

# Prevention of Atrial Fibrillation: How Important is Transseptal Atrial Conduction in Humans?

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## Editorial Comment

The article by Betts et al.<sup>1</sup> in this issue of the *Journal* reports detailed high-density mapping of left atrial (LA) endocardial activation by a noncontact system performed during sinus rhythm and coronary sinus (CS) pacing in nine patients with paroxysmal atrial fibrillation (AF). They accurately describe areas of block in the posterior LA wall in close proximity to the pulmonary veins (PVs) during sinus rhythm and CS pacing. They suggest that these lines of block contribute to the substrate for reentrant arrhythmias, including AF or LA flutter. The site of earliest LA endocardial activation was on the superior interatrial septum, anterior to the ostium of the right upper PV in 5 patients, in the midposterior septum, anterior to the ostium of the right lower PV in 2 patients, and on the anterosuperior septum in 2 patients. A vertical line of conduction block running from the superior to inferior right PVs was seen during sinus rhythm and CS pacing in 5 of 9 patients. Their results are important, emphasizing the role of a "posterior" rather "anterior" (Bachmann's bundle) site of interatrial breakthrough that is the first site to show disorganized activity at AF onset. Conduction block or delay in the posterior LA may provide the additional component allowing triggers to induce reentrant wavelets that may degenerate into AF. The maps appear to be accurate. Using a non-contact mapping system with a 64-electrode array on a 9-French balloon catheter, thousands of points can be collected and detailed LA geometry can be acquired. The entire endocardial activation can be mapped continuously during every beat in sinus rhythm as well as during CS pacing. The main limitation of the study is the lack of a control group, as mapping was not performed in patients without a history of AF.

A better understanding of transseptal activation pattern and its role in a large population of AF patients may be important for treatment, but little is known about the prevalence and clinical significance of preferential routes of conduction from the LA to the right atrium in humans.<sup>2-6</sup> The position and orientation of interatrial connections appear to be speculative and essentially based on published anatomic studies. Knowledge of the anatomic and functional components of interatrial conduction has progressed dramatically. Increased knowledge of the sequence of LA activation and the way in which triggers interact with the LA to initiate AF will be useful in the evolution of treatment strategies aimed specifically at the initiating process.<sup>3</sup> These findings

also may have important implications regarding the choice of pacing sites for atrial resynchronization to suppress AF. Progressive knowledge of location and electrophysiologic properties of these connections has been derived particularly from electroanatomic studies using different complex mapping systems including the noncontact mapping or CARTO system.<sup>3,4</sup> Different patterns of transseptal activation have been reported during pacing from LA. Although preferential routes of conduction from the LA to the right atrium usually are related to the stimulation sites, recent studies have shown that left-to-right interatrial conduction occurs predominantly through Bachmann's bundle,<sup>7,8</sup> but this is not a universal finding.<sup>9,10</sup> Clearer understanding of normal and pathological atrial conduction may create new strategies for AF prevention. Attempts to control AF by nonpharmacologic means, such as pacing and ablation, formed the impetus to use complex mapping for delineating transseptal atrial conduction in both animals and humans. These studies found that endocardial activation is far more disorganized in the LA than in the right atrium. Therefore, an LA circuit may be primarily responsible for perpetuation of AF, whereas the right atrium is activated more passively. Several studies have addressed the role of a preferential site of transseptal conduction and its ablation in prevention of AF, but the exact location of this site in AF patients has not been established. Roithinger et al.<sup>4</sup> reported at least three sites of transseptal breakthrough: region of CS os, fossa ovalis, and high anterosseptal right atrium at the putative insertion of Bachmann's bundle. They reported that the CS is a preferential pathway for left-to-right atrial conduction primarily during CS pacing. In agreement with these findings, Cox et al.<sup>11</sup> emphasized the role of cryoablation around the CS, which may constitute a connection between the LA and right atrium, for success of the maze procedure. However, limited radiofrequency applications in the area of Bachmann's bundle or midseptum also have been reported to successfully terminate AF in animals. The bundle described by Bachmann<sup>12</sup> in 1916 runs on top of the atria, eventually joining the sinus node and the LA. Through its privileged location, close to the sinus node, and its connection to the anterior internodal bundle, Bachmann's bundle is classically the preferential conduction pathway from the right atrium to the LA. However, several distinct sites of transseptal interatrial connections have been reported in the region of Koch's triangle, with left posterior extensions of the AV node, at the septal level, and at the CS level with connections between the CS muscle cover and the LA. Using a noncontact mapping system, Markides et al.<sup>3</sup> recently showed that posterior interatrial connections may be the preferential conduction pathway to the LA. Nevertheless, the LA activation pattern appears to depend on a principal line of functional conduction block that is linked to the preferential orientation of the LA subendocardial fibers. These fibers run down from the top of the LA and travel between the PV ostia before

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turning septally to reach the mitral annulus in its anterior and septal part. Betts et al.<sup>13</sup> reported prior experimental data on 13 anesthetized swine, showing that successful electrical disconnection of the atria reduces AF inducibility. The authors suggested that this approach is worthy of further evaluation as a management strategy for persistent AF, combined with device therapies. We believe that further large-scale studies are needed to assess the number and electrophysiologic characteristics of interatrial connections in patients with and without AF and their relevance for AF maintenance. Differences between the left-to-right interatrial electrical connections may exist between patients with persistent AF, paroxysmal AF, and patients without AF. Whether the preliminary observations obtained in a small series of patients have major implications for a catheter-based cure of AF and result in additional benefit in preventing AF remains unanswered. In contrast, it is conceivable that long linear lesions create new fixed obstacles to propagation, with eventual discontinuities representing an ideal substrate for large gap-related reentrant circuits. If interruption of any preferential electrical connection between the LA and right atrium by additional ablation lines results in incomplete lesions, incessant proarrhythmias likely will occur in these patients, as recently reported.<sup>14</sup>

In conclusion, the LA endocardium appears to have multiple complex patterns of activation from the right-to-the left and/or from the left-to-the right atrium during sinus rhythm and pacing. The connections may promote interatrial macroreentry, which could have an important role in AF maintenance. In patients undergoing the circumferential PV approach, the success rate in curing both paroxysmal and permanent AF is approximately 85% at a mean of 900 days after ablation.<sup>15</sup> In patients with paroxysmal AF, vagal denervation can result in about 100% success.<sup>16</sup> We postulated that one mechanism of the circumferential PV approach is ablation of right-to-left or left-to-right connections that may play a role in AF generation. Therefore, the observations reported in the study by Betts et al.<sup>1</sup> are important, suggesting that elimination of interatrial communications by catheter ablation results in cure of AF.

### References

1. Betts TR, Roberts PR, Morgan JM: High-density mapping of left atrial endocardial activation during sinus rhythm and coronary sinus pacing in patients with paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol* 2004;15:1111-1117.
2. Platonov PG, Mitrofanova LB, Chireikin LV, Olsson SB: Morphology of inter-atrial conduction routes in patients with atrial fibrillation. *Europace* 2002;4:183-192.
3. Markides V, Schilling RJ, Ho SY, Chow AWC, Davies DW, Peters NS: Characterization of left atrial activation in the intact human heart. *Circulation* 2003;107:733-739.
4. Roithinger FX, Cheng J, SippensGroenewegen A, Lee RJ, Saxon LA, Scheinman M, Lesh MD: Use of electroanatomic mapping to delineate transseptal atrial conduction in humans. *Circulation* 1999;100:1791-1797.
5. Schilling RJ, Kadish AH, Peters NS, Goldberger J, Davies DW: Endocardial mapping of atrial fibrillation in the human right atrium using a non-contact catheter. *Eur Heart J* 2000;21:550-564.
6. Scheinman MM, Yang Y: Electroanatomic analysis of sinus impulse propagation in normal human atria. *J Cardiovasc Electrophysiol* 2002;13:11-12.
7. Waldo AL, Maclean AH, Karp RB, Kouchoukos NT, James TN: Sequence of retrograde atrial activation of the human heart: correlation with P wave polarity. *Br Heart J* 1977;39:634-640.
8. Cox JL, Canavan TE, Schuessler RB, Cain ME, Lindsay BD, Stone C, Smith PK, Corr PB, Boineau JP: The surgical treatment of atrial fibrillation. II. Intraoperative electrophysiologic mapping and description of the electrophysiologic basis of atrial flutter and atrial fibrillation. *J Thorac Cardiovasc Surg* 1991;101:406-426.
9. Waldo AL, Vitikainen KJ, Hoffman BF: The sequence of retrograde atrial activation in the canine heart: Correlation with positive and negative retrograde P waves. *Circ Res* 1975;37:156-163.
10. Boineau JP, Canavan TE, Schuessler RB, Cain ME, Corr PB, Cox JL: Demonstration of a widely distributed atrial pacemaker complex in the human heart. *Circulation* 1988;77:1221-1237.
11. Cox JL, Schuessler RB, D'Agostino JD Jr, Stone CM, Chang BC, Cain ME, Corr PB, Boineau JP: The surgical treatment of atrial fibrillation, III: Development of a definitive surgical procedure. *J Thorac Cardiovasc Surg* 1991;101:569-583.
12. Bachmann G: The inter-auricular time interval. *Am J Physiol* 1916;41:309-320.
13. Betts TR, Roberts PR, Morgan JM: Feasibility of a left atrial disconnection procedure for atrial fibrillation using transcatheter radiofrequency ablation. *J Cardiovasc Electrophysiol* 2001;12:1278-1283.
14. Ernst S, Ouyang F, Lober F, Antz M, Kuck KH: Catheter-induced linear lesions in the left atrium in patients with atrial fibrillation: An electroanatomic study. *J Am Coll Cardiol* 2003;42:1271-1282.
15. Pappone C, Rosanio S, Augello G, Gallus G, Vicedomini G, Mazzone P, Gulletta S, Gugliotta F, Pappone A, Santinelli V, Tortorello V, Sala S, Zangrillo A, Crescenzi G, Benussi S, Alfieri O: 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;42:185-197.
16. Pappone C, Santinelli V, Manguso F, Vicedomini G, Gugliotta F, Augello G, Mazzone P, Tortorello V, Landoni G, Zangrillo A, Lang C, Tomita T, Mesas C, Mastella E, Alfieri O: Pulmonary vein denervation enhances long-term benefit after circumferential ablation for paroxysmal atrial fibrillation. *Circulation* 2004;109:327-334.