

Electro-anatomical mapping of the left atrium before and after cryothermal balloon isolation of the pulmonary veins

Yves Van Belle · Paul Knops · Petter Janse ·
Maximo Rivero-Ayerza · Emile Jessurun ·
Tamas Szili-Torok · Luc Jordaens

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Abstract

Introduction The 28 mm cryoballoon catheter is a device used for pulmonary vein isolation (PVI). The aim of this study was to evaluate the extent of the ablation in the antral regions of the left atrium.

Methods and Results Eighteen patients with drug refractory, symptomatic, paroxysmal AF were enrolled. A 3D electro-anatomic reconstruction of the left atrium was made before and after successful PVI with the 28 mm cryoballoon. Markers were placed at the ostium. Sixteen patients were mapped. Fourteen patients had 4 veins each, and 2 patients had a common ostium of the left sided veins. All separate ostia were isolated in the antral region. The two common ostia showed ostial isolation. There was a significant difference in vein size between the common (29 and 31 mm) and the separate ostia (19 ± 4 mm) ($p < 0.01$). The performance of an additional segmental ablation if balloon PVI did not eliminate all electrical activity, did not influence the extent of the ablation. The earliest left atrial activation during sinus rhythm was located in the superior septal region before ablation in all patients. After ablation, two patients showed a substantial downward shift towards the middle and inferior septal region respectively (NS). Four patients demonstrated a slight downward shift of the first activation.

Conclusions In cryoballoon PVI, the majority of the veins undergo antral isolation. Veins with a diameter larger than the balloon, are isolated ostially. In individual cases, the left atrial activation sequence appears to be altered after ablation.

Keywords Ablation · Arrhythmia · Cryoballoon · Cryoablation · Catheter ablation · Tachyarrhythmias · Atrial fibrillation · Pulmonary veins

1 Introduction

The cryothermal balloon, or cryoballoon, is a novel technology, developed for pulmonary vein (PV) isolation. It is a catheter based device with the potential of performing a circumferential ablation, thus isolating the PV muscular sleeves in a limited number of applications. Since cryothermia causes no PV stenosis [1–3] the ablation can safely be performed at the ostial level of the pulmonary vein, but the question remains to what extent cryoballoon ablation modifies the left atrial substrate. After a large experience in animal testing was achieved by several authors [4–7] the first human results are promising as a treatment for paroxysmal atrial fibrillation (AF) [8]. The aim of this study was to evaluate the effect of the cryothermal balloon on the antral regions of the left atrium.

2 Methods

2.1 Inclusion

Patients with documented symptomatic paroxysmal AF despite antiarrhythmic drugs, at two or more occasions,

Y. Van Belle (✉) · P. Knops · P. Janse · M. Rivero-Ayerza ·
E. Jessurun · T. Szili-Torok · L. Jordaens
Clinical Electrophysiology Unit, Department of Cardiology,
Thoraxcentre, Erasmus Medical Centre,
's Gravendijkwal 230.,
3015 CE Rotterdam, The Netherlands
e-mail: y.vanbelle@erasmusmc.nl

were accepted as candidates for this study. Exclusion criteria were: left atrial dimension > 50 mm measured in the parasternal long axis, as assessed with transthoracic echocardiography, valvular heart disease and advanced age.

2.2 Pulmonary vein isolation procedure

The procedure was performed under conscious sedation. Both femoral veins were used for venous access. A 10 Fr, intracardiac echocardiography (ICE) catheter (Flexview, EP Med Systems, New Jersey, USA) (ICE) was introduced through the left femoral vein and positioned in the right atrium. A decapolar catheter was placed in the coronary sinus. A single transeptal puncture was performed using a transeptal needle (BKR1, St Jude Medical, Minnesota, USA) and an 8 F sheath (Fastcath SL1, St Jude Medical, Minnesota, USA), guided by both intracardiac echocardiography and fluoroscopy. ICE was also used to ensure a posterior transeptal approach. A 6 Fr angiocatheter (Mach 1 MP2, Boston Scientific, Massachusetts, USA) was used to make a selective angiography of every pulmonary vein for locating the ostium. A circular mapping catheter was advanced and positioned in the antrum of each pulmonary vein to record the presence of PV-potentials. The position of the circular catheter was guided by ICE. If the patient was in AF at baseline, resistant to electrical cardioversion, he was excluded from the mapping study. A 4 mm mapping catheter was then used to create an electroanatomical reconstruction of the left atrium with a CARTO-system (Biosense Webster, California, USA) or an RPM-system (Boston Scientific, Massachusetts, USA). A high density voltage map was created of the antral pulmonary vein region, as guided by the fluoroscopic images and the ICE. Tags were placed at the position of the ostial border of the pulmonary vein. After a satisfactory electroanatomical map was achieved, the sheath was exchanged for a 14 Fr steerable sheath (FlexCath, CryoCath, Montreal, Quebec). The mapping catheter was exchanged for a 28 mm, 12 Fr double lumen cryoballoon catheter (Arctic front, Cryocath, Montreal, Quebec) (Fig. 1), and positioned over an exchange wire to occlude the ostium of each PV. Cryoenergy was given for 5 min per application. The applications per vein were directed towards the major side branches, and a minimum of two applications per vein were given. If a common left ostium was present, ablation was performed with the 28 mm cryoballoon at least twice towards the major superior and inferior side branches, so a minimum of four applications were delivered. Before targeting the right superior pulmonary vein (RSPV), a quadripolar catheter was positioned in the superior caval vein for continuous phrenic nerve stimulation during cryoapplication. At loss of capture, the ablation was

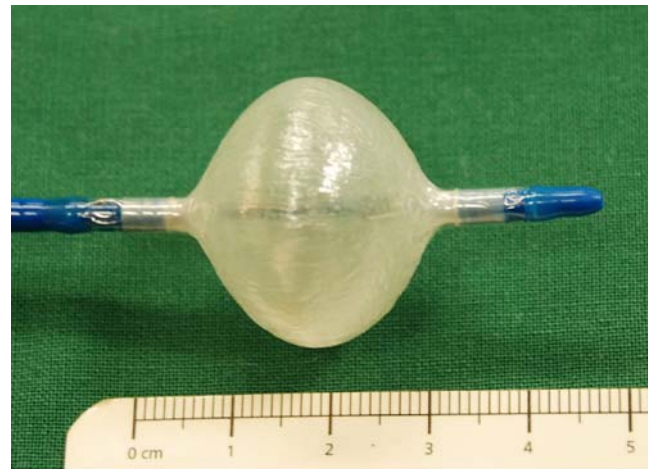


Fig. 1 Inflated 28 mm double lumen cryoballoon

instantaneously terminated. After targeting all PV's, the cryocatheter was exchanged for the circular mapping catheter to check for remaining electrical activity. If this registration showed persistence of the PV-potentials, the cryoballoon was introduced again, trying to maximize wall contact at the location of the remaining potentials (as guided by the circular catheter, ICE and fluoroscopy) and an additional two applications were given per vein. If after this second ablation attempt the activity remained present, a conventional cryocatheter (Freezor Max, Cryocath, Montreal, Quebec) was used to perform a segmental isolation through the same transeptal puncture. After obtaining isolation of all the veins, the 4 mm mapping catheter was introduced in the left atrium and a new electroanatomical map was made with special attention for mapping the ablated regions and the activation of the earliest activation site of the left atrium. Throughout the procedure, the activated clotting time was monitored every 30 min and maintained above 350 sec.

2.3 Analysis of the electroanatomical maps

The voltage map of the antral regions as guided by ICE was compared before and after ablation. The antral regions were evaluated for isolation. Local voltages of <0.05 mV were considered as ablated tissue. The location of the first activation in the left atrium during sinus rhythm was determined before and after ablation.

2.4 Statistical analysis

An unpaired Student T-test was used for comparing the diameters of the pulmonary veins. A Wilcoxon Rank test was performed for evaluating the activation change of the left atrium.

Table 1 Procedure parameters

Patient nr.	Mapping system	Balloon applications (n)	Segmental applications (n)	Fluoroscopy time(min)	Procedure time(min)	Largest diameter LSPV (mm)	Largest diameter LIPV (mm)	Largest diameter LCPV (mm)	Largest diameter RSPV (mm)	Largest diameter RIPV (mm)	Activation change
1	Carto	14	-	30	180	18.5	18.6	-	22.6	18.5	-
2	Carto	11	-	23	160	23.4	20.1	-	22.1	16.1	±
3	RPM	13	-	19	140	27.1	20.9	-	23.6	19.0	-
4	Carto	13	-	15	180	-	-	29.2	23.9	23.0	-
5	RPM	11	4	45	230	14.6	16.3	-	12.7	22.7	-
6	Carto	11	-	18	140	20.6	20.4	-	19.7	8.4	-
7	-	13	5	52	220	25.7	19.9	-	21	21.6	NA
8	Carto	12	-	37	180	19.6	17.8	-	16.4	17.6	-
9	RPM	11	-	22	120	18.8	17.9	-	23.7	19.4	+
10	Carto	10	-	26	100	22.9	18.2	-	18.1	13.5	-
11	Carto	9	3	45	240	17.8	15.7	-	21.1	18.4	±
12	Carto	13	-	21	180	-	-	31.1	23.7	18.3	-
13	RPM	14	2	53	220	24.3	18.3	-	12.7	24.9	-
14	Carto	15	-	36	200	22.6	16.3	-	21	12.7	+
15	Carto	11	-	25	150	24.2	16.6	-	18.6	12.0	±
16	Carto	13	-	16	140	23.7	15.9	-	14.6	16.1	±
17	-	13	-	34	180	25.4	17.3	-	18.6	24.9	NA
18	Carto	11	-	30	180	20.6	20.0	-	20.2	18.5	-

The pulmonary vein diameters were measured in both frontal and transverse CT slices, only the largest diameter is presented

n number, min minutes, mm millimeter, NA not available

± occurrence of large activation change

± occurrence of minor activation change

3 Results

3.1 PVI

Eighteen consecutive patients were included. Two patients were excluded for mapping due to the presence of AF, with multiple recurrences after cardioversion. The procedure data is presented in Table 1. Two patients had a common left sided ostium which was also targeted with the cryoballoon. Electrical activity was present in all of the veins. All patients underwent successful pulmonary vein isolation, with absence of PV-potentials at the end of the procedure. Mean procedure and fluoroscopy times were 174 ± 39 and 30 ± 12 min respectively. The procedure and fluoroscopy times for making the electroanatomical maps were deducted from the actual times because this was not essential in obtaining PV isolation. In 14 procedures only the cryoballoon was used, and 4 procedures required an

additional segmental approach with a linear cryocatheter. No complications occurred in this series. No phrenic nerve paralysis necessitated early termination of any RSPV ablation, no paralysis was seen at the end of the procedures.

3.2 Mapping

Qualitative assessment of the electroanatomical maps revealed antral isolation in all veins that had separate ostia. In the right sided veins, the antrum was isolated in all instances, while on the left side, the pulmonary vein anatomy was the main determinant in absence of antral isolation: the two patients with a common left sided ostium showed ostial PVI. Figure 2 shows a typical example of a voltage map during sinus rhythm before and after ablation, with complete antral isolation, also shown are the fluoroscopic images of the balloon occlusions in that same patient. Figure 3 shows a voltage map of a patient with a

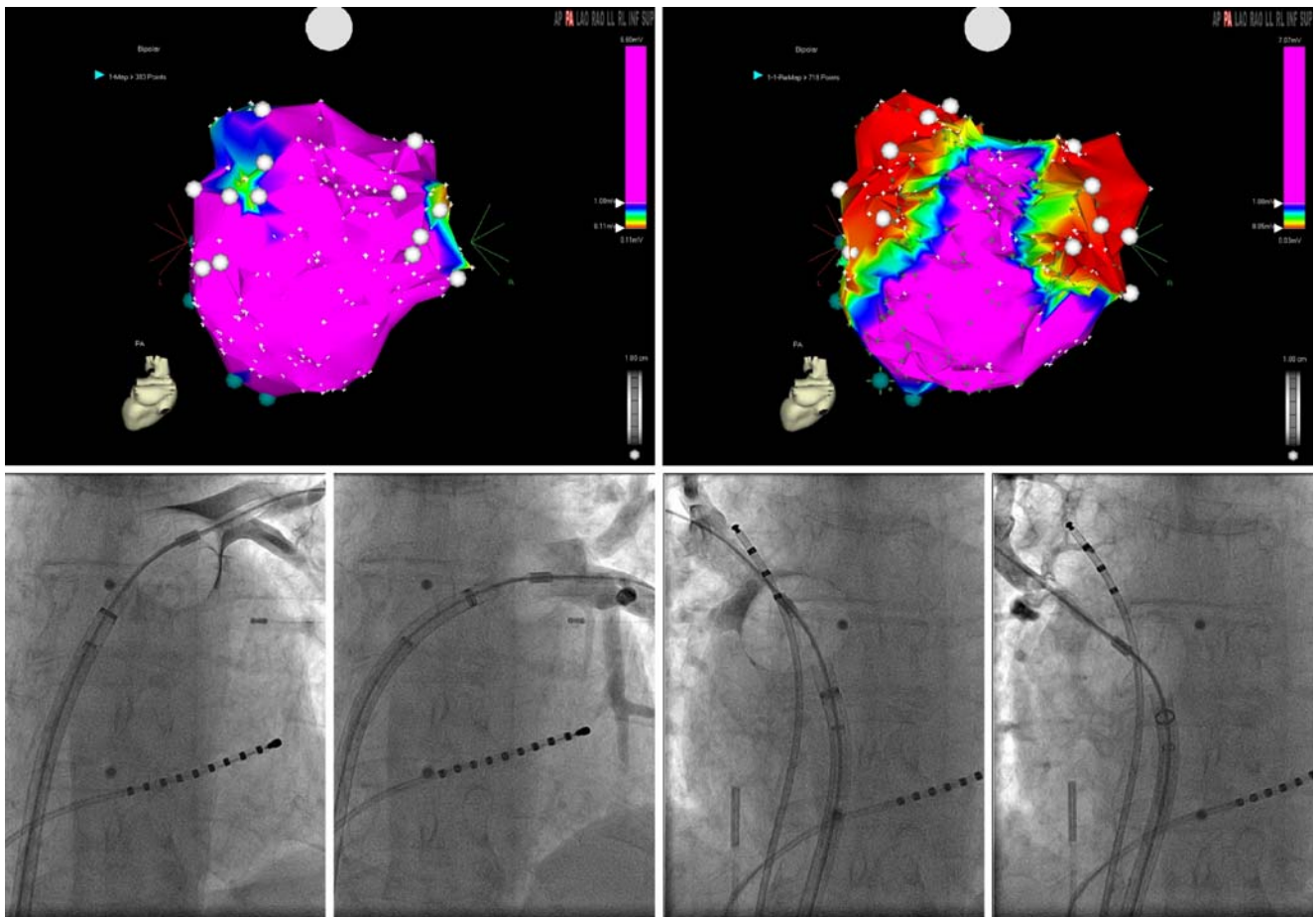


Fig. 2 Postero-anterior view of a left atrial voltage map in a patient with four separate pulmonary vein ostia, before (*upper left*) and after (*upper right*) ablation. Low voltage areas (<0.05 mV) are coloured red, white spherical markers are placed at the ostium. It is clear that the ablated region extends into the antrum. The fluoroscopic images (*below*) represent the cryoballoon occlusions during distal contrast

injection before ablation: from left to right: left upper pulmonary vein, left lower pulmonary vein, right upper pulmonary vein, right lower pulmonary vein. A decapolar coronary sinus catheter is visible in all lower images; a quadripolar catheter is visible in the two lower right images for phrenic nerve pacing during ablation of the right sided veins

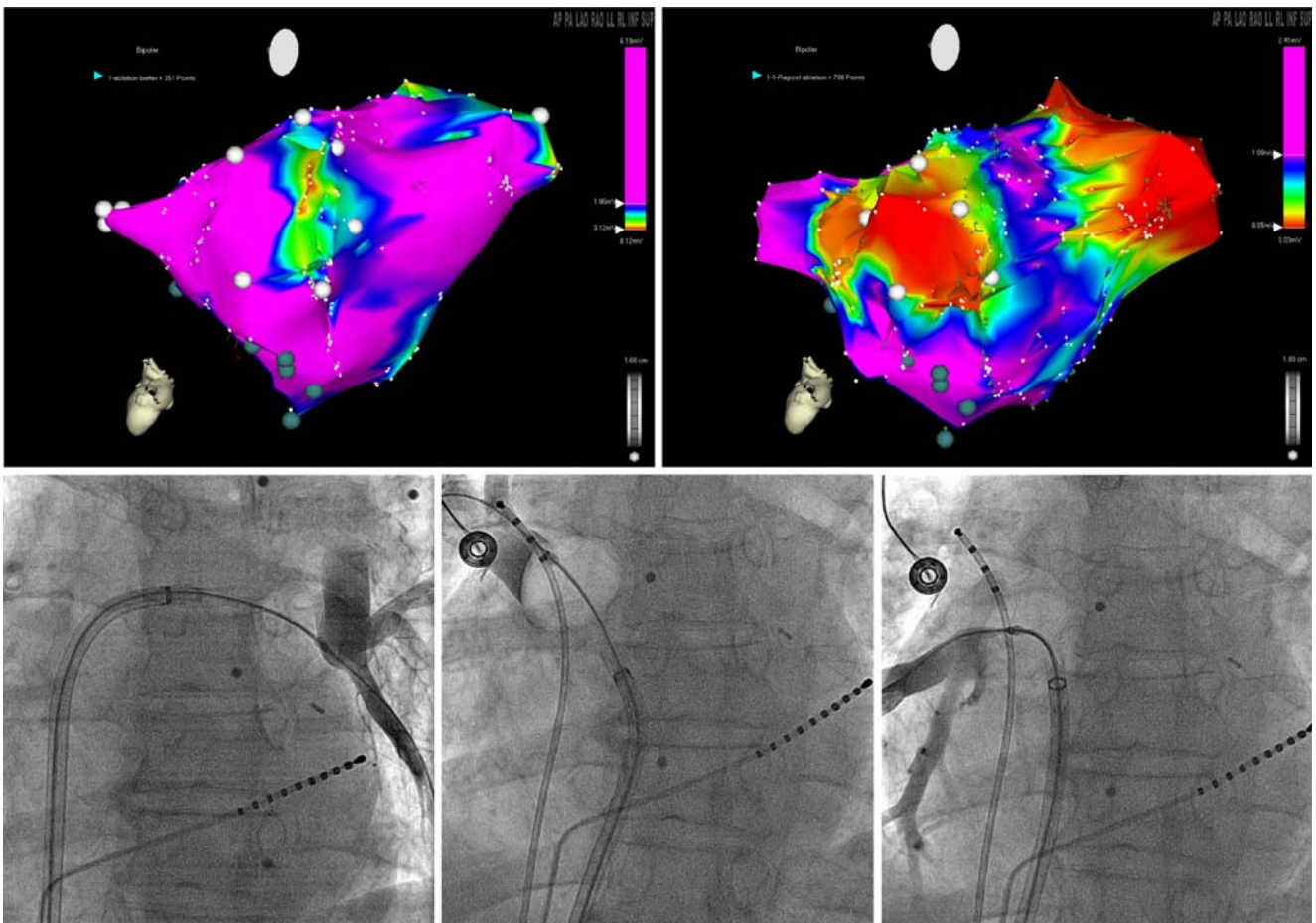


Fig. 3 Cranial left anterior oblique view of a left atrial voltage map in a patient with a left sided common pulmonary vein ostium, before (*upper left*) and after (*upper right*) ablation. Low voltage areas (<0.05 mV) are coloured red, white spherical markers are placed at the ostium. It is clear that the ablated region does not extend beyond the ostial markers. The fluoroscopic images (*below*) represent the cryoballoon occlusions during

distal contrast injection before ablation: from left to right: left common pulmonary vein, right upper pulmonary vein, right lower pulmonary vein. A decapolar coronary sinus catheter is visible in all fluoroscopic images; a quadripolar pacing catheter is visible in the middle and right lower images for phrenic nerve pacing during ablation of the right sided veins

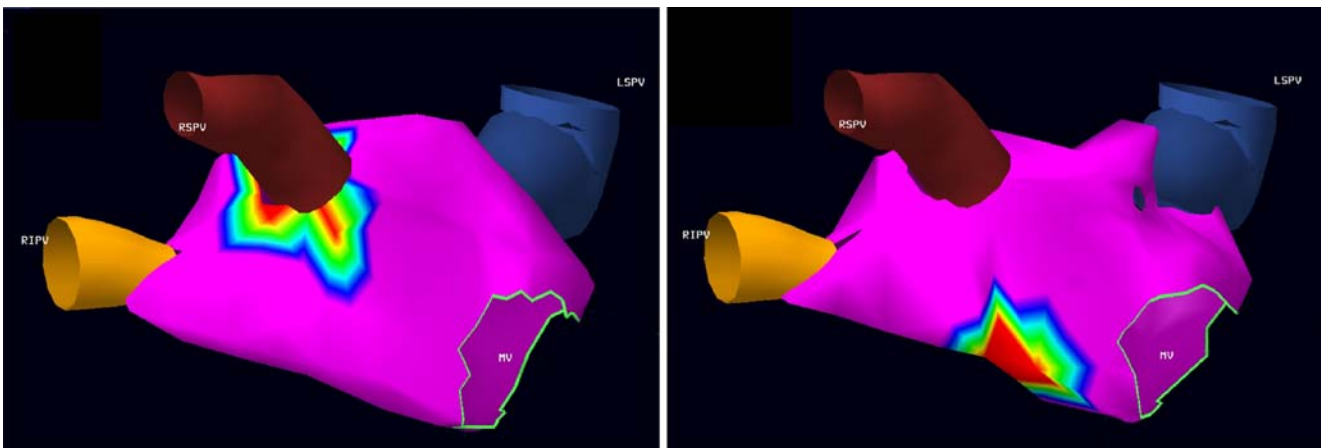


Fig. 4 Activation map of the left atrium during sinus rhythm before (*left*) and after (*right*) ablation. The earliest activation times are represented in red. It is clear that the location of the earliest left atrial activation changes from high septal before, to low septal after ablation

left sided common ostium: no antral isolation is observed around the left sided veins, only around the right sided veins. The mean of the largest diameter of the veins that showed antral isolation was 19 ± 4 mm, while the two left common ostia were 31 mm and 29 mm in their largest diameter ($p < 0.01$). The use of a linear cryocatheter for additional segmental ablation, if isolation could not be obtained with the balloon catheter, did not appear to influence the extent of the ablation in the antral region.

3.3 Activation of the left atrium

Before ablation, all of the left atria ($n=16$) showed their earliest activation site during sinus rhythm in the superior septal region. Activation mapping of the left atrium after ablation revealed a change in site of earliest activation in two patients (NS). One patient shifted his first activation point from superior towards the middle and one from superior towards the inferior region of the septum. In an additional four patients there was a minor change in activation, showing a downward shift as well, but which might have been due to a mapping artefact. An activation map is represented in Fig. 4, showing the patient switching from upper septum activation to lower septum activation of the left atrium.

4 Discussion

In cryoballoon PVI, the majority of the veins undergo antral isolation. Veins with a diameter larger than the balloon, are isolated ostially. In individual cases, the left atrial activation sequence appears to be altered after ablation.

The main finding of antral isolation by the cryoballoon seems to contradict a recent report describing ostial PVI with several other balloon based ablation systems: high intensity focused ultrasound (HIFU, ProRhythm) and endoscopic laser balloon ablation system (EAS, Cardiofocus) [9]. We believe this important difference can be explained by the inherent difference in energy delivery. Both HIFU and EAS deliver energy in a linear circumference around the balloon, aiming to create a linear circle lesion. The cryoballoon on the other hand, is less direction dependent. The refrigerant jet inside the balloon is anteriorly directed to produce the lowest ablation temperatures in a large circular zone on the anterior one third of the balloon, thus creating a wider, planar circular lesion at the balloon-tissue interface. A report recently published on the level of pulmonary vein isolation for balloon based ablation systems, described a set of eight patients ablated with a 23 mm cryoballoon [10]. This showed only ostial isolation. Our study was exclusively performed with the 28 mm cryoballoon, which could account for the discrepancy between the two findings.

In at least two cases of our cohort, we saw that the preferential conduction path from the right to the left atrium seemed to change. This was not a consistent finding for the whole group. We believe that due to the proximity of Bachmann bundle to the antral region of the RSPV [11] in some cases the conduction over this structure is delayed as a result of the ablation, also confirming the ablation of left atrial muscle tissue in the septal region. This has been proven to improve outcome with radiofrequency ablation [12] but for cryothermal ablation the clinical impact of this remains to be determined.

Common left veins were targeted in a way similar to separate veins, with a minimum of two applications directed towards their respective superior and inferior side branches each. The ablation of a common left vein posed no additional technical difficulty and was successful in electrically isolating the vein, but proved to yield a lesion not extending into the antrum, although the operators tried to perform a similar antral ablation. We found the consistent larger ostial size as the only determining factor for this phenomenon. It seems logical that a larger balloon might solve this problem. What the effect of this relatively less extended lesion is on the long term clinical outcome remains to be determined.

From our study, it can be concluded that pulmonary vein isolation with the cryoballoon consistently yields isolation in the antral region of single vein ostia, thus not only isolating the muscular PV sleeves but also extending to an antral circumferential lesion. When ablation is performed of a common ostium, the ablation is not antral, but ostial.

It remains to be determined to what extent the ablation lesion remains permanent when mapped after a long term follow-up period. The long term persistence of a left atrial activation change and the clinical significance of this is also unclear.

4.1 Limitations

Only a qualitative assessment was made of the obtained mapping data. The main reason for this was that the proximal extent of the antral region is not always well defined in all patients. Image integration could have been helpful in this respect. Since the distal boundary of the antrum is more accurately defined by the ostium, ablation was more reliable when assessed qualitatively in reference to that boundary. Therefore, the presented data show that antral ablation was present in the reported cases, but do not imply that the entire antral region was ablated. In comparison to this, circumferential ablation with radiofrequency energy is aimed at delivering ablation energy inside the antrum, thus avoiding ostial pulmonary vein stenosis, and has not been proven to isolate the antral region to its full proximal extent. A randomised comparison

to circumferential antral radiofrequency ablation would be necessary to compare any differences in the extent of the antral isolation.

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