Efficacy of Low Interatrial Septum and Right Atrial Appendage Pacing for Prevention of Permanent Atrial Fibrillation in Patients with Sinus Node Disease: Results from the Electrophysiology-Guided Pacing Site Selection (EPASS) Study

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Abstract:

**Background** - The role of pacing sites and atrial electrophysiology on the progression of AF to the permanent form in patients with SND has never been investigated. Aim of the study was to investigate the relationship between atrial electrophysiology and the efficacy of atrial pacing at the low interatrial septum (IAS) or at the right atrial appendage (RAA) to prevent persistent/permanent atrial fibrillation (AF) in patients with sinus node dysfunction (SND).

**Methods and Results** - EPASS was a prospective, controlled, randomized study. Atrial refractoriness, basal and incremental conduction times from the RAA to the Coronary Sinus ostium were measured before implantation and difference (ΔCTos) calculated. Patients with ΔCTos≥50 ms (Study Group) and those with ΔCTos<50 ms (Control Group) were randomized to RAA or IAS with algorithms for continuous atrial stimulation ON. The primary endpoint was time to development of permanent or persistent AF within a 2-year follow-up in the study group, IAS vs RAA. Data were analyzed by intention to treat. One hundred two patients (77±7 yrs, 44M) were enrolled, 69 (68%) in the study group and 33 (32%) in the control group. Of them, 97 ended the study, respectively randomized: 29 IAS vs 36 RAA and 18 IAS vs 14 RAA. After a mean follow-up of 15±7 (median 17) months, 11 (16.6%) patients in the study group met the primary endpoint: 2 IAS vs 9 RAA (log rank=3.93, P=0.047).

**Conclusions** - In patients with SND and intra-atrial conduction delay, low IAS pacing was superior to RAA pacing in preventing progression to persistent or permanent AF.

**Clinical Trial Registration** - ClinicalTrials.gov NCT00239226

**Key words:** Interatrial septum pacing, Right atrial appendage pacing, Atrial fibrillation, Sinus node disease, Electrophysiologic study
Introduction

In patients with inducible atrial fibrillation (AF), a significant prolongation of conduction times to the posterior triangle of Koch has been described (1, 2). Moreover, distal coronary sinus and interatrial septum (IAS) pacing at the coronary sinus ostium (CS-os) have been shown to be able to prevent AF induction in the setting of acute EP study, owing to a reduction of intra-atrial conduction delay of premature stimuli at the postero-septal area (2-4). A few clinical studies have reported that IAS pacing applied at either the low IAS (5) or at the Bachman bundle (6) is more effective than conventional RAA pacing in reducing symptomatic AF recurrences and progression to chronic AF in patients with bradycardia. However, this preventive effect of IAS pacing on AF has not been observed in other prospective randomized and controlled clinical studies (7, 8). The presence of shortened atrial refractoriness, atrial refractoriness dispersion and intra-atrial conduction delay have been identified as predictors of post-pacing AF occurrence in patients with SND receiving conventional RAA pacing (9, 10). The potential relationship between individual atrial electrophysiological properties and AF development during chronic atrial pacing at different atrial sites has not yet been investigated.

The goal of the present investigation was to evaluate whether chronic pacing applied at the low IAS is superior to chronic RAA pacing for the prevention of persistent or permanent AF in patients with SND and intra-atrial conduction delay to the posterior triangle of Koch, as compared with patients without any evidence of intra-atrial conduction delay during pre-implantation EP evaluation.
Methods

The EPASS was a multicenter prospective randomized and controlled study enrolling patients with SND and indication for permanent pacing. The study was approved by the local ethics committees of all participating centers. In order to be included in the study, all the following criteria had to be met: SND with a Class I indication for permanent pacing; age > 18 years; patient ability to comply with follow-up requirements; signed informed consent.

Exclusion criteria were: pregnancy, anamnestic TIA or stroke, neoplastic or any other severe disease reducing life expectancy (<3 years), heart surgery within the last 6 months, left atrial diameter > 55 mm, determined in the parasternal long-axis view, and participation in other studies.

Study protocol

The study design is outlined in Figure 1. Patients underwent EP evaluation prior to device implantation, after discontinuation of any antiarrhythmic therapy for at least 5 half-lives of the drugs. Under local anesthesia with lidocaine, two multipolar catheters were positioned at the RAA and in the coronary sinus, with the proximal pair placed at the ostium. Surface electrocardiographic leads I, II, aVF and V1 and intracardiac electrograms from the RAA and CSos, filtered at 40-500 Hz, were simultaneously displayed on a multichannel monitor, stored and printed at a paper speed of 200 mm/s. Stimulations were performed with 2-ms square wave pulses at twice the diastolic threshold. The atrial effective refractory period (ERP) at the RAA was measured by the extrastimulus technique with a step-up protocol until atrial capture. After a train of eight paced cycles at 600 ms (S1), an extrastimulus (S2) was delivered and the coupling
interval (S1S2) was increased in 10-ms steps. A1 and A2 are the atrial electrograms resulting from S1 and S2. The atrial ERP was defined as the longest S1-S2 interval that failed to result in an atrial depolarization (A2). The baseline and incremental intra-atrial conduction times from the RAA to the coronary sinus ostium (CTos and ICTos, respectively) were then measured during straight atrial pacing, 10 ms above the atrial ERP. Finally, the difference between the ICTos and the CTos was calculated (ΔCTos=S2A2os – S1A1os). On the basis of the literature data (1, 2, 9, 10) and our previous experience (11), a significant intra-atrial conduction delay to the posterior triangle of Koch area was considered to be present if the measured ΔCTos was > 50 ms. Patients with this specific EP finding were assigned to the study group, while patients with a ΔCTos <50ms were assigned to the control group. An example of a patient with ΔCTos > 50 ms is shown in Figure 2.

Patients of both groups were then randomized to RAA or low IAS pacing. Pacing site randomization was decided in real time as soon as the result of the EP study was available. Randomization was stratified by center and balanced according to history of AF, sex, age and other variables: hypertension, diabetes, coronary artery disease, NYHA functional Class, LVEF, and heart failure.

The sample size of the study was estimated for patients with ΔCTos>50ms (study group), comparing IAS vs RAA. The primary end point was time to development of persistent/permanent AF within 24 months. We hypothesized that IAS could reduce by 50% the incidence of persistent/permanent AF compared to RAA in patients with ΔCTos>50ms during 24 months follow-up. Specifically, we hypothesized that 25% of patients with ΔCTos>50ms paced at the RAA could develop persistent/permanent AF versus 12% of patients with ΔCTos>50ms paced at the IAS. The estimated sample size able to provide an 80% power to
show a difference between these 2 groups, with a probability of 95% and a drop-out <10%, is 150 patients per group. The patients in the control group were followed-up as an observational group. Data were analyzed by intention to treat. An interim analysis was planned after the enrolment of the first 100 patients to assess the prevalence of patients with ΔCTos>50ms, the incidence of adverse events in patients implanted in the IAS and to assess the preliminary results.

**The implanted pacing/sensing system**

The pacing system was implanted according to the standard clinical procedures usually applied by each investigator. All atrial leads were bipolar with a short tip-to-ring distance (<10 mm) to avoid far-field R-wave sensing in the atrium. The lead implanted at the IAS was always a screw-in Capsure-fix or Select-secure lead (Medtronic Inc). The appropriate positioning of the septal atrial lead just above the coronary sinus ostium was assessed under fluoroscopic control, using orthogonal incidences (right and left anterior oblique views). For each atrial site, pacing was accepted if the stimulation threshold was <1.5V and the sensing value was >1 mV. Septal pacing sites with ventricular far-field recordings greater than half the atrial voltage value were excluded.

The pacemakers used in this trial were the Vitatron model T-70 DDDR or Selection 9000 DDDR. Both these pacemakers have the CE mark of approval and are equipped with diagnostic and therapeutic algorithms for AF (12, 13). Device setting was aimed to continuously pace the atrium and to minimize ventricular pacing. Device programming:

- Mode: DDD or DDDR at the physician’s discretion.
- Basic rate: 60 bpm.
Diagnostic functions: all activated.

- Mode switching: AUTO (beat-to-beat).

All other parameters were programmed at the physician’s discretion.

**Follow-up evaluation**

After implantation, a lead stabilization phase of 3-5 weeks was observed: during this period each investigator optimized the device parameters for diagnostics (atrial sensing and atrial blanking) and therapies. No data regarding AF episodes or cardioversions were collected during the stabilization period.

At the end of this preliminary phase, each patient underwent the 1st follow-up examination and started the monitoring period, which 2 years if the patient did not develop permanent AF.

Regular follow-up examinations and data collection were scheduled every 6 months.

**Definitions of paroxysmal, persistent and permanent Atrial Fibrillation**

Paroxysmal Atrial Fibrillation was defined as any AF episode lasting more than 5 minutes and less than 7 days, as diagnosed by the implanted device.

Persistent Atrial Fibrillation was defined as any AF episode lasting more than 7 days, requiring cardioversion or not, as diagnosed by the implanted device.
Permanent Atrial Fibrillation was defined as the 3rd episode of persistent AF: no further follow-up for the study was scheduled in this case.

**Primary and secondary endpoints**

The primary end point was time to development of persistent/permanent AF within 24 months, IAS vs RAA, in the study group.

Secondary objectives focused on the comparison between the study group and the control group and related subgroups, through the following variables:

- Number of persistent AF episodes (> 7 days) through pacemaker telemetry.
- Time to first episode of any AF after the stabilization phase, through pacemaker telemetry.
- Duration of each AF episode (Paroxysmal and Persistent) in groups and subgroups.
- Atrial and Ventricular pacing percentage, as revealed through pacemaker telemetry.
- Symptoms collected through the Specific Symptoms Scale Questionnaire (11): palpitations, effort dyspnea, rest dyspnea, exercise intolerance, easy fatigue, chest discomfort. A global score was computed for each patient by adding the score for each single symptom.
- Hospitalizations for heart failure.

**Statistical analysis**
Continuous variables were reported as the mean ± SD. Non parametric Mann-Whitney U test was used to compare not normally distributed variables and Student’s unpaired T-test for normally distributed variables. Skewness of distributions was tested by means of the Shapiro-Wilk test. Kaplan-Meier survival estimate was obtained for the primary endpoint. Curves were compared using the log-rank test. Proportions were compared by Fisher’s exact test. A P value <0.05 was regarded as significant for the primary endpoint.

Results

The EPASS study enrolled 102 patients, 97 of whom ended the study after a mean follow-up of 15±7 months, median 17, range 3-24. The study was prematurely closed when the interim analysis showed no adverse events in patients treated with IAS pacing and the proportion of patients with persistent/permanent AF in the RAA study group was 25% as expected, vs 6.9% in the IAS study group, corresponding to a reduction much higher than 50% as hypothesized in the protocol.

In those patients with history of AF (71%), the arrhythmia was paroxysmal. Patients with history of AF had ΔCTos=64±36ms vs 60±30ms (P=0.60) in those without history of the arrhythmia. P-wave duration was significantly longer in patients paced at the RAA vs IAS, respectively: 132±11 ms vs 112±10 ms (P=0.02). Patients with a ΔCTos > 50 ms numbered 69 out of the 102 enrolled (68%). The characteristics of the patient population are shown in table 1A-B. ΔCTos differed significantly between the study group and the control group (P<0.0001), in accordance with the criteria for patient classification through the electrophysiological study.
ICTos also showed a similar difference between the 2 patient groups (P<0.001). No other parameters differed significantly among the study groups and related subgroups. Figure 3 shows the details of the patient flow from enrollment to study closure.

During the study we did not see any far-field artifact lasting more than 5 min, the threshold we considered to collect the AF episodes.

**Primary endpoint**

Kaplan-Meier curves (figure 4) showed a statistically significant difference (log rank=3.93, P=0.047) in sinus rhythm survival of IAS vs RAA patients in the study group. At the time of the study closure, permanent/persistent AF incidence was 25% vs 6.9% respectively in patients treated with RAA vs IAS pacing.

**Secondary endpoints**

There were no statistically significant differences comparing the time to permanent/persistent AF of each group, except those of the primary endpoint: IAS (study group) vs IAS (control group), log rank=0.21, P==0.64; RAA (study group) vs RAA (control group), log rank=0.13, P=0.71; IAS (control group) vs RAA (control group), log rank=0.35, P=0.55. The comparison of the overall patients in the study group (independently of pacing site) with the overall patients in the control group did not show any statistically significant difference: log rank=0.22, P=0.64.

A total of 20 persistent AF episodes were recorded during follow-up: 16 in the study group and 4 in the control group.

The time to the first AF recurrence, either paroxysmal or persistent, did not show any statistically significant difference among groups: 66 ± 89 (median 30) days in the study group IAS vs 83 ±
145 (median 9) days in the study group RAA (P=0.55); 160 ± 212 (median 50) days in the control group IAS vs 18 ± 19 (median 14) days in the control group RAA (P=0.08).

AF episodes lasting more than 24h were not significantly longer in RAA vs IAS patients. In study group patients paced in the RAA vs IAS patients the duration of the episodes was: 10.69 ± 17.52 (median 2.3) days vs 3.167 ± 3.674 (median 1.6) days, respectively (P=0.15). In control group patients, episode duration was 6.236 ± 6.675 days (median 3.4) in IAS patients vs 4.667 ± 7.122 days (median 1.85) in RAA patients (P=0.052).

AF burden (mean percentage of time spent in AF during follow-up) at the last follow-up was not significantly different between the groups: 2.44±7.70 % (median 0.0%) in IAS Study Group vs 11.30±25.40 % (median 0.0%) in RAA Study Group (P=0.25). Excluding the patients who reached the endpoint of persistent/permanent AF, so considering only PAF patients, the difference was much less remarkable: 1.06±3.22 % (median 0.0%) in IAS study Group vs 2.28±7.12 % (median 0.0%) in RAA Study Group (P=0.71).

Rate Responsive function was activated in all patients. The atrial pacing percentage was 87 ± 28 % (median 93) in the IAS study group vs 86 ± 20 % (median 99) in the RAA study group (P=0.06). In the control group the atrial pacing percentage was 88 ± 22 % (median 98) in the IAS vs 95 ± 12 % (median 99.5) in the RAA group (P=0.20).

The ventricular pacing percentage was 23 ± 34 % and 17 ± 28 % in the IAS and RAA study groups, respectively (P=0.47). The RAA control subgroup showed a higher ventricular pacing percentage than the IAS control subgroup: 40 ± 42 % vs 8 ± 13 % (P=0.037). This was probably due to shorter AV conduction times during atrial septum pacing.

Symptoms were collected at the last follow-up examination and patients compared. There were no statistically significant differences between groups: 9 ± 6 (median 8.2) in the IAS study
group vs 10 ± 8 (median 7.0) in the RAA study group (P=0.96) and 9 ± 7 (median 9.0) in the IAS control group vs 8 ± 6 (median 8.0) in the RAA control group (P=0.40).

There were 3 hospitalizations for heart failure during follow-up: one control group patient paced at the IAS in NYHA I on enrollment and 2 study group patients paced at the RAA in NYHA II on enrollment. None of them had a history of heart failure hospitalizations prior to the study. All had hypertension and EF>50 % on enrollment. None developed persistent or permanent AF during the study.

During the study antiarrhythmic medications were added in 2 patients of the study group paced in the RAA who reached the endpoint. Beta-blockers were administered in less than 10% in each group.

In the overall patient population, the number of patients who developed persistent AF during follow-up was 11/50 (22%) among those paced at the RAA, versus 4/47 (8.5%) among those paced at the IAS (P=0.09).

Neither lead displacements nor cross-over occurred in either the RAA or the IAS groups.

**Discussion**

The main finding of the EPASS study is that low IAS pacing is superior to RAA pacing in preventing persistent or permanent AF in patients with SND and intra-atrial conduction delay (ΔCTos>50 ms). On the other hand, in the absence of any intra-atrial conduction delay, low IAS and RAA pacing are not statistically different. To the best of our knowledge, this is the first study to demonstrate this finding.

Previous studies on the efficacy of atrial pacing at the low IAS for AF prevention yielded controversial results. Padeletti et al. (5) showed that rate-adaptive pacing at the triangle of Koch
is more effective than RAA pacing in preventing symptomatic recurrences of paroxysmal AF in patients with sinus bradycardia and a history of AF. However, two subsequent prospective randomized studies (7, 8) in similar patient populations failed to demonstrate this superiority of IAS to conventional appendage pacing. A major difference between all these previous studies and the present one is that we used persistent or permanent AF as the primary endpoint. Pacemakers are validated tools for atrial arrhythmia monitoring and their use has been increasingly accepted for investigations in the field of AF (11-18). The use of the data stored by the implanted devices has considerably improved our knowledge of AF, as it does not depend on unreliable subjective reports of symptoms (11-18).

One of the secondary endpoints of the EPASS study was the time to the first recurrence of any AF lasting more than 5 minutes, thus including paroxysmal AF episodes, as documented by the device diagnostics. No difference in this parameter was noted among groups and subgroups, which is in complete agreement with previous findings by Hermida (7). Progression to chronic AF was the primary endpoint of only one previously published randomized multicenter trial evaluating the efficacy of conventional RAA pacing and of Bachmann’s bundle pacing (6). Interestingly, that study found that Bachmann’s bundle pacing was more effective in attenuating the progression of AF. On analyzing our results independently of the individual atrial electrophysiology, i.e. by simply comparing the number of patients showing persistent or permanent AF in the IAS and RAA groups, we again observed less AF in patients paced at the IAS. This observation is in agreement with Bailin’s results (6).

Differences in atrial or ventricular pacing percentages cannot have influenced our results, as these percentages were the same in the different groups and subgroups.
It has been suggested that septal pacing is effective in preventing AF thanks to decreased atrial activation times (1-3, 19, 20, 21) and because it prolongs the premature interval at a critical site of slow conduction relative to the site of ectopy, as has been shown in animals and humans (4, 22). Our findings support this hypothesis: study group patients, who were selected on the basis of marked conduction delay to the posterior triangle of Koch, had less persistent or permanent AF if paced at the low IAS. Control group patients, who were selected on the basis of the absence of any conduction delay to the posterior triangle of Koch, showed the same incidence of persistent/permanent AF regardless of the pacing site. Presence of intra-atrial conduction delay may identify a subgroup of patients at particularly high risk of progression to chronic AF, and this progression might be attenuated by low IAS pacing.

Our investigation did not address the questions of whether IAS pacing is effective in preventing permanent AF or whether RAA pacing has a proarrhythmic effect. The data shown in fig 3 support the hypothesis that IAS tends to be more beneficial in patients with ΔCTos>50 ms than in those with ΔCTos <50 ms (permanent/persistent AF incidence: 6.9% vs 11%, respectively) and that RAA pacing tends to have a negative effect in patients with ΔCTos>50 ms, as compared with those with ΔCTos <50 ms (25% vs 14%, respectively). However, on the basis of these results, we cannot exclude the possibility that, in patients with SND and marked intra-atrial conduction delay, chronic atrial pacing from the RAA is in some way “pro-arrhythmic”, promoting AF to the persistent form. The possibility that RAA pacing might be pro-arrhythmic in humans was raised by Duytshaever et al. (4), who reported that pre-excitation of the low IAS by pacing at the coronary sinus ostium, or even at the right ventricle, in the presence of retrograde conduction, could prevent the initiation of paroxysms of AF triggered by single atrial premature beats, whereas pacing at the high right atrium had no preventive effect, or even had a
pro-fibrillatory effect. In their study, sinus rhythm also prolonged the coupling interval of premature beats to the coronary sinus ostium, and thus had a natural protective effect against AF induction, an effect that was completely absent during high right atrial pacing. In a previous study involving patients with SND and conduction delay to the posterior triangle of Koch randomized to receive chronic low IAS or RAA pacing, we reported a higher frequency of device-classified AF episodes in patients on RAA pacing than in those on low IAS pacing (23), a finding that had no obvious explanation. On the basis of the findings of the present study, the hypothesis that RAA pacing might be pro-arrhythmic in chronically paced SND patients remains open.

Our study clearly demonstrated that the preventive effects of chronic atrial pacing for persistent or permanent AF are not only influenced by the atrial pacing site, but also by the individual atrial EP characteristics of the patients. Patients with intra-atrial conduction delay benefited from low IAS, whereas, in the absence of any conduction delay, low IAS and RAA pacing were equivalent.

This fact, and the difference in endpoints, may explain why previous studies on IAS vs RAA pacing have yielded non-uniform results. However, in the EPASS study, pacing at the low IAS was never inferior to RAA pacing, either in study group or control group patients. This is a crucial result, which provides the rationale for supporting IAS pacing in every SND patient indicated for permanent atrial pacing. Low IAS was safe and well tolerated in every patient. No atrial lead displacement was observed and symptoms collected through the Specific Symptoms Scale did not show any difference between groups and subgroups, confirming that IAS pacing is as well tolerated as RAA pacing. We observed 3 heart failure hospitalizations throughout the follow-up, one in a control patient paced at the IAS, and two in study group patients with an
RAA lead. As none of these patients met the primary endpoint, no differences in heart failure hospitalizations were noted between IAS- and RAA-paced patients.

**Limitations**

The study was prematurely terminated after the interim analysis showed that the primary endpoint was reached without any adverse event related to IAS pacing. Consequently, the number of patients in each group was quite low.

We did not measure the effect of the different sites of atrial pacing on the intra-atrial delays. The pacemakers we used in this investigation were equipped with an algorithm for minimizing ventricular pacing (Refined Ventricular Pacing) that is an automatic hysteresis of the AV interval, non comparable with the recent algorithms for Minimum Ventricular Pacing, so we could not expect ventricular pacing percentages close to 0%. Anyway the same algorithm was activated in every patient of every group.

**Conclusion**

IAS pacing is superior to RAA pacing in preventing the development of persistent or permanent atrial fibrillation in patients with sinus node disease and intra-atrial conduction delay at the posterior triangle of Koch, as assessed by EP study.

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**Conflict of Interest Disclosures:** Giorgio Corbucci is employee of Medtronic.
References:


Table 1A  Demographics and Clinical Baseline Parameters (97 patients)

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<th>NYHA III</th>
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CAD=Coronary artery disease
Table 1B  Electrophysiological Baseline Parameters (97 patients)

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<th>AF (%)</th>
<th>ERP (ms)</th>
<th>Ctos (ms)</th>
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<td>18 (19)</td>
<td>13 (72)</td>
<td>282±53</td>
<td>67±31</td>
<td>92±39*</td>
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<td>8 (57)</td>
<td>285±37</td>
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<td>91±33*</td>
<td>26±14^</td>
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</table>

* P<0.001 vs study group; ^ P<0.0001 vs study group

IAS = Interatrial Septum; RAA = Right Atrial Appendage; NYHA = New York Heart Association class; AF = Atrial Fibrillation; ERP = Effective Refractory Period at the RAA; CTos = Conduction Time: the interval between the first intrinsic deflection of atrial electrogram recorded at the RAA and the first intrinsic deflection of atrial electrogram recorded at the coronary sinus ostium during straight atrial pacing from RAA; ICTos = Incremental Conduction Time: the interval between the first intrinsic deflection of atrial electrogram recorded at the RAA and the first intrinsic deflection of atrial electrogram recorded at the coronary sinus ostium during straight atrial pacing from RAA, delivered 10 ms above the atrial ERP; ΔICTos = difference between ICTos and CTos.
Figure Legends:

**Figure 1** - The study design. After enrollment, each patient underwent EP study, was classified on the basis of ∆CTos (> or < 50 ms) and then randomized to IAS or RAA pacing. Telemetric and ambulatory data were collected at each follow-up examination.

**Figure 2** - An example of EP signals used for measuring ∆CTos in a patient with ∆CTos > 50 ms. The incremental conduction time (ICT) is measured as the interval between the first intrinsic deflection of the atrial electrogram (S2 delivered at the RAA) and the first intrinsic deflection of the atrial electrogram recorded at the CSos (ICTos) during programmed stimulation from the high right atrium (HRA), 10 ms above the atrial ERP. Finally, the difference between the ICTos and the CTos is calculated (∆CTos=S2A2os – S1A1os).

**Figure 3** - Participant flow: 102 patients were enrolled, 97 (95%) of whom completed the study.

**Figure 4** - Probability (Kaplan-Meier curve) of maintaining sinus rhythm in patients with ∆CTos>50 ms (study group) undergoing RAA pacing or IAS pacing. The difference is statistically significant (log rank=3.93, P=0.047).
SND Pts

EP study

Study group

Pts with severe conduction delay
$\Delta CTos > 50\, ms$

Randomization IAS vs RAA pacing
Algorithms ON

IAS

RAA

Control group

Pts with normal conduction delay
$\Delta CTos < 50\, ms$

Randomization IAS vs RAA pacing
Algorithms ON

IAS

RAA

FU every 6 months until the end of the study
Participant Flow for Primary Endpoint

SND Pts; 102 enrolled

End of Stabilization Phase; 99

3 pts developed permanent AF immediately after implantation

ΔCTos > 50 ms

Study Group, 66

IAS, 29

2 (6.9%)

ΔCTos < 50 ms

Control Group, 33

IAS, 18

2 (11%)

RAA, 36

9 (25%)

2 pts were lost to FU; 97 pts ended the study

RAA, 14

2 (14%)

#(%) Pts who developed Permanent or Persistent AF
Sinus Rhythm Survival vs Time (K-M Method)

Survival Probability

Time (months)

(log rank=3.93, P=0.047)

Study group

IAS - RAA
Efficacy of Low Interatrial Septum and Right Atrial Appendage Pacing for Prevention of Permanent Atrial Fibrillation in Patients with Sinus Node Disease: Results from the Electrophysiology-Guided Pacing Site Selection (EPASS) Study

Roberto Verlato, Giovanni Luca Botto, Riccardo Massa, Claudia Amellone, Antonello Perucca, Maria Grazia Bongiorni, Emanuele Bertaglia, Vigilio Ziacchi, Marcello Piacenti, Attilio Del Rosso, Giovanni Russo, Maria Stella Baccillieri, Pietro Turrini and Giorgio Corbucci

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Supplemental Material

Appendix: List of participating hospitals and physicians:

General Hospital, Camposampiero (PD), Italy: Roberto Verlato, Maria Stella Baccillieri, Pietro Turrini
S. Anna Hospital, Como, Italy: Giovanni Luca Botto, Giovanni Russo
Molinette Hospital, Torino, Italy: Riccardo Massa, Claudia Amellone
Presidi Ospedalieri Riuniti, Borgomanero (NO), Italy: Antonello Perucca
Cisanello Hospital, Pisa, Italy: Maria Grazia Bongiorni, Giuseppe Arena
Mirano Hospital, Mirano (VE), Italy: Emanuele Bertaglia
Desenzano Hospital, Desenzano (BS), Italy: Vigilio Ziacchi, Giampaolo Gelmini
CNR, Pisa, Italy: Marcello Piacenti, Luca Panchetti, Umberto Startari
Fucecchio Hospital, Fucecchio (PI), Italy: Attilio Del Rosso, Paolo Bartoli, Vincenzo Guarnaccia.