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Clinical Benefit of Ablating Localized Sources for Human Atrial Fibrillation

The Indiana University FIRM Registry

John M. Miller, MD, Vikas Kalra, MD, Mithilesh K. Das, MD, Rahul Jain, MD, MPH, Jason B. Garlie, MD, Jordan A. Brewster, MD, Gopi Dandamudi, MD

ABSTRACT

BACKGROUND Mounting evidence shows that localized sources maintain atrial fibrillation (AF). However, it is unclear in unselected "real-world" patients if sources drive persistent atrial fibrillation (PeAF), long-standing persistent atrial fibrillation (LPeAF), or paroxysmal atrial fibrillation (PAF); if right atrial sites are important; and what the long-term success of source ablation is.

OBJECTIVES The aim of this study was to analyze the role of rotors and focal sources in a large academic registry of consecutive patients undergoing source mapping for AF.

METHODS One hundred seventy consecutive patients (mean age 59 ± 12 years, 79% men) with PAF (37%), PeAF (31%), or LPeAF (32%). Of these, 73 (43%) had undergone at least 1 prior ablation attempt (mean 1.9 ± 0.8; range: 1 to 4). Focal impulse and rotor modulation (FIRM) with an endocardial basket catheter was used in all cases.

RESULTS FIRM analysis revealed sources in the right atrium in 85% of patients (1.8 ± 1.3) and in the left atrium in 90% of patients (2.0 ± 1.3). FIRM ablation terminated AF to sinus rhythm or atrial flutter or tachycardia in 59% (PAF), 37% (PeAF), and 19% (LPeAF) of patients, with 15 of 67 terminations due to right atrial ablation. On follow-up, freedom from AF after a single FIRM procedure for the entire series was 95% (PAF), 83% (PeAF), and 82% (LPeAF) at 1 year and freedom from all atrial arrhythmias was 77% (PAF), 75% (PeAF), and 57% (LPeAF).

CONCLUSIONS In the Indiana University FIRM registry, FIRM-guided ablation produced high single-procedure success, mostly in patients with nonparoxysmal AF. Data from mapping, acute terminations, and outcomes strongly support the mechanistic role of biatrial rotors and focal sources in maintaining AF in diverse populations. Randomized trials of FIRM-guided ablation and mechanistic studies to determine how rotors form, progress, and regress are needed.
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Atrial fibrillation (AF) is the most common sustained arrhythmia (1), for which mechanistic uncertainty continues. Although the pandemic of AF is likely related to obesity and other comorbidities (1,2), it is unclear how they contribute to AF or how to reverse their effects (1). Because drug therapy for rate or rhythm control has modest success, ablation is increasingly used for symptom relief (3). However, even with current technology, the single-procedure success rate at 1 year for paroxysmal AF (PAF) is approximately 60% (4,5), and this rate is lower for persistent AF (PeAF) (6), results that are not improved by the ablation of complex fractionated electrograms or empirical linear ablation (6,7).

Mounting evidence suggests that localized rotational circuits (rotors) or focal sources comprise the electric substrate for AF; 1 strategy of identifying and treating these is focal impulse and rotor modulation (FIRM). Optical mapping, the gold standard for mapping AF (8), has recently been applied to atria from

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From the Krannert Institute of Cardiology, Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana.
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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

FIRM = focal impulse and rotor modulation

IQR = interquartile range

LA = left atrial

LPeAF = long-standing persistent atrial fibrillation

PAF = paroxysmal atrial fibrillation

PeAF = persistent atrial fibrillation

PVI = pulmonary vein isolation

RA = right atrial

RF = radiofrequency

patients with clinical AF (9). This has shown that AF is driven by stable endocardial micro-re-entrant sources where targeted ablation terminated AF (9), with transient epicardial breakthroughs or partial re-entry. These results are similar to recent clinical reports of AF sources (10) and also reconcile less stable sources seen by epicardial mapping (11). However, rotors (12) and sources (13) are not found by classical mapping, possibly because of limitations of marking electrograms in AF (14) and/or other technical limitations (15).

The aim of the IU-FIRM (Indiana University FIRM) registry was to: 1) determine if rotors and focal sources are common in a large real-world population of unselected patients with PeAF, long-standing PeAF (LPeAF), or PAF; 2) discover whether intervention at sources supports their mechanistic role across AF phenotypes; and 3) establish the "real-world" clinical outcomes of rotor- and source-based ablation.

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METHODS

STUDY DESIGN. We studied 170 consecutive patients referred to Indiana University/Methodist Hospital from January 2012 to October 2015 for ablation of symptomatic AF for standard indications (3). Subjects were ≥18 years of age, with AF despite ≥1 antiarrhythmic drug. Patients were excluded if they were unable or refused to provide written informed consent or did not have sustained AF (>5 min) during the procedure. The population included patients with PAF, PeAF, or LPeAF by standard definitions (3). This was the first ablation procedure for most patients, although 73 (43%) had undergone at least 1 prior ablation procedure. **Table 1** summarizes patient characteristics.

Each patient underwent AF mapping using a multipolar catheter inserted sequentially into both atria as previously described, followed by computational methods to interpret electrograms using repolarization and conduction dynamics to reveal sources (16). Ablation targeted the identified sources in each patient. One hundred sixty-one patients (95%) also underwent pulmonary vein isolation (PVI); the remaining 9 patients prospectively declined this. Follow-up with event and/or ambulatory monitoring or implantable device interrogation in 151 patients (89%) was used to determine clinical efficacy and establish the mechanistic impact of interventions targeting these defined mechanisms.

ELECTROPHYSIOLOGIC STUDY. Electrophysiologic study was performed after discontinuing antiarrhythmic medications for 5 half-lives (2 to 6 weeks in patients on amiodarone). Electrode catheters were advanced to the coronary sinus and right atrium and then transseptally to the left atrium. A 64-pole basket catheter (Constellation, Boston Scientific, Natick, Massachusetts [n = 44]; or FIRMap, Abbott Electrophysiology, Menlo Park, California [n = 126]) was advanced through an 8.5-F sheath to map AF in both atria in sequence. Basket sizes were selected to approximate the left atrial (LA) size on pre-procedural computed tomography or acquired electroanatomic mapping atrial "shell," then positioned to optimize fluoroscopic coverage and electrogram signals (**Figure 1**). Generally, baskets sized to fit the left atrium tended to map the right atrium well.

Digital electroanatomic atrial shells were created using Carto (Biosense Webster, Diamond Bar, California). Intravenous heparin was administered as a bolus after femoral access, followed by infusion to achieve activated clotting times >350 s. Unipolar atrial electrograms from the basket catheter were filtered at 0.05 to 500 Hz and recorded at a 1-kHz sampling frequency for export from the electrophysiological recording system (Bard/Boston Scientific, Lowell, Massachusetts).

AF was the presenting rhythm in 96 patients (57%), atrial flutter in 11 (6%), and sinus rhythm in 63 (37%). In patients presenting in sinus rhythm or in whom presenting AF or atrial flutter was terminated by ablation, AF induction was attempted using rapid pacing with or without isoproterenol (5 to 15 μg/min) or epinephrine (0.05 to 0.2 μg/kg/min) as needed.

MAPPING AF SOURCES. FIRM mapping has been described elsewhere (10). Briefly, unipolar AF electrograms recorded using basket catheters are processed using algorithms to determine propagation sequences. When deflections are monophasic or noncomplex, mapping can identify rotational or focal activations as previously illustrated (10). In cases in which AF deflections are multiphasic, the use of classical rules such as dV/dt may mark deflections within repolarization (far-field) (14). In such cases, FIRM assigns local activation on the basis of physiological information, such as action potential duration restitution (17) to account for changes in refractoriness with changes in cycle length during AF, and then applies phase analysis to identify rotors. The system (RhythmView, Abbott Electrophysiology, Menlo Park, California) then generates AF propagation maps, which are subsequently correlated to corresponding basket electrode locations within the chamber.

AF propagation (FIRM) maps were analyzed in near real time for FIRM-guided ablation at sources. Electric rotors (**Figure 2D**) were defined as rotational activation around a phase-mapped singularity that