

A biophysical model of atrial fibrillation to define the appropriate ablation pattern in modified maze[☆]

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Abstract

Objective: The surgical Maze III procedure remains the gold standard in treating atrial fibrillation (AF); however due to clinical difficulties and higher risks, less invasive ablation alternatives are clinically investigated. The present study aims to define more efficient ablation patterns of the modified maze procedure using a biophysical model of human atria with chronic AF. **Methods:** A three-dimensional model of human atria was developed using both MRI-imaging and a one-layer cellular model reproducing experimentally observed atrial cellular properties. Sustained AF could be induced by a burst-pacing protocol. Ablation lines were implemented in rendering the cardiac cells non-conductive, mimicking transmural lines. Lines were progressively implemented respectively around pulmonary veins (PV), left atrial appendage (LAA), left atrial isthmus (LAI), cavo-tricuspid isthmus (CTI), and intercaval lines (SIVC) in the computer model, defining the following patterns: P1 = PV, P2 = P1 + LAA, P3 = P2 + LAI, P4 = P3 + CTI, P5 = P3 + SIVC, P6 = P5 + CTI. Forty simulations were done for each pattern and proportion of sinus rhythm (SR) conversion and time-to-AF termination (TAFT) were assessed. **Results:** The most efficient patterns are P5, P6, and Maze III with 100% success. The main difference is expressed in decreasing mean TAFT with a correlation coefficient $R = -0.8$. There is an inflexion point for 100% success rate at a 7.5 s TAFT, meaning that no additional line is mandatory beyond pattern P5. **Conclusions:** Our biophysical model suggests that Maze III could be simplified in his right atrial pattern to a single line joining both vena cavae. This has to be confirmed in clinical settings.

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1. Introduction

Atrial fibrillation (AF) is a growing medical problem, which has been qualified as the new emerging epidemic of cardiovascular disease [1]. Various mechanisms, including rapid local ectopic activity, single-circuit re-entry, and multiple-circuit re-entry, can cause atrial fibrillation. There are implications of these mechanisms for antiarrhythmic therapy [2]. The objective of AF ablation is to create lines of conduction block to interrupt potential re-entry pathways [3]. In addition, ablation procedures were developed to eliminate foci generating ectopic beats, a source of frequent paroxysms of AF [4]. Although surgical procedures report

high success rates, the ideal location, and number of ablation lines, their best interconnection and appropriate length remain to be determined. The main problem associated with the surgical Maze is need for open-heart surgery and heavy time-consuming nature of the procedure [5]. Though, current researches on best ablation pattern are directed towards possible ways to reproduce the good results obtained with the complete Maze procedure with a minimal ablation procedure [6,7]. Intuitively, the ideal ablation pattern should be able to prevent AF with a limited number of lines of minimal length, maintaining or allowing recovery of the mechanical activity of both atria during sinus rhythm (SR) [8].

Advanced computer technology affords highly sophisticated biophysical models of AF [9–11]. These models allow the simulation of the complexity of mechanisms involved in AF, which leads not only to better understanding of the pathophysiology but also open innovative approaches to simulate potential treatment outcomes 'in silico'. When using the gold standard Maze III pattern of ablation lines, a

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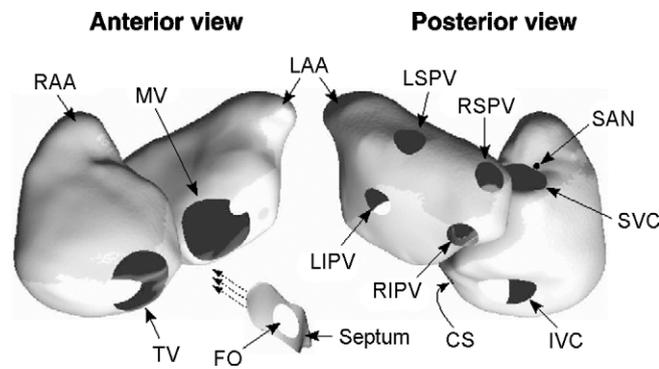


Fig. 1. 3D images of human atria based on MRI. The major vessel inlet and valves orifices are included: tricuspid valve (TV), mitral valve (MV), inferior vena cava (IVC), superior vena cava (SVC), pulmonary veins (PVs), interatrial septum with fossa ovalis (FO).

good agreement was obtained between success rate from the computer model and clinical data [12].

The present study aims to define more efficient ablation patterns of the modified maze procedure using a biophysical model of human atria with chronic AF.

2. Methods

2.1. Biophysical modeling of AF

We developed a three-dimensional biophysical model based on sliced magnetic resonance images of human atria (Fig. 1). This mono-layer geometry included the major vessel inlets, atrioventricular valve orifices, and the septal wall. The atrial surface was meshed in 100,000 triangles with 50,000 connecting nodes simulating atrial cells. Internodal propagation of electrical activity was computed as already described with an equal conductivity between them leading to a homogeneous and isotropic surface [13]. At each node, a cellular model was implemented based on published membrane kinetics model with specific modifications of ionic channel conductance allowing to reproduce atrial cellular properties [14,15]. This model requires 1 h of computation time for the simulation of 1 s of AF on a standard PC (Pentium-III 1.4 GHz). It is, therefore, the result of a careful tradeoff between model complexity, accurate representation of the human atria, and a computational load allowing the simulation of several minutes of AF.

Our basic atrial model induces sustained AF only for few seconds like in healthy human atria. Therefore, we had to modify the electrophysiological properties of our cellular model mimicking electrical remodeling as observed in patients suffering from permanent AF with baseline action potential duration (APD) set to 170 ms. After initiation of AF by burst pacing, the system evolved freely. In all cases, simulated sustained AF lasting longer than 5 min (only limited by computation time) was observed as several independent wavelets traveling randomly throughout the tissue. Two working examples of this computer model are presented, first in sinus rhythm (Movie 1) and second in atrial fibrillation (Movie 2). The simulated electrograms generated with these settings have been shown to be consistent with observations from electrograms of patients with permanent AF.

AF was initiated through wave breaks and perpetuated through functional and anatomical reentries, namely front-tail interactions and collisions with anatomical obstacles. The resulting AF patterns and electrograms have been correlated positively with clinical mapping data [16].

2.2. Ablation patterns

Ablation lines are therapeutic intervention which were simulated in the biophysical model by setting an infinite resistivity (conductivity tensor to zero) between the cardiac cells located on the ablation line, thus creating ideal continuous and transmural barrier-lesions. In this work, the different lines of our modified maze procedure [17] have been implemented progressively in the computer model in seven different patterns as shown in Fig. 2: first only pulmonary veins (PV) isolation in pattern P1, addition of left atrial appendage (LAA) ablation in pattern P2, further addition of left atrial isthmus (LAI) ablation in pattern P3. Based on pattern P3, a line in the cavo-tricuspid isthmus (CTI) was added for pattern P4 and a line from superior to inferior vena cava (SIVC), the intercaval line for pattern P5. The pattern P6 combined all the lines mentioned for P1 to P5. Finally the Maze III pattern was taken as a reference [5]. Complete isolation of the pulmonary vein region implied that no electrical activity can be propagated from the pulmonary veins to the atria. The isolated area is 11 cm², i.e. 7% of the whole atrial tissue. For the Maze III procedure, the isolated area is 32 cm², i.e. 20% of the whole atrial tissue. Because of

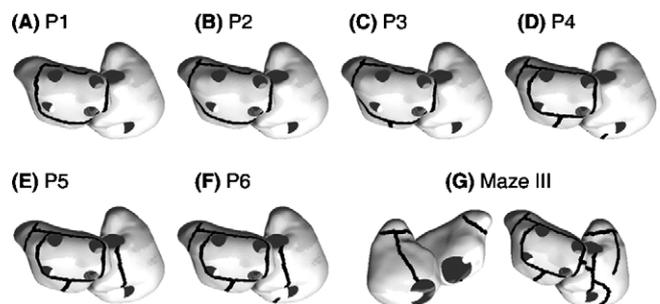


Fig. 2. Progressively implemented ablation lines (black lines). P1: Pulmonary veins isolation (PV). P2: P1 + ablation of left atrial appendage (LAA). P3: P2 + left atrial isthmus (LAI). P4: Left atrial pattern + cavo-tricuspid isthmus (CTI). P5: Left atrial pattern + superior to inferior caval veins line (SIVC). P6: P4 + P5. P7 = Maze III.

Table 1
Success rates in converting AF to sinus rhythm (SR) or atrial flutters, and mean time-to-AF termination for each progressive ablation pattern

Patterns	SR (%)	AF (%)	Flutter (%)	TAFT (s)
P1	55	42.5	2.5	13.5 ± 7.1
P2	65	25	10	13.4 ± 9.4
P3	80	20	0	11.6 ± 8.1
P4	95	5	0	9.5 ± 7.1
P5	100	0	0	7.5 ± 7.6
P6	100	0	0	5.1 ± 5.0
Maze III	100	0	0	1.3 ± 0.8

the random nature of AF, several time instants reflecting different AF states were selected as initial states for the application of the different ablation simulations. These patterns were applied instantaneously, after which the time-to-AF termination (TAFT) was documented. Ablation was defined as unsuccessful if no termination of AF occurred within 30 s (30 h computation time) after the application of the ablation lines since experiments have shown that a termination occurring after this time interval is generally due to a spontaneous termination of AF. For each defined pattern, 40 simulations of ablation were performed based on different AF states selected every second. The percentage of successful conversion to SR, the remaining atrial flutter, and the mean TAFT were computed.

3. Results

The percentages of successful conversion to SR and remaining atrial flutter based on 40 simulations for each patterns are summarized in Table 1. Three groups can be defined: first, a group with a 55–80% success rate corresponding to left atrial limited maze (P1–P3) where uncommon left atrial flutter were observed for P1 (2.5%) and P2 (10%), since both patterns did not have a line between the pulmonary veins and mitral annulus (left isthmus); second, a group with a high success rate reaching 95–100%, when adding right ablation lines (P4–P6); and finally the gold standard Maze III with a

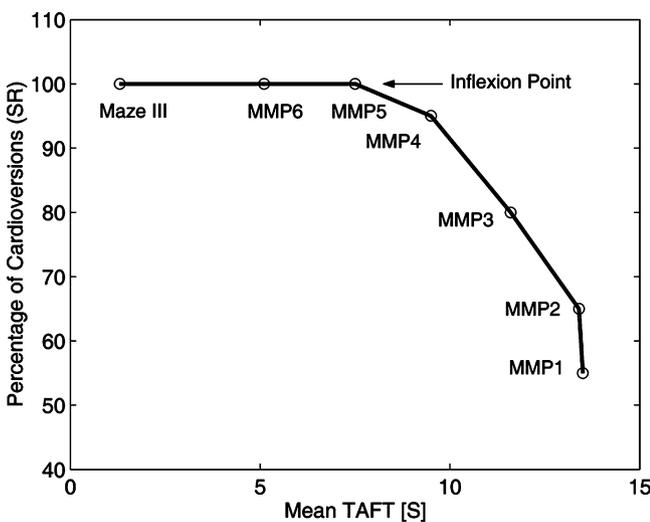


Fig. 3. Success rate of version to SR plotted against TAFT. An inflexion point to keep 100% success rate at TAFT value of 7.5 s (P5).

clear 100% success rate and minimal TAFT values with narrow standard deviation. The more complex the ablation pattern, the lower the TAFT values with a wide range of standard deviation for each ablation pattern. The most efficient patterns are P5, P6, and Maze III with 100% success. The main difference is expressed in decreasing mean TAFT value from P5 to Maze III. In Fig. 3, the success rate in terminating AF was plotted against TAFT for each different pattern. We can observe an inflexion point for 100% success rate at a TAFT value of 7.5 s (P5), signifying that no additional lines would be mandatory beyond this limit. Such an ideal pattern is simulated in the film (Movie 3).

4. Discussion

Comprehensive progress of atrial fibrillation ablation needs either experimental animal models or well-designed clinical trials. Since computer sciences have evolved, different biophysical models of AF can now be used to better understand basic mechanisms and therapeutic implications. Depending on the study design, the choice of an appropriate biophysical model can bring the best answer and approach as close as possible clinical settings. We aim to study different ablation patterns on an atrial substrate mimicking permanent AF. The biophysical model of AF presented in this study is, to our knowledge, the only model with cellular and anatomical components that is able to generate sustained AF for several minutes and to allow the study of the electrophysiological consequences of ablation lines [13]. It represents a good trade-off between realism and available computation time. On the one hand, the model needs to be complex enough to allow simulations that take into account cellular and anatomical features [7] while testing selected AF ablation patterns. On the other hand, the model was simplified to the level needed to keep the computational load within the feasibility limits set by available computer technology. The problem of inferences of computer simulations into clinical results should be addressed. Certain items are comparable, while some major differences are always present. Although anatomically correct, the necessary simplifications of the model imply several deviations from the pathophysiological reality of permanent AF. Despite the use of human atria MRI images the geometry of the biophysical model was the same in all simulations, whereas the atrial anatomy differs in each patient. Furthermore, we did not take into account organic heart diseases such as enlarged or stretched atria. This difference may be relevant because we know that left atrial size is of tremendous importance in surgical treatment of AF [8]. Like in cardio-surgical procedures, ablation lines during computer simulations were applied abruptly, corresponding to phenomena arising during myocardial revascularization. Effects of barrier-lesions on reappraisal of atrial electrical activity are tested on real time. Our model does not include anisotropic fast-conducting regions, fiber orientation, crista terminalis, and pectinate muscles, which may all play a role during AF [18]. Moreover, the present biophysical model takes into account reentrant wavelets only and not rapid foci originating from the pulmonary veins.

We defined three groups of ablation patterns. First, incremental ablation lines limited to the left atrium (P1–P3);

second, additional patterns on the right atrium (P4–P6); and finally the gold standard Maze III simulations. The first group has a success rate ranging from 55 to 80%, which corresponds to published surgical series [7,8,17,19]. Although permanent lone AF without severe organic heart disease could afford different results, we compare our simulations (pattern P3) to randomized study by Pappone and colleagues who found a 74% of patients free of recurrent AF without antiarrhythmic drug at 1 year after endovaginary pulmonary-veins isolation and left isthmus interruption [20]. Our P3 pattern showed an 80% of sinus rhythm conversion rate, statistically not different from their clinical results. These comparisons emphasized that a 'substrate' of permanent AF generates electrical and morphological remodeling that perpetuate AF in a model of multiple wavelets re-entry. As shown by patterns P1 and P2, pulmonary veins isolation is currently not efficient enough to ablate permanent AF. Indeed this limited procedure is originally intended to cure paroxysmal AF since Haissaguerre has shown PVs implications in focal firing foci [4].

Although most AF found their origin in the left atrium, about 10–20% of permanent AF originates from the right one [21]. Though in our second group, when adding right atrial ablation lines to the left maze, SR conversion rate increase from 55–80% to 95–100%. Our data showed that to cure AF originating from right atrium, the necessary and sufficient additive line is the intercaval one (P5 and P6). This finding is a new concept; it is different from the cosio isthmus ablation line, which is mandatory to ablate right typical flutter. It should be emphasized that a widespread use of the intercaval line has been related to a 5–25% of sinus node dysfunction. Routine use in clinical settings needs a thoughtful action to stay well below cavoatrial junction. This type of pattern has been tested in a clinical study by Garg and colleagues [22]. They have asked whether lesions applied only on the right atrium could ablate AF in a significant number of cases and though suppress the procedural risk associated with catheter ablation in the left atrium. These authors reported that AF was suppressed in 67% of the patients on long-term follow-up. These results are consistent with paroxysmal AF originating from multiple foci like caval veins, coronary sinus, and pectinate line [23].

Among the simulated ablation patterns, the most efficient is the Maze III procedure with a success rate of 100% and the smallest mean TAFT value of 1.3 ± 0.8 s. This ablation pattern is able to terminate AF independently of the initial states present in the atrial tissue at the moment of application of the lines. The main information to draw from the high success rate of the simulated Maze III procedure is in the efficiency of the ablation pattern in preventing AF reinitiation following a particular initial state. The success rate obtained is in agreement with clinical data, where the complete surgical Maze III pattern had the highest success rate going up to 98% [24]. Like in the Cox series performing the Maze III with the cut-and-sew technique, barrier-lesions in our model are transmural. In recent modified ablation techniques there are always doubt on transmural of the barrier-lesions afford by physical media like radiofrequency, microwave, and cryosurgery. Effect of non-transmural lesions had already been tested in our model [12]. Although anatomically correct, the necessary simplifications of the

model imply several deviations from the pathophysiological reality of permanent AF.

5. Conclusions

Our biophysical model suggests that Maze III could be simplified in his right atrial pattern to a single line joining both vena cavae. Actually, all the simulations of AF ablation we have performed 'in silico' compares pretty well with clinical rate of SR conversion published by different authors. We hope that in a near future, with refinement of modeling, each clinical setting might be studied 'in silico' to plan definitive therapeutic intervention.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.ejcts.2006.10.015](https://doi.org/10.1016/j.ejcts.2006.10.015).