Stability of Conduction Patterns in Persistent Atrial Fibrillation

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Abstract

There is a growing interest and practice of guidance of catheter ablation of atrial fibrillation (AF) by specific conduction patterns (rotors, point sources, regions of conduction slowing). Temporal stability of conduction patterns in AF has not been studied in detail.

Saventeen patients were enrolled for de novo mapping and ablation of persistent AF. Prior to pulmonary vein isolation, left atrial (LA) high density maps were collected using a 20 polar circular catheter. Conduction pattern stability was assessed using Mean Phase Coherence (MPC) of atrial electrograms. Stability was defined as the presence of several consecutive conduction patterns correlated with MPC>0.85 tolerance which constituted an individual stable pattern (SP).

LA surface coverage by SP and percentage of the time SP were present strongly depends on SP definition. For SP defined as a train of at least 3 consecutive activations, SP were found on 82% of mapped LA surface and were present 26% of the mapping time. However, if SP is defined as a train of at least 20 similar activations, the coverage drops to 15% and time SP was present to 6.5%.

In conclusion, conduction patterns during AF are short lasting. Long recordings should be analyzed before deciding on the ablation target based on specific conduction pattern.

1. Introduction

Although pulmonary vein isolation (PVI) is regarded as the cornerstone of ablation in paroxysmal AF, the optimal approach to catheter ablation of persistent atrial fibrillation (persAF) is yet to be resolved [1]. Current guidelines recommended consideration being given to more extensive linear or complex fractionated electrogram ablation, however, a series of recent randomized controlled trials have failed to demonstrate additional clinical benefit with the application of these empirically derived approaches beyond PVI [2, 3].

In this context, there is a significant interest in the development of novel approaches based on the contemporary understanding of fibrillatory dynamics to improve clinical outcomes of persAF ablation [4]. The most prominent example is the ablation targeting rotors using contact [5, 6] or non-invasive mapping approach [7]

Stability of electrical activity during AF was mainly explored in the context of electrogram fractionation [8], frequency mapping [9] or direction of wave propagation [10]. Stability of rotors mapped using basket catheter has been demonstrated in [11]. However, the findings have not been confirmed by other groups and contrasts studies on rotors stability assessed by high-density epicardial mapping [12, 13] and using body surface potential mapping [7] (all studies demonstrating short-lasting rotors).

In this study, we aimed to address the question of the stability of conduction patterns in AF. Due to a controversy regarding valid interpretation of specific conduction patterns (e.g. whether phase singularity is a rotor or an artifact related with the line of conduction block), we did not focus on specific patterns but rather looked at the stability of conduction in general.

2. Methods

2.1. Study population

The study group included 17 patients (mean age 59±9 years; 12 male) undergoing catheter ablation for persistent AF at the University Heart Center in Hamburg. Antiarrhythmic drugs, with the exception of amiodarone, were ceased at least 5 half-lives before the procedure. The study was approved by the institutional ethical committee, and all patients gave written informed consent.

2.2. Electroanatomical Mapping

Local electrograms were recorded using the circular, 20 pole mapping catheter prior to pulmonary vein isolation. The catheter was positioned at multiple sites aiming for complete coverage of the LA. A minimum of 8 s recording time was required at each site with maximum

catheter stability and tissue contact (see Figure 1). Sites with a minimum 6 simultaneously recorded electrograms with clearly visible local deflections were included in analysis.



Figure 1 Electroanatomical map of left atrium (LA). Dark dots represent data points with recorded local electrograms of 8 s duration.

2.3. Calculation of electrogram phase

Electrograms phase of was obtained using a concept of sinusoidal recomposition [14] followed by Hilbert transform. Phase of the electrogram was defined as:

$$\varphi(t) = \arctan\left(\frac{-u(t)}{H(u)(t)}\right) \tag{1}$$

where u(t) is a recomposed electrogram and H(u)(t) is a recomposed electrogram after application of Hilbert transform.

2.4. Estimation of the conduction stability

Conduction pattern stability was assessed using Mean Phase Coherence (MPC, [15]) of atrial electrograms. MPC between two consecutive local activations is defined as:

$$MPC(T_1, T_2) = \frac{1}{N} \sum_{d=1}^{N} e^{j(\varphi_d(T_1) - \varphi_d(T_2))}$$
 (2)

where T_l is the timing of the first local activation, T_2 is the timing of the following activation, N is the number of electrograms simultaneously collected at the given site, $\varphi_d(T_l)$ is the phase of the electrogram d at time T_1 and $\varphi_d(T_2)$ is the phase of the electrogram d at time T_2 . In a case both electrograms have identical phase at both times $(T_1$ and $T_2)$, MPC is equal to one. In case of uncorrelated timings electrical activity between both activations, MPC will be close to zero.

Stability was defined as the presence of several consecutive conduction patterns (defined by the parameter D) when all pairs of consecutive activations are correlated with MPC>0.85 tolerance (see Figure 2 for an example). Such set of activations constitutes an individual stable pattern (SP). Two parameters were investigated:

the coverage of the chamber by SP and percentage of the time SP were present.

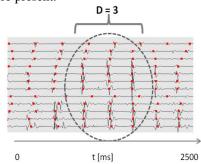


Figure 2 Example of Stable Pattern (SP) consisting of 3 consecutive activations correlated with MPC>0.85.

MPC threshold was determined arbitrarily by experienced electrophysiologist asked to identify at which MPC value the visual perception of electrogram stability is lost. resulting in value of 0.85 (see Figure 3).

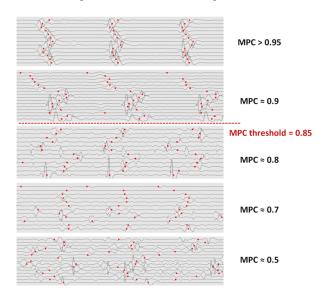


Figure 3 Example trains of activations with varying degree of coherence. Such sets were used to set define MPC threshold defining stable and unstable patterns.

3. Results

3.1. Baseline parameters

Mapping was performed successfully in all 15 cases. On average, 322±103 data points were collected for each patient. Mean AF cycle length measured at Left Atrial Appendage was 188±28 ms.

3.2. Stability analysis for D=3

Histogram of stable patterns (SP) durations for D=3

(that is, at least 3 consecutive activations form SP) is shown in Figure 4. The majority (98.2%) of SP had shorter duration than 8 s. Remaining SP (1.8%) had duration > 8 s which was not possible to determine due to a limited recorded electrogram duration. SP were found on 82% of the mapped LA surface. In total, SP were present 26% of the time.

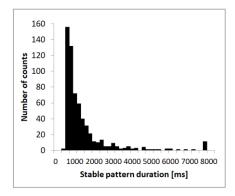


Figure 4 Histogram of identified Stable Patterns (SP) durations in case SP is defined as a train of at least 3 consecutive activations (D=3).

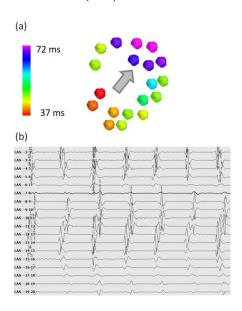
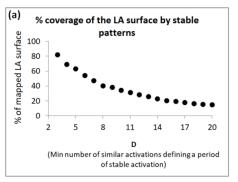


Figure 5 Example activation times in case of SP of duration > 8 s (a). Corresponding bipolar electrograms (b).

Out of 11 SP with duration > 8 s, only 7 were of sufficient electrogram quality for local activation time annotation. 6 out of 7 demonstrated 'passing wave' activation pattern: that is a progressive change of local activation times consistent with a singular wave passing through the mapping field (see Figure 5). In one case, the conduction pattern resembled a conduction block (65 ms time difference over the distance of roughly 1 cm).

3.3. Effect of D on stability assessment

LA surface coverage by SP and the percentage of the time SP was present depended on SP definition, decreasing with the increasing value of parameter D. For D=3, SP were found on 82% of mapped LA surface and were present 26% of the time. However, if SP is defined as a train of at least 20 activations (D=20), the coverage drops to 15% and time SP was present to 6.5% (see Figure 6).



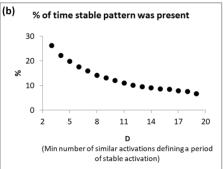


Figure 6 Percentage coverage of the LA surface by periods of stable conduction in a function of D (a). Percentage of the time stable pattern was present in a function of D (b).

4. Discussion

The main finding of this study is a poor stability of the majority (98.2%) of conduction patterns during AF. Due to a limited recording durations we can't be sure whether stable patterns of 8 s duration are not in fact stable in longer time scale. The answer to this question requires recording longer time segments during mapping.

The second important finding of this study is the sensitivity of the stability analysis on parameters used in the definition of stable conduction pattern. The definition of stability is important due to two reasons: (i) stable conduction patterns become targets in various AF catheter ablation techniques. Since time during procedure is scarce, there is a tendency to use short time segments to confirm pattern stability. Our analysis suggest that in

order to avoid false identification of SP, recording of >8 s should be used for such confirmation. Further studies are required to investigate this matter based on longer recordings. (ii) mechanistic aspect. Specific SP are interpreted as the drivers of AF (e.g. rotors, point sources of activity). Therefore, conclusions regarding general AF mechanisms strongly depend on the conduction patterns stability. Unless the driver pattern is by definition unstable in space (e.g. meandering spiral wave), it is expected this pattern to be stable in very long time frames and proper assessment of stability is crucial.

In conclusion, our findings suggest that analysis of conduction patterns stability during AF is strongly dependent on the analysis method and as such, should be quantified to allow reproduction and assessment of the criteria used to define stability.

5. Limitations

The study has following limitations: (i) arbitrary threshold defining stable conduction pattern (MPC=0.85). This parameter had to be defined based on expert opinion since the concept of stability is not a well defined property in context of electrical activity during AF. (ii) Recordings were limited to 8 s. This limitation is inherent to NavX mapping system used to collect the data allowing maximum of 8 s recordings to be collected during high-density mapping. (iii) Annotation of local deflections was challenging due to frequent occurrence of double potential and fractionation - thus, the interpretation of identified conduction patterns is rather arbitrary and should be confirmed in future studies using high density mapping.

References

- [1] A. Verma, C. Y. Jiang, T. R. Betts, J. Chen, I. Deisenhofer, R. Mantovan, *et al.*, "Approaches to catheter ablation for persistent atrial fibrillation," *N Engl J Med*, vol. 372, pp. 1812-22, May 7 2015.
- [2] J. Vogler, S. Willems, A. Sultan, D. Schreiber, J. Luker, H. Servatius, et al., "Pulmonary Vein Isolation Versus Defragmentation: The CHASE-AF Clinical Trial," J Am Coll Cardiol, vol. 66, pp. 2743-52, Dec 22 2015.
- [3] A. Verma, P. Sanders, J. Champagne, L. Macle, G. M. Nair, H. Calkins, *et al.*, "Selective Complex Fractionated Atrial Electrograms Targeting for Atrial Fibrillation Study (SELECT AF): A Multicenter, Randomized Trial," *Circulation. Arrhythmia and electrophysiology*, vol. 7, pp. 55-62, Feb 1 2014.
- [4] U. Schotten, S. Verheule, P. Kirchhof, and A. Goette, "Pathophysiological Mechanisms of Atrial Fibrillation: A Translational Appraisal," *Physiological Reviews*, vol. 91, pp. 265-325, Jan 2011.
- [5] S. M. Narayan, D. E. Krummen, and W. J. Rappel, "Clinical mapping approach to diagnose electrical rotors and focal impulse sources for human atrial

- fibrillation," *J Cardiovasc Electrophysiol*, vol. 23, pp. 447-54, May 2012.
- [6] A. S. Jadidi, H. Lehrmann, C. Keyl, J. Sorrel, V. Markstein, J. Minners, et al., "Ablation of Persistent Atrial Fibrillation Targeting Low-Voltage Areas With Selective Activation Characteristics," Circ Arrhythm Electrophysiol, vol. 9, Mar 2016.
- [7] M. Haissaguerre, M. Hocini, A. Denis, A. J. Shah, Y. Komatsu, S. Yamashita, *et al.*, "Driver domains in persistent atrial fibrillation," *Circulation*, vol. 130, pp. 530-8, Aug 12 2014.
- [8] D. H. Lau, B. Maesen, S. Zeemering, S. Verheule, H. J. Crijns, and U. Schotten, "Stability of complex fractionated atrial electrograms: a systematic review," J Cardiovasc Electrophysiol, vol. 23, pp. 980-7, Sep 2012
- [9] R. B. Schuessler, M. W. Kay, S. J. Melby, B. H. Branham, J. P. Boineau, and R. J. Damiano, Jr., "Spatial and temporal stability of the dominant frequency of activation in human atrial fibrillation," *J Electrocardiol*, vol. 39, pp. S7-12, Oct 2006.
- [10] E. P. Gerstenfeld, A. V. Sahakian, and S. Swiryn, "Evidence for transient linking of atrial excitation during atrial fibrillation in humans," *Circulation*, vol. 86, pp. 375-82, Aug 1992.
- [11] V. Swarup, T. Baykaner, A. Rostamian, J. Daubert, J. Hummel, D. E. Krummen, *et al.*, "Stability of Rotors and Focal Sources for Human Atrial Fibrillation: Focal Impulse and Rotor Mapping (FIRM) of AF Sources and Fibrillatory Conduction," *J Cardiovasc Electrophysiol*, Sep 26 2014.
- [12] P. Kuklik, S. Zeemering, A. van Hunnik, B. Maesen, L. Pison, D. Lau, et al., "Identification of Rotors during Human Atrial Fibrillation using Contact Mapping and Phase Singularity Detection: Technical Considerations," *IEEE Trans Biomed Eng*, Apr 15 2016.
- [13] T. E. Walters, G. Lee, G. Morris, S. Spence, M. Larobina, V. Atkinson, *et al.*, "Temporal Stability of Rotors and Atrial Activation Patterns in Persistent Human Atrial FibrillationA High-Density Epicardial Mapping Study of Prolonged Recordings," *JACC: Clinical Electrophysiology*, vol. 1, pp. 14-24, 2015.
- [14] P. Kuklik, S. Zeemering, B. Maesen, J. Maessen, H. Crijns, S. Verheule, *et al.*, "Reconstruction of instantaneous phase of unipolar atrial contact electrogram using a concept of sinusoidal recomposition and Hilbert transform," *IEEE Trans Biomed Eng*, Aug 20 2014.
- [15] F. Mormann, K. Lehnertz, P. David, and C. E. Elger, "Mean phase coherence as a measure for phase synchronization and its application to the EEG of epilepsy patients," *Physica D*, vol. 144, pp. 358-369, Oct 1 2000.

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