

Non-Invasive Supraventricular Tachyarrhythmia Mechanism Classification and Location based on Body Surface and Electrocardiographic Imaging biomarkers

Italo Sandoval¹, Gabriel Costa¹, Camila Restivo¹, Victor Marques², Miguel Rodrigo³, Maria de la Salud Guillem Sánchez⁴, John Sims¹, Joao Salinet¹

¹ HEartLab, Federal University of ABC, São Bernardo do Campo, São Paulo, Brazil

² Maastricht University, Maastricht, Netherlands

³ Universitat de València, València, Spain

⁴ Universitat Politècnica de València, València, Spain

Abstract

Catheter ablation presents the higher success rate in the treatment of supraventricular tachyarrhythmias. The correct location of the arrhythmogenesis and related circuits to be target is the current clinic challenge. In this study is presented a methodology based in non-invasive maps to improve diagnostic of type and mechanism location. This work ranked 40 biomarkers extracted from Phase, Dominant Frequency, Organization Index, Local Activation Time and Optical Flow maps. These maps were obtained from 22 distinct realistic arrhythmic models (AT: 8, AFL: 4 and AF: 10), on both torso and reconstructed epicardium signals (ECGi). The pipeline ranked the biomarker's contribution in the classification of the maintaining arrhythmic mechanism and its location, basing on a combination of three different indexes: Analysis of variation (ANOVA), Kendall tau and Lasso. On the torso maps, the mechanism classification obtained an overall accuracy of 0.864, with the location accuracy of 0.818, and on epicardium reconstructed maps (i.e ECGi) the accuracy is yet to be calculated. The novel Optical Flow (along with phase and frequency) related biomarkers showed a great contribution in the location and classification of the arrhythmias' mechanisms. Non-invasive maps allow classification and mechanism spatial location.

1. Introduction

The heart is a vital organ that functions as an electrical-mechanical pump, responsible for transporting essential substances to different tissues and organs in the body. Any impairment in the heart's ability to effectively pump blood can lead to dysfunction, irreversible organ damage, and even death. Factors such as genetics, aging, poor diet, a sedentary lifestyle, and excessive alcohol consumption can impact heart health and contribute to heart diseases,

including cardiac arrhythmias [1].

The three most common cardiac arrhythmias in clinical practice are atrial tachycardia (AT), atrial flutter (AFL), along with AF [2]. These arrhythmias have different underlying mechanisms: AT is characterized by localized cells firing radially in a regular high-frequency rhythm, known as an ectopic focus [2]; AFL involves a regular high-frequency rhythm propagating as a macroreentry, typically around the valves or fibrotic regions [3]; AF is characterized by uncoordinated high-frequency atrial activations, resulting in the deterioration of mechanical function and the presence of functional rotors [4]. AF is the most common cardiac arrhythmia encountered in clinical practice, affecting approximately 2% of the adult population worldwide [4]. The compromised atrial systolic and diastolic functions in AF lead to a decrease in cardiac output, increasing the risk of thromboembolic events, heart failure, and sudden arrhythmic death [5].

Currently, radiofrequency catheter ablation is used as a treatment for these three arrhythmias, and it has been shown to be safe and effective. Accurate localization of the driving mechanism is crucial for the success of the procedure, and it is typically achieved through invasive electrical mapping of the atrium [6], which increases the duration of the surgical procedure. We hypothesize that non-invasive classification and localization of cardiac arrhythmias can be achieved using biomarkers extracted using high-density body surface and ECGi Phase, Dominant Frequency, Organization Index, Local Activation Time and Optical Flow maps. If successful, these methods could serve as valuable tools to assist clinicians in planning therapeutic strategies before invasive procedures.

2. Methods

In this work, realistic in silico models were used. The models simulated the electrical behavior of the left atrium

(LA) and right atrium (RA) in the three arrhythmias. The models consist of 284,578 nodes and 1,353,783 tetrahedrons and a total of 22 simulations were conducted, each representing one of the three distinct arrhythmia mechanisms: AT (with 8 simulations), driven by an ectopic focus; AFL (with 4 simulations), driven by a macro-reentrant circuit; and AF (with 10 simulations), driven by functional rotors [7]. The system of differential equations in the atrial cell model was solved using Runge-Kutta integration.

From all simulations, the atrial geometry is simplified to a uniform triangular mesh with 2048 nodes, and the corresponding atrial electrograms (AEGM, $f_s = 500$) is obtained. The AEGM is used in a forward solution to simulate the BSPM signals referring to a torso mesh with 771 nodes, then white Gaussian noise was added to the BSPM signals with a signal-to-noise ratio (SNR) of 30, and a reduced number of leads (567) was selected [3, 7]. The BSPM signals are then used to reconstruct the AEGM (rAEGM) by applying the inverse solution and Tikhonov regularization method, such as in the ECGi technique.

In order to obtain a bi-dimensional isopotential map from the three-dimensional signals, some additional steps were made. For the BSPM the coordinates of the nodes in the torso geometry underwent cylindrical projection and were then interpolated onto a 30 by 65 grid using cubic splines. For the atria geometry a software was developed, where for each node, a 35x35 grid is created with the interpolated signals from the node's neighbors. Specifically, for each node and its neighbors, a partial mesh is created and projected onto a plane. An optimization based on the original mesh is performed to reduce the spatial deformation caused by the projection. The signals from the projected partial mesh are then interpolated into the 35x35 grid using cubic splines, generating a bi-dimensional isopotential map for each of the 2048 nodes. This projection is here called vertex-wise projection. A variation of the vertex-wise projection was made: a four view projection. This projection follows the same steps than the previous one, but selecting only four vertices, referring to the LA and the RA, and the anterior and posterior portion of the atria, the selecting a bigger neighborhood around the vertices, and interpolating in a 50x50 grid.

2.1. Biomarker Computation

44 biomarkers were extracted from different kind of maps, computed over the BSPM and rAEGM potentials from realistic in silico models, with a signal-to-noise ratio of 30. For the later one, the four-view projection was used. After, the biomarkers were ranked based on their contribution in the classification of the arrhythmias, and the best biomarkers were used in a classification model.

DF Maps: DF maps were generated using a previously

validated method based on continuous wavelet transforms [8]. Five biomarkers were calculated from the DF maps: (i) DF mean (DF- M), (ii) median (DF- Mdn), (iii) mode (DF- Mo), (iv) highest DF (HDF) and (v) inter-quartile range (IQR). Regions around the HDF value (HDFr) were identified where $|DF - HDF| \leq 1Hz$. From HDFrs, seven biomarkers were computed: (i) number of HDFrs (DF- Nr), (ii) average size (DF- Ms), (iii) standard deviation (SD, DF- SDs), (iv) percentage of the total area occupied by HDFr (DF- Ar), (v) mean (DF- MOI), (vi) standard deviation (DF- $SDOI$), and (vii) inter-quartile range (DF-IQROI) of the organization index (OI). To exclude DFs related to harmonic components or noise, which could affect HDF estimations and related biomarkers, DF values above the 90th percentile were excluded.

Phase Maps: To obtain the phase maps, a narrow 4th order Butterworth band-pass filter with a range of 2 Hz centered around the HDF value was applied to the BSPM signals. The filtered signals were then subjected to the Hilbert transform. The phase angle was computed by taking the arc-tangent of the division between the Hilbert transformed signal and the original signal [3]. The signals were downsampled to 128 Hz to reduce processing time.

Rotational activity was detected by identifying phase singularity points (SPs), which were defined as points where all phases converge. A Canny edge detector was employed to detect phase discontinuities in the phase maps, indicating shifts from $+\pi$ to $-\pi$. The endpoints of these edges were considered potential SPs. The analysis of these points involved examining the phase values of neighboring points within rings of different radii (2 to 10 cm). The phase values were obtained through interpolation based on the eight closest pixel values. Criteria were developed to classify a point as an SP, including the requirement that the phase progression on at least two rings should satisfy the following conditions: (i) the phase should progress by a minimum range of π , (ii) the progression should be ordered in at least 60% of its length, and (iii) there should be no phase discontinuities larger than π .

2.1.1. Spatiotemporal Analysis of Rotors

The distribution of SPs in space and time was analyzed based on filament maps and heatmaps (HM), calculated using a 2D histogram of SPs in the filaments over time [8]. Subsequently, eight biomarkers were determined for the filaments: (i) mean duration (Ph- Md); (ii) standard deviation of duration (Ph- SDd); (iii) mean frequency of rotation around SPs in the filaments (Ph- Mf); (iv) standard deviation of frequency (Ph- SDf); (v) average direction of rotation (+1 for clockwise and -1 for counterclockwise, Ph- MDR); (vi) filament rate over time (Ph- FIR); (vii) mean spatial displacement (Ph- MFD); and (viii) standard

deviation of displacement (Ph-*SDFD*), defined as the average displacement in each sample, calculated using the Euclidean distance between subsequent frames.

From the HM, 11 biomarkers were obtained: (i) number of regions (Ph-*Nr*); (ii) mean region size (Ph-*Mrs*); and (iii) standard deviation of region sizes (Ph-*SDrs*). The area of each region was determined as A , and the percentage of SPs in each region (pSP) was calculated. From these, the following biomarkers were obtained: (iv) mean percentage of SPs in relation to area (Ph-*MSPA*); (v) standard deviation of this percentage (Ph-*SDSPA*); (vi) number of detected SPs over time (Ph-*SPS*); (vii) percentage of SPs in each of the four subdivisions of the HM for mechanism localization; (viii) percentage of area occupied by regions (Ph-*HMrA*). Additionally, individual heatmaps were generated for each filament (HMi), and the following biomarkers were calculated: (ix) mean region size (Ph-*HMiS*); (x) mean SP density (Ph-*HMiD*); and (xi) mean area of the bounding box around each region (Ph-*HMiB*).

Optical Flow: Farneback Optical flow [9], available in the OpenCV library (v.4.5.4) for Python 3, were applied on three different maps (phase, isochronous and isopotential maps), being applied to each pair of consecutive time samples, obtaining the MVF. MVF was normalized and its temporal average calculated (nMVF). After, curl and divergent potential maps were obtained by: (i) Approximating the partial derivatives in x and y directions. Sobel filters of size of 11×11 pixels were applied to each component of the nMVF, respectively $nMVF_x$ and $nMVF_y$, providing the estimates of $\frac{\partial(nMVF_x)}{\partial x}$, $\frac{\partial(nMVF_y)}{\partial x}$, $\frac{\partial(nMVF_x)}{\partial y}$, $\frac{\partial(nMVF_y)}{\partial y}$. (ii) Next, curl and divergent maps were obtained using Equations below.

$$\text{Div. Map} = \frac{\partial(nMVF_x)}{\partial x} + \frac{\partial(nMVF_y)}{\partial y} \quad (1)$$

$$\text{Curl Map} = \frac{\partial(nMVF_y)}{\partial x} - \frac{\partial(nMVF_x)}{\partial y} \quad (2)$$

Then, for the curl maps, the average, the range and the maximum absolute value was calculated, and for the divergent maps, the average and the maximum value was calculated, totaling 5 biomarkers for each of the phase, isochronous and isopotential maps: average phase curl (OF-*PhCM*), range of phase curl (OF-*PhCR*), maximum absolute of phase curl (OF-*PhCMax*), average phase divergent (OF-*PhDM*), maximum phase divergent (OF-*PhDMax*), average isochronous curl (OF-*IsCrCM*), range of isochronous curl (OF-*IsCrCR*), maximum absolute of isochronous curl (OF-*IsCrCMax*), average of isochronous divergent (OF-*IsCrDM*), maximum of isochronous divergent (OF-*IsCrDMax*), average of isopotential curl (OF-*IsCrCM*), range of isopotential curl (OF-*IsPCR*), maximum absolute of isopotential curl (OF-*IsPCMax*), average

of isopotential divergent (OF-*IsPDM*), maximum of isopotential divergent (OF-*IsPDMMax*).

2.2. Biomarker Ranking and Classification

After computing the 44 biomarkers described above, biomarker ranking was performed using three different methods, and the scores were combined using the quadratic sum of the scores, normalized by the greatest value among the biomarkers. The ranking aimed to find the best biomarkers to discriminate: (i) Each arrhythmia from the remaining; (ii) each pair of arrhythmias; and (iii) which atrium the mechanism is located (LA or RA).

The first ranking method used was based on the analysis of variance (ANOVA) F-score, which compares the ratio between the variance of the mean for each class and the variance of the entire dataset. Higher F-scores indicate better classification performance. The second method was based on Kendall's τ coefficient, which is a suitable correlation coefficient for both quantitative and qualitative variables. The third method used Lasso's (least absolute shrinkage and selection operator) regularization for logistic regression.

After biomarker ranking, the top two biomarkers for each arrhythmia mechanism classification (MC) and the top two biomarkers for mechanism localization (ML) were selected, excluding redundant biomarkers based on their Pearson correlation coefficient. The number of selected biomarkers was chosen to avoid overfitting, considering the size of the data-set. Logistic regression algorithms from Scikit-Learn were used as classifiers, and the training and testing sets were divided using the leave-one-out method.

3. Results and Discussion

The selected biomarker for each classification task and the achieved accuracy while using it is showed in the Table 3. By combining all classifiers, the MC obtained an accuracy of 0.7272 for the BSPM analysis and 0.8636 for the ECGi analysis. Based on the ranking and the selected features, it could be seen that the novel OF biomarkers can contribute to the characterization of the three of the most common kinds of atrial arrhythmia, specially in the analysis of BSPM, been the 7 top biomarkers when summing all ranking scores. Also, the accuracy results suggest a benefit from the ECGi to the characterization of arrhythmias, however it depends on a longer and more computationally costly process.

4. Conclusions

Non-invasive maps, such as phase, dominant frequency and optical flow maps, allows extraction of biomarkers that

BSPM			
Task	Biomarker 1	Biomarker 2	Accuracy
AF/others	Ph- <i>SDSPA</i>	Ph- <i>Nr</i>	0.7727
AFL/others	DF- <i>M</i>	Ph- <i>Md</i>	0.864
AT/others	OF- <i>IPDMa</i>	DF- <i>Ms</i>	0.773
AF/AFL	DF- <i>M</i>	Ph- <i>Md</i>	0.929
AF/AT	Ph- <i>Nr</i>	OF- <i>PhDMa</i>	0.722
AFL/AT	Ph- <i>HMiD</i>	DF- <i>M</i>	0.917
LA/RA	DF- <i>Ms</i>	Ph- <i>Nr</i>	0.727

ECGi			
Task	Biomarker 1	Biomarker 2	Accuracy
AF/others	Ph- <i>SDf</i>	OF- <i>ICCMa</i>	0.6818
AFL/others	Ph- <i>HMiD</i>	DF- <i>Mo</i>	0.909
AT/others	Ph- <i>FIR</i>	OF- <i>IPCR</i>	0.818
AF/AFL	DF- <i>IQROI</i>	DF- <i>Mo</i>	0.929
AF/AT	DF- <i>IQROI</i>	OF- <i>ICCMa</i>	0.889
AFL/AT	DF- <i>IQROI</i>	OF- <i>IPCMa</i>	1.000
LA/RA	Ph- <i>HMiD</i>	Ph- <i>MFD</i>	0.777

can be used in classifiers that discriminate atrial arrhythmias and estimate the location of its mechanism. Also, the analysis of the spatial dynamic of the signals with optical flow applied to reconstructed atrial signals, obtained with ECGi, showed a great contribution to the location of arrhythmic mechanisms, such as functional rotors and ectopic foci, giving useful information prior to the invasive intervention. Analysis with BSPM and ECGi seems to have a great potential in aiding the treatment and diagnosis of atrial arrhythmias.

Acknowledgments

This study is supported by grant no. #2018/25606-2, São Paulo Research foundation (FAPESP) and CNPq INCT INTERAS. call 58/2022. J.G. Siles-Paredes is supported by grant no. #2020/03601-9, FAPESP. I. Sandoval is supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES).

References

- [1] Tortora GJ, Derrickson B. Chapter 20 - The cardiovascular system: The heart. In: B Roesch, C Stone, editors. Principles of anatomy and physiology. 11th edition. John Wiley & Sons, Inc, 2006; .
- [2] Page R, Joglar J, Caldwell M, Calkins H, Conti J, Deal B, Estes NAM, Field M, Goldberger Z, Hammill S, Indik J, Lindsay B, Olshansky B, Russo A, Shen WK, Tracy C, Al-Khatib S. 2015 acc/aha/hrs guideline for the management of adult patients with supraventricular tachycardia: a report of the american college of cardiology/american heart association task force on clinical practice guidelines and the heart

rhythm society. Journal of the American College of Cardiology 2016;67(13):e27–e115.

- [3] Marques VG, Rodrigo M, Guillem MS, et al. Characterization of atrial arrhythmias in body surface potential mapping: A computational study. Comput Biol Med 2020; 127(103904).
- [4] Hindricks G, Potpara T, Dagres N, Arbelo E, Bax J, Blomstrom-Lundqvist C, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the european association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2021;42.
- [5] Naser N, Kulic M, Dilic M, Dzibur A, Durak A, Esad, et al. The cumulative incidence of stroke, myocardial infarction, heart failure and sudden cardiac death in patients with atrial fibrillation. Med Arch 2017;71. ISSN 0350-199X.
- [6] Issa Z, Miller J, Zipes D. Clinical Arrhythmology and Electrophysiology: A Companion to Braunwald's Heart Disease. Elsevier Health Sciences, 2018.
- [7] Rodrigo M, Climent AM, Liberos A, Fernández-Avilés F, Berenfeld O, Atienza F, Guillem MS. Technical considerations on phase mapping for identification of atrial reentrant activity in direct-and inverse-computed electrograms. Circulation Arrhythmia and Electrophysiology 2017a;10(9).
- [8] Marques VG, Rodrigo M, Guillem M, Salinet J. Characterization of atrial arrhythmias in body surface potential mapping: A computational study. Computers in Biology and Medicine 2020;127.
- [9] Farnebäck G. Two-frame motion estimation based on polynomial expansion. In Bigun J, Gustavsson T (eds.), Image Analysis. Berlin, Heidelberg: Springer Berlin Heidelberg. ISBN 978-3-540-45103-7, 2003; 363–370.

Address for correspondence:

Italo Sandoval

HEartLab - Biomedical Engineering - CECS

FEderal University of ABC - UFABC

Street: Av. Anchieta, São Bernardo do Campo - SP, Brazil

E-mail: italo.sandoval@ufabc.edu.br