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Targeted Ablation at Stable Atrial Fibrillation Sources Improves Success Over Conventional Ablation In High Risk Patients A Substudy of the CONFIRM Trial

Tina Baykaner, MD, **Paul Clopton, MS**, **Gautam G. Lalani, MD**, **Amir A. Schricker, MD**, **David E. Krummen, MD**, and **Sanjiv M Narayan, MD, PhD FRCP On Behalf of the CONFIRM Investigators**
University of California and Veterans' Affairs Medical Centers, San Diego, California

Abstract

Background—Pulmonary vein (PV) isolation has disappointing results in patients with obesity, heart failure, obstructive sleep apnea (OSA) and enlarged left atria (LA), for unclear reasons. We hypothesized that these comorbidities cause higher numbers or non-PV locations of AF sources, where targeted source ablation (Focal Impulse and Rotor Modulation, FIRM) should improve the single-procedure success of ablation.

Methods—The CONFIRM trial prospectively enrolled 92 patients at 107 AF ablation procedures, in whom computational mapping identified AF rotors or focal sources. Patients underwent FIRM plus conventional ablation (FIRM-guided), or conventional ablation only, and were evaluated for recurrent AF quarterly with rigorous, often implanted, monitoring. We report the n=73 patients undergoing first ablation in whom demographic information was available (n= 52 conventional, n=21 FIRM-guided).

Results—Stable sources for AF were found in 97.1% of patients. The numbers of concurrent sources per patient (2.1±1.1) rose with LA diameter (p=0.021), lower LV ejection fraction (p=0.039), and the presence of obstructive sleep apnea (OSA, p=0.002) or hypomagnesemia (p=0.017). Right atrial sources were associated with obesity (BMI≥30 kg/m^2, p=0.015). In patients with obesity, hypertension, OSA and LA diameter > 40 mm, single-procedure freedom from AF was >80% by FIRM-guided versus <50% by conventional ablation (all; p<0.05).

Conclusion—Patients with 'difficult to treat' AF exhibit more concurrent AF sources in more widespread biatrial distributions than other patients. These mechanisms explain the disappointing

Correspondence: Sanjiv M. Narayan, MD PhD, Cardiology/111A, 3350 La Jolla Village Drive, San Diego, CA 92161 *Voice*: 858/642-1108 *Fax*: 858/552-7490, snarayan@ucsd.edu.

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results of PV isolation, and how FIRM can identify patient-specific AF sources to enable successful ablation in this population.

Keywords

Atrium; Fibrillation; Rotors; FIRM ablation; Metabolic syndrome; Sleep apnea; Clinical Trials

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The success of ablation for atrial fibrillation (AF), that conventionally targets triggers in the pulmonary veins (PV), is reduced in patients with specific comorbidities. In particular, the multi-procedure success rate from PV-isolation based AF ablation may be as low as 41% in patients with obstructive sleep apnea (OSA)[1], 73% in patients with systolic heart failure[2] and 61% in patients with metabolic syndrome[3], in whom success falls as body mass index (BMI) rises [4]. However, these disappointing results are mechanistically unexplained.

It has recently been shown that human AF may be caused by stable sources, in the form of localized spiral waves (rotors) or focal sources similar to those shown in elegant animal models[5, 6, 7]. The CONFIRM trial (CONventional ablation of AF with or without Focal Impulse and Rotor Modulation, FIRM) [8] recently showed stable sources in 97% of patients with paroxysmal and persistent AF, and is now validated in several laboratories[9, 10]. In CONFIRM, a single targeted source (FIRM) plus conventional ablation procedure increased single-procedure AF freedom to 82.4% on rigorous monitoring from 44.9% for conventional ablation alone. A recent on-treatment analysis showed that AF ablation success is highest when all sources are eliminated, either directly by FIRM or ‘coincidentally’ by PVI, intermediate if some sources are eliminated and lowest if all are missed[11].

We hypothesized that AF in patients with high-risk demographics results from higher numbers of AF sources lying remote from the PVs, that are less easily ablated coincidentally. Accordingly, we hypothesized that FIRM may improve the success of conventional ablation even in ‘difficult-to-treat’ patients. We tested our hypothesis by studying the impact of pre-specified high-risk demographics on AF rotors and focal sources, and on long-term success after FIRM-guided versus conventional ablation, in the CONFIRM trial.

METHODS

Study Design and Enrollment

CONFIRM [8] prospectively enrolled 92 subjects at 107 consecutive AF ablation procedures for standard indications. Procedures were performed by 3 investigators at 3 sites. Subjects were ≥21 years of age, with AF despite one or more class I or III anti-arrhythmic drugs. Cases were prospectively assigned 2:1 to FIRM-blinded or FIRM-guided ablation. FIRM-Guided patients were treated with targeted source ablation (FIRM) followed by conventional ablation; FIRM-blinded patients received only conventional ablation. The only exclusion was an inability or refusal to provide specific written informed consent. This report includes the n=73 patients in whom demographic information was available at their first ablation procedure for paroxysmal or persistent AF [12].

Electrophysiology Study

Electrophysiology study was performed after discontinuing anti-arrhythmic medications for 5 half lives (for amiodarone, >60 days, median 230 days). After infusing intravenous heparin to maintain activated clotting time>350 seconds, a 64-pole basket catheter (Constellation™, Boston Scientific, MA) was advanced trans-septally to map the left atrium (LA) in all patients, and also to the right atrium (RA) in n=45 patients (including all FIRM-guided cases).

Figure 1 shows biatrial baskets. AF was observed in 69 patients (including all FIRM-guided cases) including AF induced by rapid pacing or isoproterenol when required [8]. Recent studies show that induced and spontaneous AF in the same patient show very similar dominant frequency [13] and spatial patterns [14]. AF electrograms were filtered at 0.05 – 500 Hz and exported at 1kHz temporal resolution (Bard LabPro, MA).

FIRM Mapping of AF Sources

FIRM mapping has been described elsewhere [8, 14]. Briefly, AF was recorded at wide field-of-view baskets for analysis with a novel mapping system (RhythmView™, Topera, Palo Alto, California) that projects these 3 dimensional data onto grids of AF propagation. Figure 2 shows FIRM maps of AF rotors (each indicated by a red-to-blue, early-to-late spiral wave).

AF propagation (FIRM) maps were analyzed intra-procedurally to guide ablation in FIRM-Guided patients, and post-procedurally in FIRM-blinded patients. **Electrical rotors** (figure 2) were defined as sustained activation around a core, while **focal impulses** showed centrifugal activation from an origin. Rotors and focal impulses were considered mechanistic **AF sources** only if stable on repeated sampling over >30 minutes (i.e. thousands of cycles), unlike transient fibrillatory activity [15, 16].

Analysis of AF Source in Relation to Clinical Demographics

We related the numbers of AF sources to clinical variables in univariate and multivariate analyses. Being overweight was defined as 25≤BMI<30, obesity as 30≤BMI<40 and morbid obesity as BMI≥40 (in kg/m^2). CKD stages were calculated from estimated glomerular filtration rate (GFR) as stated in the U.S. National Kidney Foundation guidelines [17]. Systolic heart failure was defined as left ventricular ejection fraction ≤ 40%. LA enlargement was defined as diameter ≥ 40mm from the anteroposterior diameter on 2D transthoracic echocardiography. The presence of hypertension (HTN), diabetes mellitus (DM), OSA and other comorbidities were identified from each patient's electronic medical record.

Ablation Approach

Radiofrequency energy was delivered with a 3.5 mm tip irrigated (Thermocool, Biosense-Webster, Diamond Bar, CA) or, in heart failure subjects, 8 mm tip (Blazer, Boston Scientific, Natick, MA) catheter. In FIRM-guided subjects, FIRM was performed first via lesions to cover the AF source (rotational center of rotors, or focal source origin [8]). The endpoint was AF termination or 10 minutes' ablation (typically <5 minutes), whichever came first. If AF terminated, vigorous attempts were made to reinitiate AF. Patients in whom AF terminated but could be reinduced were labeled as 'AF slowing'. FIRM was repeated for ≤ 3 sources (≤30 minutes permitted[8]), followed by conventional ablation.

Conventional ablation [12] , performed after FIRM in FIRM-guided patients and as sole therapy in FIRM-blinded patients, was standardized to comprise wide area isolation of left and right PV pairs verified with a circular mapping catheter (Lasso, Biosense-Webster). In persistent AF, a LA roof line was also performed. Atrial tachycardia or flutter were ablated appropriately. No other ablation was performed. If AF persisted after completion of the ablation protocol, cardioversion was performed.

Post-Procedure Clinical Management

Follow up for arrhythmia recurrence met or exceeded guidelines [12]. Anti-arrhythmic medications (but not amiodarone) were continued for 3 months post-ablation, but repeat ablation was not permitted in this 'blanking period'. Subjects were evaluated quarterly for

recurrences using continuous implanted ECG monitors if possible, i.e. Reveal XT™ (Medtronic, Minneapolis, MN) once clinically available in 2009 (figure 1), or indicated pacemaker/ defibrillators. Remaining subjects received external event monitors quarterly and at times of symptoms.

Study Endpoints

The primary long-term efficacy endpoint was freedom from AF after one procedure, defined as <1% burden on continuous implanted ECG monitors (365 days/year monitoring; actual burden 0.1±0.2% in CONFIRM [8]), or <30 seconds on intermittent monitors [12] (<28 days/ year monitoring). Secondary efficacy measures included freedom from all atrial arrhythmias[8].

Statistical Analysis

Continuous data are represented as mean ± standard deviation (SD) or median and interquartile range (IQR) as appropriate. Normality was evaluated using the Kolmogorov-Smirnov test. Comparisons between 2 groups were made with Student's t-tests and summarized with means and standard deviations for independent samples if normally distributed (e.g. age, LA diameter) or, if not normally distributed, with the Mann-Whitney U test and summarized with medians and quartiles. Nominal values are expressed as n (%) and compared with chi-square tests (e.g. numbers with obesity) or the Fisher exact test when expected cell frequency was<5 (e.g. numbers with kidney disease). Associations between continuous variables were evaluated with Pearson's correlation. The comparison between two dependent correlations (e.g. rotors vs focal sources) was tested by equality of two dependent correlations [18]. The specific tests used for each comparison are indicated in the Results section. Long-term outcome was assessed and reported after a single procedure, and raw event rates were compared with chi-square tests and event-free survival plots were made by the Kaplan-Meier method and compared with log-rank tests. A probability of<0.05 was considered statistically significant throughout.

Results

The population suffered from a wide range of comorbidities, including demographic factors of high risk for recurrent AF after ablation (Table 1).

Stable Localized Sources for Human AF

Intraprocedural AF was observed in 69/73 patients, in whom FIRM mapping revealed stable AF rotors or focal sources in 67 (97.1 %) for 2.1±1.1 concurrent sources each. The number of sources in prespecified demographic subgroups is shown in Table 2. Sources lay in diverse locations in left atrium (88%; 1.37±0.9 per patient) and right atrium (71.1%; 0.91±0.7 for each patient with biatrial mapping).

FIRM often ablated sources at locations that would not be targeted conventionally. For instance, figure 2A shows concurrent biatrial sources and figure 2B shows 2 RA AF rotors that were eliminated by FIRM but may have been missed by conventional ablation.

Demographic Associations with Numbers of Concurrent AF Sources, and Source Atrium

On univariate linear regression, several demographic factors were associated with the number of concurrent AF sources per patient (Table 3). On multivariate analysis, obstructive sleep apnea (p=0.004) and systolic dysfunction (p=0.001) associated with the number of concurrent AF sources.

Since conventional ablation is mostly LA while AF sources were biatrial, we studied demographic factors associated with right (versus left) atrial AF sources (e.g. figures 2A, B). As shown in table 4, the number of RA AF sources per patient rose with increasing BMI (p=0.015). Statistical significance was unchanged when analyzing the entire population in CONFIRM (i.e. including subjects with AF despite prior PVI; data not shown).

Demographic Associations With Rotor Versus Focal AF Sources

On univariate analysis, the number of AF rotors was associated with LA diameter, systolic heart failure, low serum Magnesium, OSA and persistent AF (table 5). On multivariate analysis, systolic heart failure (p<0.001) and OSA (p=0.047) associated significantly with the number of rotors. When looking at the difference of univariate correlations between rotors and focal sources (table 5), there was a significant difference with presence of systolic heart failure (p=0.002) and serum Magnesium levels (p=0.028).

Impact of Demographic Factors on Success of Ablation

Single procedure freedom from AF was 90% for patients receiving FIRM guided ablation versus 44% for conventional ablation. The higher success of FIRM was maintained across the prespecified high-risk groups in table 6 (for AF) and table 7 (for AF/all arrhythmias), in which row 1–7 analyses use the Chi-squared test, while rows 8–10 use Fisher's exact for DM, systolic heart failure and paroxysmal AF.

Figure 3 panels A-E illustrate Kaplan-Meier curves of cumulative single-procedure freedom from AF between FIRM and conventional ablation groups for these groups. Statistical significance was unchanged when analyzing the entire population in CONFIRM (i.e. including subjects with AF despite prior PVI; data not shown).

Discussion

In AF patients in whom demographic factors would predict failure of conventional ablation, targeted elimination of stable AF rotors and focal sources performed prior to conventional ablation substantially increased single procedure success. Mechanistically, AF in patients with obstructive sleep apnea, LA enlargement, obesity, hypomagnesemia and heart failure exhibited higher numbers of concurrent AF sources, while obese patients were more likely to show AF sources in the RA remote from conventional targets. These data provide a potential unifying explanation for the disappointing results of PVI in these patients, and may help realize the goal of patient-tailored ablation at AF mechanisms [19] in a wide AF population.

Demographic Markers of Risk for AF

Incident AF has long been associated with advanced age, male gender, hypertension and heart failure [20]. More recently, incident AF has been linked with obesity and OSA [21, 22, 23], and low serum magnesium was recently shown to increase AF risk by 50% [24].

Freedom from AF after conventional ablation is also reduced by many of these same risk factors of obesity [4, 25], OSA [1, 26], systolic heart failure[2] and LA enlargement[27]. However, it has been mechanistically unexplained why these patients are 'difficult-to-treat', and thus unclear how to guide ablation procedures to circumvent these limitations.

Mechanistic Role of Stable AF Rotors and Focal Sources

This prespecified substudy of the CONFIRM trial shows that 'difficult-to-treat' AF patients show a higher number of concurrent stable AF rotors or focal sources than patients without these comorbidities. The ability of targeted FIRM ablation to maintain high long-term

outcome in these patients strengthens the mechanistic role of stable AF sources across diverse populations, as demonstrated in the CONFIRM trial and now by other laboratories [9, 10].

At the cellular and tissue level, however, it remains unclear how AF sources functionally interact with specific patterns of myofibers [28], fibrosis or scar [29], electrical remodeling [30], autonomic innervation [31] or other factors. These issues may be resolved definitively only by translational studies in models that recapitulate human AF [6, 32]. In the meanwhile, many of these results are pathophysiologically plausible in that the number of LA AF sources rose with the presence of heart failure and OSA, that increase LA pressure [33], and diabetes [34] that may cause atrial fibrosis, while RA sources rose with the presence of obesity, that can increase RA pressure [35]. Intriguingly, low serum magnesium was also associated with numbers of concurrent LA rotors, independently confirming this recent epidemiological finding [24]. Stable AF sources and their distributions may thus provide a mechanistic foundation explaining how structural and electrical remodeling interact to form AF "substrates".

Clinical Implications

The apparent complexity of AF in 'difficult-to-treat' patients, evidenced by resistance to PV isolation, may simply reflect more AF sources in diverse non-PV locations. These locations may, in turn, reflect electrical or structural 'remodeling' mechanistically related to each comorbidity. By mapping AF sources regardless of right or left atrial location, FIRM-guided ablation maintained high single-procedure success rates even in these patients. Mechanistically, these data may help develop novel approaches to ameliorate AF such as reducing pulmonary arterial pressures in OSA patients [36] or therapies for heart failure.

Limitations

The CONFIRM study was non-randomized, although subjects were enrolled, mapped and treated prospectively. CONFIRM also had an active control group (conventional ablation) compared to prior studies that compared ablation to previously ineffective drugs. Although most AF ablation trials likely underestimated AF recurrence [37], 88% of FIRM-guided patients in CONFIRM were followed using implanted cardiac devices that is more rigorous than current guidelines [12]. The present study is limited by excluding some patients from CONFIRM, but strengthened by documentation of comorbidities from each patient's electronic medical record. Notably, associations of each comorbidity with source characteristics and the benefits of FIRM-guided versus conventional ablation were statistically unchanged if examining patients with AF after prior PVI. Finally, our patient population was mostly male, although studies from other centers [9, 10] show similar FIRM-guided mapping and ablation results in women.

Conclusions

Targeted ablation at stable AF rotors and focal sources (FIRM) combined with conventional PV isolation provided significantly higher single procedure efficacy than conventional ablation alone in traditionally 'difficult-to-treat' AF patients. Mechanistically, obesity, heart failure and obstructive sleep apnea are associated with greater numbers of AF sources often remote from the pulmonary veins and in the right atrium, that can be successfully identified and treated by FIRM guided ablation yet which explains lower the success of PV isolation in this population.

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Brief Summary

Atrial Fibrillation (AF) remains a major public health problem, for which ablation is increasingly performed. However, conventional ablation for AF is disappointing in patients with specific morbidities. We found that stable localized AF rotors, recently reported by several groups, are present in higher numbers and in atypical locations in these “difficult to treat” than other AF patients. Accordingly, ablation of AF rotors (FIRM) was more successful than conventional ablation in eliminating “difficult to treat” AF.

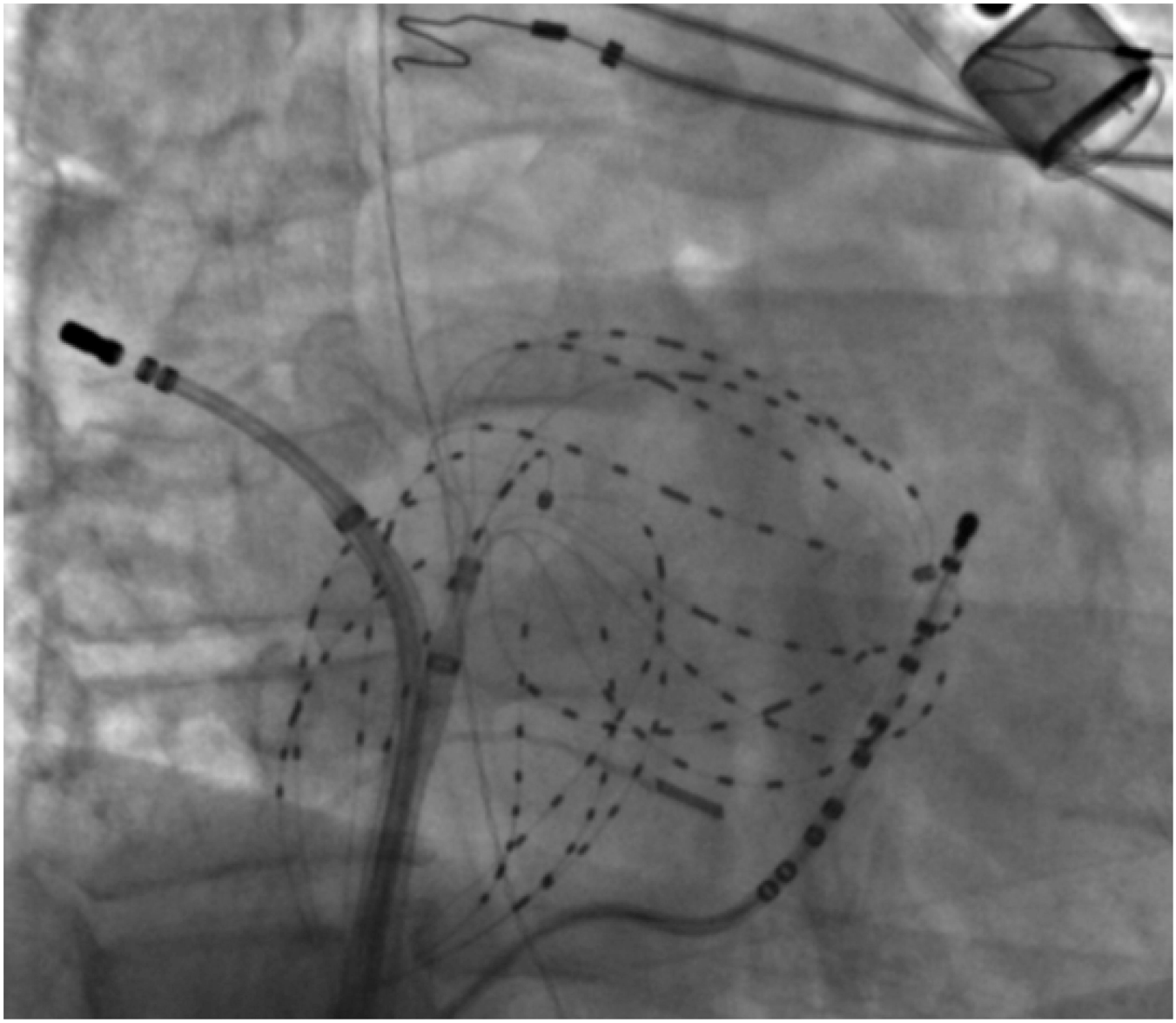
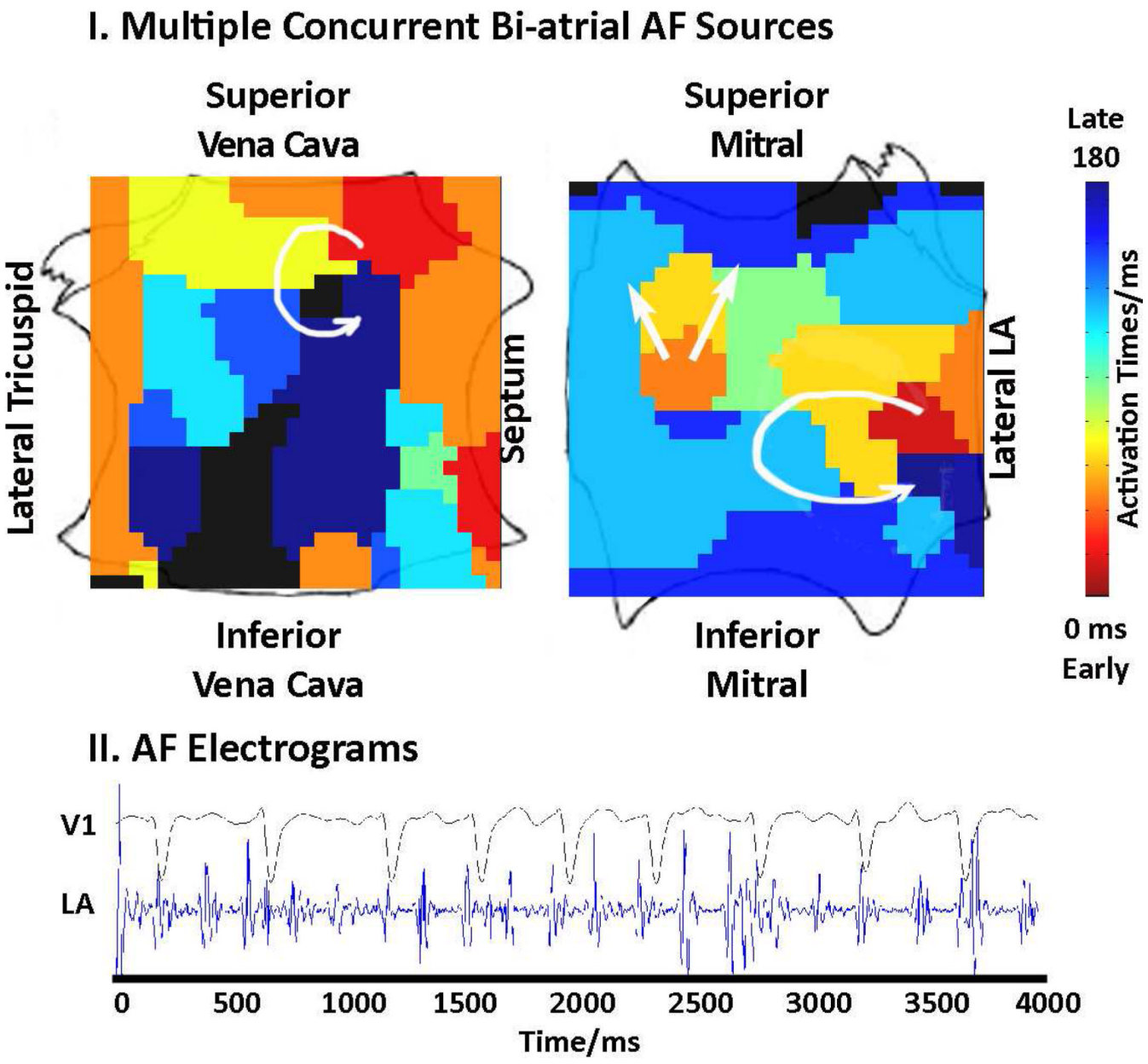


Figure 1. Focal Impulse and Rotor Mapping (FIRM) of Atrial Fibrillation, Using Contact Electrodes Widely Covering Both Atria

Fluoroscopy also shows a coronary sinus catheter, an ablation catheter, an intracardiac ultrasound catheter and an esophageal temperature probe. A subcutaneous ECG monitor, to stringently document AF recurrence, is also visible.

A



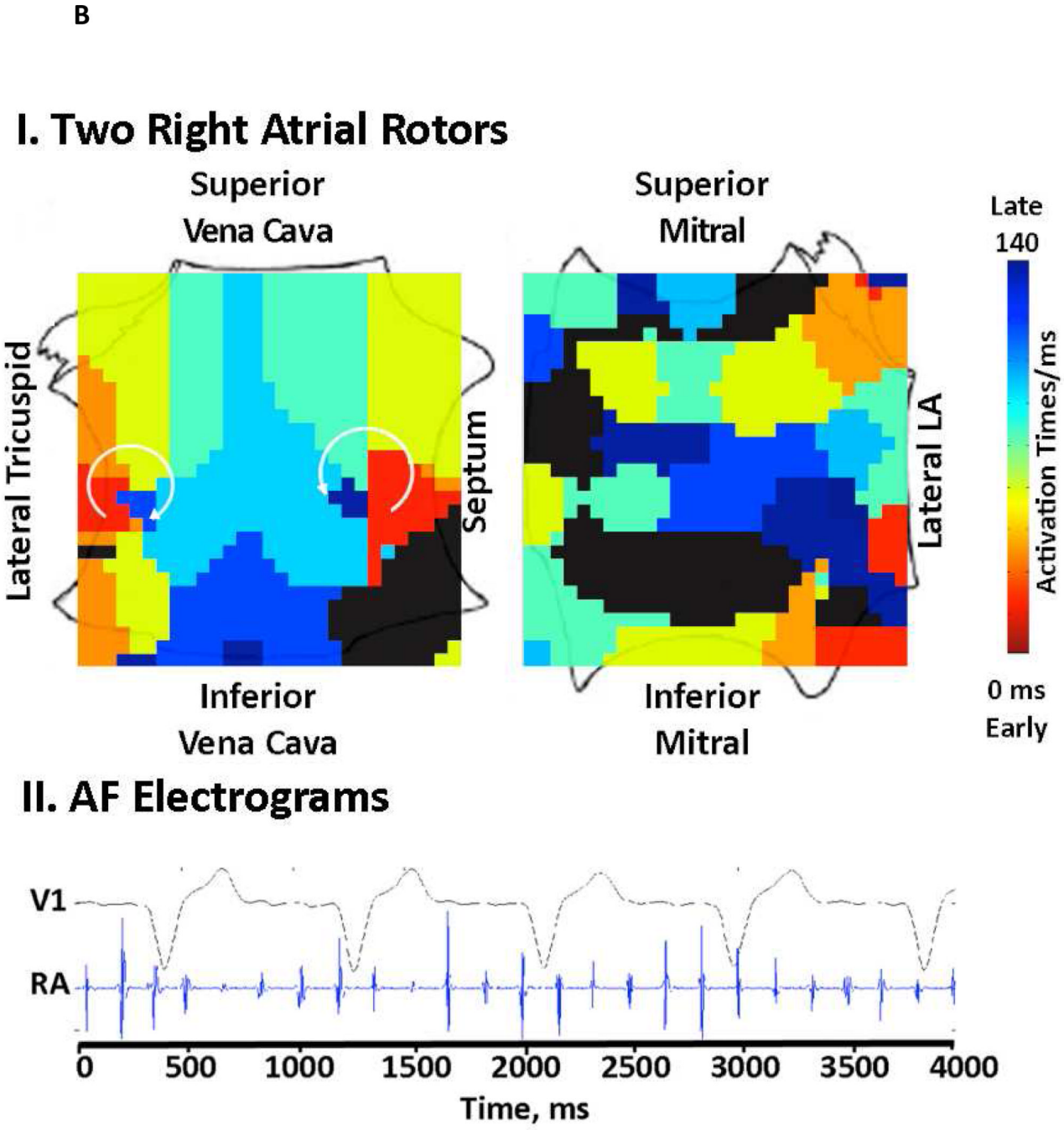
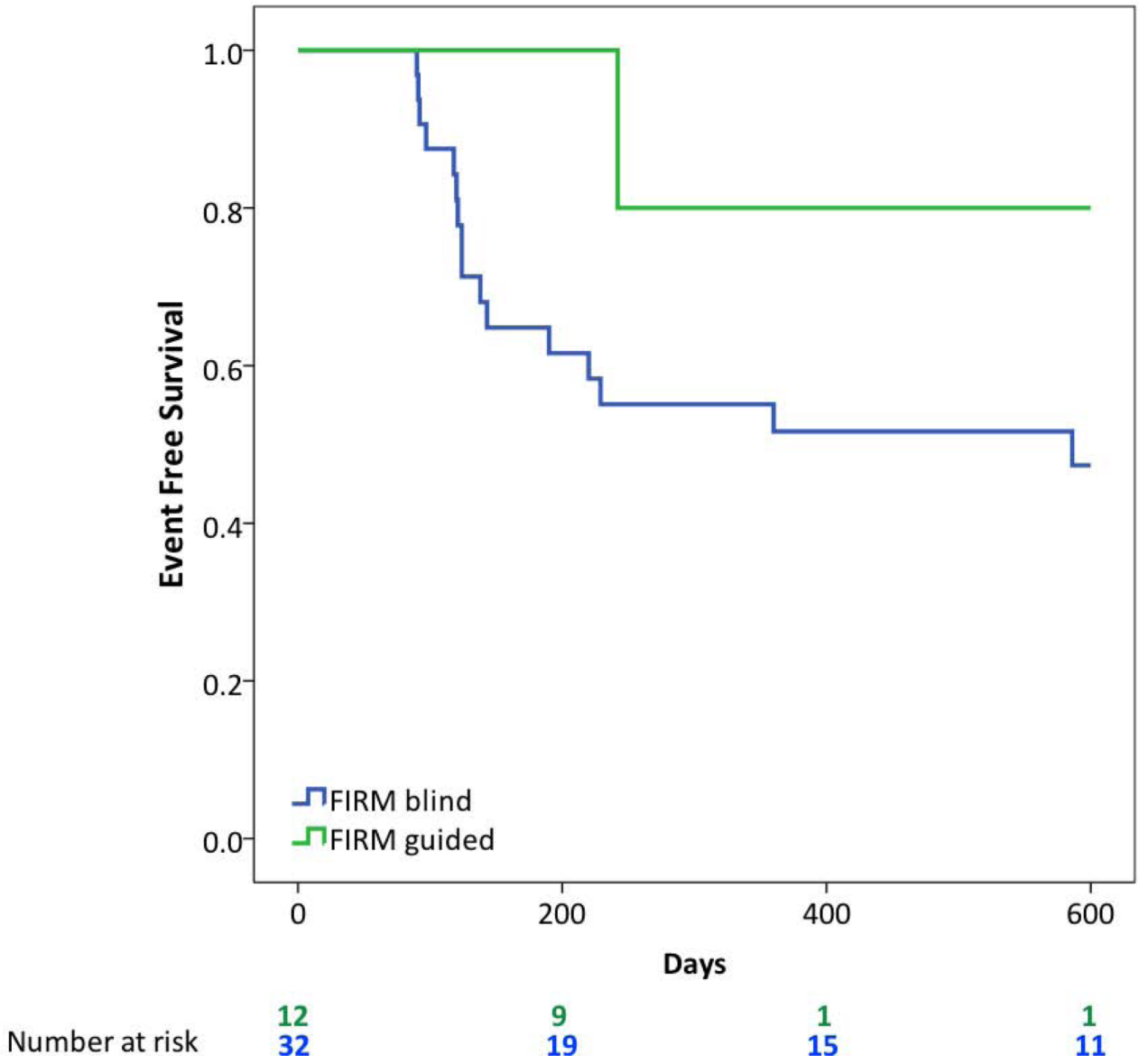


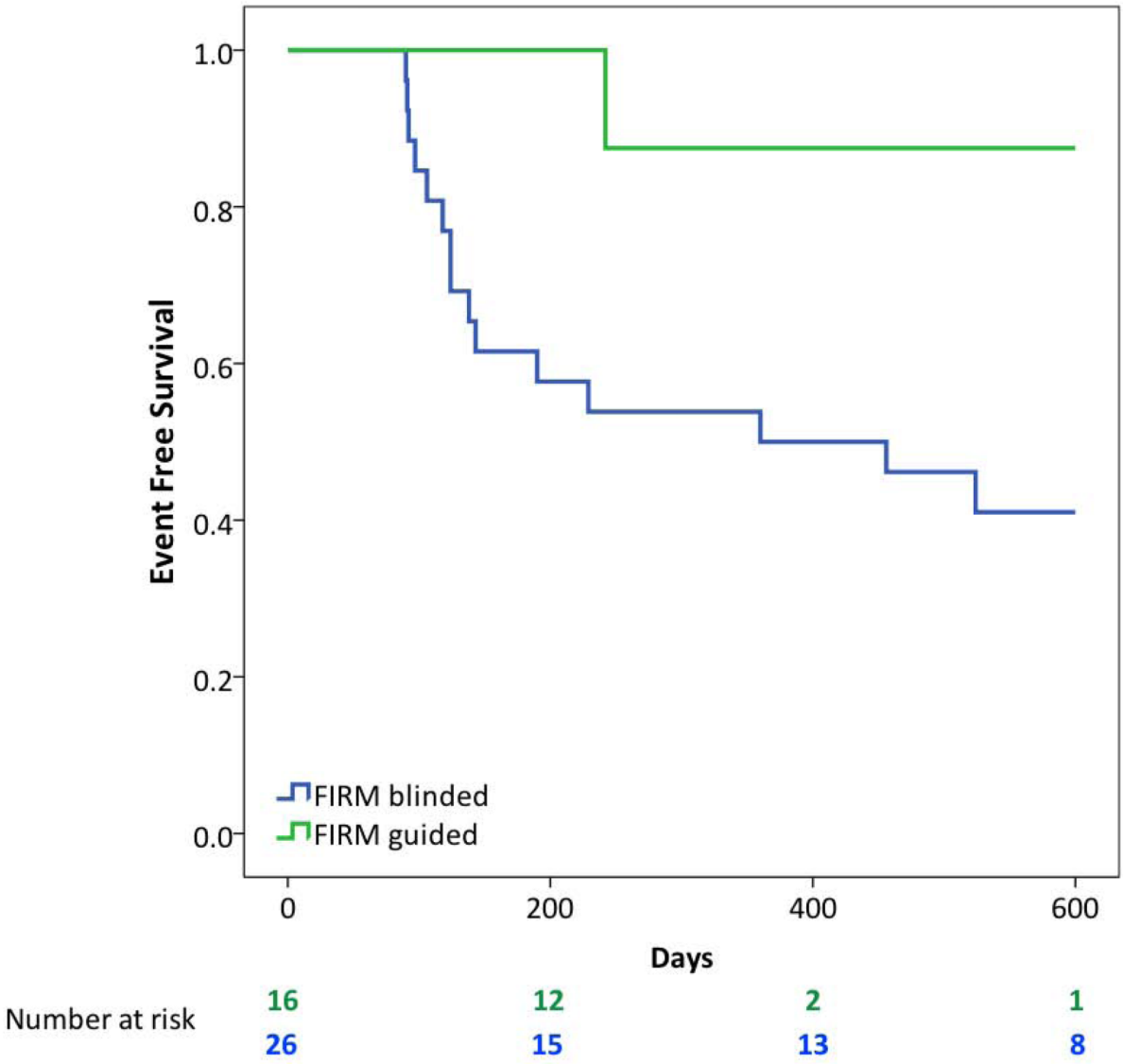
Figure 2. Multiple AF Sources in "Difficult to Treat" AF Patients

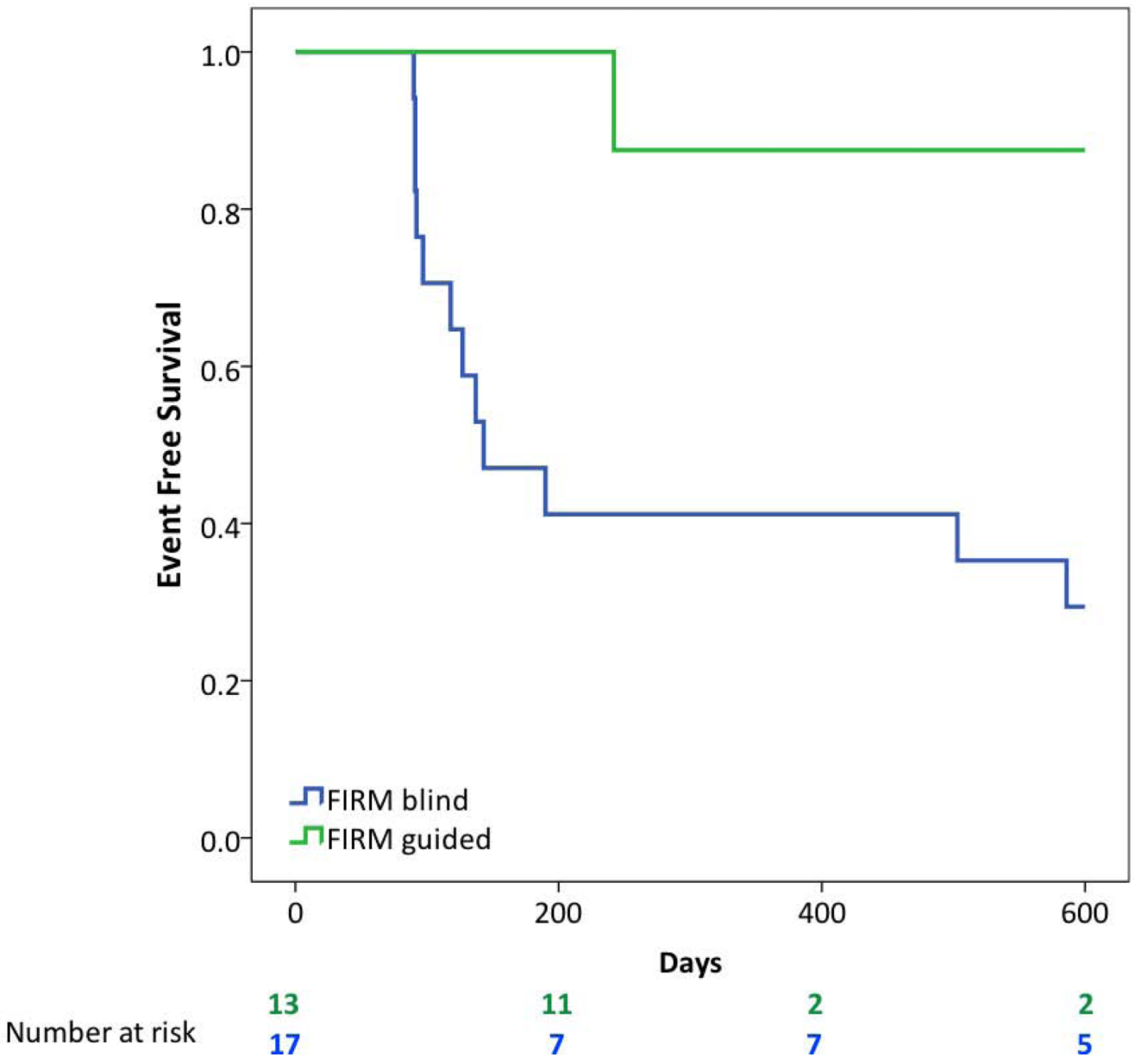
(A) Concurrent rotor and focal sources, including 2 in the LA, in a 49-year-old patient with OSA. (B) Right atrium showing 2 concurrent rotors in a 63 year old morbidly obese patient (BMI 41.9 kg/m^2), that were successfully ablated by FIRM but would not have been targeted by conventional ablation near the PVs.

(A) Single Procedure Freedom from AF in patients with obesity (p=0.048)

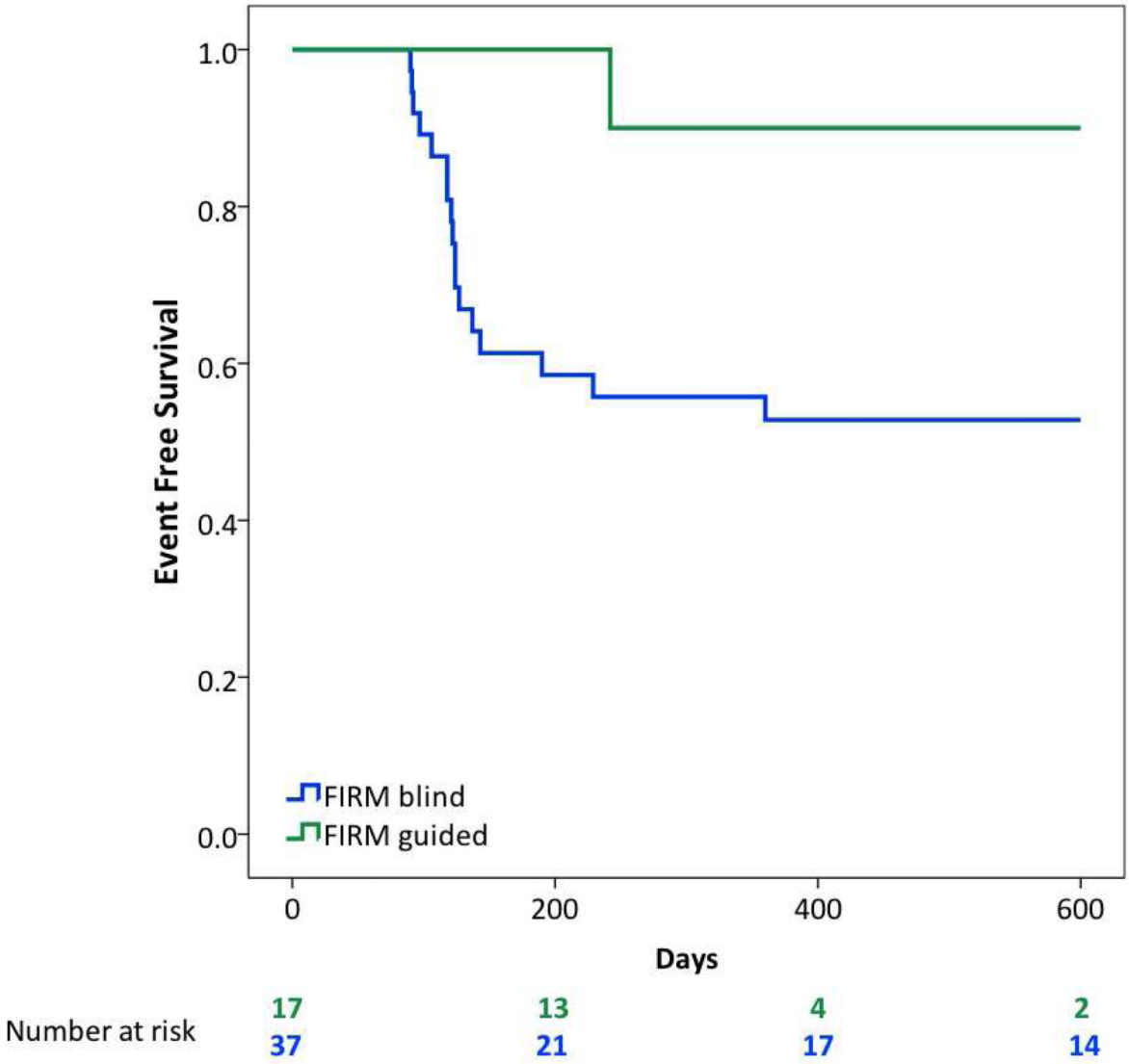


(B) Single Procedure Freedom from AF in patients with Obstructive Sleep Apnea (p=0.011)





(D) Single Procedure Freedom from AF in patients with LA enlargement (≥40mm). (p=0.009)



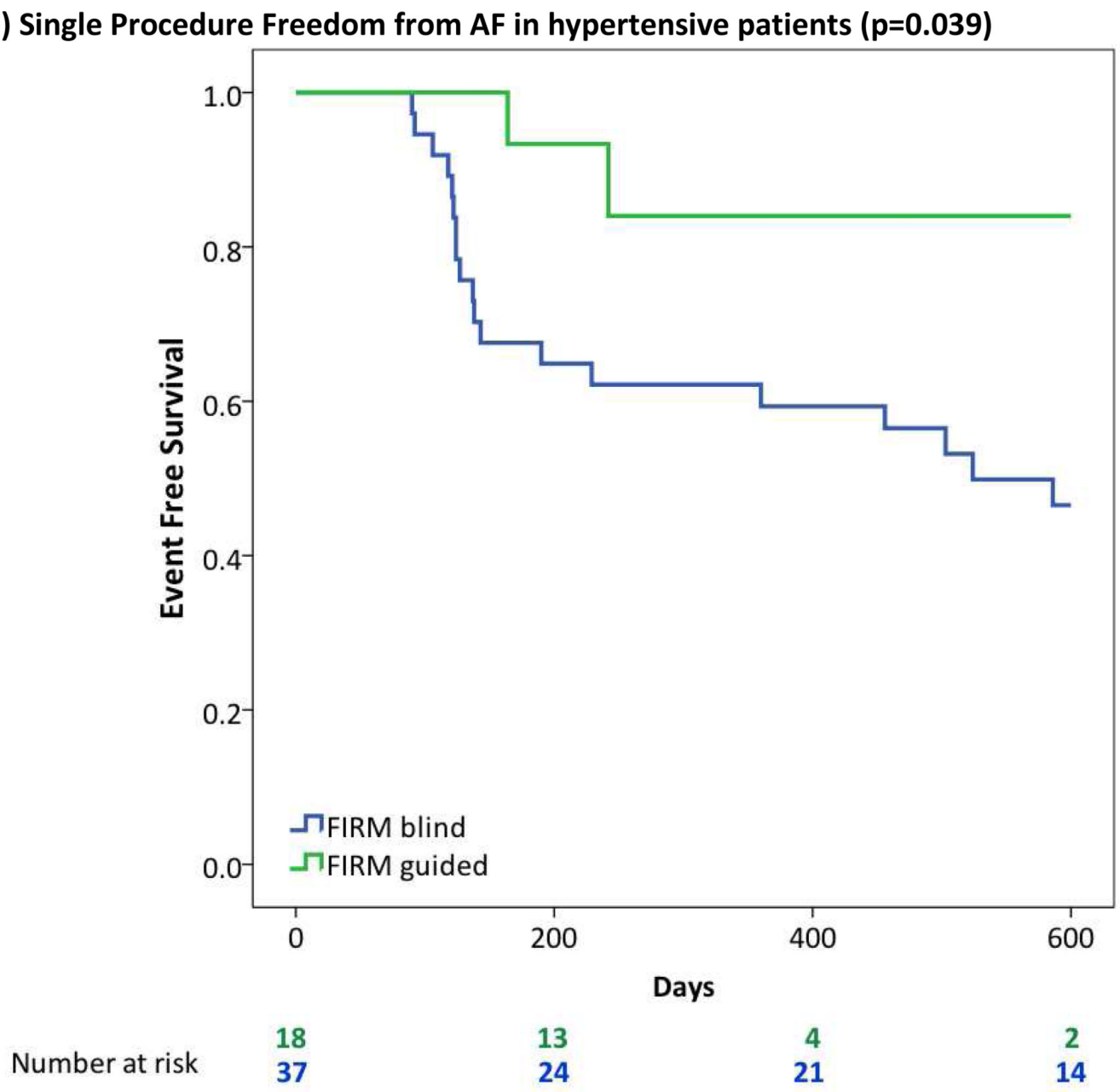


Figure 3. Cumulative Single Procedure Freedom from Atrial Fibrillation for FIRM-Guided versus Conventional Ablation for prespecified high risk subgroups

FIRM-guided provided higher freedom from AF than FIRM-blinded ablation for patients with (A) Obesity or Morbid Obesity (BMI>30), (B) Obstructive Sleep Apnea Syndrome; (C) Right Atrial Sources; (D) LA Enlargement (diameter >40 mm); (E) Hypertension.

Table 1

Clinical Characteristics

Characteristic	FIRM-blind (Conventional)	FIRM-guided	p
Type of AF	52	21	0.919
Paroxysmal AF	20	7	
Persistent AF	25	11	
Long standing persistent AF	7	3	
Age (years)	61±8.8	62±9.1	0.787
Gender (Male/Female)	N=51/1	N=19/2	0.197
LA diameter (mm)	43.8±6.6	47.4±6.8	0.042
Left Ventricular Ejection Fraction (%)	54.8±12	56.2±16	0.677
Comorbid Conditions			
Hypertension	37/52	19/21	0.125
Diabetes	17/52	9/21	0.412
BMI (mean)	31.9±5.6	33.2±5.5	0.398
Normal weight (BMI <25)	4/52	0/21	0.318
Overweight (BMI 25–29.9)	15/52	5/21	0.662
Obese (BMI 30–39.9)	28/52	12/21	0.798
Morbidly obese (BMI ≥40)	4/52	2/21	1.000
Obstructive sleep apnea	26/51	17/21	0.018
Congestive Heart Failure	10/52	5/21	0.751
Systolic heart failure (EF <40%)	6/52	5/21	0.277
Diastolic failure	4/52	0/21	0.318
BNP	206.5±186	171.5±147	0.551
Chronic Kidney Disease (CKD)	6/50	5/21	0.282
GFR, ml/min (mean)	75.8±16.3	72.6±17.6	0.486
Magnesium, mg/dl	2.05±0.18	2.05±0.17	0.940

Statistical comparisons were performed using the Chi-squared test (for incidences of persistent AF, diabetes mellitus, obstructive sleep apnea, overweight and obesity), the t-test (for age, LA diameter, LV ejection fraction, body mass index and laboratory data), and Fisher's exact test (for gender, HTN, long standing persistent AF, chronic kidney disease, congestive heart failure, normal weight and morbid obesity).

Table 2

Number of localized sources in patient subgroups

Variables	Number of Stable AF Sources	Number of Rotors	Number of Focal Sources
All	1.9±1.2	1.6±1.1	0.3±0.6
Obstructive sleep apnea	2.3±1.2	1.9±1.2	0.4±0.7
LA enlargement	2.1±1.3	1.8±1.2	0.3±0.6
Systolic heart failure	2.9±1.7	2.6±1.4	0.3±0.5
Obesity	2.1±1.4	1.8±1.2	0.3±0.6
Persistent AF	2.1±1.3	1.9±1.2	0.2±0.5
Hypertension	2.0±1.2	1.6±1.2	0.4±0.6
Diabetes Mellitus	2.1±1.5	1.6±1.4	0.5±0.8
Hyperlipidemia	2.1±1.3	1.7±1.2	0.4±0.6

Statistical analyses were done using paired samples t-test. The number of stable AF rotors was significantly higher than the number of focal sources for all subgroups ($P<0.05$ for each)

Table 3

Relationship Between Clinical Variables and the Total Numbers of Stable AF Sources on FIRM mapping

Variables	p	r
Obstructive Sleep Apnea	**0.002**	**0.364**
Systolic heart failure	**<0.001**	**0.424**
LA diameter (mm)	**0.021**	**0.283**
Magnesium (serum, mg/dL)	**0.017**	**−0.307**
New York Heart Association (NYHA) class	**0.023**	**0.274**
LV ejection fraction (%)	**0.039**	**−0.253**
Coronary artery disease	**0.050**	**0.236**
Persistent AF	**0.074**	**0.217**
Body Mass Index (BMI)	0.103	0.202
Chronic Kidney Disease (CKD)	0.176	0.167
DM	0.185	0.162
CKD stage	0.194	0.161
Hyperlipidemia	0.216	0.151
AF cycle length	0.323	−0.121
Age	0.338	0.117
Hypertension	0.349	0.114

Statistical analyses was performed using Pearson's correlation.

Table 4

Relationship of Clinical Variables to Numbers of Left versus Right Atrial AF sources

Variables	Relationship to Number of RA sources for AF		Relationship to Number of LA sources for AF	
	P	r	P	r
Systolic heart failure	0.710	0.057	<**0.001**	**0.438**
Magnesium (serum, mg/dL)	0.456	0.128	**0.003**	−**0.379**
NYHA class	0.810	0.037	**0.023**	0.274
LV ejection fraction (%)	0.458	−0.115	**0.033**	−**0.261**
OSA	0.673	0.065	**0.044**	**0.245**
Body mass index (BMI)	**0.015**	**0.367**	0.805	−0.031
LA diameter (mm)	**0.060**	**0.290**	0.166	0.173
Persistent AF	**0.115**	**0.238**	0.463	0.090
DM	0.567	−0.088	0.144	0.178
HL	0.777	−0.043	0.533	0.076

Statistical relationships Calculated Using Pearson's correlation coefficient

Table 5

Relationship of Clinical Variables to Numbers of Rotors or Focal AF sources

Variables	Relationship to AF Rotors		Relationship to AF Focal sources		Significance of difference
	p	r	P	r	p
Systolic heart failure	<**0.001**	**0.465**	0.784	−0.034	**0.002**
LA diameter (mm)	**0.002**	**0.382**	0.210	−0.156	**0.065**
Magnesium (serum, mg/dL)	**0.004**	**−0.370**	0.550	0.079	**0.028**
Persistent AF	**0.004**	**0.339**	0.096	−0.202	0.180
OSA	**0.020**	**0.282**	0.141	0.180	0.251
Body mass index (BMI)	**0.060**	**0.233**	0.743	−0.041	0.109
AF cycle length	0.223	−0.149	0.748	0.039	0.242

Statistical relationships Calculated Using Pearson's correlation coefficient and comparison of dependent correlation coefficients [18]

Table 6

Comparative Freedom from AF after FIRM-Blinded and FIRM-Guided Ablation For Prespecified Demographic Subgroups

Characteristic	Single Procedure Freedom from AF, FIRM-Blinded (Conventional)	Single Procedure Freedom from AF, FIRM-Guided	p
All patients	23/52 (44%)	17/19 (90%)	**0.001**
Obesity (BMI≥30)	14/32 (44%)	11/12 (92%)	**0.004**
Obstructive sleep apnea	10/26 (39%)	15/16 (94%)	<**0.001**
Persistent AF	12/32 (38%)	12/13 (92%)	**0.001**
HTN	16/37 (43%)	16/18 (89%)	**0.001**
Presence of RA sources	5/17 (29%)	12/13 (92%)	**0.001**
LA enlargement	19/37 (51%)	16/17 (94%)	**0.002**
DM	9/17 (53%)	6/8 (75%)	0.402
Systolic heart failure	4/6 (67%)	4/4 (100%)	0.467
Paroxysmal AF	11/20 (55%)	5/6 (83%)	0.352

Statistical differences calculated using Chi squared or Fisher's exact tests.

Table 7

Comparative Freedom from AT/AF after FIRM-Blinded and FIRM-Guided Ablation For Prespecified Demographic Subgroups

Characteristic	Single Procedure Freedom from AF/AT, FIRM-Blind (Conventional)	Single Procedure Freedom from AF/AT FIRM-Guided	p
All patients	20/52 (39%)	14/19 (74%)	**0.009**
Persistent AF	10/32 (31%)	9/13 (69%)	**0.019**
Obesity (BMI≥30)	12/32 (38%)	9/12 (75%)	**0.027**
HTN	15/37 (41%)	13/18 (72%)	**0.027**
LA enlargement	17/37 (46%)	13/17 (77%)	**0.036**
Obstructive sleep apnea	9/26 (35%)	12/16 (75%)	**0.011**
Presence of RA sources	5/17 (29%)	9/13 (69%)	**0.030**
DM	9/17 (53%)	6/8 (75%)	0.402
Systolic heart failure	3/6 (50%)	4/4 (100%)	0.200
Paroxysmal AF	10/20 (50%)	5/6 (83%)	0.197

Statistical differences calculated using chi square and Fisher's exact tests