Indian Pacing and Electrophysiology Journal 19 (2019) 129–133

Contents lists available at ScienceDirect

Indian Pacing and Electrophysiology Journal

journal homepage: www.elsevier.com/locate/IPEJ

Characterization of pulmonary vein reconnection post Cryoballoon ablation

Shivang Shah, Wenjie Xu, Evan Adelstein [1], Andrew Voigt, Samir Saba [1, 2], Sandeep Jain [*, 1]

Center for Atrial Fibrillation, Heart and Vascular Institute, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

ARTICLE INFO

Article history:
Received 17 January 2019
Accepted 18 February 2019
Available online 20 February 2019

Key words:
Achieve™
Cryoballoon
Ablation
Atrial Fibrillation
Pulmonary veins reconnections

ABSTRACT

Background: The Arctic Front Cryoballoon System is a technology in which substrate alterations in patients with atrial fibrillation (AF) recurrence have not been well characterized. In this study, we evaluated sites of pulmonary vein (PV) reconnections and the accuracy of the Achieve™ circular mapping catheter in detecting these reconnections after cryoablation.

Methods: This study included 15 patients undergoing redo AF ablation after a prior single cryoablation procedure. PV reconnection sites were determined by measuring PV signals and high output pacing from 4 vectors of the Achieve catheter. The results were compared with a roving mapping catheter guided by rotational intracardiac echocardiography (ICE) in the left atrium.

Results: All patients had PV reconnections (2.1 ± 0.8 veins/patient). The left superior PV was most commonly reconnected ($n = 11$), whereas the right inferior PV was least likely ($n = 3$). Both carinas (left: $n = 11$; right: $n = 7$) and left atrial appendage ridge ($n = 11$) were also frequently reconnected. Mapping with the Achieve catheter showed a positive predictive value (PPV) 100% and negative predictive value (NPV) 96% when compared with ICE guided mapping. In 2 patients, right superior PV reconnection was not identified by the Achieve.

Conclusion: During redo AF ablation after index cryoablation, multiple PVs are usually reconnected, with both carinas and left atrial appendage ridge being common sites of reconnection. The Achieve mapping catheter was able to identify reconnection with high positive and negative predictive values.

1. Background

Atrial Fibrillation (AF) is the most common sustained cardiac arrhythmia, impacting >25% of the population over a lifetime. AF is associated with significant morbidity and mortality, including thromboembolic complications, impaired quality of life, and diminished functional status [1–5]. Rhythm control is pursued in certain patients for the goal of minimizing and potentially eliminating symptoms associated with dysrhythmia. Multiple treatment strategies have been employed with varying success including antiarrhythmic medical therapy, surgical MAZE, and catheter-based ablation. It has been previously shown that the main trigger for paroxysmal atrial fibrillation (PAF) is ectopy arising from within the pulmonary veins (PV) [6]. Ablative therapy for PAF has therefore focused on the electrical isolation of the pulmonary veins. This has traditionally been performed using radiofrequency (RF) catheter ablation with a point-by-point technique. Cryoballoon ablation with the Arctic Front system (Medtronic, Inc., Minneapolis, MN) is a technology emerged as an alternative to radiofrequency. Cryoballoon ablation can be safely performed with a low incidence of major complications [7,8]. Cryoballoon ablation, compared with RF ablation, offers potential advantages, including shorter procedure times [9–11], decreased hospital length of stay [9], and decreased fluoroscopy time [8,10,11]. Cryoballon ablation has shown approximate 65% success rate in patients with paroxysmal atrial fibrillation and comparable to RF when studied head to head [11,12]. The mechanisms of recurrence and knowledge of site-specific pulmonary venous breakthrough may help modify the index procedure to be more robust. In addition, the utility of the Achieve™ (Medtronic, Inc., Minneapolis, MN) has been found to be effective at aiding in acute procedural success [13] and comparable to Lasso catheters [14], but has not been compared with ultrasound-guided roving

* Corresponding author.
E-mail address: jainsk@upmc.edu (S. Jain).
Peer review under responsibility of Indian Heart Rhythm Society.
[1] Research Grant from Medtronic.
[2] Research Grant from Boston Scientific.

https://doi.org/10.1016/j.ipej.2019.02.004

map catheter technique allowing for direct visualization in real time. Given the lack of rigorous evaluation, the purpose of the study was to evaluate the mechanisms of recurrent atrial fibrillation (AF) after use of the Arctic Front Ablation system. The Achieve mapping catheter was evaluated head-to-head with our current method of ultrasound guided electrogram recordings from a conventional mapping catheter in addition to high output PV pacing.

2. Methods

2.1. Patient cohort

Patients over age 18 presenting for re-do catheter ablation for AF after an index pulmonary vein isolation (PVI) procedure utilizing the Arctic Front Cryoballoon system were eligible for enrollment in this study. The group consisted of 4 patients treated with the 1st generation Arctic Front Cryoballoon system and 11 patients with the 2nd generation system. The strategy for the index ablation procedure included an occlusive venogram without intracardiac echocardiography (ICE) guidance. PV exit block was confirmed by high output pacing from within each pulmonary vein. The protocol was approved by the Institutional Review Board at the University of Pittsburgh and informed consent was obtained by the procedural electrophysiologist.

2.2. Re-do procedure

Patients underwent pre-procedural transesophageal echocardiography and CT angiogram to evaluate PV anatomy. The ablation procedure was performed under general anesthesia with double transeptal access. Index ablation utilized a dosing algorithm of 240 s x 2 applications.

PV reconnection was determined at the onset of the procedure by two separate methods: first, an Achieve mapping catheter was placed in each of the PV with evaluation for pulmonary vein potentials as well as high output pacing performed from at least 4 distinct bipoles of the Achieve catheter within each PV; secondly, a map catheter guided by rotational intracardiac echocardiography (ICE) (9 MHz, Boston Scientific) was placed in the left atrium (LA) to precisely specify catheter location. The ICE image was aligned to a horizontal carina. In those with PV re-connections, the specific locations of the breakthrough as determined by presence of PV signal or LA capture with high output (10mA/2 ms) unipolar pacing from within the veins and location of breakthrough was confirmed with ICE. The images were divided into 6 segments along a clock face within each PV and sites of PV potentials were recorded (as illustrated in Fig. 1) [15]. After this data collection, ablation strategy was as per operator discretion. Of note, patients were followed in the arrhythmia clinic and participated in a registry for clinical outcomes. For each subject enrolled, we recorded detailed baseline characteristics, including CHA_2DS_2-VASc, pulmonary vein anatomy, and cardiac studies.

2.3. Statistics

Descriptive statistics are reported as number and percentages for discrete variables and means ± standard deviation for continuous variables.

3. Results

3.1. Patient characteristics

We enrolled 15 patients from February 2014 to January 2015. All of our redo PVI patients had cryoballoon as the method of ablation for their initial PVI. They all had conventional anatomy, resulting in a total of 60 pulmonary veins. The characteristics of the patients are listed in Table 1. The mean age of the patients was 58.0 ± 9.8 years. The mean duration from the index cryoablation procedure was 15.1 ± 9.0 months. The mean CHA_2DS_2-VASc score was 1.8 ± 1.1. All of the patients had an LVEF ≥40%, were without chronic renal disease, and 1 patient had history of stroke.

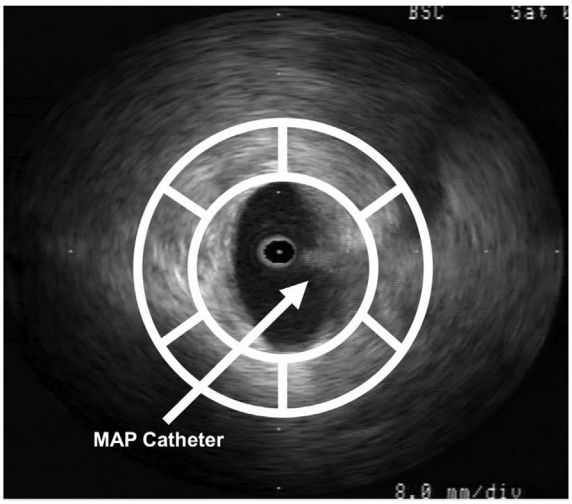

Fig. 1. Rotational intracardiac echocardiography. A mapping catheter was guided by rotational intracardiac echocardiography to determine breakthrough as seen with local signals as well as unipolar pacing. The PV was divided into six segments along a clock face to allow localization of PV reconnection.

3.2. Reconnections

All patients had at least one PV reconnection with a mean of 2.1 ± 0.8 veins reconnected per patient. The left superior PV was most commonly reconnected PV (73%), whereas the right inferior PV was least likely (20%). Both carinas (left: 73%; right: 47%) and left atrial appendage ridge (73%) were also frequently reconnected. This is further illustrated in Fig. 2. When analyzed separately, both generations of the cryoballoon showed frequent reconnections to the left atrial appendage ridge and left carina, whereas the right inferior PV was least likely to be reconnected such that the overall pattern of reconnection was similar between both generations. The site of reconnections did not change When the PV reconnections were localized on a 6 segment clock face diagram, the frequent site of reconnections were consistent with the appendage ridge and carinas. The right superior PV had frequent reconnection sites along

Table 1
Baseline patient characteristics.

Female	6 (40%)
Age (years)	58.0 ± 9.8
Hypertension	9 (60%)
Diabetes	0
Prior Stroke	1 (7%)
CHF	0
Coronary Artery Disease	2 (13%)
CABG	1 (7%)
Vascular Disease	3 (20%)
Tobacco Use	6 (40%)
Chronic Kidney Disease	0
Persistent AF	1 (7%)
$CHADS_2$	1.0 ± 0.9
CHA_2DS_2-VASc	1.8 ± 1.1
HAS-BLED	1.0 ± 0.8

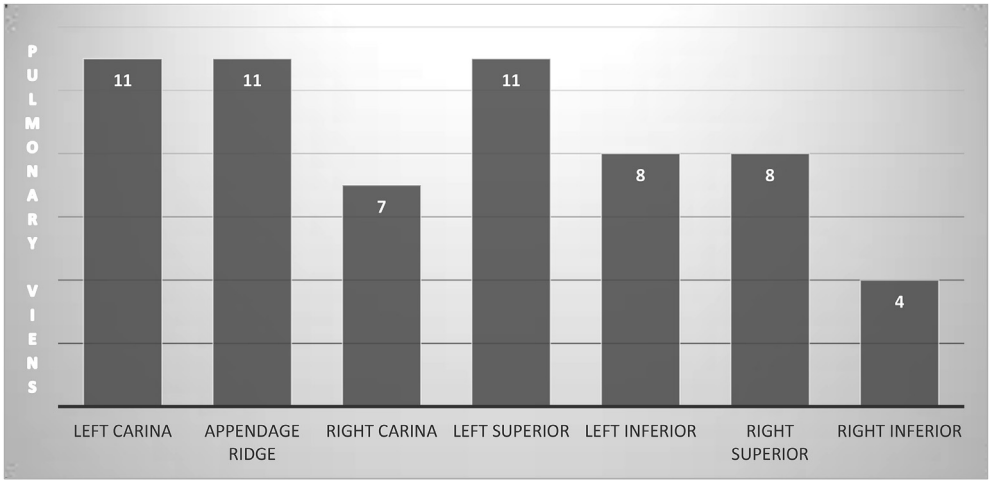

Fig. 2. Sites of pulmonary vein reconnections.

the 2 to 8 o'clock positions. These findings are shown in Fig. 3 as a density plot and in Fig. 4 in a chart format.

3.3. Comparison of entrance block by Achieve signal with exit block by achieve pacing

The Achieve catheter detected signal in 28 PVs, indicating lack of entrance block, and of the 28 PVs, capture of atrium by pacing from Achieve catheter was also demonstrated in 23 PVs, indicating the lack of exit block (1 of the PVs could not be assessed for exit block due to AF). The Achieve catheter did not detect signal in 28 PVs, of which pacing from the Achieve catheter did not capture the atrium in 25 PVs, indicating entrance and exit block (2 of the PVs could not be assessed for exit block due to AF). Overall, the presence or the lack of entrance block by Achieve signals correlate with atrial capture or non-capture by pacing from Achieve catheter.

3.4. Comparison of pulmonary vein isolation confirmation by Achieve with confirmation by ICE guided pacing

31 PVs were found to be reconnected by ICE guided pacing, of which 30 veins were also found to be reconnected by Achieve catheter. 24 PVs were found to be isolated by ICE guided pacing, compared to 25 PVs found to be isolated by Achieve catheter. In 2 patients, right superior PV reconnection was not identified by the Achieve. Also, 5 PV were excluded because of AF during the procedure or unclear signals (3 PVs for AF and 2 for unclear signals).

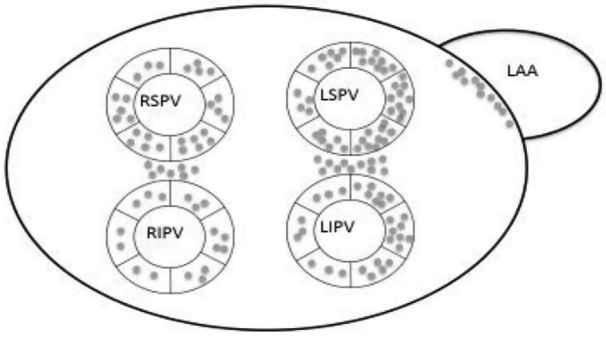

Fig. 3. Density plot of pulmonary vein reconnection sites by intracardiac echocardiography.

The 2 excluded PVs with unclear signals on the Achieve were shown to be isolated by ICE guided pacing. This data is further broken down among the PVs and shown in Fig. 5. When PV reconnection is defined by either the presence of PV signal on Achieve catheter or capture of atrial tissue by pacing within the PV, it correlated well with reconnection found by ICE guided pacing. Similarly, when acute PVI success is defined by both the lack of PV signal and lack of capture of atrial tissue by Achieve catheter, the positive predictive value (PPV) was 97% and the negative predictive value (NPV) was 92%. . Therefore, mapping with the Achieve catheter correlated well with isolation found by ICE guided pacing.

4. Conclusion

In this study, we evaluated the characteristics of pulmonary vein reconnection after an initial cryoballoon pulmonary vein isolation procedure. Patients with pulmonary vein reconnection often had multiple veins reconnected. Common areas of reconnections were the carinas and the left atrial appendage ridge. The right inferior PV usually poses special technical challenges for complete occlusion due to its location; however, in our study, it has the least number of reconnections. The most commonly reconnected vein was the left superior PV, one that is usually relatively easier to achieve complete occlusion from procedural standpoint. When the sites of reconnection are plotted into an anatomic density map, the sites with the densest rate of reconnections were the segments between the left superior PV and the left atrial appendage (Fig. 3). This is also seen in the superolateral portion of the left inferior PV. Therefore, we postulate that the increased tissue thickness of the left atrial appendage ridge could hinder complete transmural lesion and thus result in frequent reconnection of specifically the left superior PV but may also impact the left inferior PV. Dissimilarly, Kuhne et al. Furnkranz et al. demonstrated a general trend towards inferior location within the PV as site of reconnections, particularly for septal PVs, after an index cryoablation procedure [16,17]. The technique used in these studies did not have the visualization and resolution possible with ICE in the LA and also provided no data on the utility of Achieve for treatment of recurrences. With these new visualization tools, it may suggest more vigilant testing following index ablation in this region could prevent future reconnections. It may also suggest waiting longer to test for entrance and exit block and consideration of more provocative methods such as an Adenosine challenge as described [18].

We also compared the effectiveness of Achieve catheter in

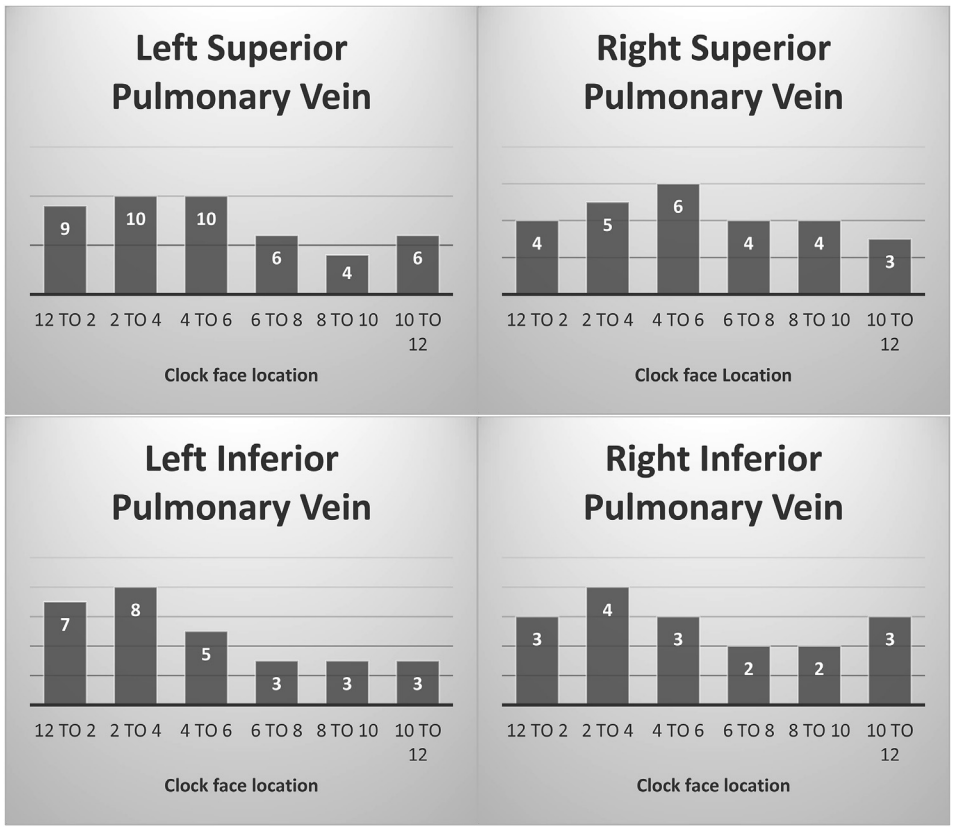

Fig. 4. Number of pulmonary vein reconnections by clock face location of each pulmonary vein.

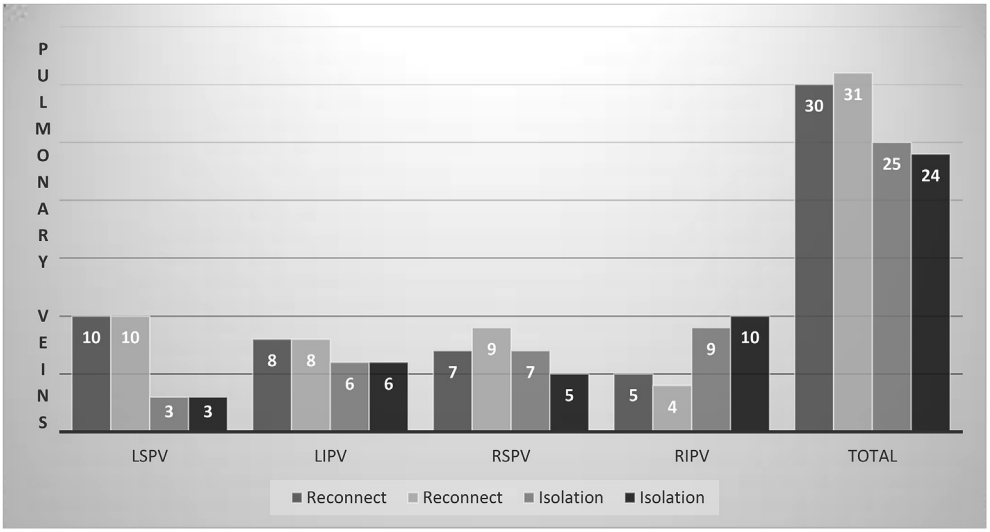

Fig. 5. Comparison OF PV reconnection/isolation by achieve vs. ice guided.

finding pulmonary vein reconnection to the gold standard ICE guided mapping catheter. The Achieve catheter was effective in confirming pulmonary vein reconnection and isolation with a PPV 97% and NPV 92% when compared to the gold standard method. We postulate that the false negative determined by the Achieve catheter may have been due to lack of contact between the electrode and the pulmonary vein tissue. Therefore, it suggests us to be more cautious in accepting no signals as truly entrance block. This may allow the need for more manipulation with the Achieve catheter and the use of a 3-D mapping system to aide in visualization of adequate tissue contact especially in larger vein sizes. The positioning of the Achieve catheter in an oblong shape along the long axis of the vessel often prevents precise localization of breakthrough signals along the cross section of the pulmonary vein. A detailed voltage map can certainly help localize sites of breakthrough but also need to be mindful of far field appendage signal which can affect interpretation.

There are several limitations in our study. First, this study was

conducted in a single center with a limited number of different operators. Unfortunately, the details of the timing of isolation often were not available as some of the initial cases were performed without an Achieve mapping catheter but rather over a guidewire. Second, the population size of this study was small with 15 patients. However, when considering the pulmonary vein reconnections, we had a total of 60 pulmonary veins, which is adequate size to investigate the present question. Despite this, there is a need for further studies with a larger patient population. This would be better powered and may detect differences in pulmonary vein characteristics leading to reconnection.

In conclusion, we found that patients usually have multiple pulmonary veins reconnected with the left superior pulmonary vein, left atrial appendage, and carinas being common sites of reconnection. The Achieve catheter is also found to be an effective tool in detecting pulmonary vein reconnection or isolation with high positive and negative predictive values.

Disclosures

The study was funded by an investigator grant from Medtronic.

References

[1] Luik A, Merkel M, Hoeren D, Riexinger T, Kieser M, Schmitt C. Rationale and design of the FreezeAF trial: a randomized controlled noninferiority trial comparing isolation of the pulmonary veins with the cryoballoon catheter versus open irrigated radiofrequency ablation in patients with paroxysmal atrial fibrillation. Am Heart J 2010 Apr;159(4):555–60. https://doi.org/10.1016/j.ahj.2010.01.008. e1.

[2] Haissaguerre M, Jais P, Shah DC, Garrigue S, Takahashi A, Lavergne T, et al. Electrophysiological end point for catheter ablation of atrial fibrillation initiated from multiple pulmonary venous foci. Circulation 2000 Mar 28;101(12):1409–17.

[3] Packer DL, Asirvatham S, Munger TM. Progress in nonpharmacologic therapy of atrial fibrillation. J Cardiovasc Electrophysiol 2003 Dec;14(12 Suppl):S296–309.

[4] Wazni OM, Marrouche NF, Martin DO, Verma A, Bhargava M, Saliba W, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. J Am Med Assoc 2005 Jun 1;293(21):2634–40.

[5] Guhl EN, Siddoway D, Adelstein E, Voigt A, Saba S, Jain SK. Efficacy of cryoballoon pulmonary vein isolation in patients with persistent atrial fibrillation. J Cardiovasc Electrophysiol 2016;27:423–7. https://doi.org/10.1111/jce.12924.

[6] Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998;339:659–66.

[7] Neumann T, Vogt J, Schumacher B, Dorszewski A, Kuniss M, Neuser H, Kurzidim K, Berkowitsch A, Koller M, Heintze J, Scholz U, Wetzel U, Schneider MA, Horstkotte D, Hamm CW, Pitschner HF. Circumferential pulmonary vein isolation with the cryoballoon technique results from a prospective 3-center study. J Am Coll Cardiol 2008 Jul 22;52(4):273–8. https://doi.org/10.1016/j.jacc.2008.04.021.

[8] Guhl EN, Siddoway D, Adelstein E, Bazaz R, Mendenhall GS, Nemec J, Saba S, Schwartzman D, Voigt A, Wang NC, Jain SK. Incidence and predictors of complications during cryoballoon pulmonary vein isolation for atrial fibrillation. J Am Heart Assoc 2016 Jul 21;5(7):e003724. https://doi.org/10.1161/JAHA.116.003724.

[9] Siddoway D, Friehling M, Voigt A, Saba S, Jain S. Improved resource utilization with similar efficacy during early adoption of cryoballoon pulmonary vein isolation as compared to radiofrequency ablation for paroxysmal atrial fibrillation. J Atr Fibrillation 2015 Mar 28:1–5.

[10] Kojodjojo P, O'Neill MD, Lim PB, Malcolm-Lawes L, Whinnett ZI, Salukhe TV, Linton NW, Lefroy D, Mason A, Wright I, Peters NS, Kanagaratnam P, Davies DW. Pulmonary venous isolation by antral ablation with a large cryoballoon for treatment of paroxysmal and persistent atrial fibrillation: medium-term outcomes and non-randomised comparison with pulmonary venous isolation by radiofrequency ablation. Heart 2010;96:1379–84.

[11] Kuck KH, Brugada J, Fürnkranz A, Metzner A, Ouyang F, Chun KR, Elvan A, ArentzT, Bestehorn K, Pocock SJ, Albenque JP, Tondo C, FIRE AND ICE Investigators. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. N Engl J Med 2016 Jun 9;374(23):2235–45. https://doi.org/10.1056/NEJMoa1602014. Epub 2016 Apr 4. PubMed PMID: 27042964.

[12] Vogt J, Heintze J, Gutleben KJ, Muntean B, Horstkotte D, Nölker G. Long-term outcomes after cryoballoon pulmonary vein isolation: results from a prospective study in 605 patients. J Am Coll Cardiol 2013 Apr 23;61(16):1707–12. https://doi.org/10.1016/j.jacc.2012.09.033. Epub 2012 Nov 28.

[13] Chierchia GB, de Asmundis C, Namdar M, Westra S, Kuniss M, Sarkozy A, Bayrak F, Ricciardi D, Casado-Arroyo R, Rodriguez Manero M, Rao JY, Smeets J, Brugada P. Pulmonary vein isolation during cryoballoon ablation using the novel Achieve inner lumen mapping catheter: a feasibility study. Europace 2012;14(7):962–7.

[14] Gang Y, Gonna H, Domenichini G, Sampson M, Aryan N, Norman M, Behr ER, Zuberi Z, Dhillon P, Gallagher MM. Evaluation of the Achieve Mapping Catheter in cryoablation for atrial fibrillation: a prospective randomized trial. J Intervent Card Electrophysiol 2016 Mar;45(2):179–87.

[15] Schwartzman D, Williams JL. Electroanatomic properties of pulmonary vein antral regions enclosed by encircling ablation lesions. Europace 2009 Apr;11(4):435–44. https://doi.org/10.1093/europace/eun361. Epub 2008 Dec 23.

[16] Kühne M, Suter Y, Altmann D, Ammann P, Schaer B, Osswald S, Sticherling C. Cryoballoon versus radiofrequency catheter ablation of paroxysmal atrial brillation: biomarkers of myocardial injury, recurrence rates, and pulmonary vein reconnection patterns. Heart Rhythm 2010;7:1770–6.

[17] Fürnkranz A, Chun KR, Nuyens D, Metzner A, Köster I, Schmidt B, Ouyang F, Kuck KH. Characterization of conduction recovery after pulmonary vein isolation using the "single big cryoballoon" technique. Heart Rhythm 2010;7(2):184–90. https://doi.org/10.1016/j.hrthm.2009.10.038. Epub 2009 Nov 10. PubMed PMID: 20129295.

[18] Wang N, Phan S, Kanagaratnam A, Kumar N, Phan K. Adenosine testing after atrial fibrillation ablation:systematic review and meta-analysis. Heart Lung Circ 2018 May;27(5):601–10.