Frequency analysis of atrial fibrillation surface and intracardiac electrograms during pulmonary vein isolation

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Aims Frequency analysis of atrial electrograms from patients diagnosed with persistent atrial fibrillation (AF) appears to be crucial in its clinical diagnosis. This work explores the fibrillatory frequency properties of both surface and intracardiac electrograms before and after pulmonary vein isolation (PVI) using three time–frequency techniques.

Methods and results Surface electrocardiograms (ECGs) of 21 patients diagnosed with persistent AF undergoing PVI were recorded. Three methods, Fourier, ensemble average, and wavelet analysis, were used to identify the dominant frequency (DF) in surface ECGs. Dominant frequency was also computed in electrograms recorded within the coronary sinus (CS). Dominant frequency measured within the CS was best estimated in surface lead V1 using both Fourier (relative error: 10.94 ± 10.37%, correlation: 0.58) and wavelet analysis (relative error: 10.97 ± 11.08%, correlation: 0.53). Ensemble average gave highest relative error (21.29 ± 18.07%) and lowest correlation (0.10). Dominant frequency decreased after right PVI. This decrease was significant (P < 0.05) in most of the patients (13, 14, and 7 out of 14 when Fourier, wavelets, and ensemble average was used; 14 in CS). Further isolation of the left pulmonary veins (PVs) yielded a significant (P < 0.05) decrease in only a few of them (3, 4, and 2 out of 14 when Fourier, wavelets, and ensemble average was used; 4 in CS).

Conclusion Wavelet and Fourier analysis are good tools for estimating the atrial fibrillatory rate from surface ECG. A drop was observed in the DF value after isolation of the right PV. However, after left PVI this decrease was smaller.

Keywords Atrial fibrillation • Dominant frequency • Frequency analysis • Pulmonary vein isolation

Introduction

Atrial fibrillation (AF) is the most common clinical cardiac arrhythmia.1 This disorder is associated with a high risk of thromboembolic events.2 In most patients, atrial fibrillation (especially the paroxysmal form) is induced by very rapid, abnormal electrical activity arising from the pulmonary veins (PVs).3 Therefore, electrical isolation of the PVs from the atria has developed as a successful procedure to cure AF, especially in patients with normal heart structure and paroxysmal AF.

Frequency analysis of AF surface electrocardiogram (ECG) has been a focus of different studies in recent years.4 The main or dominant frequency (DF) of AF has been proposed as a marker to monitor the response to several pharmacotherapies.5 This frequency can be calculated from the surface ECG using different digital signal processing techniques that include pre-processing, QRS-T subtraction,6,7 and frequency analysis of the AF.8 Typically, frequency analysis of AF signals has been performed by computation of the Fourier transform.8–12 However, Fourier is limited to the use of sinusoidal analysing functions that do not fit well with ECG waveforms. Ciaccio et al.13 proposed the ensemble average as a new method for estimating the activation rate in electrograms that they claim is more robust. Another well-known tool for frequency analysis is the wavelet transform which provides high localization in time of frequency features. Wavelets are better suited to the wave shape of the signal under study giving better time–frequency characterization than classical Fourier analysis. Wavelet analysis has been widely used in the study of ECG signals.14,15 However, the performance of
wavelet analysis as an estimator of the atrial DF has never been studied.

In this work we analyse the performance of three different methods for frequency characterization of AF signals: the Fourier transform, ensemble average analysis, and the wavelet transform. We discuss the performance of these methods as tools for estimating the DF from within AF surface ECG signals. Finally, we study the effect of pulmonary vein isolation (PVI) in DF calculated for both surface ECGs and endocardiograms recorded within the coronary sinus (CS).

**Methods**

**Clinical data**

Surface ECGs of 21 patients diagnosed with persistent AF and undergoing PVI were recorded in the electrophysiology laboratory at the Deutsches Herzcentrum Berlin (German Heart Institute Berlin). The patients were 7 women and 14 men with a mean age of 60 (±9) years. The mean value ± standard deviation (SD) number of failed antiarrhythmic drugs was 2 (±1.3).

Pulmonary vein isolation was performed with a 3.5 mm irrigated-tip ablation catheter (Navistar, Biosense Webster Inc., Diamond Bar, CA, USA). A decapolar circular mapping catheter (Lasso, Biosense Webster Inc., Diamond Bar, CA, USA) was placed at the ostial site of the PV to clearly record its electrical activity. After anatomical reconstruction of the left atrium (LA) and PVs using an electroanatomical mapping system and fusion with the computed tomography imaging of the LA (CARTO merge, Biosense Webster Inc., Diamond Bar, CA, USA), radiofrequency energy ablation was performed at the ostial site of the PV. In order to systematically evaluate the effect of electrical isolation of the PVs on DF, PVI was performed in the same order in all patients. This was by convention isolation of the right PVs, followed by isolation of the left PVs. The end point of the procedure was the complete elimination of the PV potentials in all PVs as well as induction of exit-block from the PVs (no capture of the LA during pacing at the different poles of the Lasso catheter). Adenosine-induced dormant conduction was not tested.

For every patient, six standard precordial leads (V1–V6) from surface ECG of 15–30 min length were selected from recordings performed before ablation was started. For 14 of the 21 patients in the study, data were available both after the isolation of the right PVs and at the end of the intervention when the four PVs were isolated.

In the remaining seven patients no data were available after isolation of the PVs. For those windows of a certain w that coincide with a periodicity within the segment under analysis, the power of the averaged vector will be high. Conversely, windows whose lengths do not match the periodicity of the segment will show less power, as averaging will cancel out non-periodicity.

To measure the signal power, the root-mean-square (RMS) value \(<P_w>\) of the ensemble average vector is calculated as:

\[
<P_w> = \sqrt{\frac{1}{w}} \sum_{j=1}^{w} s_{w,j}^2
\]

where \(s_{w,j}\) are the elements of the ensemble average vector of length \(w\). The length of the window \(w\) is related to frequency by the expression:

\[
f = \frac{f_s}{w}
\]

where \(f_s\) is the sampling frequency.

The DF was obtained after identifying the three higher peaks \(\left(f_1, f_2, f_3\right)\) in the RMS power and in the frequency band of 3–15 Hz. The first peak was identified as a subharmonic when it relates to other two peaks as: \(f_2 = 2 \times f_1\) and \(f_3 = 4 \times f_1\). In this case, the second peak \(f_2\) was selected as the DF. Otherwise, the frequency corresponding to the maximum peak was selected as the DF.13

**Wavelet analysis**

The continuous wavelet transform is an advanced technique for the time–frequency analysis of signals. This can be seen as a generalization of the traditional Fourier transform which, instead of sine waves for decomposition, uses a waveform or wavelet that is translated in time and stretched or squeezed, yielding better characterization of the signal under analysis. This gives higher time–frequency accuracy in localization of transitory features.17
For estimating the DF in surface ECG recordings, ventricular activity was cancelled. Continuous wavelet transform was computed using the scales corresponding to the frequency band 3–15 Hz. As a mother wavelet, the Morlet wavelet was used as it matches well with the shape of the f-wave or fibrillatory wave observed in surface ECGs. The wavelet coefficients were then summed up over the scales in order to obtain the contribution to the total energy distribution contained within the signal at each scale. Then, the scale relating to the maximum energy was identified and its corresponding frequency was defined as the DF.

Figure 1 (A) Electrocardiogram segment of 10 s length after ventricular cancellation. (B) Frequency distribution corresponding to the frequency band of 3–15 Hz calculated with Fourier, ensemble average, and wavelet analysis, respectively. Dominant frequency is observed at 5.50, 5.52, and 5.56 Hz.

Intracardiac electrogram analysis

As intracardiac electrograms contain mainly local electrical activity, no cancellation of ventricular activity is usually required, since the ventricular signal has most of its frequency content below the band of interest. Digitized signals of 10 s length, sampled at 1000 Hz (10 000 points) were considered. Then, signals were rectified. A Tukey window and zero padding were applied. Discrete Fourier transform was calculated using the FFT algorithm. The periodogram was then obtained for estimating the spectrum. The frequency resolution was 0.01 Hz. Finally, the DF was identified as the frequency relating to the maximum amplitude in the frequency band between 3 and 15 Hz. This is done independently for each of the five electrograms obtained from the...
catheter. The mean DF value is obtained as the representative DF value for each 10 s segment.

Feature extraction
All continuous data were presented as the mean value ± SD. The statistical test of Kolmogorov–Smirnov was used to compare of continuous variable distributions. Statistical significance was considered when the P value was <0.05.

Both surface and intracardiac recordings were divided into segments of 10 s length for analysis. Dominant frequency obtained at the surface ECG and in intracardiac 10 s segments were compared by computing Pearson’s correlation coefficient and by calculating the relative error expressed as

$$\Delta DF(\%) = \left| \frac{DF_{Endocardiac} - DF_{Surface}}{DF_{Endocardiac}} \right| \times 100$$

Results
Surface vs. intracardiac frequency analysis
The relationship between the atrial DF obtained at surface ECG and that obtained from intracardiac recordings at the CS was studied. The DF obtained at the CS was compared with the value obtained at each precordial ECG lead by calculating the relative error and the correlation coefficient. All recordings before, after right PVI and after all PVI, were considered.

Using Fourier analysis resulted in the lowest errors for all precordial leads, ranging from 10.94 ± 10.37% in lead V1 to 25.45 ± 27.55% for lead V4. This method also gave the highest correlation, with values ranging from 0.58 (P < 0.001) for lead V1 to 0.02 (P = 0.29) for lead V6. Secondly, wavelet analysis yielded relative errors that ranged from 10.97 ± 11.08% in lead V1 to 36.98 ± 34.94% for lead V4. Correlation values ranged from 0.53 (P < 0.001) for lead V1 down to −0.10 (P < 0.001) for lead V6. Finally ensemble average gave the higher errors (from 21.29 ± 18.07% in lead V1 to 42.99 ± 9.46% for lead V6). This technique also gave the lowest correlation with values from 0.10 (P < 0.001) in lead V2 down to −0.15 (P < 0.001) in lead V5. Results are plotted in Figure 2.

Dominant frequency distribution before vs. after pulmonary vein isolation
Changes in DF were studied before and after PVI in order to study the effect of the intervention on the atrial activation rate. Only DF calculated in surface lead V1 was considered as it had the lowest error and higher correlation with intracardiac signals measured in the CS.

Fourier and wavelet analysis gave similar DF distributions to that measured within the CS for recordings before and after PVI. Before isolation, DF obtained in surface ECG was 5.90 ± 0.94 Hz (Fourier) and 5.80 ± 0.95 (wavelet) vs. 5.90 ± 0.93 Hz in intracardiac signals. When only the right PVs were isolated, DF decreased in both Fourier (5.60 ± 0.89 Hz, P < 0.01) and wavelet analysis (5.50 ± 0.80 Hz, P < 0.01) and also in intracardiac signals (5.40 ± 0.87 Hz, P < 0.01). After the isolation of all PVs, DF decreased further down to 5.40 ± 0.65 Hz (Fourier, P < 0.01), 5.30 ± 0.70 Hz (wavelet, P < 0.01), and 5.30 ± 0.80 Hz (intracardiac, P < 0.01).

Ensemble average analysis gave a lower DF on average and a higher SD both before (4.90 ± 1.40 Hz) and after all PVI (4.80 ± 1.10 Hz). This was due to a high percentage (36.70% before and 26.10% after isolation) of subharmonic frequency (around 3 Hz) detected as DF. Electrical isolation also yielded a smaller decrease in DF when the right veins were isolated (4.90 ± 1.40 Hz before vs. 4.80 ± 1.20 Hz after right PVI, P < 0.01). When the rest of the PVs had been isolated, there was no further significant (P = 0.10) reduction in the DF.

Effect of pulmonary vein isolation on dominant frequency
The changes in the DF before and after PVI were studied in the 14 patients from whom data were available both before and after the intervention.

Dominant frequency measured in CS decreased significantly (P < 0.01) in all 14 patients when the right PVs were isolated, with a decrease of 0.53 ± 0.56 Hz in absolute values (10.72 ± 11.82% in relative values). Further isolation of the left PVs lead to a significant DF (P < 0.05) decrease in four patients (decrease of 0.26 ± 0.21 Hz and 4.61 ± 3.58%) while the rest did not have a significant (P > 0.05) change.

When Fourier analysis was used on surface ECGs, all patients showed a decrease in the DF when the right PVs were isolated. This decrease was significant (P < 0.01) in 13 of them. The difference was of 0.40 ± 0.27 Hz (6.59 ± 4.17%). Further isolation of the left PVs yielded a further significant (P < 0.05) decrease in the DF in only three of the patients. These three patients also had a significant drop in the DF measured in CS. This decrease was of 0.27 ± 0.06 Hz and 5.02 ± 1.02%. For the rest of the patients the DF did not show a significant (P > 0.05) change.

Wavelet analysis gave similar results. For all patients, DF decreased after right PVI (P < 0.01) with an absolute decrease of 0.46 ± 0.24 Hz and 7.63 ± 3.57%. Further isolation of the left PVs yielded a significant DF decrease in four patients (P < 0.05) of 0.25 ± 0.05 Hz and 4.69 ± 0.94%. These four patients were the same ones that had a drop in DF measured in CS. One patient had a small increase (P < 0.05) of 0.06 Hz (1.15%). The rest of the patients did not have a significant (P > 0.05) change.

Dominant frequency after right PVI decreased significantly (P < 0.01) in seven patients when calculated with ensemble average analysis (decrease of 0.35 ± 0.20 Hz and 6.68 ± 3.51%). Three patients had a significant (P < 0.01) increase in the DF (0.42 ± 0.36 Hz and 10.10 ± 8.49%) while four did not have a significant (P > 0.05) change. Further electrical isolation of the left PVs yielded a significant decrease (P < 0.01) in two patients of 0.38 ± 0.21 Hz (7.57 ± 3.91%). One of these two patients also had a significant drop in DF measured in CS. The other 12 did not have a significant (P > 0.05) change.

A time-frequency analysis with Fourier, ensemble average, and wavelet analysis of 1 min before, 1 min after right PVI and 1 min after intervention is plotted in Figure 3. Time–frequency analysis was performed with a window length of 10 s. For visual
representation, the output was smoothed by linear interpolation. The DF is marked by the dotted grey line. In this example the DF drops from an average of \( \approx 5.70 \) Hz before intervention down to 5.10 Hz when right PVs were isolated and again down to 5.00 Hz after ablation.

**Discussion**

**Main findings**

Dominant frequency measured in the CS was better estimated from the precordial lead V1 and using Fourier (relative error: 10.94 ± 10.37%, correlation: 0.58) or wavelet analysis (relative error: 10.97 ± 11.08%, correlation: 0.53). Ensemble average gave the highest relative error (21.29 ± 18.07%) and lowest correlation (0.10).

Dominant frequency measured in the surface lead V1 before and after right PVI showed a significant decrease when measured with all three methods (Fourier: 5.90 ± 0.94 Hz down to 5.60 ± 0.89 Hz, wavelet: 5.80 ± 0.95 Hz down to 5.50 ± 0.80 Hz, ensemble average: 4.90 ± 1.40 Hz down to 4.80 ± 1.20 Hz). Further isolation of the left PVs yielded a further decrease in DF when calculated with both Fourier (5.40 ± 0.65 Hz) and wavelet (5.30 ± 0.70 Hz) analysis. However, this decrease was smaller. Ensemble average analysis gave a lower DF on average and higher SD as compared with Fourier and wavelet transforms. These results were consistent with DF measured in intracardiac signals (5.90 ± 0.93 Hz before PVI, 5.40 ± 0.87 Hz after right PVI, and 5.30 ± 0.80 Hz after all PVI).

Isolating the right PV yielded a significant decrease in the DF in most of these patients when Fourier (decrease of 6.59 ± 4.17% and 13 patients), and wavelet (decrease of 7.63 ± 3.57% and 14 patients) transforms were used. Ensemble average gave different results, with a significant decrease in only seven patients (6.68 ± 3.51%) and a significant increment in three of them (10.10 ± 8.49%). Further isolation of left PVs yielded a smaller decrease (Fourier: three patients, 5.02 ± 1.02%; wavelet: four patients, 4.69 ± 0.94%; ensemble average: two patients, 7.57 ± 3.91%). Right PVI yielded a significant decrease in DF measured in intracardiac signals in the 14 patients (10.72 ± 11.82%), while further isolation of the left PVs yielded a significant decrease in DF in only four patients (4.61 ± 3.58%).

**Clinical interpretation and possible implications**

The mechanism of the reduction of DF after isolation of the PVs is not clear. According to experimental data,19 – 21 the posterior LA harbours regular, fast, and spatiotemporal organized activity. Fractionation of the electrical activity occurs at the interface zone between areas with fast, and areas with slower electrical activity. This could explain the genesis of the so-called complex fractionated atrial electrograms (CFAEs).22 Ablation of CFAEs is characterized by a continuous slowing of the atrial electrical activity and in many cases finally termination of AF.23 Areas of regular and fast activity (as reflected by the highest DF) have been shown to exist in the posterior or anterior LA in patients with persistent AF.24 During PVI ablative lesions are delivered close to the LA–PV junction and ~5–10 mm outside the PV ostia. It is possible that such lesions induce some degree of conduction block at the borderzone of the rapid rotors and consequently a reduction of the atrial DF, as is reflected in the results of our study. Such an
interaction with the electrophysiological substrate of the LA might at least partially explain the effectiveness of PVI as an interventional treatment in patients with persistent AF. However, after PV isolation is achieved, additional ablation lines along the roof of the LA or mitral isthmus or targeting CFAEs can further reduce DF of AF in lead V1 and in the CS. A reduction of at least 11% in the DF was reported to be necessary for long-term restoration of the sinus rhythm.

Another possible implication of our study is the evidence of a high correlation between the DF in lead V1 and the CS-catheter. None declared.

Acknowledgement

This study showed that both Fourier and wavelet analysis can be used as a guide for monitoring progression of ablation of persistent AF; our study shows that both Fourier and wavelet analysis can be used for this purpose.

Study limitations

The patient number is limited (n = 21). A larger number of subjects could lead to more consistent results. Only intracardiac signals recorded in the CS were available. However, the CS is far away from the PVs where AF sources are often located. Therefore, the variation of DF value of these sites may be limited. In this study, isolation of the right PVs was performed always before isolation of the left PVs; therefore it was not possible to explore the effect of left PVI on the DF.

Conclusion

This study showed that both Fourier and wavelet analysis are good tools to estimate the atrial electrical activity measured in the surface ECG. However, ensemble average gave a worse performance when estimating fibrillatory rate in ECG signals. It was found that standard lead V1 gave the best estimation of the atrial DF measured in the CS. Most of the patients had a significant decrease in DF when the right PVs were isolated although further isolation of the left PVs yielded a smaller decrease, which was statistically significant in fewer patients.

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References

3. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G et al. Spon-
4. Sömmma L, Stridh M, Husser D, Bollmann A, Olsson SB. Analysis of atrial fibrilla-
6. Rieti JI, Zarszoó V, Millet Roig J, García Civera R, Ruiz Granell R. Atrial activity extraction based on blind source separation as an alternative to QRST cancella-
10. Bollmann A, Mende M, Neugebauer A, Pfeffer D. Atrial fibrillation frequency pre-
dicts atrial defibrillation threshold and early arrhythmia recurrence in patients undergoing internal cardioversion of persistent atrial fibrillation. Pacing Clin Electro-
11. Romero I, Koch H, Fleck E, Kriatselis C. Study of surface electrocardiogram spec-
14. Romero I, Addison PS, Reed MJ, Grubb N, Clegg GR, Robertson CE et al. Con-
18. Fischer G, Stuhlinger MC, Nowak CN, Wieser L, Tilg B, Hintringer F. On comput-
21. Mansour M, Mandapati R, Berenfeld O, Chen J, Samie FH, Jalife J. Left-to-right gra-
29. Lin YJ, Tai CT, Kao T, Chang SL, Lo LW, Tuan TC et al. Spatiotemporal organiza-