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Difference in tissue temperature change between two cryoballoons

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ABSTRACT

Background Cryoballoon ablation, especially Arctic Front Advance Pro (AFA-Pro) (Medtronic, Minneapolis, Minnesota, USA), has been widely recognised as a standard approach to atrial fibrillation (AF). Recently, Boston Scientific has released a novel cryoballoon system (POLARx). Despite comparable acute clinical outcomes of these two cryoballoons, the recent study reported a higher complication rate, especially for phrenic nerve palsy, with POLARx. However, their impact on biological tissue remains unclear.

Objective The purpose of our study is to evaluate temperature change of biological tissue during cryoablation of each cryoballoon using a porcine experimental model.

Method A tissue-based pulmonary vein model was constructed from porcine myocardial tissue and placed on a stage designed to simulate pulmonary vein anatomy and venous flow. Controlled cryoablations of AFA-Pro and POLARx were performed in this model to evaluate the tissue temperature. A temperature sensor was set behind the muscle and cryoballoon ablation was performed after confirming the occlusion of pulmonary vein with cryoballoon.

Results The mean tissue nadir temperature during cryoablation with AFA-Pro was −41.5°C±4.9°C, while the mean tissue nadir temperature during cryoablation with POLARx was −58.4°C±5.9°C (p<0.001). The mean balloon nadir temperature during cryoablation with AFA-Pro was −54.6°C±2.6°C and the mean balloon nadir temperature during cryoablation with POLARx was −64.7°C±3.8°C (p<0.001).

Conclusion POLARx could freeze the biological tissue more strongly than AFA-Pro.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Cryoballoon ablation (Arctic Front Advance Pro (AFA-Pro) (Medtronic) and POLARx (Boston Scientific)) has been widely recognised as a standard approach to atrial fibrillation.

⇒ Despite comparable acute clinical outcomes of these two cryoballoons, their impact on biological tissue remains unclear.

WHAT THIS STUDY ADDS

⇒ Our study evaluated temperature change of biological tissue during cryoablation of each cryoballoon using a porcine experimental model.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our study revealed that POLARx could freeze the biological tissue more strongly than AFA-Pro.

⇒ We have to be more careful about phrenic nerve palsy during cryoablation with POLARx.

INTRODUCTION

Cryoballoon ablation, especially, Arctic Front Advance Pro (AFA-Pro) (Medtronic, Minneapolis, Minnesota, USA), has been widely recognised for its efficacy and feasibility as a standard approach to atrial fibrillation (AF).[1 2] Recently, a novel cryoballoon system, Boston Scientific's cryoballoon (POLARx) has become available. Cryoballoon ablation using Medtronic's AFA-Pro and Boston Scientific's cryoballoon (POLARx) have been reported to have comparable efficacy for pulmonary vein isolation in patients with AF.[3 4]

The balloon temperature during cryoballoon ablation is often used as a reference for treatment, and inadequate balloon temperature drop may be associated with recurrence of AF following cryoballoon ablation.[5] However, it is not yet known if cryoballoon temperature accurately reflects actual tissue temperature.

Although both POLARx and AFA-Pro use nitrous oxide (N_2O) (−88.2°C) for treatment, the nadir temperature of each balloon during cryoablation is different. In a previous report, the mean nadir temperature of AFA-Pro was nearly −51°C and the mean nadir temperature of POLARx was reportedly −61°C in the clinical setting.[6] Although the acute clinical outcomes of these two cryoballoons were comparable, a higher rate of phrenic nerve palsy was observed in patients treated with POLARx compared with those treated with AFA-Pro.[7] However, the effects of different balloon temperatures on the biological tissue have not been known yet. Therefore, the purpose of our study is to evaluate temperature change of biological tissue during cryoablation of each cryoballoon in an in

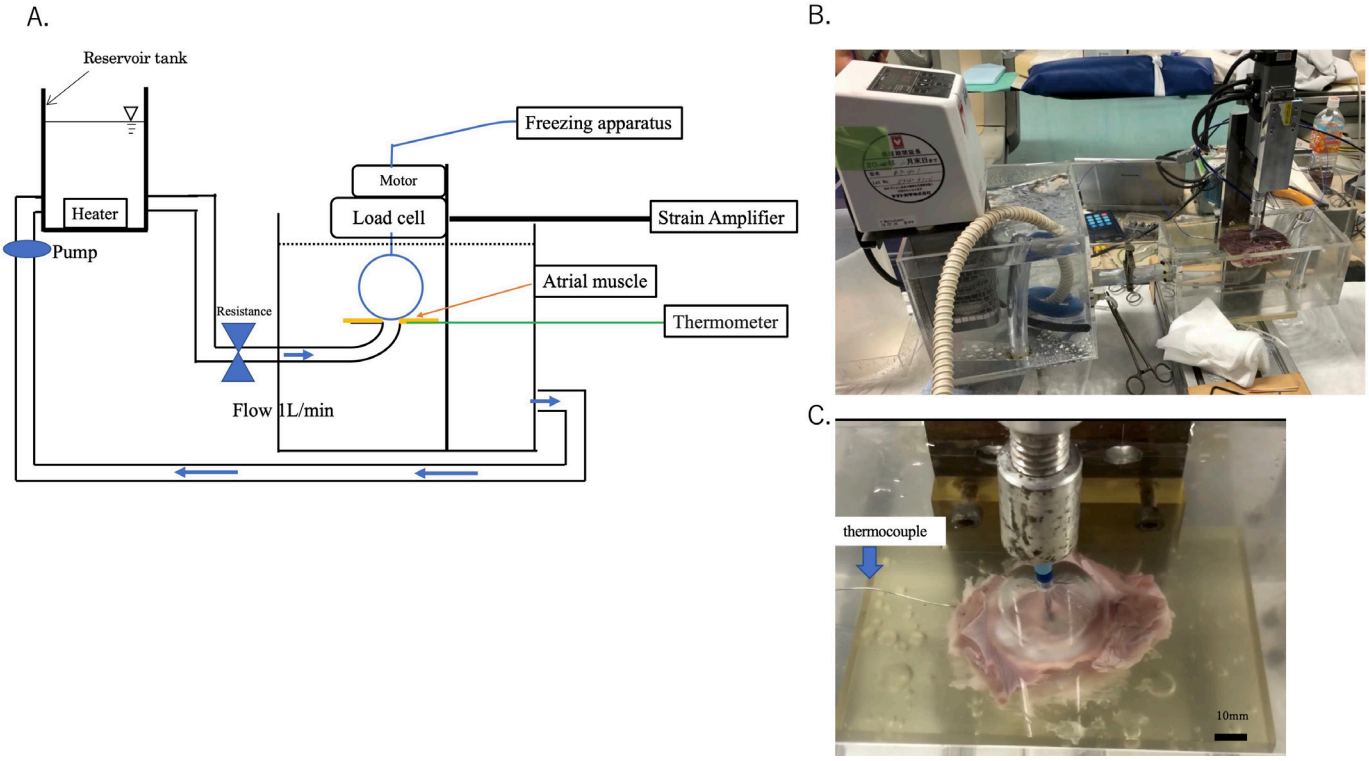

Figure 1 In vitro experimental setup. (A, B) A simulated pulmonary venous flow comes from the reserved tank through the apparatus, over the distal hemisphere of the balloon. The flow was controlled with the resistance. (C) The details of the pulmonary vein model. Thermocouple was set behind the biological tissue.

vitro model that simulates human pulmonary venous anatomy and flow.

METHOD

In vitro simulations were conducted in a plastic tank containing 0.9% normal saline, maintained at 37°C by a circulating water pump. A tissue based pulmonary vein model was constructed from porcine myocardial tissue and then placed on a stage designed to simulate pulmonary vein anatomy and venous flow. Initially, we confirmed the occlusion of the pulmonary vein model by the cryoballoon and simultaneously recorded the minimum force required to occlude the model by the cryoballoon. Cryoballoon and tissue temperatures were recorded during cryoablation. About pulmonary venous flow, the goal was to simulate a pulmonary venous flow of 1 L/min, using previous human data and the previous in vitro research model.[8 9]

In vitro experimental setup

We designed a stage with a 15 mm diameter hole in the centre based on the pulmonary vein diameter (figure 1A,B). The hole was connected to a 15 mm diameter plastic tube to maintain the flow from the tank. Fresh porcine hearts were commercially obtained, and pulmonary vein and left atrium tissue were set to the designed stage (figure 1C). The diameter of the normal human pulmonary vein ostium has been reported to be 10–13 mm, whereas the diameter of the pulmonary vein ostium measured in patients with AF has been reported to be 14–16 mm.[10 11]

The flow rate was adjusted by resistance to simulate a pulmonary vein flow rate of 1 L/min. A temperature sensor (A1.6-K-J1-M1-L300-TC1-ASP, ANRITSU METER, Japan) with a diameter of 0.5 mm was attached 5 mm under the myocardial tissue to measure temperature during cryoablation The temperature was maintained at 37°C using a thermo system (ThermoMate BF-401, Daiwa Kagaku, Japan).

Measuring the force to occlude pulmonary vein by cryoballoon

The proximal portion of the cryoballoon catheter was fixed to a pillar and connected to a motor (DRSM42RG, Oriental Motor, Japan) and a load cell (TU-MXR2(T)-g(50N), TEAC, Japan) to measure the force exerted by the catheter tip on tissue. The load cell was connected to a strain amplifier (DPM-900, KYOWA, Japan) to display the force acting on the tissue. The cryoballoon was inflated in a standard manner in a water bath and after confirming that the cryoballoon occluded the myocardial tissue with black paints, the minimum force at that point was recorded and cryoablation was initiated. The temperature of the cryoballoon and tissue temperatures were recorded after cryoablation. Seven unused pulmonary vein and atrial tissue was used for the porcine myocardium (n=7, each).

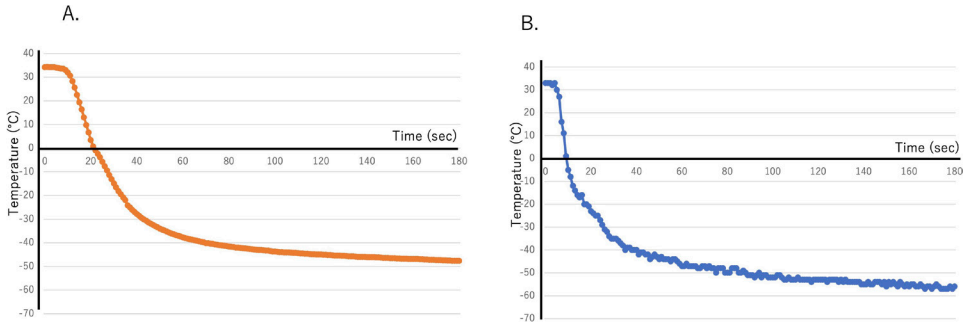

Figure 2 Examples of balloon and tissue temperature changes of Arctic Front Advance-Pro (AFA-Pro). (A) The tissue temperature change during cryoablation of AFA-Pro and the tissue nadir temperature was −47.6°C. (B) Cryoballoon temperature change of AFA-Pro and the cryoballoon nadir temperature was −56°C.

Ablation protocol

For cryoballoon ablation, Medtronic's 28 mm fourth-generation ablation catheter (AFA-Pro) and Boston Scientific's POLARx were used in our study. Cryoablation was performed for 180 s based on the previous clinical report and the freeze cycle was terminated.[12]

Outcomes

Tissue nadir temperature during cryoablation of each cryoballoon was our primary evaluation. The balloon temperature, the tissue temperature and the minimum force to occlude pulmonary vein model by cryoballoon were also evaluated.

Statistics

Continuous variables are given as mean±SD or median (quartiles) and were compared by two-sample Student's t-test, or Mann-Whitney U test, depending on the distribution of variables. A p<0.05 was considered statistically significant.

RESULT

Examples of balloon and tissue temperature changes of each cryoballoon

The tissue temperature change during cryoablation of AFA-Pro was shown in figure 2A, and the cryoballoon temperature change of AFA-Pro is shown in figure 2B. The tissue nadir temperature was −47.6°C and the cryoballoon nadir temperature was −56°C. Figure 3A shows the tissue nadir temperature change during cryoablation POLARx and figure 3B shows the balloon temperature change of the POLARx. The tissue nadir temperature was −60.0°C and the balloon temperature was −63°C during cryoablation.

Differences in tissue and cryoballoon temperatures of two cryoballoons

The mean tissue nadir temperature during cryoablation with AFA-Pro was −41.5°C±4.9°C, while the mean tissue nadir temperature during cryoablation with POLARx was −58.4°C±5.9°C, which was significantly lower for POLARx (p<0.001) (figure 4A). Additionally, the mean balloon nadir temperature during cryoablation with AFA-Pro was −54.6°C±2.6°C and the mean balloon nadir temperature during cryoablation with POLARx was −64.7°C±3.8°C, which was significantly lower for POLARx (p<0.001) (figure 4B).

The force required to occlude the pulmonary vein of two cryoballoons

The minimum force needed to occlude the pulmonary vein model by each cryoballoon was 0.85±0.24 n (86.3±24.2 gf) for AFA-Pro and 0.91±0.41 n (92.7±41.9 gf) for POLARx, but the difference was not statistically significant (p=0.731).

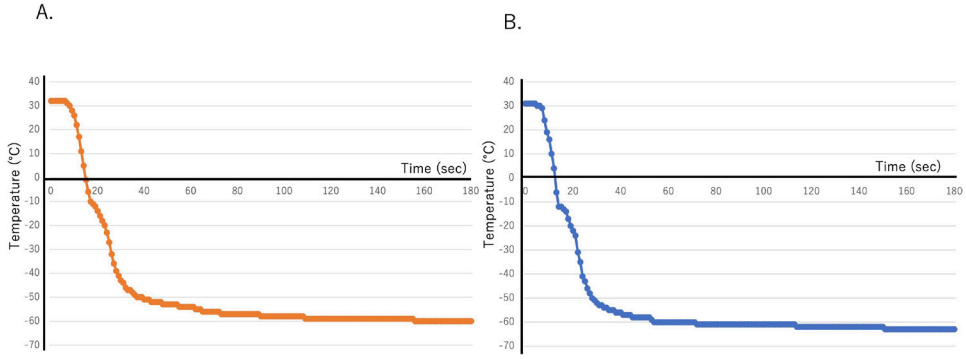

Figure 3 Examples of balloon and tissue temperature changes of POLARx. (A) The tissue temperature change during cryoablation of POLARx and the tissue nadir temperature was −60.0°C. (B) Cryoballoon temperature change of POLARx and the cryoballoon nadir temperature was −63.0°C.

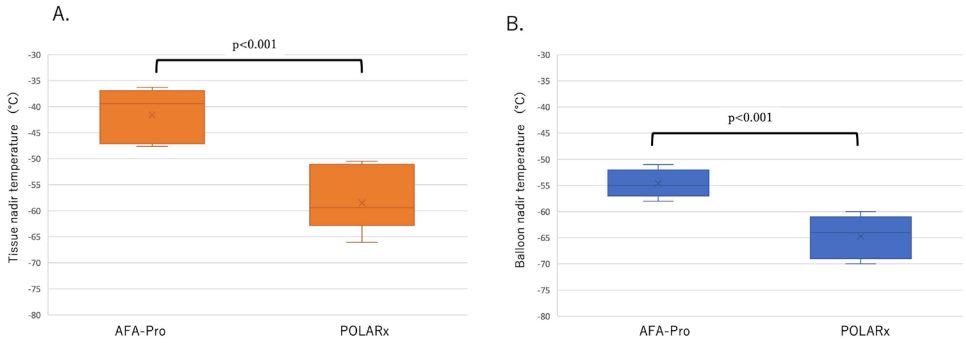

Figure 4 Differences in tissue and cryoballoon temperatures of two cryoballoons. (A) The mean tissue nadir temperature during cryoablation with Arctic Front Advance Pro (AFA-Pro) and POLARx (n=7). (B) The mean balloon nadir temperature during cryoablation with AFA-Pro and POLARx (n=7).

DISCUSSION

Our study demonstrates that POLARx can freeze biological tissue more effectively than AFA-Pro, as reflected in the balloon temperature. Moreover, even though the balloon materials of POLARx and AFA-Pro differed, the force required to occlude the pulmonary vein was not statistically different.[13]

Comparison with previously reported in vitro models of cryoballoon ablation

In this study, we constructed an experimental model to evaluate the temperature change of biological tissue treated with each cryoballoon. With regard to the experimental model's validity, a prior study investigating the temperature changes in cryocatheter (Freezor Max, Medtronic) reported that the average minimum temperature during cryoablation was −37.9°C±4.3°C, indicating that the variation observed in our study was comparable to that of the previous experimental system.[14] Another previous report evaluated temperature changes in bovine tissue using a cryoballoon (AFA: Medtronic), and this report reported that the tissue temperature dropped to −48.3°C. In this report, a thermocouple was implanted at 1 mm depth from the surface of pulmonary vein tissue. In our study, the thermocouple was placed at a deeper place of the atrial muscle, which may have resulted in a slightly higher temperature.[8]

Factors contributing to the differences of temperature variation between AFA-Pro and POLARx

From the results of this study, it can be determined that POLARx could freeze the biological tissue more strongly than AFA-Pro, and the balloon temperature was lower for POLARx. A previous study reported that POLARx could form a larger area of ice around the balloon during cryoablation with saline than AFA-Pro, which was attributed to the difference in N_2O flow rate[15] (figure 5). Table 1 summarises the characteristics of the two cryoballoons used in the study. The difference in the N_2O flow rate between the two cryoballoons could potentially explain the temperature discrepancy observed. The N_2O cooling flow rate for POLARx was 7800 standard cubic centimetres per min (sccm), which was greater than the 7200 sccm for AFA-Pro.[16]

In addition, the internal pressure of the cryoballoon during cryoablation could affect our result. The internal pressure of the cryoballoon of POLARx during cryoablation was reportedly to be 2.5 psi (0.2 atm at gauge pressure)and 18–20 psi (1.2 atm at gauge pressure) for AFA-Pro.[13] The internal pressure of POLARx is 1.2 atm (absolute pressure), which implies that the boiling point of N_2O is around −85°C based on the vapour pressure curve of N_2O published by the Linde company. On the other hand, the internal pressure of Aortic Advance Pro is 2.2 atm (absolute pressure), indicating that the boiling point of N_2O is around −75°C.[17] Recent study showed revealed a high occurrence of phrenic nerve palsy in patients treated with POLARx, which is consistent with our findings.[7] Another reason for the high frequency of phrenic nerve palsy in POLARx is the softness of the

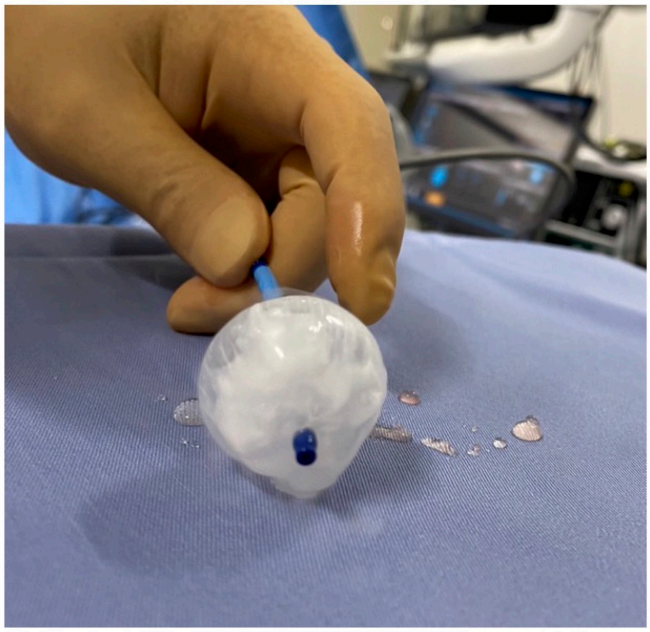

Figure 5 Ice formation with cryoablation in saline water Ice formation around cryoballoon (AFA-Pro) with saline water. AFA-Pro, Arctic Front Advance Pro.

Table 1 Different characteristics of POLARx and Arctic Front Advance Pro (AFA-Pro)

	POLARx	AFA-Pro
Sheath diameter (Fr)	12.7	12.0
N_2O fluid flow during freeze (sccm)	7800	7200
Balloon size (mm)	28	28
Pressure during freeze (psi)	2.5 psi (0.2 atm)	18–20 psi (1.2 atm)
Mean Nadir balloon temperature (°C)	−61	−51

N_2O, nitrous oxide.

POLARx. The cryoballoon of POLARx is softer than that in AFA-Pro, which could contribute to the increased occurrence of phrenic nerve palsy, possibly due to deeper freezing within the pulmonary vein. We have to be more careful about phrenic nerve palsy during cryoablation with POLARx and should take care not to freeze deeper inside the pulmonary vein during cryoablation with POLARx.

The force required to occlude pulmonary vein model by cryoballoon

There has been no study investigating the minimum force required to occlude the pulmonary vein using a cryoballoon. Our data show that the force required to occlude the pulmonary vein is not statistically different between the two cryoballoon systems, despite differences in their materials.[13 18] Some readers argue that it is necessary to compare under the same force; however, the materials of the two cryoballoons were different. One report mentioned that the material of POLARx was more flexible and shapeable than POLARX, which may require stronger force to achieve occlusion with POLARx.[15] We believe that ensuring the minimum occlusion of the biological tissue is more important than conducting research under the same force without achieving proper occlusion of the tissue.

Force for treatment: cryoballoon ablation versus radiofrequency catheter ablation

Based on our results, it appeared that cryoballoon treatment required a stronger force compared with radiofrequency (RF) catheter ablation. However, we need to consider the surface area of the cryoballoon, so the contact pressure (force adjusted for catheter surface area) should be calculated. We predict the surface area of the RF catheter (ThermoCool SmartTouch STSF, Biosense Webster) as follows: tip width=8 Fr = 2.67 mm, tip length=3.5 mm and surface area=34.9 mm. As for the cryoballoon, the surface of the cryoballoon catheter (AFA-pr) can be estimated based on an ellipse (major axis set at 14 mm, based on AFA-Pro diameter of 28 mm and minor axis set at 10.5 mm, based on half the length from the N_2O gas injection port to the cryoballoon's thermocouple). The surface area is calculated to be 2092 mm^2. A previous study suggested that it is desirable to apply a force of 10 g (0.098N) or more to energise the RF catheter,[19] and a pressure of 2.8×10^−3 N/mm^2 or more is desirable based on the surface area of the RF catheter. Based on our study's results, the pressure exerted on the pulmonary vein by the AFA-Pro cryoballoon was 0.4×10^−3 N/mm^2, indicating that the cryoballoon may treat the pulmonary vein with less force compared with the RF catheter with consideration to the surface area of catheter. One reason for the cryoballoon's ability to achieve effective treatment with less force is that the RF catheter requires point-by-point ablation, which demands more force to ablate the pulmonary vein tissue. Conversely, the cryoballoon can easily treat the pulmonary veins with less force due to the continuity of its treatment.

Limitations of this study

In this study, there are some limitations. First, the temperature change of the cryoballoon was assessed at only one point. To overcome this limitation, methods such as using more thermocouple thermometers or thermography to evaluate temperature changes at multiple points should be considered. Additionally, this study only focused on temperature changes and did not evaluate the actual histological changes in the atrium. In the future, it will be important to verify the relationship between tissue temperature changes and histological changes. Finally, we did not check whether thermocouple electrode was in direct contact with the N_2O jet or between the jets, which could affect our results.

CONCLUSION

From our study, POLARx could freeze the biological tissue more strongly than AFA-Pro. Inner pressure of cryoballoon during cryoablation and flow rate of N_2O might affect the strength of freezing between two cryoballoons.

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Contributors TH: design, data collection, analysed data, interpretation, writing original draft, critical revision of the article; KH: design, data collection; JT: design, data collection; KI: concept, design, data collection, interpretation; MM: data collection, interpretation; SS: data collection, interpretation.

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