Pulmonary Antrum Radial-Linear Ablation for Paroxysmal Atrial Fibrillation: Interim Analysis of a Multicenter Trial

Running title: Zhao et al.; Radial-linear ablation for atrial fibrillation

Xue Zhao, MD, PhD; Jiayou Zhang, MD; Jianqiang Hu, MD; Dening Liao, MD
Yinxiang Zhu, MD; Xiang Mei, MD; Jun Sheng, MD; Fang Yuan, MD; Yanping Gui, MD
Wenliang Lu, MD; Li Dai, MD; Xingui Guo, MD; Yawei Xu, MD; Yanzhou Zhang, MD
Ben He, MD; Zhengu Liu, MD, PhD

1Division of Cardiac Electrophysiology, Translational Medicine Center, Changzheng Hospital, Second Military Medical University; 2Dept of Cardiology, Huadong Hospital, Fudan University; 3Dept of Cardiology, Shanghai Tenth People’s Hospital, Tongji University; 4Dept of Cardiology, Renji Hospital, Shanghai Jiao Tong University, Shanghai, China; 5Davis Heart & Lung Research Institute & Division of Cardiovascular Medicine, Ohio State University Medical Center, Columbus, OH

Correspondence:
Xue Zhao, MD, PhD
Division of Cardiac Electrophysiology
Translational Medicine Center, Changzheng Hospital
Second Military Medical University
415 Fengyang Road
Shanghai 200003 China
Tel: 021-818-85294
Fax: 021-635-20020
E-mail: xuezhao88@yahoo.ca

Xingui Guo, MD
Department of Cardiology
Huadong Hospital
Fudan University
221 West Yanan Road
Shanghai 200040 China
Tel: 021-624-85997
E-mail: guoxinggui@yahoo.cn

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Abstract:

**Background** - Substrate abnormality in pulmonary vein (PV) antrum plays a critical role in mechanism of atrial fibrillation (AF). The present study compares the strategy of PV antrum radial-linear (PAR) ablation to encircling PV isolation for paroxysmal AF.

**Methods and Results** - A total of 86 patients with paroxysmal AF were randomly assigned to PAR ablation group or PV isolation group. The average procedure time was 161 ± 21 min in PAR ablation group and 199 ± 39 min in PV isolation group (P<0.01). The average fluoroscopy time was 25±5 min in PAR ablation group and 32±9 min in PV isolation group (P<0.001). At 14 (15-12) months of follow-up after single procedure, 31 of 42 (74%) patients in PAR ablation group and 22 of 44 patients (50%) in PV isolation group had no recurrence of AF off antiarrhythmic drug (AAD) (P=0.0249); and 36 of 42 patients (86%) in PAR ablation group and 26 of 44 patients (59%) in PV isolation group had no recurrence of AF with AAD (P=0.006). In addition, PAR ablation resulted in greater reduction of LA diameter than encircling PV isolation. Multivariable Cox regression analysis showed that only ablation strategy was independently associated with AF recurrence (HR, 0.31; 95% CI: 0.12-0.78; P=0.013). No major adverse event related to the procedures occurred.

**Conclusions** - This study suggests that PAR ablation is a potentially effective strategy for treatment of paroxysmal AF warranting further investigation.

**Clinical Trial Registration Information** - [www.chictr.org](http://www.chictr.org); Identifier: ChiCTR-TRC-11001191.

**Key words:** atrial fibrillation; catheter ablation; pulmonary vein
Curative ablation of atrial fibrillation (AF) serves two important purposes: elimination of all potential triggers and modification of atrial substrate. Although pulmonary vein (PV) isolation remains essential for most ablation procedures, the role of substrate modification has been increasingly emphasized. Although the triggers and substrate may play a different role in individual patients, considerable experimental and clinical evidence suggests that as AF progresses from paroxysmal to persistent, the atrial substrate becomes increasingly abnormal and may be a dominant factor for maintaining AF. PV isolation has been the main ablation strategy for AF ablation, however, its long-term outcome remains suboptimal. Although a significant volume of reports have claimed procedural success rates of 76% to 91%, carefully monitored clinical trials performed by experienced operators have indicated a true success rate of 66%4-5. It is therefore important to develop alternative strategies to achieve an optimal long-term outcome for AF ablation.

Encircling PV ablation or left atrial (LA) linear ablation without complete PV electrical isolation has been reported to produce a long term benefit of maintaining sinus rhythm for the majority of patients with paroxysmal or even persistent AF6-10. The areas with complex fractionated atrial electrograms (CFAEs) have been reported to potentially represent AF substrate sites and target sites for AF ablation. Multiple reentrant circuits with or without “mother rotors” in the atrial area have been proposed to be the substrate for AF11-12, alternatively, the maintenance of AF needs a critical number of circulating wavelets, each of which requires a critical excitable mass of atrial tissue. The mechanism of Maze procedure is believed to be the creation of multiple strategically placed incisions across the atria to reduce the
critical excitable mass\textsuperscript{13}.

We have proposed a novel strategy of PV antrum radial-linear (PAR) ablation as an organized modification of substrate to effectively interrupt the possible mechanisms for AF initiation and/or maintenance\textsuperscript{14}. This prospective, multicenter, randomized study was designed to compare the efficacy and safety of the new approach with the conventional PV isolation in patients with paroxysmal AF.

**Methods**

**Patient Enrollment**

The study protocol was approved by Shanghai Municipal Health Bureau and the Institutional Review Board and Ethics Committee at each of the 4 centers in Shanghai, China. All patients enrolled in the study provided written informed consent. Enrollment required at least 3 symptomatic AF episodes (at least 2 episodes verified by electrocardiogram) within 6 months before randomization, and did not respond to at least 1 antiarrhythmic drug (AAD) (class I or III). Exclusion criteria included any one of the following conditions: 1) patients with AF of more than 30 days in duration; 2) an ejection fraction of less than 40%; 3) previous AF ablation; 4) documented LA thrombus; 5) myocardial infarction within 6 months; 6) thromboembolic event in the previous 12 months; 7) severe pulmonary disease; 8) a prior valvular cardiac surgical procedure; 9) contraindication to antiarrhythmic or anticoagulation medications; and 10) LA posterioanterior diameter $>50$ mm in the parasternal long axis view (Figure 1).

The enrollment occurred between March 7, 2011, and June 12, 2011, with the last
follow-up on June 18, 2012. In this randomized trial, investigators used a computer program to assign each study participant to one of the two groups by a block randomization.

**Electrophysiology Study and Ablation Procedure**

Eighty six consecutive patients with paroxysmal AF were enrolled in this study. AAD were discontinued for a period of at least 5 half-lives prior to the procedure. Amiodarone was replaced with propafenone for at least 3 months before randomization except 1 patient in PAR ablation and 2 in PV isolation. Therapeutic anticoagulation with heparin was achieved for at least 3 days before the procedure. The procedure was performed under sedation with midazolam and fentanyl citrate. A 6F multipolar electrode catheter was placed into the coronary sinus (CS) via the left subclavian vein. Right femoral vein was used for transseptal access and ablation. Two separate transseptal procedures were made with 8F sheaths (SL1, St. Jude Medical Inc, St. Paul, MN). A 20-mm, decapolar Lasso catheter (Lasso, Biosense-Webster, Baldwin Park, CA) was used for mapping in PV areas. After transseptal access, intravenous heparin was administered. Following transseptal puncture, PV venography was performed with selective delivery of contrast into each of the PV ostia using a multipurpose angiography catheter at LAO 45° for left PVs and RAO 45° for right PVs. A 3D geometry of LA was reconstructed with CARTO system (Carto XP Navigation System, Biosense-Webster, Diamond Bar, CA). No CARTO-merge system was used in the present study.

Before ablation, a standardized atrial pacing protocol was conducted to determine AF inducibility in both groups as previously described 15. In brief, atrial burst pacing was performed in decrements from a cycle length of 250 ms down to refractoriness from the distal CS
and LA appendage. The minimum 1:1 atrial capture cycle length was identified and used to determine the pacing frequency. A train of burst pacing with $2 \times$ thresholds, pulse width of 2 ms, and duration of 10 s was delivered for AF induction. A total of 10 attempts of burst pacing were made with 5 attempts from CS and 5 from LA appendage respectively. Irregular atrial tachyarrhythmia of $\geq 30$ s was defined as inducible AF.

Radiofrequency energy was delivered to the PV antrum in the patients at a maximum temperature of 43°C, power between 25-35 W and 17 ml/min saline flow for 30 s at each lesion site with a 3.5 mm irrigated-tip ablation catheter (ThermoCool, Biosense-Webster). If for some reason the voltage reduction criteria were not met with the power of 35 W, the saline flow was increased up to 25 ml/min. During PAR ablation, if energy delivering inside PV ostium was necessary, the power was limited to 15-20 W. A successful lesion creation at each point was considered to be completed when the local bipolar voltage was decreased by 90% or to less than 0.05 mV. For patients with documented atrial flutter (AFL), the cavotricuspid isthmus was also ablated with an end point of bidirectional conduction block.

**PAR Ablation**

The ablation lines were designed based on the morphology of PVs on CT angiography before the procedure and PV venography during the procedure (Figure 2 A, B, C and D). The ablation was targeting local double potentials (the combined potentials from PV and LA) in PV antrum, which were usually characterized by atrial electrograms with deflections over 3 phases and a duration of $\geq 50$ ms or CFAEs if AF was present. All the radial-linear lesions were created with radiofrequency ablation (with the energy settings as described above) from PV ostium to the
PV-LA junction, where no PV potential was present. Each PV ostium was viewed as a clock and the ablation lines were marked as line 1, 2 and 3 separately. In the left superior PV (LSPV), line 1 started at about 2 o’clock, the anterosuperior wall of LSPV ostium, along the upper edge of left appendage to the anterosuperior wall; line 2 started at 12 o’clock towards the superior wall, and line 3 started at 9 o’clock towards the posterior wall. In the left inferior PV (LIPV), line 1 started at 3 o’clock towards the anterior wall along the lower edge of left appendage, line 2 started at 6 o’clock towards the inferior wall, and line 3 started at 9 o’clock towards the posterior wall. In the right superior PV (RSPV), line 1 started at 9 o’clock towards the anterior wall, line 2 started at 12 o’clock towards the superior wall, and line 3 started at 3 o’clock towards the posterior wall. In the right inferior PV (RIPV), line 1 started at 9 o’clock towards the anterior wall, line 2 started at 6 o’clock towards the inferior wall, and line 3 started at 3 o’clock towards the posterior wall. The completeness of linear lesions was confirmed by moving the ablation catheter back and forth along the ablation lines to check the local voltage for two times, if necessary pacing maneuvers were performed to assess line completeness.16

The procedural end point was the completion of all the designed ablation lines, conversion of AF to normal sinus rhythm, and AF becoming non-inducible with the atrial burst pacing protocol as described above. If AF was still inducible after the designed lines were completed, 1 or 2 lines in each PV would be extended for less than 5 mm towards distal PV, or 1 more line created in each PV antrum. Before and after ablation, the PV electrograms were recorded with Lasso catheter and or ablation catheter.
PV Isolation

Encircling PV ablation was performed as previously described\textsuperscript{17}. Septal and lateral continuous circular lesions around the ipsilateral PVs were created about 10 mm posterior and 5 mm anterior from the angiographically defined PV ostia. The procedural end point was PV bidirectional conduction block identified with Lasso catheter at least 30 min after ablation during sinus rhythm. LA roof line and mitral isthmus line were created if macro-reentrant atrial tachycardia occurred during the procedure.

Follow-up Protocol

After randomization, patients in PAR ablation group received radial-linear ablation in PV antrum, and patients in PV isolation group received encircling PV ablation. Patients were followed up for at least 12 months. Immediately after the procedure, all the patients were anticoagulated with warfarin with an international normalized ratio (INR) of 2-3, and AAD was given for 3 months (then discontinued), followed by metoprolol if indicated clinically. AAD was re-started for the patients with recurrent AF at the time of first recurrence in both groups and continued during the follow up. Amiodarone was administered only if propafenone was ineffective (Supplement Table 1). Electrocardiograms were obtained at every follow-up visit. After a 3-month blanking period, the patients were evaluated with an event ECG recorder (Prince 180B, China) every 3 months for three days each time until the final visit. By the end of three days of monitoring each time, the patient was evaluated by the follow up doctor. 24-hour Holter monitoring was conducted at 6 months and the final visit for all patients. The patients were also instructed to check and record their pulses for regularity and rate every day (at least five days a
week) for three min each time and whenever they had symptoms (including palpitations, shortness of breath, chest discomfort, fatigue, or dizziness) suggestive of AF.

CT angiography of LA was obtained for all patients during sinus rhythm before the procedure and 6 months after the procedure. The maximal diameter of each ostium was measured semi-automatically from the outer edges of the individual vein on CT images at the level of the ostium. Transthoracic echocardiography was obtained in sinus rhythm for all patients before the procedure and at the final visit. Ejection fraction (EF) was calculated using the modified Simpson’s method from apical four and two chamber views. LA diameter was determined in the parasternal long axis view.

All rhythm tracings were interpreted in a blinded fashion by two physicians who did not participate in the study. Recurrent AF was defined as an occurrence of AF (including AFL and atrial tachycardia (AT)) with a duration of at least 30 seconds documented by an ECG or device recording system after the 3-month blanking period until the final visit following the procedure.

Major adverse events were defined as occurrence of one of the followings: cardiac tamponade, significant PV stenosis (at least 50% reduction of PV diameter over the baseline), esophageal injury, bleeding requiring blood transfusion, pericardial effusion requiring pericardiocentesis, phrenic nerve paralysis, stroke, and acute coronary artery occlusion.

The primary end point was the proportion of patients free of recurrent AF 3 months after ablation. The secondary end points consisted of time to AF recurrence, complications and other adverse effects, change in LA dimensions and left ventricular ejection fraction.
Statistics

The primary efficacy analysis was based on an intention-to-treat analysis of all randomized patients. With an estimated success rate of 90% for PAR ablation and 70% for PV isolation, 76 patients should have been enrolled for each group, allowing for 5% dropout, for a power of 80% with Chi-Square test with 0.05 as significance level. The preplanned interim analysis was conducted when it showed the predictive probability of success to be 97.5%. The trial was stopped (although follow-up was continued) when this analysis showed the predictive probability of success to be 99%. Based on the updated study results of 86 patients, the probability of superiority was 97.51% for single procedure off AAD and 99.4% for single procedure with AAD.

Continuous variables were reported as mean ± standard deviation or median. Data for pre-ablation and post-ablation was performed with paired-sample t-test. Comparison between groups was performed with two independent sample t-test or Mann-Whitney U test (for non-normally distributed data). The categorical variables were reported as number and percentage and were analyzed using Chi-Square test. The absolute change in LA diameter among subgroups was calculated using the formula (post-ablation – pre-ablation) and analyzed using multiple comparisons in ANOVA (Dunnett’s T3). Kaplan-Meier curves were produced to obtain freedom from AF probabilities over time with one month interval and log-rank test was used for comparison. Multivariable Cox regression analysis was used to identify significant predictors of AF recurrence with consideration of clinically relevant covariates and usage of discrete time option. Variable candidates include age, gender, left ventricular ejection fraction,
LA diameter, AF duration, hypertension, diabetes mellitus, ablation strategy (PAR ablation or PV isolation), and procedure time. Variables with a p <0.05 were entered into the model and no formal test of PH assumption was applied. All tests were two-tailed and statistical significance was established at P <0.05. Analyses were performed using SPSS version17.0.

Results

Patient Characteristics

A total of 86 patients, 54 men (63%) and 32 women (37%), with the average age of 64.1±6.1 years, were enrolled. Forty-two and 44 patients were randomized to PAR ablation and PV isolation groups, respectively. The clinical characteristics of patients in both groups were shown in Table.

Procedural Results

All the patients in both groups had inducible AF prior to ablation. In PAR ablation group, the designed ablation lines were completed and AF was non-inducible in all 42 patients. Of them, 3 radial-linear lesions were performed in each PV in 38 patients; and 4 radial-linear lesions were created in LSPV and RSPV in 4 patients. One or 2 linear ablation lesions were extended less than 5 mm into PV ostium where CFAEs were recorded during AF episode in 3 patients, of whom AF episode was terminated and became not inducible. In 1 patient, ablation was performed in LA appendage to eliminate a focal trigger. In addition, the cavotricuspid isthmus linear ablation was performed on 2 patients with bidirectional block. The representative CARTO images for the ablation lesions were shown in Figure 3 A, B, C and D. After PAR
ablation, no PVs were incidentally isolated, and there were persistent PV potentials in the PVs. Delayed PV spikes might be found sometimes adjacent to ablation lines but not remote from the lines. The timing from stimulus to PV spikes was not prolonged during pacing from the coronary sinus. In the control group, PV isolation was achieved in all 44 patients with LA roof line in 2 patients, mitral isthmus line in 3 patients, and cavitricuspid isthmus line in 1 patient. No burst pacing was used to assess the effect of PV isolation. Therefore, the acute procedural success as defined was 100% in each group.

The average procedure time was 161 ± 21 min in PAR ablation group and 199 ± 39 min in PV isolation group (P<0.01). The average fluoroscopy time was 25 ± 5 min in PAR ablation group and 32 ± 9 min in PV isolation group (P<0.001). During follow-up, 2 (5%) patients underwent a second procedure in PAR ablation group, in whom no PV isolation was found before the redo procedure. One patient accepted PV isolation and the other underwent a focal ablation at LA appendage. Four (9%) patients had repeat procedure in PV isolation group, and PV reconnection was found in all these 4 patients during the redo procedure. There was no significant difference in patients with repeat procedure between the two groups (P=0.43).

**Effectiveness Outcome Analyses**

The median (interquartile range) for follow-up times was 14 (15-12) months in both groups. Kaplan-Meier curves for the effectiveness outcomes were shown in Figure 4. At 14 months after a single ablation procedure off AAD, 31/42 patients (74%) in PAR ablation group were free of AF (including AFL and AT) as compared to 22/44 (50%) in PV isolation group (P=0.0249) (Figure 4 A). At 14 months after a single ablation procedure with AAD, 36/42 patients (86%)
in PAR ablation group were free of AF as compared to 26/44 (59%) in PV isolation group
(P=0.006) (Figure 4 B). There were 5 patients free of AF in PAR ablation and 4 patients in PV isolation after a single ablation procedure on AAD. In PAR ablation group, 6 (14%) patients had recurrent AF on AAD, including 3 patients with AF, 2 with AFL and 1 with AT. In PV isolation group, 18 (41%) patients developed recurrent AF on AAD, including 16 patients with AF, 1 with AFL and 1 with AT (Figure 5). Multivariable Cox regression analysis demonstrated that only ablation strategy was identified to be independently associated with AF recurrence (HR, 0.31; 95%CI: 0.12-0.78; P=0.013).

LA Dimension
Overall, the LA diameter was significantly decreased in patients who received PAR ablation as compared to PV isolation (Figure 6 A). Subgroup analysis showed that the decrease in LA diameter occurred predominantly in patients without recurrent AF, and was more prominent in PAR ablation than PV isolation (Figure 6 B). Left ventricular ejection fraction (EF) was not significantly different post-ablation from pre-ablation in patients with PAR ablation (71.4 ± 6.2 vs 70.7 ± 4.6, P = 0.16) and PV isolation (71.8 ± 5.8 vs 70.7 ± 5.0, P = 0.16).

Adverse Events
No major adverse events including cardiac tamponade, significant PV stenosis (more than 50% narrowing), phrenic nerve paralysis, procedure-related transient ischemic attack or stroke, or atrioesophageal fistula were observed. The diameter of each PV before and after ablation was listed in Supplement Table 2. A sterile pericardial effusion developed within 2 days after ablation in 2 of 86 patients (2%), 1 in each group, but did not require pericardiocentesis. In
addition, transient sinus bradycardia occurred during ablation in 7 patients in PAR ablation group and 4 patients in PV isolation group (P > 0.05) (All these patients did not require placement of a permanent pacemaker).

Discussion

This was the first prospective multicenter randomized study showing that the novel PAR ablation was a simple, safe and effective ablation strategy for the treatment of paroxysmal AF. The new approach appeared to be more effective than PV isolation, suggesting that an organized modification of substrate in PV antria is important in eliminating the initiation and /or maintenance of AF. Indeed, multiple random propagating wavelets, autonomic innervations, ligament of Marshall, CFAE areas and even potential arrhythmogenic ostial foci, have been observed in the antrial areas as possible mechanisms for the initiation and perpetuation of AF³. All of these important mechanisms could be interrupted with PAR ablation.

The present study demonstrated the superiority of PAR ablation over PV isolation in patients with paroxysmal AF with regard to the maintenance of sinus rhythm and improvement in LA remodeling. At 14 months of follow-up, a success rate of 74% was achieved with PAR ablation after a single procedure off antiarrhythmic medication in patients with paroxysmal AF. Multivariable Cox regression analysis showed that only ablation strategy was the independent predictors for AF recurrence. Wilber and colleagues recently reported that PV isolation resulted in a success rate of 66% in patients with paroxysmal AF at the end of 9-month follow-up⁵, and PV antrum isolation achieved a success rate of 57% in patients mostly with
paroxysmal AF after a single ablation procedure at 2 years of follow-up. The outcomes of these studies were comparable to that observed in the patients with paroxysmal AF and PV isolation in the present study. Interestingly, we have also observed that PAR ablation, not PV isolation, resulted in a significant decrease in LA diameter. These data were consistent with the previous report, and supported the conclusion that maintenance of sinus rhythm was one of the key determinants for reduction in LA size. In addition, no significant complications occurred to the patients receiving the new ablation procedure, suggesting that it was at least as safe as PV isolation.

PAR ablation was a completely different strategy for AF ablation from PV isolation. The radial-linear ablation was designed to achieve an organized substrate modification in PV antria, while encircling PV ablation was intended to electrically isolate the triggers in PVs with some impact on the substrate. Another ablative strategy for substantial substrate modification was to target the CFAEs. However, this technique could involve an extensive amount of ablation in almost the entire atrium without a specific pattern anatomically. On the other hand, PAR ablation had a unified ablation pattern for all the patients with minimal individual variability, making it much easier to go through the procedure technically with shorter procedure time and less radiation exposure than PV isolation. In addition, the electrical connections from the LA to the PVs were preserved in the regions between two neighboring linear lesions during PAR ablation, thus, PV was not isolated electrically. Therefore, Lasso catheter might not be necessary, and a single transseptal puncture could be enough for the procedure.

The double potentials were the major targets of PAR ablation on the designed ablation
lines, which were usually characterized by atrial electrograms with deflections over 3 phases and duration of over 50 ms. During episodes of AF, CFAEs inside the PV ostia may suggest the existence of AF nests\textsuperscript{21}, We observed that if CFAEs were recorded along any of the linear lesions, a less than 5 mm extension of ablation into the PV ostium sometimes terminated AF, which was consistent with previous observation\textsuperscript{21}, suggesting that it usually needed more current delivering at the PV ostia.\textsuperscript{22} It had been reported that linear lesions were often arrhythmogenic due to the existence of gaps along the ablation lines\textsuperscript{23}, which could be identified with pacing capture test on the ablation lines\textsuperscript{16}. With the technique described in the present study, all the linear lesions were short that could not take long time to check the ablation lines to confirm the line completeness.

The present study did not explore the mechanism(s) for PAR ablation. However, the favorable clinical outcome of the present strategy could be related to multiple factors. The substrates for AF initiation and/or maintenance were frequently located within the PV antria\textsuperscript{3}. Usually with a total of 12 linear lesions, the radial-linear ablations could well cover both PV antral areas. Since the PV antrum was divided longitudinally by the radial-linear lesions into small regions, any current impulse would be unlikely conducted circumferentially, and thus, the localized reentrant circuits could be interrupted. The multiple random propagating wavelets could not be produced due to the loss of the structure integrity and decreased critical tissue mass in PV antrum as that in the surgical Maze procedure\textsuperscript{13}. Focal electrical discharges along the linear lesions would be eliminated as well in PV antrum or even in the ostium. In addition, the four major LA autonomic ganglionic plexi (GP) and axons were possibly targeted as well during
the creation of the ablation lesions, especially the superior left GP by line 2 and line 3 in LSPV, inferior left GP by line 2 and 3 in LIPV, anterior right GP by line 1 in RSPV and line 1 in RIPV, inferior right GP by line 2 and line 3 in RIPV. The ligament of Marshall could be interrupted with ablation line 1 and line 2 in LIPV as well as line 1 in LSPV. The GP were consistently located within the areas of CFAEs\(^{24}\) that were the main target of the radial-linear ablation as well as double potentials. In addition, ablation of the nerve cell bodies, by targeting the GP, might permanently denervate the PVs\(^ {25}\).

**Study Limitations**

The present study was focused on investigating the efficacy and safety of PAR ablation in the treatment of paroxysmal AF. Further study is needed to evaluate the therapeutic value in the patients with persistent and/or chronic AF. The follow-up was relatively short; however, a longer follow-up is ongoing for these patients. The PAR ablation was primarily performed within PV antria. It was not clear if it could be a valuable approach to the treatment of AF with its origination outside the PVs, such as right atrium or CS.

**Conclusion**

In the present study, we described a simple, safe, and effective new method for paroxysmal AF ablation with shorter procedure time and less radiation exposure than PV isolation. It required only a single transseptal puncture without the unnecessary use of Lasso catheter. The findings suggest that PAR ablation is a potentially effective strategy for treatment of paroxysmal AF warranting further investigation.
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Conflict of Interest Disclosures: None.

References:


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Table. Baseline Patient Characteristics

<table>
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<th>PV isolation (n=44)</th>
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*left ventricular ejection fraction
†For continuous variables, comparison by t test; For categorical variables, comparison by Chi-square test.
‡By Mann-Whitney U test.

Figure Legends:

Figure 1. Patient enrollment and randomization.

Figure 2. Design of ablation lines using anatomy and mapping with electrogram for PAR ablation. A and C, right PV antrum with RSPV and RIPV; B and D, left PV antrum with LSPV,
LIPV and LAA. **Up panel**, Anatomy-guided mapping with CT angiography of PVs. The red lines indicated linear ablation lesions. The ablation started from PV ostium and ended at the PV-LA junction. **Lower panel**, Electrogram-guided mapping with schematic image of PV antrum. Double potentials (PV potential combined with LA potential) or complex fractionated atrial electrograms (CFAEs) were targeted by ablation. The ablation started from PV ostium and ended at the site when only local LA potential was recorded. The black lines indicated the linear ablation lesions. Three linear lesions were marked as 1, 2 and 3 for each PV. PV, pulmonary vein; LA, left atrium; RSPV, right superior PV; RIPV, right inferior PV; LSPV, left superior PV; LIPV, left inferior PV; LAA, left atrial appendage.

**Figure 3.** Three dimensional map of the LA in different views using CARTO system. PV ostia were highlighted with white circles. Red dots indicated the linear ablation lesions. **Up panel**, a case with three radial-linear lesions created in each PV. **A**, the ablation pattern in left PV antrum; **B**, the ablation pattern in right PV antrum. **Lower panel**, a case with four radial-linear lesions created in LSPV and RSPV, and three radial-linear lesions created in LIPV and RIPV. **C**, the ablation patterns in both left and right PV antrum. **D**, the ablation pattern in right PV antrum.

**Figure 4.** Kaplan-Meier curves showing arrhythmia-free cases in patients (Pts) with paroxysmal AF. All patients in both groups survived the entire follow up. **A**, the patients free of AF after single ablation procedure off antiarrhythmic drug (AAD); **B**, the patients free of AF after single ablation procedure with AAD.
Figure 5. Flow chart of follow-up.

Figure 6. Comparison of LA dimension between PAR ablation group and PV isolation group. A, LA diameter was measured in the parasternal long axis view. *P<0.05 as compared with PV isolation group post ablation; B. The absolute change in LA diameter was calculated using the formula (post-ablation – pre-ablation). *P<0.01 compared with non-recurrent patients in PV isolation. X±SD.
204 pts assessed for eligibility

116 pts excluded
  75 pts did not meet inclusion criteria
    10 pts <3 AF episodes in 6 months before enrollment
    12 pts respond to AAD
    8 pts AF lasting longer than 30 day
    7 pts EF<40%
    6 pts previous AF ablation
    5 pts ischemic stroke
  18 pts unable to travel for follow-up
  9 pts only 1 episode verified by ECG
  41 pts refused to participate

88 pts randomized

44 pts randomized to PAR ablation
  2 pts withdrawn consent
  42 pts PAR ablation in analysis

44 pts randomized to PV isolation

44 pts PV isolation in analysis

Figure 1
Figure 2
Freedom from AF off AAD

Follow-up (months)

P=0.0249

PV isolation

PAR ablation

censored

Pts at risk

PAR ablation  42

PV isolation  44

34  34  34  34  33  33  32  31  31  31  31

29  29  25  25  25  25  25  24  22  22  22

Figure 4 A
Freedom from AF with AAD

- PV isolation
- PAR ablation
- censored

Follow-up (months)

Pts at risk
PAR ablation 42
PV isolation 44

P = 0.006

Figure 4 B
Study population
86 pts

PAR ablation
42 pts
- Free of AF off AAD: 31 Pts
- Free of AF on AAD: 5 Pts
- Recurrence of AF with AAD: 6 Pts

PV isolation
44 pts
- Free of AF off AAD: 22 Pts
- Free of AF on AAD: 4 Pts
- Recurrence of AF with AAD: 18 Pts

2nd ablation procedure
-_SHA: 1
- Focal ablation at LA appendage: 1

Free of AF on AAD: 31 Pts
Free of AF on AAD: 22 Pts
Recurrence of AF with AAD: 6 Pts
Free of AF on AAD: 4 Pts
Recurrence of AF with AAD: 18 Pts

Figure 5
Figure 6
Pulmonary Antrum Radial-Linear Ablation for Paroxysmal Atrial Fibrillation: Interim Analysis of a Multicenter Trial

Xue Zhao, Jiayou Zhang, Jianqiang Hu, Dening Liao, Yinxiang Zhu, Xiang Mei, Jun Sheng, Fang Yuan, Yanping Gui, Wenliang Lu, Li Dai, Xingui Guo, Yawei Xu, Yanzhou Zhang, Ben He and Zhenguo Liu

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SUPPLEMENTAL MATERIAL
Supplemental Table 1. AAD Administration During Follow-up

<table>
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<th>Blanking period (1-3 months after procedure)</th>
<th>Follow-up period (4-15 months after procedure)</th>
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<tr>
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<td>PAR ablation (42)</td>
<td>PV isolation (44)</td>
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<tr>
<td></td>
<td>Free of AF off AAD (31)</td>
<td>Free of AF on AAD (5)</td>
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<tr>
<td>Amiodarone</td>
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<tr>
<td>Beta-blocker</td>
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AAD indicates antiarrhythmic drug class I/III
<table>
<thead>
<tr>
<th></th>
<th>PAR ablation</th>
<th></th>
<th>PV isolation</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
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<tr>
<td>LSPV</td>
<td>21.1 ± 3.1</td>
<td>19.6 ± 4.0</td>
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<tr>
<td>LIPV</td>
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<tr>
<td>RSPV</td>
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<td>19.3 ± 3.9</td>
<td>19.5 ± 3.4</td>
<td>19.1 ± 3.6</td>
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<tr>
<td>RIPV</td>
<td>16.9 ± 2.8</td>
<td>16.4 ± 3.0</td>
<td>16.4 ± 2.6</td>
<td>16.3 ± 2.8</td>
</tr>
</tbody>
</table>

No significant difference between before and after ablation.