Europace Advance Access published January 21, 2015

Europace
doi:10.1093/europace/euu260

CLINICAL RESEARCH

Lesion formation after pulmonary vein isolation using the advance cryoballoon and the standard cryoballoon: lessons learned from late gadolinium enhancement magnetic resonance imaging

Philipp Matthias Halbfass*, Marcel Mitlacher, Oliver Turschner, Johannes Brachmann, and Christian Mahnkopf

Department of Cardiology, Klinikum Coburg, Ketschendorfer Strasse 33, 96450 Coburg, Germany

Received 10 May 2014; accepted after revision 14 August 2014

Aims To compare ablation lesion formation after pulmonary vein isolation (PVI) using the standard cryoballoon (CB-S) vs. the re-designed cryoballoon Arctic Front Advance (CB-A) using late gadolinium enhancement magnetic resonance imaging (LGE-MRI) 3 months post-ablation.

Methods and results Thirty-six consecutive patients with paroxysmal or short-lasting persistent atrial fibrillation (AF) were evaluated prospectively after PVI using the CB-S in the first 18 patients and the CB-A in the subsequent 18 patients. All patients underwent LGE-MRI and a 7-day Holter electrocardiogram monitoring 3 months after ablation. Fifty-six per cent of the patients were male (mean age 63.0 ± 9.1 years). Fifty-six per cent in the first group and 89% in the second group were free of AF recurrence 3 months after ablation ($P = 0.025$). Three months after ablation, LGE-MRI of the left atrium showed complete circular lesions in 35% of PVs in the first group and in 32% of PVs in the second group (n.s.). The left PVs showed a significantly higher proportion of PV segments with complete ablation lesions compared with the right PVs (83 vs. 34%; $P < 0.001$).

Conclusion Cardiac MRI is able to visualize induced ablation lesions after PVI and might be suitable to quantify ablation lesion amount. Ablation lesion formation did not differ significantly in patients treated with the CB-S vs. the CB-A, despite a significantly lower rate of AF recurrence after 3 months in the CB-A group. Left PVs showed a significantly higher amount of ablation lesions compared with the right PVs. Larger and randomized studies are needed to understand the relationship between representable tissue lesions and success rates.

Keywords Catheter ablation • Atrial fibrillation • Cryoballoon arctic front advance • Magnetic resonance imaging • Late gadolinium enhancement

Downloaded from by guest on March 26, 2016

Introduction

Complete electrical isolation of all pulmonary veins (PVs) is the cornerstone of catheter atrial fibrillation (AF) ablation.[1] Different ablation techniques with different energy sources are currently in use to perform PV isolation (PVI).[2–5] Frequently, more than one procedure is necessary to achieve durable long-term success without AF recurrence.[6] A main concern of PVI is the insufficient long-term permanency of ablation lines.[7–10] Cryoballoon ablation proved to be a feasible and safe alternative to radiofrequency PVI.[2,5] Recently, a newly designed cryoballoon with a novel refrigerant injection system has been introduced and approved.[11–12] These changes might result in larger and more distinct ablation lesions and thereby in higher ablation success rates. Ablation lesions after AF ablation can be visualized using late gadolinium enhancement magnetic resonance imaging (LGE-MRI).[13–15] More recently, the site of PV reconnection after an initially non-successful AF ablation procedure was compared with LGE-MRI ablation lesion delineation.[13] We report our experience

* Corresponding author. Tel: +49 9561 22 6348; fax: +49 9561 22 6349, *E-mail address*: halbfass@gmx.net

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2015. For permissions please email: journals.permissions@oup.com.

What's new?

- This is the first study comparing the re-designed cryoballoon Arctic Front Advance and the former standard cryoballoon using late gadolinium enhancement magnetic resonance imaging.
- Three months after cryoballoon atrial fibrillation ablation, the left pulmonary veins (PVs) showed more intense ablation lesions compared with the right PVs.

with ablation lesion formation detection using LGE-MRI 3 months post-ablation in patients treated with the CB-S and the CB-A.

Methods

Patients

Thirty-six consecutive patients with highly symptomatic paroxysmal or short-term persistent AF were included in the study between April and November 2012. The first 18 patients were included in the first group and treated with the CB-S until July 2012. The second treatment group consisted of the subsequent 18 patients who were treated with the CB-A. Exclusion criteria were a contraindication against MRI, left atrial (LA) appendage thrombus, severe underlying structural heart disease, and a previous LA ablation procedure.

The Arctic Front Advance Cryoballoon ablation catheter is a re-designed second-generation cryoballoon. A new vaporization technology of the refrigerant provides a larger and more homogeneous freezing area, covering the whole frontal hemisphere of the CB-A.

Ablation procedure

All PVI procedures were performed under conscious sedation with appropriate doses of fentanyl and midazolam. A single transseptal puncture was performed using a transseptal BRK-1 needle under intracardiac ultrasound (ICE) guidance (ICE Catheter ViewFlex PLUS, St Jude Medical/Irvine Biomedical, Inc.). A single 8F curved sheath (FAST-CATH, Transseptal Guiding Introducer, St Jude Medical) was positioned within the LA. Thereafter, heparin boluses were administered repeatedly to reach an activated clotting time (ACT) of 300–380 s. Further boluses were applied subsequently to maintain the target ACT during the whole procedure. Importantly, at our institution, we performed the procedure under an effective anticoagulation with an oral vitamin K antagonist in most cases. A stiff guidewire (Amplatz Extra Stiff Wire Guide 0.035″, Cook Medical) or alternatively an Inoue guidewire for transseptal access to the LA (EPFlex Feinwerktechnik GmbH) was placed through the FAST-CATH sheath. This sheath was replaced by a 12F transseptal sheath (FlexCath, Medtronic CryoCath LP), over which the cryoballoon catheter (CB-S, Arctic Front™, Medtronic, Inc.; or CB-A, Arctic Front Advance™, Medtronic, Inc.) was inserted into the LA. We used a 28 mm cryoballoon wherever possible. In patients with a PV anatomy not suitable for the 28 mm balloon, a 23 mm cryoballoon was applied. For correct placement of the balloon into the PV ostia, a circular mapping catheter (Achieve Mapping Catheter, Medtronic Ablation Frontiers) was introduced through the cryoballoon. Pulmonary vein potentials were assessed simultaneously with the Achieve mapping catheter during the freezing procedure to detect LA–PV conduction block after the beginning of the freeze.

For position control of the balloon within the PV ostium and confirmation of complete PV occlusion, contrast medium was injected from the distal lumen of the cryoballoon catheter. Each cryoballoon ablation was performed for at least 300 s. Pulmonary vein potentials were checked before and after each freeze to confirm isolation. One additional freeze was applied to each PV after confirmation of entrance block.

During freezing of the right PVs the phrenic nerve was constantly paced via the superior caval vein to check for beginning phrenic nerve palsy (PNP). The endpoint of the procedure was confirmation of entrance and exit block of each PV by placing the Achieve lasso catheter within the PV ostium.

Late gadolinium enhancement magnetic resonance imaging

Late gadolinium enhancement magnetic resonance imaging was obtained in all 36 patients 3 months post-ablation to assess the extent of non-viable tissue, using methods described in recently published manuscripts.[14,15] Briefly, all studies were performed on a 3 T Verio clinical scanner (Siemens Medical Solutions) using a TIM phased-array receiver coil. The scan was acquired 15 min following contrast agent injection (0.1 mmol/kg, Dotarem, Guerbet B.P.) using a 3D inversion recovery, respiration navigated, electrocardiogram (ECG)-gated, gradient echo pulse sequence. Typical acquisition parameters were: free-breathing using navigator gating, a transverse imaging volume with voxel size = $1.25 \times 1.25 \times 2.5$ mm^3 (reconstructed to $0.625 \times 0.625 \times 1.25$ mm^3), repetition time/echo time (TR/TE) = 5.4/2.3 ms, inversion time (TI) = 270–310 ms. GRAPPA with $R = 2$ and 46 reference lines. Electrocardiogram gating was used to acquire a small subset of phase encoding views during the diastolic phase of the LA cardiac cycle. The time interval between the R-peak of the ECG and the start of data acquisition was defined using the cine images of the LA. Fat saturation was used to suppress fat signal. The TE of the scan (2.3 ms) was chosen such that fat and water were out of phase and the signal intensity of partial volume fat-tissue voxels was reduced to allow for improved delineation of the LA wall boundary. The TI value for the LGE-MRI scan was identified using a scout scan. Typical scan time for the LGE-MRI study was 5–10 min, depending on subject respiration and heart rate.

Quantification of scar tissue using late gadolinium enhancement magnetic resonance imaging

The methods for quantification of LA scar tissue have been described previously.[14,15] Briefly, LA wall contours from the LGE-MRI images were manually segmented by experts in image processing, using the Corview image processing software (MARREK Inc.). The protocol for segmentation proceeded as follows: first, the endocardial border of the LA was defined, including an extent of PV sleeves, by manually tracing the LA–PV blood pool in each slice of the LGE-MRI volume. Secondly, the endocardial segmentation was morphologically dilated and then manually adjusted to create an assessment of the boundary of the epicardial LA surface. Finally, the endocardial segmentation was subtracted from the epicardial segmentation to define a wall segmentation, which was manually edited to exclude the mitral valve and PVs. Thus, the resulting LA wall segmentation included the 3D extent of both, the LA wall and the antral regions of the PVs.

Quantification of scar was obtained using the methods previously described elsewhere[16] using the Corview image processing software (MARREK Inc.).

Lesion formation analysis

In a lateral view, each PV ostium was divided into four quarters (left superior, right superior, left inferior, and right inferior) and it was decided,

Downloaded from by guest on March 26, 2016

whether the quarter section showed an uninterrupted ablation lesion or not. For each patient, the rate of complete ablation quarters in relation to all PV quarters was defined. In addition, it was decided, how many PVs per patient demonstrated a complete circumferential ablation lesion. This analysis was done by three experienced operators independently and blinded to the patients' allocation to the treatment group. After evaluation, a final decision on each case was made by majority or in agreement on each case with differing operator decisions.

Endpoints

The primary endpoint of the study was the ratio of PVs with visually uninterrupted circumferential ablation lesions around the PVs according to LGE-MRI in the group treated with the CB-S vs. the group treated with the CB-A. Secondary endpoints were freedom of AF recurrence 3 months after ablation and the ratio of quarter segments with complete ablation lesions around the PVs according to LGE-MRI in the CB-S vs. the CB-A group. For this purpose, LA ablation lesions were detected using LGE-MRI and quantified using the Corview software.

Statistical analysis

Continuous variables are presented as mean ± SD or median with interquartile range (IQR). Categorical variables are expressed as absolute numbers and percentages. Baseline variables were compared by an independent *t*-test (two-tailed) for all normally distributed continuous variables and by the Mann–Whitney test (two-tailed) in all not normally distributed variables. Categorical variables were tested by two-sided Fisher's exact test. Statistical analysis was performed with SPSS software. Statistical significance was assumed for $P < 0.05$.

Results

A total of 36 patients (20 men, 56%; mean age 63.0 ± 9.1 years) were treated with the standard cryoballoon ($n = 18$) or with the new Arctic Front Advance cryoballoon ($n = 18$). Twenty-five (69%) patients suffered from paroxysmal AF and 11 from short-term persistent AF (31%). Time since first diagnosed AF was median 11.5 months (6–24 months IQR) and the mean number of antiarrhythmic drugs before ablation was 0.5 ± 0.7. Both treatment groups did not differ significantly concerning patient characteristics (*Table 1*).

Procedural data and follow-up

Pulmonary vein isolation was achieved in all 70 PVs in the group of patients treated with the CB-S (3.9 ± 0.5 PVs per patient) and in all 68 PVs in the group of patients treated with the CB-A (3.8 ± 0.5 PVs per patient). Of the 18 patients in the CB-S group 2 patients had an accessory right middle PV, in the CB-A group 1 patient had an accessory right middle PV and 1 patient had a right common trunk. In each group four patients had a left common trunk (*Table 2*). In 16 patients of the first group, a 28 mm CB-S only and in 2 patients a 23 mm CB-S was used additionally to the 28 mm balloon ($n = 1$) or exclusively ($n = 1$). In 15 patients of the second group a 28 mm CB-A, in 3 patients a 23 mm CB-A was used.

The lowest mean temperature was −48 ± 8°C in the first group and −47 ± 7°C in the second group (n.s.). The mean number of freezes per PV did not differ significantly in both groups (2.66 ± 1.2 vs. 2.72 ± 1.0). Regarding the lowest mean temperature during cryoballoon ablation, the left PVs showed slightly but not significantly lower cryoballoon temperatures compared with the right PVs (−48 ± 8 vs. −46 ± 8°C; $P = 0.22$).

The degree of PV occlusion by the cryoballoon was classified into four categories with '1/4' meaning a low grade of occlusion and '4/4' describing a complete occlusion with contrast dye remaining within the PV during the whole freezing period. In both treatment groups, a '4/4' occlusion was reached in most cryoballoon applications. In cases with a '3/4' occlusion at the beginning of the freeze special manoeuvres like a 'pulldown manoeuvre' were performed during the freezing process to achieve complete occlusion. A slight temperature drop directly after this manoeuvre indicated an improvement of an initially not optimal occlusion. In case of insufficient temperature drops despite special manoeuvres, the freeze was stopped and cryoballoon positioning was repeated to achieve a better PV occlusion.

In four patients in the first group and in two patients in the second group, LGE-MRI scans were of poor quality due to rhythm- and

Table 1 Patient baseline characteristics

	Group 1 (SCB) ($n = 18$)	Group 2 (ACB) ($n = 18$)	All patients ($n = 36$)	*P* value
Male (%)	56	56	56	n.s.
Age (years)	62 ± 10	64 ± 8	63 ± 9	n.s.
Paroxysmal AF (%)	67	72	69	n.s.
Hypertension (%)	83	100	92	n.s.
CAD (%)	11	33	22	n.s.
Diabetes (%)	28	11	19	n.s.
Renal insufficiency (%)	0	0	0	n.s.
LA size (mm)	45 ± 2	46 ± 2	46 ± 2	n.s.
LVEF (% EF)	62 ± 6	63 ± 5	62 ± 6	n.s.
AADT before ablation	0.6 ± 0.7	0.4 ± 0.7	0.5 ± 0.7	n.s.
28 mm balloon *n*, (%)	17 (94)	15 (83)	32 (89)	n.s.

Data are expressed as mean ± SD, as %, or as *n* (%).
SCB, standard cryoballoon; ACB, advance cryoballoon; AADT, antiarrhythmic drug therapy; CAD, coronary artery disease.

Downloaded from by guest on March 26, 2016

Table 2 Procedural parameters

	Group 1 (SCB) (n = 18)	Group 2 (ACB) (n = 18)	All patients (n = 36)	P value
Number of veins treated	70	68	138	n.s.
Mean minimal temperature (°C)	−47.6 ± 8	−47.1 ± 7	−46.8 ± 8	n.s.
Freezing applications per vein	2.66 ± 1.2	2.72 ± 1.0	2.69 ± 1.1	n.s.
PV acute isolation (%)	100	100	100	n.s.
PV anatomy				
Normal (4 PVs)	12	12	24	n.s.
Left common Os	4	4	8	n.s.
Right common Os	0	1	1	n.s.
Accessory right PV	2	1	3	n.s.

Data are expressed as mean ± SD, as %, or as *n*.
SCB, standard cryoballoon; ACB, Advance cryoballoon.

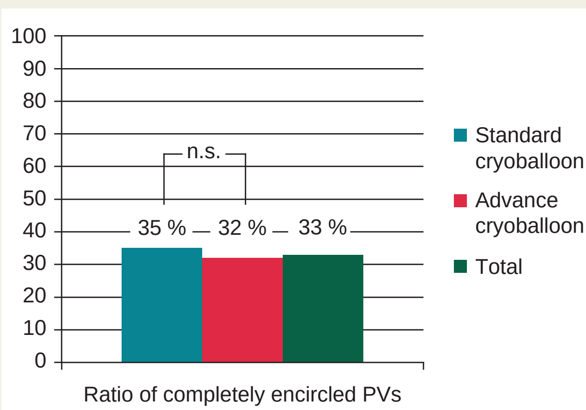

Figure 1 Ratio of circumferentially encircled PVs according to LGE-MRI 3 months after ablation.

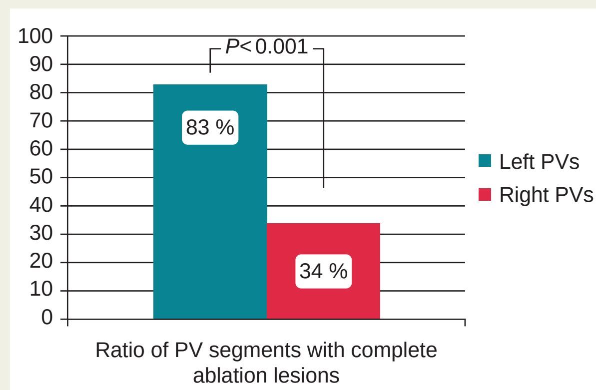

Figure 2 Ratio of quarter segments with complete ablation lesions according to LGE-MRI 3 months after ablation. The ratio of all left and all right PV segments with complete ablation lesions is given in %. PV, pulmonary vein.

breathing artefacts and therefore could not be evaluated regarding ablation lesions.

Late gadolinium enhancement magnetic resonance imaging at 3 months follow-up

Thirty LGE-MRI scans of the LA (83%) 3 months after PVI were of excellent quality for ablation lesion evaluation. The proportion of quarter segments with continuous lesions was 59% in the CB-S group and 58% in the CB-A group, which was not significantly different. Regarding the proportion of PVs with complete circular lesions, there was also no significant difference between both groups (35 vs. 32%; *Figure 1*). Comparing patients with AF recurrence with patients without AF recurrence, both groups did not differ significantly regarding the proportion of PV quarter segments with complete ablation lesions and the proportion of complete encircled PVs (60 vs. 57%; $P = 0.66$ and 32 vs. 36%; $P = 0.67$).

In the whole study cohort, all left PVs showed a significantly higher proportion of PV quarter segments with complete ablation lesions compared with the right PVs (83 vs. 34%; $P < 0.001$; *Figure 2*). And far more left PVs showed complete circumferential ablation lesions compared with the right PVs (62 vs. 7%; $P < 0.001$). When comparing the CB-S with the CB-A regarding the proportion of left PV quarter segments with ablation lesions, the difference was not significant (81 vs. 85%; $P = 0.56$).

When comparing all patients treated with a small cryoballoon or with a small and a large cryoballoon vs. all patients treated with a large cryoballoon exclusively, there was no significant difference regarding short-term AF recurrence rate or ablation lesion amount (17 vs. 30% AF recurrence, $P = 0.65$; 60 vs. 59% ratio of quarter segments with complete ablation lesions, $P = 0.93$; *Figure 3*).

Pulmonary veins with complete circumferential ablation lesions according to LGE-MRI showed slightly but not significantly lower minimal ablation target temperatures compared with PVs with incomplete ablation lesions (−47.3 ± 6.4 vs. −45.8 ± 7.6°C; P = n.s.).

Examples of LA reconstructions with complete, interrupted, and without relevant circular ablation lesions around PVs 3 months after ablation are given in *Figures 4–6*.

Downloaded from by guest on March 26, 2016

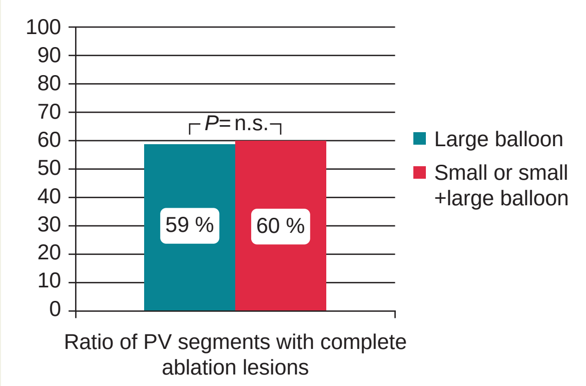

Figure 3 Ratio of quarter segments with complete ablation lesions according to LGE-MRI 3 months after ablation. The ratio of PV segments with complete ablation lesions after ablation with a large cryoballoon is displayed in green and after ablation with a small or small + large cryoballoon is displayed in red. PV, pulmonary vein.

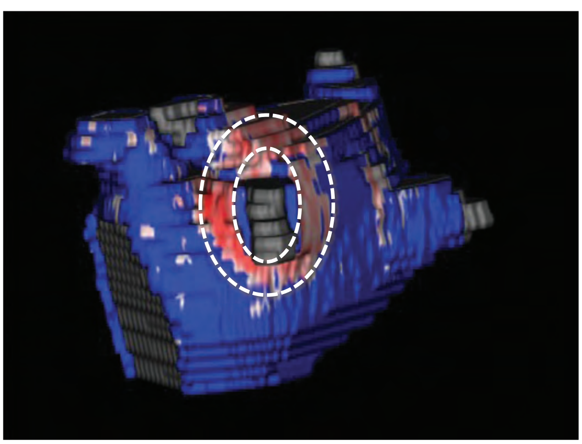

Figure 4 Late gadolinium enhancement magnetic resonance imaging reconstruction of the LA 3 months after ablation with a 28 mm advance cryoballoon. Left posterior view of the LA, healthy LA tissue is shown in blue, scar tissue is shown in red, and PV in grey. Intense continuous ring-shaped ablation lesion around the left inferior PV (dotted lines depict the ablation lesion area around the PV), nearly no scar tissue around the right inferior PV.

Atrial fibrillation recurrence and adverse events at 3 months follow-up

According to 7-day Holter ECG, 26 of 36 (72%) patients in the whole cohort were free of AF at 3-month follow-up. In the second group of patients treated with the CB-A, significantly more patients were free of AF recurrence 3 months after PVI (89 vs. 56%; $P = 0.025$).

Two procedure-related adverse events were observed during the study. One arterial aneurysm occurred in a patient of the CB-S group and one PNP occurred after freezing of the right superior PV in a patient of the CB-A group despite PNP (PNP resolved within a couple of days after the procedure). In all patients, a gastroduodenoscopy was performed before discharge after the ablation procedure. Oesophageal lesions were not seen in any of the patients. All patients in both groups underwent an MRI scan before and 3 months after ablation. In none of the patients, a PV diameter loss was seen in the follow-up MRI scan.

Discussion

The current prospective analysis is the first study comparing LA lesion formation detected by LGE-MRI short-term after PVI using one of the two currently available cryoballoon types. Recently, LGE-MRI has demonstrated to successfully delineate scar in the LA wall as a result of ablation.[14,15,17,18] Moreover, it has been demonstrated that the higher the extent of LGE after radiofrequency ablation the higher the ablation success rate was.[14,17]

According to this single-centre study, the CB-A demonstrated a safety profile comparable with that of the original CB-S, but a significantly higher short-term success rate. These results are well in line with the results reported by Fürnkranz *et al.*[19] The re-designed CB-A allows for a more homogeneous distribution of the cooling effect around a larger area of the distal balloon pole. A more homogeneously distributed freezing of the atrial tissue could increase acute and long-term PVI. Badger *et al.*[15] showed that in patients with AF recurrence after PVI, the majority of PVs were found to have regained electrical continuity in 30 of 37 PVs. If the rate of PV reconnection could be decreased, short- and long-term efficacies might increase.

Hypothesis of this study was that a more efficient cryoballoon generation results in a higher amount of ablation lesions according to LGE-MRI and in a higher short-term success rate. However, ablation lesions around the PVs in both treatment groups did not differ significantly regarding the proportion of ablated segments and the proportion of complete encircled PVs despite a significantly different short-term AF recurrence rate. These results are in contrast to the results of McGann *et al.*[14] and Peters *et al.*[17] All of the recently published work indicating the capability of LGE-MRI to predict ablation success or the site of PV reconnection analysed patients after radiofrequency ablation. Lesion formation after cryoballoon ablation might result in a different quality and amount of LGE. Also, the difference between the ablation lesion amount after using the CB-S vs. the CB-A might have been too small to be detected in a study consisting of only 36 patients. However, it is also possible that the amount of lesions and the completeness of circumferential ablation lesion sets after cryoballoon ablation do not correlate with the clinical ablation success.

When comparing all left PVs of the whole study cohort with all right PVs, the left PVs showed a significantly higher proportion of PV segments with complete ablation lesions compared with the right PVs. This is not surprising, as it is much easier to place the cryoballoon into the left PV ostia with a higher degree of PV occlusion without additional manoeuvres and a more central cryoballoon alignment than to the right ostia and with higher contact pressures of the cryoballoon to the atrial tissue. These results are well in line with the results of Badger *et al.*[15] who found higher lesion amounts around the left PVs compared with the right PVs (74 and 56% scar for left superior and left inferior PVs vs. 53 and 45% for right superior and right inferior PVs).

Downloaded from by guest on March 26, 2016

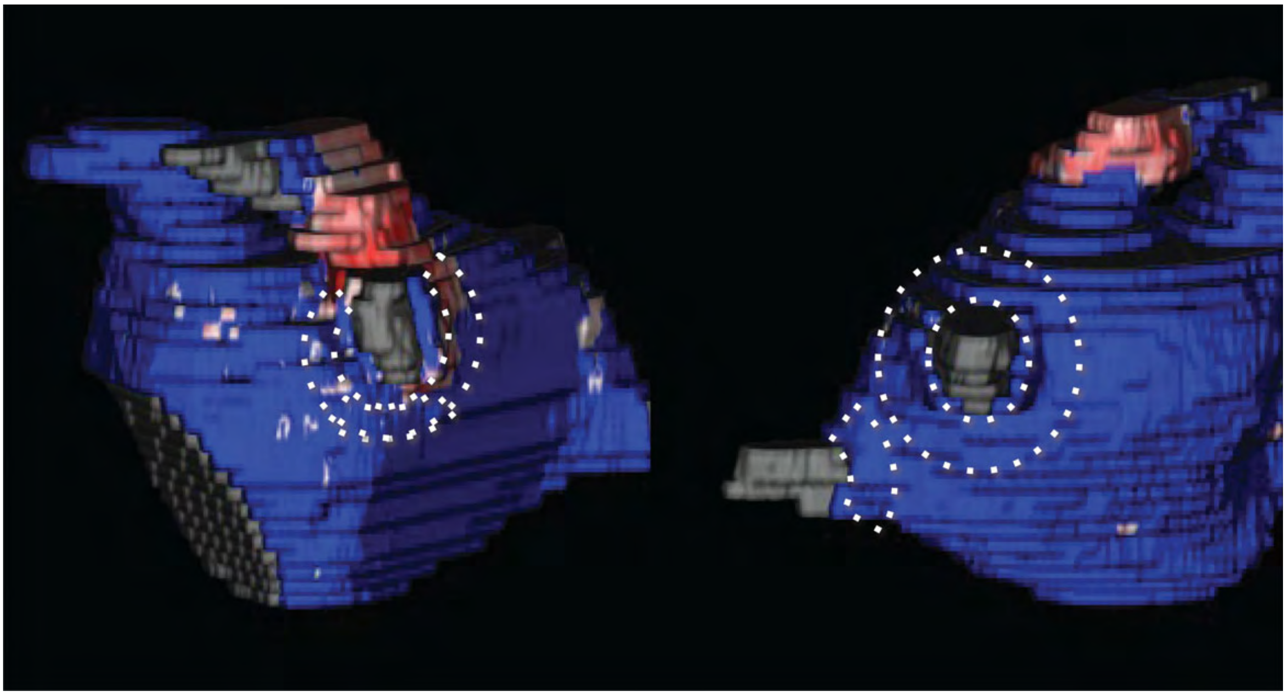

Figure 5 Late gadolinium enhancement magnetic resonance imaging reconstruction of the LA 3 months after ablation with a 28 mm advance cryoballoon. Left posterior view (left) and right anterior oblique view (right) of the LA, healthy LA tissue is shown in blue, scar tissue is shown in red. Interrupted ablation lesions around the left PVs and no relevant ablation lesions around right PVs (dotted lines depict the ostial ablation areas around the PVs).

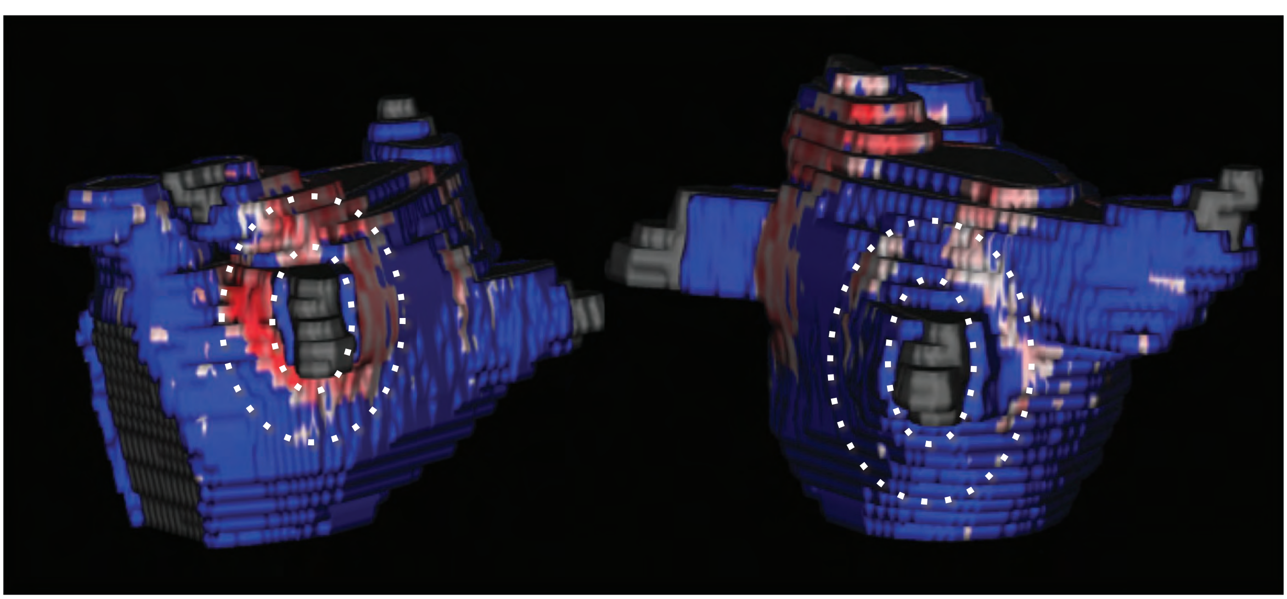

Figure 6 Late gadolinium enhancement magnetic resonance imaging reconstruction of the LA 3 months after ablation with a 28 mm advance cryoballoon. Left posterior view (left) and right posterior view (right). Left inferior PV with complete circumferential lesions, right PVs with incomplete ablation lesions (upper segments with incomplete lesion formation, lower segments without any lesion formation, dotted lines depict ostial ablation areas—typical LGE lesion pattern after cryoballoon ablation).

Downloaded from by guest on March 26, 2016

Fürnkranz *et al.*[8] found a higher conduction recovery at inferior sites especially of ipsilateral PVs and identified sharp catheter angulations with loss of central catheter alignment as a possible reason for this. This could explain why we found significantly lower lesion amounts around right compared with left PVs, despite reaching complete cryoballoon occlusion at least after additional manoeuvres in nearly all PVs. But PV reconnection is also a relevant issue concerning radiofrequency AF ablation. Lemola *et al.*[20] demonstrated that electrical PV reconnection is the most common mechanism of AF recurrence in segmental radiofrequency energy ablation.

Late gadolinium enhancement induced by ablation represents ablation tissue injury and directly indicates an ablation effect. Ranjan *et al.*[21] accurately identified ablation lesion gaps using LGE-MRI of up to 1.4 mm in a swine model. More recently, LGE-MRI was used to determine the site of PV reconnection in patients who have undergone initial AF ablation but suffered arrhythmia recurrence.[13] There is evidence that LGE-MRI is able to predict the site of reconnection after PVI in patients with AF recurrence and a redo procedure. Bisbal *et al.*[22] were able to target the site of PV reconnection in nearly all cases and gaps in roof lines in all cases in the redo procedure by LGE-MRI in their study of 15 patients with radiofrequency AF ablation. There are also controversial data reporting an insufficient accuracy to identify ablation lesions reliably in AF patients treated with radiofrequency or cryoballoon ablation.[23] However, it is reasonable to postulate a relationship between the amount of circular LGE-MRI lesions and ablation success. Nevertheless, the current study failed to demonstrate this possible association, either because the patient cohort was too small or the time between PVI and LGE-MRI was not optimal. Moreover, LGE-MRI according to the protocol used in the current study might not be suitable to detect differences in cryoballoon ablation lesions that are relevant for prediction of AF ablation outcome.

Other predictors for AF recurrence after AF ablation have recently been introduced. Besides LA diameter, type and duration of AF before ablation, and structural heart disease, the degree of LA structural remodelling is one of the predictors of AF recurrence.[24] In the current study, we did not analyse LA fibrosis indicating the degree of structural remodelling. Future studies should focus on the relationship between structural remodelling, induced scar tissue, and long-term ablation results.

Finally, there are several different issues that have to be considered as possible explanations for our finding of similar amounts of lesions and complete circumferential lesion sets around PVs in both treatment groups.

First, the small number of patients and a possibly not optimal LGE-MRI protocol or timing of MRI scans after ablation might have influenced these counterintuitive results. Secondly, cryoballoon ablation might result in a different type of LGE-MRI lesion delineation compared with RF ablation with a less distinct lesion demarcation.

Regarding success rate, the CB-A seems to be more effective than the CB-S. These results are in line with other recently published data comparing both cryoballoon types.[19]

Until now, only results of single-centre studies comparing both balloon types are available. Future larger randomized and multicentre trials should define efficacy and safety of the new cryoballoon. The amount of ablation-induced lesions around the PVs might play an important role in evaluating freezing effects after the use of the two different cryoballoons and should be a matter of investigation in future trials.

In the current study, oesophageal temperature was not measured during freezing. Important to mention, all patients included in this study underwent an endoscopic oesophageal examination routinely 1–3 days after ablation. Therefore, acute oesophageal tissue alterations would have almost certainly been diagnosed. However, Fürnkranz *et al.*[25] observed visible oesophageal lesions after the use of the CB-A in their study.

Late gadolinium enhancement magnetic resonance imaging lesion amount or pattern did not differ significantly between both cryoballoon types and between patients with or without short-term AF recurrence. It would have been of interest, if visually complete circumferential LGE-MRI lesions translated into electrically isolated PVs. In the current study, a follow-up electrophysiological (EP) study after ablation was not performed.

Limitations

Of note, the current study had an observational character. Patients were not randomized to the treatment groups and a statistical power estimation was not performed. The study included a relatively small number of patients in each treatment group. Nonetheless, both patient groups were comparable concerning patient characteristics. All patients included in the study were treated by two experienced operators according to exactly the same ablation protocol as mentioned above. A 3 month follow-up period is not sufficient to evaluate long-term ablation success. However, recent studies have shown that short-term recurrence is the strongest predictor of long-term recurrence after ablation in patients with AF. Follow-up EP studies were not performed. Therefore, PV reconnection as a possible mechanism for AF recurrence could not be confirmed. And finally, the LGE-MRI protocol and the time of MRI after ablation might not have been suitable to identify differences in ablation lesions between both treatment groups despite different ablation results. Late gadolinium enhancement magnetic resonance imaging was not able to detect a different ablation lesion amount after ablation with the CB-S vs. the CB-A in this study. However, significantly higher ablation lesion amounts in left-sided vs. right-sided PVs are well in line with the results of other studies showing higher lesion amounts of left-sided vs. right-sided PVs after RF ablation.[15] Furthermore, ablation lesions delineated by LGE-MRI were found only in the typical contact areas between cryoballoon and atrial tissue, thereby demonstrating the capability of LGE-MRI to detect cryoballoon ablation lesions.

Conclusion

Cardiac MRI is able to visualize induced ablation lesions after PVI and might be suitable to quantify ablation lesion amount. Ablation lesion formation did not differ significantly in patients treated with the CB-S vs. the CB-A despite a significantly lower rate of AF recurrence after 3 months in the CB-A group. Left PVs showed a significantly higher amount of ablation lesions compared with the right PVs. Larger and randomized studies are needed to understand the relationship between representable tissue lesions and success rates.

Downloaded from by guest on March 26, 2016

Conflict of interest: P.M.H. received travel grants from Medtronic, J.B. received travel grants and lecture fees from Biotronik and Medtronic.

References

1. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA *et al.* 2012 HRS/EHRA/ECAS Expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Europace* 2012;**14**:528–606.
2. Packer DL, Kowal RC, Wheelan KR, Irwin JM, Champagne J, Guerra PG *et al.* Cryoballoon ablation of pulmonary veins for paroxysmal atrial fibrillation: first results of the North American Arctic Front (STOP AF) Pivotal Trial. *J Am Coll Cardiol* 2013;**61**:1713–23.
3. Dukkipati SR, Neuzil P, Kautzner J, Petru J, Wichterle D, Skoda J *et al.* The durability of pulmonary vein isolation using the visually guided laser balloon catheter: multicenter results of pulmonary vein remapping studies. *Heart Rhythm* 2012;**9**:919–25.
4. Looi KL, Gajendragadkar P, Taha T, Elsik M, Scully E, Heck P *et al.* Long-term outcomes (>2 years) of atrial fibrillation ablation using a multi-electrode ablation catheter in patients with paroxysmal atrial fibrillation. *J Interv Card Electrophysiol* 2013;**36**:61–9.
5. Neumann T, Vogt J, Schumacher B, Dorszewski A, Kuniss M, Neuser H *et al.* Circumferential pulmonary vein isolation with the cryoballoon technique results from a prospective 3-center study. *J Am Coll Cardiol* 2008;**52**:273–78.
6. Kühne M, Suter Y, Altmann D, Ammann P, Schaer B, Osswald S *et al.* Cryoballoon versus radiofrequency catheter ablation of paroxysmal atrial fibrillation: biomarkers of myocardial injury, recurrence rates, and pulmonary vein reconnection patterns. *Heart Rhythm* 2010;**7**:1770–76.
7. Schade A, Langbein A, Spehl S, Barth S, Deneke T, Groschup G *et al.* Recurrence of paroxysmal atrial fibrillation after cryoisolation of the pulmonary veins. Is a 'redo' procedure using the cryoballoon useful? *J Interv Card Electrophysiol* 2013;**36**:287–95.
8. Fürnkranz A, Chun KRJ, Nuyens D, Metzner A, Köster I, Schmidt B *et al.* Characterization of conduction recovery after pulmonary vein isolation using the 'single big cryoballoon' technique. *Heart Rhythm* 2010;**7**:184–90.
9. Ahmed H, Neuzil P, Skoda J, D'Avila A, Donaldson DM, Laragy MC *et al.* The permanency of pulmonary vein isolation using a balloon cryoablation catheter. *J Cardiovasc Electrophysiol* 2010;**21**:731–37.
10. Bordignon S, Fürnkranz A, Dugo D, Perrotta L, Gunawardene M, Bode F *et al.* Improved lesion formation using the novel 28 mm cryoballoon in atrial fibrillation ablation: analysis of biomarker release. *Europace* 2014;**16**:987–93.
11. Chierchia GB, Di Giovanni G, Ciconte G, de Asmundis C, Conte G, Sieira-Moret J *et al.* Second-generation cryoballoon ablation for paroxysmal atrial fibrillation: 1-year follow-up. *Europace* 2014;**16**:639–44.
12. Straube F, Dorwarth U, Vogt J, Kuniss M, Heinz Kuck K, Tebbenjohanns J *et al.* Differences of two cryoballoon generations: insights from the prospective multicentre, multinational FREEZE Cohort Substudy. *Europace* 2014; doi:10.1093/europace/euu162.
13. Spragg DD, Khurram I, Zimmerman SL, Yarmohammadi H, Barcelon B, Needleman M *et al.* Initial experience with magnetic resonance imaging of atrial scar and co-registration with electroanatomic voltage mapping during atrial fibrillation: success and limitations. *Heart Rhythm* 2012;**9**:2003–9.
14. McGann CJ, Kholmovski EG, Oakes RS, Blauer JJ, Daccarett M, Segerson N *et al.* New magnetic resonance imaging-based method for defining the extent of left atrial wall injury after the ablation of atrial fibrillation. *J Am Coll Cardiol* 2008;**52**:1263–71.
15. Badger TJ, Daccarett M, Akoum NW, Adjei-Poku YA, Burgon NS, Haslam TS *et al.* Evaluation of left atrial lesions after initial and repeat atrial fibrillation ablation: lessons learned from delayed-enhancement MRI in repeat ablation procedures. *Circ Arrhythm Electrophysiol* 2010;**3**:249–59.
16. Perry D, Morris A, Burgon N, McGann C, MacLeod R, Cates J. Automatic classification of scar tissue in late gadolinium enhancement cardiac MRI for the assessment of left-atrial wall injury after radiofrequency ablation. *Med Imaging* 2012; doi: 10.1117/12.910833.
17. Peters DC, Wylie JV, Hauser TH, Nezafat R, Han Y, Woo JJ *et al.* Recurrence of atrial fibrillation correlates with the extent of post-procedural late gadolinium enhancement. *J Am Coll Cardiol Imaging* 2009;**2**:308–16.
18. Segerson NM, Daccarett M, Badger TJ, Shabaan A, Akoum N, Fish EN *et al.* Magnetic resonance imaging-confirmed ablative debulking of the left atrial posterior wall and septum for treatment of persistent atrial fibrillation: rationale and initial experience. *J Cardiovasc Electrophysiol* 2010;**21**:126–32.
19. Fürnkranz A, Bordignon S, Schmidt B, Gunawardene M, Schulte-Hahn B, Urban V *et al.* Improved procedural efficacy of pulmonary vein isolation using the novel second-generation cryoballoon. *J Cardiovasc Electrophysiol* 2013;**24**:492–97.
20. Lemola K, Hall B, Cheung P, Good E, Han J, Tamirisa K *et al.* Mechanism of recurrent atrial fibrillation after pulmonary vein isolation by segmental ostial ablation. *Heart Rhythm* 2004;**1**:197–202.
21. Ranjan R, Kholmovski EG, Blauer J, Vijayakumar S, Volland NA, Salama ME *et al.* Identification and acute targeting of gaps in atrial ablation lesion sets using a real-time magnetic resonance imaging system. *Circ Arrhythm Electrophysiol* 2012;**5**:1130–35.
22. Bisbal F, Guiu E, Cabanas-Grandio P, Berruezo A, Prat-Gonzalez S, Vidal B *et al.* CMR-guided approach to localize and ablate gaps in repeat AF ablation procedure. *JACC Cardiovasc imaging* 2014;**7**:653–63.
23. Hunter RJ, Jones DA, Boubertakh R, Malcolme-Lawes LC, Kanagaratnam P, Juli CF *et al.* Diagnostic accuracy of cardiac magnetic resonance imaging in the detection and characterization of left atrial catheter ablation lesions: a multicenter experience. *J Cardiovasc Electrophysiol* 2013;**24**:396–403.
24. Mahnkopf C, Badger TJ, Burgon NS, Daccarett M, Haslam TS, Badger CT *et al.* Evaluation of the left atrial substrate in patients with lone atrial fibrillation using delayed-enhanced MRI: implications for disease progression and response to catheter ablation. *Heart Rhythm* 2010;**7**:1475–81.
25. Fürnkranz A, Bordignon S, Schmidt B, Böhmig M, Böhmer MC, Bode F *et al.* Luminal esophageal temperature predicts esophageal lesions after second-generation cryoballoon pulmonary vein isolation. *Heart Rhythm* 2013;**10**:789–93.

Downloaded from by guest on March 26, 2016