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Differences in continuous spectra of fractionated electrograms in paroxysmal versus persistent atrial fibrillation

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ABSTRACT

Introduction: Quantitative measurements are helpful to discern fractionated electrograms in paroxysmal and persistent atrial fibrillation (AF), and may be useful to detect optimal ablation sites. However, electrical activation events can be transient, leading to erroneous estimates of electrogram properties. Measurement of continuous changes in electrogram frequency content may improve analysis.
Method: Fractionated local electrograms from 10 paroxysmal and 10 persistent AF patients were acquired from outside the pulmonary vein ostia and left atrial free wall using the distal bipolar ablation catheter electrode, and analyzed over continuous 16 second intervals. A New Spectral Estimator (NSE) updated the frequency spectrum and spectral parameters once per millisecond. The tallest spectral peak (dominant frequency or DF) was determined. Statistical tests of variability were used to determine significant differences between paroxysmal and persistent AF.
Results: Changes in the value of the DF over 16 seconds were caused by transient drifts in the frequency of the dominant peak, or by changes in which peak had the highest amplitude. The continuous DF and the spectral profile parameters were more highly variable in paroxysmal as compared with persistent AF patients ($p < 0.001$). There was found to be a gradient from high to low variability of DF in paroxysmal AF, from the left superior pulmonary vein antrum to the left atrial free wall.
Conclusions: The results suggest that atrial electrical activation becomes more stable and focused at a narrow frequency range in persistent as compared to paroxysmal AF. The NSE implemented for continuous update of spectral parameters, enables a rapid characterization of fractionated electrograms with high time-frequency resolution and low computational cost.

1. Background

Atrial fibrillation (AF) is the most common arrhythmia, yet optimal catheter ablation paradigms remain elusive due to incomplete understanding of the underlying mechanisms. Atrial regions with fractionated electrograms have been the topic of much discussion and interest for catheter ablation [1]. From a bioengineering perspective, AF complexity can be defined using the degree of repetitiveness (or lack thereof) in the fractionated electrogram signal [2,3]. Fractionated electrograms are composed of multiple low amplitude deflections, caused by the presence of multiple asynchronous electrical activation events [4]. When the signal is repetitive, similar electrogram shapes occur repeatedly, although not necessarily with a constant time interval between occurrences [2,3]. Greater repetition in the electrogram morphology suggests the presence of reproducible electrical activation patterns.

The frequency domain methods of AF analysis are usually based on the dominant frequency (DF), defined as the largest fundamental (nonharmonic) peak in the 3–12 Hz range of the electrogram power spectrum [5–7]. Over the range 3–12 Hz, the Fourier transform provides only 72 spectral points unless the signal length is padded with zeros. Insufficient time / frequency resolution in computing the DF may in part explain discrepancies in findings between research groups investigating the properties of fractionated electrograms [8–10]. A new spectral estimator (NSE) has been developed to address the limitations of the Fourier transform [11]. Over the range 3–12 Hz, the NSE generates 245 spectral points without padding. Both of these methods have only been implemented thus far to characterize single, static portions of the recorded AF electrogram signal, which are not useful to characterize transient temporal events and variability.

Methods with improved time-frequency resolution would be useful to characterize the quantitative spectral signature of fractionated electrograms, which likely contain transient time-frequency

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components relating to swiftly changing activation patterns, with dramatic and/or subtle shifts in frequency. If the spectral parameters of fractionated electrograms are to be used to guide catheter ablation of AF, their temporal and spatial stability becomes of critical concern. In this study, the NSE was implemented to calculate quantitative, continuous changes in spectral parameters of fractionated electrograms, and the results for paroxysmal versus persistent AF patients were graphed as time-frequency plots and compared, in an attempt to help define the potential usefulness of these parameters in guiding catheter ablation therapy. Although higher order spectral analysis and entropy methods could be used for the same purpose, the time-frequency plots were constructed as a first step in better understanding the AF data.

2. Method

2.1. Clinical data acquisition

Fractionated electrograms were recorded continuously for 16 seconds (15,632 sample points at 977 Hz sampling rate) from 10 paroxysmal and 10 persistent AF patients referred to the Columbia University Medical Center cardiac electrophysiology laboratory for catheter ablation of AF. The data was obtained from a consecutive series of patients for each type and was analyzed retrospectively. Electrograms were acquired from two sites selected at random from each of the following anatomical locations: one centimeter (CARTO measurement) from the ostia of the left superior pulmonary vein (LSPV), left inferior pulmonary vein (LIPV), right superior pulmonary vein (RSPV), right inferior pulmonary vein (RIPV), and the free wall sites in the anterior and posterior left atrium (LA). All data used for analysis were complex fractionated atrial electrograms, defined as electrograms with multiple deflections and varying patterns, with a maximum average interval of 50 milliseconds between deflections [12]. Based on these criteria, there were a total of 114 fractionated electrogram recordings analyzed from the persistent AF patients, and 90 fractionated electrogram recordings from the paroxysmal AF patients.

The acquisition and analysis of these data were approved by the Internal Review Board at Columbia University Medical Center. All patients had paroxysmal or longstanding persistent AF with no arrhythmogenic drug therapy and were undergoing catheter ablation for treatment of their AF. In paroxysmal AF patients with baseline sinus rhythm, arrhythmia was induced by rapid pacing (cycle lengths 250–200 milliseconds) from the coronary sinus or from the right atrial lateral wall. The arrhythmia was required to persist for at least 10 minutes for those signals to be included in the retrospective analysis. The underlying rhythm was AF in those patients with persistent AF. All electrograms were bandpass filtered by the acquisition system prior to digitization to remove baseline drift and high frequency noise (CardioLab, GE Healthcare, Waukesha, WI). The recordings were sampled at 977 Hz, corresponding to approximately 1 millisecond intervals, their amplitudes were measured in millivolts, and the signals were then stored to PC computer hard drive.

2.2. Quantitative analysis

The NSE has been described in detail elsewhere [11,13]. Briefly, electrogram recordings were first normalized to mean zero and unity variance. Window filtering to taper the signal is neither required nor used as a preprocessing step. The static or offline version of this technique works as follows. Electrograms were analyzed in the range 3–12 Hz in accord with prior studies [14]. This range of 3–12 Hz is equivalent to a cycle length for local electrical activation of approximately 325–81 milliseconds, respectively. To generate the power spectrum in this frequency range, the following algorithm was implemented. At 3 Hz, the time interval for periodicity of the signal is $w = 977/3\ \text{Hz} = 325$ sample points. The power at 3 Hz is determined by first averaging all sequential segments of the signal of length 325 discrete sample points over an 8 second interval. Examples of where the segments are located are shown in Fig. 1A. In this figure, a fractionated electrogram is shown, with second marks indicated by the asterisk on the abscissa. In the top panel, the horizontal bar which alternates black and gray denotes each of the first 8 segments. Each alternation in color represents 325 sample points of the signal. The signal portion above each segment is then extracted, and all extracted segments are added together to form the ensemble mean. Thus the number of segments n that are averaged over an 8 second interval is $8 \times 977 / 325 = 24$, when rounded down to the nearest integer. The sum of squares of all elements in the ensemble mean vector divided by its length w is the power. Similarly, power was computed separately for all other values of w to 977/12 Hz=81 sample points. The computed values of power were plotted to form the NSE power spectrum (245 spectral points in total). For graphing, the root mean square (RMS) power was plotted, i.e., square root of power [11].

Although calculation of one power spectrum by the NSE method is computationally expensive as compared with the Fourier Transform, continuous update of the NSE power spectrum, i.e., generation of a new spectrum with each incoming sample point of data, can be done using a more efficient formulation [15]. Rather than recalculating the ensemble average by equally weighting the n segments and summing, as in the static mode, a moving average was used to update the ensemble mean vector for the continuous mode calculation. The moving average weights the discrete signal point obtained during the current time epoch, and adds it to the appropriate element of the ensemble mean vector from the prior time epoch [15]. Thus only a few arithmetic calculations were needed for update of all ensemble mean vectors. Unlike the static mode, which used a single 8 second window for calculation, in the continuous mode, the moving average was shifted by 1 sample point to update the NSE. Over a 16 second interval, there was thus $16 \times 977 = 15{,}632$ updates in the power spectrum for each fractionated electrogram. Since each new signal point was added to the spectral calculation immediately, it was anticipated that changes in spectral characteristics would rapidly become evident in response to a change in electrogram characteristics.

2.3. Measurements and statistics

Once the power spectrum was obtained at each sample point for all fractionated electrogram recordings, spectral parameters were used to characterize their frequency content. Besides the DF, several other previously introduced spectral parameters were computed [7]. The dominant amplitude parameter (DA), which is the magnitude of the DF peak, was measured. The spectral profile parameter was calculated by normalizing the power spectrum to a range of 0–1 unit, and determining the mean (MP) and standard deviation (SP). All of these spectral parameters were shown previously to be useful for distinguishing fractionated electrograms acquired from paroxysmal versus persistent AF patients [7]. The DF, DA, MP, and SP spectral parameters were determined for each NSE power spectrum (i.e., once each sample point – approximately once per millisecond of the signal) over each 16 second fractionated electrogram interval. Each parameter was tabulated and summarized over the 16 second interval. The rank-sum test was then used to determine the