Official Title: Clinical Application Evaluation of a Novel Pulsed Field Ablation System for the Treatment of Paroxysmal Atrial Fibrillation and Its Protective Effect on Left Atrial Function

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1. Research Objectives, Significance, and Necessity

1.1 Background and Necessity

Atrial fibrillation (AF) is the most common clinical arrhythmia, with an increasing incidence due to global population aging. It significantly impacts quality of life and is a major cause of cardiogenic stroke and heart failure. Catheter ablation, particularly radiofrequency catheter ablation (RFCA), is a first-line strategy for drug-refractory paroxysmal atrial fibrillation (PAF). However, conventional thermal ablation techniques (RFCA and cryoballoon ablation) rely on non-selective tissue damage, potentially injuring adjacent structures such as the esophagus, phrenic nerve, and pulmonary veins, leading to severe complications like atrial-esophageal fistula and pulmonary vein stenosis. Furthermore, extensive myocardial necrosis and secondary fibrosis can negatively impact left atrial function.

Pulsed Field Ablation (PFA) utilizes irreversible electroporation (IRE) to create nanoscale pores in cell membranes, selectively inducing apoptosis of cardiomyocytes without thermal or cryo effects. Its core advantage lies in its high tissue selectivity, allowing for durable pulmonary vein isolation (PVI) while maximally preserving surrounding critical structures. While preliminary studies show excellent immediate safety and efficacy, its potential impact on left atrial function remains a key scientific question. We hypothesize that PFA induces milder inflammation and more favorable tissue repair, better preserving left atrial mechanical function compared to thermal ablation.

1.2 Significance of Left Atrial Function Assessment

Left atrial function includes reservoir, conduit, and booster pump functions. Speckle-tracking echocardiography (STE) derived left atrial strain (LA Strain) is a sensitive tool for early detection of left atrial dysfunction and predicts AF recurrence and stroke. This study aims to comprehensively evaluate the clinical application value of PFA and its impact on left atrial function.

2. Research Goals

2.1 Overall Goal

To evaluate the efficacy of a novel PFA catheter in treating PAF, and to elucidate

its short- and long-term impacts on left atrial structure and function.

2.2 Specific Goals

(1) Complete a single-center, randomized, controlled clinical trial comparing the efficacy, safety, and impact on left atrial function of a novel PFA catheter versus traditional RFCA in symptomatic PAF patients.

(2) Primary Efficacy Endpoints: Immediate PVI success rate, and freedom from atrial arrhythmias (>30s) at 3 and 12 months post-procedure.

(3) Primary Safety Endpoints: Incidence of cardiac tamponade, thromboembolic events, vascular complications, atrial-esophageal fistula, pulmonary vein stenosis, phrenic nerve injury, coronary spasm, hemolysis, renal impairment, and muscle injury.

(4) Secondary Endpoints:

a. Changes from baseline at 1 week, 1, 3, 6, and 12 months in: LAVI, LVEF, E/A ratio, a'/e' ratio, LASr, LAScd, and LASct.

b. Quality of life score (EQ-5D-5L).

c. Serum biomarkers: Acute myocardial injury (troponin), inflammatory response (CRP, IL-6) at baseline, 6h, and 24h post-procedure.

d. Mechanistic markers: Fibrosis-related markers (Galectin-3 and soluble ST2) at baseline and 1, 3, 6, 12 months.

3. Main Research Content

(1) Multimodal Assessment of Left Atrial Function: TTE and STE to precisely evaluate left atrial volume and function.

(2) Single-center Clinical Trial:

Design: Prospective, single-center, randomized, controlled trial.

Subjects: Symptomatic PAF patients.

Follow-up: Pre-op, 1 week, 1, 2, 3, 6, and 12 months post-op (symptom assessment, 12-lead ECG, 24h Holter, echocardiography).

(3) Data Management and Statistical Analysis: SPSS software will be used for statistical processing, including descriptive statistics, t-tests, non-parametric tests,

chi-square tests, and propensity score matching.

4. Project Innovations and Key Technical Issues

4.1 Innovations

(1) Conceptual Innovation: Expanding the treatment goal from traditional rhythm conversion to the synergistic optimization of electrophysiological stability and mechanical functional integrity, establishing "protection and improvement of left atrial function" as a key evaluation metric.

(2) Research Model Innovation: Combining multimodal imaging (ultrasound) with serum biomarkers to construct a comprehensive left atrial function evaluation system.

4.2 Key Technical Issues to be Solved

(1) Real-time monitoring of precise catheter-tissue contact and stability using ICE guidance.

(2) Establishing a standardized left atrial function analysis workflow (blinded core lab analysis).

(3) Elucidating the underlying mechanism of PFA protecting atrial function via serum fibrosis markers.

5. Research Methods and Technical Route

5.1 Patient Selection and Inclusion/Exclusion Criteria

Patients are randomized 1:1 to the PFA ablation group or the RFCA group. Perioperative management, anesthesia, and follow-up protocols are consistent between the two groups.

Inclusion Criteria:

(1) Age >= 18 years.

(2) Symptomatic paroxysmal atrial fibrillation (AF duration < 7 days).

(3) Ineffective treatment with one or more antiarrhythmic drugs (e.g., propafenone, sotalol, amiodarone).

(4) Discontinued antiarrhythmic drugs for at least 5 half-lives before the procedure.

(5) Willing to receive PFA treatment and postoperative follow-up, and able to sign informed consent.

Exclusion Criteria:

(1) Previous radiofrequency catheter ablation (RFCA) for atrial fibrillation.

(2) Presence of a cardiac pacemaker or post-left atrial appendage closure.

(3) Thrombocytopenia (PLT < 80×10^9/L) or contraindications to anticoagulation.

(4) Left atrial anterior-posterior diameter > 55 mm (by TTE, parasternal long-axis view).

(5) Left atrial (or left atrial appendage) thrombus (confirmed by TEE or MSCT).

(6) Severe structural heart disease (e.g., hypertrophic obstructive cardiomyopathy, severe valvular heart disease) or uncontrolled heart failure (NYHA class III or IV).

(7) Thyroid dysfunction (e.g., uncontrolled hyperthyroidism).

(8) Severe hepatic or renal impairment (AST or ALT >= 3 times upper limit of normal; SCr > 3.5 mg/dl or Ccr < 30 ml/min).

(9) History of stroke within the past 6 months.

(10) History of surgery within the past 3 months.

(11) Pregnant women.

(12) Life expectancy < 12 months.

5.2 Preoperative Baseline Data Collection

General data (history, physical exam, comorbidities, medications), inflammatory markers, serum biomarkers (troponin, CK, BNP, NT-proBNP), ECG (12-lead, 24h Holter), and Echocardiographic indicators (LAVI, LVEF, E/A, a'/e', LASr, LAScd, LASct).

5.3 Surgical Protocol

(1) PFA Treatment System: Composed of a PFA generator and a pulsed ablation catheter (Tianjin Yingtailiankang Medical Technology Co., Ltd.).

(2) Preoperative Preparation: Standard sterile preparation, Seldinger technique for venous access (right femoral vein), placement of sheaths (8F, 11F, 8.5F transseptal sheath). ICE catheter guidance for transseptal puncture. Heparinization (100 U/kg).

(3) Ablation Procedure: Under 3D mapping system guidance, circumferential PFA

isolation of pulmonary veins. ICE is used to assist catheter positioning and contact assessment. Sufentanil and dexmedetomidine for analgesia and sedation. Verification of PVI and PV entrance block.

(4) Grouping and Blinding: Assessor-blinded. The electrophysiologist performing the procedure is aware of the grouping, but personnel performing postoperative imaging analysis, ECG interpretation, data management, and statistical analysis are blinded.

5.4 Postoperative Follow-up

Follow-up time points: 1 day, 1 week, 1 month, 2 months, 3 months, 6 months, and 12 months post-procedure. Atrial arrhythmias occurring within 90 days post-procedure (blanking period) are not counted as recurrence.

(1) Clinical symptoms.

(2) Arrhythmia monitoring (12-lead ECG, 24h Holter).

(3) Serum biomarkers (myocardial injury, inflammation, coagulation, BNP/NT-proBNP).

(4) Imaging indicators (TTE, STE for LASr, LAScd, LASct).

(5) Quality of Life (EQ-5D-5L questionnaire).

5.5 Data Collection

Electronic Case Report Forms (eCRF) will be used.

Baseline data.

Perioperative data (procedure time, fluoroscopy time, transseptal puncture attempts, PFA parameters, immediate PVI success rate, adverse events).

Follow-up data (primary efficacy endpoints, secondary efficacy endpoints, safety endpoints).

5.6 Statistical Analysis

Sample size calculation: Based on a 12-month freedom from atrial arrhythmia survival rate (RFCA ~70%, PFA assumed ~85%, absolute advantage 15%, α=0.05, β=0.2, 10% loss to follow-up), approximately 110 patients per group are needed,

total sample size = 220.

SPSS will be used. Kaplan-Meier survival analysis for primary efficacy endpoint. Cox proportional hazards regression model for predictors of AF recurrence.

6. Project Timeline (36 Months)

Year 1 (Months 1-12): Preparation, ethics approval, team building, PFA training, standardized data collection. Patient enrollment (target 60% completion) and initial follow-ups (1 week, 1 month, 3 months).

Year 2 (Months 13-24): Core follow-up execution (3-month and 6-month follow-ups). Complete all patient enrollment. Database cleaning and formal interim analysis.

Year 3 (Months 25-36): Long-term follow-up (12 months). In-depth data mining and final statistical analysis. Writing reports, paper submission, and project acceptance preparation.

7. Expected Outcomes and Economic/Social Benefits

Expected Outcomes:

Clinical research report on PFA application evaluation and standardization.

Standardized left atrial function assessment protocol.

Theoretical mechanism elucidation of PFA protecting atrial function.

Academic outputs:

8 high-level papers (at least 2 domestic), 2 domestic patents, training 1 PhD and 2 Master's students.

Economic/Social Benefits:

PFA technology is expected to reduce severe complications (esophageal fistula, phrenic nerve injury), improve patient quality of life, and reduce medical burden (estimated saving 30,000-50,000 RMB per patient).

8. Research Foundation and Conditions

The team has over 20 years of experience in AF catheter ablation, completing over 10,000 RFCA procedures. Pre-clinical PFA animal experiments and preliminary human feasibility studies have been completed. The hospital has 4 digital catheterization labs, 3D mapping systems, ICE, and STE. Over 2,000 AF patients are

treated annually. The cooperating enterprise (Yingtailiankang) has applied for 30 national invention patents regarding PFA catheters and pulse output algorithms.

9. Risk Analysis and Countermeasures

9.1. Technical Risks: PFA is novel; long-term efficacy and optimal parameters need validation. Countermeasures: Strict preclinical basis, real-time ICE monitoring, standardized STE analysis, core lab blinded analysis.

9.2. Personnel Risks: Dependence on key experts. Countermeasures: AB 角 mechanism (backup roles), systematic training, performance incentives.

9.3. Market Risks: Competition from international giants (Medtronic, Boston Scientific). Countermeasures: Focus on "left atrial function protection" differentiation, accelerate localization, establish early clinical trust.

9.4. Policy and Regulatory Risks: Long NMPA registration cycle. Countermeasures: Early communication with NMPA, professional CRO cooperation.

9.5. Institutional/Cooperation Risks: Hospital-enterprise coordination, funding security. Countermeasures: Detailed contracts, joint management group, milestone-based funding, financial due diligence.