

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.

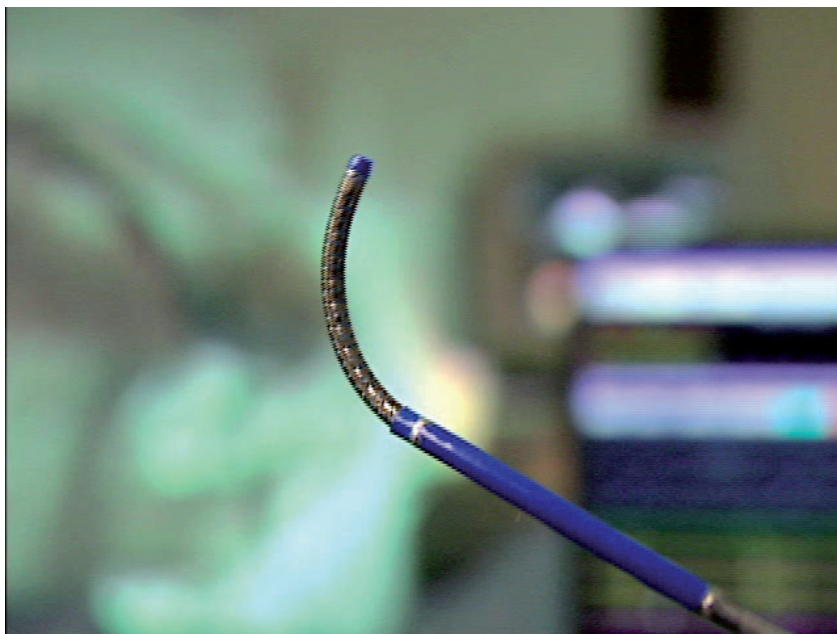


Figure 1. Steerable inner and outer guide catheter ARTISAN™ (Hansen Medical, Mountain View, CA, USA) for use with the Sensei™ Robotic Catheter System (Hansen Medical).

Image courtesy of U Meyerfeldt, Schwarzwald-Baar Klinikum Villingen-Schwenningen, Villingen, Germany.

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.

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 reversion 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

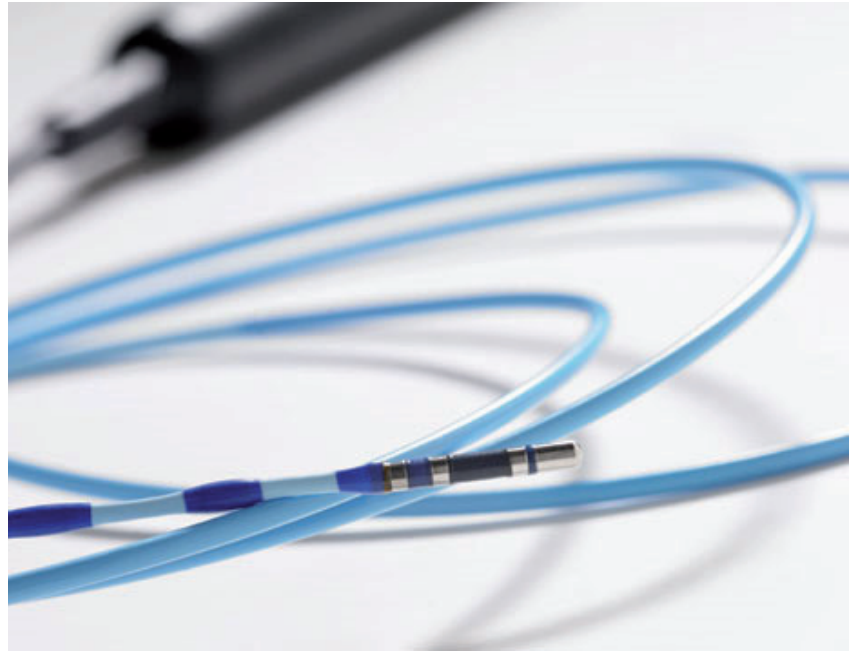


Figure 2. NAVISTAR RMT™ (Biosense Webster, CA, USA) temperature-sensing steerable navigation and ablation catheter for use in Stereotaxis NIOBE® magnetic navigation system (Biosense Webster).
Image courtesy of L von Rueden, Biosense Webster.

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

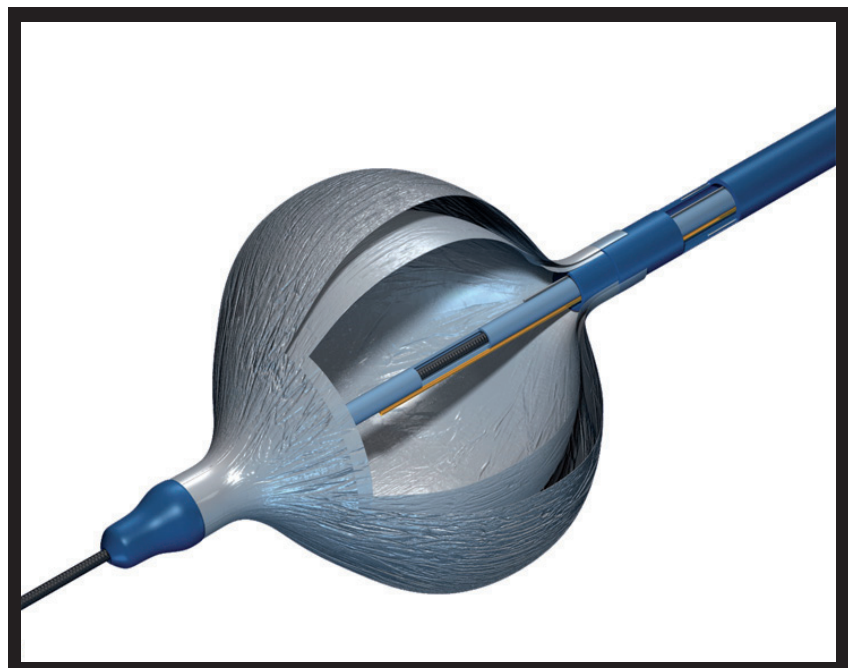


Figure 3. ArcticFront® cryoballoon catheter (Medtronic, Carlsbad, CA, USA).
Image courtesy of A Fischer, Medtronic.

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].

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

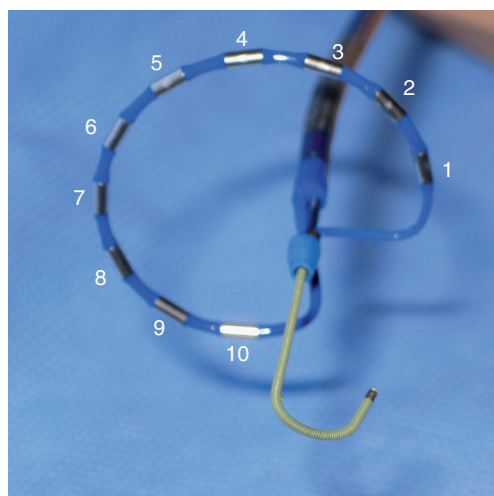


Figure 4. Decapolar PVAC™ (Medtronic, CA, USA) ablation catheter with over-the-wire technique. A total of 10 platinum electrodes are arranged on a nitinol frame array. Adjacent electrodes are used for bipolar signal acquisition (1/2, 3/4 and so on) and can be used for bipolar ablation.

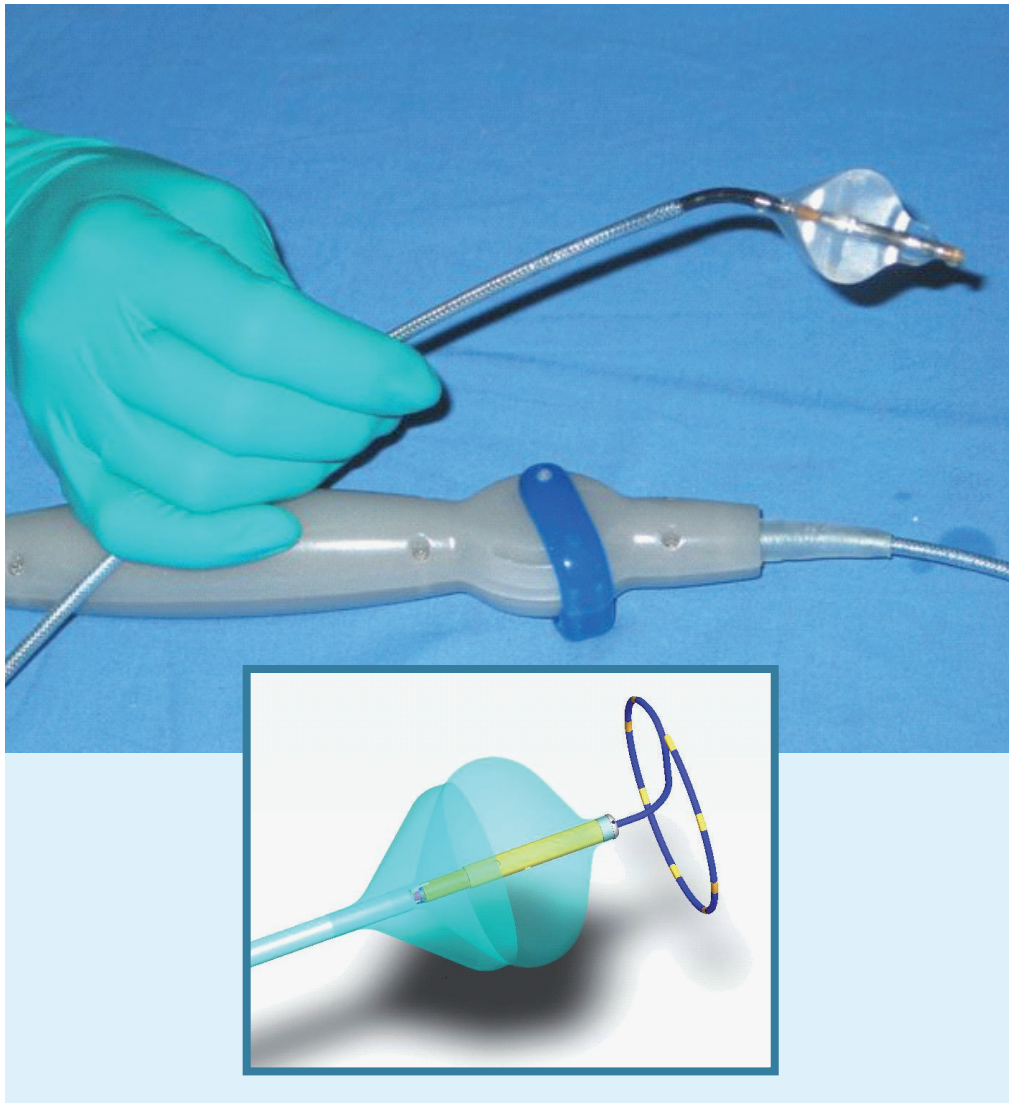


Figure 5. High-intensity-focused ultrasound balloon catheter (ProRhythm Inc., NY, USA) composed of a 10-French multilumen steerable catheter with a central lumen for a guide wire. Image courtesy of B Schmidt, St. Georg Hospital, Hamburg, Germany.

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.

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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.

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