Ablation catheters for atrial fibrillation: benefits and complications

Treatment of symptomatic atrial fibrillation by ablation has become a well-established therapeutic option. Electrophysiologists provide pulmonary vein isolation and substrate modification by using different mapping systems and ablation catheters, which differ in many technical aspects, such as the energy form applied, shape or mapping characteristics. Both cryothermal and radiofrequency energy have been routinely used for ablation therapy, but lately high-intensity-focused ultrasound has been described as a promising energy alternative. In this article we try to differentiate between the commonly used ablation catheters in atrial fibrillation ablation, reflecting on their potential in terms of efficacy, safety and feasibility.

KEYWORDS: ablation catheter ▪ atrial fibrillation ▪ cryothermal energy ▪ high-intensity-focused ultrasound ▪ pulmonary vein ablation catheter ▪ radiofrequency energy

Dong-In Shin[1,2†] & Thomas Deneke[1,3]

[†]Author for correspondence:
[1]Academic Heart Center Cologne, Urbacher Weg 19, 51149 Cologne, Germany
Tel.: +49 220 3566 1472
Fax: +49 203 566 1473
di.shin@khporz.de
[2]University of Witten-Herdecke, Germany
[3]Ruhr-University Bochum, Germany

Treatment of symptomatic and drug-refractory atrial fibrillation (AF) by ablation has been established as a feasible and effective therapy option. Since Haissaguerre's landmark findings demonstrating that electrical activity of pulmonary veins (PVs) play a crucial role in the initiation of paroxysmal AF [1], electrical isolation of PVs remain the primary goal in all ablative strategies. Despite all the technical developments in the field of mapping systems and ablation catheters, ablation of AF is still a time-consuming, skill-demanding and challenging procedure. Therefore, different ablation catheters have been developed in order to provide an effective, safe and accurate isolation of PVs.

Ablation catheters using radiofrequency energy

Most procedures for AF ablation have been performed using a single and irrigated-tip catheter (4 or 8 mm) in combination with a 3D mapping system. Owing to the complex anatomy of the left atrium and its junctions to the left atrial appendage PV, 3D mapping systems (CARTO®, Biosense Webster, CA, USA; NavX™, St. Jude Medical, MN, USA) allow an anatomical reconstruction of the left atrium and visualization of the catheter tip positioning or movement during ablation procedure. Since the introduction of image integration, a tool that allows a fusion of multislice-CT or MRI scans of the left atrium and PVs with 3D mappings during the procedure (available for CARTO and NavX), safety, efficiency and feasibility in PV isolation have been improved significantly [2]. Using radiofrequency (RF) energy, 20–30 W (temperature-controlled energy delivery) are applied by an irrigated-tip catheter. Ablation strategies differ, mainly in a segmental versus circumferential ablation line. Segmental PV isolation is achieved by an application of RF impulses at the PV ostia; owing to the increased risk of PV ostium stenosis, alternatively large circular lesions around all ipsilateral PV ostia can be performed. Both in segmental and circumferential ablation, a complete ablation line around the PV is needed to reach the procedural end point of electrical PV isolation. Using a single-tip catheter this goal is difficult to achieve and strongly dependent on the operator's manual skills and experience. Owing to undetected gaps during PV isolation, left atrial tachycardia occurs in many patients after the procedure, which are often less tolerated by patients and often as difficult to ablate by electrophysiologists than AF itself. Although creation of long linear lesions by a single-tip catheter is challenging, it offers the advantage of targeted ablation at any location in the left atrium. This is crutial for the ablation of complex fractionated atrial electrograms and difficult to perform by multielectrode ablation catheters. Furthermore, additional lines (i.e., left atrial roof line, mitral isthmus line and so on) can be performed depending on the need of left atrial substrate modification in addition to PV isolation. Studies based on RF energy ablation demonstrated single procedure efficacy of 46 to 77% in patients with paroxysmal AF after a follow-up time of 1 year [3,4], while success rates in patients with persistent AF seems to be lower with 27 to 67% [3,5]. Owing to limitations in

future medicine part of fsg

manual catheter manipulation concerning tissue contact, catheter stability or maneuverability, efforts have been made to overcome these problems by robotic or magnetic navigation. The robotic system (Sensei™ Robotic Catheter System, Hansen Medical, CA, USA) consists of a physician workstation capable of controlling a robotic catheter manipulation arm that transmits operator's movements to a steerable sheath system, consisting of an outer and inner sheath that can be controlled by the use of six pull wires. This special sheath system (Figure 1) provides a precise steering of any standard ablation catheter and can be used in combination with all available 3D mapping systems. In a single-center study by Di Biase *et al.,* safety and feasibility of this robotic catheter navigation could be demonstrated [6]. The end point of freedom from AF at the follow-up, after 3 months, could be reached in 85% of all treated patients. Furthermore, a significant reduction in fluoroscopy time, compared with manual ablation, could be achieved. Another principle of nonmanual steering of the ablation catheter was introduced in 2002 using a magnetic navigation system for ablation [7,8]. The magnetic navigation system NIOBE® (Stereotaxis, MO, USA) creates a steerable magnetic field around the patient using an outer magnetic field with 0.08 T. Small magnets are integrated in the tip of the soft ablation catheter (Figure 2), which can be steered by changing the outer magnetic field. This allows the operator to perform a mapping and ablation procedure from outside of the catheter laboratory in a fully remote-controlled way. Besides exact catheter-tip navigation and a significant reduction of operator's radiation exposure, there are few data on AF ablation using magnetic navigation owing to the late release of an open irrigated-tip catheter.

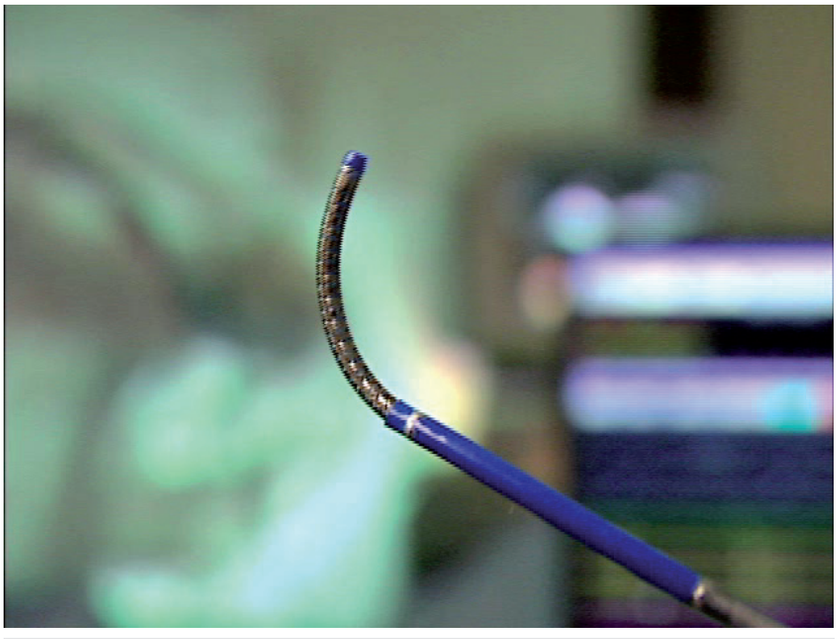

Figure 1. Steerable inner and outer guide catheter ARTISAN™ (Hansen Medical, Mountain View, CA, USA) for use with the Sensei™ Robotic Catheter System (Hansen Medical).
Image courtesy of U Meyerfeldt, Schwarzwald-Baar Klinikum Villingen-Schwenningen, Villingen, Germany.

Ablation catheters using cryothermal energy

The cryoballoon technique for AF ablation was introduced in 2005 [9] in order to overcome procedure-related complications during RF ablation, such as PV-ostium stenosis, thromboembolic events or atrial–esophageal fistula. The cryoballoon catheter (Arctic Front®, Medtronic, CA, USA) consists of a double-walled balloon that can be guided over the wire (Figure 3). Nitrous oxide is used as the refrigerant and is delivered under pressure from a console into the inner balloon chamber via a lumen within 2 mm of the catheter tip, where it undergoes a liquid-to-gas phase change resulting in the inner balloon cooling to temperatures less than -80°C. The cryoballoon is advanced into the left atrium by a steerable 12-French sheath. A central lumen in the catheter can be used for contrast injection into the PV and for a guidewire to advance the catheter to the PV orifice. Through contrast injection, peri-balloon leaks can be detected and the balloon position in the PV can be adjusted to achieve an optimal closure of the PV ostium. Cryothermal energy is delivered for 4–8 min per freeze. The histological quality of cryothermal lesions differ from RF-induced lesions in several ways. Cryolesions are homogenous with intact endothelium and are free of thrombus formation. Collagen formation of the endocardium is preserved while tissue shrinkage and destruction of the tissue structure by heating is typical in RF lesions. Furthermore, cryoablation seems to be safe with respect to PV stenosis in comparison with RF energy ablation [10]. Successful PV isolation can be performed using a cryoballoon catheter in 84–93% of targeted PVs [11,10]. A prospective three-center study by Neumann *et al.* demonstrated successful treatment of paroxysmal AF with revovery from AF in 74% of cases after a follow-up time of 6 months [10]. Owing to the limited opportunities of substrate modification persistent AF could be treated successfully in only 42% of all cases. Using the cryoballoon catheter, phrenic-nerve palsy was reported as a major complication [11], but in most cases patients recovered fully over time so the complication of

a chronic phrenic nerve palsy seems to be rare. Although there have been no reported instances of atrial–esophageal fistula after cryoablation, there is evidence that cryothermal energy is associated with esophageal injury. In an animal study by Ripley *et al.*, direct application of cryoablation and RF ablation created similar acute and chronic lesion dimensions on the esophagus of calves [12]. Furthermore, cryoballoon ablation in humans demonstrated significant decreases in luminal esophageal temperatures, resulting in esophageal ulcerations in 17% of patients [13].

Ablation using a duty-cycled decapolar mapping & ablation catheter

This ablation system consists of a 9-French, over-the-wire, steerable, decapolar circular mapping and ablation catheter (FIGURE 4), with a maximum diameter of 25 mm (PVAC™, Medtronic, CA, USA). The diameter can be changed slightly by rotating the catheter tip. The 100% platinum electrodes are arranged on an eccentric nitinol frame intended for unidirectional tissue contact. The PV ablation catheter (PVAC) delivers energy from a multichannel generator (GENius™, Medtronic, CA, USA), which is capable of simultaneously delivering RF energy in a unipolar and bipolar fashion to up to 12 electrodes on the ablation catheter. Energy can be delivered independently to any or all of the electrodes in both a unipolar and bipolar configuration. Energy is delivered via a duty-cycled (on–off period) using a phase difference between adjacent electrodes. Ablations are temperature controlled using a predefined target temperature of typically 60°C and power is limited to a maximum of 8–10 W depending on the bipolar:unipolar energy ratio. Energy can be delivered in unipolar (between each electrode and dispersive patch), bipolar (between adjacent electrode pairs) and in 4:1, 2:1 or 1:1 bipolar:unipolar ratios. The PVAC electrodes are smaller than conventional ablation catheter tips, thus a power output of 10 W allows current densities equivalent to 4 mm ablation electrodes. The first data from a prospective trial, in which paroxysmal AF was treated by the PVAC, were published by Boersma *et al.* [14]. In treating 98 consecutive patients, 100% of targeted PVs could be isolated. After a follow-up time of 6 months, 83% of treated patients demonstrated no recurrence of AF without drug therapy. Furthermore, no procedure-related complications could be observed. These findings can be supported by our own clinical experience with PVAC [SHIN DI, DENEKE T, UNPUBLISHED DATA]. We performed PV isolation by PVAC in 99 consecutive patients with a mean procedural time of 104 ± 25 min. During ablation, 386 out of 387 PVs (99.7%) were successfully isolated with the PVAC. Total RF application duration was 28 ± 8 min and radiation duration was 20.7 ± 8 min. Owing to procedural complications, two arteriovenous fistulas and one

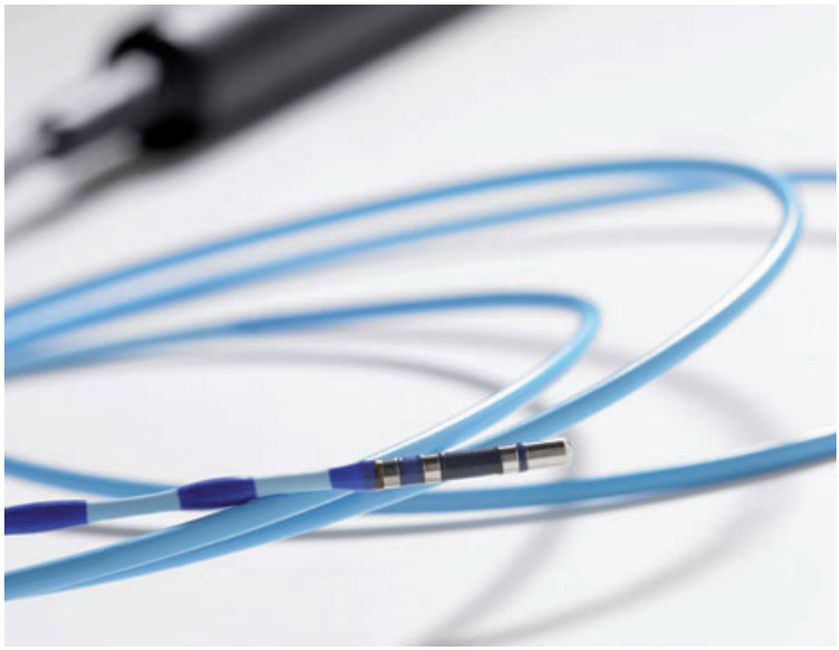

Figure 2. NAVISTAR RMT™ (Biosense Webster, CA, USA) temperature-sensing steerable navigation and ablation catheter for use in Stereotaxis NIOBE® magnetic navigation system (Biosense Webster).
Image courtesy of L von Rueden, Biosense Webster.

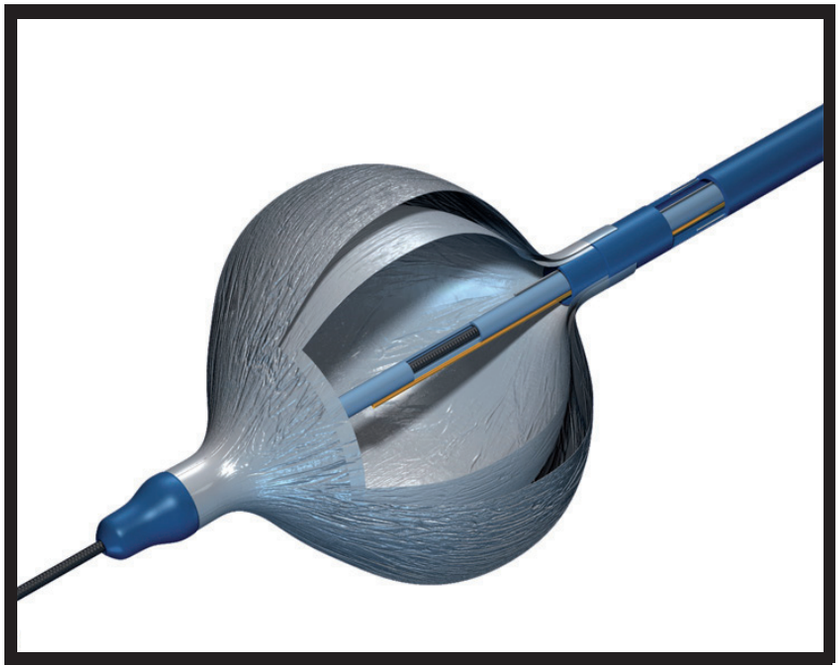

Figure 3. ArcticFront® cryoballoon catheter (Medtronic, Carlsbad, CA, USA).
Image courtesy of A Fischer, Medtronic.

reversible phrenic nerve palsy after isolation of the superior caval vein was documented. During early follow-up, after 3 months, 77% of patients with paroxysmal AF and 50% of those with persistent AF were free from AF and had been able to stop taking antiarrhythmic drugs after undergoing PV isolation alone in a single procedure. In patients with persistent AF, substrate modification is also needed to complete PV isolation. This ablation system offers three additional devices (multiarray septal ablation catheter [MASC™] multiarray ablation catheter [MAAC™] and tip-versatile ablation catheter [TVAC™]; Medtronic, CA, USA) to ablate complex fractionated atrial electrograms in the left atrial body.

Ablation catheters using high-intensity-focused ultrasound

The high-intensity-focused ultrasound (HIFU) ablation catheter (ProRhythm Inc., NY, USA) is a 10-French, steerable balloon catheter with a diameter of 24 mm and consists of two attached noncompliant balloons (Figure 5). The distal balloon is filled with a mixture of water and contrast media in a 4:1 ratio and contains a 9 MHz ultrasound crystal. The proximal balloon is filled with carbon dioxide and forms a parabolic surface at the base of the distal balloon, which reflects the ultrasound in a forward direction, focusing a 360° ring of ultrasound energy 2–6 mm in front of the distal balloon surface. The catheter has a central lumen that can be used for a guidewire (0.23") to position the balloon in the orifice of the PV in a over-the-wire mode, or for an application of contrast media. HIFU energy creates an irreversible injury to the targeted myocardium causing cell death through coagulative necrosis due to rapid (within 10 s) hyperthermal toxicity [15]. In contrast to RF-energy ablation, which depends on slow conduction heating by a close tissue-to-catheter tip contact, HIFU lesions can be induced independent of contact in a 20 mm diameter ring at a 5 mm depth [16]. Schmidt *et al.* published their data of a single-center study in which 15 patients could be enrolled for PV isolation (PVI) using a HIFU ablation balloon catheter [17]. Despite successful isolation of 89% of all targeted PVs, clinical outcome demonstrated disappointing results, with 58% of all patients being free from AF episodes. Furthermore, two patients experienced chronic phrenic nerve palsy by ablation that did not resolve after 12 months. In a canine model, Yokoyama *et al.* demonstrate that HIFU ablation can result in an esophageal ulcer when esophageal temperature was higher than 50°C and HIFU energy was applied unfocused and inside the PV [18].

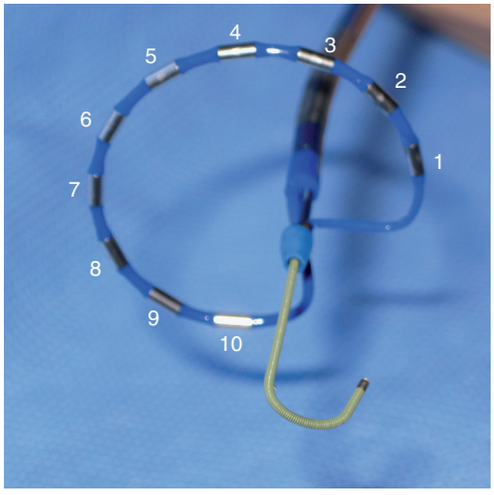

Figure 4. Decapolar PVAC™ (Medtronic, CA, USA) ablation catheter with over-the-wire technique. A total of 10 platinum electrodes are arranged on a nitinol frame array. Adjacent electrodes are used for bipolar signal acquisition (1/2, 3/4 and so on) and can be used for bipolar ablation.

Future perspective

Owing to the increasing numbers of patients with symptomatic AF, we have to face the urgent need for a feasible, safe and effective ablation technique. Performing PVI using RF energy and a single-tip catheter is associated with safety concerns, such as thromboembolic complications or atrial–esophageal fistula. Furthermore, point-by-point ablation remains a manually challenging procedure and has to deal with postprocedure rates of left atrial tachycardia up to 18–25%. The mean procedure time is strongly operator dependent, but can easily rise up to 3 or 4 h, especially in cases when additional lines of ablation or complex fractionated atrial electrograms are needed in addition to PVI. Robotic or magnetic navigation seem to overcome some of these problems, but are not available in every center yet. In our opinion, treatment for paroxysmal AF by PVI has to be achieved by a balloon or multipolar ablation catheter approach, which creates linear ablation lesions. Both PVAC and cryoballoon catheters seem to be feasible tools for a fast and safe PVI in patients with paroxysmal AF. For effective treatment of persistent AF, more tools are needed in order to perform a sufficient substrate modification. Thus, in this patient group a combination of a balloon catheter/multipolar ablation catheter approach and a single-tip-guided substrate modification could be necessary. HIFU energy seems to be a promising alternative energy form

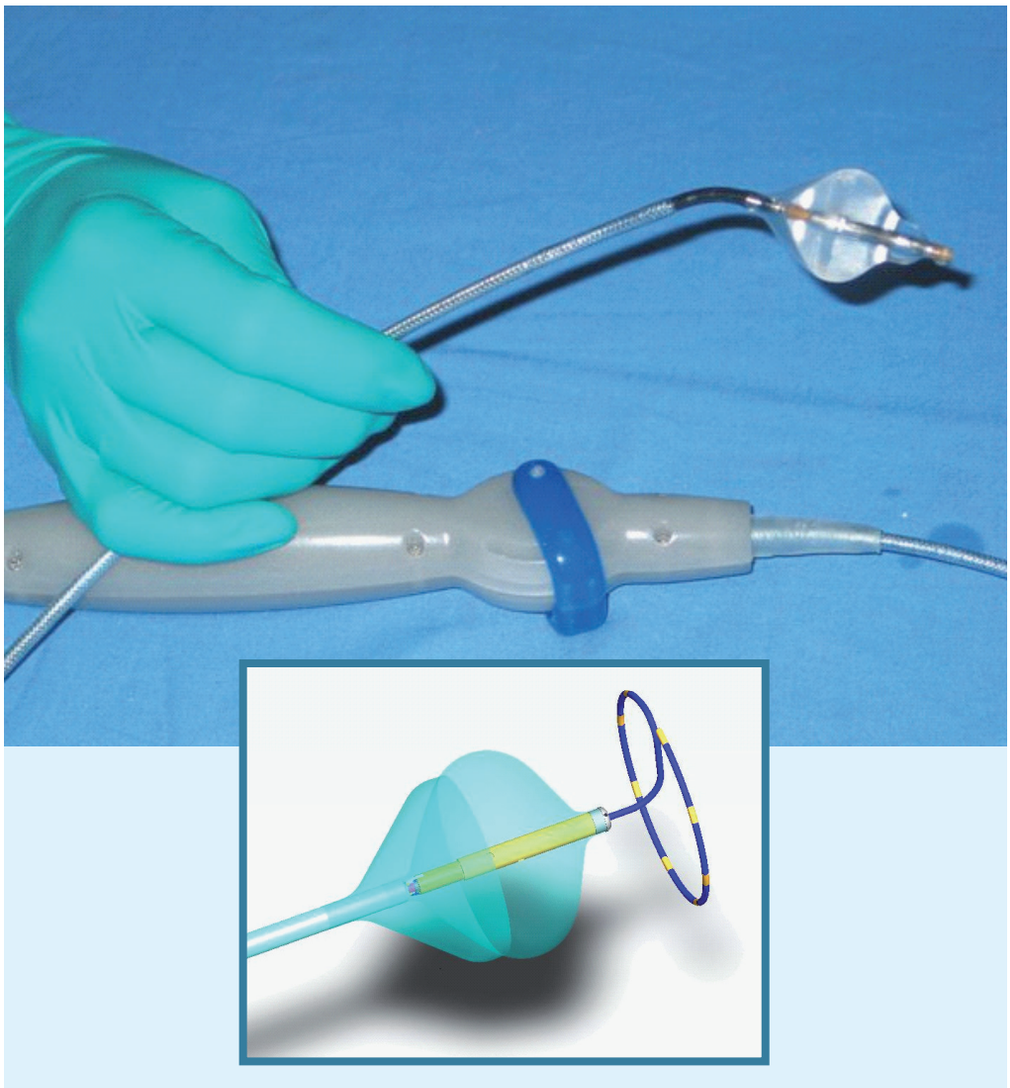

Figure 5. High-intensity-focused ultrasound balloon catheter (ProRhythm Inc., NY, USA) composed of a 10-French multilumen steerable catheter with a central lumen for a guide wire.
Image courtesy of B Schmidt, St. Georg Hospital, Hamburg, Germany.

owing to its ability to create linear lesions that are less dependent on absolute balloon–tissue contact compared with other balloon approaches, such as the cryoballoon catheter. Furthermore, the opportunity of providing visually guided energy and ablation lines might be a promising technical improvement. Owing to the complex and varied anatomy of PV ostia (e.g., single ostium, early branching, accessory PV and so on) a visually guided approach might optimize energy application in terms of safety and efficacy. A real-time visualization could be provided by endoscopic tools or real-time MRI scans, which have to be integrated in used mapping systems. Recently, Reddy *et al*. demonstrated the feasibility of a visually guided balloon catheter ablation of AF with an endoscopic ablation system (CardioFocus Inc., MA, USA) that allowed direct visualization of the target region and ablation using laser energy [19]. A total of 91% of all targeted PVs could be isolated successfully and a freedom of AF could be achieved in 60% of all patients after a drug-free period of 12 months. More data are needed to conclude if endoscopic ablation systems might be the clue to provide a safe, efficient and fast therapy in ablating AF.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Executive summary

- Ablation of atrial fibrillation (AF) is still a challenging and time consuming procedure. Efficacy, especially in the treatment of persistent AF, needs to be improved.
- Ablation by a single-tip, radiofrequency energy-delivering ablation catheter in combination with a 3D mapping system is still the most used ablation tool. Pulmonary vein isolation and substrate modification can be provided by a skilled operator. Thrombus formations, pulmonary vein stenosis, atrial–esophageal fistula and phrenic nerve palsy remain major complications. Performing linear lesions by a point-by-point ablation approach is still time consuming.
- Robotic or magnetic navigation might improve success rates, procedure time and safety when using a single-tip ablation catheter.
- The cryothermal balloon catheter is a promising tool for pulmonary vein isolation in the treatment of paroxysmal AF; substrate modification can not be achieved.
- The pulmonary vein ablation catheter (PVAC™; Medtronic, CA, USA) seems to be a feasible tool for a fast and effective pulmonary vein isolation in AF patients. Success rates are comparable to radiofrequency single-tip or cryoballoon catheters. Effectiveness of multiarray septal ablation catheter (MASC™, Medtronic), multiarray ablation catheter (MAAC™, Medtronic) and for substrate modification in treatment of persistent AF has to be studied.
- High-intensity-focused ultrasound ablation catheters (ProRhythm Inc., NY, USA) seem to be promising due to its independence on tissue–catheter contact and energy characteristics.
- If visually guided procedures can be the next step to take in order to improve effectiveness, safety of AF ablation has to be proven.

Bibliography

Papers of special note have been highlighted as:
- ▪ of interest
- ▪▪ of considerable interest

1 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.* 339, 659–666 (1998).

2 Malchano ZJ, Neuzil P, Cury RC *et al.*: Integration of cardiac CT/MR imaging with three dimensional electroanatomical mapping to guide catheter manipulation in the left atrium: implications for catheter ablation of atrial fibrillation. *J. Cardiovasc. Electrophysiol.* 17, 1221–1229 (2006).

3 Gaita F, Caponi D, Scaglione M *et al.*: Long-term clinical results of two different ablation strategies in patients with paroxysmal and persistent atrial fibrillation. *Circ. Arrhythm. Electrophysiol.* 1, 269–275 (2008).

4 Oral H, Chugh A, Good E *et al.*: A tailored approach to catheter ablation of paroxysmal atrial fibrillation. *Circulation* 113, 1824–1831 (2006).

5 Bhargava M, Di Biase L, Mohanty P *et al.*: Impact of type of atrial fibrillation and repeat catheter ablation on long-term freedom from atrial fibrillation: result from a multicenter study. *Heart Rhythm* 6, 1403–1412 (2009).

6 Di Biase L, Wang Y, Horton R: Ablation of atrial fibrillation utilizing robotic catheter navigation in comparison to manual navigation and ablation: single center experience. *J. Cardiovasc. Electrophysiol.* 20(12), 1328–1335 (2009).

7 Faddis MN, Blume W, Finney J *et al.*: Novel, magnetically guided catheter for endocardial mapping and radiofrequency catheter ablation. *Circulation* 106, 2980–2985 (2002).

8 Faddis MN, Chen J, Osborn J *et al.*: Magnetic guidance system for cardiac electrophysiology: A prospective trial of safety and efficacy in humans. *J. Am. Coll. Cardiol.* 42, 1952–1958 (2003).

9 Sarabanda A, Bunch TJ, Johnson SB *et al.*: Efficacy and safety of circumferential pulmonary vein isolation using a novel cryothermal balloon ablation system. *J. Am. Coll. Cardiol.* 46, 1902–1912 (2005).

▪ **First published manuscript describing the cryoballoon technique.**

10 Neumann T, Vogt J, Schumacher B *et al.*: Circumferential pulmonary vein isolation with the cryoballoon technique. *J. Am. Coll. Cardiol.* 52, 273–278 (2008).

▪▪ **Largest published multicenter study using the cryoballoon ablation catheter for atrial fibrillation (AF) with a success rate of 74% in paroxysmal AF and 42% in persistent AF after 6 months.**

11 Van Belle Y, Janse P, Rivero-Ayerza MJ *et al.*: Pulmonary vein isolation using an occluding cryoballoon for circumferential ablation: feasibility, complications, and short-term outcome. *Eur. Heart J.* 28, 2231–2237 (2007)

12 Ripley KL, Gage AA, Olsen DB *et al.*: Time course of esophageal lesions after catheter ablation with cryothermal and radiofrequency ablation: implication for atrio–esophageal fistula after catheter ablation for atrial fibrillation. *J. Cardiovasc. Electrophysiol.* 18, 642–646 (2007)

13 Ahmed H, Neuzil P, d'Avila A *et al.*: The esophageal effects of cryoenergy during cryoablation for atrial fibrillation. *Heart Rhythm* 6, 962–969 (2009)

14 Boersma L, Wijffels M, Oral H: Pulmonary vein isolation by duty-cycled bipolar and unipolar radiofrequency energy with a multielectrode ablation catheter. *Heart Rhythm* 5, 1635–1642 (2008).

▪▪ **First published manuscript using the pulmonary vein ablation catheter in paroxysmal AF, indicating a 6-month success rate of 83% recovery from AF.**

15 Okumura Y, Kolasa M, Johnson S *et al.*: Mechanism of tissue heating during high intensity focused ultrasound pulmonary vein isolation: implications for atrial fibrillation ablation efficacy and phrenic nerve protection. *J. Cardiovasc. Electrophysiol.* 19, 945–951 (2008).

16 Nakagawa H, Antz M, Wong T *et al.*: Initial experience using a forward directed, high-intensity focused ultrasound balloon catheter for pulmonary vein antrum isolation in patients with atrial fibrillation. *J. Cardiovasc. Electrophysiol.* 18, 136–144 (2007).

17 Schmidt B, Antz M, Ernst S *et al.*: Pulmonary vein isolation by high-intensity focused ultrasound: first in man study with a steerable balloon catheter. *Heart Rhythm* 4, 575–584 (2007).

18 Yokoyama K, Nakagawa H, Seres KA *et al.*: Focused ultrasound and side-firing unfocused ultrasound in the left atrium and inside the pulmonary vein. *Circ. Arrhythm. Electrophysiol.* 2, 41–49 (2009).

19 Reddy V, Neuzil P, Themistoclakis S: Visually guided balloon catheter ablation of atrial fibrillation. Experimental feasibility and first-in-human multicenter clinical outcome. *Circulation* 120, 12–20 (2009).

▪▪ **First manuscript describing and demonstrating the feasibility of a endoscopic ablation system, allowing visually guided ablation.**