Electrocardiographic Imaging in Atrial Fibrillation: Selection of the Optimal Tikhonov-Regularization Parameter

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Abstract

Electrocardiographic imaging (ECGI) allows evaluating the complexity of atrial fibrillation (AF) signals using the Boundary Element Method and Tikhonov regularization. An accurate ECGI reconstruction is dependent on a proper selection of the regularization parameter (λ). In this work, two ranges of λ are explored to evaluate the effect of λ on the quality of the ECGI reconstruction.

ECGIs of 20 AF patients were computed using zero (T0), first (T1) and second (T2) order Tikhonov regularization (TR) for two ranges of λ: from 10^{-9} to 10^{2} and 10^{-12} to 10^{-4}. Dominant frequencies (DF) and the number of rotors obtained with the two ranges and methods were compared.

Zero-order Tikhonov showed to be more robust in λ selection for different λ ranges. For lower λ ranges, higher DF was found (T2, $p<0.05$) and more rotors were detected for T1 and T2 ($p<0.01$). Differences between TR methods compared by λ ranges showed more variability in derived metrics for lower λ range ($p<0.01$).

Optimal ranges for λ search differ among T0, T1 and T2. Election of lower than optimal λ values result in an increased estimated electrical complexity.

1. Introduction

Electrocardiographic imaging (ECGI) is a non-invasive technique that allows computing the epicardial activity by means of the solution of the inverse problem of electrocardiography by using surface electrograms and the geometry of the torso and heart of the patient. ECGI can be used to evaluate the complexity of atrial fibrillation (AF) signals, with some correlation with intracardiac mapping [1]. Despite the demonstrated reliability of ECGI reconstructions, the obtention of ECGI signals is an ill-conditioned problem with an unknown solution, which specially for AF, is strongly dependent on the noise and quality of the signals.

The inverse problem of electrocardiography has been studied by several approaches [2], being zero-order Tikhonov regularization (TR) the most widely used. Election of the regularization parameter is usually accomplished by the L-curve method, which is based on minimizing both the norm of the regularized solution and the norm of the residual vector [3]. Tikhonov regularization method has a good performance in models of AF signals [4], but in real scenarios, the complexity and the noise of the signals affect the selection of λ. Higher λ can result in an oversmoothed ECGI, hindering an underlying atrial electrical complexity, and on the contrary, λ values closer to zero are more sensitive to little changes of the signal, amplifying artifacts caused by noise that for AF are difficult to remove. A correct λ selection depends on the performance of the method but this selection is totally dependent on the range searched for selecting the regularization parameter.

In the present study, two different ranges of λ are explored to compute the ECGI in real AF signals using zero, first and second order TR. The premise of this study is that ECGI with a good reconstruction and a correct λ selection will present lower differences between TR orders, this difference is expected to be reflected in the resulting maps and non-invasive metrics as well.

2. Material and methods

2.1. Data collection and preprocessing

The electrical activity of 20 AF patients (10 females and 10 males; 63.1 ± 7.9 years old) was recorded through Body Surface Potential Mapping with 64 electrodes prior to pulmonary vein isolation (PVI). The torso geometry of the patients and the position of electrodes were reconstructed using photogrammetry of a video of the patient [1]. The heart anatomy of each patient was obtained from a database of MRI segmented atria, by selecting the most appropriate based on the torso's geometries.

Base line of surface electrograms was removed, signals were band-pass filtered between 2 and 45 Hz. One signal per patient was selected with a mean duration of 4.61 ± 0.52s and ventricular activity was removed by using the Principal Component Analysis approach described in [5].

2.2. Inverse problem and regularization parameter selection

To compute the ECGI of each patient, the inverse problem of each signal is computed using Tikhonov regularization (TR) and L-curve optimization [6]. Tikhonov regularization allows estimating the epicardial potentials (x) by minimizing the following equation:

$$\|Ax - b\|^2 + \lambda\|Lx\|^2 \quad (1)$$

Where b are torso potentials and A the transfer matrix calculated using the Boundary Element Method between torso and atria geometries. In this study, we used three Tikhonov orders where L is a square matrix that is the identity matrix in zero-order Tikhonov, (T0), the gradient operator in first-order (T1), and the Laplacian operator in second-order Tikhonov (T2) [4]. For each method, the regularization parameter chosen is the one that minimizes equation 1. In this study, two ranges of λ were studied and compared using three different order Tikhonov regularization methods: a high range from 10^{-9} to 10^{2} and a lower range from 10^{-12} to 10^{-4}.

2.3. ECGI derived metrics and statistical analysis

After computing ECGI for both ranges and three methods, the highest dominant frequency (HDF) [7] and rotors were computed [8]. Both metrics were compared for each Tikhonov solution in both λ ranges. Absolute difference between ECGI solutions obtained with different Tikhonov orders were computed and compared between ranges. Statistical comparisons were calculated using paired t-student test and Wilcoxon rank-sum test when the normality of the metrics was not present. A p-value<0.05 was considered statistically significant.

3. Results

3.1. Regularization parameter range and optimal selection

An example of how an appropriate range of λ affects ECGI derived maps is presented in Fig. 1. Dominant frequency maps (Fig. 1A) and singularity point (SP) histograms (Fig. 1B) are presented for the three TR orders and optimal and sub-optimal λs. An optimal λ selection shows dominant frequency maps with localized areas of high frequencies (red-coloured) that match between the three TR orders, moreover, areas of HDF match clearly with SP in panel B, presenting interpretable results and reproducible between orders. When a sub-optimal λ was chosen HDF and SP are more dispersed in the presented maps, leading to non-interpretable and coherent results, which suggest that ECGI reconstruction was more affected by noise.

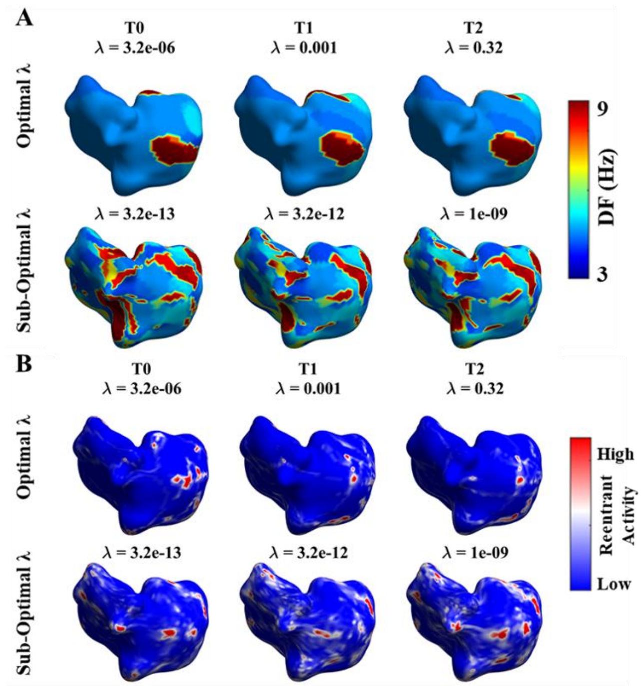

Figure 1. Dominant frequency (A) and singularity point maps (B) from an atrial fibrillation signal obtained by Tikhonov regularization of zero, first, and second-order (T0, T1, and T2). The first row of each panel represents the solution using an optimal regularization parameter (λ) and the second row a sub-optimal λ.

Two λ ranges were compared in 20 AF signals and the selected λ are represented in Fig 2. Optimal λ found in the higher range (dots) appeared in a narrow range of values with no overlap between ranges for T0 (10^{-6} to 10^{-4}), T1 (10^{-2} to 1) and T2 (1 to 100). The highest λ range showed lower variability of the optimal selection between patients with lower values for T0 compared to higher TR orders. However, when the studied λ range was lower, the variability of the λ selection between patients was higher. Zero-order Tikhonov, showed more similar results between λ ranges, being more consistent since the optimal λ belongs to the region for λ search that overlaps in both ranges. The first and second order, presented more disperse and lower λ between patients, tending to 0.

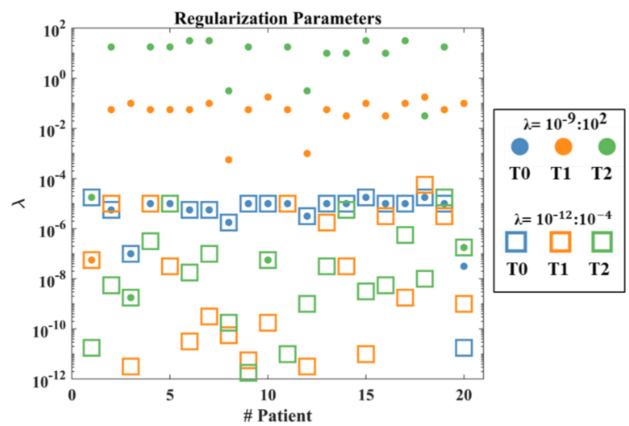

Figure 2. Results of the selected regularization parameters (λ) for a high range of λ (dots) and low range (squares) for zero, first and second order Tikhonov regularization (T0, T1 and T2, respectively).

3.2. ECGI metrics vs. regularization parameter

In Fig 3 ECGI derived metrics and how they change between the studied ranges of the regularization parameter. are represented. Results of HDF (Fig 3A) appeared in the range from 6 to 12 Hz for all the TR orders tested. Overall, we did not find any relation between HDF and λ. The number of rotors (Fig. 3B), in contrast, showed an inverse relation with λ for the three TR methods tested.

A comparative of the noninvasive metrics computed from TR methods using both λ ranges is presented in Fig 4A. As it can be observed, T0 did not show differences in the derived metrics based on λ ranges due to the lower variability in parameter selection. However, differences can be found in higher orders, that showed how lower λ ranges are related to a higher complexity of the metrics, being significantly higher for HDF (T2, $p<0.05$) and specially in the number of rotors per second ($p<0.01$) that showed higher mean values and standard deviations. In Fig 4B, the absolute difference between metrics and methods is compared in both λ ranges. It is observed that this variability is higher for the lower range, as well as its dispersion. Highest dominant frequency differences were significant only for the comparative between T0 and T2. Nevertheless, rotors per second showed statistical difference for all the comparatives ($p<0.01$), being the absolute difference between TR orders higher for the lower regularization parameters.

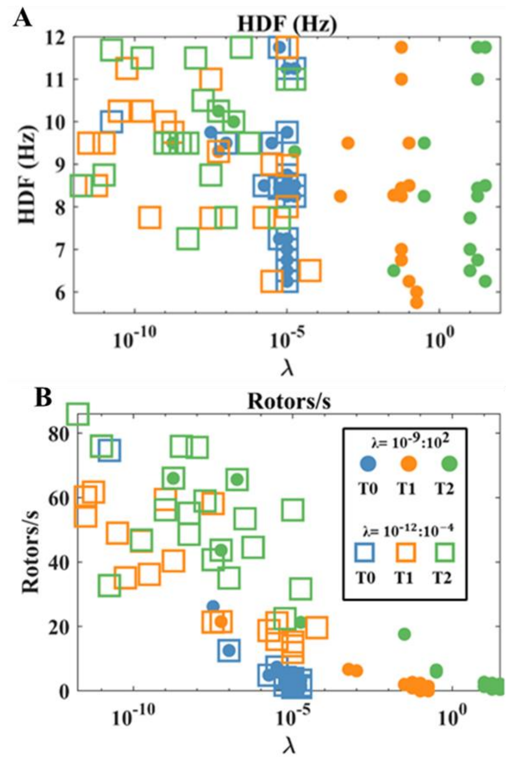

Figure 3. AF-related metrics obtained with the three TR orders versus the selected regularization parameters (λ) for a high range (dots) and low range (squares) of λ. A: Highest dominant frequency; B: rotors per second.

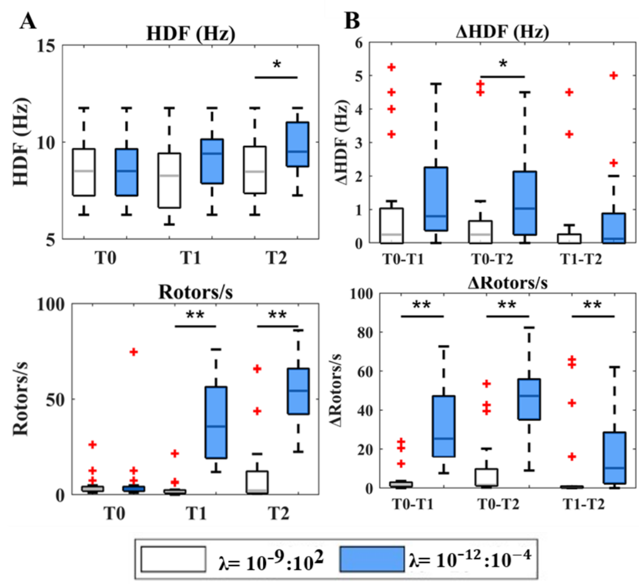

Figure 4. A. Comparison of ECGI metrics for each TR order for a high range of λ (white) and a low range of λ (blue). B. Comparison of the difference of ECGI derived metrics between TR orders and λ ranges.

4. Discussion

In this study we evaluated the relevance of the proper range selection for the calculation of the regularization parameter of the inverse problem in AF signals. Optimal regularization parameters do cluster in quite narrow ranges that are different for zero, first and second order Tikhonov regularization. Selection of a smaller regularization parameter than the optimal one does result in an increased AF complexity that may not be related to the underlying complexity.

Tikhonov regularization methods, mostly zero-order, have been preferred in the literature for ECGI resolution during AF [4], which is consistent with our study, being T0, the most consistent method in choosing the optimal λ between ranges. First and second-order solutions, showed larger λ variability, but results were more consistent for the highest λ range. Although the epicardial signal reconstruction could be oversmoothed for higher λs, T1 and T2 presented fewer differences between methods and ECGI derived metrics, suggesting a more realistic reconstruction.

ECGI obtained maps with lower λ ranges presented higher HDF and rotors per second numbers, when compared with higher λ values. Higher complexity of the resulting metrics can be produced either for a realistic ECGI approximation of a complex atria substrate or by amplification of noise and small changes in the signal due to the small regularization parameter, which is less likely due to the found errors between TR orders and the reconstructed DF and SP maps. Comparing the errors in the metrics from different orders and λ ranges could improve the quality of ECGI by choosing the λ that minimizes the errors between methods, to avoid smooth and noisy solutions. Therefore, we propose that the range of lambda values to be searched for either zero, one or second order Tikhonov regularization should be from 10^{-7} to 10^{2}.

5. Conclusions

ECGI derived metrics reflect higher complexity of AF substrate when sub-optimal values of the regularization parameter are selected for Tikhonov regularization and L-curve optimization.

A trade-off between regularization parameter range and type of inverse problem method remains critical in obtaining a good ECGI reconstruction, being the optimal ranges for λ search different among T0, T1 and T2.

Acknowledgments

This work was supported by: Instituto de Salud Carlos III, and Ministerio de Ciencia, Innovación y Universidades (supported by FEDER Fondo Europeo de Desarrollo Regional PI17/01106 and RYC2018-024346B-750), EIT Health (Activity code 19600, EIT Health is supported by EIT, a body of the European Union), Generalitat Valenciana Grants (ACIF/2020/265) and PersonalizeAF project, which received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 860974. This publication reflects only the author's view and the Agency is not responsible for any use that maybe made of the information it contains.

References

[1]M. Rodrigo et al., "Non-Invasive Assessment of Complexity of Atrial Fibrillation: Correlation with Contact Mapping and Impact of Ablation", *Circ. Arrhythmia Electrophysiol.*, vol. 13, No. 3, Feb. 2020.

[2]J. Salinet et al., "Electrocardiographic Imaging for Atrial Fibrillation: a Perspective from Computer Models and Animal Experiments to Clinical Value", *Front. Physiol.*, 2021. (Accepted for publication).

[3]C. Hansen, "Analysis of Discrete Ill-Posed Problems," *Soc. Ind. Appl. Math.*, vol. 34, no. 4, pp. 561–580, Dec. 1992.

[4]C. Figuera et al., "Regularization Techniques for ECG Imaging During Atrial Fibrillation: A Computational Study, ", *Front. Physiol.*, vol. 7, no. Oct, 2016.

[5]F. Castells, C. Mora, J. J. Rieta, D. Moratal-Pérez, and J. Millet, "Estimation of Atrial Fibrillatory Wave from Single-Lead Atrial Fibrillation Electrocardiograms Using Principal Component Analysis Concepts", *Med. Biol. Eng. Comput.*, vol. 43, no. 5, pp. 557–560, Oct. 2005.

[6]P. C. Hansen and D. P. O'Leary, "The Use of the L-Curve in the Regularization of Discrete Ill-Posed Problems", *SIAM J. Sci. Comput.*, vol. 14, no. 6, pp. 1487–1503, Nov. 1993.

[7]M. Rodrigo et al., "Highest Dominant Frequency and Rotor Postions are Robust Markers of Driver Location During Noninvasive Mapping of Atrial Fibrillation: A Computational Study", *Heart Rhythm*, vol. 14, no. 8, pp. 1224-1233, Aug. 2017.

[8] C. Fambuena et al., ''An Evaluation on the Potential Clinical Outcome Prediction of Rotor Detection in Non-Invasive Phase Maps',' *Comput. Cardiol. Conf.*, 2021. (Unpublished).

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