Highest Dominant Frequency and Rotor Positions are Stable Markers for Atrial Driver location in Non-invasive Mapping of Atrial Fibrillation

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Abstract

Inverse-computed Dominant Frequency (DF) and rotor maps have been proposed as non-invasive mapping techniques to locate atrial drivers maintaining atrial fibrillation (AF). This study evaluates the robustness of both techniques to identify atrial drivers.

Highest DF (HDF) regions and rotor position were compared with the same inverse-computed measurements on a population of 30 different mathematical AF simulations after addition of white noise to the ECG, linear and angular deviations in the location of the atria and also with varying blood conductivities.

Inverse-computed EGMs showed individually a poor correlation with the actual EGMs even in the absence of induced error sources and worsened with the artifacts. However, inverse-computed HDF regions showed stability against artifacts: from 82±18% match for the HDF region for the best conditions, down to 60±22% for the worst case. The rotor location also presented a stable measurement: the distance from the inverse-computed rotor to the actual rotor was 0.8±1.61 cm for the best conditions, 2.4±3.6 cm for 10 dB, 4.3±3.2 cm for 4 cm displacement and 4.0±2.1 cm for 36º.

Non-invasive AF driver identification based on HDF and rotor location is accurate even in the presence of noise or uncertainties in atrial location or conductivity.

1. Introduction

In the last years, Haïssaguerre et al. [1] have reported on the identification of rotors noninvasively, by using the Electrocardiographic Imaging (ECGI) technique. However, the propagation patterns that result from the inverse problem resolution during atrial fibrillation (AF) and serve as a basis for rotor identification appear to be paradoxically simple [1] as compared to those obtained with contact electrodes [2]. Since the inverse problem in AF has only been validated indirectly based on the freedom from AF after an ablation procedure [1], the validity of such approach is still a matter of debate.

In this study we make use of mathematical simulations of AF in order to evaluate the stability of non-invasive identification of AF drivers by rotors or Highest DF (HDF) regions in presence of uncertainties in the inverse solution.

2. Materials and methods

2.1. Mathematical models

A realistic 3D model of the atrial anatomy composed by 284,578 nodes [3] was used to simulate the atrial electrical activity by solving the atrial cell formulation proposed by Koïvumaki et al. [4]. Fibrotic tissue was modelled by electrically disconnecting between 20% and 60% of the total nodes. An ensemble of 30 different AF episodes was simulated, composed of 14 AF patterns driven by a single rotor at varying locations on the left atrium (LA) and 16 AF patterns driven by a single rotor at varying locations on the right atrium (RA).

The ECG potentials on the torso model were calculated by solving the forward problem of electrocardiography with the Boundary Element Method [5] in a mesh formed by 771 nodes. The electrical conductivities used were 3S/m for blood and 2S/m for the rest of the tissue [5].

Inverse-computed EGMs (icEGM) were obtained by solving the inverse problem with the zero-order Tikhonov's method in which the regularization parameter was chosen according to the L-curve method [5].

2.2. Addition of uncertainties

In order to evaluate the robustness of the inverse solutions against model uncertainties, we evaluated the accuracy of the solution under noise, errors in the location or orientation of the atria inside the torso volume and errors in the conductivity. In particular, white Gaussian

Computing in Cardiology 2016; VOL 43 ISSN: 2325-887X DOI:10.22489/CinC.2016.004-418

noise was added to the synthetic ECG signals with a signal-to-noise ratio (SNR) between 60dBs and 0dBs. Alternatively, the inverse problem was solved for displacements in the location of the atria from 0 cm to 5 cm in the lateral axis (X axis in Fig 1.A), under rotations from 0º to 45º also in the lateral axis and variations in the blood conductivity from 0.5 S/m to 9 S/m (as opposed to the 3 S/m used for the forward problem).

2.3. Rotor and DF identification

Rotor location was carried out by identification of singularity points (SP) in the phase signal map obtained with the Hilbert Transform [6]. A rotor was defined as the connection between SPs across time and only long lasting rotors, defined as those that complete at least one rotation were considered as rotors and other SPs were discarded. Histograms of rotors presence were obtained by accounting the amount of rotors in each atrial node, and the node with highest reentrant presence was considered as the rotor site [1], and their distance to the actual rotor was measured.

For the Dominant Frequency (DF) analysis, icEGMs were baseline-removed and were then low-pass filtered with a 10th-order Butterworth filter with a cut-off frequency of 10 Hz. Power spectral density of all signals was computed using Welch periodogram to determine the local DFs with a spectral resolution of 0.01Hz [7]. Highest Dominant Frequency (HDF) regions were defined as those atrial regions whose DF values presented a difference with the rotor DF lower than 0.5 Hz. Inverse-computed DF maps were compared with the departing DF maps by obtaining the concordance of the HDF region as the intersection area of departing and inverse-computed HDF regions divided by the departing HDF area.

3. Results

3.1. Illustrating example

Figure 1.A illustrates a schematic view of the 3D torso model used for the inverse solution and the atrial surface at its original position and after a displacement of 2 cm. Panels C, D and E compare the inverse-computed maps with the original maps depicted in panel B. In particular, the voltage, phase and DF maps are depicted for an AF pattern driven by a stable rotor in the posterior wall of the LA. As it can be observed, the inverse-computed voltage map is smoother than the departing EGMs; however, the potential distribution is similar. This is also evidenced in the phase map, in which the location of the singularity point is preserved. Finally, the inverse-computed DF map seems more robust to the inverse computation since the Highest Dominant Frequency (HDF) region has roughly the same distribution than the departing HDF region.

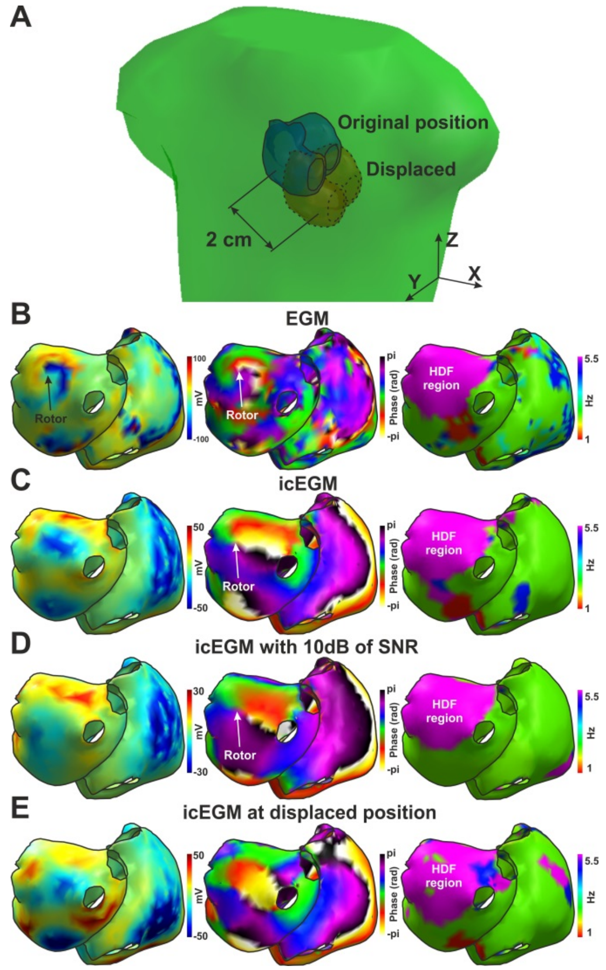

Figure 1. (A) Schematic view of the torso surface (green), atrial surface at the original position (blue) and atrial model at displaced position (red). Potential map (left), phase (center) and DF map (right) for: (B) EGM signal; (C) icEGM signal with no inaccuracies; (D) icEGM signal with 10dB of NSR; (E) icEGM signal solved at displaced (2 cm) position.

3.2. Signal correlation

Similarity of the inverse-computed signals with the departing EGMs after imposition of signal or model uncertainties was systematically evaluated in our AF model database and presented in Fig. 2. As it can be observed, the correlation coefficient for EGM signals is quite poor even in the absence of noise or model uncertainties, with a mean correlation coefficient of 0.45±0.12. Addition of white noise to the surface ECGs before computing the inverse solution decreased this correlation coefficient down to 0.18±0.1 for a 0 dB SNR. Uncertainties in the model conductivities had no effect on the accuracy of the resolution, as it can be observed in Fig. 2.B. Uncertainties in the location or orientation of the atria inside the torso volume, however, had a large impact on the correlation coefficients. Correlation coefficients decreased down to 0.01±0.02 for a 3 cm of displacement or down to 0.03±0.05 for a 27º of rotation.

3.3. Dominant frequency

Although the morphology of inverse-computed and their departing EGMs have been shown to be poorly related, they do allow for a robust estimation of the local activation rate (or DF) against signal or model uncertainties, as it can be observed in Fig. 3. Identification of the highest DF region was accomplished with a concordance above 75% for SNRs as low as 10 dB and went down to 56.5±32.3% for 0dB. Again, changes in the blood conductance did not result in perceptible changes in the HDF region concordance rate and remained stable around 85±10%. Quite notably, identification of the HDF region was very stable against uncertainties in the atrial location, with mean concordance values above 75.9±11.9%, corresponding to a 3 cm displacement. Inverse-computed DF maps were more sensitive to angular deviations, since the concordance of the HDF progressively decreased from 84.5±10.6% for 0º down to 56.2±23.0% for 45º.

3.4. Rotors

In Figure 4, the accuracy of the inverse-computed rotor estimation is presented for the entire database. The average errors under the effect of electrical noise remained stable around 1 to 1.5 cm from 60dB to 20dB. For 10dB and 0dB the average value of the error in rotor location raised up to 2.4±3.6 cm and 4.5±4.5 cm respectively, but in both cases 50% of rotors were identified with a deviation below 2 cm. Variations in blood conductance did not result in significant variations respect to the original location. Displacements in the atrial position provoked a comparable error in the inverse-computed rotor position: from 0.9±1.3 cm for a displacement of 1 cm to 4.7±3.3 cm for a displacement of 5 cm. Rotations of the atria inside the thorax also resulted in incremental errors in the inverse-computed rotor position: from 1.2±1.3 cm for 9º to 4.9±2.6 cm for 45º.

Next, the ability of the inverse solution in identifying the atrial region responsible to maintain the arrhythmia was also evaluated. The atrial surface was divided into 7 anatomical regions (left PVs, right PVs, PLAW, upper RA, lower RA, anterior LA and septum) [1] and the match between the departing and inverse-estimated driving region was quantified. As it can be observed in Fig. 5A, there was a good match for the higher SNRs, with more than 80% match, which gradually decreased with increasing noise levels down to 47% for 0dB. Blood conductance again had little effect on rotor identification. Rotor region identification was accurate for small deviations in location (< 3cm) or orientation (< 9º).

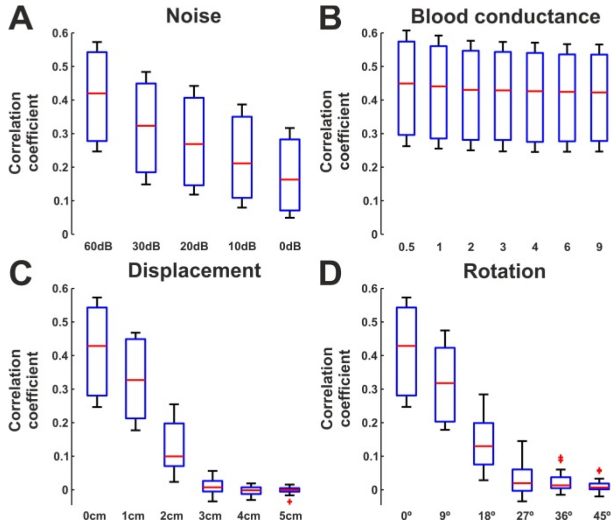

Figure 2. Correlation coefficient between icEGMs and original EGMs.

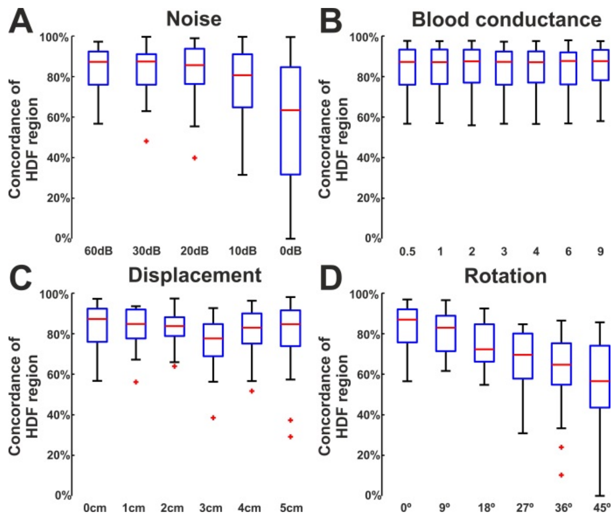

Figure 3. Concordance of inverse-computed HDF region with original HDF region under.

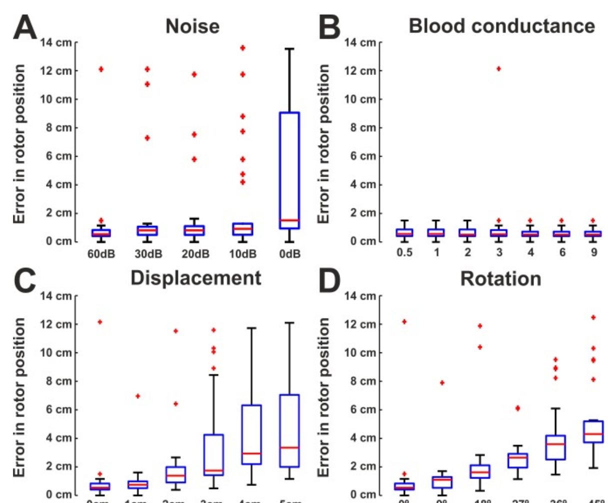

Figure 4. Error in non-invasive rotor position identification.

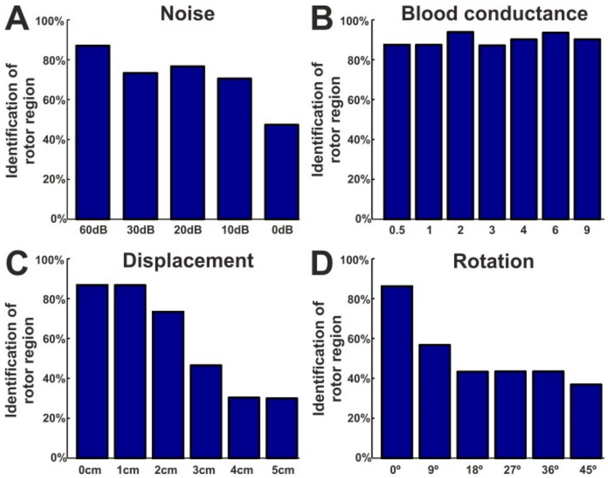

Figure 5. Non-invasive identification of the rotor region under variations.

4. Discussion

In this work we demonstrate that inverse-computed maps allow for an accurate identification of atrial drivers even in the presence of noise or model uncertainties by making use of mathematical models of human AF and torso propagation. In spite of the limited accuracy of the morphology of inverse-computed epicardial potentials, atrial drivers can be identified because the predominant activation patterns and activation rates are preserved.

We have recently shown that inverse-computed EGMs are poorly related to contact electrograms (either experimentally measured or simulated), with large relative errors in the instantaneous phase [6]. We have also demonstrated that electrical propagation through the torso is involved in a loss of pattern complexity, which is consistent with a mutual cancellation of propagation wavefronts with opposed directions [6] that may not be retrievable by solving the inverse problem. Despite this loss of information at the body surface level, surface potentials have shown to keep some relevant attributes of AF drivers both in terms of their activation frequency [7] and rotor location [6]. However, other uncertainties may add computational errors in the inverse problem resolution which may restrict the validity of such approach in the context of AF. These uncertainties include the electrical noise or the inaccuracies in the geometrical model used due to either an inaccurate volume segmentation or the dynamic position of the atria inside the thorax during heart contraction and respiration.

However, despite the non-negligible effect of signal or noise inaccuracies on the reconstructed propagation patterns, we found that activation-based parameters, such as the activation frequency or rotor location are robust against both signal and model uncertainties. This good performance of activation-based parameters suggests that the underlaying propagation patterns do reach the torso surface and can be inverse-reconstructed whereas the fibrillatory conduction that surrounds the main rotational activity cancels out and reaches the surface at a lower extent [6]. According to our results, the simple activations patterns inversely computed do not account for the complexity of true AF activation patterns, but keep key features that allow the atrial driver identification.

In this work we have made use of mathematical models in order to validate the noninvasive estimation of atrial drivers during AF because current technology does not allow validating such approach in a real scenario. An accurate validation would require a precise measurement of the transmembrane voltage in the entire atrial tissue and torso, including the endocardium, epicardium and surface ECG at multiple sites. However, the mathematical models used may not represent the whole spectrum of possible atrial substrates during AF thus our results cannot be extrapolated to a more general AF population.

Acknowledgements

Supported by: Generalitat Valenciana Grants (ACIF/2013/021); Instituto de Salud Carlos III (Ministry of Economy and Competitiveness, Spain: PI13-01882, PI13-00903 and PI14/00857); Spanish Society of Cardiology (Grant for Clinical Research in Cardiology 2015); Spanish Ministry of Science and Innovation (RIC PLE2009-0152) and Centro Nacional de Investigaciones Cardiovasculares (CNIC-13).

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