Available online at www.sciencedirect.com

ScienceDirect

Journal of Electrocardiology xx (2017) xxx – xxx

JOURNAL OF Electrocardiology

www.jecgonline.com

Impact of number of co-existing rotors and inter-electrode distance on accuracy of rotor localization☆,☆☆

Konstantinos N. Aronis, MD,[a] Hiroshi Ashikaga, MD, PhD[a,b,*]

[a] Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD, United States
[b] Department of Biomedical Engineering, Johns Hopkins University School of Medicine, Baltimore, MD, United States

Abstract

Background: Conflicting evidence exists on the efficacy of focal impulse and rotor modulation on atrial fibrillation ablation. A potential explanation is inaccurate rotor localization from multiple rotors coexistence and a relatively large (9–11 mm) inter-electrode distance (IED) of the multi-electrode basket catheter.

Methods and results: We studied a numerical model of cardiac action potential to reproduce one through seven rotors in a two-dimensional lattice. We estimated rotor location using phase singularity, Shannon entropy and dominant frequency. We then spatially downsampled the time series to create IEDs of 2–30 mm. The error of rotor localization was measured with reference to the dynamics of phase singularity at the original spatial resolution (IED = 1 mm). IED has a significant impact on the error using all the methods. When only one rotor is present, the error increases exponentially as a function of IED. At the clinical IED of 10 mm, the error is 3.8 mm (phase singularity), 3.7 mm (dominant frequency), and 11.8 mm (Shannon entropy). When there are more than one rotors, the error of rotor localization increases 10-fold. The error based on the phase singularity method at the clinical IED of 10 mm ranges from 30.0 mm (two rotors) to 96.1 mm (five rotors).

Conclusions: The magnitude of error of rotor localization using a clinically available basket catheter, in the presence of multiple rotors might be high enough to impact the accuracy of targeting during AF ablation. Improvement of catheter design and development of high-density mapping catheters may improve clinical outcomes of FIRM-guided AF ablation.

Keywords: Atrial fibrillation; Spiral wave; Rotor; Mapping; Computational model

Introduction

Spiral waves have been proposed to be drivers of atrial fibrillation (AF) [1,2], polymorphic ventricular tachycardia (VT) [3], and ventricular fibrillation (VF) [2,4]. Spiral waves result from an intrinsic property of the myocardium as a continuous, excitable system, to sustain high-frequency vortices in two dimensions (2-D), or vortex filaments in three dimensions (3-D) that are triggered by electrical stimuli during the vulnerable period [5]. The '*rotor*' of a spiral wave is a rotation center from which a 2-D spiral wave of excitation rotates outward. The dynamics of rotors are determined by complex interactions between multiple factors, including ionic currents [6], action potential duration restitution properties, conduction velocity restitution properties, wavefront curvature of spiral waves, heterogeneity and anisotropy of the media, and coexisting rotors [7,8].

Rotor mapping and targeting using focal impulse and rotor modulation (FIRM) is one of the most well-studied approaches to catheter ablation of persistent AF [9] and VF [10]. Several mechanisms have been proposed as to how focal ablation of the rotor region results in AF termination [11]. However, clinical evidence is conflicting. Early clinical trials of rotor mapping in AF ablation showed promising results [9,12,13]. The results of early clinical trials, have not been replicated in recent studies [14–17]. In addition, there is no spatial correlation between rotors identified clinically and the underlying myocardial scar tissue [18,19]. One potential explanation to account for the apparent contradiction is an error associated with spatial localization of rotors using currently available mapping technologies. Another potential

☆ Funding: This work was supported by NIH T32 training grant (5T32HL007227–42) (to K.N.A.) the W.W. Smith Charitable Trust (to H.A.), the Johns Hopkins University Institute of Clinical and Translational Research (to H.A.), and the Fondation Leducq Transatlantic Network of Excellence (to H.A.).

☆☆ Disclosures: The authors have no conflict of interest to disclose.

* Corresponding author at: Cardiac Arrhythmia Service, Johns Hopkins University School of Medicine, 600 N. Wolfe Street, Carnegie 568, Baltimore, MD 21287, United States.

E-mail address: hashika1@jhmi.edu (H. Ashikaga).

https://doi.org/10.1016/j.jelectrocard.2017.08.032
0022-0736/

explanation is that human AF is sustained by electrical activation of different cycle lengths emanating from foci and breakthrough sites [20–22].

The standard methods to identify rotors include phase mapping [2], dominant frequency [23], and Shannon entropy [24,25]. In phase mapping, the electrograms in each region are mapped to a phase from -π to +π, and a rotor can be defined as a phase singularity [26] around which the phase progresses through a complete cycle from -π to +π [27]. A stationary rotor trajectory called a '*core*' of spiral waves can also be localized as the region with the highest frequency of the electrogram called dominant frequency (DF), caused by the small path length of the rotor trajectory [1,23]. The Shannon entropy [28] of the electrogram localizes the core of spiral waves by quantifying the probability distribution of electrographic amplitudes [24]. These methods allow accurate detection of rotors in experimental (*e.g.* optical mapping) and simulation settings (*e.g.* finite element modeling) but require high spatial resolution. In contrast, the multi-electrode catheters used clinically to detect rotors have limited spatial resolution with an inter-electrode distance (IED) of 9–11 mm, which is considerably larger than the wavefront width (1–3 mm) [29,30]. Therefore, the representation of equiphase lines in phase mapping requires extensive interpolation to cover the large unexplored areas. This could erroneously join spatial points that are excited at the same time by phase mapping but actually belong to different wavefronts. In addition, interpolated equiphase lines may connect spatial points that have the same instantaneous phase value, but could belong to completely different equiphase lines.

In this study, we evaluated the impact of IED on the accuracy of rotor localization using standard methods, including phase singularity, dominant frequency and Shannon entropy in a numerical model of cardiac tissue. We tested the hypothesis that an error associated with spatial localization of the rotor or the rotor trajectory (core) increases with increasing IED, and this increase is larger when more than one rotors are present.

Materials and methods

Please refer to the *Supplemental Methods* section in the *Supplemental Material* for detailed methods. We performed data analysis using MATLAB R2017a (MathWorks Inc., Natick, MA).

Simulation of spiral waves

We simulated a system of a 2-D 12 × 12 cm^2 isotropic lattice of cardiac tissue using the Rogers-McCulloch model to represent cardiac action potential. The Rogers-McCulloch model accurately reproduces several important properties of cardiac tissue such as slowed conduction velocity, unidirectional block due to wavefront curvature, and spiral waves [31]. We converted the transmembrane potential to unipolar and bipolar voltage signal (see *Supplemental Methods* for details). The original spatial resolution is 1 × 1 mm^2. We simulated one through seven coexisting spiral waves with a time step of 0.063 msec, which was subsequently downsampled at a sampling frequency of 500 Hz to reflect realistic measurements in human clinical electrophysiology studies [32]. This resulted in seven separate time series of one through seven coexisting spiral waves for a total duration of 10 s. We chose the observation time window of 10 s according to how focal FIRM localizes the rotor. FIRM uses ~50 cycles of spiral wave to localize the rotor, and with the cycle length of 120–240 msec (250–500 bpm), the observation window required to localize the rotor is 6–12 s [33].

Phase singularity

We estimated phase singularity using the instantaneous phase of the unipolar voltage signal time series (see *Supplemental Methods* for details). The dynamics of phase singularity at the original spatial resolution (IED = 1 mm) with each number of spiral waves served as the reference standard against which the error was calculated.

Dominant frequency

We estimated the dominant frequency on bipolar voltage signals. We rectified bipolar signal and then normalized it by subtracting its mean value. We subsequently filtered frequencies <3 Hz and >15 Hz using a bandpass finite impulse response (FIR) filter. We then applied a Hanning window to attenuate the effect of abrupt changes in time domain at the beginning and end of the time series [34,35]. Subsequently we performed a discrete Fourier transform to obtain the frequency spectrum of the time series. Dominant frequency is defined as the maximal frequency of the spectrum in each cell [1,35,36] (see *Supplemental Methods* for details).

Shannon entropy

For each mesh node, the bipolar voltage signal was binned according to its amplitude with bins of fixed amplitude 0.01 AU. For each bin, the relative probability density was defined as the number of counts in an amplitude bin divided by the sum of bin counts in all bins. Using this framework, one can compute the Shannon entropy (in bits) of each time-series process (see *Supplemental Methods* for details).

Error of rotor localization as a function of inter-electrode distance

To evaluate the impact of IED on spatial localization of rotors, we spatially downsampled the lattice (IED = 1 mm) in 6 different ways such that IED = 2, 4, 8, 10, 15, and 30 mm. We then linearly interpolated the lattice to maintain the same number of cells as the original lattice (120 × 120). We applied phase singularity, dominant frequency and Shannon entropy to localize the rotor or the rotor trajectory (core) in the interpolated lattice, just as in the clinical settings. For each IED, we defined the error of rotor localization (in mm) as the 2-D Euclidian distance between the center of mass of the estimated core and that of the reference standard. The reference standard is the center of mass of each rotor core, estimated by the phase singularity