Role of Sinus Node during Atrial Fibrillation : A Novel Insight from Regional Frequency Analysis

HW Tso[1], T Kao[1], YJ Lin[2], CT Tai[2], SA Chen[2]

[1]Institute of Biomedical Engineering, National Yang-Ming University, Taipei, Taiwan
[2]Cardiovascular Research Center, Taipei Veterans General Hospital, Taipei, Taiwan

Abstract

The sinus node (SAN) is demonstrated to play a role in the genesis and the perpetuation of atrial fibrillation (AF). The sinus activation during AF is difficult to analyze with conventional electrogram recordings. The purpose of this study was to investigate the atrial substrate characteristics near the sinus node (SAN) during sinus rhythm (SR), ongoing AF and before AF termination according to the frequency analysis compared to the rest of the right atrium (RRA). The present study included 6 patients with paroxysmal AF underwent noncontact mapping for the right atrium (RA). After subtraction of QRS-T complex, regional frequency distribution was obtained from the signals of 256-equally distribution mapping site for three situations. The dominant frequency (DF), power amplitude (MP), and organization index(OI) of DF between SAN and RRA during AF were similar (p>0.1). However, the DF of SAN area became lower (p<0.001), the power amplitude of local spectra (p<0.005) was higher, and more organization (P<0.001) compared to RRA before termination of AF. In conclusion, atrial substrate around the SAN is characterized by slower atrial activity compared to the rest of the right atrium during termination of AF. The frequency analysis showed that the DF around SAN area during AF termination was similar to during SR, suggesting that the sinus automaticity was preserved with local entrance block from the rest of the atrium.

1. Introduction

Atrial fibrillation (AF) is characterized by rapid and irregular activation of the atrium. Based on revealed evidence from experimental and clinical studies, the reentrant mechanism is involved in the genesis and maintenance of AF [1,2]. The maintenance of AF depends on the presence of a number of simultaneous reentrant waves. The size of a reentrant wave is related to the wavelength that should be an important determinant of AF occurring [1,2,3].

The sinus node (SAN) is demonstrated to play a role in the genesis and the perpetuation of atrial fibrillation (AF). Previous animal study demonstrated that injury to sinus node could facilitate inducibility AF [4]. In the human, AF is also associated with abnormal SAN function [1,5]. A pioneer study by Kirchhof and Allessie et al. showed that sinus automaticity was preserved with high degree of sinoatrial entrance block during AF [6]. In previous study, we found that organized activation was observed during termination of AF by using coherence function analysis from the canine's model [7]. The purpose of the present study is to investigate the atrial substrate characteristics near the SAN during ongoing AF sustain (AFS) and immediately before AF termination (AFT), according to the frequency analysis, compared to the rest of the right atrium (RRA).

2. Methods

2.1. Study patients

This study consisted of 6 patients referred for ablation of paroxysmal AF, originated from pulmonary vein (PV, n=4), superior vena cava (SVC, n=1), crista terminalis (CT, n=1). They suffered from frequent episodes of AF for an average of 4.2 ± 2.7 years (>1 episode per week in the most recent months), and were refractory to or intolerant of 1 to 3 (mean 2±1) anti-arrhythmic drugs. Six seconds of AF maintenance, AF prior to terminated, and sinus rhythm were recovered for frequency analysis.

2.2. Non-contact mapping system

The noncontact mapping system (EnSite 3000 with Precision Software, Endocardial Solutions) had been described in detail previously [8]. In brief, the system consisted of a catheter (9F) with a multi-electrode array surrounding a 7.5- ml balloon mounted at the distal end. The system locates the three-dimensional position of the electrodes on any desired catheter relative to the multi-electrode array using a locator signal. Navigation provided the means to define a model of the chamber anatomy and to track the position of the standard contact catheters within the chamber relative to the label points of interest, such as the anatomical structure or critical zones of conduction. Virtual endocardial electrograms were mathematically reconstructed and displayed on the anatomical model, producing isopotential or isochronal color maps. According to the virtual system, we defined the location of SAN during SR.

2.3. Signal processing

After subtraction of QRS-T complex(Figure 1), filtered by 0.1-60Hz 2nd Butterworth band-pass filter, each 2 seconds of regional frequency distribution was obtained from the signals of 256-equally distribution mapping sites for SR, AFS, and AFT.

A fast Fourier transform (FFT) with a Hamming window was calculated on the resultant data segments (6 seconds, 1200 Hz sampling rate). The frequency spectra were plotted and analyzed from 0.5 to 20 Hz to include only the physiologic range of practical interest. The spectra were normalized by the maximum power of the 256 spectra (Figure 2A). For each spectrum, the largest peak was identified as the dominant frequency (DF) and the magnitude of DF as power amplitude (MP) [9].

The total power of the spectrum was calculated from between 0.5 to 20 Hz. The power under the DF was determined over a 1 Hz-window. The ratio of the DF power and its harmonics to the total power was defined as the organization index (OI) [10], representing the organization of the signals.

After signal analysis, the results of 256 signals were performed as two dimensions colored mapping. The DF mappings (Figure 3D) were consisted by 256 DFs that were determined from power-spectra. The MP and OI mappings were performed by the same way.

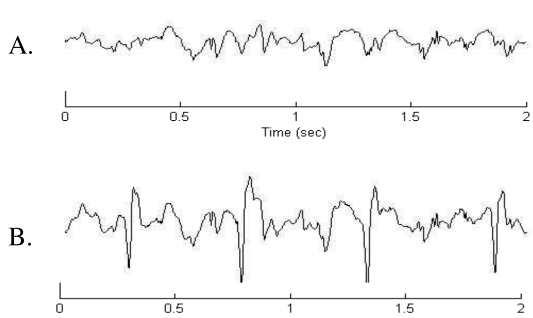

Figure 1. An example of one signal had QRS cancellation in A, and the original electrogram in B.

2.4. Statistical analysis

All data were analyzed three parameters (DF, MP, and OI) by comparing the variation of SAN and of the rest of RA respectively by using the Mann-Whiteney test. The level of significance was taken as $P<0.01$. Results are reported as mean±SD.

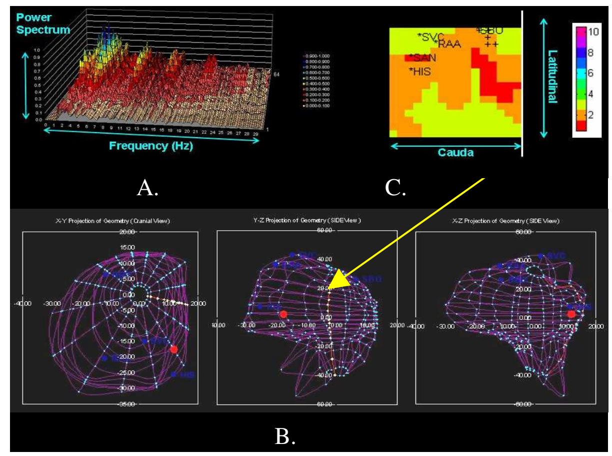

Figure 2. A.the 256 spectra were calculated by FFT show as relief map. B.the virtual electrograms were reconstructed and displayed on the three-dimensional anatomical model. C.the anatomical model was spread the plant of 256-equally distribution mapping sites.

3. Results

Ongoing AF and spontaneous termination were observed in all 6 patients with duration of 6 ± 3 min. Location of the SAN was identified by isopotential activation during SR immediately before initiation of the AF. Overall, 8 episodes of ongoing AF (2± 3 min), and 8 episodes of spontaneous termination were observed. Ensite balloon was deployed in the RA in all patients with stable balloon location through out the procedure and without complications.

3.1. An example of DF mapping

As Figure 3 and Figure 4, there were a representative example of the frequency analysis from one patient during ongoing and before AF termination, showing as regional distribution of DF in the RA. In Figure 3, we showed the distribution of electrograms with their corresponding DFs in the RA from an episode of AF. The electrograms from SAN (Figure 3A) showed rapid activity with a DF of 3.9 Hz. In Figure 3B, the recording at the middle of RA showed a DF of 4.8Hz. At the bottom of RA, the DF was 3.9 Hz (Figure 3C). Figure 3D showed the DF mapping of the whole RA with different colors as different DFs. Before AF terminated shown in Figure 4, we had the similar results in the middle and bottom of RA

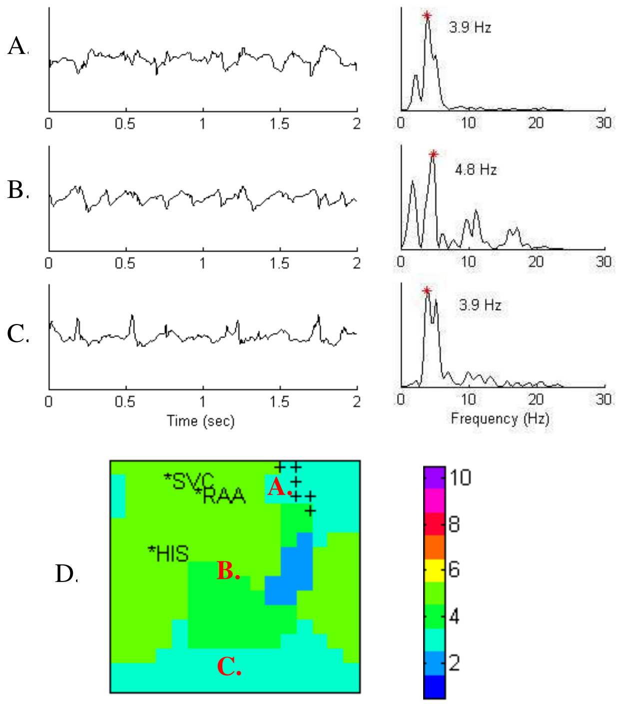

Figure 3. Spectra transformation of ongoing AF resulted form the whole RA for 2-seconds frequency analysis. A.at the SAN area, B.at the middle of RA C.at the bottom of RA. D.DF mapping in whole RA. There were the "+" symbols marked as SAN area by locator. (SVC=superior vena cava, RAA=right atrial appendage; HIS=Bundle of HIS).

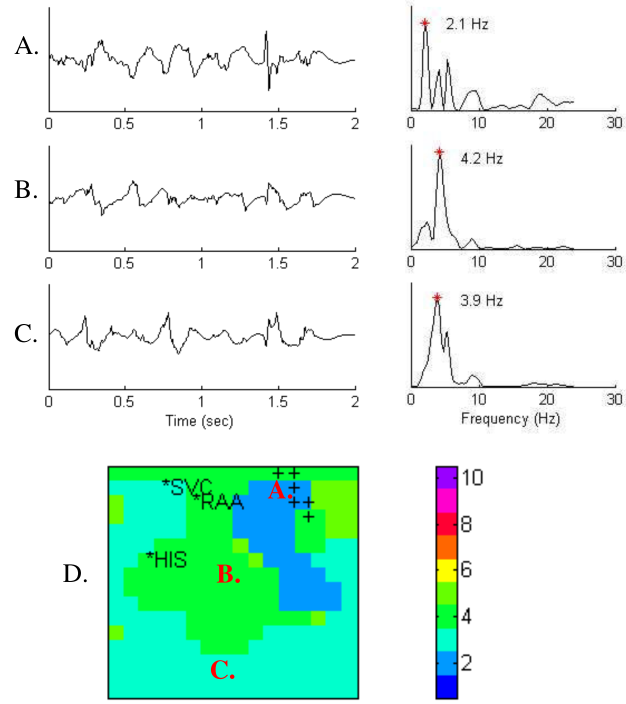

Figure 4. Spectra transformation before AF termination resulted form the whole RA for 2-seconds frequency analysis. A.at the SAN area B.at the middle of RA C.at the bottom of RA. D.DF mapping in whole RA. There're the "+" symbols marked as SAN area by locator. (SVC=superior vena cava, RAA=right atrial appendage; HIS=Bundle of HIS).

as ongoing AF(4.2 Hz and 3.9 Hz, Figure 4B,C). There was different pattern from SAN became lower frequency with a DF of 2.1Hz (Figure 4A). A low frequency region was shown around the SAN with local conduction block of AF wave fronts.

Figure 3D showed the DF distribution pattern during ongoing AF, higher DF was observed around the septum and His area, and the DF of the SAN is not different with the other part of the RA. In Figure 4D, DF around the SAN was markedly decreased, whereas the DF of RRA remained high, including the septal area. Therefore, SAN entrance block, rather than the slowing of AF activity of the driver in the PV or RRA, may account for decrease of DF within the SAN before AF termination.

3.2. The characteristic of sinus node by frequency analysis

During ongoing AF, regional frequency analysis showed that the mean DF of the SAN area (16 Mapping

Table 1. Frequency analysis result of sinus node and outside sinus node area during ongoing AF and before termination.

	Area	During ongoing AF	Immediately before AF termination
Dominant frequency (Hz)	SAN	4.53±0.84	2.73±1.03*
	RRA	4.72±0.66	5.04±1.28 *†
Magnitude power ($\times10^{-4}$ mV)	SAN	8.84±4.00	10.0±3.61
	RRA	5.40±5.65	3.91±2.65*†
Organization index	SAN	0.39±0.11	0.47±0.14
	RRA	0.40±0.12	0.36±0.10*†

* P<0.001, compared to during ongoing AF
†P < 0.001, compared to the area of sinus node (SAN).
(Abbreviation: SAN: sinus node area; RRA: the rest of the right atrium.)

sites) was similar to the RRA (240 Mapping sites) during ongoing AF (4.53±0.84 Hz vs. 4.72±0.66Hz; P>0.1). On the other hand, SAN area had lower DF compared to the rest of the RA (2.73±1.03Hz vs. 5.04±1.28Hz; P<0.001) before termination of AF. Furthermore, 2-seconds sequential frequency analysis on SAN region showed the DF of SAN became reduced before the last 2 seconds AF termination.

The MPs and OIs of the SAN area were similar to the rest of the RA during ongoing AF (Table 1). However, the MP around the SAN area was higher and the OI was also higher as compared to the rest of the RA, indicating more organized activation was presented immediately before AF ceased (Table 1).

We also performed frequency analysis immediately after AF termination. The DF of SAN before termination of AF was similar to during SR (2.72±1.03 Hz vs. 2.21±0.58 Hz; P>0.1), suggesting that sinus automaticity was preserved immediately before AF termination.

4. Conclusions

Atrial substrate around the sinus node was characterized by slower atrial activity compared to the rest of the RA before AF termination. On the other hand, the sinus node activity during ongoing AF was similar to the rest of the RA. The frequency analysis further demonstrated that the DF around SAN area during AF termination was similar to during SR, suggesting that the sinus automaticity was preserved with local entrance block from the rest of the RA.

Acknowledgements

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Address for correspondence

Han-Wen Tso
Institute of Biomedical Engineering
National Yang-Ming University
155, Sec.2,Li-Nong St., Peitou, 112, Taipei, Taiwan, R.O.C.
E-mail address: susun@bme.ym.edu.tw