

Efficient Generation of Cardiac Digital Twins for Personalized Atrial Fibrillation Treatment Using Non-Invasive ECGI Data

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Abstract

Atrial Fibrillation (AF) is a prevalent cardiac arrhythmia. AF poses significant challenges to patient well-being and longevity as current treatments are not effective and personalized as desired. While cardiac modelling has advanced considerably, the translation of these models into personalized therapies remains challenging. This paper proposes a framework leveraging Digital Twins (DTs) based on non-invasive electrocardiographic imaging (ECGI) data to enhance the planning and efficacy of ablation procedures.

The framework was validated against benchmark simulations across diverse AF scenarios utilizing a cellular automata model. DTs are personalized using ECGI-derived metrics, as Dominant Frequency (DF) maps, to modify tissue properties and simulate arrhythmia dynamics. The DF comparison between benchmark simulations and DTs shows a MAE of 1.15 Hz. Additionally, the ablation strategy effective in stopping arrhythmia in benchmark simulations also works in DTs.

The framework efficiently generates DTs that replicate benchmark dynamics using non-invasive data, with DF maps playing a crucial role in DT personalization. With its reliance on non-invasive data and efficient computational methods, the framework shows potential for real-time clinical use, assisting personalized AF ablation strategies.

In recent decades, significant advancements have been made in cardiac modeling, leading to the proposal of various models to elucidate cardiac dynamics. This progress has deepened our comprehension of cardiac arrhythmias and their treatment modalities. Over the past years, the emergence of cardiac Digital Twins (DTs) has enabled the creation of virtual replicas of patients' hearts based on their individual data. These DTs hold promise for tailoring treatments to individual patients, potentially enhancing the efficacy of ablation therapies. However, existing frameworks described in the literature may be limited in the degree of personalization, rely on invasive data, or necessitate prolonged simulation times, posing challenges for real-time clinical application for personalizing treatments on an individual patient basis[3].

Electrocardiographic imaging (ECGI) is a non-invasive technique that allows to recover cardiac electrical activity from Body Surface Potential Mapping(BSPM)[4]. ECGI has shown to retain relevant information about the spectral and rotational activity of AF patients[5],[6].

This paper presents a framework to develop DTs based on non-invasive data ECGI to aid planning of ablation procedures. We validate the proposed framework against benchmark mathematical models comparing the original benchmark models against the final DTs. We will propagate the models to the torso, do ECGI and obtain the DT based on the ECGI solution. We evaluate our framework by comparing metrics derived from both models, and testing if the same type of ablation strategy can stop the arrhythmia in both scenarios.

1. Introduction

Atrial Fibrillation (AF) is the most common type of arrhythmia in the world. It demeans the quality of life and reduces the life expectancy of the patients. Moreover, current treatments demand high budgets and are not as effective and personalized as desired[1]. Success rates of catheter ablation therapy including several procedures are in the range 50%-80%[2].

2. Methods

2.1. Benchmark cardiac simulations

AF simulations were obtained for benchmarking over a volumetric mesh with 59,208 nodes using a cellular automata (CA) model [7]. This benchmark set included

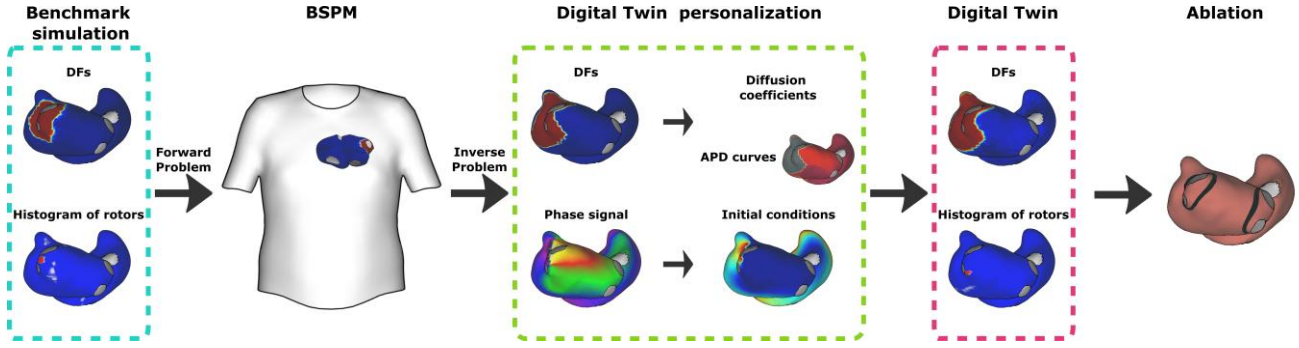


Figure 1. The proposed personalization framework. The benchmark simulation is propagated to the torso and added gaussian noise. Then the inverse problem is computed to recover the heart signal. From these signals, derivatives as Dominant Frequencies (DFs) and the phase signal transform are obtained to personalize the diffusion coefficients, APD curves and establish the initial conditions of the Digital Twin (DT). Then, the DT is obtained, and DFs and histogram of rotors are compared with the benchmark simulation. Lastly, the ablation strategy that stopped that arrhythmia in the benchmark model is also tried in the DT.

simulations where diverse regions of the tissue were modified to have shorter Action Potential Duration (APD) and lower diffusion coefficients which help to sustain the arrhythmias. Moreover, an eikonal model [8] with rotors within those areas was used for the initialization of the simulation. Each basal AF simulation lasted over 10 seconds.

Over the simulations, Dominant Frequencies (DFs) using P-welch algorithm were measured[5]. Also, histograms of rotational activity lasting greater than one rotation[6] were computed.

For each simulation, the ablation strategy which stopped the AF was found by proving diverse classical ablation therapies till one finalised the arrhythmia. For this, the ablation was introduced in the model by disconnecting the nodes related to the ablation and then the simulation was continued for 5 more seconds.

Electrograms (EGMs) were computed at the surface of heart using a shell of 4.000 nodes. The EGMs were then propagated to a torso with 678 nodes solving the forward problem using the Boundary Element Method (BEM) [9]. Lastly, gaussian noise with a signal-to-noise ratio of 10 dB was added to the surface signal.

2.2 Digital Twin personalization framework

The personalization framework to obtain the DT consisted of the following stages: ECGI calculation, DT personalization, DT simulation and evaluation. The same CA mathematical model used to obtain the benchmark simulations was used for the DT ones.

For the ECGI calculation, the forward problem torso and heart shell were used. The inverse problem was solved using zero order Tikhonov regularization and L-curve optimization[9].

For the personalization of the DT, derivatives obtained from the ECGI solution were obtained. DF maps were computed in the same way as for the benchmark

simulations. Those maps were used to determine the APD desired in the model. We based this on the inversely proportional relationship between the DF and the basic cycle length of activation. The basic cycle length consists of the sum of two terms: the APD and the diastolic interval (DI). Thus, high DF shall be related with short APD. The APDs in the used models are determined by APD curves. These curves are defined in the following way:

$$APD = A_{APD} * (1 - B_{APD} * e^{-\tau_{APD} * DI})$$

We changed the A_{APD} which determines the plateau of the curve; thus, the cell could activate at the rate seen in the DF maps. Moreover, DF maps were also used to modify the diffusion coefficient of the tissue to ensure that the tissue could activate at the expected rate.

For the model initialization, a phase Hilbert transform of ECGI signal was used. To choose the time instant, we computed the histogram of rotors of the ECGI signal. We chose a time instant where a rotor was found the nearby the centroid of the high DF area of the ECGI solution. Then phase signal of that time instant was converted into voltage for the model initialization.

Once we have the APD curves, the diffusion coefficients, and the initial conditions of the models over the heart shell, these are each interpolated to the complete heart volume. Then, the DT simulation was run for 10 seconds duration as for the original benchmark simulations.

2.3 Digital Twin evaluation

To evaluate the DTs, DF maps and histogram of rotor. Regarding the DF maps, the correlation coefficient (CC), mean absolute error (MAE) and root-mean-square error (RMSE) were calculated. The CC was also measured for the High DF regions (HDF). HDF was defined as the areas with a DF above the 85-percentile interval.

Regarding the histogram of rotors, the area over the 99.9 percentile of the map was obtained. Then, the Euclidian distance between the centroid of the high rotational area of

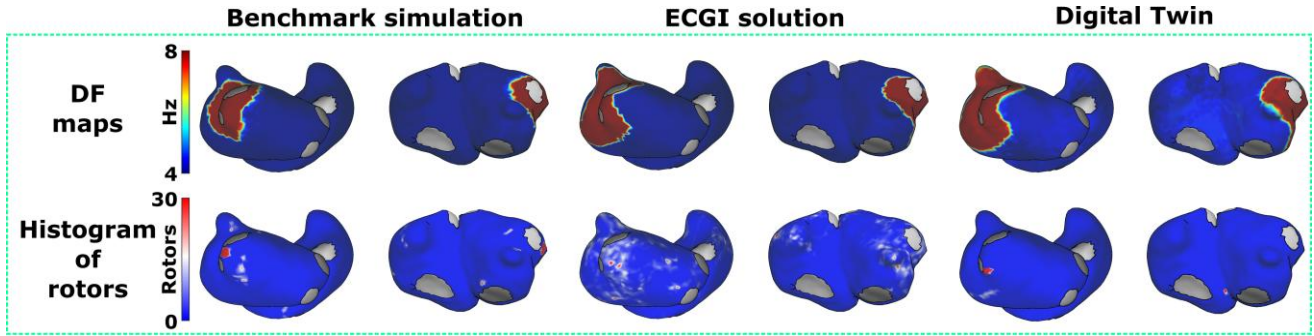


Figure 2. Summary of the results obtained for the first case. The Dominant Frequencies (DFs) maps and the histogram of rotors are illustrated for the benchmark simulation, the ECGI solution and the Digital Twin (DT).

the benchmark simulation and the one of the DT was found.

Lastly, the same ablation strategy which stopped the arrhythmia in the original benchmark model was introduced in the DT and the outcome was simulated. After five seconds, the successfulness of the ablation was checked.

3. Results

3.1 Benchmark cardiac simulations

The framework was evaluated through three benchmark simulations. For the first set-up, the region driving AF was in the left pulmonary veins and AF terminated after pulmonary vein isolation (PVI). For the second set-up, the activity driving AF was on the posterior wall and AF terminated after ablation of the roof + PVI. For the third set-up, the left atrial appendage (LAA) was the leading region and AF terminated after the ablation of LAA.

The simulations were run using a 38 CPU cores (Intel(R) Xeon(R) W-3375 CPU @ 2.50GHz). For a 10 seconds simulation, 15 seconds of computational time were required without the use of the GPU.

3.2 Digital Twin evaluation

For the first case which is shown in figure 2, the benchmark DFs and the DT ones had CC of 0.74, a MAE of 0.96 Hz and RMSE of 1.24 Hz. The HDFs presented a CC of 0.73. The Euclidian distance between the centroid of high rotational areas of the original simulation and the DT was 1.32 cm.

In the second case, the original DFs and the DT ones had CC of 0.75, a MAE of 1.08 Hz and RMSE of 1.36 Hz. The HDFs showed a CC of 0.67. The Euclidian distance between the centroid of the rotational areas was 2.31 cm.

The last case presented a CC between the DFs of 0.54, a MAE of 1.41 Hz and RMSE of 1.64 Hz. Regarding the HDFs regions, they had a CC of 0.62. The Euclidian distance between the centroid of the rotational areas was 2.14 cm.

In summary for the three cases, the DFs of the benchmark simulation and the DT had a mean CC of 0.68 (± 0.12), a mean MAE of 1.15 (± 0.23) Hz and a mean RMSE of 1.41 (± 0.21) Hz. The mean CC of the HDFs areas was 0.67 (± 0.06) and the mean distance between high rotational areas was 1.92 (± 0.53) cm.

In all set-ups, the ablation strategy which stopped the arrhythmia in the benchmark simulation also terminated the arrhythmia in the derived DT. Particularly, the impact of ablation in the first case is illustrated in Figure 3. After PVI ablation, the arrhythmia ceased both in the benchmark simulation and in the DT.

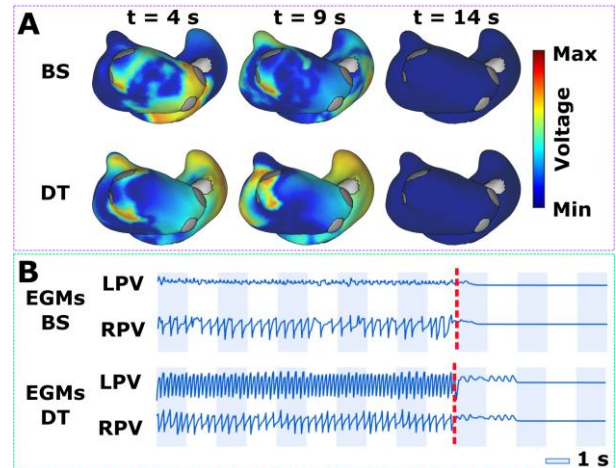


Figure 3. Summary of the propagation for the first case. In panel A, the voltage maps at 4, 9 and 14 seconds are illustrated for the benchmark simulation (BS) and the Digital Twin (DT). In panel B, two EGMs of the benchmark simulation and DT. The red line indicates the moment when the ablation was introduced. LPV: left pulmonary vein. RPV: right pulmonary vein.

4. Discussion

A framework for constructing DT based on ECGI data during AF was presented in this paper. For this a set of CA simulations were used as benchmark and propagated to the torso. Then inverse problem was solved, and metrics

derived from the ECGI solution were used for its personalization.

The presented framework utilises DF maps to modify the tissue properties. Our results showed that DF maps contain relevant information to obtain DTs with similar dynamics to the benchmark simulations. Further work can be done to expand the tuning of the A_{APD} to the rest of the parameters of the APD curve of the model. In the future, other ECGI measurable variables including conduction velocities or rotational activities can be incorporated into the framework to further expand the personalization.

Previous AF personalization frameworks either require invasive data or need long simulation times [3], [10]. Our framework only requires non-invasive data as the ECGI solution. Moreover, the used CA model allows us to obtain a 10 second simulation in just 15 seconds and without the need of a GPU.

Future efforts will focus on extending this framework to clinical applications with patients, facilitating real-time DT generation without invasive data. This advancement holds promise for tailoring ablation treatments to individual patients, enhancing treatment personalization.

5. Conclusions

The presented framework generates DT with similar dynamics to the benchmark simulations without the need of long simulation times or invasive data. This paves the way for obtaining DT during AF which can be used during real-time clinical practice to personalize the treatment of the individual patients.

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Conflict of Interests

AMC, MSG and IHR are co-founders and shareholders of Corify Care SL.

References

- [1] G. Hindricks *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): The task force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC,” *Eur Heart J*, vol. 42, no. 5, pp. 373–498, Feb. 2021.
- [2] N. Mujović, *et al.*, “Catheter ablation of atrial fibrillation: An overview for clinicians,” *Adv Ther*, vol. 34, no. 8, p. 1897, Aug. 2017.
- [3] J. Corral-Acero *et al.*, “The ‘digital twin’ to enable the vision of precision cardiology,” *Eur Heart J*, vol. 41, no. 48, pp. 4556–4564, Dec. 2020.
- [4] S. Tzeis *et al.*, “European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) expert consensus statement on catheter and surgical ablation of atrial fibrillation,” *Heart Rhythm*, vol. 0, no. 0, Apr. 2024.
- [5] M. Rodrigo *et al.*, “Highest dominant frequency and rotor positions 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.
- [6] C. Fambuena-Santos, *et al.*, “AF driver detection in pulmonary vein area by electrocardiographic imaging: Relation with a favorable outcome of pulmonary vein isolation,” *Front Physiol*, vol. 14, p. 1057700, Jan. 2023.
- [7] C. Herrero-Martin, *et al.*, “Tailoring process for the regional personalization of atrial fibrillation with a novel cardiac model,” *Comput Cardiol (2010)*, vol. 2022-September, 2022.
- [8] A. Herlin *et al.*, “Eikonal-based initiation of fibrillatory activity in thin-walled cardiac propagation models,” *Chaos*, vol. 21, no. 4, 2011.
- [9] M. Rodrigo *et al.*, “Solving inaccuracies in anatomical models for electrocardiographic inverse problem resolution by maximizing reconstruction quality,” *IEEE Trans Med Imaging*, vol. 37, no. 3, pp. 733–740, Mar. 2018.
- [10] L. Azzolin *et al.*, “AugmentA: Patient-specific augmented atrial model generation tool,” *Computerized Medical Imaging and Graphics*, vol. 108, p. 102265, Sep. 2023.

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