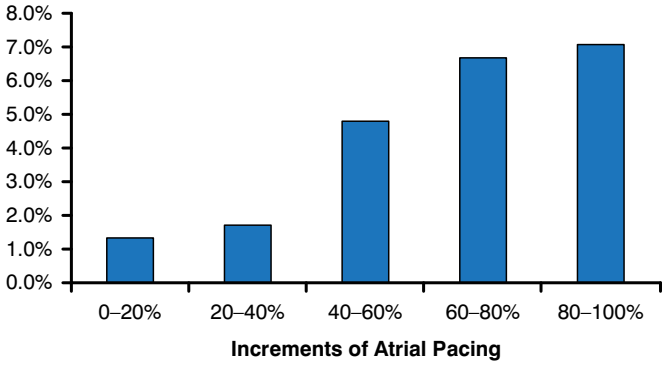
P-wave duration (Figure 1) [Kristensen L et al. *Pacing Clin Electrophysiol* 2004].

A meta-analysis has shown that the risk for AF is increased with A-pacing (Figure 2) and that rate-adaptive pacing causes more A-pacing [Elkayam LU et al. *Pacing Clin Electrophysiol* 2011]. The Advanced Elements of Pacing Randomized Controlled Trial [ADEPT] showed that there was no beneficial effect of rate-adaptive pacing on functional status or quality of life of patients with bradycardia indications for dual-chamber pacing [Lamas GA et al. *Heart Rhythm* 2007]. The Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial [ASSERT] showed that continuous atrial overdrive pacing did not prevent new-onset AF and was poorly tolerated [Hohnloser SH et al. *Heart Rhythm* 2012]. ASSERT also showed that AF >6 minutes in duration was associated with more atrial tachycardia and more thromboembolic events [Kaufman ES et al. *Heart Rhythm* 2012].

Figure 2. Atrial Pacing Increases Risk for Atrial Fibrillation



Reproduced with permission from John Wiley from Elkayam LU, Koehler JL, Sheldon TJ, et al. The influence of atrial and ventricular pacing on the incidence of atrial fibrillation: a meta-analysis. *Pacing Clin Electrophysiol* 2011;34:1593-1599.

However, it is unknown whether reducing A-pacing can reduce AF. The randomized, controlled DANPACE II trial will test in 900 patients whether dual-chamber pacing at 40 beats/min (DDD-40) reduces the incidence of AF ≥6 minutes compared with dual-chamber, adaptive-rate pacing at 60 beats/min (DDDR-60) in patients with sick sinus syndrome (SSS). Central remote monitoring will be conducted during the 2-year trial; all messages requiring clinical action will be sent to the local hospital of the patient.

The primary endpoint is the time to the first episode of pacemaker (PM)–detected AF >6 minutes. Secondary end points are the time to the first episode of PM-detected AF >6 hours and to >24 hours, number of AF episodes, percentage of time in AF, time to persistent AF, hospital admission because of AF, time to cardioversion for AF, time to PM reprogramming, time to event (stroke, transient cognitive impairment, or peripheral thromboembolism), time to death, quality of life, and 6-minute walk distance.

The inclusion criteria are patients aged ≥18 years with SSS and an indication for their first DDD PM (symptomatic sinus pause >2 seconds or sinus bradycardia with or without paroxysmal AF).

The exclusion criteria are permanent or persistent (>7 days) AF before PM implantation, persistent sinus bradycardia or symptomatic chronotropic incompetence (SCI) requiring DDD pacing at >40 beats/min, life expectancy < 1 year, grade II or III persistent AV block, indication for an implantable cardioverter-defibrillator or cardiac resynchronization therapy, pregnancy, or participation in another intervention study.

Patients with suspected SCI in the DDD-40 group will be crossed over to the DDDR-60 group after exercise testing and 24-hour Holter monitoring. After 1 month, they will be reevaluated, and patients whose symptoms are reduced will remain on DDDR-60.

Presence of IAC Delay Is Critical to Selecting Patients for IASP

Written by Mary Beth Nierengarten

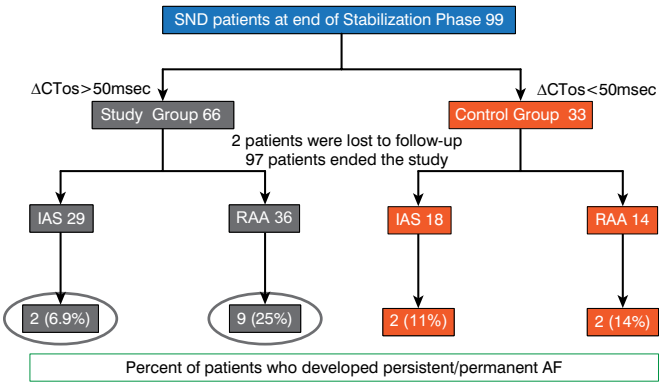
In patients with intra-atrial conduction (IAC) delay to the posterior triangle of Koch, pacing the interatrial septum (IAS) may play a role in preventing permanent or persistent atrial fibrillation (AF).

Giovanni L. Botto, MD, S. Anna Hospital, Como, Italy, presented data from the Electrophysiology-Guided Pacing Site Selection study, a prospective, active-controlled, randomized, multicenter study that assessed the efficacy of atrial pacing at the IAS versus the right atrial appendage (RAA) to prevent persistent or permanent AF in patients with sinus node disease (SND) [Verlato R et al. *Circ Arrhythm Electrophysiol* 2011].

Prior to implantation with an atrial-based pacing device, patients with SND underwent electrophysiologic studies to measure atrial refractoriness and the incremental conduction times from the RAA to the coronary sinus ostium, and the difference (ΔCTos) was calculated. Of the 102 study patients, 3 patients developed permanent AF immediately after device implantation and were excluded from the study.

Of the 99 remaining patients, 66 with IAC delay were assigned to the treatment group (ΔCTos >50 ms) and 33 to the control group (ΔCTos <50 ms). Two patients were lost to follow-up.

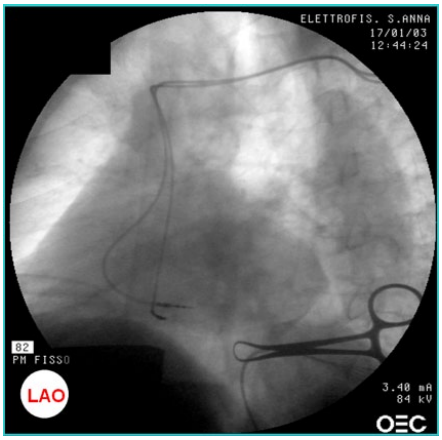
Figure 1. EPASS Trial Design



AF=atrial fibrillation; ΔCTos=change in conduction time to ostium; IAS=interatrial septum; pts=patients; RAA=right atrial appendage; SND=sinus node disease.

Reproduced with permission from Lippincott Williams & Wilkins from Verlato R, Botto GL, Massa R, et al. 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. *Circ Arrhythm Electrophysiol* 2011;4:844-850.

Figure 2. Low IASP: LAO View of Lead Positioning



IASP=interatrial septal pacing; LAO=left anterior oblique.

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Table 1. Baseline Parameters of Patients in EPASS

Patients, Number (%)	History of AF, Number (%)	ERP, mean ± SD, ms	CTos, mean ± SD, ms	ICTos, mean ± SD, ms	ΔCTos, mean ± SD, ms
IACd+ (67%)*					
Study group, IAS, 20 (30)	22 (76)	261±43	82±33	154±54	80±23
Study group, RAA, 36 (37)	23 (64)	257±40	82±35	148±45	79±27
IACd– (33%)**					
Control group, IAS, 18 (19)	13 (72)	282±53	67±31	92±39	26±14
Control group, RAA, 14 (14)	8 (57)	285±37	74±26	91±33	26±18

AF=atrial fibrillation; CTos=conduction time to ostium; ΔCTos=difference between CTos and ICTos; EPASS=Electrophysiology-Guided Pacing Site Selection; ERP; IACd=intra-atrial conduction delay; ICTos=incremental conduction time to ostium; IAS=interatrial septum; RAA=right atrial appendage.

*On November 12, 2014, this was changed from IACd (67%) to IACd+ (67%). **On November 12, 2014, this was changed from IACd (33%) to IACd– (33%).

The remaining 97 patients in the study were then randomly assigned to either RAA pacing (RAAP) or IAS pacing (IASP) with continuous atrial stimulation within each group. In the treatment group (Figure 1), 29 patients were randomized to IASP and 36 to RAAP. In the control group, 18 were randomly assigned to IASP and 14 to RAAP.

Figure 2 provides an example of the left anterior oblique view of the leads positioning in case of low IASP.

Table 1 shows the electrophysiologic baseline parameters of the study patients. The patients were assessed every 6 months. The primary end point was time to development of permanent or persistent AF in the 2-year study.

The results of the study showed that 11 patients (16.6%) in the treatment group developed permanent or persistent AF. Of these, 2 patients had IASP and 9 had RAAP (Figure 2) [Verlato R et al. *Circ Arrhythm Electrophysiol* 2011]. In the control group, 4 patients developed permanent or persistent AF, 2 with IASP and 2 with RAAP. More patients in the treatment group maintained sinus rhythm with IASP than with RAPP (p=0.047).

Prof. Botto stated that the study showed the superiority of low IASP over RAAP in preventing persistent or permanent AF in patients with sinus node disease and IAC delay to the posterior triangle of Koch.

The study also highlighted the importance of IAC delay in selecting patients who benefit from IASP, on the basis of the finding of no significant difference between low IASP and RAAP in the absence of IAC delay in the control group. Prof. Botto noted that these patients can easily be identified by a quick electrophysiologic study

during device implantation. The algorithms for continuous atrial pacing and the lead technology to permanently pace specific atrial sites are available.

No Difference in LV Function Between RV Apex or Septum Pacing

Written by Mary Beth Nierengarten

Patients with high-grade atrioventricular (AV) block and preserved baseline left ventricular (LV) function who need a high percentage of right ventricular (RV) pacing show small but significant reductions in LV ejection fraction (LVEF) over a 2-year period from pacing with either RV apex (RVA) or RV high septum (RVHS), with no difference between RVA and RVHS.

Gerry Kaye, MD, Department of Cardiology, University of Queensland, Princess Alexandra Hospital, Brisbane, Australia, presented results of the Protection of Left Ventricular Function During Right Ventricular Pacing [PROTECT-PACE; NCT00461734], a randomized, prospective, international, multicenter, single-blinded trial to compare the effect of pacing the RVA versus the RVHS on LV systolic function in patients with high-grade AV block. Full results of the study will be published in the *European Heart Journal*.

Sponsored by Medtronic UK, the study was undertaken to test the hypothesis that RVHS pacing is superior to RVA pacing in preventing LV dysfunction in patients with preserved LVEFs who need ventricular pacing. The need to examine pacing other than with the RVA is highlighted by accumulating evidence that RVA pacing has multiple deleterious effects, including the potential to result in long-term LV dysfunction.

The study included 240 patients with high-grade AV block and sinus rhythm or permanent atrial fibrillation (AF) who were randomly assigned to RVA pacing (n=120) or RVHS pacing (n=120). Patients with selected cardiac diseases were excluded, along with those with indications for implantable cardioverter-defibrillators or cardiac resynchronization therapy and those with intermittent AV block or reversible causes for AV block, those with known paroxysmal AF prior to enrollment, and those who needed amiodarone therapy within 6 months

Table 1. Patient Demographics[a]

Characteristic	RVA Pacing (n=120)	RVHS Pacing (n=120)	Total Patients Randomly Assigned (N=240)	p Value
Age, mean ± SD, years	73.7 ± 11.1	74.7 ± 10.0	74.2 ± 10.5	NS
Men	73 (60.8%)	89 (74.2%)	162 (67.5%)	0.0274
Systemic hypertension	76 (63.3%)	67 (55.8%)	143 (59.6%)	NS
Diabetes	29 (24.2%)	27 (22.5%)	56 (23.3%)	NS
Hypercholesterolemia	39 (32.5%)	46 (38.3%)	85 (35.4%)	NS
No diagnosed CV disease	22 (18.3%)	26 (21.7%)	48 (20.0%)	NS
Coronary artery disease	27 (22.5%)	31 (25.8%)	58 (24.2%)	NS
Primary/idiopathic electrical disease	24 (20.0%)	21 (17.5%)	45 (18.8%)	NS
Previous stroke	4 (3.3%)	5 (4.2%)	9 (3.8%)	NS
Transient ischemic attack	3 (2.5%)	3 (2.5%)	6 (2.5%)	NS
Previous CABG	8 (6.7%)	8 (6.7%)	16 (6.7%)	NS
Previous valvular surgery	5 (4.2%)	4 (3.3%)	9 (3.8%)	NS

CABG=coronary artery bypass grafting; CV=cardiovascular; RVA=right ventricular apex; RVHS=right ventricular high septum.

[a]Data are expressed as number (percentage) except as indicated.