# Non-invasive Detection of Reentrant Drivers during Atrial Fibrillation: a Clinical-Computational Study

Miguel Rodrigo<sup>1</sup>, Andreu M Climent<sup>2</sup>, Alejandro Liberos<sup>1</sup>, Jorge Pedrón-Torrecilla<sup>1</sup>, José Millet<sup>1</sup>, Francisco Fernández-Avilés<sup>2</sup>, Felipe Atienza<sup>2</sup>, Omer Berenfeld<sup>3</sup>, Maria S Guillem<sup>1</sup>

> <sup>1</sup>Universitat Politècnica de València, València, Spain <sup>2</sup>Hospital General Universitario Gregorio Marañón, Madrid, Spain <sup>3</sup>University of Michigan, Ann Arbor, MI, USA

#### Abstract

Reentrant drivers or mother rotors have been defined as a mechanism responsible of atrial fibrillation (AF) maintenance whose ablation can terminate the fibrillatory episodes. This study presents a novel noninvasive approach to identify atrial reentrant patterns.

High-density surface potential recordings were obtained from 14 AF patients and singularity points (SP) were located in the torso phase maps after band-pass filtering at the highest dominant frequency. An atrialtorso computer model was used to investigate the effect of the band-pass filtering on the electric potential signal.

Stable SPs were found during  $73.1\pm16.8\%$  of time after band-pass filtering vs.  $8.3\pm5.7\%$  on raw signals. Surface SPs representing atrial rotors were detected at specific torso areas related with their atrial location.

Phase analysis after band-pass filtering can detect atrial drivers, helping to plan the best therapy strategies.

#### **1.** Introduction

Novel recording techniques have demonstrated that functional reentries, or mother rotors, can be the responsible of the maintenance of fibrillatory processes during atrial fibrillation (AF), and their ablation can terminate the arrhythmia [1-3]. The identification of the fibrillatory mechanisms in each patient may help in planning the best pharmacological therapy or ablation strategy to deliver to that individual patient.

Previous studies have found a correlation between the dominant frequency (DF) distribution along the atria and the position of the atrial rotors [2-3]. Besides, it has recently been shown that non-invasive mapping allows the identification of these high DF atrial sources during human AF by using surface recordings [4]. Thus, the aim of this study is to investigate the potential use of surface mapping recordings for the detection of atrial drivers prior to the invasive interventions.

### 2. Methods

### 2.1. Patients

Surface electrocardiograms (ECG) from 14 paroxysmal and persistent AF patients were recorded using a grid of 67 electrodes on a vest covering the torso (Figure 1). Ventricular activation was removed by administration of a central venous bolus of adenosine (12-18 mg) and 4-seconds segments of surface ECGs surrounding the longest RR interval were used for the analysis. Surface potentials were baseline-subtracted and low-pass filtered at 30 Hz [5]. Power spectral density of all signals was computed to determine the local DFs and their distribution on the body surface [4].

Intracardiac electrograms (EGMs) were simultaneously obtained from both atria during the procedure by using catheters introduced via the right femoral vein. Power spectral density of EGMs was computed to determine the DF of each atrium. Surface ECGs were then filtered at the highest DF (HDF) found on the torso surface or at the highest DF found at either left atrium EGMs (LA-HDF) or right atrium EGMs (RA-HDF) by using a 2 Hz bandwidth band-pass filter.

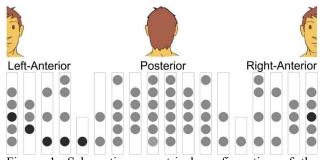


Figure 1. Schematic geometrical configuration of the surface electrodes relative to the torso. Electrodes at locations corresponding to the standard ECG precordial leads are denoted as black circles.

# 2.2. Mathematical models

Due to the difficulty in obtaining simultaneous panoramic recordings from the atria and torso surface, we had to rely on mathematical models of the electrical behaviour of the atria-torso system to investigate how the atrial reentrant patterns are projected on the torso. Our atria-torso model consisted on a spherical shell of active tissue, representing the atria, within a passive torso modelled as a uniform volume conductor bounded by a spherical surface representing the torso surface [6].

The atrial shell was divided into a 10% area with healthy conduction properties and a 90% area with fibrotic properties, resulting in a fibrillatory propagation pattern leaded by a stable rotor placed on the healthy area. The electric potential resulting from the atrial activity was studied everywhere on 20 concentric spheres from the atria to the torso by using the Boundary Element Method.

#### **2.3.** Phase singularity and filaments

Phase maps on the torso surface of patients and in each concentric layer in the computer models were obtained from the potential phase signal of each node by the Hilbert transform [7]. A singularity point (SP) was defined as the point in a phase map which is surrounded by phases from 0 to  $2\pi$ . Only those SPs that were present for the duration of at least one full rotation were considered. A filament was defined as the connection between SPs across spherical layers on the atrial-torso model at a given time.

#### 3. Results

#### 3.1. Patients

Surface phase maps recorded on the patients torso during AF showed unstable patterns prior to the HDFfiltering, as can be appreciated on Figure 2A. The SPs detected were present briefly and drifted large distances in short time. After HDF filtering of the potential signal, phase maps showed SPs more spatially and temporally stables (Figure 2B). The reentrant patterns could be observed also in the ECG signal after the HDF-filtering. Figure 2C shows a clear reentrant pattern in the filtered potential signal that corresponds to the stable SP in Figure 2B. Measurements on the rotor occurrence before and after HDF-filtering confirmed the stabilization of the SPs (Figure 2D). Stable SPs were found in unfiltered AF signals during 8.3±5.7% of the time vs. 73.1±16.8% in HDF-filtered signals (p<0.01) and the average SPs duration concomitantly increased following the HDFfiltering (160±43 ms vs. 342±138 ms, p<0.01).

The EGM simultaneously recorded to the surface potential signal allowed us to make inferences between

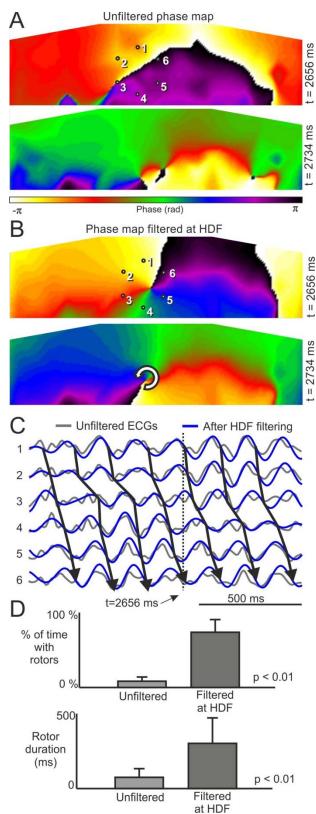


Figure 2. Surface phase maps at two selected times for unfiltered (A) and for HDF-filtered (B) potential signal. (C) ECGs at positions 1-6 in (A) and (B). (D) Surface rotor measurements over the entire cohort.

the reentrant patterns detected on the torso surface and the evidence of rotor drifting in the atria. In Figure 3A the spatial position of a torso SP that lasted for 3 seconds can be observed. It is noticeable that the EGM (Figure 3B) presented unstable morphology in intervals 1-4 and monomorphic morphology at interval 4-5, which is consistent with the observed drifting of the SP on the torso surface. It is remarkable that the detected rotors can drift out of the registered area, so the duration values described above are a conservative estimation.

The band-pass filtering at the HDF found on the atrial EGM tended to concentrate the rotor apparition at certain areas of the torso. The trajectory of a surface SP that drifted during 2 seconds on the posterior torso obtained after the LA-HDF filtering in a LA-fastest patient is depicted in Figure 4A. In Figure 4B can be observed the trajectory of a SP that drifted during 500 ms on the right anterior torso detected after the RA-HDF filtering in a RA-fastest patient. In Figure 4C, the 2-dimensional histogram of SP locations after LA-HDF filtering in patients with an inter-atrial DF gradient > 1 Hz (n=10) shows a predominant location of SPs on the posterior torso, while the histogram after RA-HDF filtering shows the predominant location on the right anterior torso. The locations of the maximal numbers of true LA or RA SPs are shown in Panels C and D to reside well within the areas demarcated by the HDFs originating either at the LA or RA (marked with dotted line), respectively, based on previous surface-atrial DF distribution correlation study [4].

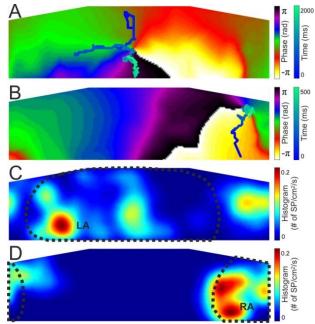


Figure 4. (A) Phase map and rotor tracking after LA-HDF. (B) Phase map and rotor tracking after RA-HDF filtering. Histogram of the rotor position for all rotors detected in patients with an inter-atrial DF gradient after LA-HDF filtering (C) and after RA-HDF filtering (D).

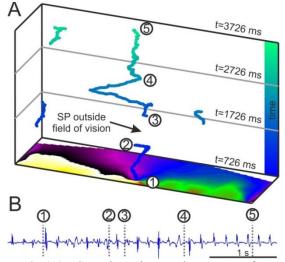


Figure 3. (A) PSs trajectories on the torso surface. (B) EGM recorded at the highest DF in the atria simultaneously to the surface recordings.

#### **3.2.** Mathematical models

Figure 5A shows the phase map at increasing distances from epicardial to surface in the atrial-torso mathematical model with a reentrant driver in the 10% of healthy tissue. Note that phase maps from raw signals showed unstable patterns due to the fibrotic activity. However, after the HDF-filtering the surface phase map became stable, showing a stable SP at the nearest point to the atrial rotor. At Figure 5B the filament distribution before and after the HDF filtering can be seen. It can be observed that HDFfiltering allows removing the activity at frequencies other than the rotor activity (fibrotic activity), projecting on the torso only the electrical activity produced by the rotor.

# 4. Discussion

In this study we show that phase maps of surface potentials during AF display unstable reentrant patterns, but after HDF-filtering they allow observing reentrant patterns with spatiotemporal stability. The short-lived and unstable surface reentrant activity in the non-filtered data is suggested by computer simulations to result from superposition of irregular electrical activity at frequencies other than the HDF which may mask the presence of the more stable reentrant activation. Furthermore, it has been found that there is a correlation between the drifting of these reentrant patterns on the torso and the EGM signal simultaneously recorded, so there is evidence that our surface reentrant patterns can be provoked by atrial reentrant drivers. Finally, it has been shown as the HDFfiltering at the bands of the right and left atrium activity reflects surface rotors in different areas of the torso which coincide with the areas in which the electrical activity of the right and left atrium are projected respectively [4].

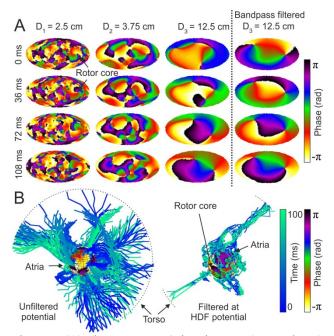


Figure 5. (A) Phase maps at 4 time instants (top to down) in 3 concentric layers at increasing distances from the epicardium (left to right) and after HDF filtering of surface potentials. (B) Temporal evolution of filaments for unfiltered potentials and for HDF-filtered potentials.

Previous studies have demonstrated that reentrant drivers can be responsible of the human AF maintenance [1-3]. Narayan et al. reported recently that rotor activity is detectable by panoramic intracardiac mapping in about 70% of 98 out of 101 AF patients and brief ablation at the centers of those rotors was effective in terminating or slowing the arrhythmia [1]. The results presented in this study are consistent with that latter evidence: the surface recordings are detecting rotor activity also in about 70% of the time during AF.

Computer simulations have demonstrated that atrial rotors, even present in small atrial areas, can be detected on the torso surface by HDF-filtering. Activity of rotors covering a small atrial portion may be masked by the electrical activity of the rest of the atria, even if it is a highly disorganized activity, so the raw potential signal may shows unstable reentrant patterns. The HDF-filtering allows attenuating the signal component provoked by the regions working in a frequency other than the rotor, remaining after the band-pass filtering only the electrical activity provoked by the reentrant driver and thus stabilizing the surface reentrant patterns.

We cannot conclusively confirm that rotational patterns observed in patients correspond to actual atrial rotors since we do not have simultaneous epicardial and/or endocardial panoramic data. However, we have made use of mathematical models to demonstrate that in case rotors are present during AF on the atria, they can be detected on the torso surface by HDF-filtering even if the rotors are present in small areas. Although the models of the atria-torso system were simple spherical models, these simple models contain the active and passive volume conductor components needed to gain insight into the mechanisms of visual rotor stabilization by HDF-filtering.

# 5. Conclusion

Phase analysis of the surface potential signal after HDF-filtering and identification of singularity points can detect the presence of atrial reentrant drivers. The detection of the AF maintenance mechanism in each individual patient may help improving the diagnosis and selecting the best therapies.

### Acknowledgements

This work was partially supported by Spanish Ministry of Economy (TEC2009-13939), by Generalitat Valenciana (GV/2012/039), by Universitat Politècnica de València (PAID-05-12) and through its research initiative program.

## References

- Narayan SM, Krummen DE, Shivkumar K, et al. Treatment of atrial fibrillation by the ablation of localized sources: CONFIRM (conventional ablation for atrial fibrillation with or without focal impulse and rotor modulation) trial. J Am Coll Cardiol 2012;60:628-36.
- [2] Atienza F, Almendral J, Jalife J, 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.
- [3] Atienza F, Almendral J, Moreno J, et al. Activation of inward rectifier potassium channels accelerates atrial fibrillation in humans: evidence for a reentrant mechanism. Circulation 2006;114:2434–42.
- [4] Guillem MS, Climent AM, Millet J, et al. Noninvasive localization of maximal frequency sites of atrial fibrillation by body surface potential mapping. Circ Arrhythm Electrophysiol 2013;6:294-301.
- [5] Guillem MS, Climent AM, Castells F, et al. Noninvasive mapping of human atrial fibrillation. J Cardiovasc Electrophysiol 2009; 20:507–13.
- [6] Rodrigo M, Climent AM, Liberos A, et al. Non-invasive location of re-entrant propagation patterns during atrial fibrillation. Computers in Cardiology 2013;40:1235-8.
- [7] Zlochiver S, Yamazaki M, Kalifa J, Berenfeld O. Rotor meandering contributes to irregularity in electrograms during atrial fibrillation. Heart Rhythm 2008;5:846-54.

Address for correspondence.

M. Rodrigo

BioITACA, Universitat Politècnica de València mirodbor@teleco.upv.es