# Non-Invasive Detection of Higher Frequency Atrial Sources During Atrial Fibrillation

Francisco Castells[1], Raúl Llinares[1], Andreu M Climent[1], Felipe Atienza[2], Jorge Igual[1], José Millet[1], Maria S Guillem[1]

[1] Universitat Politècnica de València, València, Spain
[2] Hospital General Universitario Gregorio Marañon, Madrid, Spain

## Abstract

*This study proposes a non-invasive methodology to detect higher atrial frequencies in AF patients, which may be related to localized drivers, responsible of AF maintenance. The proposed algorithm extracts a signal from a Body Surface Potential Mapping (BSPM) recording from the linear combination that maximizes a cost function that measures periodicity within a given range. By applying iteratively this algorithm in 1.5Hz-width bands from 5Hz to 20Hz in steps of 0.25Hz, several candidates for AF signals with increasing frequency are obtained. Signals with high spectral concentration, low kurtosis and repeatability in 5 consecutive steps were considered compatible with AF. Among these signals, the one with the highest frequency was selected as candidate for AF driver. This frequency was compared with spectral analysis of surface signals in segments under adenosine effects, i.e. with absence of ventricular activity.*

*The algorithm was applied to 18 BSPM recordings from AF patients. In all cases, the high frequency was consistent with the spectral analysis of the segments with adenosine. High atrial frequency values were $9.61 \pm 2.12$, spectral concentration was $0.415 \pm 0.096$ and kurtosis $0.60 \pm 0.81$. The non-invasive detection of high frequency atrial sources may help to define the most appropriate therapy, e.g. for ablation of atrial regions with high activation rates.*

## 1. Introduction

In the last years, non-invasive characterization of atrial fibrillation (AF) from the analysis of surface electrocardiograms (ECGs) has become increasingly popular, since it provides relevant information regarding atrial electrical activation. One of the parameters frequently employed is the atrial dominant frequency, or alternatively, its inverse, the atrial dominant cycle length. This parameter requires the previous estimation of the atrial activity (AA). Several methods have been proposed for this, although they can be grouped in two different strategies: (1) cancellation of ventricular waves from the subtraction of QRST templates [2] and (2) estimation of a global AA from source separation approaches [1]. Once the atrial signal is estimated, the main atrial frequency can be detected by spectral analysis. With respect to AF therapies, ablation of atrial tissue has been progressively introduced, which brought about new studies with intracardiac data. This revealed the existence in some patients of small regions with higher frequencies, which could be candidates for ablation, as being probably responsible for AF maintenance [3]. Indeed, a previous study concluded than radiofrequency ablation leading to elimination of left atrium to right atrium frequency gradients predicts long-term SR maintenance in AF patients [4]. These frequencies could be well 2 or 3Hz higher than the global atrial frequency, which can not be followed by the rest of the atrial tissue. The detection of higher atrial frequencies from non-invasive techniques would be helpful for an enhanced diagnosis and selection of the most appropriate therapy. However, this is not feasible with conventional techniques, since higher frequencies are masked by the dominant atrial frequencies (obviously, due to a larger tissue proportion). In this paper, a specific methodology for non-invasive detection of higher atrial frequencies during AF is developed.

## 2. Materials

A specific protocol for database collection was designed for this study. Since higher frequencies usually appear in small regions, they can only be observable in few sites at the surface, which could not belong to the standard 12-lead ECG. Therefore, a 64-lead BSPM system is employed instead, with the electrodes distributed all around the torso in both front and rear regions. Another key question is a reference to be compared with. In this study, a short segment free from ventricular activity was induced by adenosine administration. With this, the detection of atrial frequencies during this segment is possible without the previous estimation of the atrial signal. The reference frequency

will be the highest visible in the torso, even if it is not the dominant frequency, but only observable in few leads. An important side effect of adenosine administration is that the atrial frequency may be increased upto 1 or 2 Hz, depending on the patient. Therefore, it would be reasonable to find lower frequencies once adenosine effects are over. The database consisted of 18 BSPM recordings from consecutive AF patients.

## 3. Methods

As aforementioned, the goal of this study was to detect high frequency atrial sources, even if they present low amplitudes in comparison to the dominant AA and are only visible in few leads in non standard locations. The method for AA estimation is based on source separation strategies. The classical Blind Source Separation (BSS) approach outputs as many sources as input signals, by maximizing an independence criterion based on higher order statistics [1]. One of the limitations of this method is its reliability when several sources present quasi-Gaussian properties. These limitations are reinforced with large number of signals and low amplitudes of the signal to retrieve, which are both the case. In order to overcome these problems, an *ad hoc* method is employed, where only one source is estimated. Furthermore, instead of maximizing a independence criterion, a cost function that exploits the periodicity of the atrial signal is defined. With this, we obtain a robust, reliable and computationally efficient algorithm to estimate the desired atrial source [5]. The main drawback of this algorithm is that it requires as input parameter an approximation of the atrial frequency. Therefore, we need an additional mechanism to break this vicious circle, since the pursued parameter is, in turn, an algorithm input. The way we proceeded in this study is the following: an iterative algorithm is carried out, where the input frequency varies from 5Hz to 20Hz in steps of 0.25Hz. In each iteration we obtained a candidate to atrial source. Obviously, not all sources were consistent to an atrial fibrillatory wave. Among all signals compatible with atrial fibrillation, the signal with higher frequency was associated to our target source. The criterion to evaluate the compatibility was based on spectral concentration measurements, kurtosis and repeatability of the estimated signal source in consecutive iterations.

### 3.1. Atrial activity estimation

Considering $\mathbf{y}(\mathbf{t})$ as the ensemble of $N$ leads, the aim is to obtain a linear transformation vector $\mathbf{v}$ that retrieves an estimation of the atrial source $\hat{s}_A$:

$$\hat{s}_A(t) = \mathbf{v}^T \mathbf{y}(t), \tag{1}$$

so that the spectral power in the corresponding range of frequencies $[f_1 \ldots f_2]$ is maximized.

After a whitening process, the ECG data in $\mathbf{y}(\mathbf{t})$ are transformed into a set of uncorrelated signals $\mathbf{z}(\mathbf{t})$. The statement in (1) is then reformulated as:

$$\hat{s}_A(t) = \mathbf{w}^T \mathbf{z}(t), \tag{2}$$

where $\mathbf{w}$ is a unit vector (i.e. $\|\mathbf{w}\|^2 = 1$).

This optimization problem is then defined in the frequency domain:

$$\mathbf{w} = \arg\max_{\mathbf{w}} \left( \int_{f_1}^{f_2} \left| \hat{X}_A \left( e^{j2\pi f} \right) \right|^2 df \right), \tag{3}$$

where $\hat{X}_A \left( e^{j2\pi f} \right)$ is the Fourier Transform of $\hat{x}_A(t)$. Since $\hat{x}_A(t)$ is unknown, this problem is finally rewritten in a recursive form:

$$\mathbf{w} = \arg\max_{\mathbf{w}} \sum_{k=K_1}^{K_2} \mathbf{w}^T \hat{\mathbf{Z}} \left( e^{j2\pi f_k} \right) \hat{\mathbf{Z}}^H \left( e^{j2\pi f_k} \right) \mathbf{w}, \tag{4}$$

where $f_k$ are the spectral samples of the FFT, being $K_1, K_2$ the indexes corresponding to $f_1, f_2$, respectively. This optimization problem is then solved with a fast and reliable fixed-point algorithm.

### 3.2. Determination of high atrial frequecies

Since several atrial frequencies could be found, narrow frequency bands of 1.5Hz are explored in the range from [5..6.5]Hz to [18.5..20Hz], in steps of 0.25Hz. For each frequency band, the algorithm described in 3.1 is applied. As a result, a set of signals candidates to atrial sources is obtained. Obviously, not all them would not be consistent with AA properties. For instance, for a main frequency of 7Hz, the signal that maximized the spectral content in the range [5..6.5Hz] would be meaningless. On the other hand, this atrial source could be retrieve in successive trials when exploring consecutive frequency ranges, from [5.75Hz..7.25]Hz to [6.75..8.25]Hz.

If several atrial frequencies are present, several signals consistent with AA properties can be obtained. The challenge is to determine correctly which of them correspond to atrial sources and then discard the rest of the signals. Finally, as explained above, the objective is to determine if exists an atrial source with higher frequency than the main atrial frequency. Regarding the spectral domain and according to previous studies, the AA activity exhibits a narrow spectrum, with high spectral concentrations. On the other hand, in the temporal domain, the existence of QRS complex residua is associated with high kurtosis values. Hence, good quality in AA estimation is only possible with

low kurtosis value. Finally, a repeatability in the estimated frequency in overlapped frequency ranges is a must. Consequently, the following conditions must be accomplished to consider it as an atrial signal:

- **Spectral concentration:** $> 0.30$ and 1.7 greater than the spectral concentration of the background noise, considering it as the mean of the spectral concentration obtained in the last frequency ranges, from 18Hz to 20Hz.
- **Kurtosis:** $< 2$.
- **Frequency reapetability:** In five consecutive iterations, the frequency deviation should be $< 0.25Hz$

### 3.3.    Results validation

The reference data to be compared with is a segment free from ventricular activity, induced by adenosine administration. As the complete torso is explored with a BSPM system, higher atrial frequencies can be captured, even if there are only visible in few non-standard positions. The main advantage is that the clean atrial signal at each site is available, and therefore the frequencies are easily detected in the spectral domain.

### 4.    Results

The methods decribed above were applied to our 18 AF patients. For the sake of a better understanding, let us illustrate the results with an example. Figure 1 represents the spectral concentration, kurtosis and frequency of the retrieved signals, candidates for atrial source, as a function of the central input frequency for the AA estimation algorithm.
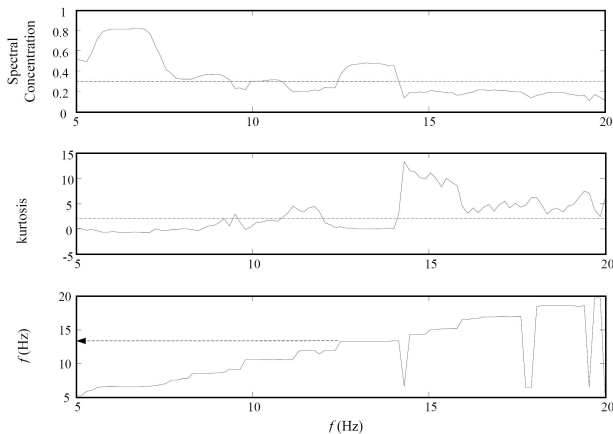


Figure 1.  Spectral concentration (top), kurtosis (center) and frequency (bottom) of the retrieved signals as a function of the central input frequency ($\pm 0.75Hz$) for the AA estimation algorithm.

Considering the spectral concentration (top), two hat-shaped segments with values well above the threshold of 0.3 and the background noise are observed. At a first glance, this would suggests the existence of at least two atrial sources. Nevertheless, in order to consider them as AA, other parameters should be analyzed. The kurtosis (center) showed a consistent behavior, with values under the threshold of 2 for those segments. Notice than at a certain point, the kurtosis rises rapidly, corresponding to background spectral concentration values. This indicates that the estimated signals at frequencies above 14Hz are not compatible with AA properties, suggesting that these frequencies are not present in the BSPM recording. Finally, the frequencies of the estimated signals reveal a flat behavior with constant values in the range corresponding to the spectral concentration plateau. This suggests that, despite sliding the frequency inputs, the estimated atrial source is equivalent for overlapped frequency ranges. Accordingly with these considerations, the searched frequency is the highest frequency that meets all requierements, in this case, 13.4Hz.

Obviously, this result should be constrated with a reference for validation. Otherwise, the 13.4Hz frequency would seem too high for being an atrial source, and the AA estimation method could be questioned. When exploring the BSPM leads, most of them only showed the lower frequency, around 6.3Hz, with slight frequency variations depending on the lead. However some few leads located at the left side of the torso also showed the higher frequency (Figure 2. Indeed, two frequency peaks at 6.0Hz and 13.5Hz can be observed. Notice also that the high frequency is not a multiple of the low frequency, hence the possibility of a harmonic should be disregarded.
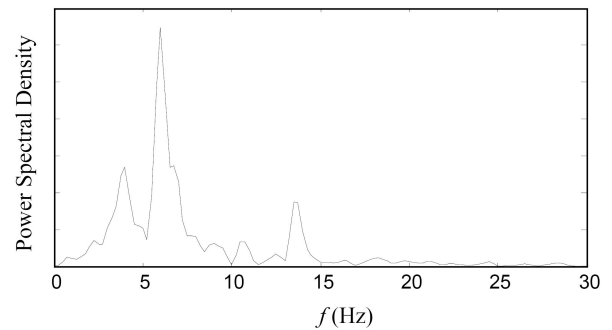


Figure 2.  Spectrum of the AA under adenosine effects at the left side of the torso.

Being $f_H$ the high atrial frequency to detect and $f_{H_{Ad}}$ the reference atrial frequency to compare with, i.e. the higher atrial rate found under adenosine effects, the results for all patients are displayed in table 4. In addition, spectral concentration and kurtosis values of the estimated signal are given. High atrial frequency values were $11.14 \pm 1.89$Hz and $9.61 \pm 2.12$Hz for adenosine and basal segments, respectively. The frequency gradient

suffered between both states was $1.53 \pm 1.27$Hz. For the estimated atrial signals (basal), spectral concentration was $0.415 \pm 0.096$ and kurtosis $0.60 \pm 0.81$.

Table 1. Atrial frequencies, spectral concentration and kurtosis values of all patients.

| Patient | $f_{H_{\text{Ad}}}$ | $f_H$ | SC | $k$ |
|---------|------|--------|------|-------|
| #1 | 9.8 | 8.3 | 0.40 | 0.89 |
| #2 | 12.9 | 10.0 | 0.37 | -0.12 |
| #3 | 13.3 | 13.9 | 0.39 | 0.24 |
| #4 | 13.6 | 13.4 | 0.45 | 0.17 |
| #5 | 9.1 | 8.6 | 0.58 | -0.41 |
| #6 | 10.8 | 9.3 | 0.37 | 1.12 |
| #7 | 7.1 | 6.5 | 0.59 | -0.35 |
| #8 | 11.0 | 8.2/10 | 0.34 | 1.52 |
| #9 | 10.0 | 8.6 | 0.50 | -0.30 |
| #10 | 10.2 | 8.7 | 0.30 | 1.71 |
| #11 | 11.6 | 11.4 | 0.30 | 1.41 |
| #12 | 11.0 | 9.0 | 0.32 | 2.00 |
| #13 | 11.7 | 9.9 | 0.35 | 0.58 |
| #14 | 13.7 | 8.6 | 0.61 | -0.12 |
| #15 | 10.4 | 8.8 | 0.40 | -0.01 |
| #16 | 9.9 | 8.0 | 0.38 | 1.74 |
| #17 | 14.5 | 13.8 | 0.41 | -0.01 |
| #18 | 9.9 | 8.2 | 0.40 | 0.77 |

## 5.  Discussion

The frequencies found for most of the patients were clearly higher than typical atrial frequencies during AF, usually between 6Hz and 8Hz. Nevertheless, the high atrial frequencies during basal state were consistent with the frequencies found under adenosine effects, which where even higher, in about 1.5Hz. This frequency gradient between both states can be well explained by drug administration. In all patients, except in patient #7, a dominant atrial component with lower frequency could be found. The presence or absence of atrial regions with higher atrial frequencies may indicate differences in the atrial substrate responsible for AF mantainance, which may lead to different diagnosis and treatment strategies. Currently, the detection of high atrial frequencies is only feasible with intracardiac exploration by means of catheterism. The possibility of inferring the existence of high frequency atrial regions from non-invasive techniques would provide enhanced AF characterization, with immediate clinical implications. A further refinement of these techniques would be the localization of this region in the left or right atrium.

## 5.1.  Study limitations

The most arguable part of the proposed technique is discerning whether a signal is compatible with AA properties or not. Although high spectral concentration, low kurtosis values and frequency repeatability are expected, the proposed thresholds are still too weak conditions. As displayed in table 4, the values of SC and $k$ are too close to the thresholds. Accordingly, more robust classification tools are required. Nevertheless, this algorithm would still work properly in a large number of patients and provide important information that could be used in future works for improved techniques.

Finally, despite using segments without ventricular activity as reference signals in this preliminary study, intracardiac recordings should be employed as the gold standard instead, since the final goal is to reflect at the surface what occurs in atrial chambers.

## 6.  Conclusions

The existence of high atrial frequency regions can be detected in a non-invasive manner from the analysis of surface signals. Since they are usually responsible for AF manteinance, the treatment strategy may involve localization and ablation of these regions. Therefore, an enhanced non-invasive characterization of AF may guide the cardiologist to next steps, for a correct diagnosis and therapy.

## References

[1] Castells F, Rieta J, Millet J, Zarzoso V. Spatio-temporal blind source separation approach to atrial activity estimation in atrial tachyarrhythmias. IEEE Trans Biomed Eng 2005;52:258-67.

[2] Stridh M, Sörnmo L. Spatiotemporal QRST cancellation techniques for analyses of atrial fibrillation. IEEE Trans Biomed Eng 2001;48:105-11.

[3] Sanders P, Berenfeld C, Hocini M, Jaïs P, et al. Spectral Analysis Identifies Sites of High-Frequency Activity Maintaining Atrial Fibrillation in Humans. Circulation 2005;112:789-97.

[4] 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 2009;6:33-40.

[5] Llinares R, Igual J, Miró Borrás J. A fixed point algorithm for extracting the atrial activity in the frequency domain. Comput Biol Med 2010;40:943-9.

Address for correspondence:

Name: Francisco Castells
ITACA Institute Universitat Politècnica de València
Camí de Vera s/n, 46022 València
Spain fcastells@eln.upv.es