Tracking of Atrial Fibrillation Drivers Based on Propagation Patterns: an In-Silico Study

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Abstract

In some persistent atrial fibrillation (AF) patients, localized drivers may sustain AF and thus could represent possible ablation targets. In this work, we test in silico the feasibility of locating AF drivers from high-density electrode grid catheter mapping. A volumetric 3D atrial model was used to simulate 8 AF episodes driven by a stable reentry around a region of scar tissue (5 left atrium [LA], 3 right atrium [RA]). Sequential mapping in 1s segments was performed with a high-density electrode grid, starting from 20 uniformly distributed regions (12 LA, 8 RA). Conduction velocities estimated for each AF cycle were used to obtain temporal and directional parameters of the propagation. Trajectories of connected activation times were used to detect reentries or radial spread of activations. If no pattern was detected, the electrode array was moved in 5mm steps upstream of the propagation direction. The algorithm obtained accuracy, sensitivity, and precision of 87.2%, 23.4%, and 56.3% for reentries and 87.0%, 8.5%, and 26.8% for radial spread of activations, respectively. Reentries were found in average within 1.52 steps/5 mm from the initial position of the grid. The results indicate that propagation patterns may be sufficient to track localized AF drivers sequentially during high-density mapping.

1. Introduction

Ablation therapy for atrial fibrillation (AF) still has suboptimal rates of success. The current cornerstone of AF ablation, pulmonary vein isolation (PVI), is efficient for paroxysmal patients, but provides progressively worse results for the more persistent cases [1]. In many such patients, the substrate may be too complex for targeted ablation due to the extensive electrophysiological and structural remodeling. At the same time, in some of those patients, the persistence of AF after PVI may be linked to the presence of localized driving mechanisms elsewhere in the atria, which could be valuable ablation targets [1].

Mechanisms such as anatomical and functional reentries, transmural breakthroughs, and ectopic foci have been suggested as possible AF drivers [1]. Previous works applied different signal analysis techniques trying to capture characteristics of these mechanisms, such as phase singularity [2], and dominant frequency [3] analyses. However, ablation strategies focused on targets suggested by such approaches still did not lead to better therapy outcomes [1]. These results may be related to technical limitations, such as low coverage or spatial resolution of existing mapping catheters [4], or to the fact that they do not reflect precisely the locations of driving mechanisms [5].

Regardless of the nature of the underlying mechanism, it is expected that repetitive conduction patterns will propagate from its starting location [6]. These patterns may be summarized as either a radial spread of activations (such as in the case of breakthroughs and foci) or reentries. Detecting such conduction patterns with good spatial resolution may lead to better localization of regions harboring AF drivers and possibly to better ablation targets.

Thus, an efficient strategy to sequentially position high-density catheters and detect conduction patterns associated with driving mechanisms may provide a fast and efficient framework that electrophysiologists could use for extra-pulmonary vein ablation of AF. To better understand how to develop such a strategy, it is relevant to study the relationship between the underlying driving mechanisms, their propagation patterns, and the data measured with the catheters. For this task, atrial computer models are a good experimental environment where the underlying conduction patterns are known and can be analyzed in depth.

In this study, we aimed to locate regions harboring driv-

ing mechanisms of AF with sequential mapping using a high-density electrode grid, based on the typical conduction patterns of reentry and radial spread of activations. We developed a strategy to track and identify such drivers, testing its performance in highly detailed AF simulations.

2. Methods

AF simulations: AF was simulated in a highly detailed volumetric three-dimensional model of the human atria, with electrophysiological properties corresponding to persistent AF patients [7]. Pacing close to a temporary block line (200 ms) generated reentries to initiate the arrhythmia. In each simulation, the atrial substrate was modified to simulate circular scars (10 mm diameter) of inactive tissue permeated by fibrotic paths [7]. The generated reentries were anchored and stabilized by these scars, creating a scenario of a repetitive and localized driving mechanism. Eight 11s simulations were generated, 5 with scars in the left atrium (LA), and 3 in the right atrium (RA). Reentry core positions over time and centers of radial spreads of activations were tracked by phase analysis and by connecting waves on the transmembrane potentials [7], respectively, and used as ground truth for the driver positions.

Tracking AF drivers: AF drivers were tracked using endocardial unipolar signals measured with a 4x4 electrode grid with 3 mm spacing to emulate a realistic clinical scenario. Starting from 20 uniformly spaced positions in both atria (12 in LA and 8 in RA), the electrode grid was used to measure sequential 1s segments of endocardial signals (Figure 1A). Activation times were obtained based on the maximum negative deflection in the electrograms. Differences in activation times were used to calculate the average AF cycle length (CL) and to estimate the conduction velocity (CV) vectors between the grid electrodes [8].

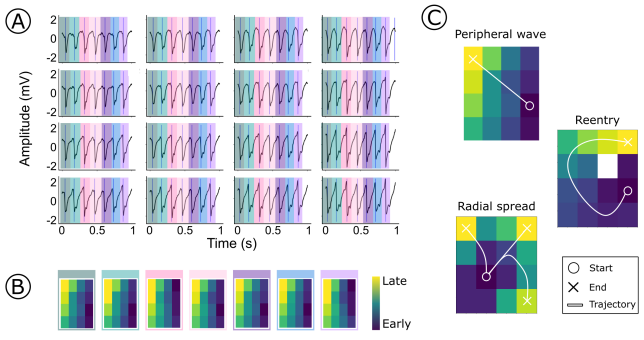

Figure 1. Algorithm for detecting driving mechanisms. Unipolar recordings (A) were divided into individual wavefronts by connecting activation times (B). Trajectories were built from each wavefront and used to detect the presence of driver-related conduction patterns (C)

At each grid position, the activation patterns of individual wavefronts were analyzed to determine if a driving mechanism was present. A wavefront is defined as a group of activation times linked between neighboring electrodes in the grid without conduction blocks (CVs < 0.1 mm/ms, Figure 1B) [8].

In each wavefront, 3 parameters were obtained to represent characteristic conduction patterns of AF drivers. Directional preferentiality was estimated as one minus the variance in angles of the CV vectors, with values ranging between 0 and 1, indicating propagation in all directions or in an uniform direction, respectively. CL coverage was estimated as the percentage of the average AF CL covered by each wavefront [9]. Finally, trajectories were estimated in each wavefront. Trajectories were defined as the paths of faster conduction between the earliest and latest activations in the electrode grid (Figure 1C). A weighted directed graph was used to calculate trajectories, with the inverse of CV values as the edge weights. A curvature score was calculated for each trajectory, defined as the sum of the angles between segments in the trajectory normalized by 2π.

Conduction patterns associated with driving mechanisms were represented by the above-mentioned parameters. A radial spread of activations, corresponding to focal points or transmural breakthroughs, was defined as a wavefront in which at least two trajectories were present, traveling in directions separated by $> 70°$, with short CL coverage (< 0.1) and directional preferentiality lower than 0.7. These thresholds corresponded to the approximate angle between two ideal trajectories traveling from the center to two corners of the grid, fast activation of the electrode grid and a moderate degree of divergence of CV directions, respectively. Radial spread of activations are associated with transmural breakthroughs or focal points. However, in the simulations used in this study, no focal points were present and breakthroughs seldom occurred repeatedly in the same regions, being mostly passive phenomena linked to the driving reentry. Thus, such activation pattern happened most commonly in sites where the the propagation comes from the contra-lateral atrium, at exit points such as the Bachmann bundle, coronary sinus, or the septal region.

Reentries were defined as wavefronts in which the maximum curvature score was > 0.3 with higher CL coverage (> 0.1). These thresholds were chosen so that at least one third of the reentry curvature ($120°$) was within the grid, given its low coverage, and to avoid confusions with radial spread of activation, respectively. If no driving mechanism could be detected, the average direction of all the CV vectors in the interval was used to estimate the preferential direction of propagation, and the electrode grid was dislocated 5 mm upstream of this direction.

The driver detection was limited to the same chamber as the initial position of the grid. The tracking algorithm ran until a reentry or radial spread of activations was located.

The quality of the driver detection was assessed based on the accuracy, sensitivity, and precision of their detection. The number of steps to locate reentries were used to evaluate the performance of the tracking strategy.

3. Results

In all simulations, a stable reentry was present close to the introduced scar regions. In 2 simulations, additional reentries appeared both in the LA and RA, with the original stable reentry occasionally meandering and/or temporarily disappearing. In 84.5% of the scenarios in which the initial placement of the grid and the stable reentry were in the same atrium, the algorithm led to this driver. The driver detection algorithm correctly located a reentry with an accuracy of 87.2% considering both atria. The sensitivity and precision of the detections were 23.4% and 56.3%. Figure 2A gives an example of the tracking algorithm, with positions where a correct (true positive, in yellow) and incorrect detection was made (false negative, in green).

Figure 2B shows the number of steps to correctly locate a reentry and to be in its vicinity (< 10mm, corresponding to regions close to the edges of the electrode grid), based on the initial distance between the starting point and a reentry. The gray dashed line represents the ideal scenario for a perfectly stable reentry and an optimal tracking algorithm, in which each 5 mm step brings the grid center closer to a reentry by the same distance. The other lines represent the obtained number of steps per 5 mm of initial distance. The algorithm required on average 1.52 steps per 5 mm of initial distance to locate correctly a reentry, which represents 8 (IQR: 5/12) repositionings of the electrode grid. The difference between the slope of the lines associated with the reentry detection and with the positioning of the grid on its vicinity highlight the limitation of the spatial coverage of the employed grid and the effectiveness of the tracking algorithm to find the region harboring a reentry.

The overall accuracy for detecting radial spread of activations was 87.0%, with sensitivity and precision of 8.5% and 26.8%, respectively. Most of these detections (88.2%) were in exit points when the driving reentry was localized in the contra-lateral atrium. These should not be interpreted as drivers, but rather as an indicative to continue the mapping in the other chamber.

4. Discussion

In this work, we introduced a strategy to adaptively locating drivers with high-density electrode grids based simply on the conduction patterns that define them. This approach is suitable for locating regions of the atria that will frequently harbor reentries or radial spread of activation, representing possible ablation targets. While we focused on stable reentries scenarios, repetitive drivers may

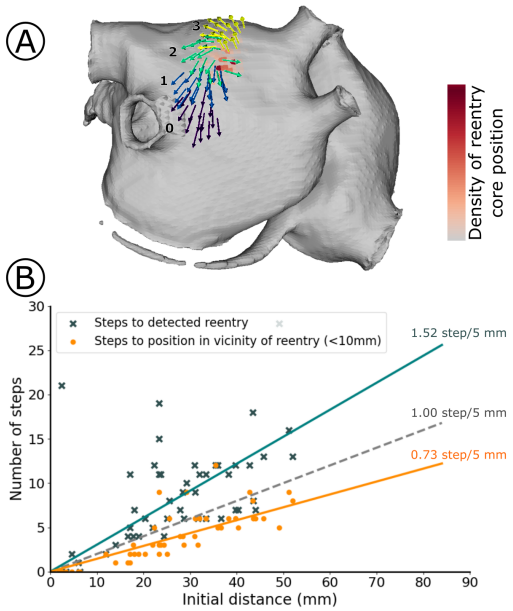

Figure 2. A) Tracking procedure example, with a false negative (green) and a true positive (yellow) reentry detection. B) Number of steps per initial distance from a reentry to locate it (blue) or to be in its vicinity (orange)

be found intermittently in the atria. The proposed strategy may therefore help electrophysiologists to accurately locate the regions where they occur.

Reentries, ectopic foci, and/or transmural breakthroughs may be responsible for maintaining AF in some patients where PVI fails in terminating the arrhythmia. While few studies have observed stable drivers in human AF [1], intermittent repetitive conduction patterns can be expected in localized regions of the atria [6]. Such regions can be ablation targets, but localizing them remains challenging due to technological limitations.

Mapping of AF and localization of eventual driving mechanisms is limited either by the spatial resolution or coverage of the employed catheters. While panoramic mapping catheters may give a better overview of the activation patterns, their lower spatial resolution may lead to false positive detection of drivers, with lower localization precision [4]. Sequential high-density mapping strategies are, on the other hand, limited by the field of view of the catheters, but provide better spatial resolution to determine the regions that may sustain driving mechanisms.

The strategy presented here is a dynamic approach to locating drivers with high-density electrode grids based simply on the conduction patterns that define them, and on the idea that the propagation of the action potentials stems from driving mechanisms. This approach is suitable for locating regions of the atria that will frequently harbor reen-

tries or radial spread of activation, representing possible ablation targets. While the scenarios presented here are of stable reentries, such repetitive drivers may be found intermittently in the atria, and the proposed strategy may help lead electrophysiologists to the regions where they occur.

The low sensitivity for both the detection of reentries and radial spread of activations may be due to the choice of thresholds for their detection. However, the selection of these values explains only partially the obtained results. Changing the threshold values is a trade-off between the sensitivity and precision, since avoiding some false negative outcomes also increased the number of false positives. The accuracy remained similar due to the high number of true negatives detected by the automated algorithm. We hypothesize that the low sensitivities are mainly a consequence of the limited coverage of the electrode grid. In situations in which reentry cores or origins of radial spread of activations are on the edges of the grid, the conduction patterns may appear as peripheral waves that, albeit curved, would not lead to the detection of the mechanism.

While the tracking strategy is efficient to bring the electrode grid to the vicinity of driving mechanisms, their automatic detection is still challenging. Nevertheless, the strategy proposed here could be of value for electrophysiologists during procedure, who may decide to obtain longer recordings and reduce the step distance to move the electrode grid when close to a driving mechanism as indicated by the tracking algorithm. The final decision of potential ablation targets should be a combination of factors evaluated by the electrophysiologist, which can consider the classification proposed here together with additional information e.g. about the underlying substrate.

5. Conclusion

This work presented an algorithm for quickly tracking and detecting rotational and radial patterns of conduction that can be associated with AF drivers, based only on activation time detection and the grid-like structure of the catheter. Improved rules for repositioning the electrode grids or human intervention may make this process even more reliable. The proposed strategy could help inform electrophysiologists and improve the selection of ablation targets for AF beyond PVI.

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