Relationship between Complex Fractionated Atrial Electrogram Patterns and Different Heart Substrate Configurations

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Abstract

Complex Fractionated Atrial Electrograms (CFAE) were identified as being symptomatic of reentrant activities. Signals recorded by an intracardiac catheter give an imprecise vision of the underlying phenomena that occur in the proarrhythmic substrate. In this study, phenomenological and ionic numerical models were used to simulate a small piece of the atrium substrate. The catheter measurement is also simulated numerically to take into account electrode particularities. Modifications were applied on the numerical substrate. Then stimulation scenarios were generated in the numerical substrate such as planar waves, stable or breaking spirals. Comparison between simulated and clinical electrograms showed common patterns.

1. Introduction

Atrial Fibrillation is initiated and perpetuated by complex phenomena. The atrium activity beyond the control of the sinoatrial node induces disorder in the whole heart rhythm. Several studies explore the underlying mechanisms of AF. Modifications in the atrial substrate such as irregularities, decreasing of the Action Potential Duration (APD) or hyper excitability can explain abnormal conduction paths and behavior. The pulmonary veins involvement is also predominant in AF genesis and has promoted curative techniques such as catheter radiofrequency ablation. The radiofrequency ablation procedure consists of an exploration of the atrium searching for AF symptomatic electrograms. These signals are the expression of the activity potentially responsible for rhythm disorder; this is the case of Complex Fractionated Atrial Electrograms (CFAE).

Complex Fractionated Atrial Electrograms are symptomatic of the mechanisms underlying the AF as activity reentries or ectopic foci. Among the wide variety of intracardiac signals, CFAE were identified as strongly associated with AF[1-3]. The ablation of CFAE sites has a major impact on cycle length increasing and leads to sinus rhythm restoration. Identification and classification of CFAE is a necessary step in the characterization of arrhythmical substrates.

Nowadays, cardiologists have learned to recognize CFAE visually. Therefore, this empirical recognition is not precise and the ablation process can be painful for the patients. Electrograms recorded from the catheter electrodes give the electrical potential of thousands of cells at a given time, yet averaging the substrate activity. Moreover the pressure exerted by the catheter tip on the substrate modifies the contact surface area.

To understand and quantify the arrhythmical substrate mechanisms from catheter electrograms, one has to mimic this kind of measurements. Numerical substrate simulations are based on mathematical models of cardiac cells. These models can reproduce qualitatively or quantitatively the behaviour of a cardiomyocyte.

This work presents two different numerical models used to simulate the behavior of an atrial cardiomyocyte. The models are applied to a 2D surface to create a numerical substrate. This substrate is then modified to induce disturbances similar to those encountered in arrhythmical substrate. Stimulations are then applied to observe interactions between the propagating waves and the substrate. Electrograms are acquired using a numerical model of the catheter tip. Resulting signals and patterns are then compared with clinical signals from ablation procedures.

2. Materials

2.1. Numerical cell models

2.1.1. Aliev Panfilov model

This behavioural model is a modification of the Fitzhugh Nagumo model of an excitable medium. It reproduces most of the basic properties of cardiac cells such as depolarization and repolarization phases of the action potential. The simplicity of this model [4] makes it possible to simulate large surface of cardiac tissue without using large computing resources. Two differential equations describe the fast and slow processes, presented here for monodomain 2D implementation:

$$\frac{\partial e}{\partial t} = \delta\nabla^2 e - k(e-a)(e-1) - er + I_{stim}, \qquad (1)$$

$$\frac{\partial r}{\partial t} = [\varepsilon + \frac{\mu_1 r}{\mu_2 + e}][-r - ke(e-b-1)].$$

Where e is the membrane potential, r is the conductance of the inward currents, these variables are dimensionless here. K, a, b, $\mu 1$, $\mu 2$ are parameters determined from experiments. With δ the diffusion parameter and ∇^2 the Laplacian operator.

I_{stim} is the potential used to initiate the first excitation.

Default values given in the Panfilov model description are:

ε=0.002; a=b=0.15; $\mu 1$=0.2; $\mu 2$= 0.3; k=8; δ=0.05

This model allows spiral waves and break up to be initiated easily.

2.1.2. Courtemanche Ramirez Nattel model

Only few mathematical ionic models describe the human atrial cell. The Courtemanche Ramirez Nattel (CRN) model provides 21 voltages variables, it uses 12 gating variables for the transmembrane currents, 3 gating variables for the Ca^{2+} release current from the SR; Ca^{2+} concentrations in the cytoplasm, NSR, and JSR; and intracellular Na^{+} and K^{+} concentrations. Details on variables calculations could be found in [5]. This model makes it possible to investigate the role of the currents involved in atrial fibrillation. For one cell, the transmembrane potential changes are driven by:

$$\frac{\partial V_m}{\partial t} = \frac{-(I_{ion} + I_{stim})}{C_m} \qquad (2)$$

Where I_{ion} is the total ionic current in pA per µF and I_{stim} is the stimulus current, C_m is the membrane capacitance in µF per unit area, V_m is the transmembrane potential in millivolts and t in milliseconds.

The model is implemented in 2D. The propagation of action potential is modeled assuming monodomain equation [6]:

$$C_m \frac{\partial V_m}{\partial t} = S_v^{-1}\nabla^2.\sigma.V_m + I_{st} - I_{ion} \qquad (3)$$

With Cm = 1(µF/cm2) representing the capacitance of the membrane, S_v = 0.24(µm^{-1}) the cell surface to volume ratio and σ = 0.5(mS/m) is the electrical conductivity tensor of atrial tissue.

2.2. Catheter representation

Thermocool WebsterBiosense catheter

The modelled catheter is a Thermocool irrigated tip ablation catheter from Biosense Webster (BiosenseWebster, Diamond Bar, CA, USA). It is used to burn areas of atrial substrate responsible for AF maintenance or triggering. The tip of the catheter is composed with four metallic electrodes used to acquire the atrial substrate fields of potentials. Most of the time, electrodes are used in pairs to acquire bipolar electrograms.

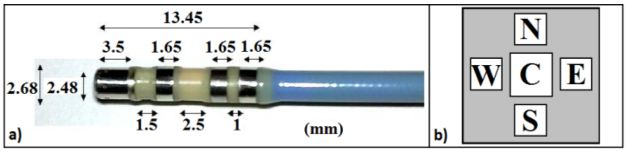

Figure 1. a) Thermocool catheter tip, electrodes size and distribution. b) Electrode disposal in the numerical substrate, representing 4 cardinal positions for a catheter acquisition. C for Center electrode represents the distal one.

The electrodes surfaces are 32.1mm² for the distal one, 13.9mm² for the 3 others. One chooses to keep one third of these values as average contact surface with the substrate. Chosen contact surface are thus 10.7mm² for the distal electrode, 4.63mm² for the 3 others. Taking into account average dimensions for a cardiomyocyte of 15µm by 100µm, about 7100 cells are covered by the distal electrode, the 3 others cover about 3000 cells each. These amounts are taking into account in further numerical simulations. Only the first electrode couple is modelled in this work.

The first derivative of the transmembrane potential was calculated [7] to retrieve extracellular potential.The extracellular potential calculated above gives a unipolar recording. The bipolar recording is the difference between two unipolar electrograms [8]. The potential recorded by an electrode is defined as the sum of potentials from cells covered by its contact surface.

In the following simulations, areas of the electrodes are modified to observe the impact on electrogram patterns as in [9]. The electrode contact surface is expressed as a ratio of the full electrode area; for instance the 1/3 ratio means that only one third of the surface touches the substrate. This approach aims to reproduce the conditions of acquisition of an intracardiac electrogram during AF radiofrequency ablation. The quality of the contact between the catheter and the substrate is not constant and plays a significant role in the appearance of signals.

3. Method

3.1. Simulation scenarios

3.1.1. Aliev Panfilov model simulations

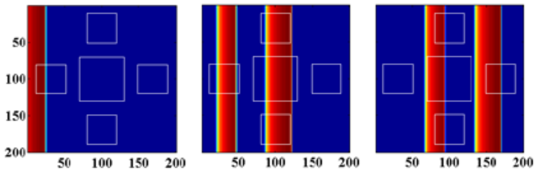

Figure 2. Planar wave simulation for Aliev Panfilov model, for times 5, 15, 35.

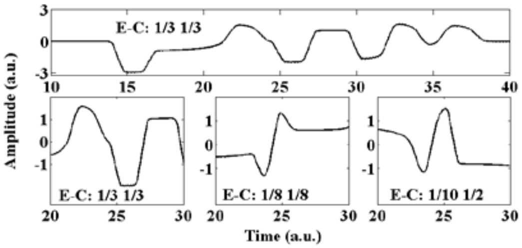

Figure 3. Bipolar electrogram from E-C electrodes with 1/3 surface ratio for the planar wave simulation. Following 3 patterns for the same activity period, recorded for 3 different electrode surface ratios.

In Fig. 3, the presented patterns illustrate the impact of the electrode surface on the signal observed. A reversal of polarity occurs between the 2nd and 3rd patterns with a 1/10 ratio for the East electrode and a 1/2 ratio for the Center one.

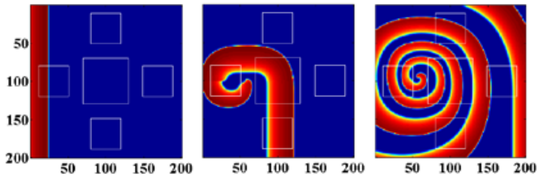

Figure 4. Spiral wave simulation for AlievPanfilov model, for times 5, 25, 45.

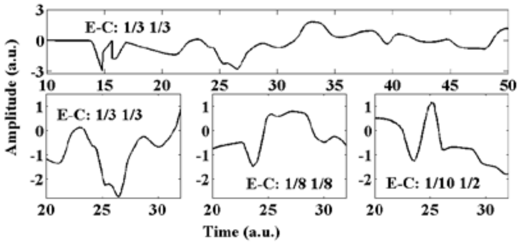

Figure 5. Bipolar electrogram from the spiral activity. E-C electrodes are used with 3 different ratios.

In Fig. 5, the 1/3 ratio yields a negative fragmented potential that becomes a positive quasi plateau using 1/8 ratio. The last pattern is comparable to that of the planar wave simulation for the same ratio (see Fig. 3).

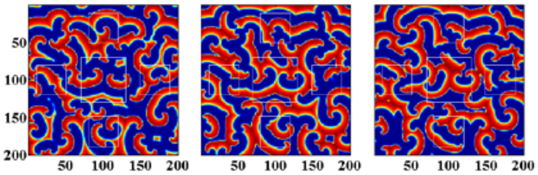

Figure 6. Breaking waves simulation for AlievPanfilov model. For times 5, 15, 35.

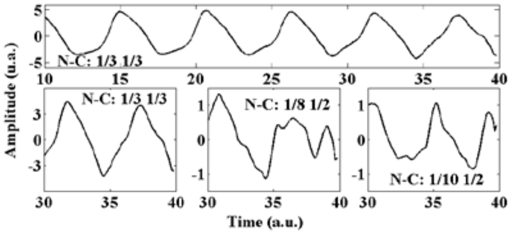

Figure 7. Bipolar electrogram from the breaking waves simulation. Recorded with N-C electrodes.

In Fig. 7, the electrogram appears to be quasi-regular. Observed regularity fades for the lasts patterns where electrodes have each a different contact ratio. It shows that synchronized wavelength activity could lead to wrongphenomenon identification.

3.1.2. CRN model simulations

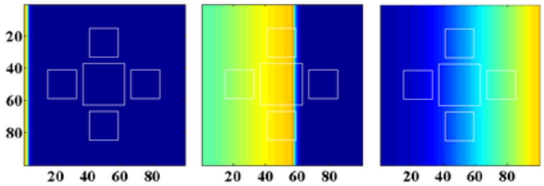

Figure 8. Planar wave simulation for CRN model, for times 12, 100, 200 ms.

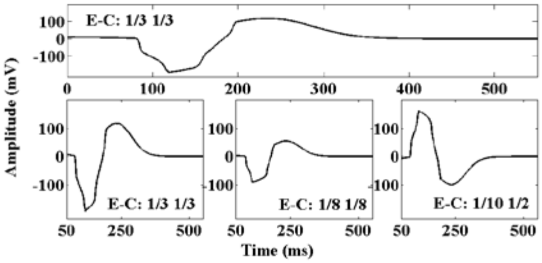

Figure 9. Bipolar electrogram for CRN planar wave simulation. Recorded with E-C electrodes, 1/3 surface ratio. Following patterns show the same activity recorded for 3 different electrode surface ratios.

In this simulation, the ratio hardly alters the observed patterns, only a polarity reversal appears in the last pattern (see Fig. 9).

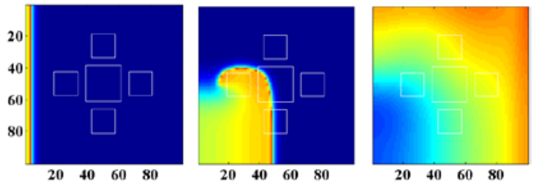

Figure 10. Pseudo-spiral wave simulation for CRN model, for times 15, 70, 150 ms.

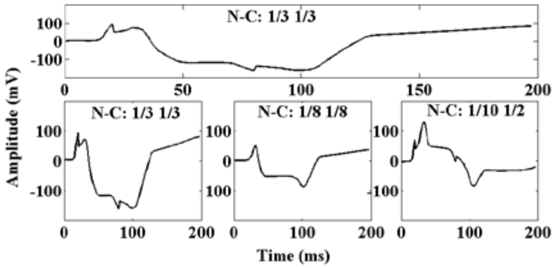

Figure 11. Bipolar electrogram from CRN pseudo-spiral wave simulation. Recorded with N-C electrodes, 1/3 surface ratio. Following 3 patterns is the same activity recorded for 3 different electrode surface ratios.

3.2. Clinical and simulated patterns comparison

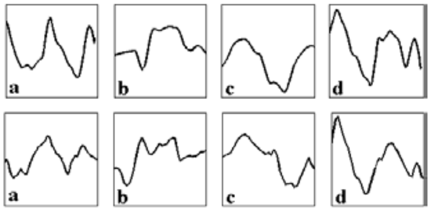

Figure 12. Patterns from simulated and clinical electrograms. The first line presents 4 patterns from the previous simulations, the 2nd line shows patterns isolated from clinical intra-atrial electrograms, recorded with a Thermocool catheter.

This small set of patterns shows similarities in the evolution of potentials for both simulated and clinical electrograms (see Fig. 12). However, simulated patterns come from known electrode contact ratios and clinical electrograms are recorded from a catheter whose contact quality is not determined.

4. Discussion

For a given activity in atrial substrate, the electrode contact surface modifies the perception of the actual potential. A bigger electrode tends to create larger electrograms with lower amplitude and smaller electrode contact surface increase the spatial resolution. Some electrograms may appear fractionated as a result of complex underlying activity or as a consequence of a specific electrode contact. This preliminary study tends to show that fractionated patterns mostly occur on complex activity scenarios such as spiral or breaking waves. Evaluate the quality of the catheter-substrate contact is a necessary step to improve AF ablation procedure.

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