Spectral Analysis of the ECG to Guide Optimal Endpoint in Catheter Ablation of Atrial Fibrillation

Raúl Alcaraz[1], Fernando Hornero[2], José J Rieta[3]

[1] Research Group in Electronic, Biomedical and Telecomm. Eng., Univ. of Castilla-La Mancha, Spain
[2] Cardiac Surgery Department, Clinical University Hospital of Valencia, Spain
[3] BioMIT.org, Electronic Engineering Department, Universitat Politecnica de Valencia, Spain

Abstract

Thanks to its high rates of success, catheter ablation (CA) is nowadays considered as the first-line therapy to treat atrial fibrillation (AF). However, a procedural consensus beyond pulmonary veins isolation (PVI) still lacks for patients with persistent AF. Nonetheless, the main goal of every CA procedure is to ablate the least amount of tissue able to render patients free from AF at long-term. Hence, the identification of an optimal CA endpoint is an interesting clinical challenge. For that purpose, the present work explores the ability of some spectral features obtained from the atrial activity (AA) reflected on the surface ECG. More precisely, the variations experienced during the procedure by the dominant atrial frequency (DAF), its 3 dB bandwidth and the median atrial frequency (MAF) are analyzed from lead V1 in 15 patients undergoing CA. The obtained results show a strong agreement between the DAF and MAF, which are able to anticipate with an accuracy between 70 and 80% the patients' rhythm after a follow-up of 3 months. As a consequence, monitoring AA spectral features could be helpful in quantifying the atrial substrate alteration provoked by CA procedures.

1. Introduction

Atrial fibrillation (AF) is the most common clinically important arrhythmia, with a recent worldwide estimate of up to 33.5 million patients, without including those with silent disease [1]. Moreover, its prevalence is expected to increase 3-fold in the next 3 decades, thus making this arrhythmia a global epidemic [2]. Unfortunately, the presence of AF is associated with increased risk of stroke and heart failure, and decreased quality of life and survival [3, 4]. Indeed, the AF-related symptoms, such as fatigue, dizziness, faintness and chest pain (among others), as well as its morbidity are responsible for frequent visits to the physician and hospitalizations, thus leading to extensive and rising costs for the Health Services [5].

Considering its natural progression, AF can be classified into three different forms [6]. It often starts as paroxysmal (self-terminating) episodes and becomes persistent or permanent with time. Paroxysmal AF is defined as attacks of AF lasting from several seconds to less than 7 days, and spontaneously reverting to sinus rhythm (SR). Persistent AF lasts more than 7 days, but responds to external interventions and SR can be restored. Finally, permanent AF does not respond to therapy and both the clinician and the patient accept to make a joint decision to stop further attempts to revert AF. Thus, only interventions to control the heart rate are pursued.

To restore SR both in paroxysmal and persistent AF patients, non-invasive pharmacological and electrical cardioversions are usually the first options [7]. However, these treatments have proven a limited effectiveness to modify the atrial substrate and, consequently, to avoid long-term AF recurrences [7]. In this context, catheter ablation (CA) has emerged in the last years as an effective tool to treat symptomatic patients with drug-refractory AF [8]. In fact, this therapy has evolved considerably to become safer and more effective and is now among the most frequently performed cardiac procedures [2].

Since Haissaguere et al. [9] demonstrated that rapid bursts of ectopic beats originating from the muscle sleeves of the pulmonary veins (PVs) were the main source of AF, its isolation remains as the "gold standard" approach [8]. However, its success rate is suboptimal especially for patients with persistent AF in whom more extensive ablation techniques have been proposed [2]. Targeting complex and fractionated atrial electrograms (CFAEs), linear ablation, and isolation of invasively or non-invasively detected drivers of AF are the most relevant complementary strategies [8]. However, recent mutli-centric studies have put a question mark about the effectiveness of these procedures compared to PVI alone, thus highlighting the need of additional clinical trials [10, 11].

Despite the lack of a procedural consensus beyond the PVI, the main goal of every CA protocol is to ablate the

 ISSN: 2325-887X DOI:10.22489/CinC.2017.339-125

least amount of tissue able to render patients free from AF at long-term [12]. Generally, most of the CA procedures finish when AF reverts and its reinduction is not possible [12]. However, no strong evidences support AF termination as a reliable indicator of clinical efficacy [12]. Thus, considering that some previous works have revealed that a decrease higher than 10% in the surface ECG dominant atrial frequency (DAF) could be an effective CA endpoint for persistent AF patients [13], this work explores the ability of two additional spectral features of the atrial activity (AA) signal for the same purpose.

2. Materials

The standard 12-lead ECG recording along with other typical intra-cardiac bipolar signals were acquired with a sampling rate of 977 Hz and 16-bit resolution during the whole CA procedure for 15 patients in persistent AF. The details related to the used CA protocol can be found in [14]. In brief, the PVI was firstly reached by creating a circumferential set of lesions. Then, those atrial points showing the highest values of DAF were ablated in a similar way. The procedure finished when AF terminated and its reinduction was impossible or when all the points with a DAF greater than 1.2 times the basal frequency were targeted. In this later case, electrical cardioversion was applied if the patient was still in AF. Three months after the procedure, 8 patients had again relapsed to AF and the remaining ones continued in SR.

3. Methods

3.1. Data preprocessing

With the aim to study the variation experimented by the analyzed spectral features, a 10 second-length ECG segment just before the CA procedure started and another one just before its end were selected from the lead V1. This lead was analyzed because it contains the highest fibrillatory waves compared to the ventricular activity [15]. Both ECG intervals were typically preprocessed to remove noise and nuisance interferences. Thus, they were filtered by using a forward/backward high-pass filtering (0.5 Hz cut-off frequency) to remove base-line wander, a low-pass filtering (70 Hz cut-off frequency) to reduce high frequency muscle noise and an adaptive notch filtering at 50 Hz to remove power-line interference [16].

3.2. Atrial activity spectral profiling

The AA component was extracted from each preprocessed ECG segment by using an adaptive QRST cancellation method [17]. The most similar 15 beats to the one under cancellation were used to generate the ventricular template for its subtraction. The power spectral density (PSD) of the resulting signal was then estimated making use of the Welch periodogram. A Hamming window of 4096 samples in length, a 50% overlapping between adjacent windowed sections and a 10240-points Fast Fourier Transform (FFT) were used as computational parameters [18].

According to many previous works [13], the highest amplitude frequency in the range of 3–9 Hz was selected as the DAF. Additionally, its 3 dB bandwidth (BW) and the median atrial frequency (MAF) of the AA spectral content were also computed. This last index was defined as the frequency dividing the PSD into two equal halves [19].

3.3. Performance assessment

The differences between the spectral indices computed for the segments before and after CA were obtained in percentage with regard to the initial value and, then, expressed as mean $\pm$ standard deviation for the patients maintaining SR and relapsing to AF after the follow-up. Additionally, the statistical differences between both groups of patients were tested by a t-Student's test. A two-tailed value of $\rho < 0.05$ was considered as statistically significant.

On the other hand, the ability of each spectral feature to discern between the two groups of patients was evaluated by means of a ROC curve. This graph is the result of plotting the proportion of true positives (TP) out of positives (sensitivity) against the proportion of false positives out of the negatives ($1-$specificity) at various threshold settings. Sensitivity was considered as the percentage of patients who maintained SR correctly classified. Similarly, the rate of patients relapsing to AF was considered as the specificity. The optimal threshold was selected as those that provided the highest percentage of patients correctly classified, i.e. the highest accuracy.

4. Results

An illustrative example of the results is shown in Fig. 1, where the segments before and after CA together with their corresponding AA signals and spectral features are displayed for a patient maintaining SR after the follow-up. Note that the spectral distribution maintains its shape after CA, but it is notably shifted towards lower frequencies. The global results have been included in Table 1 and Fig. 2. Although high dispersion can be noticed, the indices DAF and MAF reported statistically significant ($\rho < 0.05$) decreases for patients maintaining sinus rhythm compared to those relapsing to AF. Indeed, whereas no relevant changes in both parameters were observed for the second group of patients, a notable drop was seen for the first one.

In agreement with these results, the DAF and MAF also provided a promising ability to anticipate the CA outcome after the follow-up. However, the MAF reported

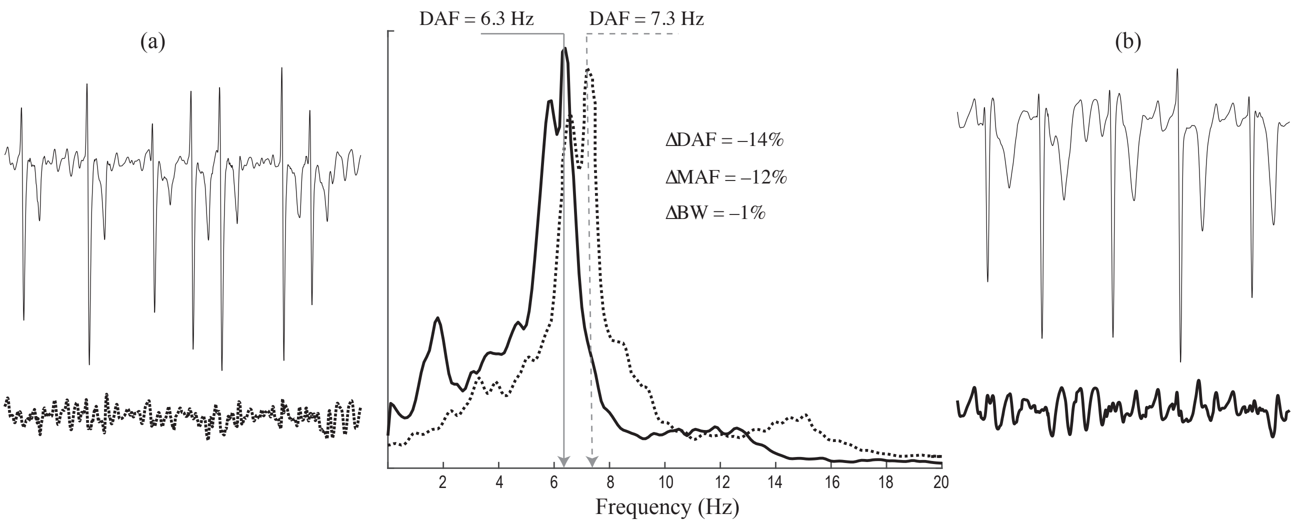

Figure 1. Example of three second-length ECG segments and their corresponding extracted atrial activity for a patient maintaining SR after the follow-up. (a) Segment before CA. (b) Segment after CA. The middle panel shows the spectral distributions for both AA segments evidencing considerable variations in the analyzed parameters after CA.

Table 1. Mean and standard deviation values for the variation experimented by the spectral indices during the CA procedure. Statistical significance (ρ) is also shown.

Index	Patients maintaining SR	Patients relapsing to AF	ρ-value
ΔDAF	$-3.56 \pm 8.93\%$	$1.27 \pm 10.32\%$	0.04
ΔBW	$0.27 \pm 6.77\%$	$0.32 \pm 9.34\%$	0.17
ΔMAF	$-2.25 \pm 7.42\%$	$0.32 \pm 9.47\%$	0.04

a slightly higher diagnostic accuracy. Thus, whereas the DAF yielded values of sensitivity, specificity and accuracy of 71.43%, 75.01% and 73.33%, the MAF presented values of 85.71%,75.01% and 80.02%, respectively.

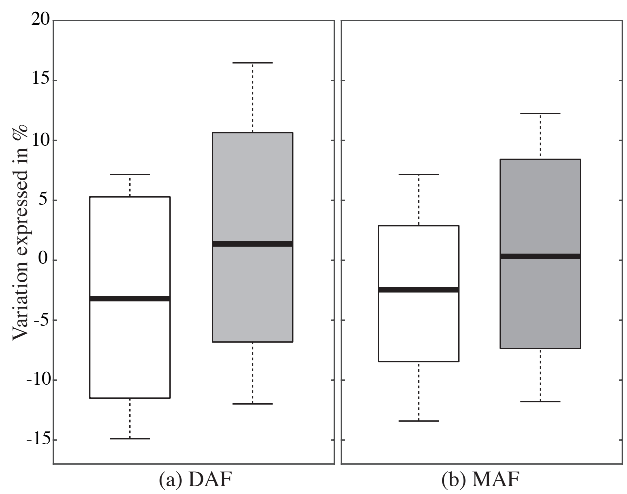

Figure 2. Boxplots of the variations obtained for the DAF (a) and MAF (b) from the patients maintaining SR (white box) and relapsing to AF (shaded box).

5. Discussion and conclusions

In contrast to previous works where the DAF has only been analyzed to estimate an optimal CA endpoint [13], two additional spectral indices, such as the DAF bandwidth and MAF, have been introduced for the first time in this context. The results show a strong agreement between the DAF and MAF, which have reported a statistically significant decrease for the patients maintaining SR after the follow-up. Although a considerably lower drop has been here observed, this result is in line with previous works where a DAF decrease higher than 10% has been identified as an effective CA endpoint [13]. Moreover, considering that lead V1 mainly reflects the fibrillatory frequency of the right atrium (RA) [20], the obtained outcome also agrees with the studies that have revealed a DAF decrease in RA for patients who remain free from AF, but not for those presenting AF recurrence, after some months [14].

Contrarily, the variation experimented during the CA procedure by the spectral concentration around the DAF, estimated through the BW, did not provide significative differences between the patients who relapsed to AF and those maintaining SR during the follow-up. To this respect, a similar result has also been reported when the index BW has been used to predict the recurrence of AF after electrical cardioversion [18]. Hence, given that both procedures of CA and electrical cardioversion provoke very different alterations on the substrate of AF, it may be concluded that this metric could also be poorly predictive of other therapeutical approaches for AF, such as pharmacological cardioversion or AF surgical ablation.

Finally, it has to be remarked that the number of analyzed patients is limited and, therefore, the obtained results must be considered with caution. Thus, although it could be suggested that non-invasive monitoring of the AA spectral features might be helpful in quantifying the atrial substrate alteration during CA and, hence, in guiding its optimal endpoint, further studies with expanded databases are mandatorily required to corroborate that finding.

Acknowledgements

Research supported by grants TEC2014–52250–R and DPI2017–83952–C3 MINECO/AEI/FEDER, UE.

References

[1] Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, Gillum RF, Kim YH, McAnulty Jr JH, Zheng ZJ, Forouzanfar MH, Naghavi M, Mensah GA, Ezzati M, Murray CJL. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. Circulation Feb 2014;129(8):837–47.

[2] Morin DP, Bernard ML, Madias C, Rogers PA, Thihalolipavan S, Estes 3rd NAM. The state of the art: Atrial fibrillation epidemiology, prevention, and treatment. Mayo Clin Proc Dec 2016;91(12):1778–1810.

[3] January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. Circulation Dec 2014; 130(23):e199–267.

[4] Freedman B, Potpara TS, Lip GYH. Stroke prevention in atrial fibrillation. Lancet Aug 2016;388(10046):806–17.

[5] Wodchis WP, Bhatia RS, Leblanc K, Meshkat N, Morra D. A review of the cost of atrial fibrillation. Value Health 2012; 15(2):240–8.

[6] Gallagher MM, Camm J. Classification of atrial fibrillation. Am J Cardiol Oct 1998;82(8A):18N–28N.

[7] Margulescu AD, Mont L. Persistent atrial fibrillation vs paroxysmal atrial fibrillation: differences in management. Expert Rev Cardiovasc Ther Aug 2017;15(8):601–618.

[8] Latchamsetty R, Morady F. Atrial fibrillation ablation. Annu Rev Med Aug 2017;.

[9] Haïssaguerre M, Jaïs P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Métayer P, Clémenty J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med Sep 1998;339(10):659–66.

[10] Verma A, Jiang Cy, Betts TR, Chen J, Deisenhofer I, Mantovan R, Macle L, Morillo CA, Haverkamp W, Weerasooriya R, Albenque JP, Nardi S, Menardi E, Novak P, Sanders P, STAR AF II Investigators. Approaches to catheter ablation for persistent atrial fibrillation. N Engl J Med May 2015;372(19):1812–22.

[11] Nattel S, Xiong F, Aguilar M. Demystifying rotors and their place in clinical translation of atrial fibrillation mechanisms. Nat Rev Cardiol Sep 2017;14(9):509–520.

[12] Baker M, Kumar P, Hummel JP, Gehi AK. Non-inducibility or termination as endpoints of atrial fibrillation ablation: What is the role? J Atr Fibrillation 2014;7(3):1125.

[13] Yoshida K, Chugh A, Good E, Crawford T, Myles J, Veerareddy S, Billakanty S, Wong WS, Ebinger M, Pelosi F, Jongnarangsin K, Bogun F, Morady F, Oral H. A critical decrease in dominant frequency and clinical outcome after catheter ablation of persistent atrial fibrillation. Heart Rhythm Mar 2010;7(3):295–302.

[14] Atienza F, Almendral J, Jalife J, Zlochiver S, et al. 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 Jan 2009;6(1):33–40.

[15] Petrutiu S, Ng J, Nijm GM, Al-Angari H, Swiryn S, Sahakian AV. Atrial fibrillation and waveform characterization. A time domain perspective in the surface ecg. IEEE Eng Med Biol Mag 2006;25(6):24–30.

[16] Sörnmo L, Laguna P. Biomedical Signal Processing in Cardiac and Neurological Applications. Elsevier Academic Press, 2005.

[17] Alcaraz R, Rieta JJ. Adaptive singular value cancelation of ventricular activity in single-lead atrial fibrillation electrocardiograms. Physiol Meas Dec 2008;29(12):1351–69.

[18] Alcaraz R, Rieta JJ. Time and frequency recurrence analysis of persistent atrial fibrillation after electrical cardioversion. Physiol Meas May 2009;30(5):479–89.

[19] Hornero R, Escudero J, Fernández A, Poza J, Gómez C. Spectral and nonlinear analyses of MEG background activity in patients with Alzheimer's disease. IEEE Trans Biomed Eng Jun 2008;55(6):1658–65.

[20] Hsu NW, Lin YJ, Tai CT, Kao T, Chang SL, Wongcharoen W, Lo LW, Udyavar AR, Hu YF, Tso HW, Higa S, Chen SA. Frequency analysis of the fibrillatory activity from surface ECG lead V1 and intracardiac recordings: implications for mapping of AF. Europace 2008;10(4):438–43.

Address for correspondence:

Raúl Alcaraz Martínez
Escuela Politécnica, Campus Universitario,
16071, Cuenca, Spain.
e–mail: raul.alcaraz@uclm.es