on the roof and lateral wall. On the posterior wall, the difference is smaller but still substantial (around 0.7 mV). However, little to no difference can then be seen in the areas around the pulmonary veins.

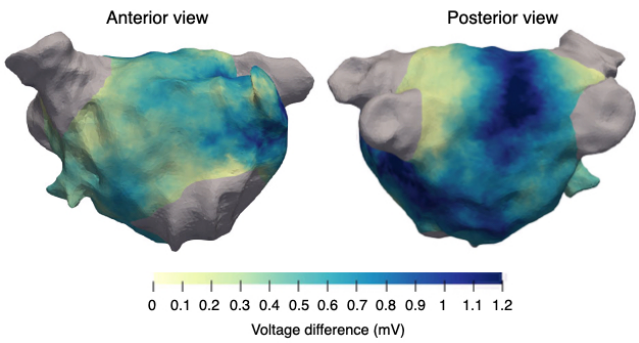

Figure 3. Difference in the mean voltage between SR and AF. The anterior view is shown on the left and the posterior view on the right.

The spread of the voltage in each of the six regions across all patients is then shown in Figure 4.

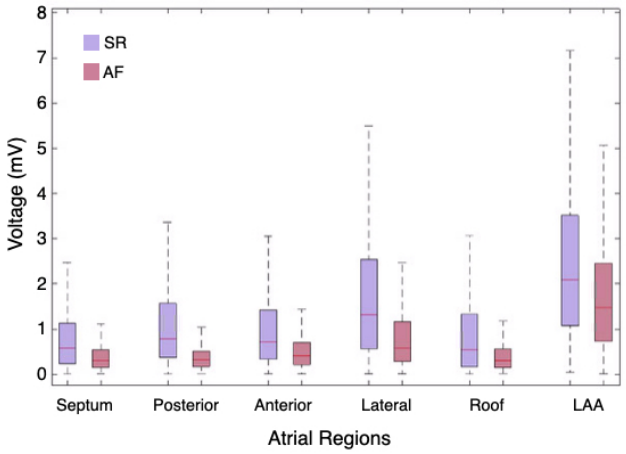

Figure 4. Boxplots showing the voltage across all patients for each region of the left atrium in SR and AF. $p < 0.001$ for SR vs. AF for all regions.

The spread of the voltage across all patients was larger in SR than AF for all regions. Using the two sample t-test, the difference between SR and AF for each region was found to be highly significant (p-value < 0.001). This is also true for the difference between each region in SR and AF. Moreover, the areas with lower voltages, thus indicating more arrhythmogenic substrate, were identified as the anterior wall, septum and roof, which is in concordance with previous studies [12, 13].

The optimal thresholds in AF for each region and corresponding accuracy values with respect to SR voltage <0.5 mV are shown in Figure 5.

The lowest agreement between SR and AF using the same threshold across all regions was found at the septum, posterior wall and the roof. When using regional thresholds, the posterior wall showed the greatest improvement, where the accuracy increased by around 10%. For the lateral wall, there was also an improvement of around 5%. However, for the other regions, the change was at maximum 1%. For each region, the optimal regional threshold was $\pm$ 0.05 mV from the optimal AF threshold when assessing all regions.

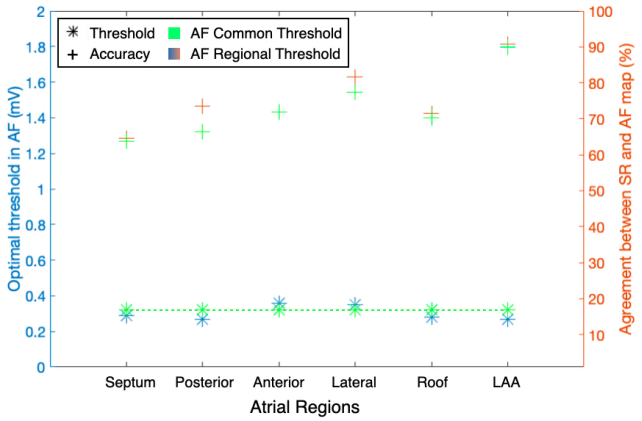

Figure 5. Optimal threshold and the corresponding accuracy for each region of the left atrium. The blue asterisks correspond to the left y-axis indicating the optimal threshold for each region in AF, with the red crosses corresponding to the right y-axis showing the accuracy for each region. The green asterisks shows the optimal AF threshold for all regions combined, and the green crosses represent the accuracy. The red cross for the anterior wall is covered by the green cross with only a 0.1% increase in accuracy.

4. Discussion

A high spatial concordance was found between the SR and AF maps, with higher voltages being located in the LAA and the lateral wall in both mapping modalities. However, some discrepancies do exist. It was identified that significant discordances in the voltage were located on the posterior and lateral wall (Figure 3 4). Nonetheless, when identifying LVA, the lateral wall had a relatively high agreement of $> 80\%$ between the SR and AF map, due to the majority of points having high voltage values. However, the accuracy for the posterior wall was $< 70\%$ when using the optimal AF threshold for the entire map. It was found that this could be improved by an additional 10% by using a specific regional threshold (Figure 5).

In this study, it was found that the areas of frequent low voltage (roof, septum and anterior wall) are coherent with previous studies [12, 13]. Interestingly, the area with the lowest concordances between the SR and AF map, the posterior wall, was also found to have one of the lowest correlations when comparing unipolar verus bipolar maps [15].

The aim of this paper was to investigate the discrepancies between SR and AF mapping and identify if using regional thresholds could improve the accuracy. For many regions, a high correlation was found between the SR and AF maps. Areas with significant discordance, on the other hand, were improved when using a regional threshold. For this study, low voltage defined as SR $< 0.5\,\mathrm{mV}$ was considered as the ground truth since it is currently widely used to identify fibrotic substrate in the atria. However, this may not lead to the optimal AF threshold being found for identifying true areas of fibrotic tissue. Further studies assessing the relationship between the AF voltage map and the MRI may provide a deeper insight regarding the optimal threshold.

5. Conclusion

In this study, the relationship between SR and AF voltage mapping was analysed. In general, areas of high and low voltage were the same in both mapping modalities. Regions with high voltage values in both maps but with greater differences between the maps typically showed a high correlation when identifying LVA. It was found that, using a universal threshold for AF mapping was sufficient for most regions with limited reduction of the accuracy. However, for the posterior wall, using a lower threshold can improve the correlation between the maps. Therefore, substrate targeted for ablation during AF mapping can be more accurately identified on the posterior wall by using a lower threshold.

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