Effect of fat layer thickness on the ablation area in pulsed electric field ablation

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ABSTRACT

Background: Pulsed electric field (PEF) ablation has recently been applied by researchers in the treatment of atrial fibrillation (AF), which is able to utilize high-voltage electric fields to produce damage to the myocardium for the purpose of treating AF. The effect of epicardial fat layer on the ablation effect has not been systematically studied. The purpose of our study was to establish a computer simulation model to rationally simplify the human organ, which was used to evaluate the effect of the fat layer on the ablation damage area. **Methods:** Firstly, by building a computational simulation model, different tissues of the heart were simplified and a three-dimensional computational model containing only the ablation device of interest was built, the ablation damage range was assessed in the post-processing interface using an electric field threshold of 400v/cm, and finally, the thickness of the fat layer was varied in order to assess the effect of the fat layer on the ablation area. **Results:** The epicardial fat layer had a weakening effect on PFA, and the total ablation depth decreased when the thickness of the fat layer increased, and when the fat layer reached 1.5 mm, the total ablation depth stabilized and the ablation depth of the myocardial layer decreased. In addition, we found a strong linear relationship between the total ablation depth and pulse voltage.

Keywords: Pulsed field ablation, computer modeling, fat, ablation area

1. INTRODUCTION

Pulsed electric field (PEF) ablation, also known as Pulsed Field Ablation (PFA), is a technique that leads to cell death in the ablation area by applying an electric field to the ablated tissue, a technique that has previously achieved better results in the treatment of tumors by applying high voltage to tumor cells, inducing pores in the cell membrane within a short period of time, resulting in an imbalance of the intracellular environmental homeostasis, and consequently leading to cell death[1-3]. In recent years, the PFA technique, as a nonthermal ablation technique, has gained widespread interest among clinicians for its unique safety profile. The use of PFA technology for pulmonary vein isolation in the endocardium for the treatment of atrial fibrillation (AF) has been widely used, and these clinical applications have demonstrated that PFA has a unique safety profile compared with other ablation techniques and that no damage is caused to the nearby tissues while pulmonary vein isolation is being performed, due to the fact that the PFA technology transmits a small amount of heat to the target tissues and that myocardial tissues are more sensitive to the electric field compared with other tissues, which makes this technique to have better tissue selectivity [4-8]. Epicardial PFA as an alternative approach to AF treatment, some researchers in a previous study found that the conductivity of fat near myocardial tissue was lower than that of myocardium, which resulted in the ablation area being almost confined to the fat layer. A subsequent researcher used computer modeling to analyze the effect of epicardial fat on the ablation area and found that the presence of fat significantly altered the normal electric field distribution. Subsequent researchers utilized the method of simulating fat by coating the surface of potatoes with butter and obtained the result that butter diminishes the depth of the ablation region in potatoes [9-11]. Currently, there are fewer studies on whether the fat layer affects the ablation effect of PFA on the ablation region. Most of the existing research cases were studied using fixed PFA parameters. The aim of our study was to investigate the ablation effect of the presence of the supraspinal myocardial fat layer on the ablation region targeted for ablation by PFA by means of multiparameter fat thickness versus multiparameter pulse voltage.

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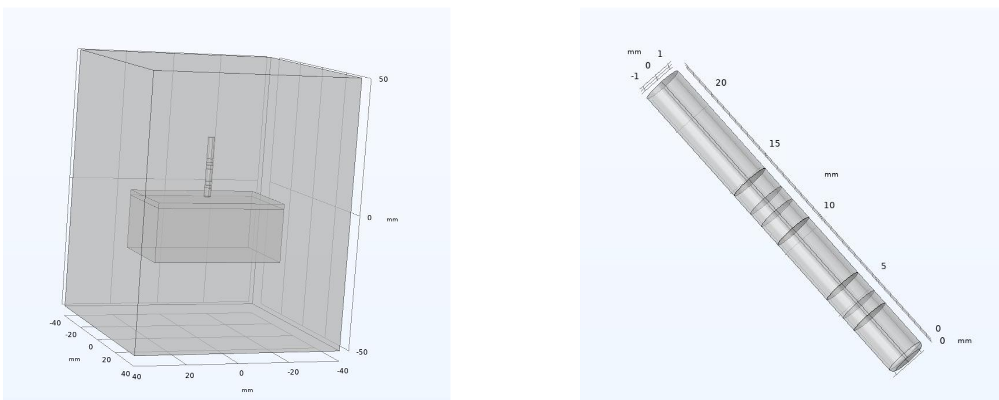
2. METHODS

2.1 Modeling

We considered building a three-dimensional computational model in the computer that contains only the ablation region of interest for the ablation catheter, which was done to reduce the complexity of the model computation, and some researchers have previously demonstrated that this model simplification method is effective in computational modeling [12-13]. In the simplified model setup, we built a 3D computational model containing only the catheter, fat, myocardium, and saline, and the whole model is shown in Figure 1A. In the model, we only consider the case where the catheter is perpendicular to the surface of the myocardium, which is to avoid the influence of the angle on the ablation effect. For the catheter model, we consider the real size of the catheter in the experiment, there are four electrodes in the ablation catheter, the height of the fourth electrode is 3.5 mm, the height of the other three electrodes is 1.5 mm, and the diameter of the catheter is 2.5 mm, and the catheter model diagram is shown in Figure 1B. We set the fat layer to be located above the myocardial layer, and in the model, the thickness of the fat layer varied between 0 and 2.5 mm, and the whole fat layer was between the myocardial layer and the catheter [9, 14].



A. Schematic diagram of the computational model

B. Catheter Model Schematic

Figure 1. Schematic diagram of the simulation model

2.2 Boundary conditions

We set the boundary conditions in the model, set the first and second electrodes of the ablation catheter as negative electrodes, and set the third and fourth electrodes of the ablation catheter as positive electrodes, and in terms of the applied voltage of the catheter, we set the voltage range between 1000 V and 1800 V, in which the ablation voltage is taken every 200, and in terms of the pulse setting, we set the applied pulse to be 2us and set 250 Pulse. In addition to this, we set the current on the surface of the model, which means that the current in the model flows between the positive and negative poles of the ablation catheter.

2.3 Material properties

The conductivity of the tissue changes during the ablation of the tissue by PFA, which is due to the fact that when the pores induced by PFA on the target tissue cells are created, it leads to a greater permeability of the cells to the electric current. Therefore, in the computational modeling, we represent this conductivity change induced by PFA during the ablation process using the sigmoid function [15-16]. The PFA process-dependent equation is shown below.

$$\sigma(E) = (\sigma_0 + \frac{\sigma_1 - \sigma_0}{1 + 10e^{-\frac{(|E| - 58{,}000)}{3000}}}) \quad (1)$$

Where σ_0 is the conductivity before electroporation and σ_1 is the conductivity after electroporation. The specific parameters are shown in Table 1 [12, 17]. Saline, Electrode and Poyurethane showed no change in conductivity during PFA.

Table 1. Parameters for model conductivity calculation

Element	Myocardium	Fat	Saline	Electrode	Poyurethane
σ_0（S/m）	0.0537	0.0377	1.392	$4.6e^{6}$	$1e^{-5}$
σ_1（S/m）	0.0281	0.0438			

2.4 Governing equations

For the model calculation problem, we use COMSOL software to solve the model numerically using the finite element method. In the electric field solution, we use the quasi-static approximation to calculate the electric field distribution. The electric field distribution is computed by solving the Laplace form of Maxwell's system of equations [14, 18].

$$\begin{cases} \nabla \cdot \left(\sigma \nabla V\right) = 0 \\ E = -\nabla V \\ J = \sigma E \end{cases} \tag{2}$$

Where is σ the conductivity of the material, V is the voltage, E is the electric field vector and J is the current density vector.

2.5 Analysis of results

We used computer simulation of different tissues of the heart and thus simulated the effect of fat on the PFA area. In the present study, we comprehensively assessed the size of the PFA region by varying the thickness of the fat layer and by using different pulse voltages. In this simulation, we used 400 V/cm as the irreversible threshold for myocardial injury, due to the fact that a large number of previous studies have reported that 400 V/cm is the minimum threshold for myocardial injury [19-21]. In our model, fat and myocardium were located in saline, which was to make the ablation model close to the real clinical ablation state.

3. RESULTS

3.1 Effect of different fat layer thickness at the same voltage

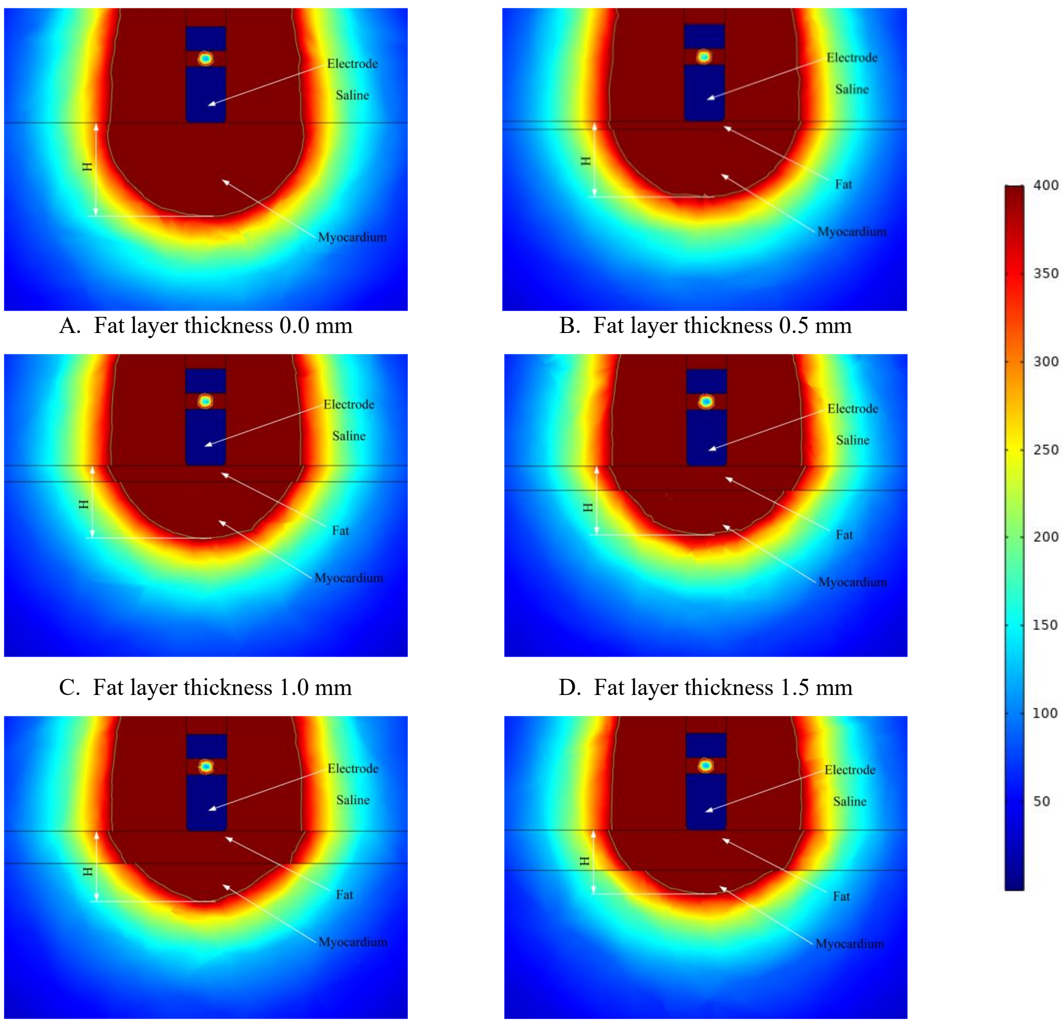
As shown in Figure 2, the energy ablation region of PFA penetrated the fat layer to produce damage to the myocardial layer. At the same pulse voltage, the depth of myocardial layer damage becomes thinner and thinner with the thickness of the fat layer, which indicates that the fat layer has an effect on the ablation depth of PFA. Figure 2 shows the ablation data for different fat layer thicknesses at a pulse voltage of 1200V. Figure 2A shows that the ablated damage depth of the myocardial layer was 5.9 mm for a fat layer thickness of 0.0 mm; Figure 2B shows that the ablated damage depth of the myocardial layer was 4.7 mm for a fat layer thickness of 0.5 mm; Figure 2C shows that the ablated damage depth of the myocardial layer was 4.4 mm for a fat layer thickness of 1.0 mm; Figure 2D shows that the ablated damage depth of the myocardial layer was 4.4 mm for a fat layer thickness of 1.5 mm. myocardial layer was ablated to a depth of injury of 4.2 mm; Figure 2E shows that the myocardial layer was ablated to a depth of injury of 4.3 mm when the thickness of the fat layer was 2.0 mm; and Figure 2F shows that the myocardial layer was ablated to a depth of injury of 3.9 mm when the thickness of the fat layer was 2.5 mm.

As shown in Figure 2, we can see that at the same pulse voltage, the total depth of PFA decreases as the thickness of the fat layer increases, which also means that the fat has a greater impediment to myocardial transmission of PFA energy compared to the fat. In terms of the ablation width of the myocardial layer, as the thickness of the fat layer increased, there was a small change in the width of the myocardial layer that was ablated when the PFA energy passed through the fat layer (fat depth 0.5 mm: myocardial layer ablation width 11.2 mm; fat depth 1.5 mm: myocardial layer ablation width 9.9 mm; and fat depth 2.5 mm: myocardial layer ablation width 7.4 mm.) Tables 2 and 3 show the ablation data at different pulse voltages. ablation data at different pulse voltages.

Table 2. 800-1200V ablation data

800V			1000V			1200V		
D	H	h	D	H	h	D	H	h
0.0	4.3	4.3	0.0	5.1	5.1	0.0	5.9	5.9
0.5	3.5	3.0	0.5	4.1	3.6	0.5	4.7	4.2
1.0	3.2	2.2	1.0	4.0	3.0	1.0	4.4	3.4
1.5	2.9	1.4	1.5	3.7	2.2	1.5	4.2	2.7
2.0	2.9	0.9	2.0	3.4	1.4	2.0	4.3	2.3
2.5	2.8	0.3	2.5	3.4	0.9	2.5	3.9	1.4

D: thickness of fat layer (mm); H: total depth of ablation (mm); h: thickness of ablated myocardium (mm)



A. Fat layer thickness 0.0 mm
B. Fat layer thickness 0.5 mm
C. Fat layer thickness 1.0 mm
D. Fat layer thickness 1.5 mm
E. Fat layer thickness 2.0 mm
F. Fat layer thickness 2.5 mm

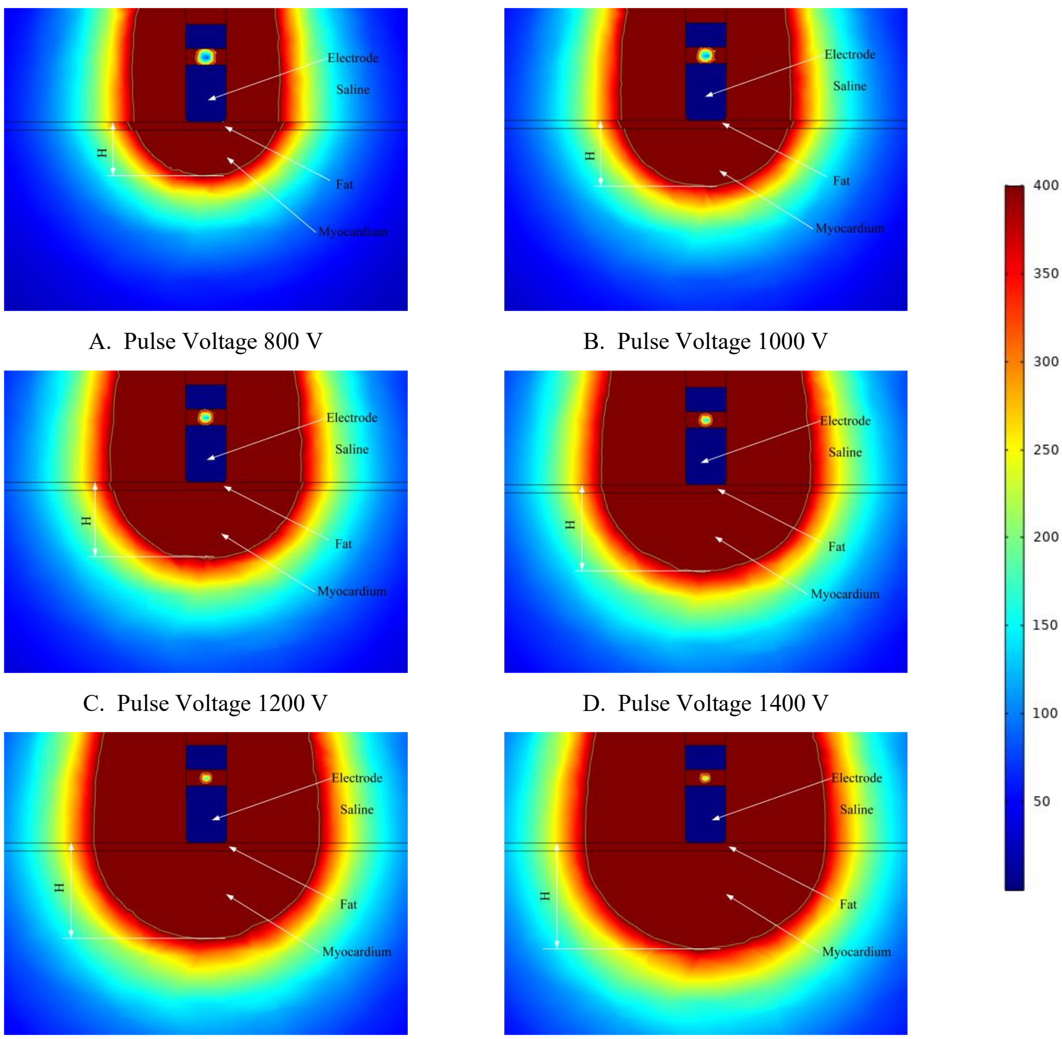
Figure 2. Ablation data for different fat layer thicknesses at a pulse voltage of 1200V.

Table 3. 1400-1800V ablation data

1400V			16000V			1800V		
D	H	h	D	H	h	D	H	h
0.0	6.5	6.5	0.0	7.3	7.3	0.0	7.9	7.9
0.5	5.4	4.9	0.5	6.0	5.5	0.5	6.6	6.1
1.0	5.0	4.0	1.0	5.7	4.7	1.0	6.0	5.0
1.5	5.0	3.5	1.5	5.3	3.8	1.5	5.8	4.3
2.0	4.5	2.5	2.0	5.3	3.3	2.0	5.5	3.5
2.5	4.4	1.9	2.5	5.2	2.7	2.5	5.4	2.9

D: thickness of fat layer (mm); H: total depth of ablation (mm); h: thickness of ablated myocardium (mm)

3.2 Effect of the same fat layer thickness at different voltages



A. Pulse Voltage 800 V

B. Pulse Voltage 1000 V

C. Pulse Voltage 1200 V

D. Pulse Voltage 1400 V

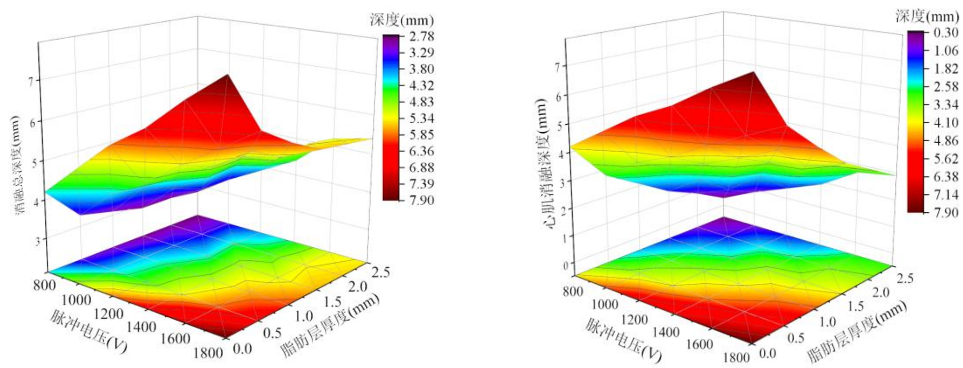
E. Pulse Voltage 1600 V

F. Pulse Voltage 1800 V

Figure 3. Ablation data at different pulse voltages for a fat layer thickness of 0.5 mm.

In order to study the effect of fat layer thickness on the ablation area more deeply, we considered the effect of the same fat layer thickness on the myocardial ablation area from the perspective of using different pulse voltages for PFA. Figure 3 shows the damage to the ablation area by PFA with pulse voltages ranging from 800 V to 1800 V at a fat layer thickness of 0.5 mm. Figure 3A shows that at a pulse voltage of 800V, the myocardial layer was ablated to a depth of 3.5 mm; Figure 3B shows that at a pulse voltage of 1000 V, the myocardial layer was ablated to a depth of 4.1 mm; Figure 3C shows that at a pulse voltage of 1200 V, the myocardial layer was ablated to a depth of 4.7 mm; Figure 3D shows that at a pulse voltage of 1400 V, the myocardial layer was ablated to a depth of 5.4 mm; Figure 3E shows that at a pulse voltage of 1600 V, the myocardial layer was ablated to a depth of 6.0 mm; and the depth of damage of the ablated myocardial layer was 6.6 mm at a pulse voltage of 1800 V as shown in Figure 3F.

From Fig. 3, we can conclude that the depth of myocardial tissue damage in the ablation region is getting deeper with the increase of pulse voltage (pulse voltage: 800 V, depth of damage: 3.5 mm; pulse voltage: 1200 V, depth of damage: 4.7 mm; pulse voltage: 1600 V, depth of damage: 6.0 mm.). However, we can see that as the voltage increases linearly, the depth of PFA damage to the myocardium does not have a linear relationship, and the ability of the voltage to damage the myocardial layer is becoming smaller. In order to understand more deeply the effect of fat layer thickness on the ablation region, we use two parameters of fat thickness and pulse voltage to make the ablation region response surface as shown in Figure 4.



A. Voltage, fat effect on total ablation depth

B. Voltage, fat effect on depth of myocardial ablation

Figure 4. Schematic diagram of ablation at different factor levels.

We show the effect of fat layer thickness and pulse voltage on the ablation area with 3D response surface plots, and we are not trying to find an optimal solution for a certain ablation depth here. From the 3D response surface plots, we can get that the total ablation depth is not linear with the linear increase of the fat layer thickness at the same pulse voltage, and with the increase of the fat layer thickness, the obstruction effect of the fat on the ablation area is more obvious. At the same fat layer thickness with the pulse voltage linearly increases the total depth of ablation is not a linear relationship, with the increase of pulse voltage, the fat on the ablation area of the obstruction effect is also more obvious.

4. DISCUSSION

4.1 Main findings

Currently, a large number of clinical experts have a strong interest in PFA for the treatment of AF, and studies have demonstrated that PFA, with its unique tissue selectivity, can effectively reduce damage to other tissues (such as esophagus, nerves, etc.) in the vicinity of the ablation area [22-24]. Some studies have demonstrated that the presence of epicardial fat layer may affect the tissue ablation effect of PFA. This may be due to the fact that the electrical conductivity of adipose tissue is smaller than that of myocardial tissue, and researchers have made studies on the effect of fat on ablation from potato experiments and other simulation experiments [9-11]. However, to date, we are not aware of any studies that have investigated the ablation effect of PFA on ablated tissue for different fat layer thicknesses and pulse voltages during epicardial ablation. To the best of our knowledge, our study is the first study to evaluate the effect of fat layer on the ablated area during epicardial ablation from multiple fat thicknesses and multiple pulse voltages using computational modeling. In our study, three-dimensional modeling was performed using computers to simulate multiple combinations of fat layer thicknesses and pulse voltages. The main results of this study are as follows:

1) The fat layer has a hindering effect on PFA ablation; the thicker the fat layer, the stronger the effect on PFA energy hindrance (under 1200 V pulse voltage, when the thickness of the fat layer comes to 2.5 mm, the total depth of ablation is 3.9 mm.).
2) At the same pulse voltage, the total depth of ablation varied less when the fat layer thickness reached 1.5 mm (under 1600 V pulse voltage, when the thickness of the fat layer comes to 1.5 mm, 2.0 mm, 2.5 mm, the total depth of ablation is 5.5 mm, 5.3 mm, 5.2 mm.).
3) At the same pulse voltage, there was a step change in the total depth of PFA ablation when the fat layer was 0.0 mm and when the fat layer was 0.5 mm (1000 V: 5.1 mm and 4.1 mm; 1400 V: 6.5 mm and 5.4 mm; 1800 V: 7.9 mm and 6.6 mm.).
4) At different pulse voltages, the total ablation depth appears to have a linear relationship with the pulse voltage when a fat layer is present (fat layer thickness 0.5 mm: total depth of ablation: 3.5 mm, 4.1 mm, 4.7 mm, 5.4 mm, 6.0 mm, 6.6 mm.).

The present study is a study of the epicardial fat layer affecting the area of PFA, and the study of the fat layer is of strong clinical relevance for the wall permeability of PFA. Our results show that due to the huge difference in electrical conductivity between the fat layer and the myocardial layer (myocardium: 0.281 S/m, fat: 0.0438 S/m.), this can lead to the fat itself being less conductive than the myocardium, in other words the value of the electric field of the myocardial layer of the same thickness is higher than that of the fat layer. This is also verified in our computational modeling, where the fat layer has a certain hindering effect on the ablation of PFA, and this hindering effect becomes progressively larger as the thickness of the fat layer increases.

For the first time, we investigated the effect of the epicardial fat layer on the ablation region using a three-dimensional model, and in our computational model, the total depth of ablation in the PFA region appeared to have a close linear relationship with the voltage, as given in Article 4 of our summary. It is worth noting that due to the large pulse voltage intervals we set, this finding still deserves a more detailed study. Meanwhile, we found that when the thickness of the fat layer reached 1.5 mm, the total depth of the PFA area changed less with the increase of the fat layer thickness under the same pulse voltage in our model, and the total depth of ablation appeared to have some retraction (1000 V: 3.7 mm, 3.4 mm, 3.4 mm; 1600 V: 5.3 mm, 5.2 mm, 5.2 mm.). In addition, our computational modeling this time did not address whether different pulses would have an effect on this ablation region hindering effect on the fat layer, which still warrants further in-depth study in the follow-up.

4.2 Limitations

We derived these data from computer modeling. We would like the data on the influence of the fat layer on ablation to come directly from carrier experiments, but so far we are not aware of any similar studies. Although we recognize the limitations of our model compared to patients, we try to approximate the real human environment in our simulations, e.g., simulation of the electrical conductivity of different tissues. In our simulations, the pulse voltage data are spaced widely, and some invisible ablation data do not seem very obvious (such as the total ablation depth is linearly related to the pulse voltage), but nevertheless, we can humanly analyze the data from more than one fat layer to obtain them.

5. SUMMARY

In this paper, we made a study on the effect of different thicknesses of fat layer on the ablation area of PFA. We found that compared with the presence of only the myocardial layer, the presence of a fat layer caused a decrease in the ablation depth of PFA, and the fat layer had a certain hindering effect on the ablation depth. When the fat layer reaches a certain thickness, the effect of the fat layer on the total depth of ablation gradually decreases. In addition, under the same thickness of fat layer and different pulse voltages, the total ablation depth seems to have a linear relationship with the pulse voltage, which needs to be verified by more detailed grading of pulse voltage. In conclusion, the presence of the fat layer is a hindrance to PFA, and we hope that different data will be available in the future to validate our work, and we also hope that our simulation data will have a positive effect on clinical studies.

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