Atrial fibrillation (AF) is the most common cardiac arrhythmia in clinical practice. It is well known that AF depends on the interaction between the “triggers” and “substrate”, and the elimination or isolation of the “trigger” can cure AF. In recent years, growing knowledge of atrial substrate mapping has helped in learning more about the maintenance of AF, and to identify the critical atrial substrate for catheter ablation, in spite of the elimination of all triggers initiating AF. However, how to identify the critical arrhythmogenic atrial substrate remained unclear. The question will be addressed in the present article.

Atrial fibrillation (AF) is the most common cardiac arrhythmia in clinical practice. It is well known that AF is characterized by a spatiotemporal organized activation, with a variable frequency and spectral morphology throughout the atria. The complex activation patterns of AF can result in fractionated signals, separated by short and variable intervals that prohibit a reliable identification of the precise local activation rate or interval (Figure 1). Furthermore, it is difficult to represent sustained episodes of AF by only a small sample of fibrillatory electrograms, within a limited period of time. One reasonable method for a transformation is to transform the time-domain electrogram signal into a frequency-domain electrogram signal, i.e. to elucidate the data beyond the time-domain electrogram. Frequency-domain signals provide a feasible method to analyze the temporal and spatial distribution of fibrillatory waves during AF. The current review focuses on the basic principles and methodology of the frequency-domain analysis using the Fast Fourier Transform (FFT), and the further clinical implications during catheter ablation of AF.

With each “normal” heartbeat (sinus rhythm), an electrical signal arising from the sinus node spreads to the right and left atria, and therefore, causes atrial depolarization. Then, the electrical impulse spreads through the atrioventricular node and further initiates ventricular depolarization. As the signal travels, it causes the heart to contract and pump blood. AF is characterized by a rapid and irregular activation of the atrium, for example, 400-600 pulses of chaotic contractions of the atrium per minute. The ventricular rate during AF is thus, no longer under the physiological control of the sinus node. An electrocardiogram (ECG) recording is necessary to diagnose AF. The diagnosis requires an ECG or rhythm strip demonstrating: 1) “absolutely” irregular RR intervals, 2) no distinct P waves on the surface ECG, and 3) an atrial cycle length (when visible) that is usually variable and less than 200 ms [1]. A brief period of AF may cause palpitations, chest discomfort and light-headedness. Sustained AF with an uncontrolled ventricular response rate can cause severe congestive heart failure [2].

It is well known that the development of AF requires a “trigger” and an anatomic or functional substrate capable of both initiation and perpetuation of AF [3]. Pulmonary Vein (PV) focal firing may trigger AF, or act as a rapid driver to maintain the arrhythmia. Catheter ablation strategies for the cure of AF have targeted isolation of the PVs, whereas additional substrate modification is required in 20% to 40% of patients with paroxysmal AF, and most with non-paroxysmal AF [4,5]. Therefore, it is important to identify the critical arrhythmogenic atrial substrate responsible for AF perpetuation, and for a further catheter ablation strategy. Three-dimensional (3D) electroanatomic mapping systems were introduced into catheter ablation of AF more than a decade ago. Currently, the Ensite NavX (St Jude Medical, Minnetonka, MN, USA) and Carto ( Biosense Webster Inc, Diamond Bar, CA, USA) systems are the most popular 3D mapping systems used worldwide, because they provide accurate visualization of the atrial anatomy and identification of the atrial substrate properties for catheter ablation of atrial arrhythmias (Figure 2).

One of the important approaches used to guide AF ablation is an analysis of the local atrial electrogram properties. A time-domain analysis refers to an evaluation of the inter-electrogram intervals by a local cycle length criterion. This involves a determination of the intervals between the local activations, with signal amplitude cutoffs and refractory period blanking, used to assess the “true” local firing and avoid contamination by far-field events and double sampling of complex signals. A frequency-domain analysis refers to the quantification of the local Dominant Frequency (DF) by spectral analysis methods incorporating the FFT [6]. Regarding the electrogram morphology analysis, all data were digitalized at 1 KHz and analyzed by a Matlab computer program. The frequency resolution was 0.54 Hz. Time-domain bipolar signals were sampled at 1200 Hz and filtered with a bandwidth from 32 to 300 Hz. Then, the data was exported to an external computer program for an electrogram analysis. The FFT analysis was performed using a Hanning window function on each segment from all recording sites in the Left Atrium (LA). The Dominant Frequency (DF) was defined as the frequency with the maximum power in the frequency range. To ensure the reliability of the DF detection, the lowest-noise signal was chosen for the analysis. The DF peaks were determined when the area...
of the dominant frequency peak over the total spectrum was higher than 0.3.

Nademene et al. [7] first described a new ablation approach to target the Complex Fractionated Atrial Electrograms (CFAEs), which were thought to indicate areas of slow conduction and/or pivot points of reentry of wavefronts. Using this approach, the critical atrial substrate could be modified and it could achieve procedural AF termination, restoration of normal sinus rhythm, and long-term maintenance of sinus rhythm. Till now, most of the electroanatomical mapping systems offered an automatic algorithm to display the CFAE distribution based on a time-domain method [8]. In 2009, Grzeda et al. [6] presented the results of an interesting theoretical analysis of time-domain versus frequency-domain approaches to the CFAE identification. The study demonstrated that the time-domain methods in targeting the AF ablation sites had a good predictive value, but were easily prone to degradation. In contrast, the frequency-domain method seems to be much more robust. The 3D electroanatomic mapping system provided specific software with a detection algorithm for CFAE identification, which included an Interval Confidence Level (ICL) and Average Complex Interval (ACI).

In this laboratory, the relationship between the different detection algorithms (ICL vs. ACI) and CFAE identification was investigated based on both time-domain and frequency-domain approaches. Time-domain CFAE mapping of the LA was performed based on the detection algorithms with the ICL and ACI under a recording duration of 5 seconds. The ICL characterized the repetitiveness of the fractionated atrial electrograms. The ACI that displayed the average value for all intervals was presented with the fractionated interval (FI). CFAEs were defined as an FI between 50-120 ms, or an ICL>5 [9]. The method of the FFT has been described previously [10]. A 6.82-second segment of data was exported to an external computer program. The FFT analysis (sampling rate, 1200 Hz; resolution, 0.14 Hz; with a Hanning window function) was performed from all recording sites (CFAEs site). The largest peak frequency of the resulting spectrum was identified as the DF. The area under the DF peaks over the total areas was defined as the Harmonic Index (HI). As shown in the example in figure 3, the color-coated electroanatomic reconstruction of the LA depicted CFAE maps based on the algorithm of the ICL (Figure 3A) and ACI (Figure 3B). The former map could highlight the rapid repetitive electrograms and the latter one could emphasize the continuous and disorganized electrograms. The area coated with the color orange represented high CFAEs sites, based on the time-domain analysis in both maps. On the other hand, the intracardiac bipolar electrograms and corresponding frequency spectra of the high CFAE sites showed a high DF in the ICL map and low HI in the ACI map, respectively. Further analysis demonstrated that the ICL value correlated with the DF (R=0.51, P<0.001), whereas the ACI value correlated better with the HI (R=0.38; P<0.01). There was no correlation between the ICL value and HI, or the FI value and DF (p>0.05) (Figure 4).
In this laboratory, the substrate modification was guided by a continuous CFAE ablation post PV isolation. Critical CFAEs in the vicinity of the highest DF sites correlated with a higher procedural AF termination rate for the CFAE ablation [11]. This finding indicated that a combined analysis of both the fractionation and frequency analysis may allow for a more specific approach, to identify the critical atrial substrate that remains after PV isolation, without unnecessary ablation of an extensive atrium myocardium. Different automatic algorithms identify critical atrial substrates with different electrogram characteristics. Higher ICL values indicated areas with rapid repetitive activities (high DF values), whereas the lower ACI values indicated areas with continuous fractionation with more disorganized signals (low HI values).

References


