NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA88; Dual-chamber pacemakers for symptomatic bradycardia due to sick sinus syndrome and/or atrioventricular block

This guidance was issued in February 2005.

The review date for this guidance is September 2011.

1. Recommendation

A review of TA88 'Dual-chamber pacemakers for symptomatic bradycardia due to sick sinus syndrome and/or atrioventricular block' will be planned into the NICE's work programme.

A revised remit will be sought from the Department of Health to clarify the indications for which the technology will be appraised. The following revised remit is suggested: *"To appraise the clinical and cost effectiveness of dual chamber (atrial and ventricular) pacemakers for the treatment of symptomatic bradycardia due to sick sinus syndrome, atrioventricular block, or a combination of sick sinus syndrome and atrioventricular block."*

That we consult on this proposal.

2. Original remit(s)

To appraise the clinical and cost effectiveness of dual chamber (atrial and ventricular) pacemakers relative to single chamber pacemakers, and to advise on the patients for whom the former would be particularly appropriate.

3. Current guidance

1.1 Dual-chamber pacing is recommended for the management of symptomatic bradycardia due to sick sinus syndrome, atrioventricular block, or a combination of sick sinus syndrome and atrioventricular block, except:

- in the management of sick sinus syndrome in patients in whom, after full evaluation, there is no evidence of impaired atrioventricular conduction; in this situation, single-chamber atrial pacing is appropriate
- in the management of atrioventricular block in patients with continuous atrial fibrillation; in this situation, single-chamber ventricular pacing is appropriate
- in the management of atrioventricular block (atrioventricular block alone, or in combination with sick sinus syndrome), when patient-specific factors,

such as frailty or the presence of comorbidities, influence the balance of risks and benefits in favour of single-chamber ventricular pacing.

The above guidance refers only to pacing for the primary indications of sick sinus syndrome and/or atrioventricular block, and does not cover more complex pacing indications.

4. Rationale[1]

According to the technology section of TA88, dual chamber pacemakers are indicated for use in the treatment of atrioventricular block in the absence of continuous atrial fibrillation, and in sick sinus syndrome with atrioventricular block. As noted in the post script to the guidance "more complex pacing indications" were not addressed. It appears that the committee recommended the technology in the patients for whom it was clinically indicated at the time; the 'exceptions' in the bulleted list relate to conditions for which the technology was not indicated or was contraindicated.

The results of the DANPACE study suggest that the indications for dual chamber pacing may be expanded to include sick sinus syndrome without atrioventricular block. The current guidance recommends single chamber pacing when there is no evidence of impaired atrioventricular conduction.

The remit for this appraisal is unusual in two ways; firstly it specifies the comparator technology and secondly it does not specify the indication for which the technology is to be appraised, but instead leaves it to the appraisal committee to advise on the patients for whom the technology would be particularly appropriate. Perhaps in line with the unusual nature of the remit, the guidance actively recommends the use of the comparator technology (single chamber pacing) for those in whom dual chamber pacing is not recommended. It would be helpful if the remit could be clarified to confirm the indications for which the technology will be appraised.

5. New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from April 2010 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below.

6. Summary of evidence and implications for review

Initial correspondence from the manufacturers of devices included in the original guidance suggests that new pacemakers have come to market for the treatment of bradycardia which would fall within the recommendations of TA88. Some of the new

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

dual chamber pacemakers provide atrial-based pacing for the treatment of sick sinus syndrome without atrioventricular block but can switch to a dual chamber pacing back-up facility in the event of atrioventricular block. Also, some pacemakers are safe to use with magnetic resonance imaging.

The original guidance (TA88) was based on four randomised controlled trials (RCTs) in which patients either received dual chamber pacemakers in both arms but were randomised to dual or single chamber pacing modes, or were randomised to receive dual or single chamber pacemaker devices. There were difficulties interpreting the evidence because the trials had been conducted in mixed groups of patients (with sick sinus syndrome, atrioventricular block and people with both conditions). The Committee also noted that some of the large RCTs included pacing modes that were not clinically appropriate (such as single chamber ventricular pacing for sick sinus syndrome without atrioventricular block). The research recommendations of TA88 referred to DANPACE, an ongoing RCT that would provide further information on the differential clinical effectiveness of these devices in people with sick sinus syndrome without atrioventricular block.

The DANPACE trial (Nielsen et al, 2011) was conducted in 1415 patients with sick sinus syndrome who were referred for first pacemaker implantation and randomly assigned a single-lead atrial pacemaker or a dual-chamber pacemaker. The results of this trial reported no statistically significant difference in death from any cause between the two groups during follow-up (29.6% in the single-pacing group compared with 27.3% in the dual-chamber group [HR = 1.06, 95% CI 0.88–1.29; p = 0.53]). Single chamber atrial pacing was associated with a higher incidence of paroxysmal atrial fibrillation (28.4% compared with 23.0% with dual chamber pacing ([HR = 1.27, 95% CI 1.03–1.56; p = 0.024]) and a two-fold increased risk of pacemaker reoperation during follow-up (22.1% in the single chamber pacing arm compared with 11.9% in the dual pacing arm (HR = 1.99, 95% CI 1.53–2.59; p < 0.001).

The authors conclude that DANPACE findings support the routine use of dual-chamber pacing in patients with sick sinus syndrome without atrioventricular block. TA88 recommends single chamber atrial pacing in patients with sick sinus syndrome and no evidence of impaired atrioventricular conduction.

Literature searches of new evidence since the review proposal of 2010 (in which there was not considered to be new evidence which would materially affect the recommendations of TA88) identified two other recent trials that evaluated different pacing modes for people with bradycardia associated with sick sinus syndrome.

In one study (Dabrowska-Kugacka et al, 2010) acute echocardiographic examination was performed in 15 healthy subjects, and in 25 patients with sinus node dysfunction and recurrent atrial fibrillation during multisite atrial pacing, single-site Bachmann's bundle pacing and coronary sinus pacing. Pacing mode had no effect on stroke volume. Coronary sinus pacing resulted in right atrial filling diminution, shortened mechanical atrioventricular delay in the right heart and diminished right ventricular inflow. The magnitude of reversion of the physiological right-to-left atrial contraction sequence was most prominent during coronary sinus pacing. Bachmann's bundle pacing provided the best atrial contraction synchrony, and had a comparable effect on global cardiac function to multisite atrial pacing. It was concluded that single-site

Bachmann's bundle pacing provided comparable haemodynamics to multisite atrial pacing and was sufficient to restore atrial contraction synchrony. Single-site coronary sinus pacing induced echocardiographic pacemaker syndrome in the right heart.

A prospective, randomised, parallel-control study (Davy et al, 2009) evaluated the SafeR mode of pacing, which combines the advantages of the atrial pacemaker mode while ensuring dual chamber pacing for backup in case atrioventricular block occurs. The study compared SafeR mode versus the dual chamber pacing mode with long atrioventricular delay (250 ms) in reducing cumulative right ventricular pacing during 1-year follow-up in recipients of dual chamber pacemakers who did not have persistent atrioventricular block or atrial fibrillation lasting >30% of the run-in phase. Patients were randomly assigned to SafeR mode (n = 141) or dual chamber mode (n = 146).There were significant differences between the groups in mean % right ventricular pacing at 1-year follow-up, with lower rates observed in the SafeR mode (4.5 ± 15.3%) compared with the dual-chamber mode (16.7 ± 28%).

In summary, some of TA88's recommendations for treating bradycardia in people with sick sinus syndrome and atrioventricular block are still applicable, but the recommendation to use single chamber atrial pacing for people with sick sinus syndrome without atrioventricular block needs updating.

7. Implementation

A submission from Implementation is included in Appendix 3.

A 2-year national survey (Network Devices Survey Group) of pacing modes for all first implants (pacemakers and implantable defibrillators) for the treatment of sick sinus syndrome in the UK in 2003 and 2004. There were 9,536 registered new implants, with 24% of patients receiving ventricular mode implants and 76% receiving dual chamber or single chamber atrial pacemaker.

Hospital Episode Statistics (HES) show that the total number of dual chamber cardiac pacemaker procedures performed in the NHS to treat bradycardia or increased between 2006 and 2011 with a higher rate of uptake for the treatment of atrioventricular block compared with sick sinus syndrome (see figure 1 in appendix 2).

A national survey conducted by the Network Devices Survey Group (Cunningham et al, 2009) that analysed adherence to TA88 in England and Wales in 2008 reported a national average of 77% single chamber atrial-based pacing in sick sinus syndrome with the rate in individual pacing centres varying between 0% to 100%.

A manufacturer noted that the current pacemaker implant/utilisation rate in England and Wales is 600–700 per million population per annum (including replacements), which is significantly below the European average of 1021 per million.

8. Equality issues

No equality issues were raised in the original guidance.

GE paper sign off: Janet Robertson, 14th September 2011

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Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A review of the guidance should be planned into the appraisal work programme.	A review of the appraisal will be planned into the NICE's work programme.	Yes
The decision to review the guidance should be deferred to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No
The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No

Options	Consequence	Selected – 'Yes/No'
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	No

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment
- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed
- The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

Technology appraisal 95: Implantable cardioverter defibrillators (ICDs) for the treatment of arrhythmias (review of TA11) Issued: January 2006. Currently under review (see below)

Technology appraisal 120: Cardiac resynchronisation therapy for the treatment of heart failure Issued: May 2007 Currently under review (see below)

Clinical guideline 36: The management of atrial fibrillation. Issued: June 2006. Consultation on a proposal to review this guideline closed on 8th August 2011, the outcome of this consultation has not yet been published.

In progress

Technology appraisal in development: Implantable cardioverter defibrillators for the treatment of arrhythmias and cardiac resynchronisation therapy for the treatment of heart failure (combined review of TA95 and TA120). Publication date tbc

Details of new products

Technology (manufacturer)	**Details (phase of development, expected launch date,)**
EnRhythm MRI SureScan (Medtronic)	The EnRhythm MRI SureScan EMDR01 IPG is an implantable medical device that monitors, detects, and treats atrial tachyarrhythmia episodes. It also provides bradycardia pacing and monitoring of ventricular tachycardia (VT) episodes. The device senses the electrical activity of the patient's heart using the sensing electrodes of the implanted leads. It then analyzes the heart rhythm based on selectable sensing and detection parameters. If the device detects an atrial tachyarrhythmia, it delivers programmed atrial ATP therapy to the patient's heart. If the device identifies a bradyarrhythmia, it delivers bradycardia pacing therapy to the patient's heart. If an MRI scan is required for a patient, the MRI SureScan pacing mode allows the patient to be safely scanned while the device continues to provide appropriate pacing. Available in Europe from 2008.

References

Dabrowska-Kugacka A, et al (2010) Single-site Bachmann's bundle pacing is beneficial while coronary sinus pacing results in echocardiographic right heart pacemaker syndrome in brady-tachycardia patients. *Circulation Journal* 74 (7), 1308–1315.

Davy J-M, et al (2009) Performance of the safeR mode in reducing right ventricular pacing in PM selected patients without AV conduction disorders: Results from the saver study. Heart Rhythm Conference: 30th Annual Scientific Sessions of the Heart Rhythm Society, Heart Rhythm 2009 Boston, MA United States. Conference Start: 20090513 Conference End: 20090516. Conference Publication: (var.pagings): S246.

Nielsen JC, et al (2011) A comparison of single-lead atrial pacing with dual-chamber pacing in sick sinus syndrome. *European Heart Journal* 32(6), 686–696.

Appendix 3 – Implementation submission

Implementation feedback - review of technology appraisals: report for guidance executive

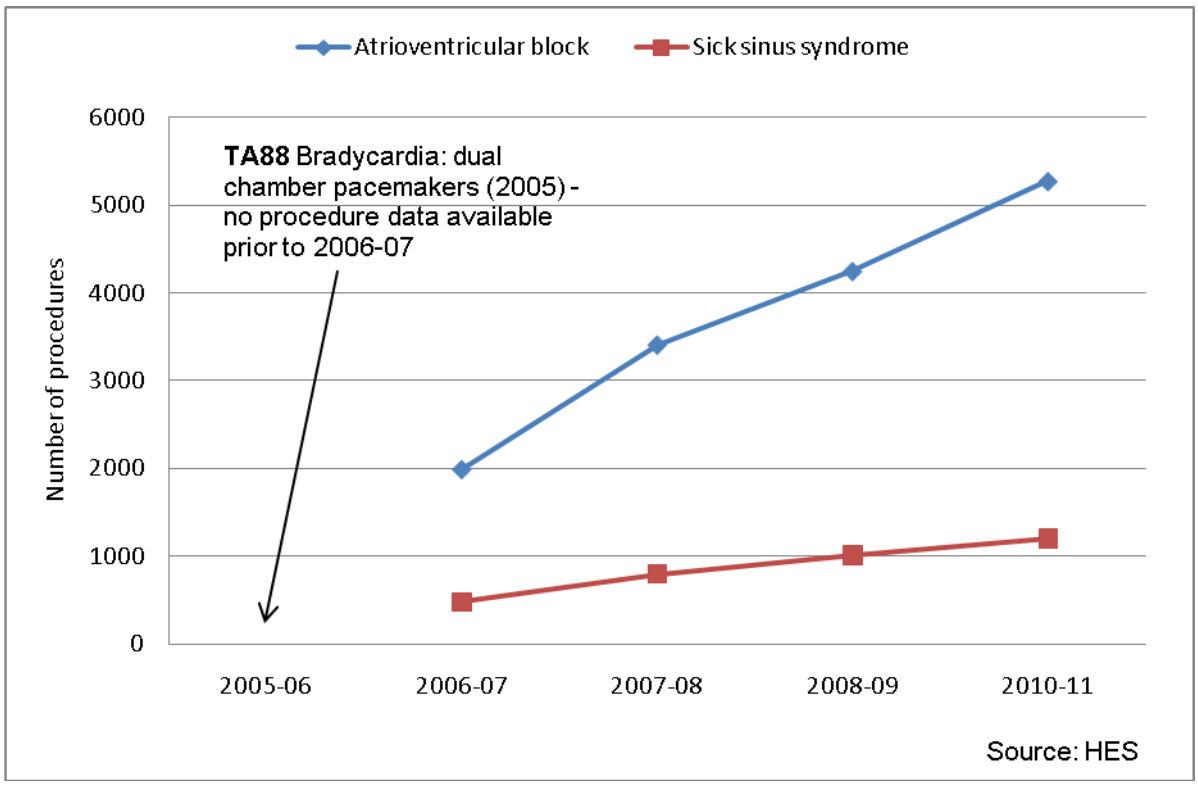
Technology Appraisal	**TA88 – Bradycardia: dual chamber pacemakers**
Implementation input required by date	**16/06/2011**

1. Routine healthcare activity data

1.1 Hospital Episodes Statistics data

This section provides information on dual chamber cardiac pacemakers for bradycardia due to sick sinus syndrome or atrioventricular block carried out in England. The data are obtained from Hospital Episode Statistics (HES). Unfortunately there is no data available prior to 2006-07; therefore it has not been possible to look at the number of procedures before the publication of TA88.

Figure1 Number of dual chamber cardiac pacemaker procedures (finished consultant episodes) performed for patients diagnosed with sick sinus syndrome or atrioventricular block in secondary care within the NHS



2. Implementation studies from published literature

Information is taken from the ERNIE website

2.1 Network Devices Survey Group (2006) Pacemakers and implantable defibrillators: a two year national survey for 2003 and 2004

The study examined, across all networks and countries in the UK, the mode prescription for all first implants registered as sick sinus syndrome, in 2003 and 2004. There were 9,536 registered new implants. 24% received ventricular mode implants (either VVI or VVIR). 76% received dual chamber or atrial mode implants. Atrial-based pacing in cardiac networks ranged from 60% to 89%.

2.2 Choo W.K et al (2009) The selection of pacing modalities according to NICE recommendations *Journal of the Royal College of Physicians* 39:113-6

The authors retrospectively studied the data of all 200 patients attending a single hospital who received single-chamber ventricular pacemakers and dual-chamber pacemakers between January 2003 and December 2005 (when when pacemakers were selected based on local experience and opinions). Compliance with NICE guidance was retrospectively found to be 72% but there was no significant difference in mortality between the compliant and non-compliant groups. The authors argue that stringent compliance with the current NICE guidance may not necessarily reduce mortality and morbidity.

2.3 Cunningham D et al (2009) Heart Rhythm Devices: UK National Survey 2008

The authors have analysed adherence to NICE guidelines by looking at new implants in England and Wales in 2008. The maximum capable mode of the implanted generator was used. The national average for atrial-based pacing in Sick Sinus Syndrome (SSS) is 77%. However, the rate in individual pacing centres varies from 0% to 100%.

3. Qualitative input from the field team

The implementation field team have recorded the following feedback in relation to this guidance:

Nothing to add at this time.