

# Wavelet Variance Differences in Atrial Fibrillation during Anaesthetic Effect

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## Abstract

*Effect of anaesthetic agents in restoration rhythm procedures during atrial fibrillation (AF) has not been fully investigated. We evaluated the effects of a widely used anaesthetic agent (propofol) in the fibrillation patterns. Intra-atrial recordings belong to 18 patients diagnosed with AF were analyzed “before” (baseline) and “during” anaesthetic infusion. The goal of this study is to characterize the variation in atrial properties along the atria in both states. The wavelet variance decomposes the variance of a time series on a scale by scale basis and hence has considerable appeal when physical phenomena are analyzed in terms of variations operating over a range of different scales. Moreover, the variance estimates are more accurately determined with a maximal-overlap version of the wavelet transform (MODWT). As mother wavelet was used the Haar wavelet where the signal was partitioned over seven scales. Wavelet analysis highlights a significant lower changes during the anaesthetic infusion respect to the basal conditions in the right atrium, with an opposite effect and non significant values in the left atrium. The proposed methodology provides an additional approach to the understanding of the role of the anaesthetic, showing a decrease in the variance inter-scales during the anaesthetic infusion in the right atrium, with the opposite effect in the left atrium.*

## 1. Introduction

Atrial Fibrillation (AF), as consequence of being the most frequent arrhythmia, has been object of numerous studies. Nowadays, it is well known that this arrhythmia is originated at the atria due to the coexistence of multiple re-entrant atrial wavelets which are often initiated by arrhythmogenic foci located at the pulmonary veins [1,2], where scientific inquiry has provided insight into what abnormal conditions affecting the basic electrophysiological state of the atria are responsible for the initiation and per-

petuation of the arrhythmia and what factors govern the response of the atrioventricular transmission system.

Between these factors related to the AF, one especially important is the role of autonomous nervous system and, in particular, the pro-arrhythmic effects of sympathetic or vagal activation. Although basic and experimental research has provided insight into the mechanisms of AF and the effects autonomous nervous system [3,4], as well as, of many antiarrhythmic drugs [5,6], the effects of the anaesthetics during AF ablation procedures [7–9] to prevent the recurrences are not completely known.

In this paper, the analysis of the propofol effects in atrial activity during AF is proposed. Propofol (2,6-diisopropylphenol) is the most common agent in restoration sinus rhythm procedures. The rapid redistribution and metabolism of this anaesthetic results in a short elimination half-life of approximately one hour, making it suitable for short-lasting sedation, i.e. in the cardioversion procedures.

To study of atrial changes provoked by the propofol infusion can be helpful the analysis of intra-cardiac recordings before and during the effects of this anaesthetic.

The main contribution of this paper is in providing the variance obtained by applying a wavelet-based time-series analysis approach, as a distinctive parameter. The notion of the scale-dependent wavelet variance, which in many ways is analogous to the more familiar frequency-dependent Fourier power spectrum, is thus a natural tool for investigating not only the scale-dependent variance, but the locations of events contributing to the variance at each scale. This feature has summarized the variation of the atrial activity extracted from the intra-cardiac recordings in different atrial regions. Finally, statistical analysis of the obtained parameters provided the quantitative difference between both groups.

## 2. Materials

All procedures were performed according to Helsinki declaration. AF intracardiac recordings were registered

in 18 patients, 14 paroxysmal AF (between the age of  $58 \pm 17$  and 69% of men) and 4 persistent AF (between the age of  $46 \pm 3$  years old, and 100% men), submitted to an AF ablation procedure immediately before and after propofol sedation (an iv bolus of 1.5-2 mg/kg, depending on weight and time to hypnosis). A 24-pole catheter (Orbiter, Bard Electrophysiology, 2-9-2mm electrode spacing) was inserted through the femoral vein and positioned in the right atrium (RA) with the distal dipoles into the coronary sinus to record left atrial electrical activity as well. The medium and proximal electrodes were located spanning the right atrial peri-tricuspid area, from the coronary sinus ostium to the upper part of the interatrial low paraseptal region including low right septum and low left septum. Using this catheter, 12 bipolar intracardiac electrograms were digitally recorded at 1 kHz sampling rate (16 bit A/D conversion; Polygraph Prucka Cardio-Lab, General Electric), which we refer to as dipole 1-2, dipole 3-4, etc. While the exact positioning of the catheter will vary from subject to subject, in general the leads 1-2, 3-4, and 5-6 are in the left atrium (LA), leads 7-8, 9-10, 11-12 are in the septum area (SA), and leads from 15-16, 17-18, ... to 23-24 are in the RA. Forty to 60 s recordings were analyzed and compared before and during the anaesthetic effect.

### 3. Methods

#### 3.1. Pyramidal algorithm discrete wavelet transform

The discrete wavelet transform (DWT) is an implementation of the wavelet transform using a discrete set of the wavelet scales and translations of the mother wavelet in new values called wavelet coefficients.

The original signal can be exactly reconstructed, if all the coefficients are retained, by working back down the pyramid, successively computing the approximation at each smaller scale. At each scale, the set of wavelet coefficients and the set of scaling coefficients are both doubled in length by inserting one zero after each sample [10].

The decomposition is performed sequentially, starting with the smallest scales and progressing to the larger scales, applied only at dyadic scales  $2^j$ .

The coefficients for scale parameter  $2^j$  are obtained by the pyramid algorithm. What this does in effect is to convolve the data with a scale-specific filter and then to sub-sample the output of  $N$  samples at intervals  $2^j$  to yield  $N/2^j$  DWT coefficients  $D_{j,n}$ , where  $j$  specifies the scale (for dilation) and  $n$  the location (for translation).

Where  $\hat{\sigma}_{u,j}^2$  is the contribution to the variance of  $u = f(x)$  for scale parameter  $2^j$  (eq. 1), known as the sample wavelet variance [11].

$$\hat{\sigma}_{u,j}^2 = \frac{1}{2^j n_j} \sum_{n=1}^{n_j} D_{j,n}^2 \quad (1)$$

#### 3.2. Maximum overlap discrete wavelet transform

Percival and Guttorp (1994) showed that the wavelet variance could be more efficiently estimated, not by subsampling the convolution of the filters with the data, but rather by retaining all the values. They called this new procedure the maximal overlap discrete wavelet transform (MODWT), and they denote the sequence of MODWT coefficients by  $d_{j,n}$ . For a sequence of MODWT coefficients the locations  $n$  progress in unit steps rather than steps of  $2^j$  as in the DWT case. That the MODWT coefficients are obtained without the subsampling step means that the new coefficients at any scale are no longer orthogonal to each other. In addition to the increased efficiency the MODWT is shift-invariant and can be readily applied to  $N$  data when  $N$  is not an integer power of 2 [11, 12].

The maximal overlap wavelet variance is defined as the eq. 2, where near the beginning and the end of the data sequence the wavelet filters overlap were discarded.

$$\hat{\sigma}_{u,j}^2 = \frac{1}{2^j \hat{n}_j} \sum_{n=1}^{\hat{n}_j} d_{j,n}^2 \quad (2)$$

Similarly the contribution to the covariance of two variables  $u = f_1(x)$  and  $v = f_2(x)$  from scale  $j$  is given as a wavelet covariance, estimated from the MODWT of the two variables by

$$\hat{C}_{u,v,j} = \frac{1}{2^j \hat{n}_j} \sum_{n=1}^{\hat{n}_j} d_{j,n}^u d_{j,n}^v \quad (3)$$

where  $d_{j,n}^u$  and  $d_{j,n}^v$  are the MODWT coefficients for scale  $2^j$  and location  $n$  for the variables  $u$  and  $v$ , respectively.

#### 3.3. Statistical analysis

The parameters are expressed as *mean*  $\pm$  *SD*. Paired t-tests were used for comparison between the 2 groups of results. Comparison of serial measures was obtained by repeated measures ANOVA coupled with the Student-Newman-Keuls test. Results were considered to be statistically significant at  $p < 0.05$ .

## 4. Results

### 4.1. Pyramid algorithm DWT results

The wavelet analysis with Haar wavelet, as mother wavelet, decomposes the variance of a time series on a scale-by-scale basis, along seven scales through a wavelet multiresolution analysis.

The results of variance measurements showed that there are differences in the RA between both states with more variability before the infusion of the anaesthetic than during its effect, on the contrary this differences were not statistical significant in the LA (Fig. 1). As well the scale to scale results showed higher differences across the highest scales.

In addition, to analyse the differences between atria in both states, the covariance measurement from two dipoles in each atrium was analysed. The results showed that the difference of covariance between the dipoles situated in the RA was statistical significant ( $p=0.019$ ) with not statistical signification in those located in LA. The mean of covariance parameter (*Cov*) is represented in Table 1, as well as the mean of difference of covariance between (*Diff. cov*) scales, and the mean of the variance along all the scales in each atrium, where it is observed that all the proposed parameters follow the same tendency than the covariance measurement.

Table 1. LA and RA variances and covariances across 7 DWT scales

DWT Param.	Basal	Propofol	Statist. Sig.
Var LA dip 1-2	$1.11 \pm 1.34$	$1.37 \pm 2.35$	$p = 0.376$
Var LA dip 3-4	$0.45 \pm 0.30$	$0.64 \pm 0.59$	$p = 0.149$
Cov LA	$-0.12 \pm 0.13$	$-0.14 \pm 0.23$	$p = 0.594$
Diff. Cov LA	$0.03 \pm 0.05$	$0.04 \pm 0.09$	$p = 0.301$
Var RA dip17-18	$1.75 \pm 1.60$	$1.03 \pm 0.85$	$p = 0.049$
Var RA dip19-20	$1.58 \pm 0.89$	$0.89 \pm 0.82$	$p = 0.004$
Cov RA	$-0.15 \pm 0.17$	$-0.06 \pm 0.09$	$p = 0.019$
Diff. Cov RA	$0.05 \pm 0.85$	$0.01 \pm 0.05$	$p = 0.012$

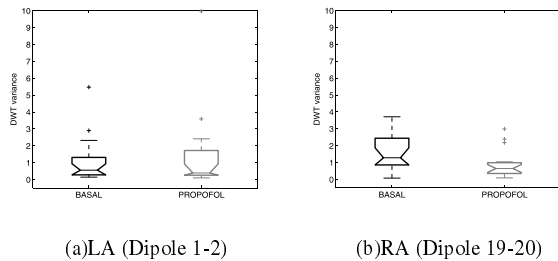


Figure 1. DWT variance of atrial activity in both atria during both states, (basal (black), propofol (grey)).

### 4.2. MODWT results

The wavelet variance is estimated for the first seven scales from the resulting MODWT wavelet coefficients, with the Haar wavelet (eq. 2). The analysis showed that in the RA the differences are higher than in the other atrium (Fig. 2), where not approaching to be statistical significant (Table 3).

In addition, the measurements of covariance between adjacent dipoles in the LA and the RA along the scales showed the same tendency as the previous analysis, where in the LA (dipoles 1-2 and 3-4) the covariance values was  $-0.33 \pm 0.52$  in basal conditions, vs.  $-1.75 \pm 6.30$  during the propofol infusion, with not statistical signification ( $p = 0.321$ ), and in the RA (dipoles 17-18 and 19-20) with  $-1.11 \pm 1.12$  in basal conditions, vs.  $-0.44 \pm 0.87$  during the anaesthetic effect, with a statistical signification of  $p=0.028$ ) (Table 3).

The analysis of the change in MODWT coefficients variance scale by scale in basal and propofol states is displayed in Table 2. It reveals a statistical significant variance differences in all the scales for the dipoles situated in the RA, with higher values in basal conditions than during the anaesthetic effect, with the opposite effect in the dipoles situated in the LA and not statistical significant variance differences.

Table 2. LA and RA variance differences (basal-propofol) in each scale of MODWT coefficients

MODWT coefficients	variance LA basal-propofol	Stat. Sig. (p)	variance RA basal-propofol	Stat. Sig. (p)
Scale 1	$-0.50 \pm 2.45$	$p=0.403$	$1.16 \pm 2.11$	$p=0.032$
Scale 2	$-1.81 \pm 8.08$	$p=0.355$	$3.59 \pm 0.65$	$p=0.032$
Scale 3	$-4.38 \pm 19.75$	$p=0.360$	$7.40 \pm 13.09$	$p=0.028$
Scale 4	$-4.44 \pm 21.23$	$p=0.388$	$7.17 \pm 11.14$	$p=0.013$
Scale 5	$-1.41 \pm 7.11$	$p=0.412$	$3.60 \pm 4.57$	$p=0.004$
Scale 6	$-0.33 \pm 1.50$	$p=0.371$	$1.39 \pm 1.89$	$p=0.006$
Scale 7	$-0.11 \pm 0.47$	$p=0.344$	$0.61 \pm 1.00$	$p=0.020$

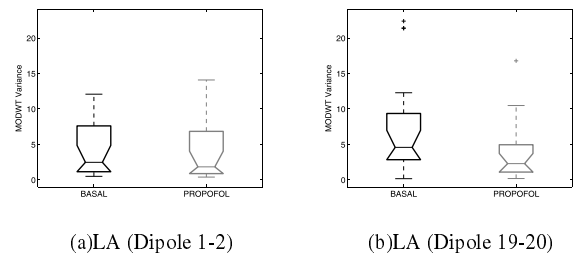


Figure 2. MODWT variance of atrial activity in both atria during both states, (basal (black), propofol (grey)).

Table 3. LA and RA variances and covariances across 7 MODWT scales

MODWT Param.	Basal	Propofol	Statist. Sig.
Var LA dip 1-2	4.94 ± 6.20	6.78 ± 13.85	$p = 0.320$
Var LA dip 3-4	1.85 ± 1.47	3.02 ± 3.73	$p = 0.163$
Cov LA	-0.33 ± 0.52	-1.75 ± 6.30	$p = 0.321$
Diff. cov LA	0.02 ± 0.04	0.03 ± 0.07	$p = 0.218$
Var RA dip 17-18	8.60 ± 3.74	6.86 ± 2.52	$p = 0.046$
Var RA dip 19-20	7.53 ± 7.21	3.92 ± 4.41	$p = 0.011$
Cov RA	-1.11 ± 1.12	-0.44 ± 0.87	$p = 0.028$
Diff cov RA	0.05 ± 0.07	0.01 ± 0.32	$p = 0.004$

## 5. Discussion and conclusions

In the present study are presented two different algorithm from wavelet transform to analyse the variability of atrial activity in patients with AF in basal conditions and under an anaesthetic effects. These algorithms are the orthogonal DWT computed using a recursive procedure known as the pyramid algorithm [10], that involves a subsampling operation, and the maximal overlap pyramid algorithm [12], which is a variation of the pyramid algorithm that eliminates subsampling and leads to efficient estimates of the wavelet variance.

Assessment of scaling behavior from an observed atrial time series is particularly appealing in the wavelet domain. The wavelet decomposition allows for a particularly revealing form of scale analysis in which the value of a derived quantity is determined using data smoothed to increasingly larger scales. The wavelet variance provides a summary of the spectral density function in this domain.

The variance and covariance wavelet-based tests of the time series showed the same tendency, as well as both methods of wavelet decomposition where it was observed a statistical significant differences in all of the scales analyzed of the dipoles situated in the RA with higher variance and covariance in basal conditions.

These results identify transient periods of wave propagation changing over space and time, with a different behavior in both chambers during the anesthetic infusion. Nevertheless, the detailed mechanisms by which this occurs require further study, and multisite mapping would be helpful to further elucidate the reason for which this difference of organization occurs.

In addition, these results coincide with other obtained in previous studies, where the dominant frequency during the anaesthetic infusion has significant differences respect to basal conditions in the RA, slowing the dominant frequency in all of right atrial region, with not statistical significant changes in the LA [13]. This study confirms a more homogeneous RA behavior with less variability during the propofol effect in patients with AF.

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