Jurnal
Teknologi

Full Paper

A REVIEW ON ATRIAL FIBRILLATION AND ITS RELATED ANALYSIS

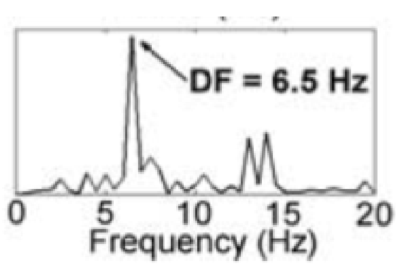
Received
15 December 2015
Received in revised form
30 March 2016
Accepted
30 May 2016

Priscilla Sim Chee Mei[a], Anita Ahmad[b*]

[a]Electronic and Computer Engineering Department, Faculty of Electrical Engineering, Universiti Teknologi Malaysia, 81310 UTM Johor Bahru, Johor, Malaysia
[b]Control and Mechatronic Engineering Department, Faculty of Electrical Engineering, Universiti Teknologi Malaysia, 81310 UTM Johor Bahru, Johor, Malaysia

*Corresponding author
anita@fke.utm.my

Graphical abstract



Abstract

Atrial fibrillation (AF) has been widely stated as the most common arrhythmias (irregularities of heart rhythm) which could lead to severe heart problem such as stroke. Many studies have been conducted to understand and explain its mechanism by analyzing its signal, in either time domain or frequency domain. This paper aims to provide basic information on the AF by reviewing relevant papers. Overall, this paper will provide review on the underlying theory of AF, AF mechanism as well as the common relevant signal processing steps and analysis.

Keywords: Arrhythmias, atrial fibrillation, signal processing

1.0 INTRODUCTION

The heart is one of the main human organs since it plays an important role in the cardiovascular system to pump blood throughout the human body for oxygen supply [1, 2]. For a normal healthy person, the heart could works normally and producing a normal sinus rhythm or heartbeat at the range of 60-100 beats per minute [1, 3]. In reality, irregularities of the heart rhythm occurred on many people, especially those who did not practice healthy lifestyle. The heart rhythm can either be too slow (known as bradycardia, less than 60 beats/minute) or too fast (known as tachycardia, more than 100 beats/minute) [1, 4, 5]. These irregularities of the heart rhythm are known as arrhythmias [1, 4-6].

Atrial fibrillation (AF) has been widely stated as the most common arrhythmias, specifically as a supraventricular tachycardia, in which it often produces fast and irregular heartbeats [1, 7-9]. There are three types of AF, namely paroxysmal, persistent and permanent [1, 5, 10]. Paroxysmal AF is AF which occurs occasionally, i.e. spontaneously terminated within 7 days, while persistent AF is one that does not stop by itself, i.e. sustained more than 7 days, but will stop if medication or cardioversion is given to help the heart return to its normal rhythm [1, 5, 11-14]. On the other hand, the permanent AF is present all the time and cannot be fixed with either medication or cardioversion [1, 5, 14, 15].

Currently, AF has been paid concern for its major cause of stroke and progressively increasing burden worldwide [1, 16-29]. For instance, a research recently done on US adult population had projected that the prevalence of AF cases will increase from 5.2 million in year 2010 up to 12.1 million in year 2030, showing the seriousness of AF epidemiology [10]. A person with lone AF might have no symptom at all [14]. However, AF patients often will experience similar symptoms as people with other types of heart problems, such as shortness of breath, heart palpitation and fatigue [1, 5]. The risk of getting AF includes factors like age, gender, and influence by other diseases such as hypertension, diabetes and increased BMI [1, 5, 16, 17, 19, 21, 22, 24-26, 28-30].

2.0 AF TREATMENT

There are three main approaches for AF treatment. First, through medication. Since AF is associated with chaotic heart activity [31, 32], antiarrhythmic drugs will be given as medication to regulate the heart rhythm or decrease the fibrillatory waves frequency in the surface ECG so that it could return to normal rhythm [1, 5, 14, 16, 29, 33-35].

Next, through surgical. This is commonly used to implant the pacemaker or implantable defibrillator invasively on the cardiac wall to help replace the function of the malfunction sinus node (the natural pacemaker of the heart) to regulate the heartbeat [16, 29].

Another approach for AF treatment is the non-surgical approach, which includes electrical cardioversion as well as catheter or radiofrequency (RF) ablation. Electrical cardioversion refers to the use of electricity apply on the patient chest using eiter paddles or patches to help reset the normal electrical conduction system of the heart. Ablation on the other hand is performed using catheter to burn the tissue suspected as the source of activation for AF [1, 36].

Catheter ablation (CA) has been a more preferable method for patients with paroxysmal and persistent AF due to about 40% higher of significant freedom rate when compare to antiarrhythmic drug treatment [1]. Besides that, CA approach could also help decrease the risk of patient getting stroke and heart failure [1]. Ablation at AF activation sites help increase the AF cycle length, means longer period, lower frequency, and help terminate paroxysmal AF [37]. Thus, CA has been widely recognized as either the first or second line treatment option for AF [38-40]. Figure 1 shows the catheter ablation insertion. The site of ablation is usually focused in the left atrium (LA) and pulmonary vein (PV) region as shown [1].

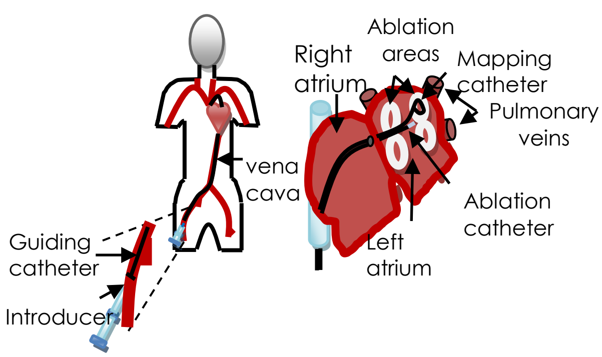


Figure 1 Ctheter ablation insertion [1]

Pulmonary vein isolation (PVI) which refers to the electrical isolation of the pulmonary veins (PVs) from the atria guiding CA, has been claimed as a potentially successful treatment for paroxysmal AF [37, 41-48]. This is due to the ability of PVs generating ectopic beats that initiate AF in majority paroxysmal AF patients [44, 49]. However, PVI is less effective for other types of AF such as persistent AF [48, 50]. Other researchers have presented another type of ablation procedure called the stepwise ablation [51]. J. Zhao *et al.* have applied stepwise linear ablation in their study and reported it as a better ablation approach without PV isolation that could produce higher ablation outcome and decrease PV stenosis risk [52].

In current, anatomical or intracardiac mapping studies have been conducted to visualize the sites of activation of AF in 3D [53]. Real-time AF mapping helps to guide the RF catheter ablation by identifying the suitable ablation target sites [6, 39, 45, 53-55]. There are a few types of left atrium mapping including conventional mapping, simultaneous noncontact mapping and circumferential mapping [45, 56]. The mapping system is feasible at estimating the dominant frequency of AF and complement the conventional ablation procedure [56, 57].

Overall, failure of AF termination using ablation might suggests problems such as wrong determination of critical AF maintenance sites, unrecognized frequency gradient or the different underlying maintenance mechanism of AF for different patients [37]. Nevertheless, the success of an approach is defined differently according to the goals or objectives of the treatment as well as the types of AF. To minimize the risk of the treatment procedure on a patient, the time of catheter insertion should be minimized while the sites for ablation should be determined accurately in a short time [1, 58].

3.0 MECHANISM AND MAINTENANCE

The AF mechanism is concerning the maintenance of AF. J. C. Pachon M *et al.* had classified the atrial muscle into two, namely the compact myocardium (CM) and fibrillary myocardium (FM) [36]. Generally, researchers believed that AF is maintained by an activation source of high frequency sites [1, 4, 32, 36, 55, 59-61], also known as FM sites or AF nest which becomes the driver maintaining AF [36]. The main FM sites include left atrium (LA) roof, LA septum, LA posterior wall and PVs area [36, 62]. These regions usually become the main target of ablation therapy [32].

Research on the AF mechanism concept started in the early 1907 by Winterberg, who hypothesized that multiple rapid firing foci which distributed throughout the atria was the source of AF [62, 63]. Next, Mines introduced the circus movement reentry theory [62, 63]. Thereafter, more researchers had tried to explain the mechanism of AF based on theories on circus movement and ectopic focus [42, 62, 63]. Moe *et al.* later explained the maintenance of AF using multiple wavelet hypothesis [1, 18, 37, 42, 59, 62, 64]. The hypothesis states that AF is sustained by a number of coexisting wavelet which propagate randomly throughout the atria during AF [1, 20, 37, 42, 62]. In other words, they postulated that AF as a turbulent and self-sustaining process which was not dependent on any driver [33, 42, 63]. Haissaguerre *et al.* had also reported that AF was triggered by repetitive rapid discharges from the PVs [33, 42].

Recent research has however claimed that the AF maintenance correlates highly with the rotors theory [62, 63]. The rotor theory was proposed by Jalife *et al.* [1, 42, 63]. They believed that AF was spatio-temporally well organized and maintained by the spiraling wavefronts produced by a rotating engine called the rotor [42, 62, 63]. The rotor was claimed as the DF source which mainly found in the posterior LA wall-PV region [62].

Besides that, cardiac autonomic ganglia which is the nervous tissue found on the heart surface are also thought to play the role in initiation and maintenance of AF [1, 49]. H. Takashima *et al.* had reported that heterogeneous conduction was observed at the roof and inferior region of the posterior LA in most of the AF patients under experiment [65]. They also claimed that the direction of the wavefronts affect the conduction properties of the posterior LA which may play an important role in the initiation and maintenance of AF thus complete isolation of the posterior LA may prevent AF [65].

4.0 AF SIGNAL PREPROCESSING

Electrocardiogram (ECG) signal is the recorded representation signal of the electrical activity of the heart [2, 3, 28, 66-69]. It has become one of the important diagnose tools for a person heart condition [2, 22, 68, 70-74]. AF ECG signal is always irregular [22]. Figure 2 shows the different pattern of a normal heartbeat signal and some abnormal signals, i.e. fast, slow and irregular. Fast heartbeat means shorter period and thus higher frequency and vice versa for a slow heartbeat.

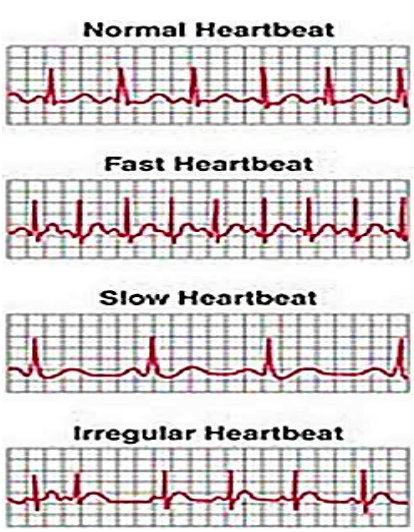


Figure 2 Normal and abnormal heartbeat patterns

Jason *et al*. mentioned that not all signals (for DF analysis) require preprocessing steps especially if the waveform of the signals are readily sinusoidal like [32]. These signals include monophasic action potential or the action potential-like signal obtained from optical mapping, as well as surface ECG fibrillatory wave (except QRS-T subtraction) [32]. However, the common local recording of atrial electrograms, either using unipolar or bipolar electrode will require signal preprocessing steps due to its typically sharp biphasic waveform [19, 32, 60]. The electrogram signal preprocessing steps include low pass filtering, QRS or QRS-T subtraction and rectification [32, 60].

4.1 Low Pass Filter

The atrial rate is in the range of (4±1 to 10±1) Hz [4, 22, 32, 35, 54, 75]. Hence, the signal greater than the frequency range should be filtered.

4.2 Ventricular Activity

Surface ECG frequency is said to be highly correlated with the intracardiac signals or atrial electrogram [23, 76-78]. In ECG signal, the QRS complex and T wave are due to the ventricular activity [1-3, 23, 54, 66-69, 73, 74, 79-84]. The ventricular activity rate might range between 10-30 Hz, which is overlapped with the AF signal [2, 19, 54]. Hence, the noise due to ventricular activity should be removed by subtracting QRS or QRS-T components of AF to avoid false determination of DF of AF [23, 54, 80, 83-85]. Surface ECG usually is used as the reference to identify the ventricular wave to be removed [2, 71, 75, 86].

4.3 QRS or QRS-T Subtraction

QRS or QRS-T subtraction is one of the important step in the signal pre-processing [41, 87]. A. Ahmad *et al.* had presented comparison on three types of QRS subtraction for atrial electrograms, namely flat, linear and spline interpolations [1, 54]. According to the result, all the three types of interpolations only show significant different in the power of the signals but not the dominant frequency [1, 54]. J. L. Salinet Jr *et al.* had proposed QRS-T subtraction approach and comparing it with average beat subtraction (ABS) and flat interpolation QRS subtraction methods [75]. The results show that QRS-T subtraction was better than QRS subtraction and almost similarly do well as the ABS method [75].

4.4 Rectification

The necessary of signal rectification for AF signal pre-processing has not been discussed by researchers. Rectification generally transform biphasic waveform into monophasic waveform using absolute value function [32]. J. Ng *et al.* had highlighted that rectification step causes the peak and troughs of signal become correspond with a sinusoid signal [32], as shown in Figure 3. However, whether this rectification step should be applied on either surface ECG signal (as reference) or atrial electrogram signal is also an issue. The similarity of a signal pattern with the sinusoid signal (in time domain) is important to reduce error when using Fourier transform method for analysis [32].

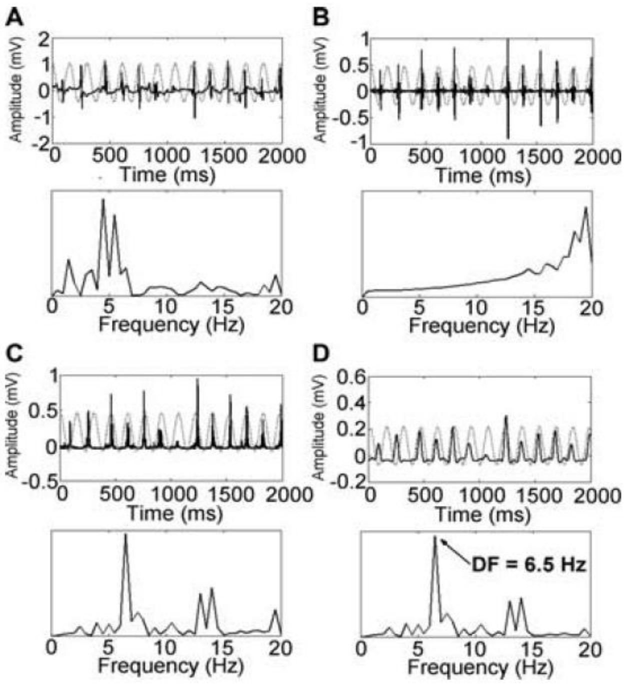


Figure 3 Common preprocessing steps that are used prior to Fast Fourier Transformation of bipolar electrograms of AF. (A) Original bipolar electrogram recording. (B) Signal after bandpass filtering from 40 to 250 Hz. (C) Signal after rectification. (D) Signal after lowpass filtering with a 20 Hz cutoff frequency [32]

5.0 TIME-FREQUENCY DOMAIN ANALYSIS

Generally, signal analysis will be either in time or frequency domain, depending on the suitability of the signal under analysis [30].

Signal interpretation in time domain is simple and showing the changes of parameters with time which is known as temporal change [23, 32, 59]. Time domain analysis usually used to determine the cycle length (CL) for the atrial electrogram [31, 59]. CL is defined as the length or period between QRS complexes or a cycle of signal [59]. According to S. Ammar *et al.*, a shorter AFCL is associated with a longer duration of AF, longer procedural time and larger left atrium diameter [88, 89]. Yet, the irregular characteristic of AF making time domain analysis becomes difficult and often being an obstacle for measurement of accurate CL [32, 59, 61].

Another approach using time domain is CFAE. CFAE was first proposed by Nademanee *et al.* as a new ablation approach in 2004 [31, 90]. CFAE was defined as fractionated atrial electrograms with at least two deflections and atrial electrograms with cycle length less than 120ms (averaged over 10s) [33]. CFAE sites was proposed as one of the important regions in the atria maintaining AF, thus also becomes the ablation target area by some researchers [13, 40, 91, 92]. However, a research done by Grzeda *et al.* in 2006 has shown that the use of CFAE method for AF sites for ablation prediction is prone to degradation [31, 92]. F. Atienza *et al.* had also concluded that CFAE ablation should not be used as a stand-alone treatment option [46].

In contrast, frequency domain analysis is more preferable for interpreting AF signal which is random and often chaotic [1, 4, 5, 31, 32, 54, 59]. The strength of different frequencies in a time interval will be represented in frequency domain so that signal will be analyzed in terms of the change in parameters such as power versus frequency [32]. Using frequency domain analysis, dominant frequency (DF) is the common parameter determined for AF activation rate estimation [18, 30-32, 41, 43, 58, 60, 91-95]. DF is defined as the frequency at which the power or magnitude of the spectrum is maximum [1, 4, 18, 31, 32, 43, 50, 59-61, 92, 95, 96]. The better the atrial electrogram signal being approximated to a sinusoidal function, with its dominant frequency equal to the activation rate, the better the DF analysis could reflect the activation rate for treatment target [60].

The FFT method is commonly applied to determine DF of AF because it is more preferable than other methods, such as the Blackman Tukey (BT), autoregressive (AR) and multiple signal classification (MUSIC) due to its fast and accurate determination [1, 4, 58]. I. Romero *et al.* had also stated that Fourier analysis was more preferable in estimating the DF based on surface ECG when compare to ensemble average method, but similarly good with the wavelet analysis [41]. FFT studies on AF had shown a leftward shift in the dominant frequency [36].

C. Tobón *et al.* had conducted study in localizing continuous ectopic sources of high frequency during AF episodes in remodeled atria, and they claimed that the organization index mapping was better than dominant frequency mapping in the case [97]. Organization index (OI) is defined as ratio of area under the DF peak and its harmonic to the total area under the spectrum [78, 94, 96]. One of the weaknesses of OI measurement is that it involves only the fundamental and the first harmonic while ignoring the higher harmonics and thus did not contribute significantly to the overall power [78].

Nevertheless, researchers have attempted to analyze AF signal using both time domain and frequency domain [15, 23, 35, 93, 98]. Researchers claimed that time domain analysis and frequency domain analysis might have unequal robustness [99]. A. Elvan *et al.* suggested that DF should be determined from intervals instead of spectral analysis because they found out that there were poor correlation between mean, median and mode of AF cycle length and DF when using spectral analysis [100].

6.0 CONCLUSION

This paper has generally provide a review on the basic underlying theory of AF, including different types of AF, symptoms, risk factors, treatment options, mechanism and maintenance as well as signal preprocessing and analysis.

More researches are expected in future to identify the true mechanism of AF and to determine the right activation factors for AF maintenance, in order to improve the clinical treatment procedure.

Acknowledgement

The authors would like to thank the Ministry of Higher Education and Universiti Teknologi Malaysia for supporting this research under Q.J130000.2523.05H60.

References

[1] A. Ahmad. 2012. Dominant Frequency Estimation For Atrial Fibrillation Studies. PhD Thesis, University of Leicester.

[2] I. Saini, D. Singh and A. Khosla. 2013. QRS Detection Using K-Nearest Neighbor Algorithm (KNN) And Evaluation On Standard ECG Databases. *Journal of Advanced Research.* 4 (4): 331-344.

[3] R. Splinter. 2010. *Handbook of Physics in Medicine and Biology*. CRC PressI Llc.

[4] A. Ahmad, S. Buyamin and N. Senin. 2013. Frequency Analysis for Surface Electrocardiogram Of Atrial Fibrillation. *Jurnal Teknologi.* 64(5).

[5] N. Senin 2012. Frequency Analysis for Surface Electrocardiogram (ECG) of Atrial Fibrillation (AF). Bachelor of Engineering (Electrical-Control and Instrumentation). Universiti Teknologi Malaysia.

[6] W.-J. Rappel and S. M. Narayan. 2013. Theoretical Considerations For Mapping Activation In Human Cardiac Fibrillation. *Chaos: An Interdisciplinary Journal of Nonlinear Science.* 23(2): 023113.

[7] O. Berenfeld. 2010. Toward Discerning The Mechanisms Of Atrial Fibrillation From Surface Electrocardiogram And Spectral Analysis. *Journal of Electrocardiology*. 43(6): 509-514.

[8] M. D. Lesh, J. M. Kalman, J. E. Olgin and W. S. Ellis. 1996. The Role Of Atrial Anatomy In Clinical Atrial Arrhythmias. *Journal of Electrocardiology.* 29: 101-113.

[9] T. Sasaki, *et al.* 2006. Morphological Properties of Atrial Fibrillation Waves in Patients with Left Ventricular Dysfunction—Spectral Analysis of Atrial Fibrillation Waves in Dilated Cardiomyopathy. *Journal of Arrhythmia*. 22(2): 92-97.

[10] S. Colilla, A. Crow, W. Petkun, D. E. Singer, T. Simon and X. Liu. 2013. Estimates of Current and Future Incidence and Prevalence of Atrial Fibrillation in the U.S. Adult Population. *The American Journal of Cardiology*. 112(8): 1142-1147.

[11] P. R. B. Barbosa, *et al*. 2006. Spectral Turbulence Analysis Of The Signal-Averaged Electrocardiogram Of The Atrial Activation As Predictor Of Recurrence Of Idiopathic And Persistent Atrial Fibrillation. *International Journal Of Cardiology.* 107(3): 307-316.

[12] H. Sohara, *et al.* 2013. Radiofrequency Hot Balloon Catheter Ablation For The Treatment Of Atrial Fibrillation: A 3-Center Study In Japan. *Journal of Arrhythmia*. 29(1): 20-27.

[13] J. Chen, *et al.* 2014. A Decade Of Complex Fractionated Electrograms Catheter-Based Ablation For Atrial Fibrillation: Literature Analysis, Meta-Analysis And Systematic Review. *IJC Heart & Vessels*. 4: 63-72.

[14] M. Zoni-Berisso, *et al.* 2013. Frequency, Patientcharacteristics, Treatment Strategies, And Resource Usage Of Atrial Fibrillation (From The Italian Survey Of Atrial Fibrillation Management [ISAF] Study). *The American Journal Of Cardiology*. 111(5): 705-711.

[15] N. Ortigosa, Ó. Cano, G. Ayala, A. Galbis and C. Fernández. 2014. Atrial Fibrillation Subtypes Classification Using The General Fourier-Family Transform. *Medical Engineering & Physics*. 36(4): 554-560.

[16] S. S. Chugh, G. A. Roth, R. F. Gillum and G. A. Mensah. 2014. Global Burden of Atrial Fibrillation in Developed and Developing Nations. *Global Heart*. 9(1): 113-119.

[17] S. S. Chugh, *et al.* 2013. Worldwide Epidemiology Of Atrial Fibrillation: A Global Burden Of Disease 2010 Study. Circulation. *CIRCULATION AHA*. 113.005119.

[18] A. Ahmad, F. S. Schlindwein, J. H. Tuan and G. A. Ng. 2010. Isoprenaline and Atropine Effect on Atrial Arrhythmias Study. *ASME 2010 10th Biennial Conference on Engineering Systems Design and Analysis*. 839-842.

[19] V. D. A. Corino, R. Sassi, L. T. Mainardi and S. Cerutti. 2006. Signal Processing Methods For Information Enhancement In Atrial Fibrillation: Spectral Analysis And Non-Linear Parameters. *Biomedical Signal Processing and Control*. 1(4): 271-281.

[20] K. Yoshida and K. Aonuma. 2012. Catheter Ablation Of Atrial Fibrillation: Past, Present, And Future Directions. *Journal of Arrhythmia*. 28(2): 83-90.

[21] E. Kodani and H. Atarashi. 2012. Prevalence Of Atrial Fibrillation In Asia And The World. *Journal of Arrhythmia*. 28(6): 330-337.

[22] R. J. Martis, U. R. Acharya, H. Prasad, C. K. Chua, C. M. Lim and J. S. Suri. 2013. Application Of Higher Order Statistics For Atrial Arrhythmia Classification. *Biomedical Signal Processing and Control.* 8(6): 888-900.

[23] S. Petrutiu, J. Ng, G. M. Nijm, H. Al-Angari, S. Swiryn and A. V. Sahakian. 2006. Atrial Fibrillation And Waveform Characterization. *Engineering in Medicine and Biology Magazine, IEEE.* 25(6): 24-30.

[24] T. N. Nguyen, S. N. Hilmer and R. G. Cumming. 2013. Review Of Epidemiology And Management Of Atrial Fibrillation In Developing Countries. *International Journal Of Cardiology*. 167(6): 2412-2420.

[25] A. Workman, G. Smith and A. Rankin. 2011. Mechanisms Of Termination And Prevention Of Atrial Fibrillation By Drug Therapy. *Pharmacology & Therapeutics.* 131(2): 221-241.

[26] B. J. Padanilam and E. N. Prystowsky. 2008. *Epidemiology of Atrial Fibrillation The Rising Prevalence*. Springer.

[27] T. M. Maddox, I. S. Nash and V. Fuster. 2008. *Economic Costs Associated With Atrial Fibrillation*. Springer.

[28] R. J. Martis, U. R. Acharya and L. C. Min. 2013. ECG Beat Classification Using PCA, LDA, ICA And Discrete Wavelet Transform. *Biomedical Signal Processing and Control.* 8(5): 437-448.

[29] R. Omar, *et al.* 2011. Atrial Fibrillation in Singapore and Malaysia: Current Trends and Future Prospects. *Journal of Arrhythmia.* 27(3): 171-185.

[30] H. Zhongchao, T. Jijun, C. Yuquan and P. Ming. 2006. A Novel spectral Analysis Method of Atrial Fibrillation Signal Based on Hilbert-Huang Transform. Engineering in Medicine and Biology Society, 2005. *IEEE-EMBS 2005. 27th Annual International Conference of the*. 17-18 Jan. 825-828.

[31] L. Yenn-Jiang. 2012. The Frequency Analysis and the Atrial Fibrillation. *Journal of Biocatalysis & Biotransformation.* 1(2): 1-2.

[32] J. Ng and J. J. Goldberger. 2007. Understanding And Interpreting Dominant Frequency Analysis Of AF

Electrograms. *Journal of Cardiovascular Electrophysiology.* 18(6): 680-685.

[33] C. K. Ching, D. Patel and A. Natale. 2007. Catheter Ablation Of Atrial Fibrillation. *Journal of Arrhythmia.* 23(2): 85-101.

[34] H. Fukaya, *et al.* 2009. Attenuating Effects of Anti-Arrhythmic Agents on Changes in Fibrillation Cycle Length in Very Early Phase Paroxysmal Atrial Fibrillation—Spectral Analysis of Fibrillation Waves in Surface ECG. *Journal of Arrhythmia.* 25(3): 135-141.

[35] M. Aunes-Jansson, N. Edvardsson, M. Stridh, L. Sörnmo, L. Frison and A. Berggren. 2013. Decrease Of The Atrial Fibrillatory Rate, Increased Organization Of The Atrial Rhythm And Termination Of Atrial Fibrillation By AZD7009. *Journal of Electrocardiology.* 46(1): 29-35.

[36] J. C. Pachon M, *et al.* 2004. A New Treatment For Atrial Fibrillation Based On Spectral Analysis To Guide The Catheter RF-Ablation. *Eurospace.* 6(6): 590-601.

[37] P. Sanders, *et al.* 2005. Spectral Analysis Identifies Sites Of High-Frequency Activity Maintaining Atrial Fibrillation In Humans. *Circulation*. 112(6): 789-797.

[38] M. Meo, V. Zarzoso, O. Meste, D. G. Latcu and N. Saoudi. 2013. Catheter Ablation Outcome Prediction In Persistent Atrial Fibrillation Using Weighted Principal Component Analysis. *Biomedical Signal Processing and Control.* 8(6): 958-968.

[39] Y. H. KIM, H. E. LIM and H. N. PAK. 2006. Use Of Three- Dimensional Mapping Systems In The Catheter Ablation Of Atrial Fibrillation. *Journal of Cardiovascular Electrophysiology*. 17(s3): S16-S22.

[40] D. Katritsis, F. M. Merchant, T. Mela, J. P. Singh, E. K. Heist and A. A. Armoundas. 2010. Catheter Ablation of Atrial FibrillationThe Search for Substrate-Driven End Points. *Journal of the American College of Cardiology.* 55(21): 2293-2298.

[41] I. Romero, E. Fleck and C. Kriatselis. 2011. Frequency Analysis Of Atrial Fibrillation Surface And Intracardiac Electrograms During Pulmonary Vein Isolation. *Cardiovasc Res*. 54(2): 204-216.

[42] M. Yamazaki and J. Jalife. 2012. Pathophysiology Of Atrial Fibrillation: From Initiation To Maintenance. *Journal of Arrhythmia.* 28(3): 129-139.

[43] Y.-J. Lin, *et al.* 2006. Frequency Analysis in Different Types of Paroxysmal Atrial Fibrillation. *Journal of the American College of Cardiology.* 47(7): 1401-1407.

[44] S.-A. Chen, *et al.* 1999. Initiation Of Atrial Fibrillation By Ectopic Beats Originating From The Pulmonary Veins Electrophysiological Characteristics, Pharmacological Responses, And Effects Of Radiofrequency Ablation. *Circulation.* 100(18): 1879-1886.

[45] G. Hindricks and H. Kottkamp. 2001. Simultaneous Noncontact Mapping Of Left Atrium In Patients With Paroxysmal Atrial Fibrillation. *Circulation*. 104(3): 297-303.

[46] F. Atienza, *et al.* 2011. Mechanisms Of Fractionated Electrograms Formation In The Posterior Left Atrium During Paroxysmal Atrial Fibrillation In Humans. *Journal of the American College of Cardiology.* 57(9): 1081-1092.

[47] T. Yamane. 2012. Current Strategies For Non-Pharmacological Therapy Of Long-Standing Persistent Atrial Fibrillation. *Journal of Arrhythmia.* 28(3): 155-161.

[48] S.-h. Wu, *et al.* 2013. Benefits And Risks Of Additional Ablation Of Complex Fractionated Atrial Electrograms For Patients With Atrial Fibrillation: A Systematic Review And Meta-Analysis. *International Journal Of Cardiology.* 169(1): 35-43.

[49] B. Scherlag, *et al.* 2005. Electrical Stimulation to Identify Neural Elements on the Heart: Their Role in Atrial Fibrillation. *Journal of Interventional Cardiac Electrophysiology.* 13(1): 37-42.

[50] E. J. Ciaccio, A. B. Biviano, A. Gambhir, J. T. Jacobson and H. Garan. 2014. Temporal Stability in the Spectral Representation of Complex Fractionated Atrial Electrograms. *Pacing and Clinical Electrophysiology.* 37(1): 79-89.

[51] M. Takahashi, et al. 2012. Outcomes After Stepwise Ablation For Persistent Atrial Fibrillation In Patients With Heart Failure. *Journal of Arrhythmia.* 28(6): 347-352.

[52] J. Zhao, Y. Yao, R. Shi, W. Huang, B. H. Smaill and N. A. Lever. 2015. Progressive Modification Of Rotors In Persistent Atrial Fibrillation By Stepwise Linear Ablation. *HeartRhythm Case Reports.* 1(1): 22-26.

[53] M. El Haddad, R. Houben, R. Stroobandt, F. Van Heuverswyn, R. Tavernier and M. Duytschaever. 2013. Algorithmic Detection Of The Beginning And End Of Bipolar Electrograms: Implications For Novel Methods To Assess Local Activation Time During Atrial Tachycardia. *Biomedical Signal Processing and Control.* 8(6): 981-991.

[54] A. Ahmad, *et al.* 2011. *QRS Subtraction For Atrial Electrograms: Flat, Linear And Spline Interpolations. Medical & Biological Engineering & Computing.* 49(11): 1321-1328.

[55] M. S. Guillem, *et al*. 2013. Noninvasive Localization Of Maximal Frequency Sites Of Atrial Fibrillation By Body Surface Potential Mapping. *Circulation: Arrhythmia and Electrophysiology*. 6(2): 294-301.

[56] S. Gojraty, N. Lavi, E. Valles, S. J. Kim, J. Michele and E. P. Gerstenfeld. 2009. Dominant Frequency Mapping Of Atrial Fibrillation: Comparison Of Contact And Noncontact Approaches. *Journal Of Cardiovascular Electrophysiology.* 20(9): 997-1004.

[57] F. Atienza, *et al.* 2009. Real-Time Dominant Frequency Mapping And Ablation Of Dominant Frequency Sites In Atrial Fibrillation With Left-To-Right Frequency Gradients Predicts Long-Term Maintenance Of Sinus Rhythm. *Heart Rhythm.* 6(1): 33-40.

[58] A. Ahmad, F. S. Schlindwein and G. A. Ng. 2010. Comparison Of Computation Time For Estimation Of Dominant Frequency Of Atrial Electrograms: Fast Fourier Transform, Blackman Tukey, Autoregressive And Multiple Signal Classification. *Journal of Biomedical Science and Engineering.* 3: 843.

[59] V. B. Traykov, R. Pap and L. Sághy. 2012. Frequency Domain Mapping Of Atrial Fibrillation-Methodology, Experimental Data And Clinical Implications. *Current Cardiology Reviews.* 8(3): 231.

[60] J. Ng, A. H. Kadish and J. J. Goldberger. 2007. Technical Considerations for Dominant Frequency Analysis. *Journal of Cardiovascular Electrophysiology.* 18(7): 757-764.

[61] J. Ng, V. Sehgal, D. Gordon and J. Goldberger. 2014. Iterative Method to Detect Atrial Activations and Measure Cycle Length from Electrograms during Atrial Fibrillation. *IEEE Trans Biomedical Engineering.* 61(2): 273-278.

[62] J. Jalife. 2003. Rotors and Spiral Waves in Atrial Fibrillation. Journal of Cardiovascular *Electrophysiology.* 14(7): 776-780.

[63] J. Jalife, O. Berenfeld and M. Mansour. 2002. Mother Rotors And Fibrillatory Conduction: A Mechanism Of Atrial Fibrillation. *Cardiovasc Res.* 54(2): 204-216.

[64] S. Nattel, A. Shiroshita-Takeshita, B. J. Brundel and L. Rivard. 2005. Mechanisms Of Atrial Fibrillation: Lessons From Animal Models. *Progress In Cardiovascular Diseases.* 48(1): 9-28.

[65] H. Takashima, *et al.* 2010. Characteristics Of The Conduction Of The Left Atrium In Atrial Fibrillation Using Non-Contact Mapping. *Journal of Cardiology*. 56(2): 166-175.

[66] Y.-C. Yeh and W.-J. Wang. 2008. QRS Complexes Detection For ECG Signal: The Difference Operation Method. *Computer Methods And Programs In Biomedicine*. 91(3): 245-254.

[67] S. Chouakri, F. Bereksi-Reguig and A. Taleb-Ahmed. 2011. QRS Complex Detection Based On Multi Wavelet Packet Decomposition. *Applied Mathematics and Computation*. 217(23): 9508-9525.

[68] S. Pal and M. Mitra. 2012. Empirical Mode Decomposition Based ECG Enhancement And QRS Detection. *Computers In Biology And Medicine*. 42(1): 83-92.

[69] Z. Zidelmal, A. Amirou, M. Adnane and A. Belouchrani. 2012. QRS Detection Based On Wavelet Coefficients. *Computer Methods And Programs In Biomedicine.* 107(3): 490-496.

[70] A. Daamouche, L. Hamami, N. Alajlan and F. Melgani. 2012. A Wavelet Optimization Approach For ECG Signal Classification. *Biomedical Signal Processing and Control.* 7(4): 342-349.

[71] H. Zhang. 2012. An Improved QRS Wave Group Detection Algorithm and Matlab Implementation. *Physics Procedia.* 25: 1010-1016.

[72] S. Banerjee, R. Gupta and M. Mitra. 2012. Delineation Of ECG Characteristic Features Using Multiresolution Wavelet Analysis Method. *Measurement.* 45(3): 474-487.

[73] M. A. Kabir and C. Shahnaz. 2012. Denoising Of ECG Signals Based On Noise Reduction Algorithms In EMD And Wavelet Domains. *Biomedical Signal Processing and Control.* 7(5): 481-489.

[74] R. Tafreshi, A. Jaleel, J. Lim and L. Tafreshi. 2014. Automated Analysis Of ECG Waveforms With Atypical QRS Complex Morphologies. *Biomedical Signal Processing and Control.* 10: 41-49.

[75] J. L. Salinet Jr, J. P. V. Madeiro, P. C. Cortez, P. J. Stafford, G. André Ng and F. S. Schlindwein. 2013. Analysis Of QRS-T Subtraction In Unipolar Atrial Fibrillation Electrograms. *Medical & Biological Engineering & Computing.* 51(12): 1381-1391.

[76] S. Uetake, *et al.* 2014. Frequency Analysis Of Surface Electrocardiograms (Ecgs) In Patients With Persistent Atrial Fibrillation: Correlation With The Intracardiac Ecgs And Implications For Radiofrequency Catheter Ablation. *Journal of Arrhythmia.* 30(6): 453-459.

[77] M. H. Raitt and W. Kusumoto. 2012. Correlations Among The Frequencies Of Atrial Activity On The Surface Electrocardiogram, Intracardiac Atrial Electrograms, And The Atrial Effective Refractory Period In Patients With Atrial Fibrillation. *Journal Of Electrocardiology*. 45 (3): 296-303.

[78] A. Buttu, *et al.* 2013. Adaptive Frequency Tracking Of The Baseline ECG Identifies The Site Of Atrial Fibrillation Termination By Catheter Ablation. *Biomedical Signal Processing and Control*. 8(6): 969-980.

[79] F. I. Donoso, R. L. Figueroa, E. A. Lecannelier, E. J. Pino and A. J. Rojas. 2013. Atrial Activity Selection For Atrial Fibrillation ECG Recordings. *Computers In Biology And Medicine.* 43(10): 1628-1636.

[80] V. D. Corino, M. W. Rivolta, R. Sassi, F. Lombardi and L. T. Mainardi. 2013. Ventricular Activity Cancellation In Electrograms During Atrial Fibrillation With Constraints On Residuals' Power. *Medical Engineering & Physics.* 35(12): 1770-1777.

[81] J. P. V. Madeiro, P. C. Cortez, J. A. L. Marques, C. R. V. Seisdedos and C. R. M. R. Sobrinho. 2012. An Innovative Approach Of QRS Segmentation Based On First-Derivative, Hilbert And Wavelet Transforms. *Medical Engineering & Physics.* 34(9): 1236-1246.

[82] S. Pal and M. Mitra. 2010. Detection Of ECG Characteristic Points Using Multiresolution Wavelet Analysis Based Selective Coefficient Method. *Measurement.* 43(2): 255-261.

[83] H.-W. Tso, Y.-J. Lin, C.-T. Tai, S.-A. Chen and T. Kao. 2012. Characteristics Of Fibrillatory Activities During Spontaneous Termination Of Paroxysmal Atrial Fibrillation: New Insight From High-Density Right Atrium Frequency Mapping. *Canadian Journal of Cardiology.* 28(1): 87-94.

[84] J. J. Rieta Ibañez and R. ALCARAZ MARTÍNEZ. 2013. Applications of Signal Analysis to Atrial Fibrillation. *Atrial Fibrillation-Mechanisms and Treatment.* 155-180.

[85] J. Mateo and J. Joaquín Rieta. 2013. Radial Basis Function Neural Networks Applied To Efficient QRST Cancellation In Atrial Fibrillation. *Computers In Biology And Medicine.* 43(2): 154-163.

[86] J. L. Salinet, A. Ahmad, P. D. Brown, P. Stafford, G. A. Ng and F. S. Schlindwein. 2010. Three-Dimensional Frequency Mapping From The Noncontact Unipolar Electrograms In Atrial Fibrillation. *Computing in Cardiology*. 26-29 Sept. 745-748.

[87] M. S. Manikandan and K. Soman. 2012. A Novel Method For Detecting R-Peaks In Electrocardiogram (ECG) Signal. *Biomedical Signal Processing and Control*. 7(2): 118-128.

[88] P. G. Platonov and F. Holmqvist. 2011. Atrial Fibrillatory Rate And Irregularity Of Ventricular Response As Predictors Of Clinical Outcome In Patients With Atrial Fibrillation. *Journal of Electrocardiology.* 44(6): 673-677.

[89] S. Ammar, *et al.* 2014. Impact Of Baseline Atrial Fibrillation Cycle Length On Acute And Long-Term Outcome Of Persistent Atrial Fibrillation Ablation. *Journal of Interventional Cardiac Electrophysiology.* 41(3): 253-259.

[90] N. Oketani, *et al.* 2012. Catheter Ablation Of Atrial Fibrillation Guided By Complex Fractionated Atrial Electrogram Mapping With Or Without Pulmonary Vein Isolation. *Journal of Arrhythmia.* 28(6): 311-323.

[91] S.-L. Chang, *et al.* 2013. Electrophysiological Characteristics Of Complex Fractionated Electrograms And High Frequency Activity In Atrial Fibrillation. *International Journal Of Cardiology*. 168(3): 2289-2299.

[92] K. R. Grzeda, S. F. Noujaim, O. Berenfeld and J. Jalife. 2009. Complex Fractionated Atrial Electrograms: Properties Of Time-Domain Versus Frequency-Domain Methods. Heart Rhythm. *The Official Journal Of The Heart Rhythm Society.* 6(10): 1475-1482.

[93] R. Zolei-Szenasi, G. Vadai, R. Pap and Z. Gingl. 2014. Enhanced Time-Domain Detection Of The Activation Frequency Of Atrial Fibrillation. *Applied Computational Intelligence And Informatics (SACI), 2014 IEEE 9th International Symposium on*. 349-353.

[94] S. Lee, K. Ryu, A. L. Waldo, C. M. Khrestian, D. M. Durand and J. Sahadevan. 2013. An Algorithm To Measure Beat- To- Beat Cycle Lengths For Assessment Of Atrial Electrogram Rate And Regularity During Atrial Fibrillation. *Journal Of Cardiovascular Electrophysiology.* 24(2): 199-206.

[95] K. Nagashima, *et al.* 2013. Termination Of Atrial Fibrillation By Ablation Of High-Dominant Frequency Sites Adjacent To Epicardial Adipose Tissue. *Journal of Arrhythmia.* 29(4): 242-243.

[96] J. W. E. Jarman, *et al.* 2014. Organizational Index Mapping to Identify Focal Sources During Persistent Atrial Fibrillation. *Journal of Cardiovascular Electrophysiology.* 25(4): 355-363.

[97] C. Tobón, J. F. Rodríguez, J. M. Ferrero, F. Hornero and J. Saiz. 2012. Dominant Frequency And Organization Index Maps In A Realistic Three-Dimensional Computational Model Of Atrial Fibrillation. *Europace.* 14: 25-32.

[98] O. Berenfeld, *et al.* 2011. Time-And Frequency-Domain Analyses Of Atrial Fibrillation Activation Rate: The Optical Mapping Reference. *Heart Rhythm*. 8(11): 1758-1765.

[99] E. J. Ciaccio, A. B. Biviano and H. Garan. 2013. Computational Method For High Resolution Spectral Analysis Of Fractionated Atrial Electrograms. *Computers In Biology And Medicine*. 43(10): 1573-1582.

[100] A. Elvan, *et al.* 2009. Dominant Frequency Of Atrial Fibrillation Correlates Poorly With Atrial Fibrillation Cycle Length. *Circulation: Arrhythmia and Electrophysiology*. 2(6): 634-644.