Online Resource

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Title: Efficacy and Safety of a Novel Pulsed Field Ablation System in Paroxysmal Atrial Fibrillation

Authors: Qiming Liu, MD, PhD,[a] Hanxiong Liu, MD,[a] Xiaoshu Cheng, MD, Zhihui Zhang, MD, PhD, Chenyang Jiang, MD, PhD, Zhiyu Ling, MD, Yan Wang, MD, PhD, Xuping Li, MD, Zhen Zhang, MD, Qi Chen, MD, Wenzhi Luo, MD, Zhenjiang Liu, MD, Duan Luo, MD, Jianhua Yu, MD, Guoshu Yang, MD, Qinmei Xiong, MD, Yan Luo, MD, Jinzhu Hu, MD, Juying Zhang, PhD, Shenghua Zhou, MD, PhD [b]

[a] These authors contributed equally to this work.

[b] Affiliation: The Second Xiangya Hospital of Central South University, Changsha, China

[b] Email: zhoushenghua@csu.edu.cn

Online Resource 1. All the Reviewed and Approved Ethics Committees

Institution	Ethics Approval Number
The Second Xiangya Hospital of Central South University	(2023) Lun Shen Di (K587) Hao Orig. No.: (2023)伦审第(K587)号
Sir Run Run Shaw Hospital Affiliated to Zhejiang University School of Medicine	Shao Yifu Yiyuan Lun Shen 2023 Xie Di 0624 Hao Orig. No.: 邵逸夫医院伦审 2023 械第 0624 号
The Second Affiliated Hospital of Nanchang University	Qi Lin Shen [2022] Di (13) Hao-02 Hao Orig. No.: 器临审[2022]第(13)号-02 号
The Third People's Hospital of Chengdu	QX-2022-004-03
The Third Xiangya Hospital of Central South University	Kuai 23825 Orig. No.: 快 23825
Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology	[2022] Lun Shen Zi (183)-1 Hao Orig. No.: [2022]伦审字(183)-1 号
The Second Affiliated Hospital of Chongqing Medical University	2022 Nian Lun Shen (104)-1 Hao Orig. No.:2022 年伦审(104)-1 号

Online Resource 2. Inclusion / Exclusion Criteria

Inclusion criteria:

1) Age 18 to 80 years old.

2) Patients with symptomatic paroxysmal atrial fibrillation.

3) Be willing to participate in the clinical trial, receive follow-up as required by the protocol and sign the informed consent form.

Exclusion criteria:

1) Previous ablation of atrial fibrillation, atrial tachycardia or atypical atrial flutter.

2) Preoperative atrial tachycardia (≥ 30 s) and atypical atrial flutter.

3) Implantation of cardiac pacemaker, valve or pulmonary vein stent.

4) History of cardiac surgery.

5) Hemorrhagic stroke within 6 months.

6) Transient ischemic attack or ischemic stroke within 1 month.

7) History of myocardial infarction or percutaneous transluminal coronary angioplasty within 3 months.

8) Hypertrophic cardiomyopathy.

9) Rheumatic heart disease.

10) Moderate to severe aortic valve disease, moderate to severe mitral stenosis, and severe other valve disease.

11) Mental disorder or history of mental illness and inability to cooperate autonomously.

12) Left atrial anteroposterior diameter > 50 mm.

13) Left ventricular ejection fraction < 40%.

14) Left atrial thrombosis.

15) Diaphragmatic paralysis.

16) Lactating, pregnant or planning or potentially pregnant women.

17) Expected lifetime < 12 months.

18) Participating in other interventional clinical investigations.

19) Not suitable for inclusion in the clinical investigation by the judgment of the investigator.

Online Resource 3. Induction and Ablation Protocol

First, pulmonary vein isolation (PVI) was performed. Then, atrial fibrillation (AF) was induced by rapid atrial pacing (15-beat drive train at an amplitude of 10 mA and a pulse width of 2 ms; decrementing from 300 to 200 ms in steps of 10 ms with a 5-second pause between drive trains). If non-pulmonary vein (Non-PV) triggers were not identified, a sustained infusion of isoproterenol (ISP, 1–5 μg/min) was administered. Non-PV triggers were defined as the earliest site where ectopic beats initiated AF. Identified Non-PV triggers were subsequently ablated. Finally, induced atrial flutter and/or atrial tachycardia would be addressed with targeted linear ablation of the critical isthmus or focal ablation at the site of origin, as appropriate. During ablation, operators adjusted catheter contact based on real-time contact force feedback for procedural guidance, without modulating energy delivery.

Online Resource 4. ECG Examination Compliance

Visits	3-mo	6-mo	12-mo	Unscheduled
Examination, % (n) [a]				
12-lead ECG	62.1 (100)	59.0 (95)	0 (0)	90.0 (9)
24-h Holter	42.2 (68)	49.7 (80)	100.0 (158 [b])	40.0 (4)
Completion rate, % (n)	98.1 (158/161)	99.4 (160/161)	100.0 (158/158 [b])	100.0 (10/10)

[a] Some patients completed both 12-lead ECG and 24-h Holter examinations at the same visit.

[b] 158 patients (98.1%, 158/161) completed 12-month follow-up, with 100% completion in 24-h Holter examination.

ECG, electrocardiogram

Online Resource 5. Analysis of Atrial Flutter Recurrence Patterns

A detailed analysis of the six patients with atrial flutter (AFL) recurrence revealed two distinct patterns based on whether cavotricuspid isthmus (CTI) ablation was performed during the index procedure.

Group A: Recurrence despite prior CTI ablation (n = 3). Three patients presented with typical AFL (two also had concomitant atypical AFL) and all underwent CTI ablation during the index procedure. While AFL recurrence in these patients may reflect late conduction recovery, potentially attributable to reversible electroporation [1,2], it is noteworthy that among the 13 patients who underwent CTI ablation in our study, only one developed recurrent typical AFL (1/13, 7.7%). This rate is numerically lower than the 11.9% reported in a prior study of concomitant CTI ablation [1].

Group B: Recurrence without prior CTI ablation (n = 3). Three patients had no documented typical AFL at baseline and therefore did not undergo CTI ablation. Two of these three also experienced atrial fibrillation recurrence. In the absence of repeat mapping, it remains unclear whether these episodes represent iatrogenic results of left atrium ablation or previously concealed reentrant circuits unmasked after AF elimination [3].

Online Resource 6. Logistic Regression Analysis of Primary Effectiveness Failure (Effectiveness Cohort, n=161)

	Univariable analysis [a]			Multivariable analysis		
	N	**OR (95% CI)**	**P-value**	**N**	**OR (95% CI)**	**P-value**
Age (≥65 vs <65 years)	161	1.3 (0.6, 2.83)	0.50			
Age (≥75 vs <75 years)	161	1.22 (0.41, 3.6)	0.72			
Sex (female vs male)	161	0.71 (0.33, 1.56)	0.41			
BMI category (overweight vs normal) [b]	161	1.29 (0.56, 2.96)	0.54			
BMI category (obese vs normal) [b]	161	1.35 (0.33, 5.47)	0.67			
Years since first PAF episode (≥1 vs < 1)	155	0.97 (0.89, 1.05)	0.51			
Hypertension (yes vs no)	161	1.94 (0.62, 5.99)	0.25			
Diabetes (yes vs no)	161	1.24 (0.55, 2.77)	0.60			
Coronary artery disease (yes vs no)	161	0.64 (0.25, 1.61)	0.35			
Cerebrovascular disease (yes vs no)	161	1.2 (0.48, 2.96)	0.69			
Congenital heart disease (yes vs no)	161	4.23 (0.57, 31.27)	0.16	161	2.31 (0.23, 22.76)	0.48
Preoperative AAD	161	1.01 (0.46, 2.24)	0.96			

		Univariable analysis [a]			Multivariable analysis	
administration (yes vs no)						
Left atrial diameter (> 38 vs ≤38 mm)	161	2.47 (1.11, 5,47)	0.03	161	2.42 (1.02, 5.75)	0.045
LVEF (> 60 vs ≤60%)	161	0.62 (0.25, 1.56)	0.31			
Anesthesia mode (general or local anesthesia)	161	0.5 (0.22, 1.15)	0.10	161	0.49 (0.2, 1.22)	0.13
Contact force (> 5 & <10 vs ≤5 g)	161	0.96 (0.39, 2.32)	0.93			
Contact force (> 5 & <10 vs ≥10 g)	161	0.72 (0.19, 2.72)	0.63			
Concomitant atrial arrhythmia (yes vs no)	161	4.65 (1.7, 12.72)	0.003	161	4.03 (1.4, 11.59)	0.01
Combined Non-PV [c] ablation (yes vs no)	161	1.16 (0.45, 2.99)	0.75			

[a] If any statistically significant associations were observed at a *P*-value <0.20, the variables were considered for the multivariable model. In case of severe multicollinearity, only one variable was selected for the multivariable model.

[b] Three participants were underweight and were grouped with the normal participants.

[c] Non-PV indicates the ablation targets outside the pulmonary veins.

AADs, antiarrhythmic drugs; BMI, body mass index; LVEF, left ventricular ejection fraction; PAF, paroxysmal atrial fibrillation.

Online Resource 7. Adverse Events

Event Category	Events, n (%) [a]
Abdominal discomfort	6 (4.8)
Abnormal liver function	6 (4.8)
Acute appendicitis	1 (0.8)
Anorectal disorder	5 (4)
Atrial flutter	1 (0.8)
Atrial premature	1 (0.8)
Atrial tachycardia	1 (0.8)
Bleeding at puncture site	1 (0.8)
Bronchial asthma	1 (0.8)
Cervical spondylosis	1 (0.8)
Chronic kidney disease	2 (1.6)
Coronary artery disease	3 (2.4)
COVID-19 infection	15 (12.1)
Dizziness	2 (1.6)
Dysuria	2 (1.6)
Eye disorder	6 (4.8)
Fever	2 (1.6)
Gastritis	1 (0.8)
Gastrointestinal bleeding	2 (1.6)
Gout	2 (1.6)

Event Category	Events, n (%) [a]
Headache	1 (0.8)
Helicobacter pylori infection	1 (0.8)
Hepatic cyst	1 (0.8)
Hyperthyroidism	1 (0.8)
Hypokalemia	6 (4.8)
Moderate to severe mixed ventilatory dysfunction	1 (0.8)
Obstructive sleep apnea	1 (0.8)
Pain at puncture site	5 (4)
Peripheral joint disorder	3 (2.4)
Posterior circulation ischemia	1 (0.8)
Premature atrial and ventricular contractions	1 (0.8)
Prostatitis	1 (0.8)
Recurrent depressive disorder	1 (0.8)
Respiratory tract infection (non-COVID-19)	14 (11.3)
Rib fracture	1 (0.8)
Sinus arrest (vasovagal reaction)	1 (0.8)
Sinus bradycardia	3 (2.4)
Skin disorder	7 (5.6)
Sleep disorder	2 (1.6)
Subclinical hypothyroidism	2 (1.6)
Thyroid nodule	1 (0.8)

Event Category	Events, n (%) [a]
Urinary tract disorder	3 (2.4)
Uterine leiomyoma	1 (0.8)
Vaginal disorder	2 (1.6)
Ventricular premature	1 (0.8)
Vestibular neuronitis	1 (0.8)

[a] A total of 124 adverse events occurred in 71 patients.

Online Resource 8. Serious Adverse Events

Event Category	Events, n (%) [a]
Acute appendicitis	1 (3.4)
Atrial arrhythmias (atrial tachycardia and atrial flutter)	1 (3.4)
Atrial fibrillation	3 (10.3)
Atrial flutter	2 (6.9)
Atrial premature	1 (3.4)
Atrial tachycardia	1 (3.4)
Bilateral knee osteoarthritis	1 (3.4)
Cataract (left eye)	1 (3.4)
Cataract (right eye)	1 (3.4)
Chest pain	1 (3.4)
Coronary artery disease (stable angina)	1 (3.4)
Coronary spasm	1 (3.4)
COVID-19 pneumonia	1 (3.4)
Epiretinal membrane (bilateral eyes)	1 (3.4)
Epiretinal membrane (right eye)	1 (3.4)
Erosive gastritis	1 (3.4)
Hepatic insufficiency	1 (3.4)
Hypertension	1 (3.4)
Mixed hemorrhoids	1 (3.4)
Posterior circulation ischemia	1 (3.4)

Event Category	Events, n (%) [a]
Reflux esophagitis	1 (3.4)
Renal calculus with hydronephrosis and infection	1 (3.4)
Sepsis (respiratory infection associated with COPD, fatal)	1 (3.4)
Thyroid nodule	1 (3.4)
Tuberculous meningitis	1 (3.4)
Ventricular arrhythmias (ventricular premature, paroxysmal ventricular tachycardia)	1 (3.4)

[a] A total of 29 serious adverse events occurred in 25 patients.

References

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