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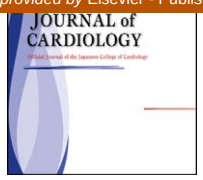

Original article

# Low atrial septal pacing with dual-chamber pacemakers reduces atrial fibrillation in sick sinus syndrome

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**KEYWORDS**
Pacemakers;
Pacing;
Atrial fibrillation;
Low atrial septum;
Sick sinus syndrome

**Summary**
*Background:* Sick sinus syndrome (SSS) is often complicated with the additional presence of atrial fibrillation (AF). Atrial septal pacing, compared with right atrial appendage (RAA) pacing, shortens the atrial conduction time and reduces the dispersion of the refractoriness. However, low atrial septal (LAS) pacing's efficacy for preventing AF in SSS remains controversial in Japan.
*Methods and results:* We analyzed 95 consecutive patients with SSS who underwent dual-chamber pacemaker implantations. Forty-two patients (44%) had a history of AF at the time of the pacemaker implantation. In the group without a history of AF, LAS pacing was performed in 17 patients, and RAA pacing in 36 patients. In the group with a history of AF, LAS pacing was performed in 15 patients, and RAA pacing in 27 patients. We evaluated whether LAS pacing prevented the development of de novo AF and the persistence of AF after pacemaker implantations. No significant differences were found in the baseline characteristics between the RAA and LAS groups regardless of an AF history. During a 1-year follow-up period, in the SSS patients without a history of AF, 19.0% (7/36) of the RAA group developed de novo AF, however, 5.9% (1/17) of the LAS group developed de novo AF ($p = 0.20$). On the other hand, in the SSS patients with a history of AF, 22.0% (6/27) of the RAA group developed persistent AF, but none of the LAS group developed any persistent AF ($p = 0.049$). There were no post-operative complications related to the LAS pacing.
*Conclusions:* LAS pacing is safe and feasible. LAS pacing may prevent the progression to persistent AF in SSS patients with dual-chamber pacemakers.


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## Introduction

Atrial fibrillation (AF) is the most common cardiac rhythm disturbance and contributes substantially to cardiac morbidity and mortality. It carries a considerable risk of thromboembolisms and sustained AF, with an uncontrolled ventricular response rate, and can cause congestive heart failure with an increased risk of death [1]. AF is frequently encountered in pacemaker patients, most commonly in those with sick sinus syndrome (SSS) [2—4]. Atrial pacing was reported to be effective for the prevention of AF because of the suppression of premature atrial contractions that initiate reentry and predispose to AF [5—9]. Furthermore, atrial septal pacing, compared with right atrial appendage (RAA) pacing, shortens the atrial conduction time and reduces the dispersion of the refractoriness [10,11]. However, whether low atrial septal (LAS) pacing can reduce the initiation and maintenance of AF clinically remains controversial. We sought to compare standard RAA lead implantations with LAS lead implantations for the prevention of AF in SSS patients with dual-chamber pacemakers, based on whether or not they had a history of AF.

## Methods

### Study protocol

Between January 2002 and June 2007, 95 consecutive SSS patients (average age 72 ± 9 years, 39 males) with standard indications for a dual chamber pacemaker were retrospectively analyzed. The follow-up period was defined as 1 year. Patients with SSS associated with acquired second- or third-degree atrioventricular block and those with less than a 1-year follow-up were excluded from this study. Forty-two patients (44%) had a history of AF at the time of the pacemaker implantation. In the group without a history of AF, LAS pacing was performed in 17 patients, and RAA pacing in 36 patients. In the group with a history of AF, LAS pacing was performed in 15 patients, and RAA pacing in 27 patients (Fig. 1). The implantable devices were an Intelis II DR ($n = 3$), Nexus DR ($n = 2$) (Guidant Corp., St. Paul, MN, USA), Kappa DR ($n = 13$) (Medtronic Inc., Minneapolis, MN, USA), Affinity DR ($n = 7$), Integrity DR ($n = 9$), and Identity DR ($n = 61$) (St Jude Medical, Sylmar, CA, USA). The atrial leads implanted were a ThinLine II EZ 438-35S ($n = 5$) (Guidant Corp.), Capsure FIX 5068 ($n = 13$) (Medtronic Inc.), Tendril 1488T ($n = 41$) and Tendril 1688T ($n = 36$) (St Jude Medical). The tip to ring spacing of all the atrial leads was ≧10 mm. The lower rate was set between 50 and 70 bpm (mean 59 ± 6 bpm), and the programmed AV delay between 150 ms and 300 ms (mean 212 ± 40 ms). The ventricular leads were all inserted in the apex. The mode switch features were all programmed to occur for atrial rates of >225 bpm and the bipolar atrial sensitivity was set to 0.5 mV or at a 4:1 safety margin, whichever yielded the more sensitive setting. The post-ventricular atrial blanking (PVAB) period was programmed to be adapted on an individual basis after specific assessment for the presence of a far-field R-wave if the interval from the ventricular stimulus to the far-field signal exceeded the minimal programmed PVAB interval. Patients underwent a clinical assessment, standard 12-lead electrocardiogram (ECG), recording and interrogation of their pacemaker at the pacemaker clinic.

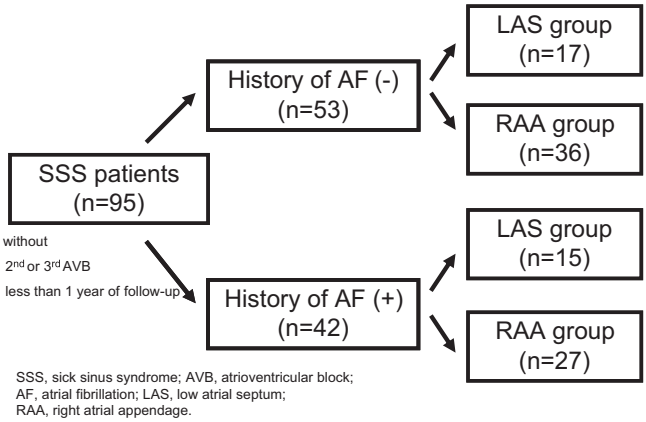


**Figure 1** This shows the allocation of the patients. Ninety-five consecutive sick sinus syndrome (SSS) patients were analyzed. Patients with SSS associated with acquired second- or third-degree atrioventricular block (AVB) and those with less than a 1-year of follow-up were excluded from this study. Forty-two patients (44%) had a history of atrial fibrillation (AF) at the time of the pacemaker implantation. In the group without a history of AF, low atrial septal (LAS) pacing was performed in 17 patients, and right atrial appendage (RAA) pacing in 36. In the group with a history of AF, LAS pacing was performed in 15 patients, and RAA pacing in 27.

### Lead implantation procedure

An active fixation lead was placed into the RAA using the standard technique. The lead position was confirmed via fluoroscopy (Fig. 2A and B). During the LAS lead implantation, an atrial lead was introduced into the right atrium using standard techniques. With fluoroscopy in the left anterior oblique (LAO) position, the lead was rotated toward the interatrial septum around the coronary sinus ostium using a Locator™ (St Jude Medical) (Fig. 3A and B). We confirmed that atrial pacing exhibited negative P waves in leads II, III, and aVf of the 12-lead ECG (Fig. 4).

### Definitions

A history of AF was defined as the occurrence of any of the following two circumstances:

(1) Formerly documented AF already having been recorded in a 12-lead ECG or Holter ECG.
(2) The presence of both more than 1 min of mode switching and documented AF on the intracardiac electrograms within 1 week after the pacemaker implantation.

De novo AF was defined as the presence of both more than 1 min of mode switching and documented AF on the intracardiac electrograms 1 week after the pacemaker implantation.

Persistent AF was defined as the occurrence of any of the following three circumstances [12]:

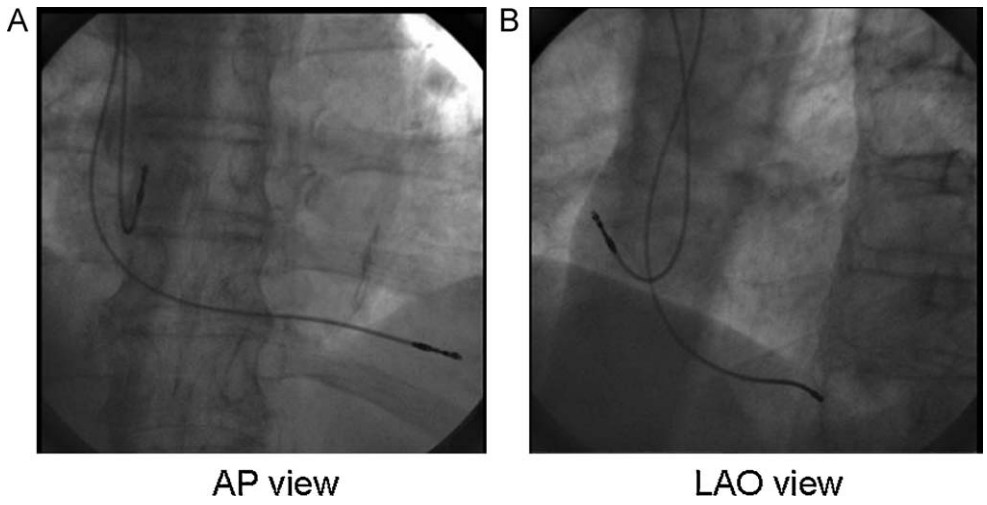


**Figure 2** X ray showing the atrial lead implanted in the right atrial appendage. (A) Anteroposterior (AP) view. (B) Left anterior oblique (LAO) view.

(1) Two consecutive visits in which AF was present.
(2) At least 22 h of AF for at least 7 consecutive days, detected by means of the diagnostic data stored in the pacemaker.
(3) At least 22 h of AF per day for fewer than 7 consecutive days if an interruption by electrical or pharmacologic cardioversion occurred.

### Evaluation

We evaluated the patients as follows:

(1) The efficacy of the prevention of AF during LAS pacing.
   (a) The prevention of de novo AF in patients without a history of AF.
   (b) The prevention of the progression to persistent AF in patients with a history of AF.
(2) The safety of LAS pacing: the post operative complications.

### Statistical analysis

An independent-sample *t*-test and Pearson $\chi^2$ test were used to compare the quantitative and categorical variables between groups, respectively. All continuous data were expressed as the mean $\pm$ SD. A $p < 0.05$ was considered statistically significant.

## Results

### Patients without a history of AF

There were no statistical differences regarding the age, gender, history of hypertension or diabetes mellitus, B-type

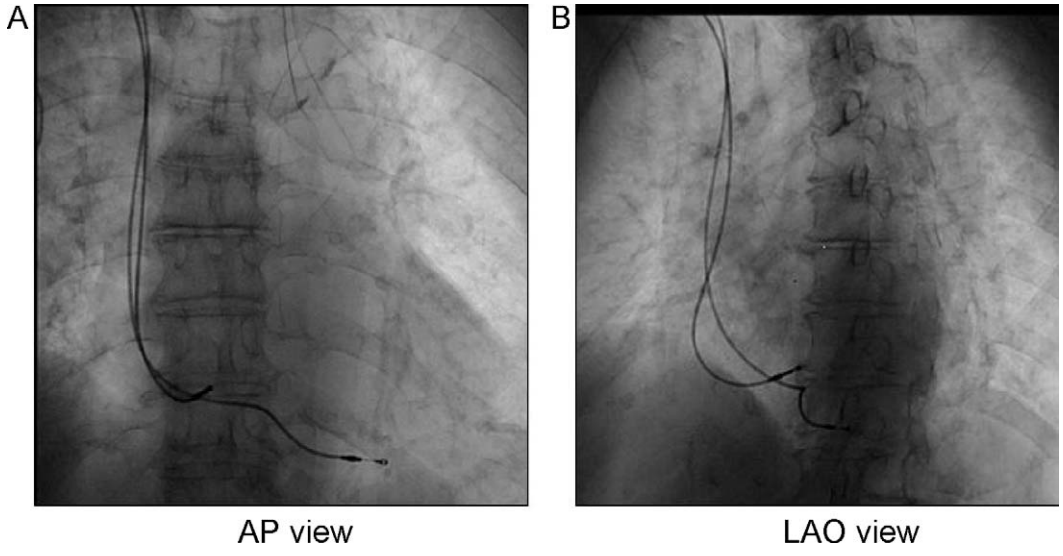


**Figure 3** X ray showing the atrial lead implanted in the low atrial septum. (A) Anteroposterior (AP) view. (B) Left anterior oblique (LAO) view.

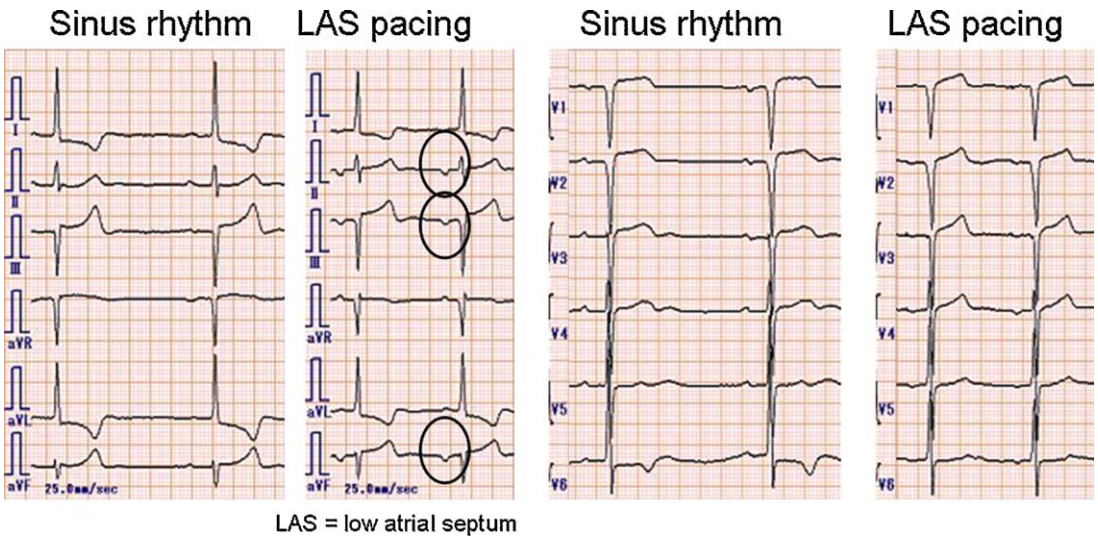


**Figure 4** Twelve-lead electrocardiogram. The left side shows normal sinus rhythm and the right side low atrial septal (LAS) pacing. The P waves in leads II, III, and aVf are inverted and negative during low atrial septal pacing. The P wave width shortened from 110 ms to 100 ms.

natriuretic peptide (BNP) level, or echocardiographic parameters, including the ejection fraction or left atrium diameters. The medical treatment during the follow-up period was similar between the LAS and RAA groups (Table 1). At the time of the pacemaker implantations, the atrial and ventricular thresholds and P-wave and R-wave sensing data were also similar between the LAS and RAA groups. The AF Suppression™ algorithm (St Jude Medical) was not used in the SSS patients without a history of AF. During a 1-year follow-up period, the cumulative percent of atrial paced beats (Cum%AP) was similar between the LAS and RAA groups (51% vs. 57%, respectively; $p = 0.49$), however the cumulative percent of ventricular paced beats (Cum%VP) was lower in the LAS group than in the RAA group (10% vs. 28%, respectively; $p = 0.03$) (Table 2). As a result, 19.0% (7/36) of the patients in the RAA group developed de novo AF, but only 5.9% (1/17) of those in the LAS group developed de novo AF. However, there was no statistical difference between the two groups ($p = 0.20$) (Fig. 5).

**Table 1** Baseline characteristics of the patients without a history of atrial fibrillation (AF).

| | LAS ($n = 17$) | RAA ($n = 36$) | $P$ |
|---|---|---|---|
| Age (years) | $72 \pm 10$ | $69 \pm 13$ | 0.39 |
| Male gender, % ($n$) | 47(8) | 39(14) | 0.57 |
| Hypertension, % ($n$) | 71(12) | 64(23) | 0.23 |
| Diabetes mellitus, % ($n$) | 18(3) | 17(6) | 0.93 |
| Structural heart disease, % ($n$) | 12(2) | 33(12) | 0.10 |
| Hemodialysis, % ($n$) | 6(1) | 3(1) | 0.59 |
| Complication of I degree AVB, % ($n$) | 6(1) | 11(4) | 0.54 |
| Echocardiographic parameters | | | |
| LVDd (mm) | $46 \pm 5$ | $48 \pm 6$ | 0.36 |
| LVDs (mm) | $27 \pm 5$ | $30 \pm 7$ | 0.19 |
| LAD (mm) | $39 \pm 6$ | $36 \pm 8$ | 0.26 |
| EF (%) | $72 \pm 8$ | $68 \pm 11$ | 0.24 |
| BNP (pg/ml) | $279 \pm 666$ | $136 \pm 242$ | 0.49 |
| Medications | | | |
| Sodium channel blocker, % ($n$) | 6(1) | 8(3) | 0.69 |
| β Blocker, % ($n$) | 0(0) | 11(4) | 0.13 |
| ACEI and/or ARB, % ($n$) | 35(6) | 39(14) | 0.63 |
| Statin, % ($n$) | 6(1) | 19(7) | 0.20 |

LAS, low atrial septum; RAA, right atrial appendage; AVB, atrioventricular block; LVDd, diastolic left ventricular dimension; LVDs, systolic left ventricular dimension; LAD, left atrial dimension; EF, ejection fraction; BNP, B-type natriuretic peptide; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker.

**Table 2** Pacemaker function during the implantation and follow-up.

| | SSS without a history of AF | | | SSS with a history of AF | | |
|---|---|---|---|---|---|---|
| | LAS ($n=17$) | RAA ($n=36$) | *P* | LAS ($n=15$) | RAA ($n=27$) | *P* |
| Pacemaker implantation | | | | | | |
| Atrial threshold (V) | $0.8\pm0.6$ | $0.7\pm0.3$ | 0.20 | $0.8\pm0.5$ | $0.8\pm0.5$ | 0.96 |
| P-wave sensing (mV) | $2.0\pm1.3$ | $2.4\pm1.3$ | 0.42 | $2.4\pm0.7$ | $2.1\pm1.4$ | 0.49 |
| Ventricular threshold (V) | $0.2\pm0.1$ | $0.3\pm0.4$ | 0.54 | $0.2\pm0.1$ | $0.2\pm0.1$ | 0.97 |
| R-wave sensing (mV) | $13.8\pm6.5$ | $14.7\pm5.9$ | 0.62 | $16.3\pm6.7$ | $15.2\pm6.0$ | 0.58 |
| Follow-up | | | | | | |
| AFS on more than 3 months | 0(0) | 0(0) | 1.0 | 40(6) | 26(7) | 0.34 |
| Cumulative % atrial paced (%) | $51\pm25$ | $57\pm30$ | 0.49 | $59\pm25$ | $59\pm25$ | 0.81 |
| Cumulative % ventricular paced (%) | $10\pm13$ | $28\pm31$ | 0.03 | $32\pm37$ | $37\pm38$ | 0.68 |

SSS, sick sinus syndrome; AF, atrial fibrillation; LAS, low atrial septum; RAA, right atrial appendage; AFS, atrial fibrillation suppression.

## Patients with a history of AF

There were no statistical differences regarding the age, gender, history of hypertension or diabetes mellitus, BNP level, or echocardiographic parameters, including the ejection fraction or left atrium diameters. The medical treatment was similar between the LAS and RAA groups (Table 3). The medical treatment shown in Table 3 consisted of only routine medications. The occurrence of atrial arrhythmias is not included in that table. During the pacemaker implantations, the atrial and ventricular thresholds and P-wave and R-wave sensing data were also similar between the LAS and RAA groups. During the follow-up period, the Cum%AP and Cum%VP were similar between the LAS and RAA groups (59% vs. 59%, $p=0.81$; 32% vs. 37%, $p=0.68$, respectively) (Table 2). The utility of the AF Suppression™ algorithm after more than 3 months from the implantation was also similar (40% vs. 27%, $p=0.34$). As a result, 22.0% (6/27) of the patients in the RAA group developed persistent AF, but none of those in the LAS group developed persistent AF ($p=0.049$) (Fig. 5).

## Post-operative complications

During the follow-up period, there were no atrial lead dislodgements, perforations, pericarditis, or diaphragmatic pacing events noted. The atrial thresholds and P-wave sensing issues did not change between data obtained immediately after the implantation and at 1-year follow-up. There were no known patient deaths related to pacemaker complications.

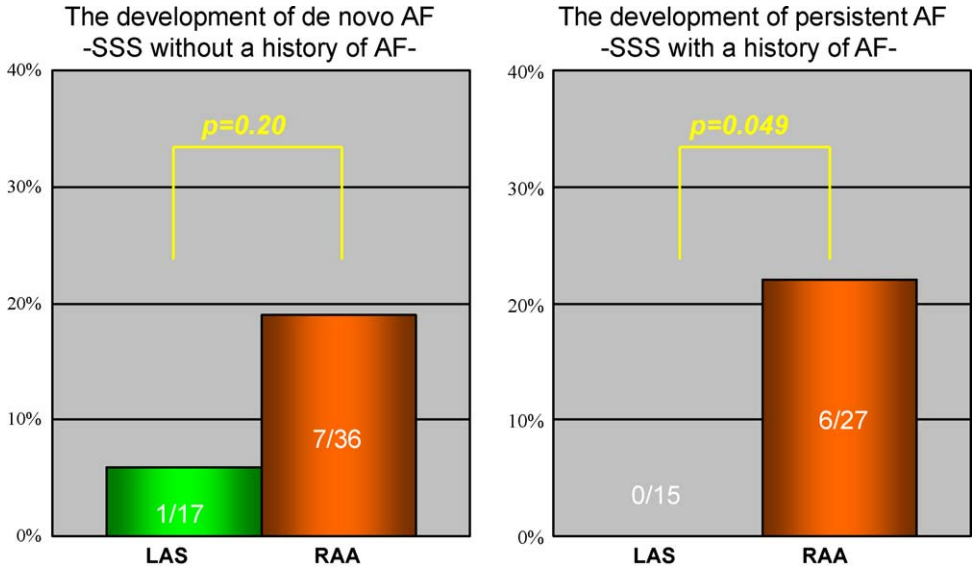


**Figure 5** The development of atrial fibrillation (AF) (follow-up period; 9 months) is shown in this figure. In the sick sinus syndrome (SSS) patients without a history of AF, 19.0% (7/36) of the patients in the right atrial appendage (RAA) pacing group developed de novo AF, but only 5.9% (1/17) of those in the low atrial septal (LAS) pacing group developed de novo AF ($p=0.20$). On the other hand, in the SSS patients with a history of AF, 22.0% (6/27) of the patients in the RAA group developed persistent AF, but none in the LAS group developed persistent AF ($p=0.049$).

**Table 3** Baseline characteristics of the patients with a history of atrial fibrillation (AF).

| | LAS ($n=15$) | RAA ($n=27$) | $P$ |
|---|---|---|---|
| Age (years) | 73 ± 8 | 73 ± 7 | 0.90 |
| Male gender, % ($n$) | 53(8) | 37(10) | 0.31 |
| Hypertension, % ($n$) | 60(9) | 59(22) | 0.13 |
| Diabetes mellitus, % ($n$) | 20(3) | 15(4) | 0.67 |
| Structural heart disease, % ($n$) | 40(6) | 37(10) | 0.92 |
| Hemodialysis, % ($n$) | 13(2) | 4(1) | 0.26 |
| Complication of I degree AVB, % ($n$) | 7(1) | 0(0) | 0.17 |
| Echocardiographic parameters | | | |
| LVDd (mm) | 46 ± 4 | 48 ± 6 | 0.42 |
| LVDs (mm) | 28 ± 5 | 30 ± 7 | 0.35 |
| LAD (mm) | 40 ± 4 | 42 ± 7 | 0.57 |
| EF (%) | 71 ± 10 | 67 ± 11 | 0.38 |
| BNP (pg/ml) | 452 ± 962 | 157 ± 239 | 0.25 |
| Medications | | | |
| Sodium channel blocker, % ($n$) | 33(5) | 19(5) | 0.31 |
| β Blocker, % ($n$) | 20(3) | 19(5) | 0.95 |
| ACEI and/or ARB, % ($n$) | 20(3) | 33(9) | 0.32 |
| Statin, % ($n$) | 13(2) | 19(5) | 0.59 |

LAS, low atrial septum; RAA, right atrial appendage; AVB, atrioventricular block; LVDd, diastolic left ventricular dimension; LVDs, systolic left ventricular dimension; LAD, left atrial dimension; EF, ejection fraction; BNP, B-type natriuretic peptide; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker.

## Discussion

This observational study suggested that LAS pacing was effective for preventing the persistence of AF in patients with SSS undergoing dual-chamber pacemaker implantations, and the pacing thresholds and sensing data were similar to that of RAA pacing. In recent years, various types of atrial pacing that might reduce the occurrence of AF have been studied. Several reports have suggested that site-specific atrial pacing, e.g. high atrial septal pacing, that is Bachmann's bundle, low atrial septal, LA, or dual-site atrial pacing, might be more effective by virtue of shortening the total interatrial activation times. Multi site pacing has generally positive results [13—16]. However, the usual methods of bi-atrial stimulation require two leads: one placed in the RA and another in the LA, using the coronary sinus. The LA lead can be placed by inserting a lead in the proximal coronary sinus. This approach has the disadvantage of requiring an extra lead, which increases the cost and difficulty of the implant procedure. Atrial septal pacing is a simple method, which may produce simultaneous bi-atrial stimulation, using a single lead. Prior clinical trials of atrial septal pacing have produced mixed results [15—27]. The study by Bailin of Bachmann's bundle pacing showed positive results with a longer survival-free rate of AF as compared with RAA pacing [24]. A study by Padeletti et al. in 2001 showed the benefit of septal pacing in 46 patients randomized to RAA pacing or septal pacing in the prevention of paroxysmal AF [25]. Pacing from the atrial septum was reported to shorten the atrial conduction time and improve the dispersion of the refractoriness [10]. As shown in Fig. 4, the P wave width shortened with pacing from 110 ms to 100 ms. Consequently, atrial pacing was able to inhibit the triggered premature atrial conducted beats from the pulmonary veins (PVs) due to a shorter conduction time between the atrial pacing from the LAS and PVs, as compared to the atrial pacing from the RAA. Moreover, an improvement in the dispersion of the refractoriness may modify the atrial substrate and inhibit the progression to persistent AF. However, a later, large multi-center study of the combined effect of septal pacing and AT/AF tachycardia pacing prevention algorithms failed to show the benefit of atrial septal pacing [26,27]. Sweeney et al. reported that unnecessary ventricular pacing correlated with the persistence of AF in patients with SSS [12], however the previous studies having a short AV delay and higher Cum%VP may have induced the onset of AF regardless of the region of the atrial leads. In this study, the AV interval was dependent on the discretion of the physician, but ventricular sensing took precedence as often as possible. In the group with a history of AF, due to frequent mode switches from DDD to DDIR during AF, the atrial pacing sites were not affected by the AV intervals, and the Cum%VP was similar between the two groups. However, the Cum%VP was lower for LAS pacing than RAA pacing because of the shorter conduction time from the atrial pacing site to the ventricular sensing site in those without a history of AF. In the SSS patients with long PQ intervals, LAS pacing may be more effective when considering the Cum%VP. Some patients with a history of AF had a high frequency of mode switches, but remained in sinus or a pacing rhythm. This suggests that LAS pacing may be more effective than RAA pacing in inhibiting the progression to persistent AF in patients with a large sized LA. On the other hand, Bachmann's bundle pacing showed positive results, however, the atrial lead placement was much easier at the LAS using a Locator™ than in Bachmann's bundle region, and the ascending aorta is located behind Bachmann's bundle anatomically, so implantations of the atrial screw-in lead may involve the risk of a perforation of the ascending aorta [28].

The limitations of this study may include the following. First, the follow-up periods were relatively short. Longer term results are desirable. Second, the programmed AV delays were dependent on the discretion of the physicians, however, ventricular sensing was given precedence as often as possible. Third, asymptomatic and unrecognized AF may be included in the SSS patients without a history of AF because asymptomatic and unrecognized AF was very common in those with SSS. The use of only the 12-lead ECG and Holter ECG recordings before the pacemaker implantations was insufficient for detecting the AF episodes, so we defined the patients with a history of AF as those having more than 1 min of mode switching within 1 week after the pacemaker implantation as well as any documented AF in the 12-lead ECG and Holter ECG recordings. Fourth, the allocation to LAS and RAA pacing was not parallel. An allocation bias may have affected the results, however, the SSS patients were consecutive patients and there were no statistical differences in the patient background between the LAS and RAA groups. We expect there would be the same results for the safety and efficacy of LAS pacing. Fifth, all right ventricular (RV) leads were implanted in the RV apex. RV septal pacing affects a different ventricular motion [29] than RV apex pacing, and consequently may affect the development of AF and progression to persistent AF. However, the Cum%Vp was relatively low in the SSS patients, and we expect there would be the same results regardless of the RV pacing site. Sixth, this study had a small sample size and used an observational and non-randomized analysis. A large, prospective, and multi-center trial may be required.

## Conclusions

LAS pacing is safe and feasible. LAS pacing, compared to traditional RAA pacing, may inhibit the maintenance of AF in SSS patients with paroxysmal AF.

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