# Original Article The efficacy, feasibility and safety of a novel wire-guided ablation catheter for ablation of the right superior pulmonary vein: an experimental study in pigs

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Abstract: The efficacy, feasibility of use and safety of a novel wire-guided ablation catheter for atrial fibrillation ablation was evaluated experimentally. Pigs (n = 8) were sedated, intubated and randomized into wire-guided and general saline-irrigated ablation catheter experimental groups (n = 4 per group) successively, in a randomized paired study design. Catheters were inserted into the coronary sinus or right atrial appendage via the femoral vein. Transseptal puncture was guided by X-ray. The left atrium (LA) and right superior pulmonary vein (RSPV) were reconstructed using EnSite Velocity<sup>™</sup> mapping. Contact-mapping and contact-ablation were performed in the antrum of the RSPV. Average procedure and exposure times of circumferential RSPV ablation and RSPV-antrum radial-linear ablation were shorter in pigs who received wire-guided catheter ablation compared with those who received salineirrigated catheter ablation (procedure time:  $22.5 \pm 3.8$  vs.  $32.5 \pm 5.1$  min, and  $11.3 \pm 1.9$  vs.  $15.8 \pm 2.5$  min, respectively; P < 0.001) (exposure time: 7.5 ± 1.1 vs. 11.4 ± 2.2 min, and 3.4 ± 0.5 vs. 6.7 ± 1.3 min, respectively; P< 0.001). During ablation, the catheter fell into the right atrium fewer times, and took less time to re-insert into the LA, in the wire-guided compared with the saline-irrigated catheter group  $(0.7 \pm 0.8 \text{ vs. } 5.1 \pm 1.3 \text{ times}$ , and  $1.0 \pm 0.2$ vs. 5.0 ± 0.9 min, respectively; P < 0.001). There were no guidewire-associated thromboses and no scratches, tears or thrombiin in the RSPV intima during the experimental period. The findings indicate that the stability, accuracy of positioning and safety of the wire-guided ablation catheter are superior to the general saline-irrigated ablation catheter for ablation of the RSPV.

Keywords: Pulmonary vein, atrial fibrillation, radiofrequency ablation, ablation catheter

#### Introduction

Circumferential pulmonary vein (PV) ablation is a classical surgical approach for the treatment of atrial fibrillation (AF), but requires complete encirclement of the PV orifice in order to electrically isolate the PVs. The critical factor for achieving PV isolation is that all ablation sites must completely penetratethe the atrial muscle layer [1, 2]. Generally, the procedure takes at least 30 minutes for an experienced electrophysiological physician to perform, and can take significantly longer if the practitioner is inexperienced [3]. Furthermore, during the ablation procedure, the direction and distance of travel of the ablation catheter in the left atrium (LA) are poorly controlled, resulting in contact instability and gap formation which can lead to recovery of PV connections and the recurrence of AF after ablation [4, 5].

Effective manipulation of the ablation catheter in the LA is therefore critical to ensuring the success and efficiency of AF ablation. Clinical trials have demonstrated that the major risk factor for the recurrence of AF after PV isolation is the recovery of electrical connections between the PVs and the LA [6]. The recovery of PV connections is dependent on many factors. These include the thickness of the local atrial muscle as well as the positioning and stability of the catheter [7]. The local potential amplitude partially and indirectly reflects the stability and tightness of the contact between the cath-



**Figure 1.** Wire-guided ablation catheter applied in mapping of the left atrium of experimental pigs. A. Wire-guided ablation catheter. The guidewire is shown protruding out from the guidewire distal hole lumen (black arrow). B. Wire-guided ablation catheter positioning and mapping of the RSPV. The guidewire was pushed into the distal RSPV. The mapping electrode was placed in the RA appendage.

eter and the atrial wall [8]. Although the use of a pressure sensing catheter provides an effective means of monitoring catheter manipulation and positioning in order to prevent unstable contact, the success of the procedure is still heavily reliant on the experience of the practitioner [4, 9]. Conventional ablation catheters are typically non-wire-guided ablation catheters that are only suitable for the single-target fixed discharge ablation of paroxysmal supraventricular tachycardias. They are not suitable for multi-target mobile discharge ablation of AF.

A novel wire-guided ablation catheter that is based on the principle of compasses for drawing a circle, may have potential in improving both catheter manipulation and the accuracy of catheter positioning and contacting. The aim of this study was to evaluate the efficacy, safety and feasibility of use of a novel wire-guided ablation catheter for ablation of the right superior pulmonary vein (RSPV), in pigs.

#### Materials and methods

# Experimental materials

The experimental protocol was approved by the Ethics Committees of the Second Military Medical University and Fudan University. The procedures were performed on eight Bama pigs (body weight 50-55 kg), provided by Shanghai Jiaotong University Experimental Animal Center. The novel catheter employed was a wire-guided cold saline-irrigated ablation catheter (Triguy<sup>™</sup>, HuiTai Medical Devices Co., Ltd, Shenzhen, China) based on an 8Fr cold saline-irrigated ablation catheter (4 mm tip) with an additional guidewire lumen. The proximal opening of the guidewire lumen was in the ablation catheter tail, and the distal opening was in the junction between the adjustable and non-adjustable curve segment, forming an angle of 90° after the bend of the ablation catheter tip. The hydrophilic guidewire (0.038") (Terumo Corporation, Maimaigi-choFujinomiya, Japan) and guidewire lumen were aligned together (Figure 1A and 1B). The EnSiteNavX three-dimen-

sional electro-anatomical mapping system (St. Jude Medical Inc., Saint Paul, US) and an IBI-1500T11 radio frequency ablation generator (St. Jude Medical Inc., Saint Paul, US) were used to perform LA and PV model reconstruction and radio frequency current discharge, respectively. An electrophysiological recorder (Segmentation Tool Version 1.0, St. Jude Medical Inc., Saint Paul, US) was used to record 12-lead body surface electrocardiograms (ECGs) and intracardiac ECGs.

# Experimental procedures

Animals were sedated with ketamine (10 mg/ kg, i.m.) and atropine (0.04 mg/kg, i.m.), and retained on the operating table in a supine position for 10 minutes in order to establish intravenous access. Eight pigs underwent endotracheal intubation with an ID7.0 mm catheter, and were mechanically ventilated (A/C model, frequency: 20 beats/min, tidal volume 350-400 ml, respiratory ratio 1:2, oxygen concentration: 60%). General anesthesia was maintained with sevoflurane (1-5%), ketamine (10 mg/kg), and vecuronium (0.04 mg/kg), administered intravenously [10]. The multipolar electrode catheter was inserted into the coronary sinus or the right atrial appendage via the right femoral vein. Transseptal puncture was guided by X-ray at the position of the apex to the xiphoid process. After transseptal puncture, an unfractionated heparin bolus (100 IU/ kg) was administered, and activated clotting time (ACT) remained at  $\geq$  300 seconds.



**Figure 2.** Schematic diagram of the contact/mapping approach. A. Schematic diagram of circumferential PV discontinuous contact. Discontinuous contact/mapping was performed at four separate sites around the circumference of the RSVP (the upper, lower, left and right). B. Schematic diagram of circumferential PV continuous contact. Circumferential PV continuous contact/mapping was performed around the circumference of the RSPV-antrum. C. Schematic diagram of RSPV-antrum radial-liner continuous contact. Contact/mapping was performed at four separate radial-linear sites of the RSPV in the RSPV antrum (upper and lower, before and after). Red dots represent mapping sites; PV: pulmonary vein; RSPV: right superior PV.

ostia, and 20 ml of the X-ray contrast agent (Hengrui Medicine Co., Ltd., Jiangsu, China) was injected for RSPV angiography. To determine the RSPV venography, RSPV angiography images were taken in the following projection positions: poster anterior, right anterior, oblique 45°, left anterior oblique 45°, andhead position 10°. The RSPV ostia was defined as the maximal inflection between the PV lumen and the LA body in pulmonary venography. The diameter of the ostia in the right anterior oblique 45° position was measured with digital calipers (GE medical, Advantx LCV+, USA).

#### Study design

To enable direct comparison of the operating performance of the two catheters, individual animals were randomized into the wire-guided ablation catheter group and the general salineirrigated ablation catheter group, successively. The experimental protocol included contactmapping and contact-ablation in the RSPV antrum. Contact-mapping comprised of circumferential RSPV contact and RSPV antrum radiallinear contact, and contact-ablation comprised of circumferential RSPV ablation and RSPV antrum radial-linear ablation [11]. The sites of circumferential RSPV contact and ablation were both approximately 0.5 cm outside the RSPV ostium. During experimentation, it was found that the probability of the catheter unintentionally falling into the right atrium (RA), and the success of the catheter re-entering the LA, were significantly different between the two treatment groups. The occurrence of this phenomenon was therefore observed and recorded during the experiments, so that it could be incorporated into the analyses. After completion of the experiment, the LA and PV ablation tissues were excised for gross and histopathological observation.

#### RSPV angiography

After transseptal puncture, the catheter sheath was aligned with the lower part of the RSPV

#### Contact-mapping

The major differences between the wire-guided and general saline-irrigated ablation catheters are manifested in their controllability and stability in operation. Therefore, the contact-mapping phase was initially designed to enable comparison of the procedure time and exposure time of the two types of catheter at four separate sites of the circumferential RSPV, as well as along the circumferential RSPV, and radial-linear contact-mapping in the RSPVantrum, for each experimental animal. Standards for contact/mapping under X-ray fluoroscopy were: contacting at each site for at least three seconds, maintaining stability of the ablation catheter and acquiring a clear and stable maximum local potential. Contact-mapping did not involve ablation.

Following atrial septal puncture, the sheath of the catheter entered the LA and PV, and the guidewire was then pushed into the distal RSPV via the guidewire lumen. At that point, the guidewire became a supporting rotating shaft and turned into an axis for the ablation catheter. The ablation catheter was then rotated clockwise or counterclockwise around the guidewire to reach the preset mapping sites. Contact and ablation were achieved by bending or sliding the ablation catheter against the contact-mapping site. The distal catheter rotation was between 0-90°, with the electrode rota-

Animal	Weight (kg)	Heart rate (beats/min)	Oxygen saturation (%)	Ablation energy (W)	Ablation temperature (°C)	Complications		
#1	53.2	105	98	30	43	Ν		
#2	52.8	96	99	30	43	Ν		
#3	51.3	100	97	30	43	Ν		
#4	52.0	109	95	30	43	PT		
#5	54.4	103	96	30	43	Ν		
#6	53.6	99	97	30	43	Ν		
#7	52.9	108	98	30	43	Ν		

Table 1. Basic study parameters

PT: pericardial tamponade.

tional radius increasing when the distal curve was narrowed, and reducing when it was released. Macrocyclic and microcyclic mapping were performed when the distal electrode had alarge radius of curvature and a small radius of curvature, respectively. Observation targets included: (1) circumferential RSPV discontinuous contact, which consisted of the ablation catheter sequentially contact-mapping the four scheduled separated sites in the upper, lower, left and right side of the circumference of the RSPV (as shown in Figure 2A); (2) circumferential RSPV continuous contact, which consisted of theablation catheter successively contactmapping the scheduled successive mapping sites along the circumference of the RSPV (as shown in Figure 2B); (3) RSPV-antrum radiallinear continuous contact, which consisted of the ablation catheter successively contactmapping the four scheduled mapping sites along the longitudinal axis of the RSPV-antrum. Local double potentials were targeted from the PV ostiumto the PV-LA junction where there was no PVpotential, and the ablation catheter was slowly and continuously retracted to the LA side, along the preset line (as shown in Figure 2C).

# Contact-ablation

The circumferential RSPV ablations were perfrmed approximately 0.5 cm outside of the RSPV ostia, and elimination of the electrical potentials between the PV and the LA was the endpoint of the procedure. The RSPV-antrum radial-linear ablation target was local double potentials between the PV ostium to PV-LA junction, where there was no PV potential. The ablation catheter was moved backwards and forwards twice to check for local potentials, and four radial-linear ablation lines were completed. The radio frequency was delivered to the PV antrum at a maximum temperature of 43°C, power between 25 and 35 W and a saline flow rate of 17 ml/ min for each lesion. The ablation catheter was transferred to the next target ablation site when the local potential had disappeared or decreased by more than 90%.

# Re-insertion of the ablation catheter into the LA

If, during the experimental procedure, the ablation catheter unintentionally fell into the RA, it had to be re-inserted into the LA before ablation could continue. The number of times the ablation catheter unintentionally fell into the RA and the duration of time it took for it to be reinserted into the LA from the previous atrialseptal puncture hole, were recorded and compared between the two catheter types (wire-guided and general saline-irrigated).

# Pathological observations

As part of the gross pathological inspection, the heart was excised and flushed with saline and the guidewire was installed into the RSPV after the animals had been euthanized. Lesions in the atrial septal puncture, atrial endometrium, RSPV ostium, LA appendage, pulmonary vein outer membrane, and the atrial pericardial surface were examined. The presence of mural thrombus in the distal opening of the guidewire and along the guidewire surface was grossly examined. The RSPV was slit open and carefully observed. For histological evaluation, tissue samples were taken from the RSPV, fixed in 10% buffered formalin, embedded in paraffin, cut into 3 µm thick sections, stained with hematoxylin-eosin (H&E) stain, and analyzed under light microscopy (x200) with an Olympus BX43 microscope.

# Statistical analysis

Continuous variables that were normally distributed were presented as means  $\pm$  standard deviation (SD); non-normally distributed variables were reported as medians and interquartile ranges (IQR). The means of two continuous

	Wire-guided ablation catheter (n = 7)	General saline-irrigated ablation catheter (n = 7)	P value
Circumferential RSPV discontinuous contact			
Procedure time (min)	4.2 ± 0.6	9.8 ± 1.6	< 0.001
Exposure time (min)	1.3 ± 0.2	2.6 ± 0.6	< 0.001
Circumferential RSPV continuous contact			
Procedure time (min)	13.9 ± 1.9	21.9 ± 3.2	< 0.001
Exposure time (min)	5.9 ± 1.0	10.6 ± 2.3	< 0.001
RSPV-antrum radial-linear continuous contact			
Procedure time (min)	8.2 ± 1.1	13.7 ± 1.8	< 0.001
Exposure time (min)	2.7 ± 0.4	5.5 ± 1.1	< 0.001

#### Table 2. Contact/mapping of ablation catheter

PSPV: right superior pulmonary vein.



Figure 3. Three dimensional schematic of Contact/ablation sites. The LA and RSPV were reconstructed using the EnSite Velocity<sup>™</sup> mapping system. Red dots represent circumferential RSPV ablation sites; yellow dots represent RSPV-antrum radial-liner ablation sites. LA: left atrium. RSPV: right superior pulmonary vein.

normally distributed variables were compared using the Paired Sample Student's T-test. Data were analysed by SPSS version 19.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism 6 Software (GraphPad Software Inc., SanDiego, CA, USA) was used to construct the schematic diagrams. A *P* value of < 0.05 was considered statistically significant.

#### Results

#### Basic study parameters

Pericardial tamponade occurred in two animals during experimentation, one of which died. Seven animals completed the protocol. The mean diameter of the RSPV, this being the largest point of rotation between the PV and LA, was  $14.0 \pm 2.1 \text{ mm}$  (n = 7), as shown by the RSPV angiography (**Table 1**).

#### Contact-mapping

The circumferential RSPV discontinuous contact procedures as well as the circumferential RSPV continuous contact and RSPV-antrum radiallinear continuous contact procedures were each conducted in the same animal successively. The average procedure and exposure times were significantly less in the wire-guided ablation catheter group than in the paired general saline-irrigated ablation catheter group (P < 0.05) (**Table 2**).

#### Contact/Ablation

The average procedure times of the circumferential RSPV ablation and the RSPV-antrum radial-linear ablation were significantly shorter in the wire-guided ablation catheter group compared with the general saline-irrigated ablation catheter group (22.5  $\pm$  3.8 min vs. 32.5  $\pm$  5.1 min, and 11.3 ± 1.9 min vs. 15.8 ± 2.5 min, respectively) (P < 0.001) (Figure 3). The average exposure times of these ablation procedures were also significantly shorter in the wireguided versus the general saline-irrigated ablation catheter groups (7.5 ± 1.1 min vs.  $11.4 \pm 2.2$  min, and  $3.4 \pm 0.5$  min vs.  $6.7 \pm 1.3$ min, respectively) (P < 0.001) (Figure 3). The magnitude of the differences in procedure time and exposure time were, respectively, 30.8%



**Figure 4.** Average procedure times of circumferential RSPV ablation and RSPV-antrum radial-liner ablation in pigs treated with the novel wire-guided ablation catheter and a traditional saline-irrigated ablation catheter. \*: P < 0.05; \*\*: P < 0.001.



Figure 5. Average exposure times of circumferential RSPV ablation and RSPV-antrum radial-liner ablation in pigs treated with the novel wire-guided ablation catheter and a traditional saline-irrigated ablation catheter. RSPV: right superior pulmonary vein. \*: P < 0.05; \*\*: P < 0.001.

and 34.2% for the circumferential RSPV ablation, and 28.5% and 49.3% for the RSPVantrum radial-linear ablation (**Figures 4** and **5**).

# Re-insertion of the ablation catheter into the LA

During the LA ablation procedure, the ablation catheter unintentionally fell into the RA an average of 0.7  $\pm$  0.8 times in the wire-guided ablation catheter group. This was significantly fewer than that in the general saline-irrigated ablation catheter group (5.1  $\pm$  1.3 times) (*P* < 0.001) (**Figure 6A**). The time taken to re-insert the ablation catheter into the LA from the previous atrial septal puncture hole was also significantly less in the wire-guided ablation catheter group compared with the general saline-irrigated ablation catheter group (1.0  $\pm$  0.2 min vs. 5.0  $\pm$  0.9 min) (*P* < 0.001) (**Figure 6B**).

#### Gross pathology observations

From the intimal side of the left superior pulmonary vein (LSPV), the proximal PV with its muscular sleeve appeared red in color, like the LA, while the distal PV without a muscle sleeve appeared white (**Figure 7A**). The RSPV ostia appeared dark red, with visible swelling and the presence of bulging lesions. Its surface was stained with blood, and part of the area appeared dark brown following circumferential RSPV ablation (**Figure 7B**). In the longitudinal view of the RSPV, the rough circumferential ablation lesions and associated blood were visible in the RSPV-antrum. The PV intima was smooth and no guidewire related injuries or attached thrombi were visible (**Figure 7C**).

#### Histological observations

Tissue transmural injury and coagulation necrosis was visible in the longitudinal sections of the RSPV-antrum radial-linear ablation lesions. The cell structure appeared normal and no obvious endarterectomy detachments were visible (**Figure 7D**).

#### Safety outcome

The pericardial tamponade that occurred in two animals during experimentation resulted from transseptal puncture. One of the affected animals died and the other survived through to completion of the experiment after pericardiocentesis. There was no evidence of PV stenosis either during or after surgery. No thromboses were found on the LA appendage, the guidewire lumen distal aperture or the guidewire surface, andno scratches, tears or thromboses in the RSPV intimaor esophageal injuries were detected in any of the animals.

#### Discussion

This study has evaluated the efficacy and feasibility of using of a novel wire-guided ablation catheter for contact-mapping and contact/ ablation procedures in the RSPV of experimental pigs. The RSPV of pigs has been used in this study because the anatomy of swine RSPV is the closest to that of human beings [12]. The results have demonstrated that the wire-guided catheter has good controllability and higher stability when compared with a general salineirrigated ablation catheter, and significantly reduces both the procedure time and the expo-



**Figure 6.** Comparison of the average number of times the ablation catheter fell into the RA and had to be re-inserted into the LA in pigs treated with the novel wire-guided ablation catheter and a traditional aline-irrigated ablation catheter, and of the duration of re-insertion. LA: left atrium, and RA: right atrium. \*: P < 0.05; \*\*: P < 0.001.



**Figure 7.** Pathological observations of tissue specimens from pigs treated with the novel wire-guided ablation catheter and a traditional saline-irrigated ablation catheter. A. View of the LSPV intima without ablation. The proximal PV with muscle sleeve appears red in color like the LA, while the distal PV without muscle sleeve was white in color. B. View of the RSPV after circumferential RSPV ablation. The RSPV ostia was manifested as dark red, with visible swelling and bulging lesions. The surface was stained with blood, and part of the area was dark brown. C. Longitudinal view of the RSPV. The rough circumferential ablation lesions, with associated blood, were visible in the RSPV-antrum. The PV intima was smooth and no guidewire related injuries were evident. D. Longitudinal section of the RSPV-antrum radial-liner ablation lesions along the PV long axis. LSPV: left superior pulmonary vein, PV: pulmonary vein, LA: left atrium, and RSPV: right superior PV.

sure time. In addition, in the presence of a guidewire, the ablation catheter can more easily be re-insertedinto the LA from the previous atrial septal puncture holein the event that it unintentionally falls into the RA during the ablation procedure. Moreover, no obvious injury to

the RSPV was caused by the guidewire.

The effective manipulation of the ablation catheter in the LA, coupled with the accuracy of positioning and stability of the contactsmade with the ablation targets, are the most critical factors to ensuring the success and efficacy of AF ablation. For inexperienced electrophysiological physicians, owing to the difficult positioning and contact instability of traditional (saline-irrigated) ablation catheters, their subiective movement can be inconsistent with or evencontrary to the actual movement of ablation catheter, both in direction and distance [4]. In recent years, a number of improved AF ablation catheters have been developed, with the sole purpose of improving their controllability and increasing their contact stability.

The introduction of the pressure sensing catheter has significantly increased the longterm success rate of AF ablation. It has reduced the level of distortion in the 3D modelling process that can be caused by the presence of low or high pressure, and thus helps to improve the authenticity and accuracy of threedimensional mapping. In addition, a pressure sensing catheter has advantages in improving the ablation success rate and in reducing the likelihood of complications arising, by facilitating efficacious and safe contact and

ablation, with less dependence on the 'handfeel' of the practitioner [13, 14]. Currently, novel available catheter options include a fixedcurved MARQ catheter [15], PV ablation catheter (PVAC) [10], multi-polar cold saline-irrigated radiofrequency ablation catheter, and a cryoballoon for PV cryoablation [16]. The nonadjustable catheter model increases the stability of catheter contact, but the flexibility of the catheter contact is then lost.

A wire-guided ablation catheter is based on the principle of compasses for drawing a circle, and has a simple structure. When the guide-wire is fixed into the PV, the ablation catheter does not leave PV-antrum. no matter how much the ablation catheter is rotated. As a result, the catheter can achieve more accurate and stable contact with the ablation site (s), regardless of how rapidly or flexibly it is rotated. The wire-guided ablation catheter can be used not only for circumferential PV ablation, but also in LA or RA linear ablation, and apart from the treatment of AF, it is also applicable to right ventricular outflow tract ventricular tachycardia ablation. When the guidewire is inserted into the superior vena cava, the wire-guided ablation catheter can be used in RA ablation, including for the treatment of atrial tachycardia, dual atrioventricular nodal pathways and right heart bypass, and especially foranteroseptal accessory pathway ablation. When the guidewire is inserted into the pulmonary artery, the wire-guided ablation catheter can be used for right ventricular outflow tract ablation. in the treatment of conditions such as right ventricular premature contraction and tachycardia.

The purpose of the contact-mapping conducted in the present study was to enable evaluation of the controllability of the wire-guided ablation catheter in the same animal more comprehensively. In contact-mapping, the ablation catheter was maintained in the target locations for only three seconds with low power discharge, which results in little tissue injury to the atrium and PV, and enables repeated observation. The aim of the circumferential RSPV continuous contact is to stimulate circumferential PV ablation. The ablation catheter is rotated around the guidewire using the principle of compasses and circumferential PV ablation with appropriate pushing or bending of the catheter was completed. Circumferential RSPV discontinuous contact is designed to simulate the process of additional ablation after circumferential PV ablation has been conducted, and to enable assessment of the accuracy of positioning and contacting of the ablation catheter. The RSPVantrum radial-linear continuous contact aims to stimulate LA linear ablation, with the ablation catheter only just positioned on and making contact along the planned ablation line. The

RSPV-antrum radial-linear ablation was then achieved by pushing or bending the catheter. During operation of the wire-guided catheter, there is no need to be concerned about it causing excessive deflection or displacement, for reasons stated above, unless the guidewire causes prolapse of the PV. Therefore, the wireguided ablation catheter greatly increases the stability of catheter manipulation and shortens the training period for less experienced physicians. The results of the contact-mapping have demonstrated that the controllability of the wire-guided ablation catheter is superior to the general saline-irrigated ablation catheter in achieving circumferential PV continuous contact, discontinuous contact and linear contact.

In terms of contact/ablation, the present study has shown experimentally, in pigs, that the wire-guided ablation catheter markedly decreases both the average procedure time and the exposure time of circumferential RSPV ablation and of RSPV-antrum radial-liner ablation, which is consistent with the findings of the contact-mapping part of the study. The advantages of the wire-guided ablation catheter compared with the general saline-irrigated catheter are dependent on the guidewire itself, which plays an important role in aiding the movement of the catheter and in achieving contact with ablation sites. The guidewire and ablation catheter electrode are maintained at a certain angle, so the guidewire cannot establish contact with the ablation electrode and impede its contact during electrical discharge. Thus, the guidewire does not have a negative impact on the efficacy of the ablation, but can actually improve its efficacy because of the increased stability of contact that is achieved. The pathology examinations confirmed that both the wireguided ablation catheter group and general saline-irrigated ablation catheter group exhibited visible transmural tissue injury as a result of PV tissue ablation, indicating success of the procedure.

The main processes of clinical AF ablation involve the manipulation of the catheter in the LA, and a common event is that the general saline-irrigated ablation catheter falls into the RA, especially in RSPV ablation. If the ablation catheter cannot be re-inserted into the LA after several attempts, it is necessary to repeat transseptal puncture [17]. However, this requires the use of an adequate amount of heparin, which therefore increases the risk of bleeding [18]. In the present study, it was observed that the wire-guided ablation catheter had superiority over the traditional salineirrigated catheter inreducing the likelihood of the catheter falling into the RA. In the event that this does occur, the wire-guided catheter can be manipulated very easily (and more quickly) along the axis of the guide-wire though the original atrial septal puncture and into the LA again because the guidewire still remains in the LA. The convenient transportation of the catheter between the RA and the LA is enabled by the use of the wire-guided ablation catheter, and unnecessary manipulations and exposure time can also be reduced.

During catheter manipulation, in the majority of cases the guidewire remains in the PV cavity and keeps constant motion with the PV. Therefore, it was considered important as part of the present study to observe whether its presence in the PV would create friction with and pressure on the PV. In order to prevent this potential damage of the guidewire on the PV intima, it is important that a hydrophilic wire with a soft bending front and a smooth surface should be selected. Furthermore, the distal hole of guidewire lumen should be installed with an anti-leakage locking device to prevent the backflow of blood, but also to prevent the slippage of the guidewire. Moreover, heparin saline could be transfused into the guide-wire lumen side hole to prevent thrombogenesis occurring in the guidewire lumen and the proximal hole. Our anatomical and histological observations revealed no injuries to or thromboses in the PV intima, suggesting that the wire-guided ablation cathetercan be used with a high degree of safety.

# Study limitations

Apart from its successful application in AF ablation, the wire-guided ablation catheter should, in theory, also be appropriate for use in RA, right ventricular and other arrhythmia ablation. However, the present study did not evaluate these other applications specifically. The procedural endpoint of local ablation was when the local potential disappeared or decreased by more than 90% [2]. However, we did not analyze the histological pathology of all ablation sites in every experimental animal. In the limited sample size, contact/mapping and contact/ ablation were performed. Theoretically, the low energy power of the catheter electrode and short time of discharge would be unlikely to cause intimal injury. However, further studies

with a larger sample size are required to confirm the findings.

#### Conclusions

This study has provided experimental evidence that the controllability of the wire-guided ablation catheter is superior to that of the general saline-irrigated ablation catheter for ablation of the RSPV, and that it can be used with a high degree of safety. The direction and distance of travel along the PV can be more reliably controlled with the wire-guided ablation catheter, and it can be more accurately positioned into target ablation sites, improving contact with them.

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# Disclosure of conflict of interest

#### None.

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#### References

- Seshadri N, Marrouche N, Wilber D, Packer D and Natale A. Pulmonary vein isolation for treatment of atrial fibrillation: recent updates. Pacing Clin Electrophysiol 2003; 26: 1636-1640.
- [2] le Polain de Waroux JB, Talajic M, Khairy P, Guerra PG, Roy D, Thibault B, Dubuc M and Macle L. Pulmonary vein isolation for the treatment of atrial fibrillation: past, present and future. Future Cardiol 2010; 6: 51-66.

- [3] Pappone C, Oreto G, Rosanio S, Vicedomini G, Tocchi M, Gugliotta F, Salvati A, Dicandia C, Calabro MP, Mazzone P, Ficarra E, Di Gioia C, Gulletta S, Nardi S, Santinelli V, Benussi S and Alfieri O. Atrial electroanatomic remodeling after circumferential radiofrequency pulmonary vein ablation: efficacy of an anatomic approach in a large cohort of patients with atrial fibrillation. Circulation 2001; 104: 2539-2544.
- [4] Makimoto H, Tilz RR, Lin T, Rillig A, Mathew S, Deiss S, Wissner E, Metzner A, Rausch P, Bardyszewski A, Zhang Q, Kamioka M, Leme C, Kuck KH and Ouyang F. Incidence and anatomical locations of catheter instability during circumferential pulmonary vein isolation using contact force. Int Heart J 2014; 55: 249-255.
- [5] Jiang RH, Po SS, Tung R, Liu Q, Sheng X, Zhang ZW, Sun YX, Yu L, Zhang P, Fu GS and Jiang CY. Incidence of pulmonary vein conduction recovery in patients without clinical recurrence after ablation of paroxysmal atrial fibrillation: mechanistic implications. Heart Rhythm 2014; 11: 969-976.
- [6] Ouyang F, Antz M, Ernst S, Hachiya H, Mavrakis H, Deger FT, Schaumann A, Chun J, Falk P, Hennig D, Liu X, Bänsch D and Kuck KH. Recovered pulmonary vein conduction as a dominant factor for recurrent atrial tachyarrhythmias after complete circular isolation of the pulmonary veins: lessons from double Lasso technique. Circulation 2005; 111: 127-135.
- [7] Yamada T, Murakami Y, Okada T, Okamoto M, Shimizu T, Toyama J, Yoshida Y, Tsuboi N, Ito T, Muto M, Kondo T, Inden Y, Hirai M and Murohara T. Incidence, location, and cause of recovery of electrical connections between the pulmonary veins and the left atrium after pulmonary vein isolation. Europace 2006; 8: 182-188.
- [8] Nakagawa H, Kautzner J, Natale A, Peichl P, Cihak R, Wichterle D, Ikeda A, Santangeli P, Di Biase L and Jackman WM. Locations of high contact force during left atrial mapping in atrial fibrillation patients: electrogram amplitude and impedance are poor predictors of electrode-tissue contact force for ablation of atrial fibrillation. Circ Arrhythm Electrophysiol 2013; 6: 746-753.
- [9] Thiagalingam A, D'Avila A, Foley L, Guerrero JL, Lambert H, Leo G, Ruskin JN and Reddy VY. Importance of catheter contact force during irrigated radiofrequency ablation: evaluation in a porcine ex vivo model using a force-sensing catheter. J Cardiovasc Electrophysiol 2010; 21: 806-811.
- [10] Wijffels MC, Van Oosterhout M, Boersma LV, Werneth R, Kunis C, Hu B, Beekman JD and Vos MA. Characterization of in vitro and in vivo lesions made by a novel multichannel ablation generator and a circumlinear decapolar ablation catheter. J Cardiovasc Electrophysiol 2009; 20: 1142-1148.

- [11] Zhao X, Zhang J, Hu J, Liao D, Zhu Y, Mei X, Sheng J, Yuan F, Gui Y, Lu W, Dai L, Guo X, Xu Y, Zhang Y, He B and Liu Z. Pulmonary antrum radial-linear ablation for paroxysmal atrial fibrillation: interim analysis of a multicenter trial. Circ Arrhythm Electrophysiol 2013; 6: 310-317.
- [12] Gerstenfeld EP and Michele J. Pulmonary vein isolation using a compliant endoscopic laser balloon ablation system in a swine model. J Interv Card Electrophysiol 2010; 29: 1-9.
- [13] Natale A, Reddy VY, Monir G, Wilber DJ, Lindsay BD, McElderry HT, Kantipudi C, Mansour MC, Melby DP, Packer DL, Nakagawa H, Zhang B, Stagg RB, Boo LM and Marchlinski FE. Paroxysmal AF catheter ablation with a contact force sensing catheter: results of the prospective, multicenter SMART-AF trial. J Am Coll Cardiol 2014; 64: 647-656.
- [14] Reddy VY, Dukkipati SR, Neuzil P, Natale A, Albenque JP, Kautzner J, Shah D, Michaud G, Wharton M, Harari D, Mahapatra S, Lambert H and Mansour M. Randomized, controlled trial of the safety and effectiveness of a contact force-sensing irrigated catheter for ablation of paroxysmal atrial fibrillation: results of the tacticath contact force ablation catheter study for atrial fibrillation (TOCCASTAR) study. Circulation 2015; 132: 907-915.
- [15] Deneke T, Schade A, Muller P, Schmitt R, Christopoulos G, Krug J, Szollosi G, Mugge A, Kerber S and Nentwich K. Acute safety and efficacy of a novel multipolar irrigated radiofrequency ablation catheter for pulmonary vein isolation. J Cardiovasc Electrophysiol 2014; 25: 339-345.
- [16] Kuck KH and Furnkranz A. Cryoballoon ablation of atrial fibrillation. J Cardiovasc Electrophysiol 2010; 21: 1427-1431.
- [17] Marcus GM, Ren X, Tseng ZH, Badhwar N, Lee BK, Lee RJ, Foster E and Olgin JE. Repeat transseptal catheterization after ablation for atrial fibrillation. J Cardiovasc Electrophysiol 2007; 18: 55-59.
- [18] Winkle RA, Mead RH, Engel G and Patrawala RA. Safety of lower activated clotting times during atrial fibrillation ablation using open irrigated tip catheters and a single transseptal puncture. Am J Cardiol 2011; 107: 704-708.