

# Atrial fibrillation

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## CATHETER ABLATION OF ATRIAL FIBRILLATION: TRIGGERS AND SUBSTRATE

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**Achieving and maintaining sinus rhythm in patients with atrial fibrillation (AF) is an attractive therapeutic goal. While antiarrhythmic therapy to maintain sinus rhythm has been demonstrated to be of limited efficacy, preliminary evidence suggests a beneficial effect of catheter ablation strategies to maintain sinus rhythm. The importance of the interaction between the triggers and substrate in the development of AF is well recognized. Catheter ablation strategies are centered on pulmonary vein ablation. However, it is becoming evident that most patients with chronic or persistent AF and 30-40% with paroxysmal AF will require additional substrate modification to improve the outcomes of AF ablation.**

### Background

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in humans, increasing with each decade of life to a prevalence of 5.9% in the population over 65 years of age. It results in an increased mortality and significant morbidity related to thromboembolic stroke, loss of atrial systole, and tachycardia-mediated atrial and ventricular cardiomyopathy<sup>1</sup>. Management strategies have been two tiered, either rate control coupled with anticoagulation or the restoration and maintenance of sinus rhythm.

Evidence from several studies demonstrates improvements in symptoms and left ventricular function with a strategy of rate

control by ablation and pacing. However, there are attractive theoretical benefits for a strategy aiming at the maintenance of sinus rhythm and cure of AF. Recent studies evaluating a pharmacological strategy to maintain sinus rhythm have suggested a limited efficacy and value, at least in older patients and those with persistent AF or structural heart disease<sup>2-4</sup>.

In contrast, emerging evidence suggests a clinical benefit of maintaining sinus rhythm with the cessation of antiarrhythmic agents using catheter ablation strategies. These benefits have been observed with a significant improvement of symptoms<sup>5</sup> and the prevention of sinus pauses on termination of AF<sup>6</sup>. In addition, a large series on AF ablation, although non-randomized, has suggested a survival benefit with the maintenance of sinus rhythm following ablation of AF<sup>5</sup>.

This review will focus on the current catheter-based mapping and ablation techniques targeting the triggers and substrate of AF to achieve the maintenance of sinus rhythm.

### Pulmonary vein ablation to eliminate the triggers of atrial fibrillation

While a number of sites within the atria have been reported to initiate AF, the pulmonary veins (PVs) are recognized as the dominant source of triggers initiating AF in many clinical situations<sup>7-10</sup>. Spontaneous activity arising from the PVs can manifest in a spectrum of atrial arrhythmias, isolated extrasystoles, slow atrial rhythms, and atrial tachycardia<sup>8</sup>. Rapid sustained focal discharges (sometimes for hours, days or longer) may drive sustained AF (true "focal" AF) but more commonly short bursts initiate AF in patients with the appropriate substrate<sup>8</sup>. PV triggers in patients with AF may occur from multiple PVs and also multiple foci within any given PV<sup>11</sup>. As such, the

catheter approach to PV ablation has progressively expanded to proximal (ostial) ablation with the aim of electrically isolating all PVs.

Circumferential mapping catheters have enabled the evaluation of the perimetric distribution and activation sequence of PV activity<sup>12</sup>. Such mapping has demonstrated that PV potentials reflecting local striated muscle were present over a variable extent (varying also from one vein to the next) of the perimeter and that PV muscle activation was often sequential from the segment with earliest activation. Ablation of the PVs guided by circumferential mapping is performed 1 cm from the ostium of both right PVs as well as for the posterior and superior aspects of the left PVs, to minimize the risk of PV stenosis. However, when ablation is required at the anterior portions of the left PVs, energy is delivered within the first millimeters of the PV (rather than the posterior wall of appendage) to achieve effective disconnection. Radiofrequency energy is delivered for 30 s at each point and this application is prolonged for 1-2 min when a change occurred in morphology or sequence of the PV potentials as determined by circumferential mapping. The procedural endpoint is the total disconnection or dissociation of the PV. Additional ostial applications to eliminate all ostial PV potentials, notably between the PVs and at their posterior wall, reduce the risk of recurrence due to ostial foci. While the use of a circumferential mapping catheter provides not only electrophysiological guidance but also an anatomic framework for PV ablation, several tools have evolved to further assist this process. These include electroanatomic mapping, intracardiac echocardiography, and various catheter localization systems (LocaLisa, NavX). Using any combination of these tools, PV electrical isolation is being performed within 1-2 hours in most experienced centers.

Reports of the immediate procedural success have ranged from 94 to 100%<sup>13,14</sup>. The long-term success rates for PV electrical isolation have been approximately 70% without antiarrhythmic agents, with Oral et al.<sup>15</sup> reporting an 85% success. Pappone et al.<sup>16</sup> have questioned the need for PV electrical isolation to achieve the clinical suppression of arrhythmia and have proposed an "anatomical approach", helped by the on-line examination of local potentials. However, recurrence of AF is frequently reported to occur in association with recovery of PV conduction<sup>17,18</sup>. In addition, a recent study evaluating a purely anatomic approach without the target of PV isolation has suggested that only 38% of patients remained arrhythmia-free without antiarrhythmic agents during follow-up<sup>19</sup>. Thus, while PV isolation may not be essential, it seems desirable in the ablation of AF.

The most concerning complication of these procedures is PV stenosis<sup>20</sup>. The current incidence of angiographic PV stenosis (> 50% reduction in venous diameter) is < 2% with most patients being asymptomatic. This incidence is reduced significantly with lower power ostial ablation and operator experience. Only 2 of over 1800 patients at our institution have required PV dilation and stenting.

## Ablation of the substrate for atrial fibrillation

In most patients with chronic AF and in 30-40% of patients with paroxysmal AF, PV isolation alone (without antiarrhythmic agents) is insufficient to maintain sinus rhythm<sup>13,17,21,22</sup>. Therefore, improved mapping techniques for non-PV foci or modification of the substrate itself are required to further improve the long-term outcome of catheter ablation in these patients. Emerging evidence in humans suggests that the substrate for AF may relate to diffuse atrial structural remodeling and its electrophysiological consequences<sup>23,24</sup>. In addition, surgically created linear compartmentalization of the atria (the Maze operation) is associated with the long-term suppression of AF<sup>25</sup>. As such, linear catheter ablation has been evaluated to modify the substrate for AF.

These studies have confirmed that while in a small subgroup of patients the dominant substrate for AF may be within the right atrium<sup>26</sup>, substrate modification is most effective when ablation is performed in the left atrium or both atria<sup>7,27-33</sup>. Furthermore, achieving complete linear conduction block was technically challenging with incomplete linear lesions being associated with the frequent development of left atrial macroreentry and recurrence of arrhythmia<sup>34</sup>. In addition, these procedures were associated with prolonged procedural and fluoroscopic durations that were prohibitive for a wider application.

Recently, more limited linear ablation is being evaluated to enhance the achievement of complete linear conduction block with reasonable procedural duration and fluoroscopic exposure. An initial strategy based firmly in experimental evidence was one of transecting the Bachmann's bundle. Such transection was achieved by linear ablation joining the two superior PVs and then joining this line to the anterior mitral annulus. While being technically challenging with linear conduction block being confirmed in only 58% of patients, such ablation was associated with the termination of AF during ablation in 60% of patients in AF. However, perhaps the most limiting factor of this procedure was the prolongation of the P wave duration associated with a characteristic change in the P wave morphology and the significant delay in lateral left atrial activation, at times occurring after ventricular contraction.

We have recently evaluated ablation of the mitral isthmus (left inferior PV to the lateral mitral annulus). This region is particularly attractive as target for substrate modification as it is short in length and its proximity to the coronary sinus allows optimal positioning of catheters to confirm linear conduction block. While being short, when combined with PV ablation it results in a contiguous line of conduction block that transects the posterior lateral left atrium (analogous to the conduction block created by cavotricuspid isthmus ablation being extended by the crista terminalis). Conduction block at the mitral isthmus can be achieved in 92% of cases with paroxysmal AF and was associated with 88% of

patients being arrhythmia-free without the use of antiarrhythmic agents at  $10 \pm 5$  months of follow-up. Importantly, there was no change in atrial activation as a result of mitral isthmus ablation during sinus rhythm. Preliminary data utilizing this procedure in patients with chronic AF suggest that at a follow-up of  $6 \pm 5$  months, 75% of patients remained in sinus rhythm.

## Conclusion

Recent studies have resulted in significant improvements in our understanding of AF and have led to catheter ablation techniques that have demonstrated the feasibility of achieving cure. Ablation limited to the PVs and mappable non-PV foci provides a success rate of approximately 70% in paroxysmal AF and much less in chronic AF. These results are further improved by additional substrate modification. While the maintenance of sinus rhythm without the use of antiarrhythmic drugs is likely to be achievable in many patients with relief of symptoms, further studies are required to confirm the long-term clinical benefit of such a strategy to allow the wider application of these techniques to patients with AF.

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## References

1. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation* 1998; 98: 946-52.
2. Hohnloser SH, Kuck KH, Lillenthal J. Rhythm or rate control in atrial fibrillation - pharmacological intervention in atrial fibrillation (PIAF): a randomised trial. *Lancet* 2000; 356: 1789-94.
3. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002; 347: 1825-33.
4. Van Gelder IC, Hagens VE, Bosker HA, Kingma JH. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *N Engl J Med* 2002; 347: 1834-40.
5. Pappone C, Rosanio S, Augello G, Gallus G. Mortality, morbidity, and quality of life after circumferential pulmonary vein ablation for atrial fibrillation: outcomes from a controlled nonrandomized long-term study. *J Am Coll Cardiol* 2003; 42: 185-97.
6. Hocini M, Sanders P, Deisenhofer I, Jais P. Reverse remodeling of sinus node function after catheter ablation of atrial fibrillation in patients with prolonged sinus pauses. *Circulation* 2003; 108: 1172-5.
7. Haissaguerre M, Jais P, Shah DC, Gencel L. Right and left atrial radiofrequency catheter therapy of paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol* 1996; 7: 1132-44.
8. Haissaguerre M, Jais P, Shah DC, Takahashi A. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998; 339: 659-66.
9. Jais P, Haissaguerre M, Shah DC, Chouairi S. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation* 1997; 95: 572-6.
10. Chen SA, Hsieh MH, Tai CT, Tsai CF. Initiation of atrial fibrillation by ectopic beats originating from the pulmonary veins: electrophysiological characteristics, pharmacological responses, and effects of radiofrequency ablation. *Circulation* 1999; 100: 1879-86.
11. Hocini M, Haissaguerre M, Shah D, Jais P. Multiple sources initiating atrial fibrillation from a single pulmonary vein identified by a circumferential catheter. *Pacing Clin Electrophysiol* 2000; 23: 1828-31.
12. Haissaguerre M, Shah DC, Jais P, Hocini M. Electrophysiological breakthroughs from the left atrium to the pulmonary veins. *Circulation* 2000; 102: 2463-5.
13. Oral H, Knight BP, Tada H, Ozaydin M. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. *Circulation* 2002; 105: 1077-81.
14. Macle L, Jais P, Weerasooriya R, Hocini M. Irrigated-tip catheter ablation of pulmonary veins for treatment of atrial fibrillation. *J Cardiovasc Electrophysiol* 2002; 13: 1067-73.
15. Oral H, Knight BP, Ozaydin M, Chugh A. Segmental ostial ablation to isolate the pulmonary veins during atrial fibrillation: feasibility and mechanistic insights. *Circulation* 2002; 106: 1256-62.
16. Pappone C, Rosanio S, Oreto G, Tocchi M. Circumferential radiofrequency ablation of pulmonary vein ostia: a new anatomic approach for curing atrial fibrillation. *Circulation* 2000; 102: 2619-28.
17. Kanagaratnam L, Tomassoni G, Schweikert R, Pavia S. Empirical pulmonary vein isolation in patients with chronic atrial fibrillation using a three-dimensional nonfluoroscopic mapping system: long-term follow-up. *Pacing Clin Electrophysiol* 2001; 24: 1774-9.
18. Cappato R, Negroni S, Pecora D, Bentivegna S. Prospective assessment of late conduction recurrence across radiofrequency lesions producing electrical disconnection at the pulmonary vein ostium in patients with atrial fibrillation. *Circulation* 2003; 108: 1599-604.
19. Stabile G, Turco P, La Rocca V, Nocerino P. Is pulmonary vein isolation necessary for curing atrial fibrillation? *Circulation* 2003; 108: 657-60.
20. Robbins IM, Colvin EV, Doyle TP, Kemp WE. Pulmonary vein stenosis after catheter ablation of atrial fibrillation. *Circulation* 1998; 9: 1769-75.
21. Haissaguerre M, Jais P, Shah DC, Arentz T. Catheter ablation of chronic atrial fibrillation targeting the reinitiating triggers. *J Cardiovasc Electrophysiol* 2000; 11: 2-10.
22. Oral H, Scharf C, Chugh A, Hall B. Catheter ablation for paroxysmal atrial fibrillation: segmental pulmonary vein ostial ablation versus left atrial ablation. *Circulation* 2003; 108: 2355-60.
23. Sanders P, Morton JB, Davidson NC, Spence SJ. Electrical remodeling of the atria in congestive heart failure. Electrophysiological and electroanatomic mapping in humans. *Circulation* 2003; 108: 1461-9.
24. Sanders P, Morton JB, Spence SJ, Kistler PM. Electrophysiologic and electroanatomic characterization of the atria in sinus node disease: evidence of diffuse atrial remodeling. *Circulation*, in press.

25. Cox JL, Ad N, Palazzo T, Fitzpatrick S. Current status of the Maze procedure for the treatment of atrial fibrillation. *Semin Thorac Cardiovasc Surg* 2000; 12: 15-9.
26. Liu TY, Tai CT, Chen SA. Treatment of atrial fibrillation by catheter ablation of conduction gaps in the crista terminalis and cavotricuspid isthmus of the right atrium. *J Cardiovasc Electrophysiol* 2002; 13: 1044-6.
27. Jais P, Shah DC, Takahashi A, Hocini M. Long-term follow-up after right atrial radiofrequency catheter treatment of paroxysmal atrial fibrillation. *Pacing Clin Electrophysiol* 1998; 21: 2533-8.
28. Gaita F, Riccardi R, Calo L, Scaglione M. Atrial mapping and radiofrequency catheter ablation in patients with idiopathic atrial fibrillation. Electrophysiological findings and ablation results. *Circulation* 1998; 97: 2136-45.
29. Garg A, Finneran W, Mollerus M, Birgersdotter-Green U. Right atrial compartmentalization using radiofrequency catheter ablation for management of patients with refractory atrial fibrillation. *J Cardiovasc Electrophysiol* 1999; 10: 763-71.
30. Ernst S, Schluter M, Ouyang F, Khanedani A. Modification of the substrate for maintenance of idiopathic human atrial fibrillation: efficacy of radiofrequency ablation using non-fluoroscopic catheter guidance. *Circulation* 1999; 100: 2085-92.
31. Jais P, Shah DC, Haissaguerre M, Takahashi A. Efficacy and safety of septal and left-atrial linear ablation for atrial fibrillation. *Am J Cardiol* 1999; 84: 139R-146R.
32. Pappone C, Oreto G, Lamberti F, Vicedomini G. Catheter ablation of paroxysmal atrial fibrillation using a three-dimensional mapping system. *Circulation* 1999; 100: 1203-8.
33. Packer DL. Linear ablation for atrial fibrillation: the pendulum swings back. In: Zipes DP, Haissaguerre M, eds. *Catheter ablation of atrial arrhythmias*. Armonk, NY: Futura Publishing Company, 2002: 107-28.
34. Ernst S, Ouyang F, Lober F, Antz M. Catheter-induced linear lesions in the left atrium in patients with atrial fibrillation: an electroanatomic study. *J Am Coll Cardiol* 2003; 42: 1271-82.