Table 1. SARA Exclusion Criteria

Age <18 or >70 years
Long-standing persistent AF
Advanced remodeling stage (LA >50 mm)
Hyper- or hypothyroidism
Hypertrophic cardiomyopathy
Implanted pacemaker or defibrillator
Moderate or severe mitral disease or mitral prosthesis
Left ventricular ejection fraction <30%
Prior ablation procedure
Contraindication for oral anticoagulation
Ative infection or sepsis
Pregnancy
Unstable angina or acute myocardial infarction ≤3 months*
Life expectancy <12 months
Mental disease or inability to give informed consent
Disease contraindicating ablation or ADT

ADT=antiarrhythmic drug therapy; AF=atrial fibrillation; LA=left atrium; SARA=Study of Ablation Versus Antiarrhythmic Drugs in Persistent Atrial Fibrillation.

*On November 12, 2014, this was changed from £3 months to ≤ 3 months.

symptomatic, persistent AF at 12 months of follow-up. Eligible patients were those with symptomatic, persistent AF (>7 days or ≤7 days requiring cardioversion) who were refractory to at least 1 class 1 or class 3 antiarrhythmic drug. Exclusion criteria are outlined in Table 1.

The study's primary outcome measure was any episode of atrial fibrillation (AF) or atrial flutter (AFL) lasting >24 hours or requiring cardioversion after a 3-month blanking period, the time during which recurrences of AF were not included in the data analysis. Secondary outcomes included negative recurrence of AF or AFL, need for cardioversion, arrhythmia-related hospitalizations, and quality-of-life measures. More than 75% of patients were men, with a mean age of 55 years, and patients were randomly assigned to receive either CA (n=98) or ADT (n=48). Patients were seen at 1, 3, 6, and 12 months and underwent 24-hour Holter monitoring at 3, 6, and 12 months.

Prof. Mont then reviewed the primary endpoint from both the intention-to-treat (ITT) and per protocol (PP) populations. In the ITT analysis, significantly more patients who underwent CA were free of the primary endpoint compared with the ADT group (70.4% vs 43.7%, p=0.002; absolute risk reduction, 26.6%; 95% CI, 10.0 to 43.3). In the PP analysis, CA was again significantly superior to ADT in reducing episodes of AF or AFL lasting >24 hours or requiring cardioversion (72.8% vs 43.8%, p<0.001). Compared with the ADT group, the CA group also showed higher probability of remaining free of sustained AF recurrence or AFL (p<0.001). There were significant differences favoring CA for negative recurrence of AF or AFL and the need for cardioversion, but not the other secondary outcomes.

No deaths or strokes occurred in either group. The incidence of adverse events in the CA group (ITT population) was 6.1% and included pericarditis (n=2), pericardial effusion (n=1), minor vascular complications (n=3), and pulmonary vein stenosis (n=1). In the ADT group, there were 2 adverse events: 1 episode of flecainide intoxication and 1 minor vascular access complication. Although not seen in this analysis, new data suggest that patients who underwent ablation experienced increased quality of life, not seen with patients treated with pharmacotherapy [Wynn GJ et al. *Europace* 2014].

Prof. Mont concluded that CA is superior to medical therapy as a strategy for maintenance of sinus rhythm in patients with persistent AF at 12-month follow-up. Longer follow-up will determine the durability of CA for persistent AF.

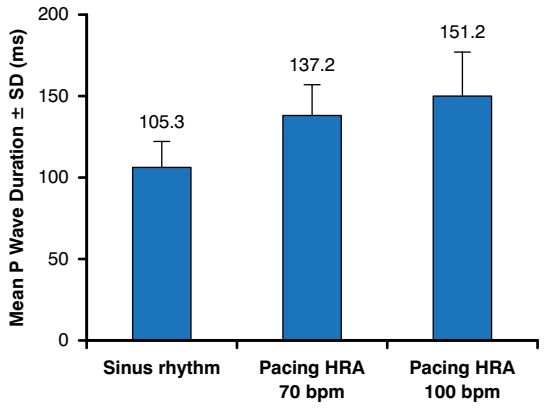
New Study to Test Effect of Reducing A-Pacing on AF

Written by Mary Beth Nierengarten

Jens Cosedis Nielsen, MD, Aarhus University Hospital, Skejby, Denmark, reviewed the background and design for the Reducing Atrial Pacing Rate to Reduce Atrial Fibrillation in Patients With Sick Sinus Syndrome study [DANPACE II; NCT02034526].

Atrial (A)-pacing may lead to prolonged and abnormal atrial activation and prolonged atrioventricular (AV) conduction, which in turn may increase ventricular pacing and thus may lead to atrial fibrillation (AF). A-pacing has been shown to cause P-wave prolongation, to induce P-wave axis changes, and to increase

Figure 1. Effect of Atrial Pacing on P-Wave Duration



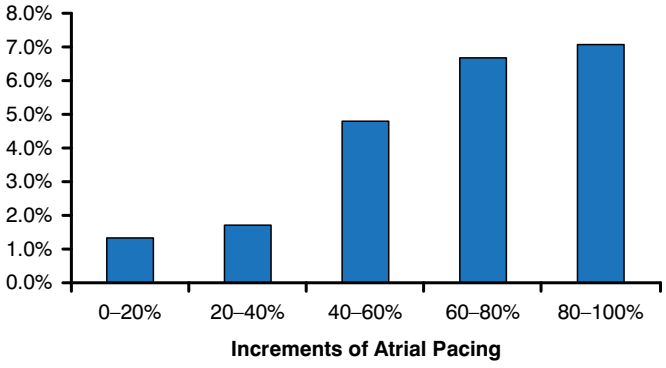
HRA=pacing at the high-rate atrium.

Reproduced with permission from John Wiley from Kristensen L, Nielsen JC, Mortensen PT, et al. Sinus and paced P wave duration and dispersion as predictors of atrial fibrillation after pacemaker implantation in patients with isolated sick sinus syndrome. *Pacing Clin Electrophysiol* 2004;27:606-614.

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.