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EDITORIAL COMMENT

Highest Dominant Frequencies in Atrial Fibrillation

A New Target for Ablation?*

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Until recently, the most widely accepted mechanism of atrial fibrillation (AF) was the “multiple wavelet” hypothesis as described by Moe and Abildskov (1) in 1959. The discovery by Haissaguerre et al. (2) in 1998 that focal ablation could eliminate paroxysmal AF in selected patients represented a major therapeutic advance. A more important consequence of that discovery was the revival of the concept that AF could result from a rapidly firing focus. This theory was described in 1925 by Sir Thomas Lewis (3), who observed that “. . . fibrillation, like flutter, may also on occasion be terminated in the auricle by cold or pressure very locally applied.” Additional support for this alternative view came later from Scherf et al. (4,5), who used local application of

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aconitine to induce AF and then demonstrated that obliteration of the site of aconitine application resulted in the termination of AF. This concept initially was not accepted by electrophysiologists, perhaps because of the limited investigative methodologies available at that time, which prevented exhaustive characterization of electrical wave propagation. With the development of high-resolution mapping techniques such as optical mapping, this task became achievable. A series of studies from the laboratory of Jalife et al. (6–10) described vortex-like re-entry (rotors) around minuscule cores, with high-frequency periodic activity in the posterior left atrium and the pulmonary vein ostia. Rapid and successive electrical impulses emanating from these rotors propagate throughout the atria and interact with functional and/or anatomical obstacles, leading to fragmentation and wavelets formation. This “fibrillatory conduction” results in the seemingly random electrical activity that characterizes AF.

The report by Lin et al. (11) in this issue of the *Journal* describes frequency gradients in different types of paroxysmal AF. The concept of frequency gradient has been reported previously. A left-to-right gradient was first demonstrated in animal models of acute AF (9). A more recent

study demonstrated the presence of a left-to-right frequency gradient in patients with paroxysmal AF (12). However, the important and novel finding in the report by Lin et al. (11) is that the highest dominant frequency is not always in the left atrium but shifts to the right atrium when AF is initiated in the superior vena cava. This discovery represents yet another strong validation for mother rotors and fibrillatory conduction as a mechanism of atrial fibrillation. The rotors initiating and maintaining AF operate at a very high frequency. The rest of the atria cannot follow in a 1:1 fashion and interatrial and intraatrial conduction block results in reduction of the frequency in areas far from the site of AF origin.

A rapidly firing focus with fibrillatory conduction and a resulting frequency gradient clearly seems to be the underlying mechanism of AF in some patients. Important unanswered questions include whether or not this mechanism explains AF in all patients and, more specifically, whether this mechanism underlies both paroxysmal and permanent AF. In addition, it remains to be determined whether AF in humans can be consistently eliminated by ablation of areas of highest dominant frequencies. Thus far, the existing evidence from human and animal studies supports the role of a rapidly firing focus in AF. One animal study in dogs with chronic AF demonstrated that local ablation of areas of shortest cycle length in the posterior left atrium caused termination of the arrhythmia (13). A recent study by Sanders et al. (14) reported that ablation of sites of high dominant frequencies resulted in prolongation of AF cycle length and termination of this arrhythmia in a large percentage of patients. The lower success rate of pulmonary vein isolation in patients with persistent or permanent AF compared with paroxysmal AF does not refute the concept of rapidly firing foci and fibrillatory conduction as a mechanism of AF. The lower success rate in this group of patients may be explained by the fact that these patients often have left atrial disease, resulting in electrophysiological and anatomic heterogeneity, which enables the formation of stable rotors in areas outside the pulmonary veins, such as the posterior, inferior, and septal parts of the left atrium, which could drive AF. In this situation, one would expect that frequency gradients would be less prominent because of the increased numbers of rotors. The presence of foci of rapid electrical activity in areas outside the pulmonary veins also may explain the increased success rate with ablation strategies using large left atrial encirclement lesions of the pulmonary veins (15–17), as well as ablation of areas of rapid fractionated electrograms (18). These lesions sets may encompass areas in the atria that could harbor rapidly firing foci.

Atrial fibrillation increasingly is being recognized as a deterministic process resulting from rapidly firing foci and fibrillatory conduction rather than a fundamentally turbulent and self-sustaining process. More studies are needed to confirm the role of high-frequency areas in driving and sustaining AF. In addition, the development of newer

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technologies incorporating methods of frequency analysis, such as the fast Fourier transform, to guide rapid identification and catheter ablation of high-frequency sites will be of utmost importance in furthering the exploration of the dominant frequency hypothesis.

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