J Interv Card Electrophysiol (2006) 17:103–109
DOI 10.1007/s10840-006-9066-9

Pulmonary vein isolation and linear lesions in atrial fibrillation ablation

Imran Sheikh · David Krum · Ryan Cooley · Anwer Dhala · Zalmen Blanck · Atul Bhatia · Vikram Nangia · Masood Akhtar · Jasbir Sra

Received: 4 August 2006 / Accepted: 29 November 2006 / Published online: 23 February 2007

Abstract
Background Various strategies have been used for atrial fibrillation (AF) ablation. It is unclear whether adding linear lesions to pulmonary vein (PV) isolation has significant advantages.
Objectives We assessed the clinical benefit of adding linear lesions in patients undergoing PV isolation for AF.
Methods One hundred patients (63 male and 37 female; mean age of 59±11 years) with documented paroxysmal AF were included in the study. Patients were randomized into two groups. The first group underwent PV isolation alone. The second group underwent PV isolation and had two linear lesions created; one line between the superior PVs, and a second line from the left inferior PV to the mitral valve annulus. Patients' clinical progress after the ablation was evaluated and compared at 1, 3, and 9 months after their respective ablation procedures.
Results The linear lesions group maintained sinus rhythm and had fewer symptoms than the lone PV isolation group (86 vs. 58%, respectively) ($p<0.05$) at 1 month. At 9 months, when patients who reverted to AF underwent additional management to regain sinus rhythm (90 vs. 82%, respectively) (p=NS), there was no statistical difference between the groups regarding the use of antiarrhythmics, the need for electrical cardioversion, and subjective improvement.
Conclusion The addition of linear lesions to PV isolation more effectively achieved sinus rhythm initially and fewer patients required additional management to maintain their rhythm when compared to patients who underwent lone PV isolation. However, at 9 months, the overall results were similar in both groups.

Keywords Atrial fibrillation · Ablation procedures · Pulmonary vein isolation · Linear lesions

I. Sheikh · D. Krum · R. Cooley · A. Dhala · Z. Blanck · A. Bhatia · V. Nangia · M. Akhtar · J. Sra
Electrophysiology Laboratories,
Aurora Sinai/Aurora St. Luke's Medical Centers,
University of Wisconsin School of Medicine and Public Health,
Milwaukee Clinical Campus,
Milwaukee, WI, USA

J. Sra (✉)
2801 W. Kinnickinnic River Pkwy #777,
Milwaukee, WI 53215, USA
e-mail: bdanek@hrtcare.com

1 Introduction

Over the last decade, various strategies have been introduced to more precisely and efficiently ablate atrial fibrillation (AF). After Haissaaguerre et al. reported that electrical isolation of the PV is advantageous in terminating AF [1], procedures have been aimed at a more anatomically-based approach to AF ablation with isolation of the PVs and the use of empiric ablation lines to prevent reentry loops [2–5]. However, it is difficult to create contiguous and transmural lines using the currently available technology and the success rate of non-contiguous and non-transmural lines is quite inadequate [6, 7]. It is often difficult to convince patients to undergo a second or a third complicated procedure with the inherent risks and the possibility of somewhat limited success [8]. Our study monitored the clinical course of two groups of patients with paroxysmal AF after they underwent a single ablation procedure, with special attention to the use of antiarrhythmic medication. The first group underwent lone PV isolation. The second group underwent PV isolation with two sets of linear lesions created in the left atrium; one from the left inferior

PV to the mitral valve annulus and another between the superior PVs. The purpose of the study was to determine if creating linear lesions during PV isolation more effectively achieved sinus rhythm in patients with paroxysmal AF.

2 Methods

2.1 Study patients

The clinical results of 100 consecutive randomized patients who underwent AF ablation were compared. Sixty-three males and 37 females, with a mean age of 59±11 years and documented AF, were included in the study. Table 1 depicts the clinical characteristics of these patients. Selection criteria for AF ablation included the following: (1) patients suffering multiple and frequent highly symptomatic episodes of AF (at least twice a month for three consecutive months), (2) AF that had been refractory to antiarrhythmic therapy or the patient was unable to tolerate antiarrhythmic therapy. Only those patients whose post ablation follow-up could be conducted at our outpatient clinic were included in the study. Patients who had undergone prior AF ablation procedures or those with permanent or persistent AF were excluded. The first month post ablation, all patients were continued on antiarrhythmic medication. Months number two and three post ablation were considered a titration phase in which attempts were made to wean off antiarrhythmic medication. Patients were then followed clinically after the titration phase for 6 months. The primary end point was freedom from AF after a single ablation procedure, either with or without the use of antiarrhythmics. The secondary end point was improvement in symptoms during the 6 months after the titration phase. All patients gave informed consent for the procedure.

Table 1 Clinical characteristics

	Lone pulmonary vein isolation	Pulmonary vein isolation with linear lesions
Number of patients*	50	50
Age	60±12	61±10
Gender	16 female, 34 male	21 female, 29 male
Ejection fraction (%)	54±12	53±14
Left atrial size cm^2	4.02±0.71	4.12±0.65
Failed amiodarone (prior to ablation)	22	20

*All patients were required to experience at least two symptomatic episodes a month for three consecutive months to be included in the study. The overall number of symptomatic episodes prior to ablation was not statistically different between the two groups.
p=NS for all categories

2.2 Ablation groups

Prior to the procedure, antiarrhythmic medications were discontinued for five half-lives (amiodarone was discontinued 2 weeks prior and warfarin was discontinued 72 hours prior to the procedure). 3D computed tomography was performed on all patients to assess the PV anatomy prior to the ablation. A transesophageal echocardiogram (TEE) was completed on all patients to rule out intracardiac thrombus. Patients were randomized as to which approach would be used during their ablation. Group I included 50 patients who underwent lone PV isolation. Group II included 50 patients who underwent PV isolation and the creation of two lines of ablation, one from the left inferior PV to the mitral valve annulus and another connecting the superior PVs. A single operator conducted the patients' ablation procedures and the same electrophysiologist was responsible for their post ablation clinical management.

2.3 Pulmonary vein isolation technique

Quadripolar catheters were placed at the high right atrium, His bundle, and the right ventricular apex. A detailed electrophysiology procedure was performed at baseline and during isoproterenol infusion (2–4 mcg/min). A decapolar catheter was placed in the coronary sinus. A CardioLab™ electrophysiology system (GE Healthcare, Waukesha, WI, USA) was used for electrophysiological monitoring. Patients were anesthesized with intravenous propofol. Hemodynamic monitoring was continuous. Left atrial access was obtained via transseptal puncture with TEE and fluoroscopic assistance. In addition to a mapping/ablation catheter, the Basket (Boston Scientific/EP Technologies, Boston, MA, USA) or Lasso catheter (Biosense Webster, Diamond Bar, CA, USA) was positioned in the left atrium via an introducer sheath. An activated clotting time (ACT) of approximately 300–350 sec was maintained throughout the procedure with intravenous heparin.

Contrast PV angiograms were used to assist in identifying the PV anatomy and ostial region. In the first 20 patients (ten in each group) the Lasso catheter was placed in the PVs as near to the ostium as possible, and recordings taken circumferentially around the ostium of the veins using adjacent pairs of electrodes on the catheter (Fig. 1). Pacing of the distal coronary sinus was utilized during ablation in the left PVs to assist in separating atrial recordings from PV potentials. Electrical isolation of the veins was then performed sequentially at sites proximal to the catheter location. The distal electrode of the mapping and ablation catheter was placed in close proximity to the electrode on the Lasso catheter with the earliest PV potential. Radiofrequency energy was applied using temperature control (50–55°C for 40–60 sec). Radiofrequency energy was delivered at the

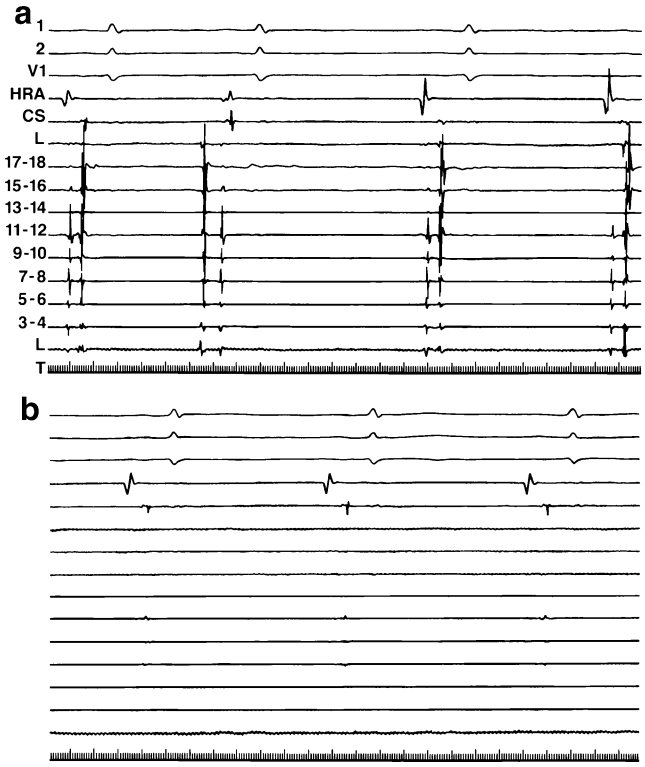

Fig. 1 Pulmonary vein isolation using Lasso catheter. Surface ECG and intracardiac tracings before (*top panel*) and after ablation (*bottom panel*) for paroxysmal atrial fibrillation is shown

most proximal or ostial aspect of the vein possible. This process was repeated until the vein was fully isolated electrically. The Lasso catheter was then moved to the next PV and the process was repeated until all PVs were isolated. If the PV (usually the right inferior PV) was too small for the Lasso catheter to be positioned adequately, attempts were made to ablate the PV potentials using the mapping and ablation catheter. Electroanatomical mapping (Biosense Webster, Diamond Bar, CA, USA) was utilized to assist in correlating the position of the ablation catheter with the Lasso or the Basket catheter and to record lesion locations.

The Astronomer location system (Boston Scientific/EP Technologies, Boston, MA, USA) was utilized for ablation procedures with the Basket catheter in the last 80 patients (40 in each group). This system informs the operator when another catheter comes into contact with an electrode on the Basket catheter, and is helpful in positioning the ablation catheter at the intended ablation site. Mapping and ablation of the pulmonary veins using the Basket catheter (Fig. 2) was performed in a similar fashion as was used with the Lasso catheter, except for the following: since the Basket catheter has electrodes arranged in a series of splines, sequential activation along the length as well as the circumference of the PVs can be recorded. This helps in determining the segment of the myocardial sleeve displaying first PV potential. Using this information, ablation was performed successively until the vein was fully electrically isolated. The same ablation parameters described in the previous section were used. Following isolation of a PV, the Basket catheter and the mapping and ablation catheter were placed in the next PV and the process was repeated until all PVs were electrically silent.

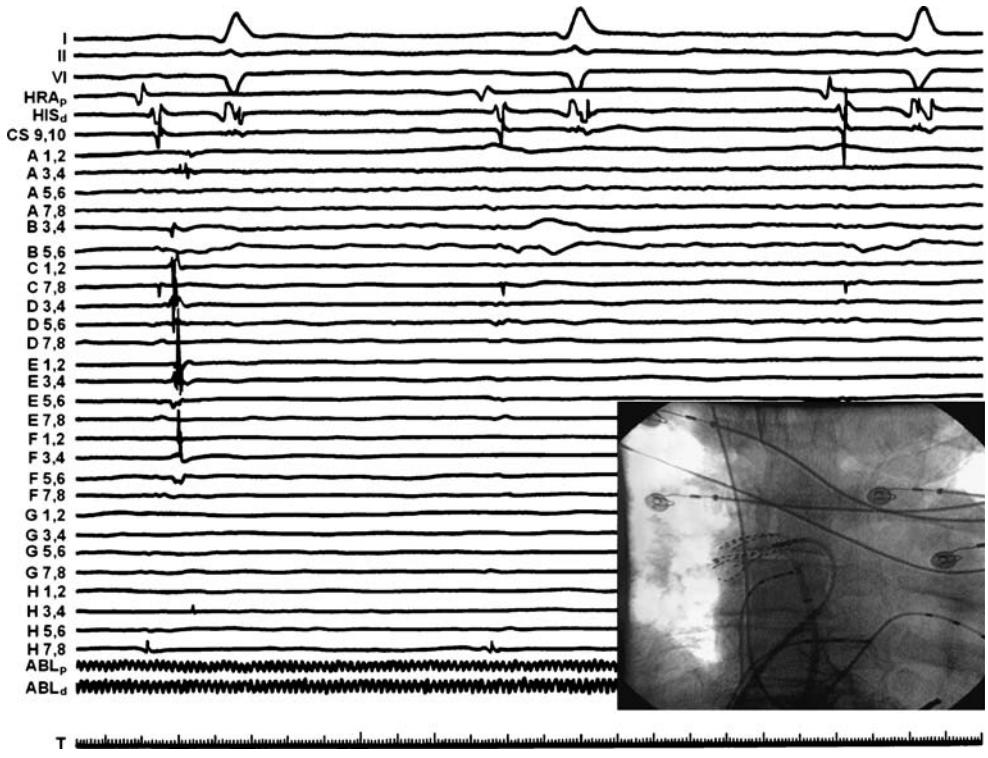

Fig. 2 Pulmonary vein isolation using multi electrode Basket catheter. Surface ECG and intracardiac tracings during ablation are shown. Ablation at the earliest pulmonary vein potential leads to complete electrical isolation of the pulmonary vein

2.4 Pulmonary vein isolation and linear lesions

In the second group of patients, after the PVs were isolated as described, two different sets of linear lesions were created in the left atrium; one line extended from the left inferior PV to the mitral valve annulus and another line was made connecting the superior PVs using the electroanatomic mapping system. Figure 3 is a diagrammatic representation of the linear lines created in addition to the PV isolation in the patients. All attempts were made to create transmural and contiguous lesions, but there was no check to see whether conduction was blocked completely across these lines.

2.5 Follow-up

All patients were initially continued on antiarrhythmic medication post ablation. At one-month follow-up, if there was no recurrence of AF lasting longer than 10 min on two separate occasions, the antiarrhythmic drug was discontinued. Following this, patients went through a two-month titration phase to see if antiarrhythmic medications were needed. All patients were then followed up for an additional 6 months at minimum. Patients were seen in the clinic at least every 2 months. Electrocardiograms were completed on each visit and, if indicated based on symptomology or rhythm tracing, a holter or event recorder was used for monitoring. Patients were also encouraged to call if they had any symptoms. All patients received a post ablation echocardiogram to screen for evidence of pulmonary vein stenosis.

2.6 Post ablation clinical outcome

Patients' clinical progress was recorded at 1, 3 and 9 months (months two and three after the ablation were considered a titration phase during which antiarrhythmic weaning was attempted). The categories of clinical progress that were recorded included: (1) maintenance of normal sinus rhythm, (2) subjective symptomatic improvement, (3) antiarrhythmic use, and (4) the need for electrical cardioversion.

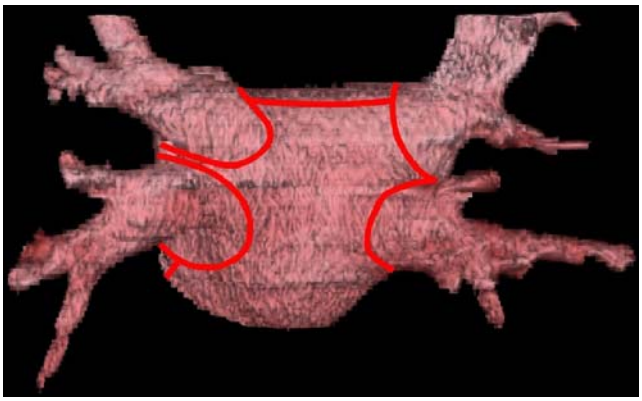

Fig. 3 Location of linear lesions made during ablation. Postero-superior 3D CT image of a segmented left atrium with approximate location of linear lesions

3 Statistical analysis

Comparisons between the categories of clinical progress listed above were made with data using the Fischer's exact test. $P \leq 0.05$ was considered statistically significant.

4 Results

4.1 Patient population

The procedure was completed in all 100 patients. All patients had failed at least one antiarrhythmic medication prior to the ablation procedure. In addition, 22 patients in the PV isolation alone group and 20 patients in the PV isolation plus linear lesion group had failed amiodarone prior to ablation.

4.2 Pulmonary vein isolation group

The procedure was completed in all 50 patients. Figures 1 and 2 depict complete electrical isolation of the PVs using the Lasso and Basket techniques. Post procedure, 21 patients reverted to AF in the first month. Of these patients, sinus rhythm was achieved in 13 patients after: five patients' antiarrhythmic were up-titrated, five patients were started on a different antiarrhythmic than that started post procedure, three patients required electrical cardioversion with antiarrhythmic up-titration. Three patients with typical atrial flutter were successfully ablated.

At 9 months (Table 1), 9 (18%) patients who underwent lone PV isolation remained in AF despite the use of antiarrhythmic medications. Twenty-seven (54%) were using antiarrhythmics to maintain a sinus rhythm. Of these, eight patients were using a smaller dose of a previously failed drug and, in 10 of the patients on amiodarone prior to ablation, the drug could either be discontinued or changed to a less toxic drug.

4.3 Pulmonary vein isolation with linear lesions group

The procedure was completed in all 50 patients. Figure 3 is a diagrammatic representation of the ablation lines created in addition to the PV isolation. Post procedure, seven (14%) patients reverted to AF. In these patients, sinus rhythm was achieved after: one patient's antiarrhythmic was up-titrated and two patients underwent electrical cardioversion with antiarrhythmic up-titration. AF could not be converted in

Table 2 Clinical follow-up

	Lone pulmonary vein isolation *n* (%)	Pulmonary vein isolation with linear lesions *n* (%)	*p* value
Sinus rhythm (initial*)	29 (58)	43 (86)	$p \leq 0.5$
Sinus rhythm (final**)	41 (82)	45 (90)	*p*=NS
Symptomatic improvement	40 (80)	43 (86)	*p*=NS
Using antiarrhythmics	27 (54)	31 (62)	*p*=NS
Electrical cardioversion performed	3 (6)	2 (4)	*p*=NS
Fluoroscopic time (min)	79±10	88±15	*p*=NS
Procedural complications	3 (6)	0	*p*=NS

*Initial statistics: patients' rhythm was monitored at 1-month post ablation.
**Final statistics at nine months: patients maintained in sinus rhythm after the titration phase (months 2 and 3 post ablation). Patients' rhythm were monitor on scheduled follow-up ECGs and, if symptomology provoked, by the use of holter or event monitors.

four patients. One patient had new onset, typical counter-clockwise flutter and was successfully ablated.

At 9 months (Table 2), of the total patients who underwent PV isolation with the addition of linear lesions, one additional patient reverted to AF after the initial one-month period. Thus a total of 45 (90%) patients were in sinus rhythm, 31 (62%) patients required antiarrhythmic drugs. Of these, two patients' antiarrhythmics were being down-titrated, and two required electrical cardioversion. In addition, amiodarone was stopped or changed to a less toxic drug in 10 of the 20 patients who were taking amiodarone prior to the ablation.

4.4 Comparison of the two groups

Six categories of clinical follow-up are depicted in Table 2. With regards to maintenance of sinus rhythm and symptomatic improvement, patients who underwent PV isolation with linear lesions showed initial post procedural success over the lone PV isolation group (86 vs. 58%, $p \leq 0.05$). At 9 months, following the interventions listed above for patients who had reverted to AF, the final success rate was essentially equal between the two groups (90 vs. 82%, *p*= NS). Both groups similarly used antiarrhythmics, required electric cardioversion, and had similar symptomatic improvement. However, there were more interventions required in terms of antiarrhythmic drug titration in patients with PV isolation alone as more patients had recurrence during the first month after the ablation.

4.5 Complications

The overall difference in complication rates between the two groups was not statistically significant. The lone PV isolation group experienced three (6%) complications: one patient suffered cardiac tamponade requiring surgical placement of a pericardial window, one patient suffered a transient ischemic attack with no residual neurologic symptoms, and the third patient experienced a small pericardial effusion with pericarditis which resolved with medical therapy. There were no complications in the group receiving linear lesions. During the follow-up period, none of the patients experienced symptoms suspicious of PV stenosis.

5 Discussion

Transvenous catheter ablation procedures are currently of interest in the treatment of patients with AF. Many patients are severely symptomatic and unable to find relief with current antiarrhythmic therapy. Areas of concern relating to the use of ablation for AF include: maintaining sinus rhythm post ablation, relieving patients' symptoms, safety, and the need for repeat ablations. This study evaluated paroxysmal AF patients at 1, 3 and 9 months post ablation and assessed the clinical advantage of adding linear lesions to PV isolation during a single AF ablation. Despite an early advantage seen with the linear lesion technique, long-term efficacy of both lone PV isolation and PV isolation with linear lesions was similar. However, a significant number of patients in both groups could be maintained in sinus rhythm on previously ineffective and less toxic antiarrhythmic drugs. Given the long procedure time of the lone PV isolation ablation, and some reluctance on the part of patients to undergo repeated ablations (often required with this technique) with the incremental increase in risk, the addition of linear lesions might afford an alternative strategy in some patients.

5.1 Success of ablation in the two groups

Reported lone PV isolation success rates in maintaining sinus rhythm have been between 50 and 60% (1–5). Our results with PV isolation correlate fairly well with the results in these prior studies (58% initially and 82% at 9 months). Success rates in maintaining sinus rhythm were higher initially (86%) when linear lesions were also created between the superior

PVs and between the left inferior PV and the mitral valve annulus. Additional benefits of the creation of linear lesions could be due to ablation of ganglionated plexi, fractionated electrograms and prevention of post ablation flutters [9, 10]. However, long-term results (lone PV isolation vs. PV isolation with linear lesions: 82 vs. 90%) were not statistically significant between the two groups, suggesting that some of the initial benefits from these additional lines could have disappeared either due to resumption of conduction across these lines or reinnervation of vagal plexi in some instances. This may be the reason why antiarrhythmics could not be discontinued. As shown in recent studies, it is not easy to create transmural and contiguous lines and the presence of gaps in lesion lines usually leads to inadequate endpoints [6]. Furthermore, another study showed a significant resumption of conduction recurrence in many patients when they were followed up sequentially by electrophysiological studies after AF ablation [7].

5.2 Use of antiarrhythmics

Although one of the goals of ablation therapy is to relieve patients from taking antiarrhythmic medication, we found a significant percentage of post ablation patients still required antiarrhythmics at 9 months. Our lesion sets were not different than those described in the literature and all attempts were made to isolate all the PVs and give complete linear lines. Prior studies have reported approximately 62–92% (2, 3, 5) of PV isolation patients are free of antiarrhythmic drug use long-term. Perhaps our results varied from these prior studies because our criteria differed on how patients were initiated and maintained on antiarrhythmics and how we measured recurrence of AF during our follow-up. However, regardless of being maintained on antiarrhythmics, a vast majority of patients still reported significant improvement in symptoms after a single ablation. In addition, we found that patients responded to antiarrhythmic medications which had previously failed to achieve a response, at lower than pre ablation dosages, and, in a significant number of patients, amiodarone was discontinued.

5.3 Limitations

Our primary endpoint did not include electrophysiology studies to define arrhythmias that occurred after the initial ablation. We also did not assess for complete conduction block across the lines. Contiguous, transmural linear lesions may give better results in patients undergoing PV isolation along with linear lesions but they are difficult to achieve [11, 12]. However, there is not a consensus on this in the literature, with some investigators suggesting that contiguous transmural ablation lines may not be required to achieve the desired endpoint [3, 4].

Amiodarone was discontinued 2 weeks prior to the respective ablation procedure. This may have affected the ability to achieve pure pulmonary vein isolation.

Post-procedure AF recurrence was checked on scheduled follow-up ECGs and, if symptomology provoked, by the use of an event or holter monitor. This follow-up method may have missed asymptomatic AF and thus overestimated our success rate.

5.4 Future considerations

It is generally accepted that PV isolation is necessary in the ablation of AF. However, as shown in this and other studies, isolation of the PVs alone may not be sufficient to achieve the ultimate end point, high success rate without the need for antiarrhythmic therapy. As currently available technologies do not depict precisely the anatomy of the left atrium, important developments, including an attempt to more precisely and efficiently define the left atrial anatomy and visualize it in real time, should further help achieve this goal [13, 14].

The addition of linear lesions to PV isolation more effectively achieved sinus rhythm and improvement of symptoms earlier on in patients with paroxysmal AF. However, the benefits of this approach did not include discontinuation of antiarrhythmic medication. In both groups, the addition of antiarrhythmic drugs can maintain sinus rhythm and improve symptoms after a single ablation in most patients.

Acknowledgments The authors would like to gratefully acknowledge the help of Pat Strommen and Janet Babe in acquiring data, Alfred J. Anderson for statistical analysis, Brian Miller and Brian Schurrer in preparing illustrations, and Barbara Danek in editing the manuscript.

References

1. Haissaguerre, M., Jais, P., Shah, D. C., Takahashi, A., Hocini, M., Quiniou, G., et al. (1998). Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *New England Journal of Medicine, 339*, 659–666.
2. Chen, S. A., Hsieh, M. H., Tai, C. T., Tsai, C. F., Prakash, V. S., Yu, W. C., et al. (1999). Initiation of atrial fibrillation by ectopic beats originating from the pulmonary veins: Electrophysiological characteristics, pharmacological responses and effects of radiofrequency ablation. *Circulation, 100*, 1879–1886.
3. Pappone, C., Rosanio, S., Oreto, G., Tocchi, M., Gugliotta, F., Vicedomini, G., et al. (2000). Circumferential radiofrequency ablation of pulmonary vein ostia: A new anatomic approach for curing atrial fibrillation. *Circulation, 102*, 2619–2628.

4. Oral, H., Knight, B. P., Tada, H., Ozaydin, M.,Chugh, A., Hassan S., et al. (2002). Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. *Circulation, 105*, 1077–1081.
5. Marchlinski, F. E., Callans, D., Dixit, S., Gerstenfeld, E. P., Rho, R., Ren, J. F., et al. (2003). Efficacy and safety of targeted focal ablation versus PV isolation assisted by magnetic electroanatomic mapping. *Journal of Cardiovascular Electrophysiology, 14*, 358–365.
6. Ernst, S. Ouyang, F., Lober, F., Antz, M., & Kuck, K. H. (2003). Catheter-inducted linear lesions in the left atrium in patients with atrial fibrillation: An electroanatomic study. *Journal of the American College of Cardiology, 42*, 1271–1282.
7. Cappato, R., Calkins, H., Chen, S. A., Davies, W., Iesaka, Y., Kalman, J., et al. (2005). Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circulation, 111*, 1100–1105.
8. Pappone, C., Santinelli, V., Manguso, F., Vicedomini G., Gugliotta F., Augello G., et al. (2004). Pulmonary vein denervation enhances long-term benefit after circumferential ablation for paroxysmal atrial fibrillation. *Circulation, 109*, 327–334.
9. Nademanee, K., McKenzie, J., Kosar, E., Schwab, M., Sunsaneewitayakul, B., Vasavakul T., et al. (2004). A new approach for catheter ablation of atrial fibrillation: Mapping of the electrophysiologic substrate. *Journal of the American College of Cardiology, 43*, 2044–2053.
10. Cappato, R., Negroni, S., Pecora, D., Bentivegna, S., Lupo, P. P., Carolei, A., et al. (2003). Prospective assessment of late conduction recurrence across radiofrequency lesions producing electrical disconnection at the pulmonary vein ostium in patients with atrial fibrillation. *Circulation, 108*, 1599–1604.
11. Jais, P., Hocini, M., Hsu, L. F., Sanders, P., Scavee, C., Weerasooriya, R., et al. (2004). Technique and results of linear ablation at the mitral isthmus. *Circulation, 110*, 2966–3002.
12. Hocini, M., Jais, P., Sanders, P., Takahashi, Y., Rotter, M., Rostock, T., et al. (2005). Techniques, evaluation, and consequences of linear block at the left atrial roof in paroxysmal atrial fibrillation: A prospective randomized study. *Circulation, 112*, 3688–3696.
13. Sra, J., Krum, D., Malloy, A., Vass, M., Belanger, B., Soubelet, E., et al. (2005). Registration of three-dimensional left atrial computed tomographic images with projection images obtained using fluoroscopy. *Circulation, 112*, 3763–3768.
14. Ector, J., De Buck, S., Adams, J., Dymarkowski, S., Bogaert, J., Maes, F., et al. (2005). Cardiac three-dimensional magnetic resonance imaging and fluoroscopy merging: A new approach for electroanatomic mapping to assist catheter ablation. *Circulation, 112*, 3769–3776.