Complex Fractionated Atrial Electrograms
A Worthwhile Target for Ablation of Atrial Fibrillation?

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Since its inception in the 1990s, catheter ablation of atrial fibrillation (AF) has been a continuously evolving procedure. Ablation strategies have adapted to advances in technology including new catheter designs, innovations in mapping systems, and alternative energy sources. Moreover, catheter ablation has stimulated and responded to an improved understanding of the mechanisms of initiation and perpetuation of AF. Over the past 15 years, many centers have spent considerable effort in defining optimal ablation strategies for elimination of paroxysmal and nonparoxysmal AF.

The pulmonary veins were recognized early by Haissaguerre et al.1,2 as a frequent source of triggers for AF. Pulmonary vein isolation quickly became the cornerstone of catheter ablation of AF and sparked its rise as a promising tool to eliminate symptomatic and drug-refractory AF.3,4 This was first performed by ostial ablation, but, because of the risk of pulmonary vein stenosis and recognition of vital antral drivers, an antral pulmonary vein isolation (APVI) strategy evolved.3,5 Adjuvants to APVI have been proposed, including ablation of complex fractionated atrial electrograms (CFAE). Initial experience suggested that CFAE ablation is a viable stand-alone strategy,6 but this experience has not been reproducible.7,8 The more frequent use of CFAE-guided ablation is as adjuvant therapy to APVI, particularly in nonparoxysmal AF.

In this issue of Circulation: Arrhythmia and Electrophysiology, Li et al9 provide a meta-analysis highlighting the impact of ablation of CFAEs in addition to APVI for improved maintenance of sinus rhythm in patients with nonparoxysmal AF. This benefit was not realized in patients with paroxysmal AF. The lack of incremental value of CFAE ablation in patients with paroxysmal AF is consistent with the primary role of the pulmonary veins in triggering and maintaining episodes of AF, such that APVI typically is sufficient therapy. In contrast, APVI by itself usually is insufficient for persistent AF because of mechanisms of AF within the atrial substrate.

The emergence of CFAE ablation as an adjuvant ablation strategy is due at least in part to its ease of usage. Potential target sites can be identified rapidly by visual inspection or with automated software incorporated into electroanatomic mapping systems. The response to ablation can be immediately verified through signal abatement or defractionation.

To fully evaluate the effect of CFAE ablation on atrial substrate, we must explore its definition and the etiology of fractionated signals and recognize some limitations inherent to CFAE-guided ablation. As recognized by Li et al, variable criteria have been used to identify CFAEs. Among the definitions of CFAEs are continuous atrial electrogram activity, complex fractionated potentials, or simply atrial electrograms with short mean cycle lengths.6,10 Although the different criteria ultimately may result in targeting similar regions, the variation in definitions can make it difficult to compare results across studies and to interpret the pathophysiologic significance of CFAEs. CFAEs are believed to indicate areas of conduction slowing or block, anchor points for continuous reentry, locations bordering high-frequency sites where fibrillatory conduction and wave break occur, overlap of multiple activation waves, or sites of autonomic innervation.6,11–13 Although ablation of CFAEs has shown clinical efficacy, CFAEs are a nonspecific marker of important target sites because they can be generated by passive mechanisms that play no role in the maintenance of AF. This can lead to extensive ablation of noncritical areas, long procedure times, an increased risk of collateral damage, and more fluoroscopy exposure. Because of this limitation, the quest for more efficient methods to identify the critical AF substrate is ongoing.

Among the alternative ablation strategies being studied are ablation of ganglionated plexi, linear ablation, and ablation of sites with high dominant frequency (DF). Proponents of the DF approach argue that this is more specific than CFAEs at identifying the critical atrial substrate. Jalife et al.11,14 have demonstrated that high DF sites correlate with anchor points of high-frequency rotors believed to be pivotal in the maintenance of AF. These sites typically show rapid periodicity but lack significant fractionation. Sites of wave break adjacent to areas of maximal periodicity often display the greatest fractionation, and targeting these sites of fractionation may produce obstacles to propagation of the high-frequency sources.11 This provides a possible explanation for the clinical efficacy of CFAE ablation. Although targeting sites of high DF may be useful, it is currently limited by several factors including constraints in high-resolution mapping to accurately identify locations of high DF. Also, rapid and accurate real-time analysis is not yet universally available. Furthermore, the temporal stability of high DF sites has been challenged. However, if these and other issues are addressed, ablation guided by DF analysis may become a practical option.
At this juncture, ablation of CFAEs as adjunctive therapy to APVI offers a readily available and practical strategy to improve success in ablation of nonparoxysmal AF. The reasons for its efficacy have been debated and despite its lack of specificity, meaningful alterations to atrial substrate do result. Proposed explanations have included elimination of sites of AF wavelet reentry, containment of high-frequency sources, alterations in autonomic input into the atria, or simply debulking of the atrial substrate.\(^6,11,13,15,16\) The lack of specificity of CFAEs does remain a concern. Furthermore, there is a considerable failure rate to achieve sinus rhythm. This may be partly due to deficiencies in current techniques to identify CFAEs, our inability to adequately ablate this substrate, or inherent limitations in CFAE analysis to unveil all areas critical for AF maintenance. The likely explanation is a combination of all three. We look forward to refinements in the identification of critical CFAEs and the development of new ablation tools that are more efficient than conventional catheters used for point-by-point ablation.

**Disclosures**

Dr Morady is a consultant for Medtronic and in the past 12 months has received lecture honoraria from Boston Scientific, St Jude, and Biotronik.

**References**


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