Ann. Ist. Super. Sanità, vol. 37, n. 3 (2001), pp. 319-324

Extraction of physiological and clinical information from intra-atrial electrograms during atrial fibrillation: review of methods

Vincenzo BARBARO, Pietro BARTOLINI, Giovanni CALCAGNINI and Federica CENSI

Laboratorio di Ingegneria Biomedica, Istituto Superiore di Sanità, Rome, Italy

Summary. - This paper presents a review of the evolution of methods and algorithms for the analysis of intra-atrial recordings, with special emphasis to the extraction of physiological and clinical information during atrial fibrillation. The principal time-domain and frequency-domain methods of electrogram analyses are described, and their physiological interpretation and clinical applications are discussed. In addition, the recent findings from complex system theory and chaos theory approaches are highlighted.

Key words: atrial fibrillation, time-domain analysis, frequency-domain analysis, complex non linear analysis theory.

Riassunto *(Estrazione di informazioni fisiologiche e cliniche da elettrogrammi intra-atriali durante fibrillazione atriale: rassegna dei metodi)*. - Questo lavoro presenta una rassegna sull'evoluzione di metodi e algoritmi per l'analisi di registrazioni intra-atriali, con particolare enfasi all'estrazione di informazioni cliniche e fisiologiche durante fibrillazione atriale. Sono descritti i principali metodi di analisi operanti nel dominio del tempo e della frequenza, e sono discusse le interpretazioni fisiologiche e le applicazioni cliniche. Inoltre, sono riportati i recenti risultati ottenuti dalla teoria del caos e dei sistemi complessi.

Parole chiave: fibrillazione atriale, analisi nel tempo, analisi in frequenza, analisi non lineare.

Introduction

Although most of the research dealing with automated processing and analysis of intracardiac signals have been devoted to methods and schemes for recognition and classification of cardiac arrhythmias in implantable devices, interest has recently grown for developing methods aimed at electrophysiological investigations.

The early methods were mainly based on measurements derived from atrial rate and, to a minor extent, from simple morphological analysis such as the probability density function and the frequency domain analysis [1].

The main limitations in developing innovative algorithms for implantable devices are represented by the computational costs, the available amount of data stored and the power consumption of dedicated hardware.

Concerning the electrophysiological investigation, these limitations no longer apply. Poligraphic systems available allow long and accurate recordings. Multipolar catheters make available multiple synchronous recordings from different sites/chambers, and computational costs do not represent a real problem for most of the computers commercially available. These factors may explain the fast increase of interest in signal processing of intracardiac electrograms observed over the last years.

The main goals of the electrophysiological studies in patients with atrial fibrillation (AF) are: investigation of the wavefronts propagation and study of the mechanisms responsible for reentry and self-sustaining of the arrhythmia; the assessment of the electrophysiological properties of the cardiac substrate to monitor and eventually optimize the pharmacological treatment; the identification of points/sites sustaining the arrhythmia to identify regions candidate to ablation.

The first attempt to describe the morphology of bipolar endocardial recordings during AF was made by Wells *et al.* [2], who gave qualitative criteria for scoring the organization of single bipolar recordings, and identified four types of AF. From then on, the assessment of the organization of bipolar recordings has mostly been achieved by visual scoring by experts. Of course this approach is time consuming and can lead to results which are neither objective nor reproducible.

A different approach consists in the analysis of the mechanism of propagation of the depolarization wavefronts. In 1985, Allessie *et al.* [3] mapped the cardiac electrical activity during AF and provided the first experimental evidence supporting Moe's multiple

wavelets hypothesis [4-6]. According to this hypothesis during AF several wavefronts of electrical activity propagate randomly throughout the surface of both atria forming complex and ever-changing patterns of electrical activity. Following these findings several authors investigated the propagation of multiple wavefronts and the interactions with anatomical and functional obstacles [7-11].

A third approach focuses on the importance of ectopic foci, first theorised by Scherf *et al.* [12, 13]. It is now clear that in some patients with AF, rapidly firing atrial foci can be identified, usually located in the superior pulmonary vein [14].

Although the early studies dealing with these approaches mostly relied on visual analysis of recorded data, important contributions and innovative concepts and methods have come from the fields of signal processing, stochastic process theory and non-linear dynamics. This paper is aimed at presenting a review of the evolution of these methods from past to present and a description of ongoing experimental works.

The manuscript is organized as follows: methods are grouped as time-domain, frequency domain and non-linear dynamics approaches. The electrophysiological interpretation of each method is discussed within each subsection. Then a general discussion on the consolidated and ongoing results is presented.

Analysis methods

Time-domain analysis

Time-domain methods mainly originate from the attempt to automate procedures usually performed by visual scoring of the signals in order to increase the reproducibility of the results, the amount of data which can be analyzed, and their popularity in clinical investigations. The large number of studies using the FF intervals are paradigmatic of this evolution. Nevertheless, several sophisticated time-domain methods are also available; they go far beyond the simple automation of visual scoring.

The main time-domain methods used so far to analyze intra-atrial electrograms are summarized in Table 1. Botteron *et al.* first proposed a method for assessing the extent of spatial organization during AF [15], by estimating the cross-correlation of closely spaced bipolar endocardial recordings. They found that the atrial activation processes during AF are spatially correlated, with the degree of correlation decaying monotonically with the distance of the bipoles.

Jais *et al.* computed the complex electrical activity (CEA) time as the percentage duration of electrograms showing either continuous electrical activity or FF intervals < 100 ms [16]. Although the methods is mainly qualitative and operator dependent, they found significant differences among atrial regions, with the septal and posterior areas more disorganized than the lateral and anterior regions.

The method proposed by Sih *et al.* was aimed at obtaining an high temporal resolution estimation of the synchrony between bipoles. It measures the short-duration linear relationship between two electrograms by a mean-squared error algorithm [17]. The algorithm measures the organization in terms of extent of predictability by linear algorithm. It turned out to be highly sensitive to different levels of organization and to have a high temporal resolution [17].

Barbaro *et al.* compared various time- and frequency-domain methods and demonstrated that the parameter which best discriminates AF types, according to Wells criteria, was the number of occurrences; i.e. the percentage number of points laying on the baseline [18].

Censi *et al.* used the recurrence plot analysis of the atrial period series to assess the degree of organization of local activation processes during AF [19]. They showed that a certain degree of organization during AF can be detected as spatio-temporal recurrent patterns of the coupling between the atrial depolarization periods at two atrial sites, and demonstrated that there is a deterministic mechanism underlying the seemingly random atrial activation processes during AF.

It is interesting to observe that, given the lack of a rigorous definition of organization, some methods measure features somewhat related to the coupling between electrograms, while others focus on single electrogram features, either from a morphological or dynamical point of view.

It should also be mentioned that some authors analysed the sequence of FF interval, rather than the raw signals. Two major attractive reasons lay behind the use of the FF interval series. Firstly, several methods developed in heart rate variability analysis can be easily adapted to FF intervals analysis (spectral analysis, measures from complex dynamics theory, symbolic dynamics, to name a few). Secondly, from a physiological viewpoint, FF interval values are related to local electrophysiological properties of the tissues, such as the excitable gab and the refractoriness [20, 21].

Frequency-domain analysis

The estimation of the frequency content of the time series is valid alternative to the time-domain methods, since it may enlighten properties and structures which can not be easily detected in the time-domain. Spectral estimation has sound theoretical bases, but only recently it has been applied to the analysis of intra-atrial electrograms. Table 2 summarizes the main frequency-domain methods used to the analysis of AF from intra-atrial signals.

Table 1. - Main time-domain methods to analyze atrial fibrillation

Authors	Method	Catheter type	Protocol	Results	Comments
Botteron *et al.* 1995 [15]	Cross-correlation, space constant calculation	Linear, right atrium and coronary sinus	Chronic and induced AF, 10 patients	Space constant correlates to the tissue wavelength	Robust pre-processing method which preclude the necessity of activation time estimation Low computational cost
Jais *et al.* 1996 [16]	Complex electrical activity and FF interval	Linear, right atrium and coronary sinus	25 patients	Posterior and septal regions show higher complexity than lateral and anterior	Not quantitative evaluation of organization
Sih *et al.* 1999 [17]	Adaptive filtering	Linear, right atrium	Induced AF, 19 dogs, vagal stimulation, adenosine	Decrease of organization with vagal stimulation	Sensitive to changes in AF organization High temporal resolution (300 ms)
Barbaro *et al.* 2000 [18]	Comparison of time domain and frequency domain	Linear, right atrium and coronary sinus	Chronic and paroximal AF, 23 patients	Number of points laying on the baseline closely fit the Wells' criteria	High temporal resolution (2 s) Low computational cost
Censi *et al.* 2000 [19]	Recurrence plot analysis	Linear, right atrium and coronary sinus	Chronic AF, 19 patients	Instances of deterministic patterns in the coupling between activation sequences Low sensitivity of linear analysis	Needing of activation sequence estimation Medium computation cost

Table 2. - Main frequency-domain methods to analyze atrial fibrillation

Authors	Method	Catheter type	Protocol	Results	Comments
Sahakian *et al.* 1992 [22]	Magnitude-squared coherence spectra	Linear	Sinus rhythm, atrial flutter, atrial fibrillation	Extraction of time-varying relationship between activity at two sites	Low temporal resolution (4.27 seconds)
Lovett *et al.* 1997 [25]	Coherence spectrogram	Linear	7 patients with atrial fibrillation during procainamide infusion	Both gradual and abrupt coherence increase in concomitance with conversion	High temporal resolution (1 second)
Jalife *et al.* 1998 [26]	Spectral estimation	High resolution optical mapping and linear catheter	*In vitro* experiments	Detection of dominant frequency peaks in both electrograms and optical recordings	Innovative link between spectral analysis and electrophysiological properties

Sahakian *et al.* first proposed an improved method of calculating magnitude-squared coherence spectra on pairs of short-duration electrogram recordings, to characterize atrial activity during AF [22]. The obtained high-resolution spectra made it possible to examine the time-varying relationship between activity at two sites, and may be used for constructing coherence maps [23]. When used to monitor the modality of sinus rhythm restoration, by drug administration, the spectral coherence did not demonstrate a progressive increase in the organization of AF prior to termination [24]. A modified spectral coherence estimation, featuring an higher temporal resolution and based on a particular time-frequency representation, showed that the conversion to sinus rhythm is concomitant with an increase in coherence and with the emergence of

structured time-frequency topography [25]. The observed transient electrical organization in the atria during AF was not detectable by previous low-resolution coherence studies. This new method presents a number of advantages over previous proposed coherence estimators and over conventional time-frequency representation, since it is sensitive only to phase-locked power shared between two signals in time and frequency.

An innovative use of spectral estimation has been proposed by Jalife *et al.*, who attempted to identify reentrant sources of activation [26]. They estimated the dominant frequency sources that are hypothesised to maintain the fibrillation. Although data were collected *in vitro* by optical recordings, the idea behind this study is certainly innovative, and *in vivo* application using the last generation mapping technique (basket catheter and/or non-contact) may be foreseen.

Complex dynamics theory approach

Methods derived from non-linear dynamical systems theory have been largely developed over the last three decades for the analysis of experimental time series. Such methods extract from a measured time series quantities representative of the dynamical behavior of the system.

The activation patterns behind the electrical activity of the heart during AF have often been characterized as random phenomena. However, the electrophysiological properties of the atria as well as their anatomy do not change during AF, suggesting that an underlying order could exist. Non-linear mechanisms of propagation of depolarization wavefronts in cardiac tissues have been recently hypothesised and investigated in various experimental and theoretical models [27-29]. The evidence collected prompts the development and testing of new non-linear tools in the analysis of endocardial signals.

In this context, the theory of non-linear dynamical systems aims at describing the electrical activity of the heart in space and time and to obtain insight into the underlying physiological processes from the measured epicardial and/or endocardial signals.

Table 3 shows the main complex dynamics theory-based methods to analyze AF.

In 1995, Hoekstra *et al*. first performed a non-linear analysis of single epicardial atrial electrograms during AF based on the estimation of their correlation dimension (CD) and correlation entropy (CE) in a reconstructed state-space (embedding procedure) [30]. Their results turned out to be consistent with the characterization of activation patterns determined by high density mapping. In addition, they found that all electrograms of AF of type I (according to Wells' criteria) performed a non-linear behaviour, and those showing a fully developed AF (type III) do not perform features of low-dimensional chaos.

Pitschner *et al*. used multipolar basket catheter to map the complex pattern of electrical activity of the right atrium in 9 AF-induced patients [31]. They measured the correlation dimension of the electrograms and found that the area anterior to the tricuspid valve was characterized by more chaotic activation patterns.

More recently, Berkowitsch *et al*. used a combination of symbolic dynamics and adaptive power estimation to compute the normalized algorithmic complexity of 31 electrograms recorded from a multipolar basket catheter in 25 patients [32]. They found that the right atrium could be divided in high- and low complexity areas according to individual patterns, even if a significant increase of the normalized algorithmic complexity has been found in the cranio-caudal direction. They also found that the administration of propafenone caused the enlargement of the low complexity areas.

Table 3. - Main complex dynamics theory-based methods to analyze atrial fibrillation

Authors	Method	Catheter type	Protocol	Results	Comments
Hoekstra *et al.* 1995 [30]	Correlation dimension and correlation entropy	Linear, right atrium	Chronic AF, 25 patients	Correlation dimension and correlation entropy correlate with the AF types	Needing of high density mapping High computational cost
Pitschner *et al.* 1998 [31]	Fractal dimension	Basket, right atrium	Intermittent AF, 9 patients	Higher fractal dimension in the areas anterior to the tricuspid valve Significant intra-individual differences	Needing for long recordings, hard computation, no real time
Berkowitsch *et al.* 2000 [32]	Algorithmic complexity	Basket, right atrium	Propafenone, 25 patients	Individual patterns of complexity Propafenone enlarged the areas with low complexity	Hard computation

Discussion

The technological development in the endocardial catheters has dramatically increased the number of channels available. Linear catheters have up to 24 electrodes, and recently, the basket catheter and the non-contact catheter, have been introduced. The basket catheter allows 64 simultaneous unipolar recordings or up to 56 bipolars over a quasi-spherical region. The non-contact system records 64 unipolar floating (non contact) signals and mathematically reconstructs up to 3360 unipolar endocardial signals. Compared to traditional linear catheters, both these systems significantly improve the number of sites simultaneously recorded, thus reducing the time needed for an extensive mapping of the atria. Such amount of data renew the interest for sophisticated signal processing methods. However, the potentialities of these catheters are still unexplored [31-35]. Presumably, the lack of specific methods of analysis and representation of these data might have contributed to their limited clinical use. Most of the methods proposed so far can be adapted and/or extended to multipolar recordings from the last generation catheters. It should be stressed that the geometry of the bipoles may affect the results of the analysis. Baerman *et al.* [36] recorded endocardial signals from four different bipole configurations and found that changes in bipole configuration resulted in profound changes in calculated atrial rate, signal amplitude, and electrogram amplitude probability density function. Electrogram median frequency turned out to be a robust measure despite multiple configurations. The effect on other measures such us correlation dimension or frequency domain indexes has to carefully evaluated, to allow comparisons from studies using different catheters.

The main attempts to interpret the signal processing indexes in term of electrophysiological properties or mechanisms use the concepts of organization, synchronization and complexity. Unfortunately standard definitions of these terms in the context of the AF phenomenon do not exist. This makes difficult either to compare results from different studies and to give interpretations to novel indexes. Indeed the term organization was first introduced by Wells [2], and it is widely used in the medical community, although it is based on visual inspection of electrograms. Sih *et al.* acknowledged the confusion between organization and synchronization [17] and pointed out the vagueness of the term "organization" itself. They also suggested an interesting interpretation of "organization" in terms of number of propagating wavelets entering the region explored by the electrodes. The synchronization, instead, may be defined more precisely and also may be interpreted in term of propagation of the same wavefront through different regions.

The term complexity has been used with different meanings in the analysis of atrial electrograms to described "complicated" waveforms and/or dynamics. However this term should be restricted to results obtained using that branch of system theory commonly knows as non-linear dynamics. The interpretation of the results derived from non-linear dynamics and chaos theory is difficult in many biological areas. The rational of such approaches is somewhat different with respect to other signal processing methods: the biological reality is investigated in its global rather than specific behavior. Authors following these approaches point out the ability of these methods to uncover the hidden deterministic mechanisms underlying the processes investigated. Nevertheless, the question whether AF is stochastic rather than deterministic is still debated.

The signal processing methods may also help in designing new approaches to the ablation therapy of AF, by identifying electrophysiological rather than anatomical sites candidate to be ablated. This idea stems from recent experimental evidences that the electrophysiological properties of the fibrillating atrial tissue feature individual patterns rather than common distribution [16, 35, 37, 38]. None of the various methods proposed in literature has yet demonstrated to be useful for the identification of regions sustaining AF.

The use of signal processing methods as a guide to radiofrequency ablation poses the constraint of a high computation speed. Only a limited number of the proposed methods fulfill the constraints of a real-time application. If a region were identified as a potential candidate for ablation, a real-time application would admit ablating using the catheter itself as spatial reference, regardless of its exact anatomical position.

The advances of the catheter technology and the availability of sophisticated concepts and ideas in the field of signal processing and information theory constitute a very promising base for a sound and profitable collaboration between engineers and medical doctors facing the electrophysiological challenges.

Submitted on invitation.
Accepted on 29 March 2001.

REFERENCES

1. Paul VE, O'Nunain S, Malik M, Camm AJ. Temporal electrogram analysis: algorithm development. *Pacing Clin Electrophysiol* 1990;13:1943-7.

2. Wells JL, Karp RB, Kouchoukos NT, MacLean WA, James TN, Waldo AL. Characterization of atrial fibrillation in man: studies following open-heart surgery. *PACE* 1978;1:426-38.

3. Allessie MA, Lammers WE, Bonke FI. Experimental evaluation of Moe's multiple wavelet hypothesis of atrial fibrillation. In: Zipes DP, Jalife J (Ed.). *Cardiac electrophysiology and arrhythmias.* New York: Grune and Stratton; 1985. p. 265-76.

4. Moe GK. On the multiple wavelet hypothesis of atrial fibrillation. *Arch Int Pharmacodyn Ther* 1962;140:83-188.

5. Moe GK, Rheinboldt WC, Abildskov JA. A computer model of atrial fibrillation. *Am Heart J* 1964;67:200-20.

6. Allessie MA, Konings K, Kirchhof CJ, Wijffels M. Electrophysiologic mechanisms of perpetuation of atrial fibrillation. *Am J Cardiol.* 1996;77:10A-23A.

7. Skanes AC, Gray RA, Zuur CL, Jalife J. Spatio-temporal patterns of atrial fibrillation: role of the subendocardial structure. *Semin Interv Cardiol* 1997;2:185-93.

8. Jalife J, Berenfeld O, Skanes A, Mandapati R. Mechanisms of atrial fibrillation: mother rotors or multiple daughter wavelets, or both? *J Cardiovasc Electrophysiol* 1998;9:S2-12.

9. Schuessler RB, Kawamoto T, Hand DE, Mitsuno M, Bromberg BI, Cox JL, Boineau JP. Simultaneous epicardial and endocardial activation sequence mapping in the isolated canine right atrium. *Circulation* 1993;88:250-63.

10. Ortiz J, Niwano S, Abe H, Rudy Y, Johnson NJ, Waldo AL. Mapping the conversion of atrial flutter to atrial fibrillation and atrial fibrillation to atrial flutter. Insights into mechanisms. *Circ Res* 1994;74:882-94.

11. Konings KT, Smeets JL, Penn OC, Wellens HJ, Allessie MA. Configuration of unipolar atrial electrograms during electrically induced atrial fibrillation in humans. *Circulation* 1997;95:1231-41.

12. Scherf D, Romano FJ, Terranova R. Experimental setudies on auricular flutter and auricular fibrillation. *Am Heart J* 1948;36:241-51.

13. Scherf D, Schaffer AI, Blumenfeld S. Mechanism of flutter and fibrillation. *Arch Intern Med* 1953;91:333-52.

14. Jais P, Haissaguerre M, Shah DC, Chouairi S, Gencel L, Hocini M, Clementy J. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation* 1997;95:572-6.

15. Botteron GW, Smith JM. A technique for measurements of the extent of spatial organization of atrial activation during atrial fibrillation in the intact human heart. *IEEE Trans Biom Eng* 1995;42:579-86.

16. Jais P, Haissaguerre M, Shah DC, Chouairi S, Clementy J. Regional disparities of endocardial atrial activation in paroxysmal atrial fibrillation. *PACE* 1996;19:1998-2003.

17. Sih HJ, Zipes DP, Berbari EJ, Olgin JE. A high temporal resolution algorithm for quantifying organization during atrial fibrillation. *IEEE Trans BME* 1999;46:440-50.

18. Barbaro V, Bartolini P, Calcagnini G, Morelli S, Michelucci A, Gensini G. Automated classification of human atrial fibrillation from intraatrial electrograms. *Pacing Clin Electrophysiol* 2000;23:192-202.

19. Censi F, Barbaro V, Bartolini P, Calcagnini G, Michelucci A, Gensini GF, Cerutti S. Recurrent patterns of atrial depolarization during atrial fibrillation assessed by recurrence plot quantification. *Ann Biomed Eng* 2000;28:61-70.

20. Michelucci A, Padeletti L, Fradella GA. Atrial refractoriness and spontaneous or induced atrial fibrillation. *Acta Cardiol* 1982;37:333-44.

21. Misier AR, Opthof T, van Hemel NM, Defauw JJ, de Bakker JM, Janse MJ, van Capelle FJ. Increased dispersion of "refractoriness" in patients with idiopathic paroxysmal atrial fibrillation. *J Am Coll Cardiol* 1992;19:1531-5.

22. Sahakian A, Ropella K, Swiryn S. Atrial electrograms and the characterization of atrial fibrillation. *J Electrocardiol* 1992;24 Suppl:131-3.

23. Ropella KM, Sahakian AV, Baerman JM, Swiryn S. The coherence spectrum. A quantitative discriminator of fibrillatory and nonfibrillatory cardiac rhythms. *Circulation* 1989;80:112-9.

24. Sih HJ, Ropella KM, Swiryn S, Gerstenfeld EP, Sahakian AV. Observations from intraatrial recordings on the termination of electrically induced atrial fibrillation in humans. *Pacing Clin Electrophysiol* 1994;17:1231-42.

25. Lovett EG, Ropella KM. Time-frequency coherence analysis of atrial fibrillation termination during procainamide administration. *Ann Biomed Eng* 1997;25:975-84.

26. Jalife J, Berenfeld O, Skanes A, Mandapati R. Mechanisms of atrial fibrillation: mother rotors or multiple daughter wavelets, or both? *J Cardiovasc Electrophysiol* 1998;9:S2-12.

27. Chialvo DR, Gilmour RF, Jalife J. Low dimensional chaos in cardiac tissue. *Nature* 1990;343:653-57.

28. Garfinkel A, Chen PS, Walter DO, Karagueuzian HS, Kogan B, Evans BJ, Karpoukhin M, Hwang C, Uchida T, Gotoh M, Nwasakwa O, Sager P, Weiss JN. Quasiperiodicity and chaos in cardiac fibrillation. *J Clin Invest* 1997;99:305-14.

29. Witkowski FX, Kavanagh KM, Penkoske PA, Plonsey R, Spano ML, Ditto WL, Kaplan DT. Evidence for determinism in ventricular fibrillation. *Phys Rev Lett* 1995;75:1230-33.

30. Hoekstra BP, Diks CG, Allessie MA, DeGoede J. Non-linear analysis of epicardial atrial electrograms of electrically induced atrial fibrillation in man. *J Cardiovasc Electrophysiol* 1995;6:419-40.

31. Pitschner HF, Berkovic A, Grumbrecht S, Neuzner J. Multielectrode basket catheter mapping for human atrial fibrillation. *J Cardiovasc Electrophysiol* 1998;9:S48-56.

32. Berkowitsch A, Carlsson J, Erdogan A, Neuzner J, Pitschner HF. Electrophysiological heterogeneity of atrial fibrillation and local effect of propafenone in the human right atrium: analysis based on symbolic dynamics. *J Interv Card Electrophysiol* 2000;4:383-94.

33. Jenkins KJ, Walsh EP, Colan ED, Bergau DM, Saul JP, Lock JE. Multipolar endocardial mapping of the right atrium during cardiac catheterization: description of a new technique. *J Am Coll Cardiol* 1993;22:1105-10.

34. Triedman JK, Jenkins KJ, Colan SD, Van Praagh R, Lock JE, Walsh EP. Multipolar endocardial mapping of the right heart using a basket catheter: acute and chronic animal studies. *PACE* 1997;20:51-9.

35. Schilling RJ, Kadish AH, Peters NS, Goldberger J, Davies DW. Endocardial mapping of atrial fibrillation in the human right atrium using a non-contact catheter. *Eur Hearth* 2000;21:550-64.

36. Baerman JM, Ropella KM, Sahakian AV, Kirsh JA, Swiryn S. Effect of bipole configuration on atrial electrograms during atrial fibrillation. *Pacing Clin Electrophysiol* 1990;13:78-87.

37. Gaita F, Riccardi R, Calò L, Scaglione M, Garberoglio L, Antolini R, Kirchner M, Lamberti F, Richiardi E. Atrial mapping and radiofrequency catheter ablation in patients with idiopathic atrial fibrillation. Electrophysiological findings and ablation results. *Circulation* 1998;97:2136-45.

38. Roithinger FX, SippensGroenewegen A, Karch MR, Steiner PR, Ellis WS, Lesh MD. Organized activation during atrial fibrillation in man: endocardial and electrocardiographic manifestations. *J Cardiovasc Electrophysiol* 1998;9:451-61.