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Preliminary Simulation Study of Atrial Fibrillation Treatment Procedure Based on A Detailed Human Atrial Model

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Abstract

Atrial Fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical practice. Surgical ablation is a therapeutic procedure that creates lines of conduction block to interrupt the maintenance of AF. However, surgical AF ablation procedures are largely based on empirical considerations, and may not be optimized. In this study, based on a detailed human atrial model with fiber orientation, eight AF surgical ablation procedures, including the clinical gold standard Cox-Maze III, incomplete Maze-III, mini-Maze, and 5 modified Maze-III procedures, were simulated and evaluated. The simulation results indicated the importance of the ablation line from the connection of superior and inferior vena cava to the atrial septum, and also showed that, in comparison with the clinical standard Maze-III procedure, our modified Maze-III procedures with fewer ablation lines achieved similar ablation effectiveness. In conclusion, this preliminary simulation study has demonstrated that current surgical AF ablation procedure is not optimal and a refinement could be suggested. It also suggests that computational heart modeling and simulation is an important tool to evaluate AF treatment strategies.

Keywords: Atrial Fibrillation; Heart modeling and simulation; Maze procedure

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice. When it occurs, the atrial rate can reach 400-600 beats per minute. The incidence rate of AF increases with age [1,2], affecting 0.5% of people aged over 50 years with an increase to 18% of people aged 80-90 years [3]. It is projected that by 2050, 2% of the general population will have AF, which poses an important public problem [4].

Different hypotheses, including the multiple-wavelet hypothesis [5], mother rotor hypothesis [6] and focal triggers and drivers from the Pulmonary Veins (PVs) [7] etc., have been proposed to understand the perpetuation of AF, however, the

exact mechanism has not yet been fully known. There are two main pharmacological strategies to treat patients with AF: rhythm control and rate control [8]. The beta-blockers and digoxin are often used to reduce heart rate. Pharmacological approaches have been attempted to convert AF to sinus rhythm, however, many of such drugs are not very effective to maintain sinus rhythm in long term and are associated with a significant number of side effects and complications. Surgical ablation is a therapeutic procedure that creates lines of conduction block to interrupt the maintenance of AF. Ablation techniques initially designed to cure AF have also been very useful to provide a better understanding on the pathophysiological mechanisms of AF initiation and maintenance. It has been widely accepted that Cox-Maze III [9] approach is now considered to be the clinical gold standard treatment approach.

Surgical AF ablation is largely based on empirical considerations, and usually evaluated in clinical studies or animal experiments. These ablation procedures may not be optimized, and therefore, need to be refined. With the development of heart modeling from the molecular level to the whole organ, and with the advantages of repeatability and reproducibility of using the modeling approach, AF has been computationally simulated, providing a better understanding on the mechanism of AF initiation and maintenance [10-12]. Computational heart modeling and simulation has also been used to assess the efficiency of AF treatment techniques.

Currently, there are several main international research groups actively engaged in AF ablation simulation work. They are Patrick Ruchat's group at Swiss Federal Institute of Technology, Switzerland, Matthias Reumann group at the University of Karlsruhe, Germany and Minki Hwang's group at Yonsei University, Republic of Korea. Ruchat's group established a single three-dimensional homogeneous atrial model based on the Magnetic Resonance Imaging (MRI) slices of human atrial tissue [13]. Minki Hwang's group developed a computational platform for virtual AF ablation. Their atrial model contained the main entrance of vessels, atrioventricular valves and diaphragm

walls, including the Tricuspid Valve (TV), Mitral Valve (MV), Inferior Vena Cava (IVC), Superior Vena Cava (SVC), PVs and the Fossa Ovalis (FO), has been used to simulate chronic AF ablation where they concluded the importance of performing both the left and right AF ablations [14]. However, Ruchat's model was quite simple without the atrial conduction system and other important parts of the atria, such as the Crista Terminalis (CT), Pectinate Muscle (PM) and Bachmann Bundle (BB), etc. Reumann's group established another three-dimensional anatomical model based on a virtual female cardiac dataset. Their model included a detailed structural anisotropy of the atria with the Sinoatrial Node (SAN), Atrioventricular Ring (AVR), Atrioventricular Node (AVN), Pulmonary Vein (PV), Left Atrial Appendage (LAA), CT, PM, BB and the thickness of the atrial wall [15]. Although Reumann's atrial model has included the elements that are essential to induce AF, it was only a cellular automata model without taking the atrial fiber orientation into account. Additionally, they only simulated the ablation of the left atrium, not the right atrium.

The aim of this study was to simulate and evaluate eight different surgical AF ablation procedures, including the clinical gold standard Cox-Maze III [9], incomplete Maze-III, Mini-Maze, and 5 modified Maze-III procedures proposed by us. The computational simulation was based on a detailed human atrial anatomic model with fiber orientation that has been previously published by us [16,17].

Materials and Methods

Three-dimensional human atrial anatomic model with fiber orientation

AF heart model was constructed based on healthy adult

male heart specimen who was collected from a healthy adult male in Zhujiang Hospital, Southern Medical University, P. R. China, with an approval from the Ethics Committee of Southern Medical University. The Chinese law of heart research has been strictly followed. The heart specimen was scanned using a spiral computerized tomography (Philips / Brilliance 64). Its size was 512×512 pixel, and the spatial resolution was 0.3574×0.3574×0.33 mm. The reconstructed 3D human atrial anatomic model with fiber orientation is shown in Figure 1. The action potentials of the central sinoatrial node (SAN), peripheral SAN, Atrial Muscle (AM), Crista Terminalis (CT) and Pectinate Muscles (PM) used in our simulation are given in Figure 2. The details of the reconstruction of the human atrial model and the atrial cell models can be found in our previous publications [16,17].

Numerical computation of excitation conduction

The monodomain equation was used to simulate the excitation conduction, which is expressed as follows [18];

$$\frac{\partial V_m}{\partial t} = \nabla \cdot (D \nabla V_m) - \frac{I_{ion} + I_{applied}}{C_m}$$

$$D = \frac{G_i}{S_v C_m} \quad (1)$$

where;

S_v is the surface volume ratio of cells (μm^{-1}), with the value of $4\mu\text{m}^{-1}$. Since our cell models were based on the model of

Figure 1: Anatomical illustration of a human atrial model with fiber orientation.

(a) is the posterior view of the atria; (b) is the conduction bundles in the atria; (c) is the transparent display of the conduction bundles and atrial muscles; (d) is anterior view of the fiber orientation within the atrial anatomic model and (e) is the posterior view (f) Represents the inclination (top) and transverse (bottom) angles of one cross section of the atria in (a).

BB: Bachmann Bundle; CT: Crista Terminalis; CS: Coronary Sinus; FO: Fossa Oval; FOE: Edge of the Fossa Oval; LPM: Left Atrium Pectinate Muscle; PV: Pulmonary Vein; SAN: Sinus Node; RAM: Right Atrial Muscles; RPM: Right Atrium Pectinate Muscle; SVC: Superior Vena Cava

Figure 2: Action potential (AP) models used in our simulation. (a) AP of central SAN; (b) AP of peripheral SAN, Atrial Musle (AM), Crista Terminalis (CT) and Pectinate Muscles (PM).

Courtemanche et al. [19], all cell types in this study have the same S_v values. C_m is the specific capacitance (pF), G_i is the bulk intracellular conductivity (mS/cm), V_m is the transmembrane potential (mV), I_{applied} is the transmembrane stimulating current density and I_{ion} is the sum of all transmembrane ionic currents (pA/pF). More details about this equation have been explained in reference [18].

In this study, the finite difference method was used to calculate equation (1), because of its simplicity and suitability for the parallel computation. The excitation conduction model was computed on a Dawning TC4000L server. It had multiple symmetrical parallel processor containing a management node and 10 computation nodes, and each computation node contained two Intel Xeon e5335 processors (each 4-core), 4G memory and 160G hard drive. The total theoretical computing capacity was up to 184 Gflops. MPICH2 was used to achieve each computing node communication. Entire calculation time was about six hours for each atrial excitation conduction cycle, with a time step of 0.04 ms.

Simulation of AF

There are three types of AF: paroxysmal, persistent and permanent. In our simulation, we didn't take the AF types into account, because the atrial anatomy is based on a normal human heart. However, the single cell model was based on persistent or permanent AF patients. In the simulation, AF episode was defined if AF was induced with the lasting time more than 5 seconds.

AF has been shown to shorten the atrial effective refractory period, reduce action potential duration, and slow down the excitation conduction. The main mechanism of atrial electrical

remodeling involves the reconstruction of different ion channels, mainly including I_{K1} , I_{CaL} , I_{to} and I_{na} . In this study, the AF-induced electrical remodeling cell model was modified from Courtemanche et al. [19] to incorporate the experimental data measured by Bosch et al. [20]. The ectopic foci pacing protocol [12] was used to initiate AF: a voltage stimulus of 10mv was given at the SAN for 1ms. After 400 ms, a train of ectopic foci (≤ 5) was delivered at the atria next to left superior pulmonary vein with the voltage stimulus strength of 20mv for 1ms. After a sufficient time, the planer wave was broken into wavelets, and the AF was then sustained. The conduction velocity in the simulation is defined as the distance between two points divided by the corresponding activation time.

Simulation of AF ablation procedures

By setting the atrial cells on the ablation line to be dead cells where V is set to be 0 mV, the surgical ablation of AF can be simulated. If AF disappeared within 5s, the AF termination was considered to be successful. Otherwise, it was an invalid ablation approach.

In this study, 8 surgical AF ablation procedures were simulated and evaluated with the Time-to-AF Termination (TAFT) recorded. They included the standard Maze-III, incomplete Maze III, Mini-Maze [21], and 5 modified Maze-III procedures proposed by us. The details of these procedures with ablation lines are shown in Figure 3 and Table 1.

Results

Figure 4 shows the simulation result of AF. AF was sustained for over 10 s. Applying the standard clinical Maze- III procedure, the sustained AF was terminated within 4 s, as shown in Figure 5.

Figure 6 and 7 show the simulation results of incomplete Maze-III and Mini-Maze ablations. It can be seen that, under both ablation procedures, AF was not terminated. That's because the vein tissue where the atrium connected to the superior and inferior vena cava was not ablated, resulting in that the electrical excitation could still bypass the superior and inferior vena cava for the AF to be maintained.

Figure 8-12 show the simulation results of our five modified Maze III ablation procedures. Under all these modified procedures, AF was successfully terminated within 4.4 s, with the range between 3.8 s and 4.4 s. The AF termination time is given and compared in Table 2. It can be seen that our modified Maze-III procedures achieved similar ablation effectiveness in comparison with the standard Maze-III ablation.

Discussion

In the study, we simulated and compared the successful rate with different surgical AF ablation lines. Based on a detailed anatomical structure of the human atrial model, 8 different surgical AF ablation procedures have been simulated, with the AF termination time obtained. The simulation results indicated the importance of ablation lines on the right atrium where connected to the superior and inferior vena cava. If these ablation lines were excluded, AF usually could not be terminated (Figure 3(b-

Figure 3: Eight surgical AF ablation procedures simulated in this study. The ablation lines are also illustrated. (a) Standard Maze-III; (b) Incomplete Maze-III; (c) Mini-Maze; (d)-(h) 5 modified Maze III procedures; they were simply referred to Modified 1, 2, 3, 4 and 5 procedures. The details of the ablation lines used in each procedure are also provided in Table 1.

Table 1: Ablation lines used in each of the eight procedures.

Ablation procedure	Ablation lines									
	LAA	PV	LPV→LAA	IPV→MV	RAA	SIVC	SIVC→AS	SIVC→TC	RAA→RA	RAA→TV
Standard Maze-III	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Incomplete Maze-III	Y	Y	Y	Y	Y	Y	Incomplete	Y	Y	Y
Mini-Maze	Y	Y	Y	Y	Y					
Modified 1	Y	Y	Y	Y	Y	Y	Y		Y	Y
Modified 2	Y	Y	Y		Y	Y	Y	Y	Y	Y
Modified 3	Y	Y	Y	Y	Y	Y	Y	Y	Y	
Modified 4	Y	Y	Y	Y	Y	Y	Y	Y		Y
Modified 5	Y	Y	Y	Y	Y	Y	Y			Y

LAA: left atrial appendage;
PV: ablation lines around each four pulmonary veins;
LPV→LAA: from left pulmonary vein to the left atrial appendage;
IPV→MV: from inferior pulmonary vein to the mitral valve;
RAA: right atrial appendage;
SIVC: ablation line jointing the posterior wall of superior and inferior vena cava;
SIVC→AS: from the connection of superior and inferior vena cava to the atrial septum;
SIVC→TC: from the connection of superior and inferior vena cava to the terminal crest;
RAA→RA: from the right atrial appendage to the right atrium high lateral wall;
RAA→TV: from the right atrial appendage to the tricuspid valve.

Figure 4: Simulation result of sustained AF.

Figure 5: Simulation result of standard Maze-III ablation procedure.

Figure 6: Simulation result of incomplete Maze III ablation.

Figure 7: Simulation result of Mini-Maze procedure.

Figure 8: Simulation result of Modified 1 ablation procedure.

Figure 9: Simulation result of Modified 2 ablation procedure.

Figure 10: The simulation result of Modified 3 ablation procedure.

Figure 11: Simulation result of Modified 4 ablation procedure.

Figure 12: Simulation result of Modified 5 ablation procedure.

Table 2: Comparison of simulation results from the 8 ablation procedures. TAFT: Time of Atrial Fibrillation Temination.

Ablation procedure	Ablation description	AF termination	TAFT(s)	No. of ablation lines
Standard Maze-III	Figure 3 (a)	Yes	4.0	10
Incomplete Maze-III	Figure 3 (b)	No	—	10
Mini-Maze	Figure 3 (c)	No	—	5
Modified 1	Figure 3 (d)	Yes	4.3	9
Modified 2	Figure 3 (e)	Yes	4.3	9
Modified 3	Figure 3 (f)	Yes	4.1	9
Modified 4	Figure 3 (g)	Yes	3.8	9
Modified 5	Figure 3 (h)	Yes	4.4	8

c), Figure 6 and 7). Our simulation results also showed that our modified Maze-III procedures with fewer ablation lines than the clinical standard Maze-III procedure could still achieve good AF ablation effectiveness, providing the advantages to simplify the AF treatment procedure.

Our modified procedures required fewer ablation lines compared with the previous work by Patrick Ruchat et al. [13,14] and Matthias Reumann et al. [15], and our human atrial model offered more detailed anatomical structure and conduction system. In particular, our atrial model includes the fiber orientation which has not been taken into account by other published modeling studies. It is well known that fiber orientation plays an important role in excitation conduction, resulting in more reasonable simulation results.

There are several limitations in this study. First, since our three-dimensional simulation of AF ablation is very time-consuming; only a few AF ablation procedures were preliminarily simulated. In the future, other clinical AF ablation procedures should be simulated and compared with clinical outcome. Second, our atrial model itself could be refined further. For instance, the atrial tissue fibrosis should be considered for AF simulation, since the effect of atrial tissue fibrosis on the left atrium is a major determinant of the progression of AF [22]. Fibroblast proliferation not only alters cardiac excitation conduction, but also changes cardiac mechanical contraction [23,24]. Furthermore, the simulation results of AF ablation procedures should be evaluated with animal experiments or clinical trials. Finally, additional ablation lines are reserved only for a subgroup of patients. Especially right atrial ablation lines are abandoned due to a higher complication rate. Further investigation of the underlying mechanisms of the induced AF and the possibility of AF re-induction using the computer modeling approaches are also worth exploring.

Conclusions

The preliminary simulation study has demonstrated that clinical standard surgical AF ablation procedure is not optimal and could be further improved. It also suggests that computational heart modeling and simulation is an important tool to evaluate surgical AF ablation procedure, and may also for evaluation AF radiofrequency catheter ablation techniques [25].

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Declarations

The author(s) certify that there is no conflict of interest with any financial/research/academic organization, with regards to the content/research work discussed in the manuscript.

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