The Future of Pulmonary Vein Isolation – Single-shot Devices, Remote Navigation or Improving Conventional Radiofrequency Delivery by Contact Monitoring and Lesion Characterisation?

David Filgueiras-Rama¹ and Jose L Merino²

1. Cardiac Electrophysiologist; 2. Head of the Robotic Cardiac Electrophysiology and Arrhythmia Unit, Department of Cardiology, Hospital Universitario La Paz, Madrid, Spain

Abstract

Pulmonary vein isolation is the main goal of atrial fibrillation (AF) ablation to date. Lack of isolation is associated with an increased risk of AF recurrences. Precise navigation to specific target sites, catheter stability and appropriate contact force are requisites for effective radiofrequency applications. Conventional manual-guided point-by-point radiofrequency energy delivery shows limitations to reach them, especially when performed by non-experienced electrophysiologists. New technological alternatives are rapidly arising and becoming clinically available to overcome some of the manual-guided radiofrequency delivery shortcomings. Here, we review the most recent clinical data, potential advantages, shortcomings and future directions of the new ablation strategies for pulmonary vein isolation.

Keywords

Atrial fibrillation, cryoballoon, ablation, remote navigation, electromagnets, contact force, radiofrequency, endoscopic guided, laser energy

Disclosure: The authors have no conflicts of interest to declare.

Received: 12 November 2012 **Accepted:** 20 February 2013 **Citation:** *Arrhythmia & Electrophysiology Review* 2013;**2**(1):59–64 **Access at:** www.AERjournal.com

Correspondence: Jose L Merino, Hospital Universitario La Paz, Robotic Cardiac Electrophysiology and Arrhythmia Unit, Department of Cardiology, Paseo de la Castellana 261, 1st floor, 28046 Madrid, Spain. E: jlmerino@arritmias.net

Atrial fibrillation (AF) is the most common sustained arrhythmia in the clinical practice.¹ The prevalence of the arrhythmia is progressively increasing in developed countries and moreover, it is expected to affect up to 12 million people only in the US by 2050.² Antiarrhythmic drugs continue to represent the first-line of treatment in AF patients, either to restore sinus rhythm or to prevent recurrences.³ However, current antiarrhythmic drugs usually do not achieve complete elimination of the arrhythmia burden and do not have a wide safety profile.^{4,5} Surgical elimination of certain arrhythmogenic substrates such as AF may represent a therapeutic option.⁶ However, nowadays catheter-based ablation is the most common alternative to treat symptomatic patients when antiarrhythmic drugs fail.³ The cornerstone radiofrequency (RF) catheter-based procedure pioneered by Haïssaguerre and colleagues, of ablating ectopic triggers that arise from the pulmonary veins (PV) in paroxysmal AF,⁷ has progressively evolved to new technical developments aiming to simplify pulmonary vein isolation and increase safety.⁸ To reach such objectives it is essential to increase catheter stability, achieve predictable lesion formation, reduce procedure and X-ray exposure time, and make simple and automatic either different steps or the whole procedure by using an anatomically-based ablation approach.

The so-called single-shot devices for PV isolation, robotic catheter navigation and ablation, contact force-controlled catheter ablation and new realtime imaging of endocardial ablation are the main available technological breakthroughs intending to overcome some of the conventional manual-guided RF delivery shortcomings. The present review is focused on compiling current clinical data, potential advantages and shortcomings of these new ablation strategies for PV isolation.

Single-shot Devices

Several single-shot devices have been developed in recent years to facilitate PV isolation, based on the encouraging aim of achieving complete isolation of the vein after one single application (single-shot) using circular catheters or balloon-like ablation devices. Among these devices, high-intensity focused ultrasound (HIFU) applied via a balloon catheter (BC) integrates a 9 megahertz (MHz) ultrasound crystal, which generates a ring of ultrasound energy at the base of the balloon. The third generation of HIFU-BC (12 French of outer diameter) is steerable through a pull wire mechanism integrated in the handle of the catheter and is available in balloon sizes (sonication ring diameter) of 24 millimetres (mm) (20 mm), 27 mm (25 mm) and 32 mm (30 mm), respectively (ProRhythm Inc, Ronkonkoma, New York, US). The catheter also has a lumen for insertion of a hexapolar spiral mapping catheter to record PV potentials. Beyond the circumferential lesion design instead of point-by-point ablation, the technology has the potential benefit of not being critically dependent on balloon-to-tissue contact. Initial reports using first and second generation HIFU balloon catheters showed long procedure times and limited efficacy to isolate all the PV in 50 % of patients.⁹ In addition, the risk profile was unacceptable for a non-life-threatening arrhythmia. Serious complications such as phrenic nerve palsy and deleterious atrial–oesophageal fistula were reported.^{10,11} Later series using a technically improved third generation HIFU balloon demonstrated acute pulmonary vein isolation in 80 % of all PV. Moreover, 60 % of veins were isolated after a single shot. No atrial–oesophageal fistula was reported and the incidence of phrenic nerve palsy was comparable to other balloon technologies (~5 %).¹² Despite of technical improvements, navigation and positioning are still challenging and its clinical use has been halted.

The pulmonary vein ablation catheter (PVAC) consists of a 9 French (Fr), over-the-wire, multi-electrode circular mapping and ablation catheter (Medtronic Ablation Frontiers LLC, Carlsbad, CA, US). The system is designed to apply duty-cycled phased unipolar and bipolar RF energy over all 10 PVAC electrodes positioned at the antral part of the PV. Its use was associated with 99 % acute isolation of the PV and 85 % of freedom from AF at six months of follow-up.¹³ Clinical success rates of PV isolation are similar to conventional point-by-point ablation using a three-dimensional (3D) navigation system. However, total procedural and fluoroscopic times seem to be significantly shorter by using the PVAC.¹⁴ Safety concerns were raised after its use was associated with much higher incidence of new embolic events detected by cerebral magnetic resonance imaging.¹⁵ The ongoing Multi-Array Ablation of Pulmonary Veins for Paroxysmal Atrial Fibrillation (MAP-PAF) trial will provide additional information about efficacy and safety of the PVAC technology.

Widely established is the use of cryothermal therapy, which has shown to theoretically overcome some of the shortcomings of RF delivery. Cryoablation lesions show well demarcated margins with preservation of basic underlying tissue architecture.^{16,17} Tissue necrosis is progressively established in the absence of significant alteration of tissue structure at thaw. Moreover, in experimental models cryoenergy is significantly less thrombogenic than RF ablation with no correlation between cryoenergy lesion size and thrombus formation.^{16,18} Lack of pain during cryothermal lesions, less destruction to surrounding vasculature and lesion reversibility with applications that do not achieve a temperature of less than -30 degrees Celsius are advantages for ablation of certain arrhythmogenic substrates.¹⁹⁻²¹ Cryoablation in the coronary sinus may also benefit of less risk of adjacent coronary artery damage.²⁰

In PV isolation, where large areas of the endocardium are ablated, less endothelial disruption might decrease the risk of thrombi-related complications. PV isolation using a balloon-based cryocatheter may facilitate the procedure compared with point-by-point ablation using a focal catheter. Altogether this makes cryoballoon ablation an attractive alternative for AF ablation. The ablation technique requires a balloon catheter, which is cooled using nitrous oxide (N₂O). The balloon shaft is introduced into the left atrium through a 14 Fr steerable sheath. The shaft has a central lumen that allows advancing either a wire or a small calibre circular mapping catheter for supporting and engaging the vein or confirming isolation, respectively. An alternative to confirm PV isolation is the use of a circular multipolar catheter advanced into the left atrium through a second trans-septal puncture. The central lumen also allows saline and contrast injection at the balloon tip, which is typically used to confirm complete occlusion before starting freezing.²² Although two balloon sizes are available (23 and 28 mm diameter), it seems more convenient to use the 28 mm diameter to keep the balloon at the antrum, therefore decreasing the risk of PV stenosis.²³

Recent clinical reports show that approximately 92 % of the PV can be successfully isolated using a balloon-only approach.²³⁻²⁵ Moreover, at 8–12 weeks after the index procedure almost 90 % of the PV remain isolated.²⁶ Acute reconnection limited to the right inferior PV may be observed in up to 2.8 % of veins within a 60-minute post-ablation observation period.²⁷ Long-term results after paroxysmal AF ablation vary depending on individual series and consideration of a blanking period. Thus, one-year freedom from recurrent paroxysmal AF was ~70 % considering a three-month blanking period using a cryoablation approach.^{24,28,29}

No differences in recurrence rates have also been reported in series comparing cryoballoon ablation versus RF ablation.²⁹⁻³¹ Conversely, maintenance of sinus rhythm at one-year, using a cryoablation approach and considering a three-month blanking period, is achieved in ~45 % of persistent AF patients.^{26,29} Combining cryoballoon PV isolation with additional electrogram-guided RF ablation and linear lesions has been reported to increase AF freedom to 86 % at six-months.³²

Some of the complications observed during RF delivery are also eliminated with cryoballoon ablation. A significant incidence (~17 %) of asymptomatic and self-healed oesophageal ulcerations can be observed after cryoballoon ablation.^{33,34} To our knowledge only one anecdotal atrial-oesophageal fistula formation has been reported using cryoablation.³⁵ The incidence of other procedure-related complications such as pericardial effusion, tamponade, femoral vein access complications, cerebral embolism and stroke are similar to segmental PV isolation using a 4 mm irrigated-tip RF catheter.^{28,36,37} However, two complications may be considered specially relevant when using cryoballoon ablation – phrenic nerve palsy and PV stenosis. The incidence of persistent phrenic nerve palsy after the procedure is ~4 % with delay recovery (one-year) observed in the vast majority of patients (93 % of cases).^{23,28} Cryothermal lesions in the right pulmonary veins and predominantly in the right superior pulmonary vein are consistently described as the most sensitive region to develop phrenic nerve palsy. Pacing the right phrenic nerve from a catheter positioned in the superior vena cava helps to detect the complication early during cryoballoon ablation of the right PV. Loss of capture or weakening of the right hemidiaphragm movements should lead the application to stop immediately.^{22,23} The incidence of PV stenosis varies depending on the definition used to consider stenosis. Thus, the incidence of PV stenosis resulting in symptoms or requiring intervention is ~0.2 %.²⁵ The incidence of other complications, such as asymptomatic gastroparesis and symptomatic inappropriate sinus tachycardia, have not been systematically assessed in clinical trials and may appear in up to 9 % and 1 % of cryoballoon ablation procedures, respectively.³⁸

Using the 28 mm diameter balloon may avoid excessive progression into the vein and reduce both phrenic nerve palsy and PV stenosis.^{22,23} Kuck et al. have also suggested the potential benefit of bigger balloons (32 mm diameter) to decrease these complications.²³

More anecdotal is the use of the RF hot balloon catheter (Hayama Arrhythmia Institute, Kanagawa, Japan) based on RF delivery between a coil electrode inside the balloon and the four cutaneous electrode patches on the patient's back to induce capacitive-type heating of the balloon.^{39,40} The technique allows isolation of the PV and posterior left atrium. No major collateral complications have been reported and the incidence of transient right phrenic nerve palsy was only 1 % in the largest series to date.⁴⁰ However, the lack of multicentre studies and limited follow-up do not allow to fully evaluate the efficacy of the RF hot balloon catheter for the treatment of AF.

Pulmonary Vein Isolation by Remote Navigation

Manipulating catheters inside the vascular system and cardiac chambers requires a skilled electrophysiologist working under fluoroscopic guidance. In AF ablation this may result in significant X-ray exposure, which is highly dependent on operator skills. Although, cryoballoon ablation has been reported to decrease X-ray exposure and total procedure time,²⁹ it still requires skilled electrophysiologist to properly place the cryoballoon in the PV antrum, especially in the right

pulmonary veins. The operator also needs to stay in the operation room during the entire procedure. In addition, the constant beating of the heart makes stability one of the main problems of RF delivery in certain target cardiac regions. New remote navigation systems have recently been developed with the objective of overcoming such limitations and allowing the operators to be away from the X-ray source while they are moving the catheters inside the cardiovascular system.^{41–43} Four major remote navigation systems are currently commercially available – the Sensei® X system from Hansen Medical (Mountain View, CA, US),⁴⁴ the Amigo™ Remote Catheter System by Catheter Robotics Inc (Mount Olive, NJ, US), the Niobe® Magnetic Navigation System from Stereotaxis (St Louis, MO, US)^{41,45} and the Catheter Guidance, Control and Imaging (CGCI) system from Magenetics Inc (Inglewood, CA, US).^{42,46}

The Sensei system is based on two steerable sheaths, through which any conventional catheter can be introduced for further manipulation via a pull-wire mechanism by a robotic arm fixed at a standard fluoroscopy table. The Amigo system is based on a mechanical catheter manipulator and a remote control handle that enables the user to manipulate a standard, conventional, electrophysiology catheter through the full range of its three functions – insertion/withdrawal, deflection and rotation.⁴⁷ The Niobe system is based on two permanent magnets positioned on each side of patient's body to create a uniform magnetic field (up to 0.08 Tesla). Special catheters with magnets affixed to their distal end can be navigated within the cardiac chambers by changing the orientation of the external magnetic fields. The CGCI system employs eight powerful electromagnets to produce a highly agile magnetic field (up to 0.16 Tesla) within an effective control area optimised to focus and contain the magnetic field almost entirely within the magnetic chamber. The magnetic field generators provide torque and force for moving, positioning and directing the tip of a catheter equipped with three permanent magnet pellets attached to its distal end.

PV isolation reports in paroxysmal and persistent AF patients using the Sensei system have consistently shown significant shortening of the fluoroscopy time.^{48–52} Remote isolation of the PV showed similar midterm follow-up (six-months to one-year) free of atrial arrhythmias to manual point-by-point radiofrequency delivery. Without adjunctive antiarrhythmic drugs ≈70 % of paroxysmal AF patients remained free of atrial arrhythmias.^{50–52} Initial reports using the Sensei system had raised the concern of higher rate of cardiac tamponade than conventional manual RF delivery⁵³, which might be related to remote manipulation of the stiff steerable Artisan catheter (Hansen Medical, Mountain View, CA, US). Further experience and introduction of a special feature of the system to indirectly estimate catheter contact force on the tissue (IntelliSense) have shown that tamponade rates are not greater than the conventional manual approach and may be more related to different temperature and power RF settings.^{50,52} High incidence of oesophageal ulcerations has been reported by Tilz et al. during PV isolation using 30 watts (W) along the posterior wall. The use of power limit to 20 W along the posterior wall in combination with an oesophageal temperature limit of 41 degrees Celsius significantly reduced the risk of oesophageal injury.⁵⁴ Considering that remote navigation may provide higher stability and subsequent more predictable RF lesions,⁵⁵ it seems reasonable to limit application time at a single spot to 20 seconds, concomitantly to set up maximum power at 30 W and decrease it to 15–20 W when ablating on the posterior wall.

The more simplified and less costly approach of the Amigo System has shown accurate remote manipulation and adequate tissue contact of conventional catheters in animal experiments, with the advantage of manual override allowing the operator to quickly gain manual control of the catheter if for any reason this should be necessary.⁴⁷ However and similar to the Sensei system, the use of mechanical forces to drive the catheter does not represent a technological advance over manual manipulation. In addition, although the system is designed to operate with a variety of catheters, up-to-date it only operates with Biosense Webster and Boston Scientific catheters.

Remote magnetic navigation and PV isolation using the Niobe system has also demonstrated to be feasible and safe. Initial series reported longer procedure time and shorter fluoroscopy time,^{56,57} along with potential easier navigation to reach the right PV.⁵⁶ Further introduction of magnetic irrigated-tip catheters and larger series confirmed high rates of acute isolation of all PV (≈90 %) and similar rates of patients remaining free from AF after midterm follow-up (6–18 months) compared with conventional manual RF approach (≈70 %).^{58,59} Ablation times were longer in the magnetic navigation group compared with the manual approach. The latter could be explained by less effective linear lesions using remote magnetic ablation due to lower maximal endocardial force exerted by the remote magnetic navigation system to the magnetic catheter tip compared with manually-applied force to the conventional ablation catheter tip.⁶⁰ A trend towards reduced major complications in the remote magnetic navigation group has also been described in the largest series to date.⁵⁸

The recently introduced CGCI system is based on eight coil-core electromagnets, which generate a dynamic magnetic field focused on the heart.^{42,46} The system produces magnetic fields 10 to 20 times less in intensity than magnetic resonance imaging and no magnetic fields are generated when it is not in magnetic guidance mode. The latter allows undisturbed use of other electronic medical equipment and eliminates the need for additional shielding of the procedure room. The Robotic system includes an operation console, the CGCI controller computer and a motorised linear catheter advancement mechanism. The system uses a standard three-axis joystick, which is used to rotate the magnetic field and manually advance or retract the catheter. A 3D Controller is used to push the catheter in any screen-oriented direction. The system may potentially overcome some of the limitations of the former Niobe system. Endocardial contact force and navigation inside the cardiac chambers may substantially improve by increasing the strength of the magnetic field magnitude (up to 0.16 Tesla).^{42,57} Continuous and rapid shaping and reshaping of the magnetic field, rather than moving external magnets to change the magnetic field, provides instantaneously transmitted changes to the tip of the magnetised catheter leading to almost realtime remote navigation. In automatic mode the CGCI system also provides a true closed-loop servo system that has the ability to keep the catheter tip on a desired anatomic target by continuously adjusting the direction and intensity of the magnetic fields.⁶¹

Experimental data in pigs have demonstrated reproducible navigation and accurate and rapid catheter positioning on the selected ablation targets within the atrial chambers. Once the ablation target is localised, the system has the ability to navigate the catheter tip to the selected target despite the cardiac motion and anatomical irregularities.⁶¹ Furthermore, necropsy studies in the same animals revealed that the majority of RF lesions were transmural (lesion depth: 78.5 ± 12.1 % of

entire left atrial wall thickness).⁶¹ Initial reports in humans also confirmed the feasibility and safety of the system to navigate and ablate left atrium arrhythmogenic substrates.⁶² Clinical trials are ongoing and will provide further evidence of potential advantages described in experimental studies and recent human reports.

Radiofrequency-based Pulmonary Vein Isolation by Contact Monitoring

Catheter contact force is a major determinant of the lesion size. Experimental data in canine thigh muscle preparations have shown that irrigated catheter RF power at 30 W and contact force ranged from 30 to 40 grams (g) produced larger and deeper lesions than those produced at high power (50 W) and lower contact force (2–10 g).⁶³ Higher contact force increases the incidence of steam pop and thrombus formation,⁶⁴ therefore contact forces between 10 and 30 g and power settings to 30 W may achieve reasonable lesion size and depth as well as minimal incidence of thrombus formation and steam pops.⁶³ The technology is based on ablation catheters with an integrated fibre-optic force sensor for realtime measurement of tip electrode-tissue contact forces (TactiCath, Endosense SA, Switzerland).⁶³

AF recurrences after PV isolation are mainly related with PV reconnection.^{65,66} While insufficient contact force may result in an ineffective lesion, excessive contact force may result in complications such as heart wall perforation, steam pops, thrombus formation or oesophageal injury.^{54,67,68} From the foregoing we can safely propose that catheter contact sensors might allow the creation of more uniform ablation lesions and increase the safety of RF delivery. Less experienced electrophysiologists might ensure less variability in manipulations and avoid excessive contact force. During mapping within scarred regions, operators might also be able to distinguish whether low electrogram amplitude is due to scarring or poor catheter contact.

Recent clinical reports have shown that realtime contact force technology is safe during PV isolation in paroxysmal AF patients.⁶⁹ In fact, high transient force events during catheter manipulation may be associated with cardiac tamponade. Thus, Shah et al. have suggested that it may be prudent to avoid contact forces exceeding 100 g during catheter manipulation and ablation, especially in the vicinity of recently ablated sites.⁷⁰ Realtime contact force feedback may also play a role to avoid excessive force during non-fluoroscopic guided procedures.⁷¹ Results from the EFFICAS studies showed that optimal contact force (>10 g) and good catheter stability, by reducing the ablations with low force-time integral (FTI <400 g), increased the efficacy of ablation during PV isolation.⁷² Larger series are needed to determine the potential role of contact force-sensing catheters to increase the safety and effectiveness of RF PV isolation.

Realtime Lesion Characterisation During Pulmonary Vein Isolation

Lack of realtime ablation lesion monitoring remains a major limitation of current ablation approaches. The latter leads to the inability of electrophysiologists to place ablation lesions with a high level of anatomic accuracy and absence of direct feedback on endocardial lesion formation. Direct visualisation of lesion formation during endocardial ablation is being sought after by different technological approaches. Ultrasound monitoring, endoscopic visualisation and optical coherence tomography are some of those technologies.^{73–75} Beyond experimental reports, endoscopically-guided laser ablation has been used in few clinical series showing promising outcomes.

A novel compliant balloon ablation catheter able to deliver visually-guided short arcs/spots of laser energy has been tested in recent preclinical and clinical series to determine if visual guidance could safely achieve reliable and persistent PV isolation.^{73,76–78} The Endoscopic Ablation System by CardioFocus Inc (Marlborough, MA, US) consists of a deflectable 12 F (internal diameter) delivery sheath and the ablation balloon catheter. The central catheter shaft houses a 2 F fibre-optic endoscope that enables direct visualisation of the cardiac anatomy once the balloon has been inflated. Laser energy (980 nanometres [nm]) can be delivered via a second fibre to the desired ablation zones. An internal cooling mechanism circulates sterile deuterium oxide (D₂O) within the balloon for cooling purposes.^{73,77} The catheter balloon allows treatment of PV from 9 to 35 mm in diameter.

Initial clinical and experimental series reported successful acute PV isolation in 91–100 % of paroxysmal AF patients and animals studied.^{73,76} The use of a compliant balloon able to better conform to the atrial anatomy may have explained the differences in acute isolation outcomes between initial series.⁷⁶ Further experience and multicentre trials have achieved acute PV isolation in 98 % of the targeted veins, along with ≈60 % of paroxysmal AF patients free of symptomatic and/or documented recurrence suggestive of AF after 13 months of follow-up, including a blanking period of three months.⁷⁸ After two procedures and 12 months of follow-up, the drug-free rate of freedom from AF or atrial tachycardia has been reported as 71 %.⁷⁹ Similar to other ablation strategies the recurrences are mainly related to electrical reconduction of previously isolated PV.^{73,78,80}

To date a limited number of patients have undergone PV isolation using the visually-guided laser ablation catheter, which makes it difficult to report the complication rates beyond anecdotal cases. Overall, it seems to show lower incidence of phrenic nerve palsy and PV stenosis than the cryoballoon approach.^{78,81} The incidence of oesophageal thermal lesions is similar to radiofrequency-based or cryothermal-based PV isolation (≈18 %).^{33,34,78,82} To our knowledge, no atrial-oesophageal fistula has been reported to date. A compliant catheter balloon along with the ability to titrate energy may potentially decrease injury to adjacent structures such as the oesophagus and the phrenic nerve. Several authors have mentioned the limitation of lacking an over-the-wire system to direct and stabilise the balloon catheter within the left atrium or PV, which may also explain few reported cases of atrial perforation and cardiac tamponade.^{77,78} Larger clinical trials are necessary to compare the clinical efficacy with other ablation strategies such as RF and cryothermal ablation.

Future Directions and Conclusions

Technological breakthroughs are aiming to increase successful long-term isolation of the PV with no risk of adverse events. Current ablation technologies individually provide some advantages over conventional point-by-point RF ablation. Cryoballoon ablation lesions seem to be more uniform, less thrombogenic and pain-free. Remote navigation improves navigation reproducibility, catheter stability and substantially decreases X-ray exposure. Realtime contact force catheters may decrease the risk of complications such as steam pop, thrombus and atrial wall rupture. New realtime visualisation of ablation lesions may also increase safety and accuracy of ablation. However, none of the approaches have demonstrated higher rates of long-term PV isolation and AF-free compared with RF ablation by experienced operators. Combining robotic navigation with realtime contact force catheters and direct visualisation of the atrial cavities may be a

feasible approach to increase accurate PV isolation and decrease the risk of complications. Due to economic and technological limitations, remote and combined technologies will be likely very limited to tertiary medical centres. Conversely, the use of single-shot devices will certainly increase in secondary centres.

It should be noticed that new approaches aiming to understand the mechanisms underlying AF, especially in persistent AF patients, have to be developed to increase the long-term freedom from recurrent AF. Thus, physiologically-guided computational mapping during AF has recently shown localised sources sustaining the arrhythmia in 96 % of AF patients.⁸³ Moreover, those sources were mainly classified as re-entrant sources, which were widely spread around the left

atrium from case to case. The number of sources was significantly higher in persistent AF than paroxysmal AF patients. Interestingly, AF terminated in 56 % of cases after ablation of the primary source without performing PV isolation. Conversely, AF termination was only achieved in 20 % of cases that underwent conventional PV isolation. Freedom from AF was also significantly higher in the source-based guided ablation group compared with the conventional PV isolation group.⁸⁴ Such results are very striking and encouraging. In fact, this new approach raises important mechanistic considerations in AF ablation, which looked forgotten during the last few years of the AF ablation era. However, the mapping strategy is still unknown for the vast majority of the electrophysiologist and the results have only been reported from a couple of centres. ■

- Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. *Am J Cardiol* 1998;**82**:2N-9N.
- Miyasaka Y, Barnes ME, Gersh BJ, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. *Circulation* 2006;**114**:119-25.
- Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Europace* 2010;**12**:1360-420.
- Køber L, Torp-Pedersen C, McMurray JJ, et al. Increased mortality after dronedarone therapy for severe heart failure. *N Engl J Med* 2008;**358**:2678-87.
- Lafuente-Lafuente C, Mouly S, Longás-Tejero MA, et al. Antiarrhythmic drugs for maintaining sinus rhythm after cardioversion of atrial fibrillation: a systematic review of randomized controlled trials. *Arch Intern Med* 2006;**166**:719-28.
- Prasad SM, Maniar HS, Camillo CJ, et al. The Cox maze III procedure for atrial fibrillation: long-term efficacy in patients undergoing lone versus concomitant procedures. *J Thorac Cardiovasc Surg* 2003;**126**:1822-8.
- Haissaguerre M, Jais 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.
- Karch MR, Zrenner B, Delsenhofer I, et al. Freedom from atrial tachyarrhythmias after catheter ablation of atrial fibrillation: a randomized comparison between 2 current ablation strategies. *Circulation* 2005;**111**:2875-80.
- Metzner A, Chun KR, Neven K, et al. Long-term clinical outcome following pulmonary vein isolation with high-intensity focused ultrasound balloon catheters in patients with paroxysmal atrial fibrillation. *Europace* 2010;**12**:188-93.
- Antz M, Chun KR, Ouyang F, Kuck KH. Ablation of atrial fibrillation in humans using a balloon-based ablation system: Identification of the site of phrenic nerve damage using pacing maneuvers and CARTO. *J Cardiovasc Electrophysiol* 2006;**17**:1242-5.
- Borchert B, Lawrenz T, Hansky B, Stellbrink C. Lethal atrioesophageal fistula after pulmonary vein isolation using high-intensity focused ultrasound (HIFU). *Heart Rhythm* 2008;**5**:145-8.
- Schmidt B, Chun KR, Metzner A, et al. Pulmonary vein isolation with high-intensity focused ultrasound: results from the HIFU 12F study. *Europace* 2009;**11**:1281-8.
- Wieczorek M, Hoeltgen R, Brueck M, et al. Pulmonary vein isolation by duty-cycled bipolar and unipolar antrum ablation using a novel multielectrode ablation catheter system: first clinical results. *J Interv Card Electrophysiol* 2010;**27**:23-31.
- Bulava A, Haniš J, Sitek D, et al. Catheter ablation for paroxysmal atrial fibrillation: a randomized comparison between multielectrode catheter and point-by-point ablation. *Pacing Clin Electrophysiol* 2010;**33**:1039-46.
- Herrera Sikiódy C, Deneke T, Hocini M, et al. Incidence of asymptomatic intracranial embolic events after pulmonary vein isolation: comparison of different atrial fibrillation ablation technologies in a multicenter study. *J Am Coll Cardiol* 2011;**58**:681-8.
- Dubuc M, Talajic M, Roy D, et al. Feasibility of cardiac cryoablation using a transvenous steerable electrode catheter. *J Interv Card Electrophysiol* 1998;**2**:285-92.
- Lustgarten DL, Keane D, Ruskin J. Cryothermal ablation: mechanism of tissue injury and current experience in the treatment of tachyarrhythmias. *Prog Cardiovasc Dis* 1999;**41**:481-98.
- Khairy P, Chauvet P, Lehmann J, et al. Lower incidence of thrombus formation with cryoenergy versus radiofrequency catheter ablation. *Circulation* 2003;**107**:2045-50.
- Friedman PL, Dubuc M, Green MS, et al. Catheter cryoablation of supraventricular tachycardia: results of the multicenter prospective "frosty" trial. *Heart rhythm* 2004;**1**:129-38.
- Aoyama H, Nakagawa H, Pitha JV, et al. Comparison of cryothermia and radiofrequency current in safety and efficacy of catheter ablation within the canine coronary sinus close to the left circumflex coronary artery. *J Cardiovasc Electrophysiol* 2005;**16**:1218-26.
- Lemola K, Dubuc M, Khairy P. Transcatheter cryoablation part ii: Clinical utility. *Pacing Clin Electrophysiol* 2008;**31**:235-44.
- Ozcan C, Ruskin J, Mansour M. Cryoballoon catheter ablation in atrial fibrillation. *Cardiol Res Pract* 2011;**2011**:256347.
- Kuck KH, Fürnkranz A. Cryoballoon ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2010;**21**:1427-31.
- Neumann T, Vogt J, Schumacher B, et al. Circumferential pulmonary vein isolation with the cryoballoon technique results from a prospective 3-center study. *J Am Coll Cardiol* 2008;**52**:273-8.
- Andrade JG, Khairy P, Guerra PG, et al. Efficacy and safety of cryoballoon ablation for atrial fibrillation: a systematic review of published studies. *Heart rhythm* 2011;**8**:1444-51.
- Ahmed H, Neuzil P, Skoda J, et al. The permanency of pulmonary vein isolation using a balloon cryoablation catheter. *J Cardiovasc Electrophysiol* 2010;**21**:731-7.
- Chierchia GB, de Asmundis C, Müller-Burri SA, et al. Early recovery of pulmonary vein conduction after cryoballoon ablation for paroxysmal atrial fibrillation: a prospective study. *Europace* 2009;**11**:445-9.
- Packer DL, Irwin JM, Champagne J, 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* 2010;**55**:E3015-6.
- Kojodjojo P, O'Neill MD, Lim PB, et al. 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.
- Kühne M, Suter Y, Altmann D, 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**:1770-6.
- Linhart M, Bellmann B, Mittmann-Braun E, et al. Comparison of cryoballoon and radiofrequency ablation of pulmonary veins in 40 patients with paroxysmal atrial fibrillation: a case-control study. *J Cardiovasc Electrophysiol* 2009;**20**:1343-8.
- Mansour M, Forleo GB, Pappalardo A, et al. Combined use of cryoballoon and focal open-irrigation radiofrequency ablation for treatment of persistent atrial fibrillation: results from a pilot study. *Heart rhythm* 2010;**7**:452-8.
- Ahmed H, Neuzil P, d'Avila A, et al. The esophageal effects of cryoenergy during cryoablation for atrial fibrillation. *Heart rhythm* 2009;**6**:962-9.
- Fürnkranz A, Chun KR, Metzner A, et al. Esophageal endoscopy results after pulmonary vein isolation using the single big cryoballoon technique. *J Cardiovasc Electrophysiol* 2010;**21**:869-74.
- Stöckigt F, Schrickel JW, Andrieu R, Lickfett L. Atri-esophageal fistula after cryoballoon pulmonary vein isolation. *J Cardiovasc Electrophysiol* 2012;**23**:1254-7.
- Sauren LD, VAN Belle Y, DE Roy L, et al. Transcranial measurement of cerebral microembolic signals during endocardial pulmonary vein isolation: comparison of three different ablation techniques. *J Cardiovasc Electrophysiol* 2009;**20**:1102-7.
- Chierchia GB, Capulzini L, Droogmans S, et al. Pericardial effusion in atrial fibrillation ablation: a comparison between cryoballoon and radiofrequency pulmonary vein isolation. *Europace* 2010;**12**:337-41.
- Guiot A, Savouiré A, Godin B, Anselme F. Collateral nervous damages after cryoballoon pulmonary vein isolation. *J Cardiovasc Electrophysiol* 2012;**23**:346-51.
- Tanaka K, Satake S, Saito S, et al. A new radiofrequency thermal balloon catheter for pulmonary vein isolation. *J Am Coll Cardiol* 2001;**38**:2079-86.
- Sohara H, Takeda H, Ueno H, et al. Feasibility of the radiofrequency hot balloon catheter for isolation of the posterior left atrium and pulmonary veins for the treatment of atrial fibrillation. *Circ Arrhythm Electrophysiol* 2009;**2**:225-32.
- Ernst S, Ouyang F, Linder C, et al. Initial experience with remote catheter ablation using a novel magnetic navigation system: magnetic remote catheter ablation. *Circulation* 2004;**109**:1472-5.
- Nguyen BL, Merino JL, Gang ES. Remote Navigation for Ablation Procedures – A New Step Forward in the Treatment of Cardiac Arrhythmias. *European Cardiology* 2010;**6**:50-6.
- Schmidt B, Chun KR, Tilz RR, et al. Remote navigation systems in electrophysiology. *Europace* 2008;**10** Suppl 3:iii57-61.
- Al-Ahmad A, Grossman JD, Wang PJ. Early experience with a computerized robotically controlled catheter system. *J Interv Card Electrophysiol* 2005;**12**:199-202.
- Ray IB, Dukkipati S, Houghtaling C, et al. Initial experience with a novel remote-guided magnetic catheter navigation system for left ventricular scar mapping and ablation in a porcine model of healed myocardial infarction. *J Cardiovasc Electrophysiol* 2007;**18**:520-5.
- Nguyen BL, Farkas L, Marx B, et al. The lobed magnetic field: initial animal validation of a new remote EP catheter guidance and control system. Heart Rhythm Society's 30th Annual Scientific Sessions, Boston, MA, US, 13-19 May 2009.
- Knight B, Ayers GM, Cohen TJ. Robotic positioning of standard electrophysiology catheters: a novel approach to catheter robotics. *J Invasive Cardiol* 2008;**20**:250-3.
- Kautzner J, Peichl P, Čihák R, et al. Early experience with robotic navigation for catheter ablation of paroxysmal atrial fibrillation. *Pacing Clin Electrophysiol* 2009;**32** Suppl 1:S163-6.
- Di Biase L, Wang Y, Horton R, et al. Ablation of atrial fibrillation utilizing robotic catheter navigation in comparison to manual navigation and ablation: single-center experience. *J Cardiovasc Electrophysiol* 2009;**20**:1328-35.
- Steven D, Servatius H, Rostock T, et al. Reduced fluoroscopy during atrial fibrillation ablation: benefits of robotic guided navigation. *J Cardiovasc Electrophysiol* 2010;**21**:6-12.
- Schmidt B, Tilz RR, Neven K, et al. Remote robotic navigation and electroanatomic mapping for ablation of atrial fibrillation: considerations for navigation and impact on procedural outcome. *Circ Arrhythm Electrophysiol* 2009;**2**:120-8.
- Hlivák P, Mlochová H, Peichl P, et al. Robotic navigation in catheter ablation for paroxysmal atrial fibrillation: midterm efficacy and predictors of postablation arrhythmia recurrences. *J Cardiovasc Electrophysiol* 2011;**22**:534-40.
- Saliba W, Reddy VY, Wazni O, et al. Atrial fibrillation ablation using a robotic catheter remote control system: initial human experience and long-term follow-up results. *J Am Coll Cardiol* 2008;**51**:2407-11.
- Tilz RR, Chun KR, Metzner A, et al. Unexpected high incidence of esophageal injury following pulmonary vein isolation using robotic navigation. *J Cardiovasc Electrophysiol* 2010;**21**:853-8.
- Davis DR, Tang AS, Gollub MH, et al. Remote magnetic navigation-assisted catheter ablation enhances catheter stability and ablation success with lower catheter temperatures. *Pacing Clin Electrophysiol* 2008;**31**:893-8.
- Pappone C, Vicedomini G, Manguso F, et al. Robotic magnetic navigation for atrial fibrillation ablation. *J Am Coll Cardiol* 2006;**47**:1390-400.
- Di Biase L, Fahmy TS, Patel D, et al. Remote magnetic navigation: human experience in pulmonary vein ablation. *J Am Coll Cardiol* 2007;**50**:868-74.
- Arya A, Zaker-Shahrak R, Sommer P, et al. Catheter ablation of atrial fibrillation using remote magnetic catheter navigation: a case-control study. *Europace* 2011;**13**:45-50.
- Lüthje L, Vollmann D, Seegers J, et al. Remote magnetic versus manual catheter navigation for circumferential pulmonary vein ablation in patients with atrial fibrillation. *Clin Res Cardiol* 2011;**100**:1003-11.
- Faddis MN, Blume W, Finney J, et al. Novel, magnetically guided catheter for endocardial mapping and radiofrequency catheter ablation. *Circulation* 2002;**106**:2980-5.
- Gang ES, Nguyen BL, Shachar Y, et al. Dynamically shaped magnetic fields: Initial animal validation of a new remote electrophysiology catheter guidance and control system. *Circ Arrhythm Electrophysiol* 2011;**4**:770-7.
- Merino JL. Introduction to the magnetecs system: Can it facilitate atrial fibrillation ablation? Heart Rhythm Society's 33rd Annual Scientific Sessions, Boston, Massachusetts, US, May 9-12 2012.
- Yokoyama K, Nakagawa H, Shah DC, et al. Novel contact force sensor incorporated in irrigated radiofrequency ablation catheter predicts lesion size and incidence of steam pop and

- thrombus. *Circ Arrhythm Electrophysiol* 2008;**1**:354–62.
64. Yokoyama K, Nakagawa H, Wittkamp FH, et al. Comparison of electrode cooling between internal and open irrigation in radiofrequency ablation lesion depth and incidence of thrombus and steam pop. *Circulation* 2006;**113**:11–9.
65. Lemola K, Hall B, Cheung P, et al. Mechanisms of recurrent atrial fibrillation after pulmonary vein isolation by segmental ostial ablation. *Heart rhythm* 2004;**1**:197–202.
66. Miller MA, d'Avila A, Dukkipati SR, et al. Acute electrical isolation is a necessary but insufficient endpoint for achieving durable PV isolation: the importance of closing the visual gap. *Europace* 2012;**14**:653–60.
67. Kuck KH, Reddy VY, Schmidt B, et al. A novel radiofrequency ablation catheter using contact force sensing: Toccata study. *Heart Rhythm* 2012;**9**:18–23.
68. Thiagalingam A, D'Avila A, Foley L, et al. Importance of catheter contact force during irrigated radiofrequency ablation: Evaluation in a porcine ex vivo model using a force-sensing catheter. *J Cardiovasc Electrophysiol* 2010;**21**:806–11.
69. Kuck KH, Reddy VY, Schmidt B, et al. A novel radiofrequency ablation catheter using contact force sensing: Toccata study. *Heart rhythm* 2012;**9**:18–23.
70. Shah D, Lambert H, Langenkamp A, et al. Catheter tip force required for mechanical perforation of porcine cardiac chambers. *Europace* 2011;**13**:277–83.
71. Kerst G, Weig HJ, Weretka S, et al. Contact force-controlled zero-fluoroscopy catheter ablation of right-sided and left atrial arrhythmia substrates. *Heart rhythm* 2012;**9**:709–14.
72. Wissner E, Petru J, Metzner A, et al. The efficacy studies: Reducing low force-time integral (fti) radiofrequency applications improves procedural efficacy during pulmonary vein isolation. *American Heart Association Scientific Sessions*, Orlando, Florida, US, 12–16 November 2011.
73. Reddy VY, Neuzil P, Themistoclakis S, et al. Visually-guided balloon catheter ablation of atrial fibrillation: experimental feasibility and first-in-human multicenter clinical outcome. *Circulation* 2009;**120**:12–20.
74. Fleming CP, Rosenthal N, Rollins AM, Arrud M. First in vivo Real-Time Imaging of Endocardial Radiofrequency Ablation by Optical Coherence Tomography: Implications on Safety and The Birth of “Electro-structural” Substrate-Guided Ablation. *The Journal of Innovations in Cardiac Rhythm Management* 2011;**2**:199–201.
75. Varghese T, Zagzebski JA, Chen Q, et al. Ultrasound monitoring of temperature change during radiofrequency ablation: preliminary in-vivo results. *Ultrasound Med Biol* 2002;**28**:321–9.
76. Dukkipati SR, Neuzil P, Skoda J, et al. Visual balloon-guided point-by-point ablation: reliable, reproducible, and persistent pulmonary vein isolation. *Circ Arrhythm Electrophysiol* 2010;**3**:266–73.
77. Schmidt B, Metzner A, Chun KR, et al. Feasibility of circumferential pulmonary vein isolation using a novel endoscopic ablation system. *Circ Arrhythm Electrophysiol* 2010;**3**:481–8.
78. Metzner A, Schmidt B, Fuernkranz A, et al. One-year clinical outcome after pulmonary vein isolation using the novel endoscopic ablation system in patients with paroxysmal atrial fibrillation. *Heart rhythm* 2011;**8**:988–93.
79. Dukkipati SR, Neuzil P, Kautzner 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.
80. Ouyang F, Antz M, Ernst S, et al. Recovered pulmonary vein conduction as a dominant factor for recurrent atrial tachyarrhythmias after complete circular isolation of the pulmonary veins: lessons from double Lasso technique. *Circulation* 2005;**111**:127–35.
81. Chun KR, Schmidt B, Metzner A, et al. The ‘single big cryoballoon’ technique for acute pulmonary vein isolation in patients with paroxysmal atrial fibrillation: a prospective observational single centre study. *Eur Heart J* 2009;**30**:699–709.
82. Halm U, Gaspar T, Zachäus M, et al. Thermal esophageal lesions after radiofrequency catheter ablation of left atrial arrhythmias. *Am J Gastroenterol* 2010;**105**:551–6.
83. Narayan SM, Krummen DE, Rappel WJ. Clinical mapping approach to diagnose electrical rotors and focal impulse sources for human atrial fibrillation. *J Cardiovasc Electrophysiol* 2012;**23**:447–54.
84. Narayan SM, Krummen DE, Shivkumar K, et al. Treatment of atrial fibrillation by the ablation of localized sources: CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) trial. *J Am Coll Cardiol* 2012;**60**:628–36.