RADAR-AF Trial

A Randomized Multicenter Comparison of **R**adiofrequency Catheter **A**blation of **D**rivers vs. Circumferential Pulmonary Vein Isolation in Patients with **A**trial Fib**R**illation

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on behalf of the RADAR-AF Investigators

RADAR – AF

http://clinicaltrials.gov : NCT00674401.

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Background

- Empiric circumferential pulmonary vein isolation (CPVI) is the therapy of choice for drug-refractory AF, but results are suboptimal.[1]
- The outcomes of mechanistically-based strategies aimed at targeting atrial fibrillation drivers are unknown.[2,3]

Objective

To determine the efficacy and safety of high-frequency source ablation (HFSA) compared to CPVI in pts with symptomatic drug-refractory AF.

1. Calkins *et al.* 2012 HRS Expert Consensus Statement AF ablation. 2. Haissaguerre *et al. NEJM* 1998; 339(10):659–666; 3. Atienza *et al. Heart Rhythm* 2009;6(1):33– 40.

Methods

- Prospective, multi-center, single blinded, randomized (1:1) clinical trial.
- Navigation system: Ensite NavX v8.0 (St Jude Medical, Mn) DF mapping software.
- Ablation: 3.5 mm irrigated tip catheter
- Sample size was calculated assuming CPVI 83% freedom from AF/AT recurrence: 115 patients, 90% power with respect to non-inferiority. Non-inferiority was concluded if the lower limit of the one sided 95% CI was >-16%.
- Follow-up: ECG & 48-hrs Holter at 3, 6, 12 months
- Intention-to-treat analysis.

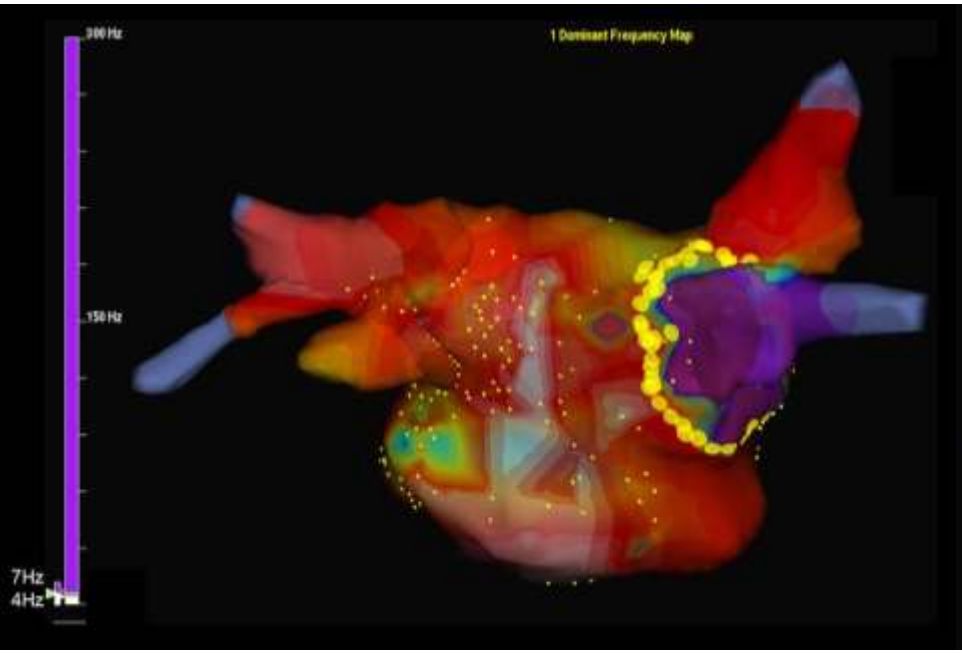
Methods

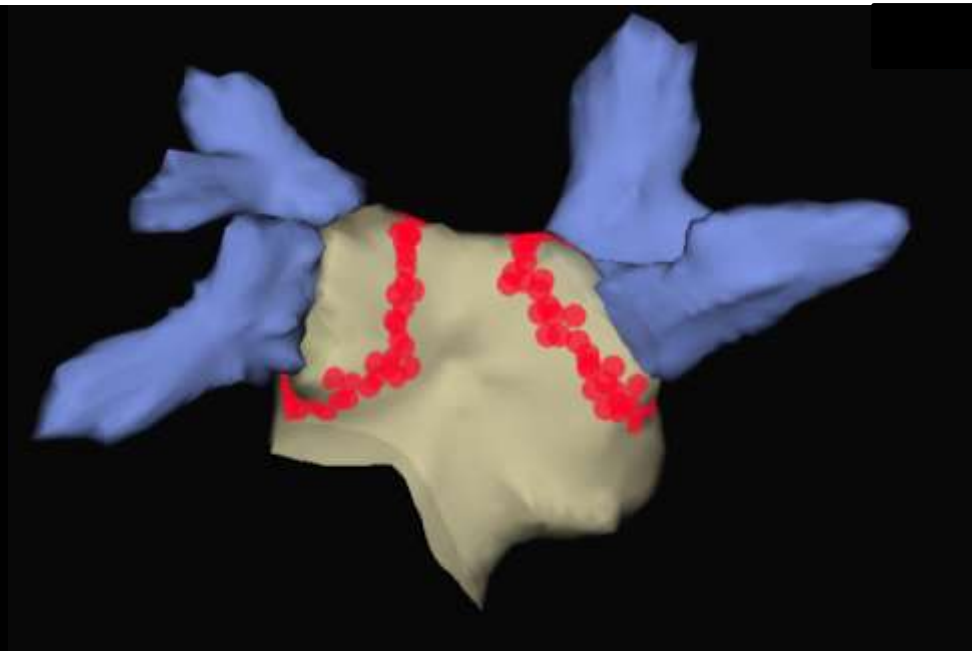
- Primary Endpoint:
  - Freedom from AF at 6 months post-first ablation procedure off antiarrhythmic medications.
- Secondary Endpoints:
  - Freedom from AF at 6 and 12 months post-ablation off/on antiarrhythmic drugs
  - Freedom from AT/AF at 6 and 12 months post-ablation off/on antiarrhythmic drugs
  - Incidence of peri-procedural complications
  - Overall adverse events
  - Quality of life

Ablation Strategy

Paroxysmal AF:

High Frequency Sites Ablation vs. Circumferential PV Isolation



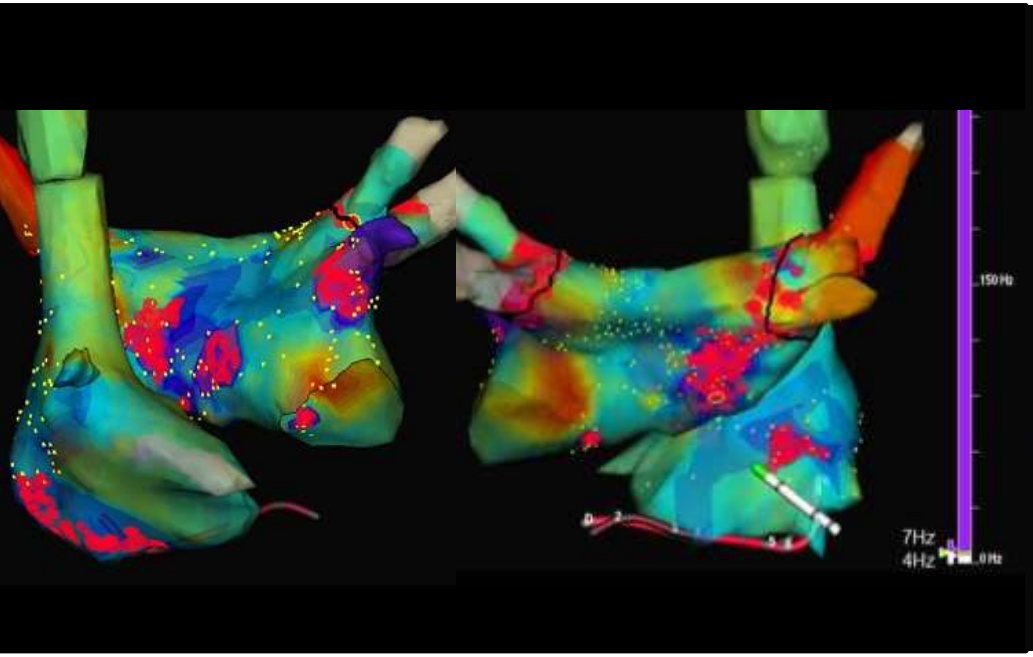


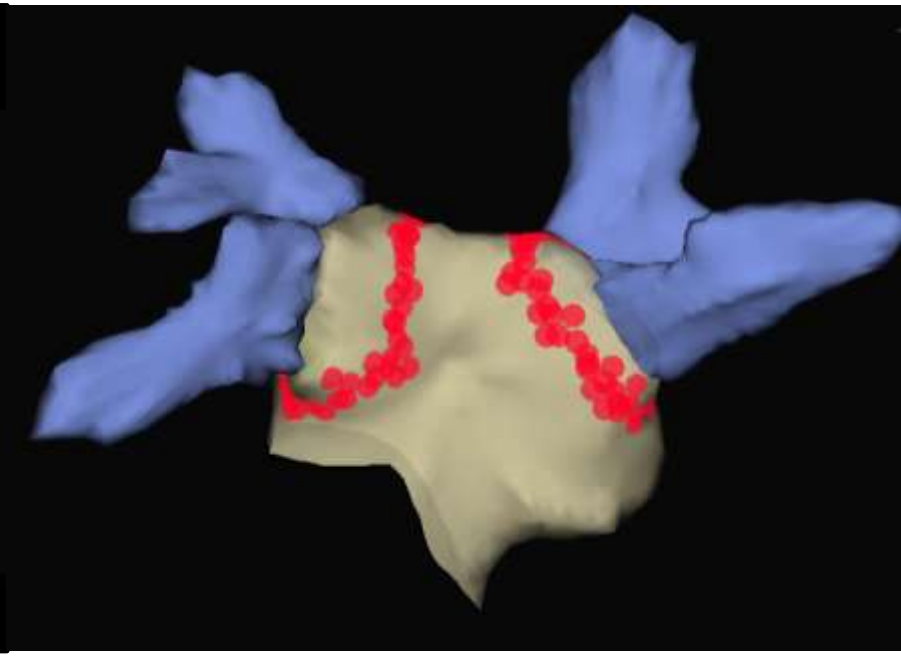
Non-inferiority design

Ablation Strategy

Persistent AF:

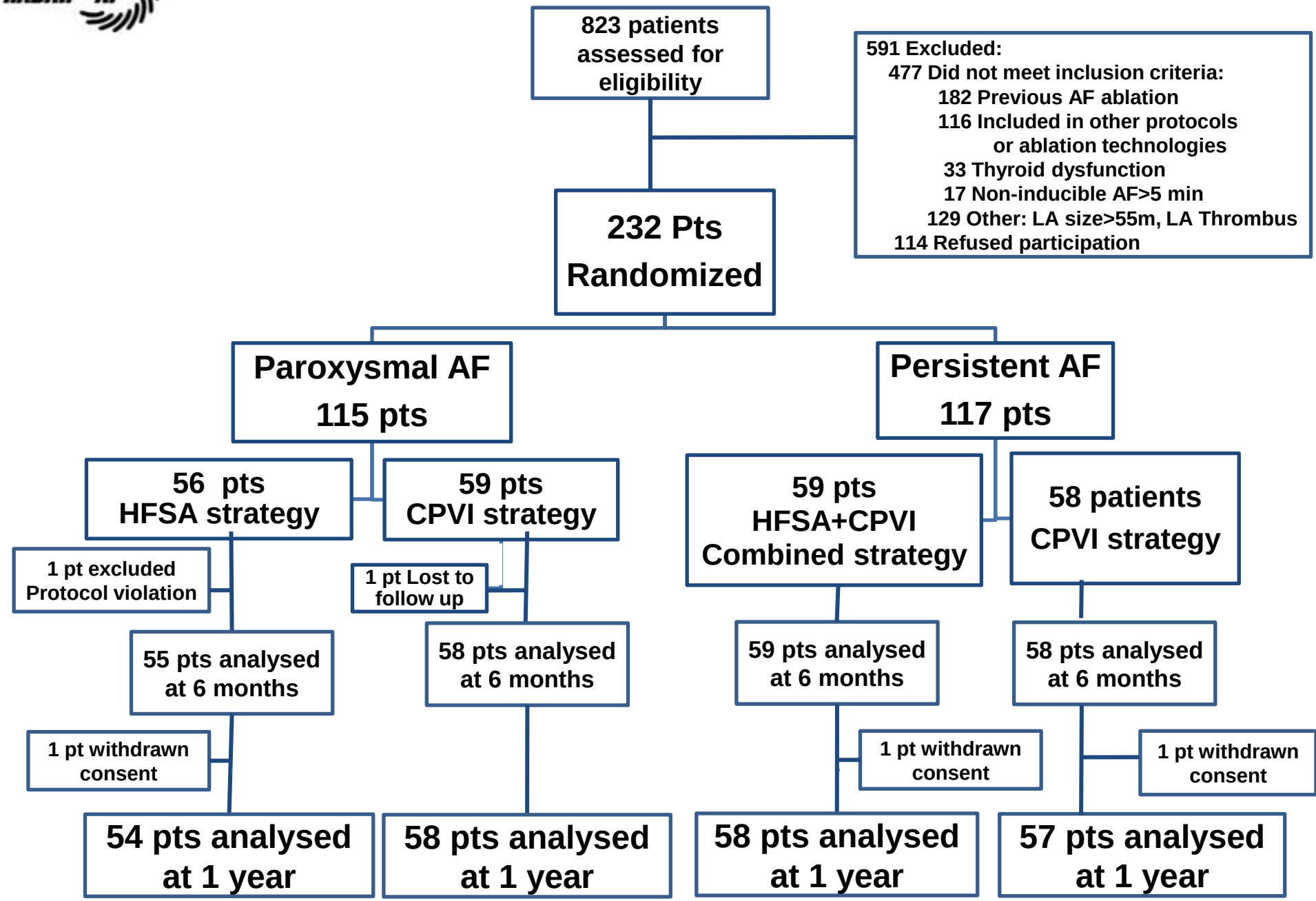
High Frequency Sites Ablation + CPVI vs. Circumferential PV Isolation





Superiority design

Flow Chart


823 patients assessed for eligibility
591 Excluded:
477 Did not meet inclusion criteria:
182 Previous AF ablation
116 Included in other protocols or ablation technologies
33 Thyroid dysfunction
17 Non-inducible AF>5 min
129 Other: LA size>55m, LA Thrombus
114 Refused participation
232 Pts Randomized
Paroxysmal AF 115 pts
Persistent AF 117 pts
56 pts HFSA strategy
59 pts CPVI strategy
59 pts HFSA+CPVI Combined strategy
58 patients CPVI strategy
1 pt excluded Protocol violation
1 pt Lost to follow up
55 pts analysed at 6 months
58 pts analysed at 6 months
59 pts analysed at 6 months
58 pts analysed at 6 months
1 pt withdrawn consent
1 pt withdrawn consent
1 pt withdrawn consent
54 pts analysed at 1 year
58 pts analysed at 1 year
58 pts analysed at 1 year
57 pts analysed at 1 year

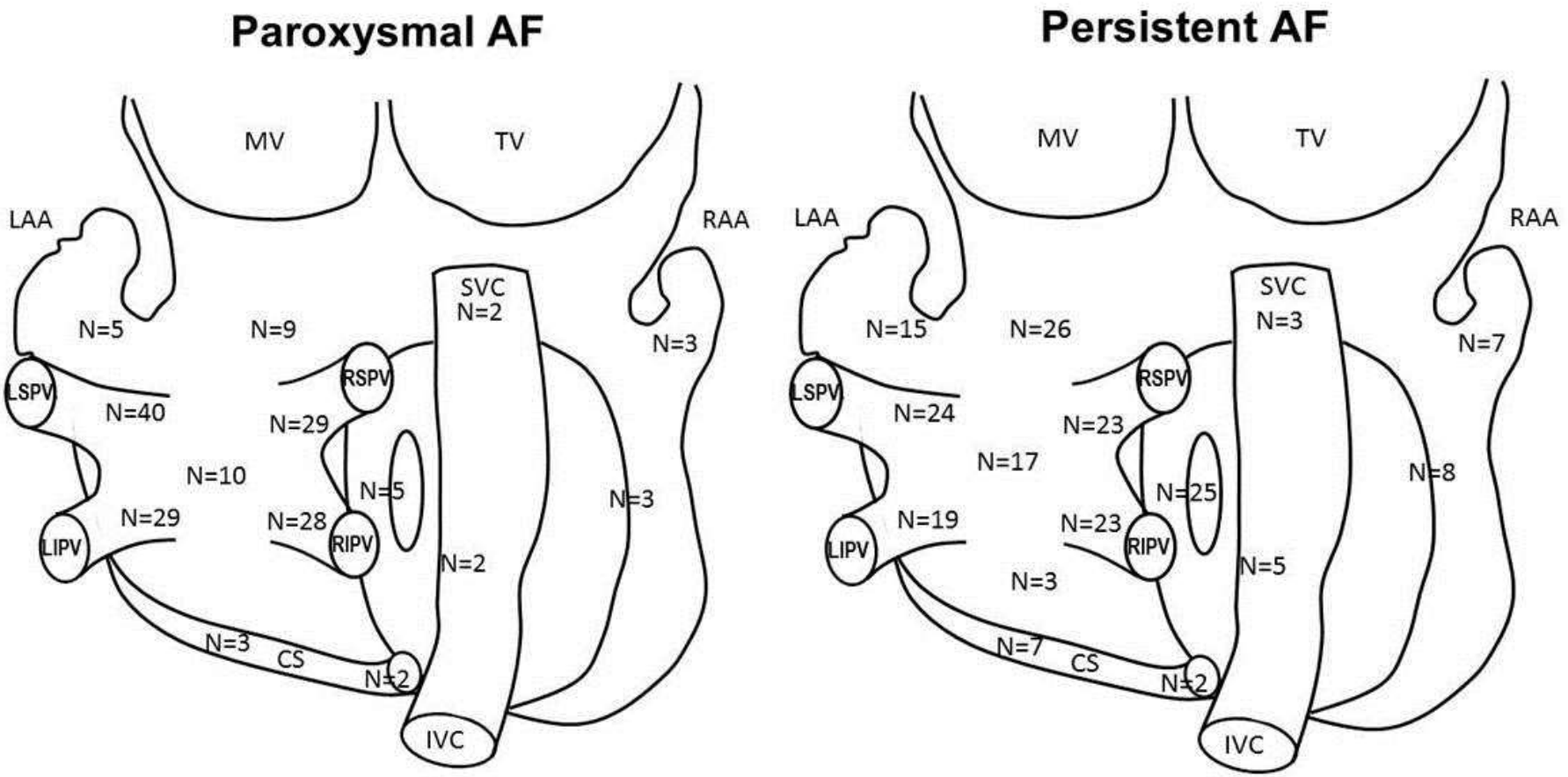
Baseline Characteristics

	Paroxysmal AF (N=113)		
	CPVI (N=58)	HFSA (N=55)	p-value
Male	49 (84%)	40 (73%)	0.168
Age, yrs	53±10	54±12	0.693
BMI, Kg/m2	27.5±4.2	28±3.1	0.439
Hypertension	17 (29%)	24 (44%)	0.123
Dyslipemia	16 (27%)	22 (40%)	0.171
Diabetes	2 (3%)	3 (5%)	0.674
Stroke/TIA	2 (3%)	0	
Heart Disease	7 (12%)	12 (22%)	0.211
Valvular disease	4 (7%)	4 (7%)	1.0
AF duration (yrs)	6.3±7.3	5.9±6	0.896
LVEF (%)	62±6	63±6	0.466
LA diameter (mm)	40±5	40±6	0.791
NYHA class I ≥II	52 (90%) 6 (10%)	51 (93%) 4 (7%)	0.743
$CHADS_2$ score 0 1 ≥2	36 (62%) 19 (33%) 3 (5%)	29 (53%) 22 (40%) 4 (7%)	0.595
Prior AAD 1 2 >3	33 (57%) 21 (36%) 4 (7%)	40 (73%) 10 (18%) 5 (9%)	0.139

Procedural Characteristics

	Paroxysmal AF		
	CPVI (N=58)	HFSA (N=55)	P-value
Induced AF	46 (81%)	49 (89%)	0.26
Mean AF cycle length, ms	172±35	176±33	0.55
DF mapping time, min	NA	31 (16)	NA
Fluoroscopy time, min	70±72	59±28	0.3
Total Procedure time, min	215±66	228±65	0.31
Nº HFS, median (IQR)	NA	3 (2-4)	NA
Nº Ablated HFS, median (IQR)	NA	2.87 (2-3)	NA
Non-ablated HFS	NA	18	NA
Isolated pulmonary veins, mean (95% CI)	3.79 (3.65-3.93)	2.22 (1.92-2.52)	<0.001
Additional LA lines	3	0	NA
RF time, min	42±28	33±26	0.08
SR conversion during abl.	16 (28%)	25 (45%)	<0.05
Redo procedures	17 (29%)	13 (24%)	0.5

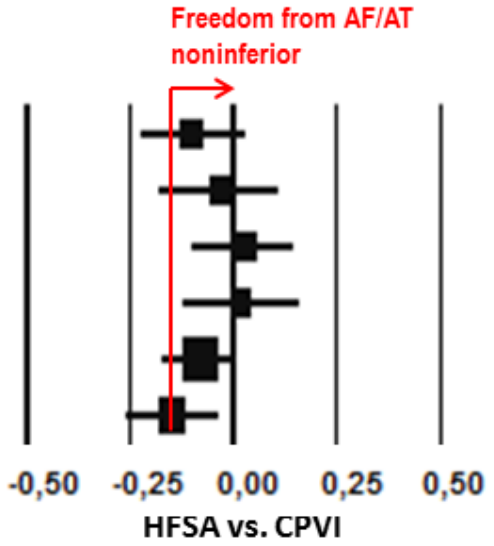
High Frequency Sites Distribution



Efficacy and Safety Endpoints

Paroxysmal Atrial Fibrillation

	Risk Diff.	Standard Error	Lower Limit	Upper Limit	p-Value for Noninferiority	p-Value for Superiority
Freedom from AF 6 months	-0.100	0.078	-0.228	0.028	0.23	0.2
Freedom from AF/AT 6 mths	-0.035	0.088	-0.180	0.110	0.08	0.69
Freedom from AF 1 year	0.022	0.075	-0.102	0.145	0.008	0.39
Freedom from AF/AT 1 year	0.017	0.084	-0.121	0.154	0.02	0.42
Periprocedural AE	-0.083	0.055	-0.173	0.007		0.13
Serious AE	-0.150	0.068	-0.263	-0.038		0.03

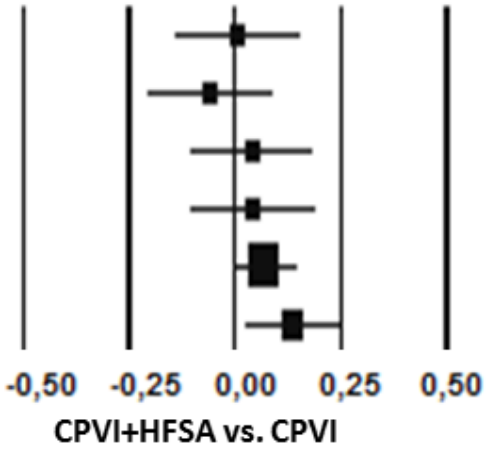


	HFSA	CPVI
Freedom from AF at 6 months	40 (73%)	48 (83%)
Freedom from Atrial Tachyarrhythmias at 6 months	36 (66%)	40 (69%)
Freedom from AF at 1 year	44 (82%)	46 (79%)
Freedom from Atrial Tachyarrhythmias at 1 year	40 (74%)	42 (72%)
Procedure related adverse events	3 (6%)	8 (14%)
Serious adverse events	5 (9%)	14 (24%)

Efficacy and Safety Endpoints

Persistent Atrial Fibrillation

	Risk Diff.	Standard Error	Lower Limit	Upper Limit	p-Value for Superiority
Freedom from AF 6 months	0.007	0.090	-0.142	0.155	0.94
Freedom from AF/AT 6 mths	-0.061	0.091	-0.211	0.088	0.50
Freedom from AF 1 year	0.041	0.088	-0.104	0.185	0.32
Freedom from AF/AT 1 year	0.041	0.090	-0.106	0.189	0.32
Periprocedural AE	0.067	0.045	-0.009	0.143	0.15
Serious AE	0.134	0.068	0.021	0.246	0.05



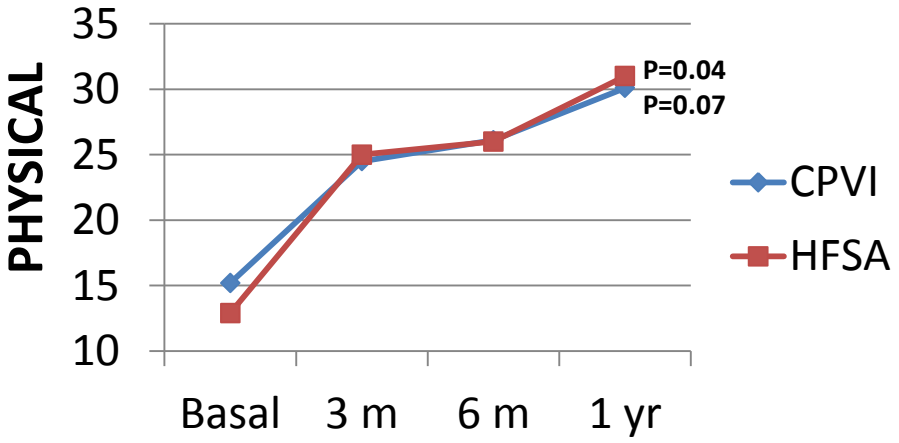
	CPVI+HFSA	CPVI
Freedom from AF at 6 months	36 (61%)	35 (60%)
Freedom from Atrial Tachyarrhythmias at 6 months	33 (56%)	35 (60%)
Freedom from AF at 1 year	40 (69%)	37 (65%)
Freedom from Atrial Tachyarrhythmias at 1 year	38 (66%)	35 (61%)
Procedure related adverse events	6 (10%)	2 (3%)
Serious adverse events	14 (24%)	6 (10%)

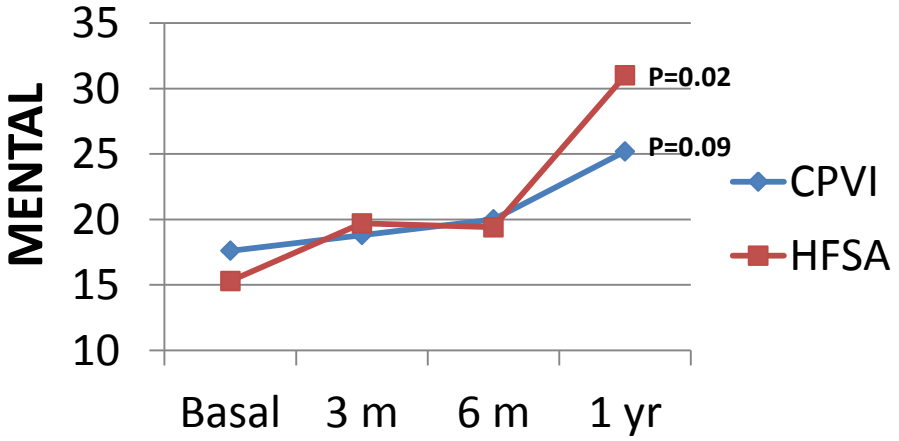
Serious Adverse Events

	Paroxysmal AF	
	CPVI	HFSA
Procedural Adverse Events		
Pericarditis/Chest pain	1	
Tamponade	2	1
Pericardial effusion conservatively treated	2	
Vascular complications	1	1
Pleural effusion		
Pneumonia <1 month	1	
PV estenosis		1
Urinary tract infection	1	
Adverse events >1 month after the procedure		
Hypotension/HF following CVE for AF		1
AF/AT/Flutter requiring hospitalization/ablation	5	1
Syncope		
Thyroid dysfunction		
Bleeding after surgery	1	
Chest pain		1
Stroke after NOAC switching		
Traumatism	1	
Pharmacologic AV block		

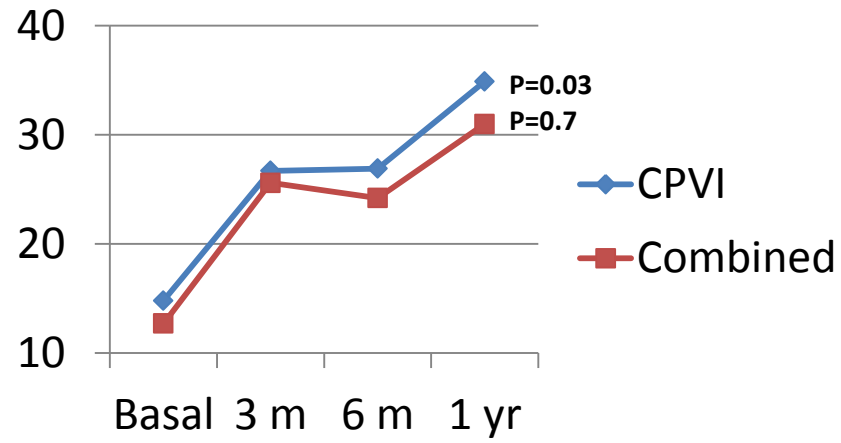
Quality of Life Atrial Fibrillation Questionnaire

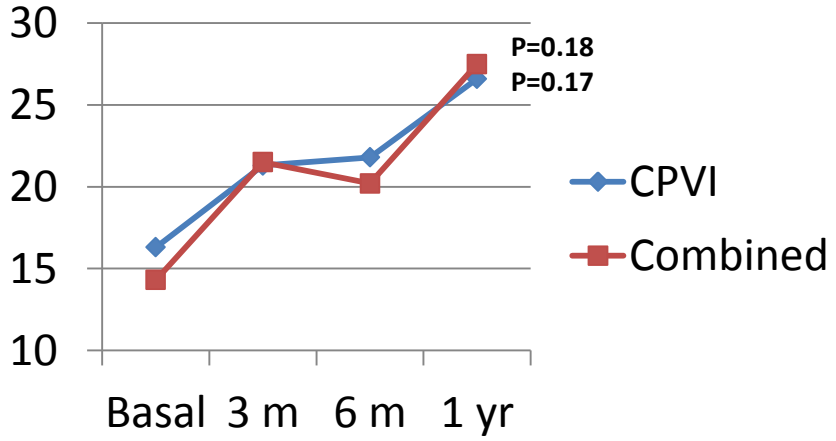
Paroxysmal AF





Persistent AF





Conclusions

- **In Paroxysmal AF:**
  - HFSA did not reach statistical significance for noninferiority compared to CPVI to achieve freedom from AF at 6 months after a single ablation procedure.
  - HFSA was noninferior to CPVI to achieve freedom of AF & freedom from atrial tachyarrhythmias at 1 year, with a lower incidence of severe adverse events.
- **In Persistent AF:** CPVI+HFSA offered no incremental value with a trend for an increase in complications risk.
- These results may offer a novel mechanistic treatment paradigm for paroxysmal atrial fibrillation.