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Journal of Atrial Fibrillation

Review of Dominant Frequency Analysis in Atrial Fibrillation

Rakesh Latchamsetty, MD, Abraham G Kocheril, MD.

University of Illinois at Chicago, Section of Cardiology

Abstract

Significant advancements have been made in the technology and approach to catheter ablation of atrial fibrillation (AF). Pulmonary vein isolation has emerged as the dominant strategy in this procedure and has fueled innovations in catheter design as well as various mapping and navigation systems. Mapping and targeting of complex fractionated atrial electrograms has also emerged as an additional or alternate strategy employed by some ablationists. Recently, attention is being drawn to a new approach targeting atrial sites with high dominant frequencies (DF) derived from their electrograms. This article is a review of the basic concepts of DF, the relevant literature behind DF analysis in AF, and the potential clinical applicability of DF analysis for catheter ablation.

Key Words: Dominant Frequency, Atrial Fibrillation, Ablation

Abbreviations: AF - atrial fibrillation; CFAE – complex fractionated atrial electrogram; DF - dominant frequency

Introduction

Despite the vast extent of resources devoted to its understanding and treatment, atrial fibrillation (AF) remains the most significant clinical arrhythmia in terms of its morbidity and continues to challenge us to fully uncover its elusive mechanisms. This is not to say, however, that there has not been significant progress made. On the contrary, remarkable strides have been made both in the basic science laboratory to uncover the mechanisms by which the arrhythmia is generated and sustained, and in clinical studies of treatment. Catheter ablation has emerged as an important therapy in drug refractory AF and has brought with it continuously improving technology in areas including catheter design, mapping systems, and overall ablation strategy.

Catheter-based pulmonary vein isolation as a means to electrically isolate triggers of AF has significantly improved success at maintaining sinus rhythm (particularly in paroxysmal AF) but has not eliminated AF altogether. Permanent maintenance of pulmonary vein electrical isolation can often prove to be challenging, and important sources outside the pulmonary veins and predominantly in the left atrium remain. Targeting areas of complex fractionated atrial electrograms (CFAE), although reported with varying degrees of efficacy, is believed to modify important sites for the mainte maintenance

Corresponding Address :Rakesh Latchamsetty, University of Illinois at Chicago, Section of Cardiology, 4766 Park Road, Ann Arbor, MI 48103.

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of AF. As an adjunct to pulmonary vein isolation, CFAE ablation has gained some favor as a means to tailor ablation to a given patient. ¹

Recently, significant attention has been directed toward utilizing dominant frequency (DF) analysis to highlight sites of rapid and consistent periodicity which are believed to represent likely targets for maintenance of AF.² This article provides an overview of the basic concepts behind DF analysis, reviews the pertinent data regarding its application to AF, and discusses the current and future status of its clinical application.

Mechanisms of Atrial Fibrillation

Multiple theories regarding the initiation and maintenance of AF have been introduced and evolved our understanding of this arrhythmia since at least the beginning of the twentieth century when Winterberg, et al. in 1907 described AF as due to multiple rapidly firing atrial foci .^{3, 4} In 1914, Mines promoted the theory of circus movement as the key reentrant mechanism to perpetuate AF.⁵ In 1964, Moe et al. described AF as a self sustaining process of multiple randomly propagating wavelets made possible by an atrial substrate of heterogeneous refractoriness. ^{6,} ⁷ Challenging this, at least in some cases of AF, has been the theory of mother rotors, described by Jalife, et al. as discrete self sustaining reentrant foci that may provide the engine for the maintenance of AF. These rotors tend to anchor to various anatomical substrates, thereby maintaining a relatively fixed location and giving off multiple randomly circulating wavelets. These wavelets then propagate throughout the atria with varying amounts of degradation (fibrillatory conduction⁸) as they encounter the heterogeneous tissue of the left and right atria and their connections. ³ The presence of these rotors have been studied through optical mapping of the left atrium and their periodicities have been shown to match with electrogram frequencies at those locations.⁹ Identifying the sites of these rotors by their rapid and periodic deflections on electrograms is the aim of frequency analysis.

Understanding Dominant Frequencies

In its application with respect to AF, the fundamental goal of DF analysis for any given location is to find the activation rate of the dominant atrial signal at that site. The standard approach during electrophysiology studies utilizes a time domain analysis where the amplitude of the signal as seen on the electrogram is plotted against time. However, during AF, the varying amplitude and morphologies of the atrial signals often preclude accurate measurement of atrial cycle lengths. DF analysis, however, dissects the electrogram into components of varying frequencies and creates a power spectrum based on their amplitudes. Ultimately, the "dominant" or highest amplitude frequency is identified and used to determine the activation rate of the primary atrial signal from that location .¹⁰ Below is a more detailed description on the specific algorithms used in DF analysis.

Initially, an electrogram from a given atrial site is obtained over a period of about five seconds .¹¹ This "time domain" signal then undergoes a Fast Fourier Transform to display a power spectrum of its frequencies and ultimately to identify a DF. The fundamental principle behind the Fourier Transform is that any time series (such as an atrial electrogram) can be portrayed as a sum of a discrete set of sinusoidal waves of specific frequencies, amplitudes, and phase shifts. After the signal is broken into these compository waves, a power spectrum of their frequencies is created and a DF can be identified (figure 1). The term "Fast" Fourier transformation implies that the time sample analyzed is of a power of 2 which lends itself to a more efficient and quick analysis.

In order to provide a cleaner or more discrete frequency power spectrum from biphasic electrogram recordings, signals need to undergo several processing steps including bandpass filtering, re tification, mand signal tapering. Band-pass filtering serves to attenuate signal "noise" outside a specified desired frequency range and highlights deflections that represent local atrial depolarization. Rectification converts the biphasic signal to a monophasic one more easily represented by a sinusoidal wave; and signal tapering reduces to baseline the signals at the two ends of a specified time "window" to prevent incompletely recorded deflections from affecting the data .^{10, 12} All these steps serve to "clean" the frequency spectrum and help elucidate the dominant atrial waveform and its periodicity.

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Figure 1: Frequency spectrum derived from an atrial electrogram.

A. Bipolar left atrial electrogram from a patient in atrial fibrillation. This signal, after undergoing several processing steps (including bandpass filtering and rectification) is broken down by Fourier transformation to its component sinsusoidal waves. B. Examples of sine waves of varying frequency, amplitude and phases are pictured.

C. Ultimately the power spectrum of the different frequencies are plotted and the dominant frequency is identified.



Any atrial site can be examined utilizing the methods detailed above and a DF can be assigned to each of these sites. Ultimately, the implication in targeting sites with high DFs for ablation is that they potentially represent the location of rotors that may be responsible for the maintenance of AF.

Several studies have suggested that in both animal and human hearts in AF, left atrium and pulmonary vein sites tend to have higher DFs than the right atrium, thereby representing a left to right DF gradient. ^{11, 13, 14} Lazar et al. demonstrated the presence of this gradient correlated with a higher probability of successful ablation through pulmonary vein isolation .¹³ However, whether high DF sites in the pulmonary veins correlate with their identification as triggering foci remains unclear as the tissue characteristics have not yet been fully described. In an animal model of Langendorff- perfused sheep hearts in AF, Jalife et al. elegantly demonstrated this left to right atrium gradient and showed its path of decrementation as it crossed Bachman's bundle from the left atrium into the right atrium. ¹⁴ All these findings support the theory that periodic and relatively stationary high frequency sources to maintain AF may be present in the left atrium and can therefore represent potential targets for therapy of AF.

Clinical Use of Dominant Frequency Analysis

Based on the concept of high DF sites representing potential sources maintaining AF, its specific clinical application is still being determined. Sanders

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et al. demonstrated in a study where the operators during AF ablation were blinded to the DF analysis, ablation at a high DF site was more likely to prolong the AF cycle length ¹⁵ Also, in paroxysmal AF the majority of AF termination occurred while ablating a high DF site. Furthermore, a difference in DF distribution was seen where patients with paroxysmal AF had high DF sites that were more likely to lie in the pulmonary vein whereas in persistent AF, left atrial DFs were often higher. Some groups are also beginning to perform real time analysis of DF to guide ablation. When targetinghigh DF sites, Atienza et al. have seen a higher probability of remaining free from (arrhythmia or) AF when successfully ablating DFmax sites or abolishing the left to right atrium DF gradient.¹⁶

While a definitive role for DF analysis to guide ablation is yet to be established and varying accounts of its efficacy have been presented, this concept is certainly one that warrants further clinical evaluation. Targeting of high DF sites may ultimately have an expanded role in AF ablation, particularly as an adjunct to pulmonary vein isolation. The ex act strategy for DF based ablation is still being developed and this process will certainly face a number of challenges. Among these is the dynamic nature of DF spectra during PVI and left atrial ablation which may require remapping of DF sites during the procedure. Software and catheter design may also need to be improved to provide more efficient and accurate real time DF maps. Also, different strategies may prevail between chronic and paroxysmal AF patients, especially in relation to its use with pulmonary vein isolation. Other potential obstacles to accurate DF analysis such as far-field signals, signal alteration around scars, and prior ablation lesions setting up local reentry will also need to be addressed.

However, with innovations such as catheter systems that can deliver a large number of electrodes to the atria and noncontact mapping, evaluating the substrate for high DF sites will likely become more efficient. Furthermore, ongoing clinical investigation is advancing our understanding of the clinical significance of high DF sites and strategies on how and when to map and ablate at these sites are being developed. If these advancements in design and refinement of strategies to target DF sites prove to increase success rates, curative ablation of AF may be accomplished with less atrial damage than current approaches.

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