A biophysical model of atrial fibrillation ablation: what can a surgeon learn from a computer model?

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Aims Surgical ablation procedures for treating atrial fibrillation have been shown to be highly successful. However, the ideal ablation pattern still remains to be determined. This article reports on a systematic study of the effectiveness of the performance of different ablation line patterns.

Methods and results This study of ablation line patterns was performed in a biophysical model of human atria by combining basic lines: (i) in the right atrium: isthmus line, line between vena cavae and appendage line and (ii) in the left atrium: several versions of pulmonary vein isolation, connection of pulmonary veins, isthmus line, and appendage line. Success rates and the presence of residual atrial flutter were documented. Basic patterns yielded conversion rates of only 10–25 and 10–55% in the right and the left atria, respectively. The best result for pulmonary vein isolation was obtained when a single closed line encompassed all veins (55%). Combination of lines in the right/left atrium only led to a success rate of 65/80%. Higher rates, up to 90–100%, could be obtained if right and left lines were combined. The inclusion of a left isthmus line was found to be essential for avoiding uncommon left atrial flutter.

Conclusion Some patterns studied achieved a high conversion rate, although using a smaller number of lines than those of the Maze III procedure. The biophysical atrial model is shown to be effective in the search for promising alternative ablation strategies.

KEYWORDS Atrial fibrillation; Computer modelling; Ablation; Surgery

Introduction

Atrial fibrillation (AF) is a growing problem that needs to be treated to prevent its impact on mortality because of severe complications such as haemodynamic dysfunctions (loss of atrial mechanical activity and irregular ventricular response that can lead to low cardiac output and heart failure) and stroke. This problem is approached differently by electrophysiologists and surgeons. From the electrophysiologist’s point of view, propagation of electrical activity makes the heart beat about 4 \times 10^7 per year. From the surgeon’s point of view, the heart is a pump circulating about 4 \times 10^6 litres of blood per year. Electrophysiologists are concerned about rhythm disturbances, whereas surgeons by a decrease in the transport of blood. However, whatever the focus of interest might be, there is no reliable biological model available for a pre-evaluation of the effectiveness of therapeutic interventions. Today, most treatments for AF are based on empirical considerations, or clinical studies and many underlying mechanisms remain unclear.

Surgical ablation of AF aims at creating lines of block to interrupt electrical conduction and, as a result, prevent the AF re-entrant process. The surgical Maze III procedure by Cox et al.² is the gold standard for patients undergoing open heart surgery for concomitant surgery such as valve replacement or coronary bypass. Although Cox et al.¹,³ reported excellent long-term results, the ideal AF ablation pattern still remains to be determined. This pattern should be able to terminate AF and prevent its re-occurrence with a limited number of ablation lines having minimal length, although allowing a correct mechanical activity/blood pumping during normal sinus rhythm. Furthermore, it would be desirable to apply this pattern with a method that is less invasive than surgery such as radiofrequency, microwave, or cryoablation. No significant difference in the post-operative sinus conversion rate could be seen between the classical ‘cut and sew’ and the alternative sources of energy that were used to treat AF.⁶

The evaluation of different lesion patterns is usually performed in clinical studies or animal experiments. Computer modelling is a rapidly growing field, which is an additional tool in testing AF ablation patterns. The main advantages are the access to any value of interest and the repeatability of experiments in controlled conditions. Several computer
models of atria have been developed over the last decades. Moe et al.\textsuperscript{7} developed the first model of AF in the 1960s using cellular automata. Later, more sophisticated models were published, taking into account several aspects of the complex atrial anatomy.\textsuperscript{8,11} Existing models differ in the tradeoff made between accuracy of the anatomical representation and the computational load. Modelling of ablation procedures requires simulations of long periods of AF on a computer modelling scale (several minutes instead of several seconds generally). The heavy computational demand of the advanced available atrial models precludes their use in this type of analysis. Therefore, a simpler model requiring far less computation effort was designed such that sufficient realism for the particular application was retained.\textsuperscript{12} Good agreement was previously obtained between ablation success rates obtained from this computer model and those reported from clinical procedures.\textsuperscript{12,13}

We have used this biophysical model of AF ablation to systematically study the performance of each ablation line generally performed by surgeons separately, as well as several of their possible combinations.

**Methods**

**Biophysical model of atrial fibrillation**

The biophysical model of AF used in this study was specifically designed to take into account the main aspects of human atrial geometry, based on magnetic resonance images, while restricting computational load. As shown in Figure 1, the openings in the geometry of the connections to the valves and major vessels are represented. Next to the overall geometry, these openings are essential elements of the geometry, as atrial activation has to propagate around these orifices. The geometry was presented by a monolayer structure with homogeneous properties. The atrial tissue was discretized using a triangular mesh, the edges of which had an average length of 0.6 mm. At each node of the mesh, the electric activity was modelled by membrane kinetics models adjusted to match human atrial properties.\textsuperscript{14,15} The resulting computational load (burden) is one hour of PC processor work to model one second of atrial activity.

The biophysical model allows the simulation of different types of arrhythmias. Various conditions for initiation and perpetuation of AF in this model have been studied and were found to be in agreement with the limited available experimental data, either from detailed mapping on small segments of atrial tissue or from spot check recordings more widely spaced, as is obtained for electrophysiological (EP) studies.\textsuperscript{16}

The study is based on a model of chronic AF in the form of sustained multiple re-entrant wavelets. The model tissue substrate of AF was set up on electrophysiological data recorded in patients suffering from permanent AF.\textsuperscript{15} Atrial fibrillation was initiated by rapid burst pacing in the sino-atrial node region, leading to sustained AF, which continued unless terminated by an intervention such as the application of ablation lines.

**Testing of ablation patterns**

In the computer model, after AF had been initiated, ablation was simulated by instantaneously assigning an infinite resistivity between the cells located on the lines of the pattern studied. In this monolayer model, this completely blocked propagation across these lines, thus simulating a perfect (transmural) ablation.\textsuperscript{12}

For testing each of the ablation line patterns, the following procedure was carried out (Figure 2). As a first step, as described

![Figure 1](image_url)
earlier, sustained chronic AF was initiated by means of burst pacing. A database comprising 40 different simulated AF states was created by randomly selecting and storing subsequent states of AF. These 40 states differ in the activity present in the tissue, such as the number of wavelets. The ablation patterns were applied instantaneously and were considered successful if AF termination was observed within an arbitrary period of 30 s. A detailed analysis of the activity following the application of lines indeed showed that termination occurring after this period was generally because of spontaneous events. When applied to the AF database, the percentage of the 40 simulations in which AF terminated was taken as the success rate of the ablation procedure. In addition to the percentage of return to sinus rhythm, the conversion to atrial flutter was also documented.

The AF ablation patterns tested included those commonly performed by surgeons (Figure 3). Different versions of the individual lines present in a full Maze III procedure, both in the right and left atria, were tested individually as well as several combinations of these lines in increasing numbers. Basic ablation lines in the right atrium were an isthmus line (RAI), a line between vena cavae (SIVC), and an appendage line (RAA). Basic ablation lines in the left atrium were several versions of pulmonary vein isolation (one by one IPV1, two by two IPV2, and four together IPV4), a connection of pulmonary veins (CPV), an isthmus line (LAI), and an appendage line (LAA). Each ablation pattern required a simulation time of a total of up to 20 min (40 different AF states times 30 s, less if AF terminated sooner). Generally, this took several hours of simulated AF and several days of computation time on a set of several PCs.

Results
The best result and the shortest time to AF termination were obtained in the computer model with the standard Maze III procedure (100%), which was used as a reference in this study. The percentages of successful conversion to sinus rhythm are summarized in Table 1. This table contains three parts ordered by increasing number of lines in each part: (i) right lines only, (ii) left lines only, and (iii) both right and left lines.

Each basic ablation pattern presented in Figure 3 was evaluated individually. For the right atrium, the basic patterns yielded conversion rates of 10–25%. For the left atrium, conversion rate was higher by 10–55%, but with a possibility of conversion into uncommon left atrial flutter. If we compare the different possibilities for isolation of pulmonary veins, the best result was obtained when a single closed ablation line encompassed all four veins (55%), or when they were connected together with the addition of the left isthmus line (60%). The best result in the right atrium, with 65% conversion, was obtained by combining all basic lines, whereas a combination of all left lines lead to a success rate of 80%. Higher rates could be obtained only if right and left lines were combined. Some patterns achieved the maximum conversion rate using a smaller number of ablation lines than the Maze III procedure. This was the case for the patterns combining an optimal isolation of pulmonary veins, the left isthmus line, and the line between vena cavae in the right atrium. We could also observe that the left isthmus line is required in the left atrium in order to avoid the occurrence of uncommon left atrial flutter at some stage after the ablation.

Discussion
Computer modelling has some limitations, which render the comparison with clinical data sometimes difficult. The timescales of computer modelling and clinical data are very different. The longest computer-simulated AF lasts only a few minutes, whereas AF in reality can last for days, months, or years. To overcome this problem, this model of chronic AF was developed by introducing electrical remodelling as
observed in atrial cells after 1 or 2 weeks of pacing-induced AF with arrhythmia becoming self-sustained and atrial effective refractory period markedly shortened. Therefore, it is only the transition phase, following the application of the ablation lines, that is modelled. Long-term effects of ablation cannot be studied clearly by means of this approach.

In this type of study, the geometry and electrophysiological properties are the same in all experiments, and the comparison of the effectiveness of the different ablation line patterns is devoid of confounding factors such as differences between patients and their clinical condition. The results shown here relate to chronic AF involving multiple re-entrant wavelets. Other types of AF, such as the ones involving rapid foci originating from the pulmonary veins as observed during paroxysmal AF, which may create differences in success rate for the lines located in the left atrium, could also be studied by means of similar models with different properties.

Despite some of the limitations, the biophysical model is an interesting tool to assess surgical ablation patterns for patients suffering from permanent AF. It offers the possibility to test lines in a ‘reversible’ way in a human model and to observe the AF termination process in detail. A previous comparison between simulations performed with this model and patients who underwent radiofrequency ablation showed a positive correlation for conversion rates to sinus rhythm and residual atrial flutter. Therefore, conversion rates can be studied realistically for different patterns in the case of chronic substrates of AF, which is the usually the case when surgeons perform ablation procedures during open heart surgery.

The results obtained for the simulated Maze III procedure are comparable with clinical data reported for this pattern, showing a long-term success rate ranging from 80 to 99%. The success rate obtained for the simulations of this pattern is very high (100%) because all the lines created are perfect and non-conducting, which may not be the case in reality. Indeed, previous simulation studies have shown that performance can decrease with Maze III from 100 to 80% for a gap of 3 mm located in the line connecting the pulmonary veins and mitral annulus. This decrease in performance is linked to the apparition of a residual atypical atrial flutter around the mitral valve.

The systematic testing of the ablation lines composing the Maze III patterns confirmed the need of having lines in both the right and left atria. This study is a generalization of the study presented by Ruchat et al., in which a minimal ablation pattern was defined by successfully adding ablation lines until a full Maze III procedure, suggesting that ablation in the right atrium could be simplified to a single line joining both vena cavae. The results shown in Table 1 indicate that combination of lines only in the right/left atrium may lead to a success rate in the range 10–65/10–85%. The maximum conversion rates obtained are comparable with the published results of clinical studies: long-term success rate of atrial compartmentalization of 67% and long-term success rate of pulmonary vein ablation of 82%.

Figure 3 Systematic testing of ablation patterns with a comparison to Maze III as a reference. Patterns in the right atrium: right isthmus line between tricuspid valve and inferior vena cava (RAI), line between superior and inferior vena cava (SIVC), and right atrial appendage line (RAA). Patterns in the left atrium: isolation of pulmonary veins one by one at 5 mm distance to ostia (IPVI), isolation of pulmonary veins two by two with a 5 mm distance between ablated areas (IPV2), isolation of four pulmonary veins (IPV4), IPV4 and left atrial isthmus line between inferior pulmonary veins and mitral valve (LAI), connection of three pulmonary veins (CPV) and LAI, left atrial appendage line (LAA).
As could be expected, individual lines generally have little impact on AF (10–25%). A noteworthy exception formed the isolation of pulmonary veins with a success rate in the range 20–55%. Isolation of pulmonary veins can be performed using different approaches, mostly developed to treat paroxysmal AF. The situation is different in the case of permanent AF, and our study shows that better conversion rates are obtained if all pulmonary veins are encompassed by one single closed ablation line rather than ablated individually. In our case, this is due to the fact that one area will be less likely to generate wavebreaks sustaining AF.

Our simulation studies indicated that all basic lines in the left atrium can lead to atypical atrial flutter, whereas this is not the case for right lines. These atrial flutters can be stopped by the introduction of a left atrial isthmus line. This line should be transmural to be effective. In the case of isolation of pulmonary veins one by one or two by two, the rate of residual atrial flutter is also dependent on the size of the area between ablated zones, as shown in a previous study.

Combination of lines in both the right and left atria increased conversion rate in the range 90–100% (assuming perfect transmural lines). This biophysical model gives some insight into the ablation process for an optimal minimal pattern. One or two lines are required in the right atrium, but the line choice does not seem to be critical. For the left atrium, the critical areas to be ablated are the pulmonary vein region and the left isthmus line.

Table 1  Success rates in converting AF to sinus rhythm for each simulated ablation pattern

<table>
<thead>
<tr>
<th>Ablation pattern</th>
<th>Sinus rhythm (%)</th>
<th>Atrial flutter R/L</th>
<th>Ablation lines</th>
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</thead>
<tbody>
<tr>
<td>RAA</td>
<td>10</td>
<td>No</td>
<td>R</td>
</tr>
<tr>
<td>RAI</td>
<td>20</td>
<td>No</td>
<td>R</td>
</tr>
<tr>
<td>SIVC</td>
<td>25</td>
<td>No</td>
<td>R</td>
</tr>
<tr>
<td>RAI+SIVC</td>
<td>60</td>
<td>No</td>
<td>R</td>
</tr>
<tr>
<td>RAI+SIVC+RAA</td>
<td>65</td>
<td>No</td>
<td>R</td>
</tr>
<tr>
<td>LAI</td>
<td>10</td>
<td>No</td>
<td>L</td>
</tr>
<tr>
<td>IPV1</td>
<td>20</td>
<td>Yes</td>
<td>L</td>
</tr>
<tr>
<td>IPV2</td>
<td>50</td>
<td>Yes</td>
<td>L</td>
</tr>
<tr>
<td>IPV4</td>
<td>55</td>
<td>Yes</td>
<td>L</td>
</tr>
<tr>
<td>CPV+LAI</td>
<td>60</td>
<td>No</td>
<td>L</td>
</tr>
<tr>
<td>IPV4+LAI</td>
<td>65</td>
<td>No</td>
<td>L</td>
</tr>
<tr>
<td>IPV4+LAA</td>
<td>65</td>
<td>Yes</td>
<td>L</td>
</tr>
<tr>
<td>IPV4+LAI+LAA</td>
<td>80</td>
<td>No</td>
<td>L</td>
</tr>
<tr>
<td>CPV+LAI+RAI</td>
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<td>No</td>
<td>R+L</td>
</tr>
<tr>
<td>CPV+LAI+SIVC</td>
<td>100</td>
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<td>R+L</td>
</tr>
<tr>
<td>IPV4+LAI+LAA+RAA</td>
<td>90</td>
<td>No</td>
<td>R+L</td>
</tr>
<tr>
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<td>R+L</td>
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<tr>
<td>IPV4+LAI+LAA+SIVC</td>
<td>100</td>
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<td>R+L</td>
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<tr>
<td>Maze III</td>
<td>100%</td>
<td>No</td>
<td>R+L</td>
</tr>
</tbody>
</table>

The possible conversion to atrial flutter is also indicated. Patterns are ordered as follows: (i) patterns involving right atrium only (R) with increasing number of lines; (ii) patterns involving left atrium only (L) with increasing number of lines; (iii) patterns involving both right and left atria (R/L) with increasing number of lines; and (iv) Maze III. In this table, all the lines required to isolate pulmonary veins are counted as one line.

Conclusion

This model-based study aimed at identifying ablation patterns with high conversion rates, similar to the best ones reported in the literature, although causing less damage to the tissue. A potential pattern that came up so far is the isolation of the pulmonary veins combined with a left isthmus line to prevent atrial flutter and a line between vena cavae or a right atrial isthmus line.

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