

Atrial Fibrillation Ablation: State of the Art

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Among several catheter-based strategies for curing atrial fibrillation (AF), 2 approaches have emerged as dominant strategies in current clinical practice: ostial segmental disconnection of all pulmonary veins (PVs) from the adjacent atrial tissue and circumferential PV ablation, first reported by our laboratory in Milan. The cure for AF by circumferential PV ablation has had a dramatic impact on morbidity, quality of life, and even mortality in patients with the most frequent cardiac arrhythmia. The last 10 years of AF ablation are characterized by a better understanding of AF mechanisms as well as by new and evolving concepts associated with innovation in technologies. We recently demonstrated, for the first time, the role of vagal denervation in enhancing long-term benefits from circumferential PV ablation. Unlike other strategies, our strategy was associated with high success rates in both paroxysmal and chronic AF. As a result, our initial approach did not substantially change over time, and now we have long-term results after >3 years of follow-up. Recently, we demonstrated the safety and feasibility of remote magnetic navigation of a soft magnetic-tip catheter within the left atrium, even at challenging sites for both mapping and ablation in patients with AF. Use of a robotic navigation system has begun a new era in interventional cardiac electrophysiology—without risk of major complications, such as cardiac tamponade or atrioesophageal fistula, even in less experienced laboratories. © 2005 Elsevier Inc. All rights reserved. (Am J Cardiol 2005;96[suppl]:59L–64L)

Currently, atrial fibrillation (AF) is a source of considerable concern, and its impact is likely to be amplified as the estimated number of patients affected by AF is expected to increase nearly 2.5-fold over the next 50 years. AF is associated with an increased number of emergency department visits and hospitalizations, and frequent electrical cardioversions may be required despite the use of antiarrhythmic drugs. These observations indicate how imperative it is to promote coordinated efforts on behalf of cardiologists, electrophysiologists, neurologists, and primary care providers to meet the increasing challenge of stroke prevention and rhythm management in the growing population with AF. Catheter ablation to cure AF has now evolved as an established method for treating this common rhythm disorder. Catheter ablation of AF is now performed on a daily basis in electrophysiology laboratories in most regions of the world. Cure of AF has had a dramatic impact on quality of life, morbidity, and mortality. The first decade of AF ablation was characterized by new observations and concepts as well as improvement in technology. Most current treatment approaches for AF aim at ablation around the pulmonary veins (PVs) with or without additional ablation lesion

lines, a procedure that yields low complication rates and high success rates in both paroxysmal and chronic AF.^{1–10} Electrical isolation of the PV from the atrial substrate provides an electrophysiologically based end point that serves to prevent propagation of arrhythmogenic impulses from the PV to the atria, eliminating this region from the substrate capable of maintaining AF. However, electrical isolation of the PV may not be required, as demonstrated by circumferential PV ablation (CPVA): a >80% reduction in the bipolar voltage amplitude in the ablation lines of CPVA results in even greater long-term success.

The AF Follow-up Investigation of Rhythm Management (AFFIRM) showed that a rhythm control strategy confers no survival advantage over rate control among patients with AF who had risk factors for stroke.^{11,12} However, drug inefficacy or adverse drug effects, or both, can easily account for the absence of a survival benefit of rhythm control. We have found that in both ablation and antiarrhythmic treatment groups, sinus rhythm (SR) maintenance is associated with significantly lower mortality and adverse event rates, calling into question the results of 3 recent AF trials (the Pharmacological Intervention in Atrial Fibrillation [PIAF]¹² trial, AFFIRM,¹¹ and the Rate Control Versus Electrical Cardioversion for Persistent Atrial Fibrillation [RACE]^{12a} trial). Our results suggest that catheter ablation for curing AF is effective in the long term and will continue to improve with further technologic advances.¹³

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Current Atrial Fibrillation Ablation Strategies: Comparative Data

Among several catheter-based strategies for AF treatment, 2 have emerged as dominant strategies in current clinical practice: 1 is aimed at ostial segmental disconnection of all PVs from the adjacent atrial tissue, and the other is aimed at anatomic circumferential ablation outside the PV ostia with additional lines as first described by our group.¹ Is either of the 2 ablation strategies superior to the other, since the 2 proposed strategies are based on different rationales, require different methods, and aim for different end points? If other atrial tissue, including areas adjacent to the orifice of the PVs and left posterior wall, are also involved in the mechanism responsible for AF, ablation around these critical areas becomes a relevant part of the strategy and an innovative, challenging concept. To investigate whether 1 of the 2 ablation strategies is superior to the other, segmental ostial ablation was compared with the circumferential left atrial (LA) ablation strategy in a randomized study in 80 patients with paroxysmal AF.⁶ The end point of the study was freedom from symptomatic AF in the absence of drug therapy after a single ablation procedure. In this study, symptomatic paroxysmal AF was eliminated more reliably by LA ablation that encircled the PVs than by segmental ostial ablation of the 4 PVs. The circumferential LA ablation strategy was found to be significantly more effective than segmental ostial ablation, with a success rate at 6 months of 87% and 67%, respectively. The procedure duration with both approaches was about 2.5 hours, although 50% shorter fluoroscopy times were reported. No difference in complication rates between the 2 ablation strategies was reported. At 6 months, 67% of patients randomized to segmental ablation were in SR without a repeat procedure, as were 88% of those randomized to CPVA. Among patients with recurrent AF after segmental isolation who were subsequently treated with CPVA, the Michigan group did not observe AF recurrences. Unlike PV isolation alone, CPVA may eliminate PV triggers—anchor points for rotors or “mother waves” that drive AF as well as affect the vein of Marshall, which has LA insertion in close proximity to the left superior PV (LSPV). CPVA also excludes approximately 25% to 30% of the posterior LA wall, limiting the area available for circulating wavelets that may perpetuate AF. These findings suggest that LA ablation to encircle the PVs is preferable to segmental ostial ablation alone as the first approach. In the last several years, most electrophysiologic groups, including the pioneering group of Bordeaux, progressively and substantially changed their initial strategy from focal to more extensive lesions for better success rates with lower risks, especially in patients with chronic AF. We believe that the 2 initially different strategies have now reported similar success rates and are tending toward a unified strategy, ie, the circumferential approach.¹³ Actually, it appears that disconnection alone is insufficient; an

enlarged ablation design inclusive of additional lesion lines is indeed crucial to cure patients with AF.

Atrial Fibrillation Mechanisms

To assess whether 1 strategy is superior to the other, it is crucial to understand the mechanisms that underlie human AF since the 2 proposed strategies are based on different rationales. The mechanisms of AF are complex and not yet well defined (Figure 1).^{8,10,14–16} Improvements in catheter ablation techniques essentially depend on better understanding of the mechanisms of this arrhythmia. Chronic AF is a highly heterogeneous and complex disease, and there are different mechanisms in different patients. However, it has become increasingly evident that AF is a disease of the posterior wall of the left atrium. The circumferential LA ablation strategy, including ablation lines in the posterior left atrium and mitral isthmus, has several possible mechanisms of action: (1) PV isolation, at least to some degree; (2) elimination of anchor points for mother waves, or rotors that may generate AF, at or near the LA-PV junction; (3) ablation of other potential trigger sites, such as the vein of Marshall and the posterior LA wall; (4) ablation of right LA connections that may play a role in generating AF; (5) atrial debulking to provide less space for circulating wavelets; and (6) complete PV vagal denervation. Some or all of these factors may explain why CPVA is superior to PV isolation alone for both paroxysmal and chronic AF. Also, we recently demonstrated and localized vagal fibers and/or ganglia around PV ostia at the venoatrial junction. Their ablation results in heart rate variability attenuation during follow-up and no AF recurrence in almost all patients in whom it is possible to elicit and ablate such vagal reflexes (overall, 30% of patients in our series). The usual sites of LA lesions required to ablate AF coincide with regions of vagal innervation. CPVA is able to eliminate both the triggers and the substrate, including local vagal denervation.

Anatomic Considerations

PV anatomic variability may have potential implications in the choice of the ablation approach. In patients with such PV anatomic variations, the circumferential approach is more favorable. One such variation is the presence of a common ostium of the left PVs, occurring in $\leq 32\%$ of patients undergoing PV isolation. Such common ostia typically are too large to allow a stable position of the circumferential mapping catheter. Another anatomic variation is the presence of a right middle-lobe PV, present in $\leq 21\%$ of patients. When present, this vein typically is separated from the right superior and right inferior PVs by a narrow rim of atrial tissue. This predisposes to sliding of the ablating catheter into the variant PV during ablation. Another anatomic finding that renders an extraostial isolation more

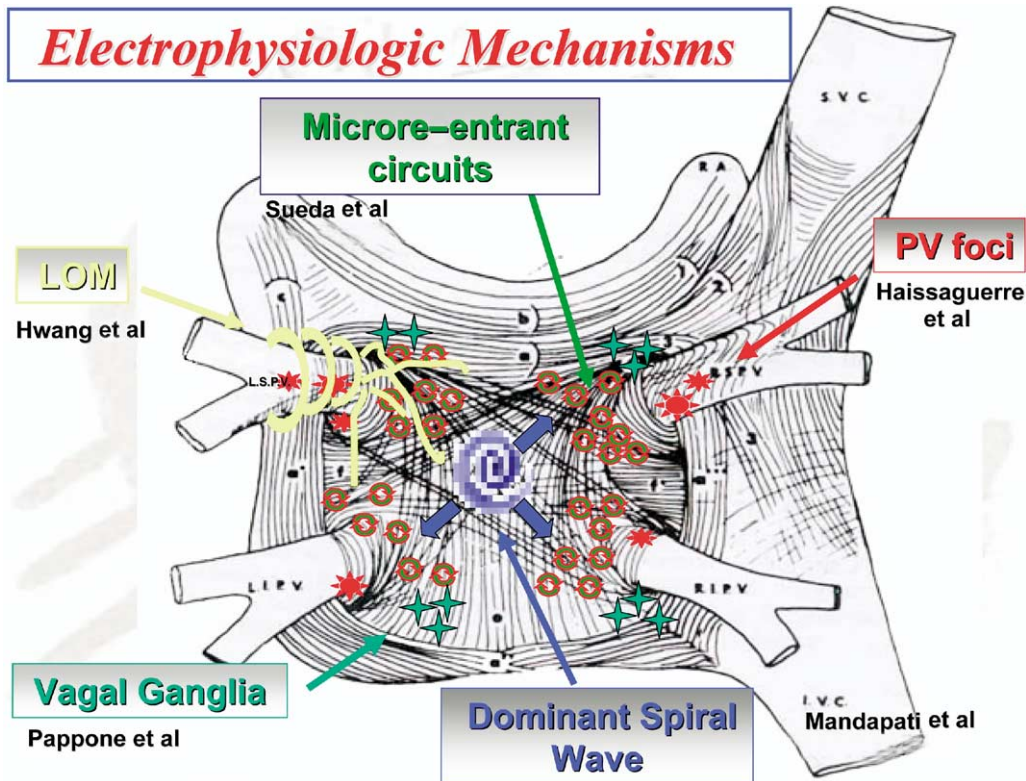


Figure 1. In the posterior left atrial (LA) wall, rotor-driven atrial fibrillation amenable to catheter ablation using an extensive approach is shown. Emphasis is on the crucial role of the pulmonary vein (PV)-LA junction for successful ablation of atrial fibrillation. IVC = inferior vena cava; LIPV = left inferior PV; LOM = ligament of Marshall; LSPV = left superior PV; RA = right atrial; RIPV = right inferior PV; RSPV = right superior PV; SVC = superior vena cava. (Adapted from *Circulation*,^{8,14,15} *N Engl J Med*,¹⁰ and *Ann Thorac Surg*.¹⁶)

Table 1
Complication rates following circumferential pulmonary vein (PV) ablation

Complication	Rate (%)
Death	0.0
Pericardial effusion	0.1
Stroke	0.03
Transient ischemic attack	0.2
Tamponade	0.1
Atrioesophageal fistula	0.03
PV stenosis	0.0
Incisional left atrial tachycardia	6.0

favorable is an ostial diameter <10 mm. Radiofrequency (RF) applications at a small ostium carry a higher than usual risk of PV stenosis.

Circumferential Pulmonary Vein Ablation Technique

Patient population and selection: Over the last 5 years, >6,000 patients with either paroxysmal or chronic AF, many of whom had associated structural heart disease, were referred to our department for circumferential PV ablation. In our series the presence of heart failure, coronary artery disease, and mechanical prosthetic valves did not affect the outcome.

Mapping and ablation procedure: Three catheters are usually used: (1) a standard bipolar or quadripolar catheter in the right ventricular apex to provide backup pacing, (2) a quadripolar catheter in the coronary sinus to allow pacing of the left atrium, and (3) a deflectable ablation catheter to be advanced through the transseptal sheath. A pigtail catheter is temporarily positioned above the aortic valve to act as a landmark at the time of transseptal puncture. A reference patch is also placed on the back of the patient. A 3-dimensional reconstruction of the left atrium is created with an electroanatomic mapping system. Tubular models of the PVs and the outline of the mitral valve annulus are also depicted as anatomic landmarks for the navigation system,

and we create the map by entering each PV in turn (Figure 2). Three locations are recorded along the mitral annulus to tag the valve orifice. To secure PV entry, we use 3 criteria based on (1) fluoroscopy, (2) impedance, and (3) electrical activity. Entry into the vein is clearly identified because the catheter leaves the cardiac shadow on fluoroscopy, impedance usually increases >140 to 150Ω , and electrical activity disappears. To better differentiate between PVs and the left atrium, we use voltage criteria (fractionation of the local bipolar electrogram) and impedance (an increase of $>4 \Omega$ above mean LA impedance) to define the PV ostium. Anatomic appearance clearly acts as added confirmation of catheter entry into the PV ostium, and an 8-mm tip-deflectable catheter or a 4-mm tip-irrigated catheter is used for mapping and ablation. The mapping and ablation procedures are performed by using the coronary sinus atrial signal if the patient is in SR, or the right ventricular signal if the patient is in AF, as the synchronization trigger for the CARTO (Biosense Webster, Inc., Diamond Bar, CA) system. Each endocardial location is recorded while a stable catheter position is maintained, as assessed by both end-diastolic stability (a distance of 2 mm between 2 successive locations) and local activation time stability. Atrial volumes are calculated at the end of diastole independently of the underlying rhythm (AF or SR). The mapping catheter is introduced into the left atrium under fluoroscopic guidance, and its location is recorded relative to the location of the fixed reference. Usually, 100 points are required to create adequate maps of the left atrium and PVs, and ≤ 200 points for accurate mapping of LA tachycardia. Anatomic reconstruction of the left atrium obtained with the CARTO system or Endocardial Solutions (St. Paul, MN) system is reliable compared with magnetic resonance imaging. By moving the catheter inside the heart, the mapping system continuously analyzes its location and orientation and presents it to the user on the monitor of a graphic workstation, thereby allowing navigation without the use of fluoroscopy. The mapping procedure is performed by moving the catheter to numerous sequential points within the left atrium and PVs, and establishing the location in 3-dimensional space together with the local unipolar and bipolar voltages and the local activation time relative to the chosen reference interval. The acquired information is then color coded and displayed. As each new site is acquired, reconstruction is progressively updated in real time to create 3-dimensional chamber geometry color coded with activation time. Additionally, collected data can be displayed as voltage maps depicting the magnitude of the local peak voltage in a 3-dimensional model. The chamber geometry is reconstructed in real time by interpolation of the acquired points. Local activation times can be used to create activation maps, which are important when mapping and ablating focal or macroreentrant atrial tachycardia but are not used during ablation in patients with AF.

Ablation strategy: Our initial ablation strategy was to encircle the 4 PVs by creating circumferential lesions around each PV. These lines consisted of contiguous focal lesions deployed at >5 mm from the PV ostia. However, since 2001, additional ablation lines on the posterior wall connecting both the superior and inferior PVs and the mitral annulus to the left inferior PV (mitral isthmus line) are created (Figure 2) to prevent postablation LA flutter.^{8,9} RF current is usually applied with a target temperature of 55°C to 65°C and a maximum power of 100 W. CPVA is performed 1 to 2 cm from the PV ostia to encircle each PV. RF energy is applied in the posterior wall with a maximum power of 50 W and a temperature target of 55°C to minimize the risk of injury. RF energy is applied continuously on the circumferential planned ablation lines as the catheter is gradually dragged along the line. Continuous catheter movement, often in a to-and-fro fashion over a point, helps keep catheter-tip temperature down by means of passive cooling. The end point of ablation is voltage abatement of the local atrial electrogram by 90% or to <0.05 mV. In some patients, if necessary, additional ablation lines are created along the LA roof, septum/anterior wall, or along the posterior mitral annulus. On average, a total of 10 to 15 seconds of RF is required. Circumferential ablation lines are usually created by starting at the lateral mitral annulus and withdrawing posteriorly and then anteriorly to left-sided PVs, passing between the LSPV and the LA appendage before completing the circumferential line on the posterior wall of the left atrium. The "ridge" between the LSPV and LA appendage can be identified by fragmented electrograms resulting from the collision of activity from the LA appendage and LSPV/left atrium. We observed termination of AF during the procedure in about one third of patients. If AF does not terminate during RF, transthoracic cardioversion is performed at the end of the procedure. If there is immediate recurrence of AF after cardioversion, completeness of the lines is reassessed. Ablation is performed in the cavotricuspid isthmus in patients with a history of typical atrial flutter; in patients with cavotricuspid isthmus-dependent atrial flutter, it is induced by atrial pacing.

PV innervation and denervation: Potential vagal target sites are identified during the procedure in $\geq 33\%$ of patients.⁴ Vagal reflexes are considered sinus bradycardia (<40 beats per minute), asystole, atrioventricular block, or hypotension that occurs within a few seconds of the onset of RF application. If a reflex is elicited, RF energy is delivered until such reflexes are abolished or for ≤ 30 seconds. The end point for ablation at these sites is termination of the reflex that is followed by sinus tachycardia or AF. Failure to reproduce the reflexes with repeat RF is considered confirmation of denervation. Complete local vagal denervation is confirmed by the abolition of all vagal reflexes. The most common sites are tagged on electroanatomic maps.⁴

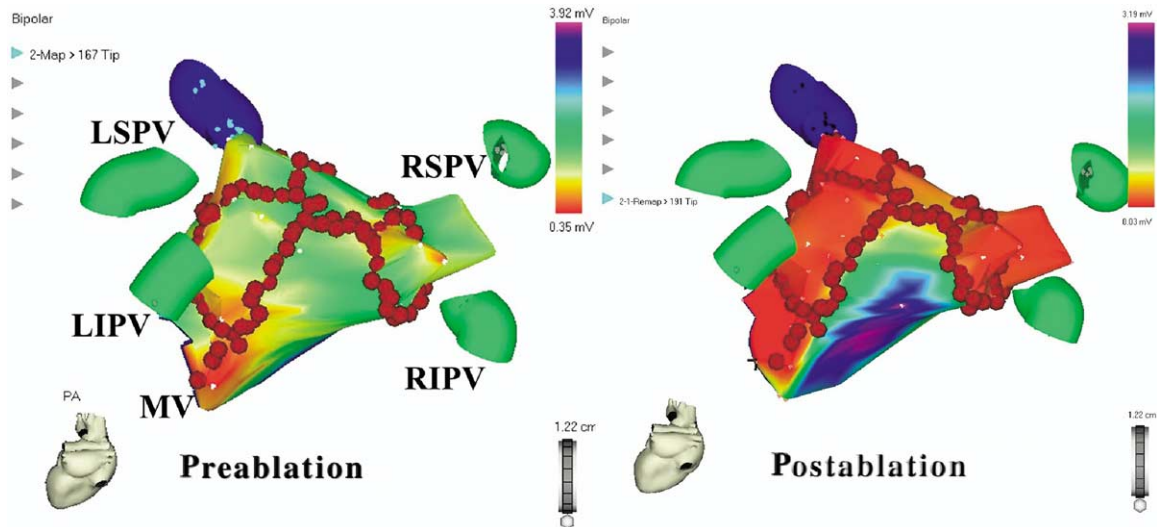


Figure 2. Preablation and postablation electroanatomic left atrial maps. Circular radiofrequency lesions are created around each pulmonary vein (PV) ostium, constituting the standard ablation set for circumferential PV ablation. Additional linear lesions connect both the right-sided and left-sided PVs. The mitral isthmus line connecting the mitral annulus and the left inferior PV (LIPV) to prevent left atrial incisional tachycardia is evident. LSPV = left superior PV; MV = mitral valve; PA = pulmonary artery; RIPV = right inferior PV; RSPV = right superior PV.

Among patients in SR, postablation remapping is performed using the preablation map for the acquisition of new points to permit accurate comparison of pre- and post-RF bipolar voltage maps. Among patients in AF, after restoration of SR, postablation remapping is performed with the anatomic map acquired during AF to have the same landmarks and lesion tags for accurate lesion validation. Gaps are defined as breakthroughs in an ablated area and identified by sites with single potentials as well as by early local activation. The completeness of the mitral isthmus lesion line is usually demonstrated during coronary sinus pacing by endocardial and coronary sinus mapping to seek widely spaced double potentials across the line of block. In our experience, after block is achieved, the double-potential interval at the mitral isthmus during coronary sinus pacing is usually approximately 150 msec, depending on the atrial dimensions and the extent of scarring and lesion creation.⁸ If incomplete block is revealed by impulse propagation across the line, further RF applications are made to complete the line of block.

In patients who are in AF at the beginning of the procedure, RF ablation is performed without an initial attempt at cardioversion. If AF does not terminate during ablation, cardioversion is performed at the end of the procedure.

Safety and Efficacy

Complications of circumferential LA ablation are reported in Table 1. Postablation LA flutter is relatively common but usually does not require a repeat procedure because it generally resolves spontaneously within 5 months after the index procedure. Atrioesophageal fistula is rare, but its occurrence is dramatic and devastating.⁵ Lower RF energy

application is recommended when ablating on the LA posterior wall; at present, the line is made on the posterior wall near the roof of the left atrium, where the left atrium is not in direct contact with the esophagus. Success rates are approximately 90% among patients with paroxysmal AF and 80% among those with chronic AF. In patients with paroxysmal AF in whom vagal reflexes are elicited and abolished by RF application, the long-term success rate is approximately 100%.⁴ A recent randomized study by our laboratory demonstrated that early recurrence of AF or iatrogenic LA tachycardia may occur within the first few months after the procedure, particularly in patients without additional ablation lines; usually they do not require a repeat procedure because the condition resolves spontaneously during long-term follow-up.⁸ Another recent randomized study by our laboratory demonstrated that CPVA is superior to administration of amiodarone in maintaining long-term SR in patients with chronic AF.

Anatomic, Electrical, and Functional Remodeling After Pulmonary Vein Ablation

Restoration of SR after ablation (usually by 5-month follow-up) results in “reverse” electrical and mechanical atrial remodeling and improved atrial function. Enlarged atria may become smaller, and this is associated with both electrical and mechanical changes. Among patients with mitral regurgitation who undergo ablation, anatomic remodeling is more pronounced and, interestingly, is associated with reduced mitral regurgitation and improved left ventricular function compared with patients in whom SR is maintained by drugs alone. In our experience, anatomic, electrical, and functional remodeling after ablation is associated with a

good long-term outcome in patients with either paroxysmal or chronic AF.

Future Directions

Remote magnetic catheter navigation system for mapping and ablation of AF—a new era in interventional electrophysiology: A novel and promising approach to transcatheter AF ablation is the robotic magnetic navigation system for accurate mapping and ablation. The initial experience with this system in our laboratory has shown that the remote control of a soft magnetic catheter in patients with either paroxysmal or chronic AF is safe and feasible. This navigation system is integrated with a newly developed electroanatomic CARTO RMT (Biosense Webster, Inc.) mapping system. A special magnetic 4-mm tip mapping and ablation catheter with a location sensor, the NaviStar-RMT catheter, has been developed to function with both magnetic navigation and the CARTO system. The CARTO RMT system sends real-time catheter-tip location and orientation data to the magnetic navigation system. Magnetic field orientations corresponding to specific map points can be stored on the navigation system and reapplied, if desired, to return to previously visited locations on the map, repeatedly and accurately. We have now developed a remote mapping and ablation protocol for circumferential PV ablation procedures.⁹ The learning curve is not long and is limited to the first case. No complication has been observed.

On the basis of our experience with this remote navigation technology in patients with node-reentrant atrioventricular reciprocating tachycardia and/or accessory pathways, as well as in patients with AF, we believe a new era in interventional electrophysiology is beginning. Magnetic catheters can now be navigated in the left atrium more precisely and safely than achieved manually, without risk of major complications, even in less experienced centers.

Conclusion

The circumferential PV approach to ablation can be safely performed in most patients with either paroxysmal or chronic AF, with high success rates that are maintained over the long term. With practice and new technology development, the procedure can be accomplished more quickly and can be safely performed even in less experienced centers, thus improving patient tolerance and exposing the patient to less risk.

- Pappone C, Rosanio S, Oreto G, Tocchi M, Gugliotta F, Vicedomini G, Salvati A, Dicandia C, Mazzone P, Santinelli V, Gulletta S, Chierchia S. Circumferential radiofrequency ablation of pulmonary vein ostia: a new anatomic approach for curing atrial fibrillation. *Circulation* 2000;102:2619–2628.
- Pappone C, Oreto G, Rosanio S, Vicedomini G, Tocchi M, Gugliotta F, Salvati A, Dicandia C, Calabro MP, Mazzone P, et al. Atrial electroanatomic remodeling after circumferential radiofrequency PV ablation. Efficacy of an anatomic approach in a large cohort of patients with AF. *Circulation* 2001;104:2539–2544.
- Pappone C, Rosanio S, Augello G, Gallus G, Vicedomini G, Mazzone P, Gulletta S, Gugliotta F, Pappone A, Santinelli V, et al. Mortality, morbidity, and quality of life after circumferential PV ablation for AF: outcomes from a controlled nonrandomized long-term study. *J Am Coll Cardiol* 2003;42:185–197.
- Pappone C, Santinelli V, Manguso F, Vicedomini G, Gugliotta F, Augello G, Mazzone P, Tortoriello W, Landoni G, Zangrillo A, et al. PV denervation enhances long term benefit after circumferential ablation for paroxysmal AF. *Circulation* 2004;109:327–334.
- Pappone C, Oral H, Santinelli V, Vicedomini G, Lang CC, Manguso F, Torracca L, Benussi S, Alfieri O, Hong R, et al. Atrio-esophageal fistula as a complication of percutaneous transcatheter ablation of AF. *Circulation* 2004;109:2724–2726.
- Oral H, Scharf C, Chugh A, Hall B, Cheung P, Good E, Veerareddy S, Pelosi F, Morady F. Catheter ablation for paroxysmal AF: segmental PV ostial ablation vs. left atrial ablation. *Circulation* 2003;108:2355–2360.
- Oral H, Knight BP, Tada H, Ozaydin M, Chugh A, Hassan S, Scharf C, Lai SW, Greenstein R, Pelosi F Jr, et al. PV isolation for paroxysmal and persistent AF. *Circulation* 2002;105:1077–1081.
- Pappone C, Manguso F, Vicedomini G, Gugliotta F, Santinelli O, Ferro A, Gulletta S, Sala S, Sora N, Paglino G, et al. Prevention of iatrogenic atrial tachycardia after ablation of atrial fibrillation: a prospective randomized study comparing circumferential pulmonary vein ablation with a modified approach. *Circulation* 2004;110:3036–3042.
- Pappone C, Santinelli V. The who, what, why, and how-to guide for circumferential pulmonary vein ablation. *J Cardiovasc Electrophysiol* 2004;15:1226–1230.
- Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Metayer P, Clementy J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339:659–666.
- Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, Rosenberg Y, Schron EB, Kellen JC, Greene HL, Mickel MC, Dalquist JE, et al, for the AF Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with AF. *N Engl J Med* 2002;347:1825–1833.
- Hohnloser SH, Kuck KH. Randomized trial of rhythm or rate control in atrial fibrillation: the Pharmacological Intervention in Atrial Fibrillation Trial (PIAF). *Eur Heart J* 2001;22:801–802.
- Van Gelder IC, Hagens VE, Bosker HA, Kingma JH, Kamp O, Kingma T, Said SA, Darmanata JI, Timmermans AJ, Tijssen JG, et al, for the Rate Control versus Electrical Cardioversion for Persistent AF Study Group. A comparison of rate control and rhythm control in patients with recurrent persistent AF. *N Engl J Med* 2002;347:1834–1840.
- Pappone C, Santinelli V. Towards a unified strategy for atrial fibrillation ablation? *Eur Heart J* 2005;26:696–704.
- Hwang C, Wu TJ, Doshi RN, Peter CT, Chen PS. Vein of Marshall cannulation for the analysis of electrical activity in patients with focal atrial fibrillation. *Circulation* 2000;101:1503–1505.
- Mandapati R, Skanes A, Chen J, Berenfeld O, Jalife J. Stable micro-reentrant sources as a mechanism of atrial fibrillation in the isolated sheep heart. *Circulation* 2000;101:194–199.
- Sueda T, Nagata H, Orihashi K, Morita S, Okada K, Sueshiro M, Hirai S, Matsuura Y. Efficacy of a simple left atrial procedure for chronic atrial fibrillation in mitral valve operations. *Ann Thorac Surg* 1997;63:1070–1075.