Characterization of Conduction Velocity From Intracavitary Electrical Recordings During Atrial Fibrillation

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Abstract

Regional characterization of the atrial substrate using biomarkers like conduction velocity (CV) could improve understanding of atrial fibrillation (AF) mechanisms in each patient and enhance ablation strategies.

A technique for measuring CV in endocardial recordings was developed based on multiple approaches. To ensure robustness, two signal preprocessing techniques were combined with two strategies for detecting delays between signals (by identifying activations and using cross-correlation) for each trio of nearby electrodes. An acceptance criterion for the measurements was established based on consistency.

The CV measurement technique was applied to 64-channel atrial electrograms from 12 patients (70 ± 5 y.o.) during AF. Velocity measurements were obtained with median 336 mm/s [IQR 248 - 438 mm/s]. In addition, different velocity distributions were obtained for each patient, ranging from 291 mm/s to 441 mm/s, with regional variations. We compared the CV results of patients grouped according to different clinical characteristics and found that, among other results, patients with a longer duration of AF had a lower CV, while those without posterior AF recurrence had an increased CV.

This technique will enable personalized atrial substrate characterization, improving ablation procedure guidance.

1. Introduction

The specific mechanisms of initiation and maintenance of atrial fibrillation (AF) are still not fully understood, causing ablation procedures to have suboptimal results.

Alteration of the atrial substrate in terms of conduction velocity and action potential duration, which is accentuated with disease progression, is associated with AF mechanisms. Therefore, a better understanding of the pathophysiology of AF requires analysis and characterization of regional biomarkers that can help to better guide ablation procedures.

Conduction velocity (CV), or action potential wavefront propagation velocity, is a regional parameter, which varies spatially and depends on tissue conditions. As AF progresses, electrical remodeling leads to a global decrease in CV, just as fibrotic infiltration causes a local reduction in velocity [1]. Regional CV is an electrophysiological parameter that can be important for diagnosis and ablation planning. It has been observed that in arrhythmic areas during AF, the CV is reduced, and these areas of decreased CV can harbor functional reentries or rotors. These regions are target areas for ablation, especially in cases where pulmonary vein isolation fails to terminate AF. Additionally, a difference in CV between two regions can lead to chaotic wavefront propagation.

Several authors have developed in-vivo CV measurement techniques from endocardial recordings based on different approaches such as polynomial fitting [2], cosine fitting [3] or even, techniques that consider electrode deformation [4]. Most of these studies have measured CV in patients in sinus rhythm or during pacing. However, it has been reported that during AF episodes the CV is lower and may have different distributions [5], so a method to assess CV during AF is needed.

The chaotic activity that occurs during AF and wavefront collisions make CV estimation under these conditions complex. This work presents a new method to increase the robustness of CV measurements in intracardiac signals by combining multiple approaches.

2. Materials and Methods

2.1. Intracavitary signals

Left atrial (LA) intracavitary recordings during AF episodes of 60 s and 64 channels from 12 patients (7 men, 70 ± 5 y.o.) obtained at Stanford Hospital (CA, USA) during ablation procedures were used. For each signal the electrode location was also available.

To eliminate ventricular interference of the signals, QRS complexes were detected and canceled. In addition, to clean the atrial signals from artifacts, they were preprocessed using two different techniques: 45 Hz low pass filter to remove high frequency noise and 2 - 20 Hz band pass filter to keep only the spectral band in which the

atrial activity has higher power [6].

2.2. Measurement of conduction velocity

CV was measured in each activation in sets of 3 signals grouped according to the proximity of their recording electrodes, and only groups with an inter-electrode distance of less than 15 mm any pair of electrodes were taken into account. From the calculation of relative differences in activation time between the 3 signals, the conduction in the vicinity of the electrodes was approximated to a plane wave and the CV in the direction of propagation was calculated (Figure 1).

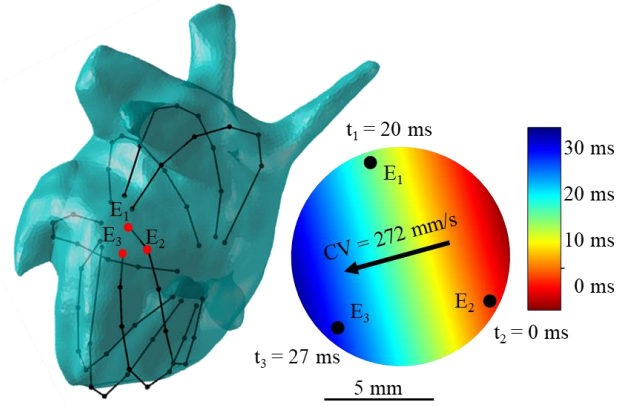

Figure 1. Location of the 64 measurement electrodes inside left atrium and example of CV calculation in a group of 3 electrodes based on the delay between their activations.

For each group of electrodes, 4 CV measurements were obtained at each activation, combining the two signal preprocessing techniques and two methods of detecting delay in activation time between them. The first one consists of obtaining the instant of activation of each signal from the classical method of detecting the maximum in the time derivative of the potential (Figure 2a). The second approach measures the delay between the signals as the time lag that maximizes their cross-correlation, calculated in windows of size equal to their cycle length (Figure 2b). To ensure the robustness of the measurements, an acceptance criterion was added based on the consistency of the results obtained with the different methods. CV measurements were accepted if the samples obtained at the same location with the 4 approaches and during the 60 s of recording were within a clinically realistic range (150 to 1500 mm/s) and at least 40% of them were within ± 150 mm/s with respect to their median. Two examples of application of this criterion are shown in Figure 3, in panel a the measurements were accepted and in panel b they were rejected.

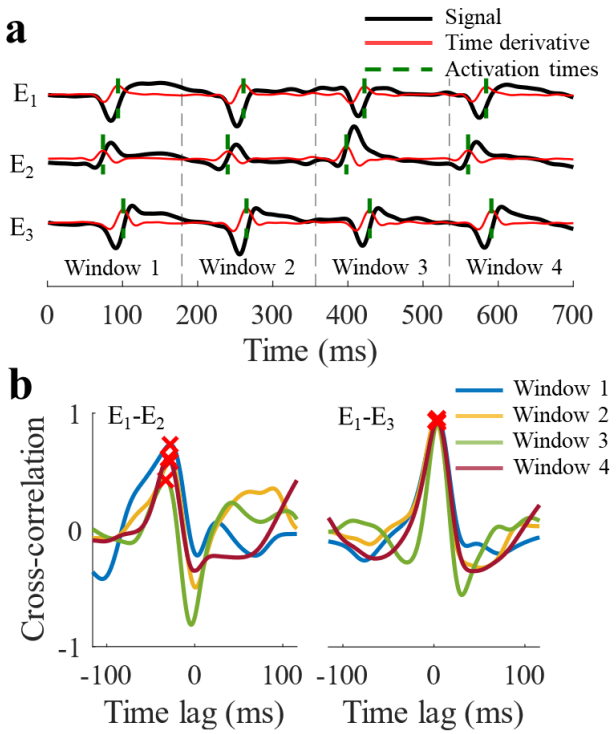

Figure 2. Example of calculation of relative differences in activation times between 3 signals during 4 activations a) detecting the maximum in the time derivative (green dashed lines) and b) from the maximum cross-correlation.

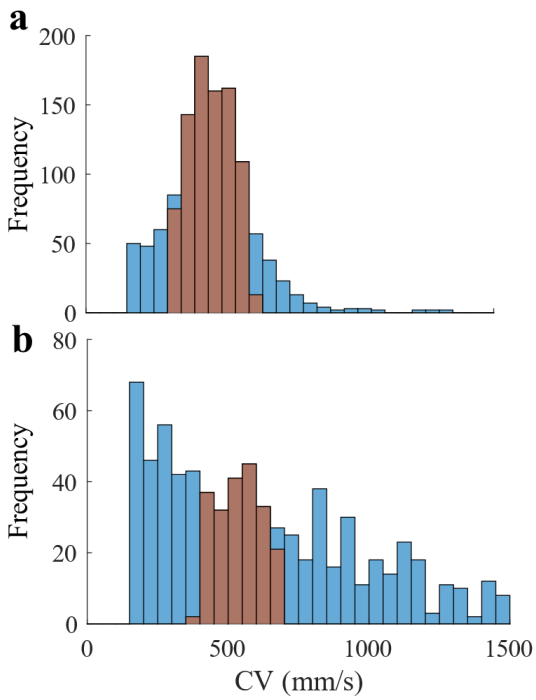

Figure 3. Example of the acceptance criteria of CV measurements. Blue: histogram of all CV measurements; orange: CV measurements at median ± 150 mm/s. The measurements were accepted in a) and rejected in b).

3. Results

From the intracavitary recordings of the 12 AF patients, CV measurements were obtained with median 336 mm/s [IQR 248 - 438 mm/s]. A different range of CV values was obtained for each subject, allowing differentiation between slower and faster atrial fibrillation phenotypes (Figure 4a). The lowest velocity value was obtained for patient 10 (P10) with a median of 291 mm/s [IQR 226 - 381 mm/s] and the highest for patient 1 (P1) with a median of 441 mm/s [IQR 326 - 595 mm/s]. In addition, for each patient, CV measurements were performed for 21 to 56 regions according to the electrode position, with 43 ± 15% of them exceeding the acceptance criteria. Thus, heterogeneous velocity distributions in space were obtained. In the case of patient 5, velocity measurements were accepted in 17 different regions and measurements ranging from 179 mm/s [IQR 164 - 245 mm/s] in the slowest region (R1, corresponding to the right pulmonary veins) to 882 mm/s [IQR 820 - 995 mm/s] in the fastest (R3, corresponding to the posterior wall) were obtained (Figure 4b).

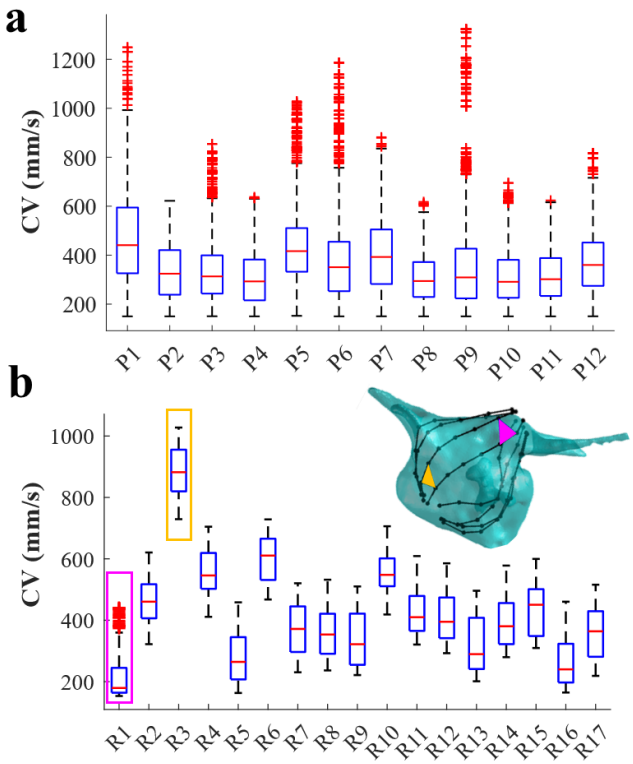

Figure 4. CV measurement. a) Distribution along 12 patients grouping all electrode sets. b) Distribution along 17 regions of patient P5 (pink: slowest CV region; yellow: fastest)

To analyze the variation in CV according to the clinical profile of the patients, CV values obtained were compared according to different pathological and therapeutic characteristics of the patients studied (Figure 5).

Patients differed little, in terms of CV, by classic markers such as type of AF, as patients with persistent or long-term AF presented slightly higher values than patients with paroxysmal AF (347 vs 324 mm/s, p<0.001). However, notable differences were seen by the duration of the pathology. It was obtained that patients with more than 1000 days of AF presented a decreased CV with respect to patients with short-duration AF (315 vs 354 mm/s, p<0.001), although, in relation to the procedure and therapy applied to the patients, it was obtained that in patients with previous ablation, notably higher CVs were measured with respect to de-novo ablations (365 vs 317 mm/s, p<0.001). Finally, it was observed that the CV measured in these patients was linked to the long-term success of therapy, since patients without AF recurrence after the blanking period presented a slightly higher CV than recurrent patients (336 vs 318 mm/s, p<0.001).

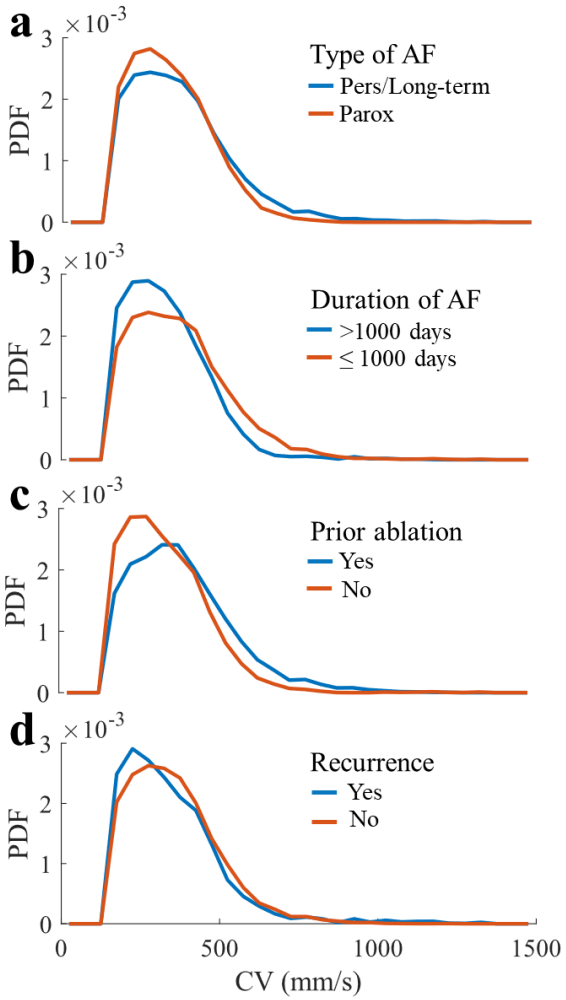

Figure 5. Comparison of CV distributions measured in patients stratified according to a) type of AF, b) duration of AF, c) existence of previous ablation, and d) recurrence after the blanking period.

4. Discussion and Conclusions

In this study it was developed a new method for measuring CV from endocardial recordings applied to 12 patients during AF. The multiple-approach methodology provides robustness to the measurements obtained, which are only accepted if there is consistency between the results obtained by the different methods. Local CV measurements have been obtained in regions with distances of less than 15 mm defined by the position of the electrodes. In this way, it is possible to regionally characterize each area of the atrium and to locate potentially proarrhythmic areas and, therefore, targets for ablation.

In addition, different velocity profiles have been obtained for each patient analyzed. The CV measurements obtained in each patient from their electrograms can be used to develop Digital Twins that reproduce not only the patient's anatomy, but also the propagation velocity of the wavefronts. In this way, it will be possible to test with a greater degree of personalization the therapies applied or to predict the outcome of the interventions.

Since clinical data on the patients were also available, it was possible to compare the distributions of velocity measurements according to different markers, taking into account the degree of disease and the therapies received by the patients. In patients with long-standing AF (> 1000 days), the lower CV is because the processes of remodeling and fibrosis generation are at a more advanced stage [7]. On the other hand, pretreatment with a previous ablation procedure increased the CV of patients. This could be since the application of this therapy manages to slow down the progression of the disease by slowing down the remodeling processes.

In this study, the CV measurement technique was applied to electrograms recorded in the left atrium, since its relevance in the maintenance of AF is known. However, it is necessary to consider recordings from both atria to validate the measurement technique. In addition, CV has been measured in recordings from 12 AF patients. This work needs to be extended to a larger number of patients to validate and generalize the results obtained.

The technique for robust measurements of CV during AF developed in this work may help to improve guidance models for ablation procedures by including patient-specific characterization of the substrate, which may increase the success of therapies compared to classical stratification.

Acknowledgments

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References

[1] T. Itoh, M. Kimura, S. Sasaki, S. Owada et al., "High correlation of estimated local conduction velocity with natural logarithm of bipolar electrogram amplitude in the reentry circuit of atrial flutter," *Journal of Cardiovascular Electrophysiology*, vol. 25, no. 4, pp. 387-394, April, 2014.

[2] A. R. Barnette, P.V. Bayly, S. Zhang, G.P. Walcott et al., "Estimation of 3-D conduction velocity vector fields from cardiac mapping data," *IEEE Transactions on Biomedical Engineering*, vol. 47, no. 8, pp. 1027-1035, August, 2000.

[3] F. M. Weber, A. Luik, C. Schilling, G. Seemann et al., "Conduction velocity restitution of the human atrium - an efficient measurement protocol for clinical electrophysiological studies," *IEEE Transactions on Bio-medical Engineering*, vol. 58, no. 9, pp. 2648-2655, September, 2011.

[4] B. Verman, T. Oesterlein, A. Loewe, A. Luik et al., "Regional conduction velocity calculation from clinical multichannel electrograms in human atria," *Computers in Biology and Medicine*, vol. 92, pp. 188-196, January, 2018.

[5] K. T. Konings, C.J. Kirchhof, J. R. Smeets, H. J. Wellens, et al., "High-density mapping of electrically induced atrial fibrillation in humans," *Circulation*, vol. 89, no. 4, pp. 1665-1680, April, 1994.

[6] I. Romero, E.Fleck and C. Kriatselis, "Frequency analysis of atrial fibrillation surface and intracardiac electrograms during pulmonary vein isolation," *Europace: Journal of the Working Groups on Cardiac Pacing, Arrhythmias, and Cardiac Cellular Electrophysiology of the European Society of Cardiology*, vol. 13, no. 9, pp. 1340-1345, September, 2011.

[7] J. Jalife and K. Kaur, "Atrial remodeling, fibrosis, and atrial fibrillation," *Trends in Cardiovascular Medicine*, vol. 25, no. 6, pp. 475-484, August, 2015.

[8] G. Tacoy, M.K. Akboga, C. Yayla, A. Akyel et al., "The effect of statin treatment on P-wave characteristics and atrial conduction time," *Kardiol Pol*, vol. 73, no. 9, pp. 747-452, May, 2019.

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