

Acute response and rhythm outcome after the patchy late-gadolinium enhancement site catheter ablation in patients with persistent atrial fibrillation

kunihiko kiuchi¹, Koji Fukuzawa¹, Mitsuru Takami¹, yoshiaki watanabe¹, Yu Izawa¹, Mayumi Shigeru¹, hiroyuki oonishi², hideya suehiro¹, tomomi akita¹, makoto takemoto¹, atsusuke yatomi¹, Toshihiro Nakamura³, jun sakai¹, Kazutaka Nakasone¹, Yusuke Sonoda¹, Kyoko Yamamoto¹, Hiroyuki Takahara¹, noriyuki negi⁴, katsusuke kyotani⁵, Atsushi Kono¹, and Ken-ichi Hirata¹

¹Kobe University Graduate School of Medicine

²Kobe Circulation Clinic

³Kobe University

⁴Kobe University Hospital

⁵KOBE UNIVERSITY HOSPITAL

October 30, 2020

Abstract

Background: Computer simulation model demonstrated that atrial fibrillation (AF) driver attached to the patchy fibrosis assessed by late gadolinium enhancement magnetic resonance imaging (LGE-MRI). However, it has not been well elucidated in patients with persistent AF. The aim of this study is to investigate whether radiofrequency (RF) application on the patchy LGE site (PLS) could terminate AF or convert to atrial tachycardia (AT) and improve the rhythm outcome. Methods: A total of 31 consecutive persistent AF patients with PLS were enrolled (PLS ablation group, mean age: 69 ± 8 years, mean left atrial diameter: 42 ± 6 mm). AF direct termination or AT conversion during RF application on the PLS were defined as favorable response. The rhythm outcome was compared between the PLS ablation group and the propensity matched conventional ablation group. Results: Favorable response was found in 15 (48%) of 31 patients (AF termination in 7, AT conversion in 8 patients). AF recurrence at 12 months follow-up was significantly less in the PLS group as compared to the control group (4 (13%) of 31 patients vs. 11 (35%) of 31 patients, log-rank $p = 0.019$). In patients with favorable response, AT recurred in 1 (7%) of 15 patients but AF. Conclusions: The PLS ablation could terminate AF or convert to AT in half of the patients and improve the rhythm outcome as compared to the conventional ablation. No AF recurrence was documented in patients with a favorable response.

Acute response and rhythm outcome after the patchy late-gadolinium enhancement site catheter ablation in patients with persistent atrial fibrillation

Kunihiko Kiuchi, MD, FHRS+, Koji Fukuzawa, MD+, Mitsuru Takami, MD+, Yoshiaki Watanabe, MD++, Yu Izawa, MD+, Mayumi Shigeru, MD§,

Hiroyuki Oonishi, RT§, Hideya Suehiro, MD+, Tomomi Akita, MD+,

Makoto Takemoto, MD+, Atsusuke Yatomi MD+, Toshihiro Nakamura MD+,

Jun Sakai MD+, Kazutaka Nakasone, MD+, Yusuke Sonoda, MD+,

Kyoko Yamamoto, MD+, Hiroyuki Takahara, MD+, Noriyuki Negi, RT P,

Katsusuke Kyotani, RT P, Atsushi Kono, MD++, Ken-ichi Hirata, MD+

+Section of Arrhythmia, Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine

++Division of Radiology, Department of Internal Medicine, Kobe University Graduate School of Medicine
SSKobe Circulation Clinic

PDivision of Diagnostic Imaging, Department of Diagnostic Radiology, Kobe University Hospital

7-5-2 *Kusunoki-cho*

Chuo-ku, Kobe city, Japan

Financial support: none

Short title: LGE-site as AF substrate

Total word count: 4922

Conflicts of Interest

The Section of Arrhythmia was supported by an endowment from Medtronic JAPAN and Abbott JAPAN. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Address: Kunihiko Kiuchi, MD, FHRS (corresponding author)

Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe University Hospital

7-5-2 *Kusunoki-cho, Chuo-ku, Kobe city, Japan*

Fax: (81)-78-382-5859

Telephone: (81)-78-382-5846

E-mail:kunihikokiuchi@yahoo.co.jp

Abstract

Background: Computer simulation model demonstrated that atrial fibrillation (AF) driver attached to the patchy fibrosis assessed by late gadolinium enhancement magnetic resonance imaging (LGE-MRI). However, it has not been well elucidated in patients with persistent AF. The aim of this study is to investigate whether radiofrequency (RF) application on the patchy LGE site (PLS) could terminate AF or convert to atrial tachycardia (AT) and improve the rhythm outcome. **Methods:** A total of 31 consecutive persistent AF patients with PLS were enrolled (PLS ablation group, mean age: 69 +/- 8 years, mean left atrial diameter: 42 +/- 6 mm). AF direct termination or AT conversion during RF application on the PLS were defined as favorable response. The rhythm outcome was compared between the PLS ablation group and the propensity matched conventional ablation group. **Results:** Favorable response was found in 15 (48%) of 31 patients (AF termination in 7, AT conversion in 8 patients). AF recurrence at 12 months follow-up was significantly less in the PLS group as compared to the control group (4 (13%) of 31 patients vs. 11 (35%) of 31 patients, log-rank $p = 0.019$). In patients with favorable response, AT recurred in 1 (7%) of 15 patients but AF. **Conclusions:** The PLS ablation could terminate AF or convert to AT in half of the patients and improve the rhythm outcome as compared to the conventional ablation. No AF recurrence was documented in patients with a favorable response.

Key Words : atrial fibrillation; fibrosis; late-gadolinium enhancement MRI; catheter ablation; rhythm outcome

Abbreviations

AF = atrial fibrillation

AT = atrial tachycardia

BNP = brain natriuretic peptide

CE-MRA = contrast enhancement magnetic resonance angiography

FFE = fast field echo

LA = left atrium

LAA = left atrium appendage

LAD = left atrial diameter

LVEF = left ventricular ejection fraction

LGE MRI = late-gadolinium enhancement magnetic resonance imaging

PLS = patchy late-gadolinium enhancement site

PV = pulmonary vein

PVI = pulmonary vein isolation

RFCA = radiofrequency catheter ablation

SM = substrate modification

Introduction

STAR AF II clinical trial demonstrated no benefit of either linear ablation or ablation of complex fractionated electrograms in addition to pulmonary vein isolation (PVI).¹ However, the impact of PVI on the rhythm outcome was not enough in patients with persistent atrial fibrillation (AF). AF termination was considered the factor predicting freedom from arrhythmia recurrence in patients with persistent AF during long-term follow-up, but it was still in debate.² The rate of AF termination during the procedure could range from 10 to 40%, which depended on the ablation strategy such PVI alone, PVI plus ablation of complex fractionated atrial electrograms (CFAEs), PVI plus a linear ablation or FIRM-guided ablation.²⁻⁵ Late gadolinium enhancement magnetic resonance imaging (LGE-MRI) based computer simulation model has demonstrated that meandering re-entrant AF driver attached to patchy fibrosis.⁶ Boyle and Trayanova et al. have recently introduced a technology for the targeted ablation of persistent AF patients with atrial fibrosis, and demonstrated the feasibility of the technology to guide patient treatment in a prospective study of 10 patients. Although it was a proof-of-concept feasibility study of the technology, the AF termination rate and rhythm outcome were likely excellent.⁷ This indicated that the importance of targeting of the fibrotic tissue specifically associating with AF driver. We hypothesized that radiofrequency (RF) application on the patchy LGE site (PLS ablation) could eliminate the possible AF driver which resulted in AF termination and improving the rhythm outcome. The primary goal of this study was to determine whether the PLS ablation could terminate AF. The secondary goal was to determine whether the PLS ablation could improve the rhythm outcome as compared to the conventional ablation in patients with persistent AF.

Methods

Patient population

A total of 31 consecutive persistent AF patients with patchy LGE site were enrolled in this study (PLS group). The chronic kidney disease patients were excluded from this study, because no LGE-MRI could be performed before ablation. As a control group, propensity matched 62 patients with or without the patchy LGE site were selected from Kobe University AF registry including a total 241 persistent AF patients who underwent conventional catheter ablation (31 in the control group with the patchy LGE site, 31 in the control group without the patchy LGE site). The study design and flowchart were shown in Figure 1. The study

was approved by the local ethics committee and complied with the Declaration of Helsinki (Committee of 2020.7.21., Approval No. B200121).

Late-Gadolinium enhancement MRI acquisition

All patients underwent contrast enhanced MR imaging using a 1.5-T MR system (Achiva, Philips Medical, Best, The Netherlands) equipped with a 5-channel cardiac coil one to three months before the AF ablation. This scan technique has been established, and the acquired images were used for the AF ablation procedure.^{8,9} First, contrast enhancement–magnetic resonance angiography (CE-MRA) of the PV–LA anatomy was acquired with a breath-hold 3D fast field echo (FFE) sequence in the coronal plane during the first pass of a contrast agent (gadobutrol, Gadovist; Bayer Yakuhin, Osaka, Japan) injection at a dose of 0.1 mmol/kg. The purpose of the scanning in the coronal plane was to reduce the number of acquisition slices and shorten the breath holding time. Then the LGE-MRI of the LA with the PVs was acquired using a 3D inversion recovery, respiration navigated, electrocardiogram-gated, T1-FFE sequence in the transverse plane 15 minutes after the contrast injection, which has been previously reported. The typical parameters were as follows: repetition time /echo time = 4.7 / 1.5 ms, voxel size = 1.43 x 1.43 x 2.40 mm (reconstructed to 0.63 x 0.63 x 1.20 mm), flip angle = 15deg, SENSE = 1.8, and 80 reference lines. The inversion time (TI) was set at 280 – 320 ms, using a Look-Locker scan. In case of AF, the data acquisition was performed with the shortest trigger delay of cardiac synchronization. In case of sinus rhythm, the data acquisition was performed during the mid-diastolic phase of the left ventricle. The typical scan time for the LGE-MRI study was 7 to 12 minutes depending on the patient’s heart rate and respiration pattern. The images of the CE-MRA, and LGE-MRI were transferred to customized software (MRI LADE Analysis; PixSpace Inc, Fukuoka, Japan) for a further image post processing and image analysis.

3D visualization of LGE site

The method of the 3D visualization for the LGE site was as follows. First, the LA was segmented semi-manually by contouring the endocardial and epicardial borders of the atrium, including the PVs. Second, the mean value and SD of the voxel intensity was measured on the “healthy” LA wall where no hyper-enhanced areas in the LGE-MRI were involved. Third, a voxel intensity histogram analysis of the LA wall identified LGEs as intensities >2 SD on the “healthy” LA wall. Furthermore, the degree of the intensity was categorized by color-coded scaling (green: $> 1SD$; yellow: $2 - 3SD$; and red: $> 3SD$). Finally, a 3D reconstruction of the color-coded LGE and volume-rendered LA and PV image generated from the CE-MRA were fused semi-automatically. The LGE site was defined as a site with a signal intensity of $> 1SD$.

Definition of the ‘patchy’ LGE site

The LGE site was classified into the dense or patchy LGE site. An animal study reported that the maximum gap length with conduction block was 4 mm.¹⁰ According to the result, the patchy LGE site was defined as the site where the at least two small LGE could distributed within 5mm diameter (Figure 2). Based on this definition, the patchy LGE site appeared inhomogeneous infiltration of atrial tissue by LGE, while the dense LGE site appeared homogenous and strong infiltration of atrial tissue by LGE.

PLS ablation and conventional ablation

Prior to the procedure, transesophageal echocardiography was performed to exclude any thrombus formation. Patients were studied under dexmedetomidine hydrochloride sedation while breathing spontaneously. Standard electrode catheters were placed in the right ventricular apex and coronary sinus after which a single transeptal puncture was performed. Unfractionated heparin was administered in a bolus form before the transeptal puncture to maintain an activated clotting time of >350 s.

Mapping and ablation were performed using a NavX system (Abbott, Chicago, IL) or CARTO3 (Biosense Webster, Diamond Bar, CA, USA) as a guide after integration of a three-dimensional (3D) model of the anatomy of the LA and PVs obtained from pre-interventional computed tomography (CT) or magnetic resonance imaging (MRI). Prior to the ablation, the circular mapping catheter (Optima, Abbott, Chicago,

IL; Carto Lasso, Biosense Webster, Diamond Bar, CA) and ablation catheter-reconstructed LA posterior anatomies were aligned with the MRI.

RF alternating current was delivered in a unipolar mode between the irrigated tip electrode of the ablation catheter (TactiCath™, Abbott, Chicago, IL; SmartTouch ThermoCool, Biosense Webster) and an external back-patch electrode. The initial RF generator setting consisted of maximal RF power of 30 to 35W. All patients underwent an extensive encircling pulmonary vein isolation. RF applications were performed in a “point by point” manner. For each RF application, the target CF was 5 – 30 g, and the target lesion size index (LSI) or ablation index (AI) was 5.2 or 500, respectively.⁹ The RF application time was routinely limited 10s when ablating the posterior wall according to the esophageal temperature measured with an esophageal temperature probe (SensiTherm, Abbott, Chicago, IL). Catheter navigation was performed with a steerable sheath (Agillis, Abbott, Chicago, IL). Conventional ablation strategy including the PVI, non-PV foci ablation, linear ablation, CFAE ablation and low voltage area (LVA) ablation depended on the operator discussion.

In the PLS group, PVI or PVI plus Box lesion were predefined based on the LGE-MRI. If the patchy LGE was found at the PV antrum or left atrial posterior wall, PVI plus Box lesion was attempted. If not, only PVI was performed. After complete PVI or PVI plus Box was confirmed, RF application at the patchy LGE site in a point by point manner. Even though AF could be terminated during the PLS ablation, RF application continued till it covered the all patchy LGE sites. If AF could convert to AT during the PLS ablation, mapping and ablation was performed for the AT termination. AF termination or AT conversion during PLS ablation were defined as a favorable response positive. If no favorable respond could be achieved, cardio version was performed. After the procedure, we performed a stimulation protocol (burst pacing from the CS with 300 ms, 250 ms, and 200 ms for 10s each) to test the inducibility. Holter ECGs were performed immediately after the procedure and after 6, and 12 months for all patients. If symptoms occurred outside the recording period, patients were requested to contact our institution or the referring physician to obtain ECG documentation. AF and AT episodes lasting >30 s was considered recurrences.

Ablation strategies promising AF termination and eliminating recurrence

To determine the ablation strategy associated with terminating AF and maintaining SR, a total of 241 persistent AF patients who underwent catheter ablation were recruited from the Kobe University AF registry database. Based on the ablation summary, the patients were classified into the following four groups: 1) PVI group, 2) PVI plus substrate modification including linear, CFAE and LVZ ablation group (PVI plus SM group), 3) PVI plus Box lesion group (Box lesion group) and 4) PLS ablation group. The ratio of AF termination and AF recurrence during the follow-up period were assessed among four groups.

Statistical analysis

Continuous data were presented as the mean± standard deviation. Continuous variables were compared by means of 1-way ANOVA and post hoc analysis with Bonferroni correction for multiple comparisons of data if normally distributed, or the Kruskal-Wallis test, if skewed. Categorical variables were analyzed with the Fisher’s exact test. To compare the rhythm outcome between the PLS ablation and conventional ablation, age, gender, left atrial diameter (LAD), left ventricular ejection fraction (LVEF) and creatinine level matched conventional ablation group were selected as a conventional ablation group. The cumulative incidence of AF recurrence was determined by the Kaplan-Meier method. The survival analysis between PLS ablation group and conventional ablation group was performed using a log-rank test. Cox proportional hazards regression models were used to estimate hazard ratios and 95% CIs for AF recurrence. Variables in the multivariable Cox proportional hazards regression model included each ablation strategy, age, gender, LAD and LVEF with P<0.05 using unadjusted Cox proportional hazard regression analysis. Multivariate logistic regression models were used to estimate hazard ratios and 95% CIs for AF termination. A value of p<0.05 was considered statistically significant. All statistical analyses were performed using EZR on R commander, version 1.36 or SPSS, Release 24 software (SPSS, Chicago, IL, USA).

Results

Patient and procedural characteristics

The patient and procedural characteristics are shown in Table 1. Although age, gender, left atrial diameter (LAD) and left ventricular ejection fraction (LVEF), creatinine level was matched, the other patient characteristics including CHADS2 score, brain natriuretic peptide (BNP) level were also comparative between the PLS and the control. As for the ablation procedure in the control group with patchy LGE site, pulmonary vein isolation (PVI), PVI plus substrate modification including linear ablation, complex fractionated atrial electrograms (CFAE) ablation, low-voltage area (LVA) ablation and PVI plus Box lesion were performed in 17 (55%), 4 (13%) and 10 (32%) of 31 patients, respectively. In the control group without patchy LGE site, pulmonary vein isolation (PVI), PVI plus substrate modification including linear ablation, complex fractionated atrial electrograms (CFAE) ablation, low-voltage area (LVA) ablation and PVI plus Box lesion were performed in 27 (88%), 2 (6%) and 2 (6%) of 31 patients, respectively. As for the procedural characteristics, the procedure time were comparative among the groups, but the fluoroscopy time was significantly longer in the PLS group than that in the control group without patchy LGE site (fluoroscopic time: 22 ± 11 min and 16 ± 4 min, $p = 0.01$).

The distribution of the PLS

A total of 69 PLS were found in 31 patients. The distribution of the PLS was shown in Figure 3. 23 (33%) and 22 (32%) of the 69 PLS were found around PV antrum and left atrial appendage (LAA) base, respectively. Subsequently, 9 (13%), 6 (9%), 5 (7%), 4 (6%) of the 69 PLS were found around the left atrial septum, left atrial posterior wall, left atrial roof and left atrial bottom, respectively.

Favorable response and rhythm outcome

Favorable response was found in 15 (48%) of the 31 patients in the PLS group, while no favorable response in the control group. Of the patients with favorable response, AF termination could be documented in 7 (23%) patients and AT conversion in 8 (26%) patients. AT could be mapped and terminated by the RF application. At the end of the procedure, AF inducibility by burst pacing could be reduced in 26 (84%) patients.

The AF/ AT recurrence at 12 months after the procedure was significantly less in the PLS groups as compared to the control group with patchy LGE site (4 [13%] vs. 11 [36%], log-rank test $p = 0.034$) (Figure 4A). AF/AT recurrence was likely less in the patients with favorable response as compared to those without one (1 (7%) of 15 vs. 3 (19%) of 16 patients, $p = 0.090$). Of note, the patient with a favorable response had AT recurrence but not AF. Representative case was shown in Figure 5. The PLS could be found at the LA septum and LAA base where RF application could terminate AF. Of interest, AF/AT recurrence were comparative between the PLS ablation group and the conventional ablation group without the patchy LGE site (4 [13%] vs. 5 [16%], log-rank test $p = 0.710$) (Figure 4B).

Ablation strategies promising AF termination and eliminating recurrence

As for the AF termination, unadjusted logistic regression analysis identified 2 ablation strategies associated with favorable response: PLS ablation and PVI. Of interest, the PLS ablation and PVI were positively and negatively associated with favorable response, respectively. According to the multivariate logistic regression analysis, the most predictive model of favorable response consisted of the PLS ablation (Table 2).

As for the AF/AT recurrence, unadjusted Cox proportional hazard regression analysis identified 2 factors associated with AF/AT recurrence: PLS ablation and LVEF. According to the multivariate Cox proportional hazard regression analysis, the most predictive model of AF/AT recurrence consisted of the PLS ablation (Table 3).

Discussion

Main findings

The study presented here demonstrated that significant impact of the PLS ablation in patients with persistent

AF. With the primary goal of our study to determine whether the PLS ablation could terminate AF, we concluded that the ratio of AF termination during the PLS ablation was almost 50%. The secondary goal was to assess whether the rhythm outcome after the PLS ablation could be improved as compared to that after conventional ablation. During a median 9 months follow-up, the AF recurrence was significantly less in the PLS ablation group as compared to the conventional ablation group. Furthermore, we concluded by means of multivariate analysis that the PLS ablation was only associated with a freedom from the AF recurrence.

Distribution of AF substrate

To date, atrial fibrosis, LVA, CFAE, AF rotor were considered as AF substrates.^{3,11-14} The left atrial fibrosis was visualized by the LGE-MRI and the LGE site was heterogeneously distributed in AF patients. Higuchi et al. reported that the LGE site was highly distributed in the left PV antrum near the posterior wall side and spread on the posterior and anterior wall with AF progression.¹⁵ The LGE was more widely distributed in patients with persistent AF compared with patients with paroxysmal AF, especially on the posterior and anterior wall. Notably, the LGE site was likely distributed around LAA on the anterior wall in the progressed AF patients. Our study also demonstrated that the patchy LGE site was predominantly distributed at PV antrum and LAA base, which was completely consistent with their results.

The LVA was reported to be mainly found in LA septum, anterior LA and LA posterior.¹⁶ Of interest, Chen et al. reported that LGE sites were present at 61% of LVAs, whereas LVAs were present at 28% of LGE sites.¹⁷ Those findings indicated that the distribution of the LGE sites could not completely overlapped with that of the LVAs. The LVA distribution could depend on the mapping resolution, pacing site, cardiac rhythm or use of the cardioversion. Furthermore, the patchy LGE site was sometimes underestimated which depended on the visualization method. This might be the reason why the distribution of the LVA were not completely concordant with that of the LGE.

The distribution of CFAE were most commonly located in the LA posterior and PV antral region.¹⁸ The distribution of spatiotemporal electrogram dispersion area were equally distributed at PV, LAA, LA posterior, LA anterior and LA roof. The distribution was unlikely similar to that of the patchy LGE site. The relationship between CFAE, spatiotemporal electrogram dispersion area, LVA and atrial fibrosis were complex and it was still in debate.

AF driver detected by a 252-electrode vest for body surface mapping were predominantly located in the PV antrum and LA bottom, subsequently around the LAA.¹⁹ Their results were likely consistent with our results. Cochet et al. concluded that the number of AF driver related to the extent of LGE, with the location of AF driver clustering to LGE sites.²⁰ This strongly indicated that the LGE site could be one of the possible AF substrates and it was considered as an ablation target, which strongly supported our ablation strategy.

AF termination and rhythm outcome

The importance of AF termination as a procedural endpoint that correlates positively with rhythm outcome is still in debate. AF termed in 51% of catheter ablation using a sequential biatrial linear defragmentation approach. Miyazaki et al. reported that AF termination was the sole factor predicting freedom from both arrhythmia recurrence and crossover to rate control strategies during long-term follow-up.² While, in the subgroup analysis of STAR AF II, AF termed in 8% of the PVI, 45% in the PVI plus CFAE ablation and 22% of the PVI plus linear ablation and the AF termination could not predict the better rhythm outcome.⁴ This discrepancy might be caused by 1) multiple procedure or single procedure, 2) follow-up period (60 months vs. 18 months). CFAE ablation was associated with a high likelihood of AT as the mode of arrhythmia recurrence. Actually, linear ablation was mainly performed for macro-reentrant ATs in the 2nd procedure. Of note, the AF recurrence was significantly less after eliminating AT after index procedure when 2nd or 3rd session was mainly performed from 4 to 28 months after the initial procedure. In our study, the mode of the arrhythmia recurrence was perimitral AT in one patient with a favorable response. Thus, no AF recurrence was found in patients with a favorable response. We speculated that AF termination during RF application could reduce the AF recurrence, however, additional RF application could have a potential risk of increasing the AT substrate. The PLS ablation provide the relatively high AF termination and the excellent outcome,

however, the ablation target area should have been more specifically focused and we should have used the time for creating a durable PVI and linear lesion. Recently, Ashihara et al. had developed a novel online real-time phase mapping system: ExTRa Mapping.¹³ By using this novel system, we reported the case in which RF application at the AF rotor area overlapped with the PLS could convert AF to common atrial flutter.²¹ We would like to hope that this real-time mapping system and LGE-MRI assessment could make it possible to intervention on the specific AF substrate.

PLS as AF substrate

LGE-MRI based computer simulation model demonstrated that meandering re-entrant AF driver was localized in boundary zones between fibrotic and non-fibrotic tissue characterized with high fibrosis density and entropy where the lower local conduction velocity was documented.^{20,22} Furthermore, they has demonstrated that the residual fibrosis after catheter ablation might be attributable to preserved re-entrant drivers and the emergence of new re-entrant driver.²³ This strongly indicated that the all fibrosis with high density and entropy were possible ablation targets. Therefore, the RF application at the PLS was continued, even in cases where AF termination was achieved during the procedure. Recently, Boyle et al. had presented the computationally guided personalized targeted ablation as a proof-of -concept feasibility study.⁷ Furthermore, they suggested that LGE-MRI based computationally guided ablation could provide not only accurate prediction of AF ablation targets but could overcome the prolonged procedure time and higher radiation exposure due to the difficulty of a conventional mapping of atrial electrical activity. In our study, both procedure time and fluoroscopy time were acceptable as compared to that of conventional ablation procedure, because additional target site was predefined by the preprocedural LGE-MRI and no further mapping was necessary during the procedure. We would hope that the PLS ablation could improve the rhythm outcome in persistent AF patients without increasing of the procedure time and radiation exposure.

Study limitations

Our study had several limitations. First, the sample size was small and the follow-up period was relatively short. Second, the PLS was assessed on the LA but not the right atrium (RA). Further PLS ablation at the RA could influence the rhythm outcome. To clarify this issue, further study should be needed.

Conclusions

The PLS ablation could terminate AF or convert to AT in half of the patients and no AF recurrence in patients with a favorable response. The rhythm outcome could be improved without compromising both procedure time and radiation exposure as compared to conventional catheter ablation.

Acknowledgements

We would like to thank Mr. Tsuyoshi Sakamoto for his development of the specially customized software (MRI LADE Analysis, PixSpace Inc., Fukuoka, Japan).

Figure Legends

Figure 1. Study design and flowchart

AF = atrial fibrillation, LGE = late-gadolinium enhancement

Figure 2. Definition of the PLS

A: patchy and dense LGE pattern. B: 3D LGE-MRI fused with CE-MRA. Lower panel depicted the patchy and dense LGE sites. Of note, ablation targets were the patchy LGE sites but the dense one. MA = mitral annulus, LGE-MRI = late-gadolinium enhancement magnetic resonance imaging, CE-MRA = contrast enhancement magnetic resonance angiography

Figure 3. Distribution of the PLS

The left and right panels illustrated the distribution of the PLS in the posterior-anterior view and anterior – posterior view. The PLS was predominantly found around PV antrum and LAA base.

PLS = patchy late-gadolinium enhancement site, PV = pulmonary vein, LAA = left atrium appendage

Figure 4. Kaplan-Meier curve of freedom from AF/AT for each group

AF = atrial fibrillation, AT = atrial tachycardia, PLS = patchy LGE site

Figure 5. PLS ablation in the representative case

A: The left panel showed the LGE-MRI. The right panel showed the 3D LGE-MRI fused with CE-MRA using by specially customized software. The white arrow and red dotted circle indicated the PLS around LAA base.

B: RF application at the PLS by using NavX system. The light blue electrogram indicated the atrial signal recorded by the ring catheter in the LAA. The LAA electrograms were organized and terminated during RF application. The 3D tags indicated the RF application points. The yellow one indicated AF termination points.

LGE-MRI = late-gadolinium enhancement magnetic resonance imaging, CE-MRA = contrast enhancement magnetic resonance angiography, PLS = patchy LGE site, LAA = left atrial appendage, RF = radiofrequency

References

1. Verma A, Jiang CY, Betts TR, et al. Approaches to catheter ablation for persistent atrial fibrillation. *N Engl J Med.* 2015;372(19):1812-1822.
2. Miyazaki S, Taniguchi H, Kusa S, et al. Five-year follow-up outcome after catheter ablation of persistent atrial fibrillation using a sequential biatrial linear defragmentation approach: What does atrial fibrillation termination during the procedure imply? *Heart Rhythm.* 2017;14(1):34-40.
3. Kirzner JM, Raelson CA, Liu CF, et al. Effects of focal impulse and rotor modulation-guided ablation on atrial arrhythmia termination and inducibility: Impact on outcomes after treatment of persistent atrial fibrillation. *J Cardiovasc Electrophysiol.* 2019;30(12):2773-2781.
4. Kochhauser S, Jiang CY, Betts TR, et al. Impact of acute atrial fibrillation termination and prolongation of atrial fibrillation cycle length on the outcome of ablation of persistent atrial fibrillation: A substudy of the STAR AF II trial. *Heart Rhythm.* 2017;14(4):476-483.
5. Chauhan VS, Verma A, Nayyar S, et al. Focal source and trigger mapping in atrial fibrillation: Randomized controlled trial evaluating a novel adjunctive ablation strategy. *Heart Rhythm.* 2020;17(5 Pt A):683-691.
6. Zahid S, Cochet H, Boyle PM, et al. Patient-derived models link re-entrant driver localization in atrial fibrillation to fibrosis spatial pattern. *Cardiovasc Res.* 2016;110(3):443-454.
7. Boyle PM, Zghaib T, Zahid S, et al. Computationally guided personalized targeted ablation of persistent atrial fibrillation. *Nat Biomed Eng.* 2019;3(11):870-879.
8. Akita T, Kiuchi K, Fukuzawa K, et al. Lesion distribution after cryoballoon ablation and hotballoon ablation: Late-gadolinium enhancement magnetic resonance imaging analysis. *J Cardiovasc Electrophysiol.* 2019;30(10):1830-1840.
9. Kurose J, Kiuchi K, Fukuzawa K, et al. Lesion characteristics between cryoballoon ablation and radiofrequency ablation with a contact-force sensing catheter: late-gadolinium enhancement magnetic resonance imaging assessment. *J Cardiovasc Electrophysiol.* 2020.
10. Ranjan R, Kato R, Zviman MM, et al. Gaps in the ablation line as a potential cause of recovery from electrical isolation and their visualization using MRI. *Circ Arrhythm Electrophysiol.* 2011;4(3):279-286.
11. Kircher S, Arya A, Altmann D, et al. Individually tailored vs. standardized substrate modification during radiofrequency catheter ablation for atrial fibrillation: a randomized study. *Europace.* 2018;20(11):1766-1775.

12. Ohe M, Haraguchi G, Kumanomido J, et al. New tailored approach using a revised assessment of fragmented potentials for persistent atrial fibrillation: Early area defragmentation by modified CFAE module. *J Cardiovasc Electrophysiol*. 2019;30(6):844-853.
13. Sakata K, Okuyama Y, Ozawa T, et al. Not all rotors, effective ablation targets for nonparoxysmal atrial fibrillation, are included in areas suggested by conventional indirect indicators of atrial fibrillation drivers: ExTRa Mapping project. *J Arrhythm*. 2018;34(2):176-184.
14. McGann C, Akoum N, Patel A, et al. Atrial fibrillation ablation outcome is predicted by left atrial remodeling on MRI. *Circ Arrhythm Electrophysiol*. 2014;7(1):23-30.
15. Higuchi K, Cates J, Gardner G, et al. The Spatial Distribution of Late Gadolinium Enhancement of Left Atrial Magnetic Resonance Imaging in Patients With Atrial Fibrillation. *JACC Clin Electrophysiol*. 2018;4(1):49-58.
16. Rolf S, Kircher S, Arya A, et al. Tailored atrial substrate modification based on low-voltage areas in catheter ablation of atrial fibrillation. *Circ Arrhythm Electrophysiol*. 2014;7(5):825-833.
17. Chen J, Arentz T, Cochet H, et al. Extent and spatial distribution of left atrial arrhythmogenic sites, late gadolinium enhancement at magnetic resonance imaging, and low-voltage areas in patients with persistent atrial fibrillation: comparison of imaging vs. electrical parameters of fibrosis and arrhythmogenesis. *Europace*. 2019;21(10):1484-1493.
18. Verma A, Sanders P, Champagne J, et al. Selective complex fractionated atrial electrograms targeting for atrial fibrillation study (SELECT AF): a multicenter, randomized trial. *Circ Arrhythm Electrophysiol*. 2014;7(1):55-62.
19. Lim HS, Hocini M, Dubois R, et al. Complexity and Distribution of Drivers in Relation to Duration of Persistent Atrial Fibrillation. *Journal of the American College of Cardiology*. 2017;69(10):1257-1269.
20. Cochet H, Dubois R, Yamashita S, et al. Relationship Between Fibrosis Detected on Late Gadolinium-Enhanced Cardiac Magnetic Resonance and Re-Entrant Activity Assessed With Electrocardiographic Imaging in Human Persistent Atrial Fibrillation. *JACC Clin Electrophysiol*. 2018;4(1):17-29.
21. Nakamura T, Kiuchi K, Fukuzawa K, et al. Successful modulation of atrial fibrillation drivers anchoring to fibrotic tissue after box isolation using an online real-time phase mapping system: ExTRa Mapping. *J Arrhythm*. 2019;35(5):733-736.
22. Fukumoto K, Habibi M, Ipek EG, et al. Association of Left Atrial Local Conduction Velocity With Late Gadolinium Enhancement on Cardiac Magnetic Resonance in Patients With Atrial Fibrillation. *Circ Arrhythm Electrophysiol*. 2016;9(3):e002897.
23. Ali RL, Hakim JB, Boyle PM, et al. Arrhythmogenic propensity of the fibrotic substrate after atrial fibrillation ablation: a longitudinal study using magnetic resonance imaging-based atrial models. *Cardiovasc Res*. 2019;115(12):1757-1765.

Figure 1

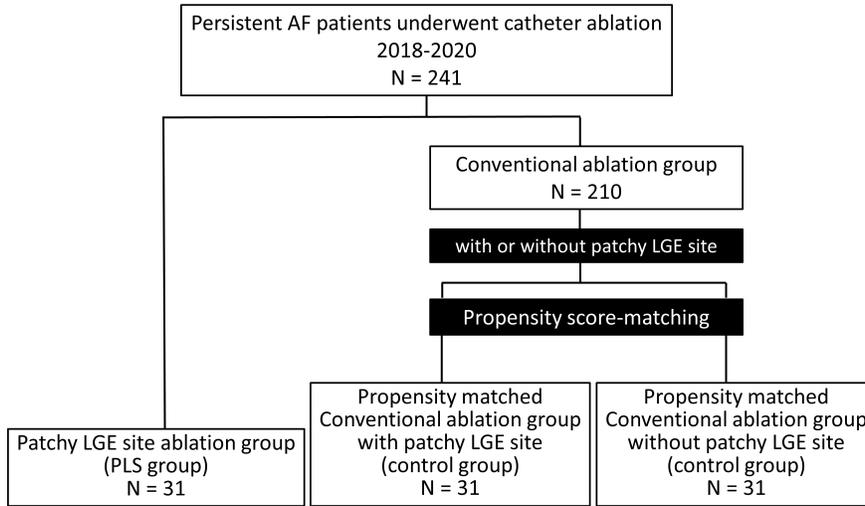


Figure 2

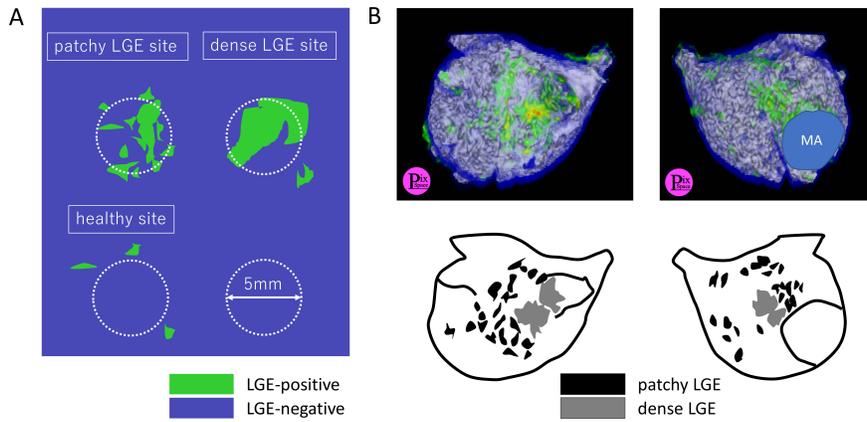


Figure 3

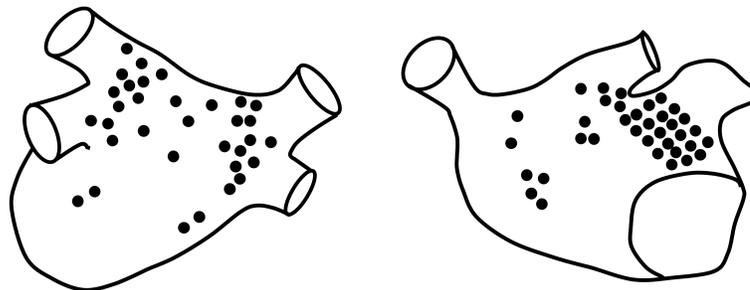


Figure 4

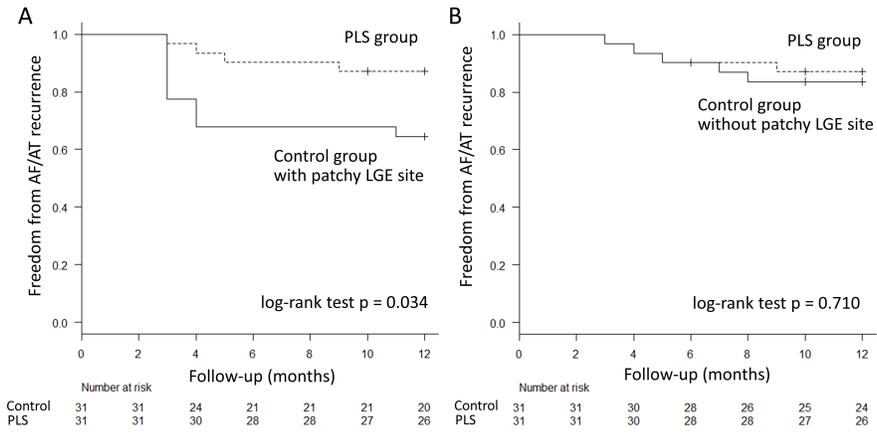
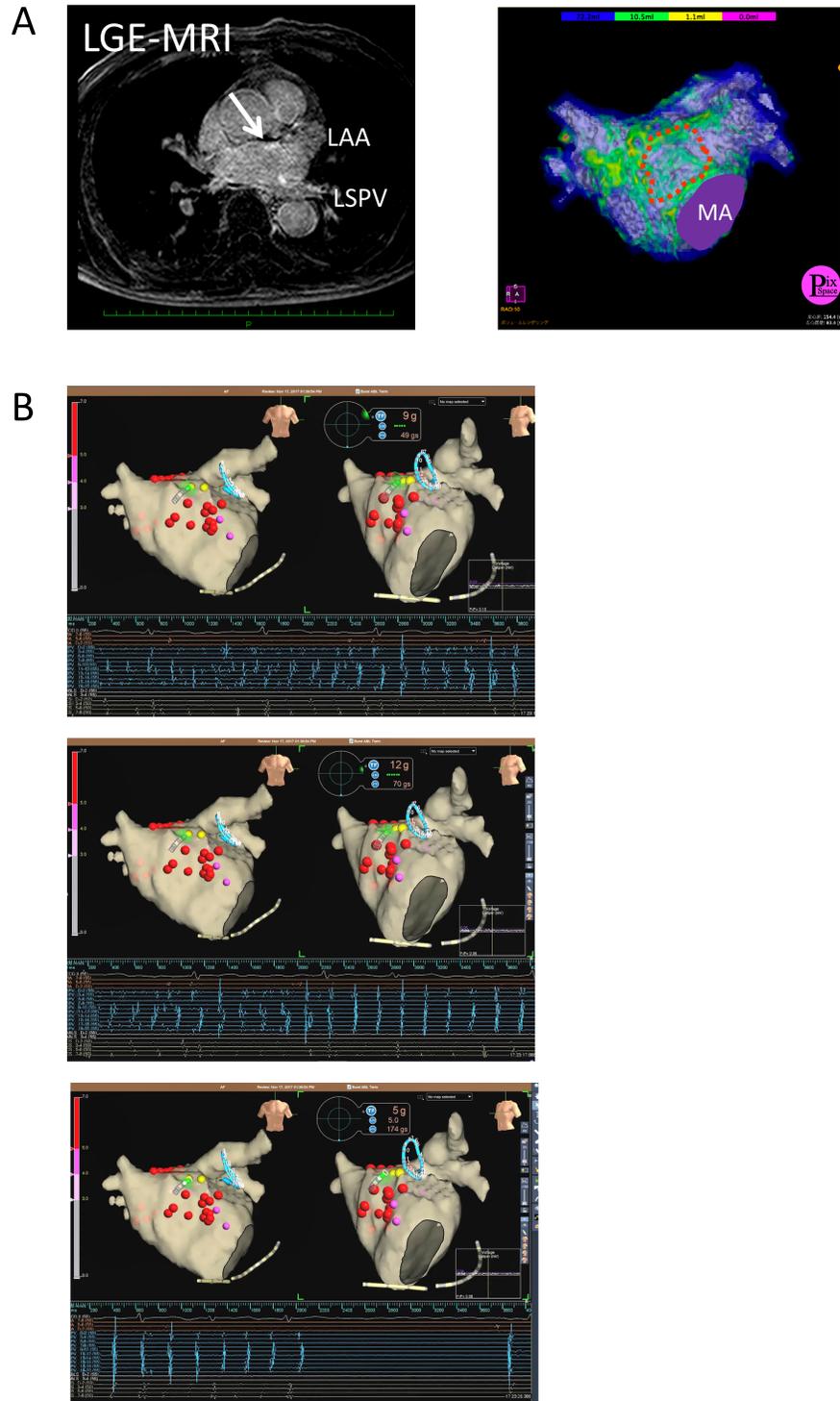


Figure 5



Hosted file

Table1_20201003.pdf available at <https://authorea.com/users/360600/articles/489872-acute-response-and-rhythm-outcome-after-the-patchy-late-gadolinium-enhancement-site-catheter-ablation-in-patients-with-persistent-atrial-fibrillation>

Hosted file

Table2.pdf available at <https://authorea.com/users/360600/articles/489872-acute-response-and-rhythm-outcome-after-the-patchy-late-gadolinium-enhancement-site-catheter-ablation-in-patients-with-persistent-atrial-fibrillation>

Hosted file

Table3.pdf available at <https://authorea.com/users/360600/articles/489872-acute-response-and-rhythm-outcome-after-the-patchy-late-gadolinium-enhancement-site-catheter-ablation-in-patients-with-persistent-atrial-fibrillation>