Local Atrial Conduction Velocity During Pacing as Indication of Atrial Fibrillation Substrate Complexity

Frank van Rosmalen[1,3], Laurent Pison[2], Tammo Delhaas[1], Harry J.G.M. Crijns[3], Stef Zeemering[4], Ulrich Schotten[4]

[1]Department of Biomedical Engineering, CARIM, Maastricht University, Maastricht, The Netherlands
[2]Department of Cardiology, Ziekenhuis Oost Limburg, Genk, Belgium
[3]Department of Cardiology, CARIM, Maastricht University Medical Center+, Maastricht, The Netherlands
[4]Department of Physiology, CARIM, Maastricht University, Maastricht, The Netherlands

Abstract

***Background**: Pulmonary vein isolation (PVI) as treatment for atrial fibrillation (AF) is not effective in up to 60% of patients with persistent AF; AF drivers outside of the pulmonary veins can contribute to AF recurrences after PVI. In this study we explored the potential use of local conduction velocity (CV) during pacing as a marker of left atrial (LA) substrate complexity.*

***Methods:** LA activation times were recorded for 7 AF patients during coronary sinus (CS) pacing before PVI using a Pentaray catheter. Activation times were relative to the CS pacing spike. LA activation locations were triangularized to calculate CV: the local direction and speed of the activation wave front. CV was quantified by the total CV distribution.*

***Results:** A mean of 1622 CVs were calculated per patient. Distribution of CVs showed a similar morphology, with median CVs in the range [0.26, 0.36] and interquartile ranges in the range [0.29, 0.39].*

***Conclusion:** This study shows that although it is feasible to calculate CVs based on sequential CARTO mapping of the LA during CS pacing, the resulting distribution of CVs using this procedure is not necessarily able to identify substrate complexity because of the large similarity between distributions and the relatively small differences in medians.*

1. Introduction

Pulmonary vein isolation (PVI) for termination of atrial fibrillation (AF) is not effective in up to 60% of patients with persistent AF.[1] One reason for this low success rate can be AF drivers or re-entry mediated by a complex substrate, like fibrosis, that are located outside of the pulmonary veins (PVs). Since PVI does not focus on atrial tissue outside of the pulmonary vein area, substrate complexity in the LA can contribute to AF recurrences after PVI. The current guidelines offer no ablation options for patients with AF recurrences presenting with isolated PVs.[2] This shows the need for a patient specific ablation approach. An important step towards a patient specific ablation approach is the quantification of substrate complexity. Fibrosis is a strong determinant of atrial conduction disturbances. Differences in local conduction velocity (CV) between patients may indicate different degrees of structural remodeling and might as such be used as a surrogate marker for substrate complexity. In this study we explored the potential use of local conduction velocity during left atrial pacing as a marker of left atrial substrate complexity, by computing 3D maps of LA activation and conduction velocity and comparing local CV distributions between patients.

Table 1. Patient characteristics.

Patient	Sex	Age	Type of AF
1	Male	58	Paroxysmal
2	Female	58	Paroxysmal
3	Female	69	Persistent
4	Male	70	Paroxysmal
5	Female	65	Persistent
6	Male	75	Persistent
7	Female	67	Persistent

2. Methods

2.1. Study population

7 patients (4 female) were included in this study. Patient details are summarized in table 1. Written

informed consent was obtained from every patient and the study protocol was approved by the hospital's ethics committee.

2.2. Mapping procedure

All procedures were performed under general anesthesia. Electroanatomical mapping using the CARTO system was performed before PVI. A 20 electrode, star shaped catheter (PentaRay, Biosense-Webster) was used to obtain a three-dimensional mesh representing the anatomy of the LA, and to collect bipolar electrical signals from the atrial wall. The catheter consisted of 10 bipolar electrodes divided over 5 splines arranged in a star shape, with a 1mm electrode size and an inter electrode distance of 4mm.

A 10-electrode catheter (WEBSTER® CS, Biosense-Webster) was placed in the CS and used for pacing to obtain a stable rhythm during recording of the signals. Pacing was performed on the distal electrodes of the CS catheter with a cycle length of 600ms.

The electrophysiologist aimed to cover the total LA by sequential mapping. Signals were recorded in 2500ms bins and together with the location of their recording stored for offline analysis. Every bin consisted of signals and locations of the mapping catheter electrodes, the signals and location of the CS catheter, and ECG limb lead signals.

2.3. Activation detection

Offline analysis was performed using Matlab 2018a (Mathworks, Natick, MA, USA). All recorded signals were detrended by subtraction of a second order Savitszky-Golay filter with a span of 201 samples. A fifth order, type-II Chebyshev filter was used to filter powerline harmonics.

ECG R-peaks and pacing spikes on the CS signals were detected using a peak finding algorithm, searching for the highest peaks with a minimum spacing of 500ms. Mapping catheter peaks were detected based on a minimal peak-to-peak voltage of 0.4mV. Peaks in the mapping catheter signals from 40ms before until 100ms after the R-peak were blanked.

The CS signal pacing spike was used as a reference for turning mapping catheter activations into local activation times (LAT). In this way, all sequentially recorded beats could be aggregated into one global beat and an LAT map could be constructed.

All LATs were assigned to the closest node on the anatomy mesh. Multiple activations assigned to the same node (including multiple activations in the same 2500ms recording) were averaged after checking for outliers. All projected LATs were compared to all neighbours within a 2mm radius and outliers were removed using Matlabs generalized extreme Studentized deviate test for outliers with a threshold factor of 0.9.

2.4. Conduction velocity calculation

The algorithm to calculate CV in the direction of wavefront propagation based on three-dimensional mapping data was introduced by Kojodjojo et al.[3], and expanded upon by Verma et al.[4]. In short, LATs on the anatomy shell are organized into triangles, and the difference in LATs and the distance over the shell between the triangle points is used to calculate the local velocity vector.

The following constraints were implemented:

- The minimum angle (for all triangle corners) was set to at least 30° to avoid long, stretched triangles.
- The minimum LAT difference between points in the triangle was set to 2ms to exclude the situation where the same activation is registered by multiple electrodes
- The maximum distance between triangle points, measured over the shell, was set to 10mm to ensure the measured CV was indeed a local CV.
- The minimum distance between triangle points, measured over the shell, was set to 1.5mm.
- The minimum CV between points on the triangles was set to 0.2, to avoid measuring over lines of blocked conduction.

LAT and CVs are presented in two ways: histograms showing the distribution of LATs and local CVs, and a LAT and CV map, showing how the LATs and CVs are distributed over the atrium. Based on literature, CVs were considered slow when below 0.2 mm/ms, and high when above 1.5 mm/ms.[5]

3. Results

Results are shown in Figure 1. A median of 3122 (minimum: 2335 maximum: 4881) signals per patient were used to calculate the activation times. Calculated activations follow the expected pattern from the CS region towards the right pulmonary veins in all patients. CV could be calculated for a mean of 1623 (standard deviation: 144) points per patient. All patients showed a CV distributions where most of the calculated CVs were to the left (slow) side of the distribution (median CVs range [0.26, 0.36] and interquartile ranges in the range [0.29, 0.39]).

In all patients we observed regions of low and high CVs. Slow CVs were often localized in clusters near the mitral valve area and near the PV ostia, whereas fast CVs were more often distributed in smaller patches over the left atrium.

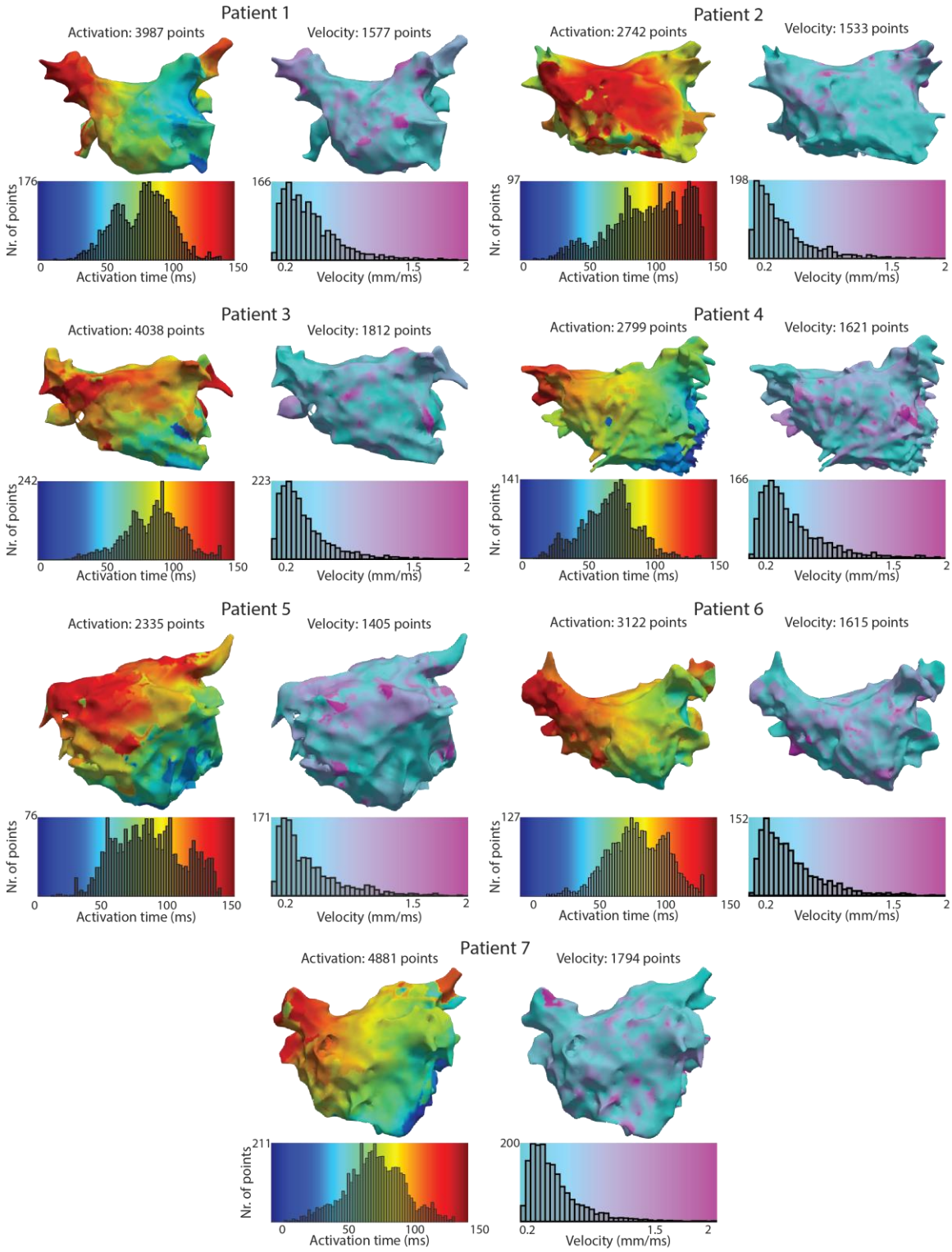

Figure 1. Results of local activation time and conduction velocity calculations for all patients. Top left panel shows the spatial distribution of activation times, using the color scale as indicated by the bottom left panel. The left bottom panel shows the histogram of activations. Top right panel shows the spatial distribution of conduction velocity using the color scale as indicated by the bottom right panel. The bottom right panel shows the histogram of conduction velocities. Note that the Y-axis differs between the histograms to better show the shape of the histogram.

4. Discussion

This study shows that it is feasible to calculate CVs based on sequential CARTO mapping of the left atrium during CS pacing. The resulting distribution of CVs using this method is not necessarily able to identify substrate complexity because of the large similarity between distributions and the relatively small differences in medians.

The median CVs computed in this study fall within the range of CVs found by a similar study using the triangulation technique to find CVs on AF patients using CS pacing ([0.16-0.95 mm/ms]), although this study used data of only 4 patients.[4] In contrast, a study into age related changes in atrial electrophysiology in 15 non-AF patients, using the same techniques, found higher mean CVs ranging from 0.57 to 0.99ms/ms.[3]. All patients in our study however were older AF patients, potentially lowering the observed CV. Moreover, the automated CV calculation method was able to use many more data compared to the previously mentioned studies, leading to a CV estimate that is more representative of the distribution of the CV over the whole left atrium.

Zones of slow CV are seen mostly around the mitral valve area and near the PV ostia. The mitral valve area is known to contain more fibrous tissue, which can explain the slow CVs in this area. The slow CVs near the PV ostia can be caused by erroneously assignment of LATs. Because the mesh shape is less regular around the PV ostia, an activation belonging to (for instance) the anterior part of the ostium can be projected on the posterior part. This can lead to a triangle with a long delay over a short distance, resulting in a low conduction velocity.

The CV distributions are dominated by slow CVs, potentially caused by measurements on the mitral valve area and erroneous assignment of LATs in the PV ostiumarea. This slow CV dominance might hide details in the medium- to fast CV part of the distribution. Although medium- to fast CV areas are still visible on the CV map, for AF substrate complexity quantification it would be preferable to be able to detect CV anomalies in the distribution. In future work, the PVs and mitral valve area can be excluded from the analysis, as the goal of the method is to quantify substrate outside of the PVs.

This study only looked at CV distribution without a priori knowledge of the existence of fibrosis in the atria. In future work we aim to study CV distribution in combination with late gadolinium enhancement cardiovascular magnetic resonance imaging, voltage mapping or fractionation mapping to co-localize the identified regions with aberrant CVs to sites with indications for structural remodeling.

References

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Address for correspondence:

Frank van Rosmalen
P.O. Box 616
6200 MD Maastricht
The Netherlands
f.vanrosmalen@maastrichtuniversity.nl