Horizon Scanning Report

Remote-controlled catheter navigation systems

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HealthPACT Secretariat

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A normal heart in sinus rhythm contracts 60 to 100 times per minute, however abnormal electrical signals may cause the muscle fibres in the atria to contract out of time, resulting in atrial fibrillation (AF). Symptoms of AF include an irregular pulse, fatigue, exercise intolerance, dizziness, fainting and general weakness. Atrial fibrillation is the most common sustained cardiac rhythm disturbance, affecting approximately two per cent of the population, with the prevalence increasing with age.

A number of options are available for the treatment of AF depending on the severity of the symptoms, including medication, cardioversion or ablation procedures. Catheter ablation is rarely used as a first-line treatment option for atrial fibrillation. The primary indication for catheter ablation is the persistence of atrial fibrillation which is refractory to anti-arrhythmic medication. Ablation aims to isolate regions of abnormal electrical signals or cardiac arrhythmia, identified by mapping studies, thus restoring the normal heart rhythm.

During manual catheter ablation the physician manually manipulates the catheters through the heart using direct visual feedback from fluoroscopic images taken in real time. Manual ablation exposes the physician and patient to high levels of ionising radiation. Robotic systems such as the Niobe® and the Sensei® perform guidance, mapping and ablation remotely, exposing the physician to markedly reduced levels of radiation. Both remote navigation systems (RNS) consist of an operating console that can be located outside the operating room, reducing radiation exposure to the majority of the attending medical staff. The console features a work station with either a joystick or a computer mouse used to guide the ablation catheter, and multiple screens alongside each other to visualise the electrogram generated throughout the ablation procedure, the 3D constructed image, which can be rotated in any plane, and fluoroscopic images of the heart.

The Sensei® operates using an electromechanical “master-slave” system. The robotic catheter control system steers the ablation catheter within the heart via a pull-wire mechanism, with its movements controlled by the robot arm or the “slave” system, which is fixed at the patient’s table. The “slave” receives input from the “master” that transmits the operator’s three-dimensional movements using the joy stick, moving the catheters in the heart according to the images generated by the mapping system. The Niobe® uses a magnetic field to guide catheters with magnetic tips. The Niobe® consists of two, large permanent magnets which are placed on either side of the patient and emit a uniform low-intensity magnetic field (0.10 Tesla). As such, an electrophysiology laboratory equipped with the Niobe® system must be custom made with magnetic...
shielding and all of its equipment must be magnetic field compatible. The magnetic ablation catheter aligns parallel to the external magnetic field and is navigated through the heart by changing the orientation of the outer magnets to each other and thus changing the orientation of the magnetic field, which is controlled by a computer interface system. Changes in the magnetic field deflect and move the ablation catheter allowing for small movements (1° and 1mm).

_Hansen Sensei®X remote navigation system_

Common adverse events reported by studies which employed the Hansen Sensei®X included iatrogenic septal defect, which may result in thromboembolism, and oesophageal lesions, which may lead to the development of serious adverse events including atrio-oesophageal fistulas. In the two studies which reported these outcomes all patients healed by end of follow-up with no sequelae. Three out of the six remaining studies included for assessment reported low rates of potentially serious adverse events (1-10%), including pericardial tamponade, pericardial effusion and perforation. Although these adverse events were considered serious, all patients were successfully treated without further sequelae. Levels of patient and operator radiation exposure were described by some studies, with either a decrease or no difference reported. It is unclear from these studies whether or not the reported radiation doses for patients or the operators are significant in terms of a cumulative dose. It should also be noted that the radiation exposure values reported in these studies had large standard deviations indicating considerable variation in the amount of exposure.

Four of the eight included studies reported on post-ablation procedure success using the Hansen Sensei®X. Two studies reported no statistically significant difference in success rates between patients with AF in the RNS and manual groups. However one comparative study noted a significant different in the success rates of patients treated for atrial flutter with RNS compared to manual ablation ($p = 0.03$). The majority of patients successfully treated remained free from AF or atrial flutter symptoms at end of follow-up in both the manual and the RNS groups. Two of the included studies reported on the learning curve involved with the use of RNS, with the first set of RNS patients taking a significantly longer time than patients treated later, indicating that it took at least 10 patients for operator familiarity with the remote navigation technique. Four comparative studies reported a significant decrease in fluoroscopy time using RNS compared to manual ablation.
A lower level of evidence was available for the assessment of the effectiveness of the Niobe®, with only two well-designed prospective comparative studies included for evaluation.

Low rates of adverse events were reported by the included studies, ranging from 2.2 to five per cent. Only one study reported on the level of radiation exposure to the patient, which was significantly less in the RNS ablation group compared to the manual group ($p = 0.032$).

No difference in procedural success rates between RNS and manual ablation were reported by two comparative studies, and of those patients who were symptom free immediately post-ablation, the majority remained symptom free at end of 6-12-month follow-up. Procedural success rates for AF or atrial flutter ablation varied from 93 to 100 per cent in the lower level evidence studies. The case series with the longest follow-up (mean 426 days) reported 70 per cent of patients with AF remained symptom-free at study end.

Conflicting results regarding the length of procedure time were reported. The best quality study reported a significantly longer procedure time for remote navigation compared to manual navigation, however another comparative study reported significantly less procedure time for patients in the RNS group compared to the manual ablation group. A learning curve was reported by two poorer quality studies; a decrease in procedure time correlated with increased operator experience.

No cost-effectiveness studies on either the Niobe® or Sensei® remote navigation systems were identified for inclusion in this assessment, however a cost-consequences analysis may be the more appropriate economic analysis to conduct. The main health outcome when using remote navigation systems is reduced radiation exposure to the patient and especially, the clinician. The included studies refer to surrogate outcomes of length of exposure (as a measure of dose) but do not provide evidence of how this reduction translates into a health benefit. We have sought this evidence elsewhere but have not been successful. Thus it is not possible to assess the health consequences of the capital investment in excess of $1 million combined with the ongoing maintenance costs.

The Hansen Sensei®X and Niobe® remote navigation systems are, in some ways, ethically uncontroversial. They would replace existing treatment regimes with new regimes that are as effective as the old, they can be provided in the same institutional settings, and they rely on similar patterns of training for operators as have been developed in the past for previous treatments. The key ethical question that remains is whether the reductions in fluoroscopy time that they offer are of clinical relevance for patients and operators.
In summary, both the Hansen Sensei®X and Niobe® remote navigation systems appear to be as effective as manual ablation for the treatment of atrial fibrillation and atrial flutter. Few adverse events occurred in both groups and reduced radiation exposure for patients and the operator were reported by the majority of studies which reported this as an outcome. All studies reported a significant decrease in fluoroscopy time compared to manual ablation, which would correlate with a corresponding decrease in radiation exposure and dose to the patient and operator alike. Although conflicting results were reported regarding procedure time, with some studies reporting an increase, a decrease or no difference in procedure time with the RNS systems, most studies reported that these differences could be explained by the learning curve associated with the use of the RNS system. Immediate success rates of the procedure, indicated by freedom from symptoms, were similar for both systems, ranging from 88-100 per cent, which was sustained at 5-12 month follow-up in 70-91 per cent of patients.
Introduction

The National Horizon Scanning Unit, AHTA, School of Population Health and Clinical Practice, University of Adelaide, on behalf of the Medical Services Advisory Committee (MSAC), has undertaken an Horizon Scanning Report to provide advice to the Health Policy Advisory Committee on Technology (Health PACT) on the state of play of the introduction and use of remote catheter navigation systems.

Two companies, Stereotaxis Inc (Missouri, USA) and Hansen Medical (California, USA), currently provide remote robotic catheter navigation systems for catheter-based electrophysiology and coronary procedures among cardiac patients. Robotic catheter navigation is currently in limited use in Australia and is offered through specialist cardiologists.

This Horizon Scanning Report is intended for the use of health planners and policy makers. It provides an assessment of the current state of development of remote-controlled catheter navigation systems, its present use, the potential future application of the technology, and its likely impact on the Australian health care system.

This Horizon Scanning Report is a preliminary statement of the safety, effectiveness, cost-effectiveness and ethical considerations associated with remote-controlled catheter navigation systems.
Background

The heart consists of four chambers: two upper chambers (atria) and two lower (ventricles). Oxygen depleted blood enters the right atrium, which contracts and sends the blood into the right ventricle, which then pumps the blood to the lungs for oxygenation. Oxygenated blood returns from the lungs to the heart via the left atrium and is finally pumped to the rest of the body when the left ventricle contracts. In a normal heart this occurs 60 to 100 times per minute. Contraction of the atria is initiated by electrical signals which emanate from the sinus node, situated at the top of the right atrium. These electrical signals travel rapidly throughout the atria to ensure that all muscle fibres contract in the appropriate sequence, pushing the blood into the ventricles. The atrioventricular node passes on these electrical signals causing the ventricles to contract after they have filled with blood from the atria. This normal, regular heart rhythm is referred to as sinus rhythm (Figure 1) (NHF 2008).

Abnormal electrical signals, originating from the pulmonary veins, cause the muscle fibres in the atria to contract out of time, resulting in atrial fibrillation (Figure 2). These abnormal signals may pass on to the ventricles, causing a rapid and irregular heartbeat. Patients with atrial fibrillation (AF) may be aware of this irregular heartbeat and feel a “fluttering” of the heart. Symptoms include an irregular pulse, fatigue, exercise intolerance, dizziness, fainting and general weakness as the heart is not working efficiently. Atrial fibrillation may occur as a one-off episode, or may be paroxysmal or persistent. The most common causes of atrial fibrillation include long-term high blood pressure, coronary heart disease, valvular heart disease and, less commonly,
hyperthyroidism. Atrial fibrillation may also be associated with excessive caffeine or alcohol intake (NHF 2008).

Due to impaired blood flow, atrial fibrillation may cause blood to pool in the heart, which may lead to the formation of a blood clot. If the blood clot breaks up it may be carried through the bloodstream, blocking smaller vessels and reducing blood supply to organs. If this occurs in vessels supplying the brain, a stroke may result. In people aged over 65 years with untreated atrial fibrillation, the risk of experiencing a stroke is approximately one in 20, which is five to six times higher than in those without AF. The risk of stroke increases in individuals with AF and other co-morbidities, including diabetes and high blood pressure (NHF 2008).

People suspected of having AF should undergo an electrocardiogram (ECG) and echocardiography to confirm the diagnosis and to rule out any other underlying cause of disease (NHF 2008). A number of options are available for the treatment of atrial fibrillation, depending on the severity of the symptoms, including medication, cardioversion or ablation procedures. Catheter ablation is rarely used as a first-line treatment option for atrial fibrillation. The primary indication for catheter ablation is the persistence of atrial fibrillation which is refractory to anti-arrhythmic medication. Catheter ablation may be indicated in symptomatic patients with heart failure and/or reduced ejection fraction. Patients undergoing catheter ablation require careful anti-coagulation therapy before, during and after the procedure to prevent left atrium thrombus formation (Calkins et al 2007; Darge et al 2009).

**Figure 2** Heart and ECG trace demonstrating atrial fibrillation (NZGG 2006)
Description of the technology

The procedure

There are currently two remote-controlled catheter systems in use world-wide: the Sensei® X Robotic Catheter System, manufactured by Hansen Medical and the Niobe® Magnetic Navigation System manufactured by Stereotaxis Inc.

Mapping

Successful ablation relies on detailed cardiac mapping and the ability to navigate catheters to specific ablation targets. Both manual and remote navigation ablation rely on cardiovascular mapping systems to record cardiac electrical activity and the anatomy of the heart to elucidate the region of abnormal electrical activity (cardiac arrhythmia) and the potential source of atrial fibrillation. Patients are placed under a C-arm fluoroscopic system which consists of an X-ray source and a fluorescent screen, giving the physician real-time feedback on the positioning of the catheter (Figure 3). The catheter is introduced via the femoral vein and is guided up to the heart into the left atrium. Once the catheter is in place and mapping is completed, the data obtained are visualised and interpreted by a mapping system (Malkin et al 2005).

![Fluoroscopic imaging system](image)

**Figure 3** The fluoroscopic imaging system indicating the X-ray source, fluorescent screen for image capture and monitors for image display (Siemens AG)

Three-dimensional, non-fluoroscopic mapping systems have been developed that continuously analyse information obtained from the catheters inside the heart. There are two main 3D mapping systems both of which can be used with the Sensei®: the CARTO (Biosense-Webster, USA) and the Ensite NavX (St Jude Medical, USA), however only the CARTO system can be used with
the Niobe®. There are several other mapping systems on the market including RPM (Boston Scientific, USA) and LocaLisa (Medtronic, USA). When used with the Niobe®, the mapping systems ascertain the location and orientation of the mapping/ablation catheter using three ultra-low magnetic fields (10⁻¹² Tesla) which are emitted from a unit placed under the operating table. The tip of the catheter contains location sensors and the catheter position and orientation is calculated by the strength of the magnetic fields. The catheter is guided by fluoroscopy into the coronary sinus and throughout the left atrium. The signal from the tip of the catheter is used to generate marker points, which are then used to create a 3D map of the cardiac geometry (see video for demonstration). Sites that require ablation can be tagged for later reference (Pappone & Santinelli 2007a). The CARTO system only allows the use of Biosense-Webster catheters (Packer 2005). The NavX mapping system produces 3D images by localising the position of the catheter using changes in impedance in the x, y and z-axis of an electronic field generated by three pairs of patches placed on the patient’s chest. Three dimensional images are generated by the computer program mapping thousands of marker points, creating a 3D image of the heart. The NavX is compatible with any brand of catheter, including bidirectional steerable catheters, and can simultaneously display up to 12 catheters and 64 electrodes (Pappone & Santinelli 2007a). The use of the CARTO and NavX 3D-mapping systems reduces the amount of fluoroscopy exposure for the patient and cardiologist. Once the patient is anaesthetised, fluoroscopy is used to initially position the circular mapping catheter in the left atrium and mapping can proceed without the need for further fluoroscopy until the catheters are moved manually to the next pulmonary vein for further mapping (Figure 4) (personal communication Flinders Private Hospital).
The Hansen Medical Sensei®X remote robotic navigation system

The Hansen Medical Sensei® remote robotic navigation system consists of an operating console that can be located outside the operating room, reducing radiation exposure to the majority of the attending medical staff. The console features a work station with the IntelliSense® joystick and multiple screens alongside each other to visualise the electrogram generated throughout the ablation procedure, the 3D constructed image, which can be rotated in any plane, and the fluoroscopic image (Figure 5, 6 and 7) (Dewire & Calkins 2010).

The Sensei® operates using an electromechanical “master-slave” system. The robotic catheter control system steers the ablation catheter within the heart via a pull-wire mechanism, with its movements controlled by the robot arm or the “slave” system, which is fixed at the patient’s table (Figure 6). The “slave” receives input from the “master” that transmits the operator’s three-dimensional movements using the joy stick, moving the catheters in the heart according to the images generated by the mapping system (Ernst 2008).
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Figure 6  The remote catheter manipulator

Figure 7  The Hansen CoHesion™ 3D visualisation module demonstrating the instinctive motion “joy stick” (printed with permission Hansen Medical Inc).
Several single-use only catheters are used simultaneously during ablation including the ring mapping catheter (6 French), the coronary sinus catheter (7 Fr) and the steerable Artisan™ ablation catheter. The Artisan™ consists of an outer sheaf, which is 14 Fr, with the ablation catheter (10.5 Fr) sitting inside and able to protrude and retract from the outer sheath. The sheath is required to supply a platform for the movement of the ablation catheter. The size of the Artisan™ catheter, which at 14 French is considerably larger than those used in conventional manual ablation (8 Fr), has caused some concern with regard to post-operative bleeding events. However, the administration of protamine to reverse the effects of the administered heparin immediately after the ablation procedure may negate the effect of using such a large catheter (personal communication Flinders Private Hospital). In addition, the Artisan™ catheter cannot accommodate the Brockenbrough needle used to create the transseptal puncture, providing access to the pulmonary veins in the left atrium. Using the Artisan™ catheter a single puncture, double-transseptal approach may be used, however this may result in a large iatrogenic atrial septal defect when both the conventional and Artisan™ sheath are introduced into the left atrium (Rillig et al 2010b).

When ablation begins only the steerable catheter is moved using the Sensei®, with the remaining catheters moved into the four pulmonary veins manually under fluoroscopic guidance. The steerable catheter navigates around the pulmonary veins one by one, ablating small defined regions, isolating each vein. These regions correspond to lines on the electrogram and the effect of ablation in that region can be immediately assessed by the electrical activity on the electrogram, with the signal indicating to the cardiologist whether more ablation is required (Figure 8). Most ablation catheters are irrigated constantly with saline to reduce temperatures, allowing ablation to occur at 50 watts. Early users of the Sensei® reported difficulties with the Sensei® in regard to the amount of pressure applied during ablation (personal communication Flinders Private Hospital).

Excessive force may result in pressure and over-heating complications, which may lead to adverse events including perforation or stroke. Too little force may result in lesions that are small in volume and depth which may not be effective in eliminating AF (Burkhardt & Natale 2009). To rectify this, new models of the Sensei® have a built-in pressure sensor, Intellisense, which continuously measure the force applied by the catheter and alerts the operator both visually (pressure readout on screen) and physically (the joy stick

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1 The French scale or French gauge system (Fr) is used to measure the size (diameter) of a catheter. 1 Fr = 0.33 mm, and therefore the diameter of the catheter in millimetres can be determined by dividing the French size by 3: D (mm) = Fr/3
vibrates) to pressures that exceed a set threshold. In addition, the system has an auto-retract button which can immediately retract the catheter sheath away from the surface of the heart by a few millimetres. Contrast media may be administered to visualise on the fluoroscopic images, and therefore to avoid direct contact with, the oesophagus during ablation, avoiding the potential for a serious adverse event (personal communication Flinders Private Hospital).

It has been estimated that the use of the Hansen Sensei® for AF ablation results in a 35 per cent reduction in fluoroscopy exposure time for the operator (Dewire & Calkins 2010).

*The Niobe® remote magnetic navigation system*

The basic principles of the Niobe® navigation system are similar to that of the Sensei®X, in that once mapping has been completed, the operator navigates the ablation catheter using a mouse and scroll button, instead of a joystick, from a separate control room whilst visualising the 3D and fluoroscopic images on screens (Figure 9).
The fundamental difference between the two systems is that the Niobe® uses a magnetic field to guide catheters with magnetic tips, whereas the Hansen system uses electromechanical guidance. The Niobe® consists of two, large permanent magnets which are placed on either side of the patient and emit a uniform low-intensity magnetic field (0.08-0.10 Tesla) with an approximate volume of 15-20 cm diameter inside the patient’s chest (Figure 10) (Ganji et al 2009; Schmidt et al 2008). The strength of the magnetic field decreases markedly when moving away from this point. To employ the Niobe® system the electrophysiology laboratory must be custom made with magnetic shielding and all of its equipment must be compatible with a magnetic field. In addition, the presence of the magnets may limit the rotation of the C-arm of the fluoroscope.
It is also recommended that all clinical staff involved in the use of the Niobe® undergo a magnetic safety course. Although the Niobe® system is not recommended to be used in patients with metallic implants (Fu et al 2009), implants such as hip and knee replacements are considered safe and aneurysm clips are now non-ferro-magnetic. Cardiologists may err on the side of caution when treating patients who are pacemaker dependent and use the manual technique, however as patients undergo pacing during the procedure it is feasible to reset the pacemaker after treatment (personal communication Device Technologies Australia). A recent in vitro study found that interference of the magnetic RNS with pacemakers or defibrillator devices not connected to leads is rare and does not result in permanent damage to most of the devices tested. There was a small subset of devices that were prone to reprogramming after magnetic field exposure, in a similar manner to the power-reset mode. All of these devices were easily reprogrammed to the initial settings. These results may vary if the study was conducted with the devices connected to leads (Jilek et al 2010).

Catheters used in the Niobe® system do not need to be sheathed and can therefore be much smaller in comparison to those used with the Sensei®. Due to the absence of a sheath, diagnostic and ablation catheters such as the Celsius® RMT (7.0 Fr) and Navistar™ RMT (7.5 Fr) are soft and flexible and can therefore navigate tortuous anatomy (Burkhardt & Natale 2009). The magnetic ablation catheter aligns parallel to the external magnetic field and is navigated through the heart by changing the orientation of the outer magnets to each other and thus changing the orientation of the magnetic field, which is controlled by the computer interface system (Navigant). Changes in the magnetic field deflect and move the ablation catheter allowing for movements as small as 1° and 1mm. The ablation catheter is advanced and retracted in the heart by a mechanical device, the Cardiodrive. Irrigated catheters have been available for use with the Niobe® since 2009 (Chun et al 2008; Ganji et al 2009; Schmidt et al 2008; Thornton & Jordaens 2007). Ablation is usually performed at a temperature of 65°C and a power limit of 50 W (Pappone & Santinelli 2007b).

Procedure time with the use of either the Niobe® or the Sensei® is approximately 2.5-4 hours depending on the complexity of the procedure, similar to the time taken for manual ablation (Schmidt et al 2008).

**Intended purpose**

Patients with AF for whom other treatment options have failed or are not a suitable option may undergo an ablation procedure in an electrophysiological laboratory to isolate the abnormal AF electrical signal, restoring normal heart rhythm. Ablation involves the electrical isolation of the heart tissue which is
contributing to the arrhythmia by the creation of insulation lesion lines. There are two types of ablation procedures: catheter and surgical ablation (see comparator section) (NHF 2008). To gain access to the left atrium for encircling the pulmonary veins, a transeptal puncture is required, usually using a Brockenbrough needle but may be achieved with the application of radiofrequency current. A double puncture may be required to accommodate the mapping and ablation catheters. Some studies have reported on the presence of a persistent iatrogenic septal defect after transseptal puncture (Rillig et al 2010b). During catheter ablation, a catheter, with an electrode at the tip, is inserted into a blood vessel in the leg and guided up to the heart. The heart is first “mapped” by the cardiologist to identify the region of abnormal electrical activity. The electrode is moved along the inner walls of the heart, measuring the electrical activity. The heart is then “paced” placing an electrical current into the conductive pathways, attempting to invoke an arrhythmia. Once the region of interest has been identified, the tip of the catheter emits radiofrequency waves to burn a small area of tissue and inactivate the electrical signal. Robotic systems such as the Niobe® and the Sensei® do these three steps; guidance, mapping and ablation, remotely, exposing the physician to markedly reduced levels of radiation (NHF 2008).

Clinical need and burden of disease

Atrial fibrillation is the most common sustained cardiac rhythm disturbance, affecting approximately two per cent of the population. The prevalence of AF increases with age with approximately five per cent of individuals aged over 65 years affected. Haemodynamic impairment and thromboembolic events related to AF result in significant morbidity, mortality, and cost (NHF 2008). As previously mentioned, the most common causes of atrial fibrillation include long-term high blood pressure and coronary heart disease, valvular heart disease and, less commonly, hyperthyroidism. The most common form of heart disease is coronary or ischaemic heart disease (CHD). There are two major types of CHD: acute myocardial infarction (AMI) also known as a heart attack, and angina. A heart attack occurs when a blood vessel supplying the heart is suddenly totally blocked, causing damage to the heart muscle. The main symptom of a heart attack is a severe and continuous chest pain. A heart attack may be fatal if the blockage to the artery is not removed. Angina is a chronic condition which occurs due to a temporary insufficiency of blood supply to the heart, resulting in intermittent chest pain. Angina usually occurs in individuals, who have significant narrowing of the heart’s arteries due to plaque, when there is an unmet demand for increased blood flow due to exercise or strong emotion (AIHW 2010a).
In Australia, it has been estimated that in 2007–08, 684,800 Australians had long-term CHD, with an overall burden of disease of nine per cent of the population. Of these it was estimated that 353,000 individuals had angina and 449,000 had other ischaemic heart diseases or heart attack. In 2007-08, there were approximately 6.8 per cent of Australians aged 55–64 years with long-term CHD, however this rate increases markedly with age with CHD occurring in approximately 19.9 per cent of those aged 75 years and over. After adjusting for age, rates for CHD were twice as high for males (4.4%) than females (2.3%). Although the prevalence of CHD remains high, the rate of death from CHD has decreased over time. During the period 1998–2007, the age-standardised rate of death from CHD fell by 40 per cent for both males and females, mainly due to improved survival after a cardiac event. Despite this, CHD is still the largest single cause of death in Australia, accounting for 16.5 per cent of all deaths (22,727) in 2007, with the majority of deaths occurring in individuals aged 75 years and over. In 2007, the age-standardised rate of CHD death for males and females was 126.3 and 72.5 per 100,000, respectively (AIHW 2010a).

During the period 2007-08, there were 620,443 public hospital separations for ischaemic heart disease. Acute myocardial infarction (ICD-10 code I21) accounted for 300,689 of these with an average length of stay of 5.4 days. Angina pectoris (I20) and chronic ischaemic heart disease (I25) accounted for 216,560 and 99,710 separations, respectively, both with an average length of stay (ALOS) of 3.0 days (AIHW 2010b). High blood pressure may also result in AF and during the same period, 2007-08, there were 6,104 (ALOS 3.3 days) and 427 (ALOS 6.6 days) public hospital separations for essential primary hypertension (I10) and hypertensive heart disease (I11), respectively (AIHW 2010b).

During the same year there were 47,164 public hospital separations for atrial fibrillation and flutter (I48), representing 145,200 patient days with an average length of stay of 3.1 days. The majority of these cases (76%) occurred in patients aged 60 years and over (AIHW 2010b).

There are two Medicare Benefit Schedule (MBS) item numbers for electrophysiological studies (MBS Online). Item number 38209 relates to “cardiac electrophysiological studies up to and including 3 catheter investigation of any one or more of syncope, atrioventricular conduction, sinus node function or simple ventricular tachycardia studies”. Item number 38212 relates to “cardiac electrophysiological studies with four or more catheter supra-ventricular tachycardia investigation; or complex tachycardia inductions, or multiple catheter mapping, or acute intravenous anti-arrhythmic drug testing with pre and post drug inductions; or catheter ablation to intentionally induce complete AV block; or intra-operative mapping; or
electrophysiological services during defibrillator implantation”. In the period July 2009 to June 2010 there were 7,894 MBS claims for both of these item numbers, with the majority for item number 38212 (7,236). For the same period there were 7,437 MBS claims for the item number 38353, for the insertion, removal or replacement of a permanent cardiac pacemaker (not biventricular pacing). These item numbers may give an indication of the maximum number of ablation procedures performed in private hospitals.

Atrial fibrillation may result in stroke, which is the most common cause of cerebrovascular death. Stroke occurs when a blood vessel leading to the brain is blocked by a clot (ischaemic stroke) or bleeds (haemorrhagic stroke). Although haemorrhagic strokes are less common than ischaemic strokes they have a higher fatality rate. As well as causing death, stroke results in high levels of disability in the community. An estimated 60,000 stroke events occur in Australia every year and the majority of these (70%) are first-ever strokes. In 2007, cerebrovascular disease accounted for 11,491 deaths (8.3% of all deaths), with stroke (8,623 deaths) and its resulting disorders (2,398) accounting for 96 per cent (11,021) of these deaths. Death from cerebrovascular disease occurred mainly in individuals aged 75 years or over (83.9%). In 2007 the overall age standardised rate of death from stroke was approximately 48 per 100,000 persons (AIHW 2010a).

During 2007-08 there were 391,310 public hospital separations for cerebrovascular diseases (I60 – I69). Of these, the greatest proportion was for cerebral infarction (I63) with 183,595 separations (ALOS 11.1 days) followed by stroke (I64, not specified as haemorrhage or infarction) with 68,884 separations (ALOS 7.9 days) (AIHW 2010b).

Recent data from New Zealand are difficult to obtain. In the year 2000, it was reported that cardiovascular disease, including cerebrovascular disease, was the leading cause of mortality in New Zealand, accounting for 40 per cent of all deaths. In the 30-years from 1970 to 2000, the age-standardised death rates for coronary heart disease have fallen by 61 and 56 per cent in males and females, respectively. Of these deaths, 22 per cent died from coronary heart and eight per cent from cerebrovascular disease. However, in the last decade of that period the decline in mortality for both men and women has only been 3.7 per cent. A total of 5,973 individuals died from coronary heart disease in the year 2000, at an age standardised rate of 82 per 100,000 persons. The age standardised mortality rate for males was double that for females at 114 and 56 per 100,000, respectively. The age standardised mortality rate for cerebrovascular disease was similar for males and females, with an overall rate of 33 per 100,000 persons. Mortality rates for coronary heart disease were considerably higher in the Māori and Pacific Islander populations compared to the general population. Māori males and females had an age standardised
mortality rate of 201 and 114 per 100,000, respectively. Pacific Islander males also had a high age standardised rate of mortality at 201 per 100,000, however the rate for Pacific Islander females approached that of the general population at 67 per 100,000. In addition, mortality rates from cardiac dysrhythmias (ICD-10 I47-I49) differed markedly according to ethnic origin. Māori males and females had an age standardised mortality rate of seven and six per 100,000, respectively for cardiac dysrhythmia (abnormal rhythm), compared to 85 and 142 per 100,000 for males and females in the general population (Hay 2004).

In New Zealand during the period 2006-07, there were 25,968 hospital separations for ischaemic heart disease with an average length of stay of 7.5 days. Angina pectoris (I20) and acute myocardial infarction (I21) accounted for 10,429 and 13,116 of these separations, with an average length of stay of 4.2 and 7.7 days respectively. During the same period, there were 7,605 public hospital separations for atrial fibrillation and flutter (I48) with an average length of stay of 4.2 days. During 2006-07 there were 8,742 public hospital separations for cerebrovascular diseases (I60 – I69) with an average length of stay of 46.4 days. Of these, the greatest proportion was for cerebral infarction (I63) with 3,410 separations (ALOS 11.8 days) followed by stroke (I64, not specified as haemorrhage or infarction) with 2,406 separations (ALOS 116.4 days) (Ministry of Health 2010).

Stage of development

There are currently two remote-controlled catheter systems listed on the Australian Therapeutic Goods Administration (TGA) register. The Sensei® X Robotic Catheter System, manufactured by Hansen Medical and distributed by St Jude Medical Australia Pty Ltd, was registered in November 2008 (ARTG 157314) and the Artisan steerable guide catheter for use with the system (ARTG 160366) was registered in March 2009. The latest model of the Sensei® was listed on the FDA in August 2009 (K091808), however the 510(K) summary includes the following proviso that the Sensei® is “designed to facilitate manipulation, positioning and control of mapping percutaneous catheters within the atria of the heart” and that “The safety and effectiveness of this device for use with cardiac ablation catheters, in the treatment of cardiac arrhythmias including atrial fibrillation, have not been established”. In addition “The Office of Device Evaluation has determined that there is a reasonable likelihood that this device will be used for an intended use not identified in the proposed labeling and that such use could cause harm. Therefore, in accordance with Section 513(i)(1)(E) of the Act, the following limitation must appear in the labeling, on the packaging for the Artisan Steerable Guide Catheter and Sheath, on the Remote Catheter Manipulator, and the Workstation: The safety and effectiveness of this device for use with


Cardiac ablation catheters, in the treatment of cardiac arrhythmias including atrial fibrillation, have not been established. Furthermore, this warning must be prominently displayed on the Remote Catheter Manipulator, Workstation, all labeling, including pouch box, and carton labels, instructions for use and other promotional materials, in close proximity to the trade name, of a similar point size, and in bold print. Please note that the above labeling limitations are required by Section 513(i)(1)(E) of the Act. Therefore, a new 510(k) is required before these limitations are modified in any way or removed from the device's labeling.” (FDA 2009). The Hansen Sensei® therefore has FDA clearance to perform mapping procedures, however clinicians in the US are using it “off-label” to perform ablation procedures under experimental conditions (Fu et al 2009).

However, on the 12th May 2010 Hansen Medical announced that it had received conditional Investigational Device Exemption (IDE) approval from the FDA authorising a clinical trial to investigate use of the Sensei® X and the Artisan™ Control Catheter for treatment of AF. The trial expects to enrol 300 patients with symptomatic, drug-refractory paroxysmal AF at a 2:1 ratio and evaluate robotic technique versus manual technique for the ablation of AF. The trial will be conducted in 14 centres worldwide. The primary endpoints are safety of the procedure and freedom from AF symptoms at one year (Marketwire Inc 2010).

There are currently 91 Sensei® systems installed and operational worldwide, with more than 2,500 procedures performed using it (personal communication St Jude Medical Australia). The Sensei® X is currently installed and in use in only two locations in the southern hemisphere: one in South Africa and one at Flinders Private Hospital, South Australia. Two cardiologists from Flinders Private Hospital have undergone training in the United States to use the Sensei® X and to date approximately 16 procedures have been conducted (Pengelley 2010). In addition, cardiologists from the Royal Adelaide Hospital, South Australia have also undergone training in the United States (personal communication St Jude Medical Australia).

The Niobe® Magnetic Navigation System manufactured by Stereotaxis Inc and distributed by Device Technologies Australia Pty Ltd, was listed on the TGA in February 2008 (ARTG 149569). A number of catheters can be used in conjunction with the Niobe® system including the CELCIUS® RMT diagnostic/ablation steerable irrigated catheter (ARTG 141097) manufactured by Biosense Webster Inc and distributed by Johnson and Johnson Medical Pty Ltd. In addition, the Stereotaxis Cardiodrive catheter advancement system was registered on the TGA in February 2008 (ARTG 149570). The Niobe® was first registered on the FDA in 2003 (K021555). A large number of the Niobe® systems are installed worldwide with the majority in the US or Europe. A
number of the systems are installed in the Asia-Pacific region, including China, Taiwan, Korea and Singapore. There is one Niobe® system installed in Australia at the Westmead Hospital, New South Wales. Clinical staff at Westmead are currently treating patients with ventricular tachycardia, atrioventricular nodal re-entrant tachycardia as well atrial fibrillation in addition to performing percutaneous coronary interventions. Approximately 3-5 procedures per week are currently being conducted at Westmead and to date there have been over 75 procedures performed. Approximately one third of these procedures are for AF, another third a combination of supraventricular or ventricular tachycardia and 10 per cent are for atrial flutter performed (personal communication Device Technologies Australia).

There are in the region of 200 Niobe® units installed worldwide and approximately 30,000 procedures have been performed (personal communication Device Technologies Australia).

There are numerous centres in Australia that treat atrial fibrillation patients with conventional ablation techniques: Flinders Private Hospital and the Royal Adelaide Hospital in South Australia, the Monash Medical Centre, The Alfred, The Austin Hospital and The Royal Melbourne Hospital in Victoria; Fremantle Hospital, the Royal Perth Hospital and the Hollywood Private Hospital in Western Australia; The Prince Charles Hospital, Princess Alexandra Hospital, St Andrews Hospital and the Queensland Cardiovascular Group in Queensland; and the Royal Prince Alfred Hospital, Westmead Hospital, Lake Macquarie Hospital and the Mater Hospital in New South Wales (Ryan 2009 and personal communication St Jude Medical). In New Zealand several centres which perform coronary artery bypass graft and angioplasty procedures and at least three of these centres perform AF ablations: the City Hospital in Auckland, Waikato Hospital in Hamilton and Christchurch Hospital.

There are at least two other robotic catheter navigation systems in development. An Israeli company now based in the USA, Corindus Inc (Massachusetts, USA), is developing the CorPath® 200 System, which is similar to the Hansen Sensei® system. This system is intended to be used for remote navigation for guide-wire, balloon and stent manipulation during percutaneous coronary interventions (PCI). The CorPath® aims to reduce the amount of radiation surgeons are exposed to at the same time as improving the precision of balloon and stent positioning and as a result improve clinical outcomes for patients. Corindus expect to commence clinical trials with the CorPath® system in 2010 (Corindus Inc 2010). One preliminary study has been conducted using the CorPath® system (Beyar et al 2006), however the system has not, as yet, received FDA approval and is not available in Australia or New Zealand. Catheter Robotics Inc (USA) is also developing a remote catheter navigation system called Amigo™. This device is currently limited to
investigational use by the FDA (Catheter Robotics Inc 2010). One preliminary study has been conducted using the Amigo™ system (Knight et al 2008). A single arm safety/efficacy study using the Amigo™ system was registered (ClinicalTrials.gov Identifier: NCT01139814) in June 2010 and intends to recruit approximately 200 patients with atrial flutter or ventricular tachycardia who require right sided electrophysiology mapping studies.
Treatment alternatives

Existing comparators

Surgical treatment options to address the underlying cause of atrial fibrillation are available usually as a concomitant procedure whilst a valve or CABG procedure is performed. Coronary heart disease is procedurally treated by percutaneous coronary interventions (PCIs) and coronary artery bypass grafting (CABG). To assess the health of the coronary arteries, coronary angiography is performed to identify arteries which may be narrowed or blocked. A catheter is inserted into the heart via an artery, usually in the groin, and after injection with a visualising dye, X-rays of the arteries are taken. Patients with narrowing of the arteries may be treated with a PCI, with or without stenting. Patients with complete blockages may need to undergo a CABG procedure, which uses blood vessel grafts, usually from the patient’s leg, chest or arm (AIHW 2010a).

A number of options are available for the treatment of atrial fibrillation depending on the severity of the symptoms, including medication, cardioversion or ablation procedures.

Most patients diagnosed with AF will be prescribed an anticoagulant, either aspirin or warfarin, to prevent clot formation. Although warfarin is more effective than aspirin in reducing the risk of stroke, it is associated with severe side effects including excessive bleeding. In addition, patients may be prescribed medication which aims to slow the heart rate by increasing the time taken for the ventricles to fill and contract (beta-blockers, digoxin and some calcium channel blockers). Anti-arrhythmic drugs may also be prescribed, including solatol, flecainide and amiodarone, which aim to maintain a normal heart rhythm (NHF 2008).

Cardioversion, either electrical or pharmacological, aims to restore a normal heart beat after a prolonged or severe episode of AF. During electrical cardioversion, the patient is sedated or anaesthetised and an electrical “shock” is applied to the heart via external defibrillator pads placed on the chest. The shock is synchronised to correspond to the R wave of the QRS complex on the ECG (Figure 11). Ventricular fibrillation may be induced if the electrical shock is delivered during the refractory period on the ECG. The same anti-arrhythmic drugs, as described above, which may be given long-term to maintain patients with AF after electrical cardioversion, may be prescribed to achieve pharmacological cardioversion (NHF 2008; 2010).
As described previously, patients with AF for whom cardioversion has failed or medication is not a suitable option may undergo an ablation procedure in an electrophysiological laboratory to eliminate the abnormal electrical signal. Manual catheter ablation proceeds as described previously, where the catheter is guided to the heart, the heart is mapped to identify regions of abnormal electrical activity, and then these regions are ablated. Catheters used for manual ablation are smaller than those used for remote catheter ablation (usually 8Fr or 2.7mm in diameter). During manual ablation the patient is placed in a fluoroscope, which consists of an X-ray source and a fluorescent screen, and the physician manually manipulates the catheters through direct visual feedback from fluoroscopic images taken in real time. Manual ablation exposes the physician and patient to high levels of ionising radiation (Beyar 2010). The physician is required to wear a heavy lead apron to reduce radiation exposure, which has lead to some physicians developing orthopaedic problems. These two factors are hazardous to the physicians performing the ablation and may reduce the number of procedures they are capable of performing in a set time period.

Patients should be followed up three months post-ablation and then every six months for two years. Warfarin is recommended for all patients for at least two months post-ablation and continuation of warfarin therapy past this point should be based on the patient’s risk factors for stroke. Patients should not undergo repeat ablation procedures within three months of the initial procedure (Calkins et al 2007; Darge et al 2009). Catheter ablation is associated with an approximate six per cent risk of complications, including thromboembolism, direct injury to cardiac structures by the catheter.
(perforation) and thermal injury to adjacent tissue. Cardiac tamponade\(^2\) occurs during other electrophysiology procedures but has a higher incidence (2-6%) during AF ablation due to the need of systemic anticoagulation. Cardiac tamponade can usually be reversed by the reversal of anticoagulation with protamine. Pulmonary vein stenosis\(^3\) is one of the commonest reported complications of AF ablation with reported incidence rates ranging from 1-38 per cent, which may be caused by thermal injury to the pulmonary vein musculature. One of the rarest (<0.25%) complications of AF ablation is atrio-oesophageal fistula formation, which occurs due to direct damage to the oesophagus during ablation and carries a 50 per cent risk of mortality (Calkins et al 2007; Darge et al 2009).

Four recent randomised controlled trials compared patients treated with catheter ablation to those treated with anti-arrhythmic medication. At 12-months follow-up, the number of patients free from symptoms of atrial fibrillation post-catheter ablation in the four trials were 87, 56, 86 and 75 per cent, compared to 37, 9, 22 and 7 per cent of patients in the medication arm of the four trials (Calkins et al 2007).

Other, not widely used, ablation techniques include cryo-ablation, where the region of interest is frozen using a coolant supplied via the inserted catheter; and microwave ablation, where tissue is ablated by the microwave energy "cooking" the adjacent tissue, and ultrasonic ablation, creating a heating effect by mechanical vibration (Beyar 2010; Dewire & Calkins 2010). Surgical ablation is rarely used and is usually conducted only when other heart surgery is necessary. During surgical ablation a number of ablation lines are made in the atria around the pulmonary veins, isolating the abnormal electrical signals and preventing them from travelling throughout the atria (NHF 2008).

A pacemaker may also be implanted to control the electrical signals of the heart (NHF 2008). The use of magnetic resonance imaging guidance for catheter ablation has also been discussed in a bid to reduce both patient and physician radiation exposure, however no studies have been reported as yet that have used this technique (Dewire & Calkins 2010).

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\(^2\) Cardiac tamponade: mechanical compression of the heart by large amounts of fluid or blood within the pericardial space that limits the normal range of motion and function of the heart.

\(^3\) Stenosis: a narrowing or constriction of the diameter of a bodily passage or orifice.
Clinical outcomes

Safety

Hansen Sensei® remote navigation system

There are currently seven listings concerning the Hansen Sensei® navigation system on the FDA MAUDE database, which lists incidents associated with medical devices that have malfunctioned and caused serious injury or death. All of the reported incidents occurred between October 2007 and July 2008 and are likely to be a result of the learning curve associated with the use of the navigation system. Five of the reported incidents involved the use of the Artisan catheter. Of these, one involved a malfunction of the catheter with a leak being detected after the catheter was introduced into the right atria. The catheter was removed and there was no patient injury. The remaining four incidents involving the Artisan catheter were all procedure related, all of which resulted in patients experiencing an effusion. Pericardiocentesis was performed and all patients were stabilised without further incident. The two remaining incidents involved the Sensei catheter, one of which involved a system malfunction which resulted in a modification of the software to all Hansen Sensei® systems. The remaining incident appeared to involve a malfunction with the system not manipulating the catheter in the posterior direction. As a result, the patient suffered an effusion, which was detected in recovery and pericardiocentesis was performed. No deaths were reported (FDA 2010).

There were eight papers included for assessment that reported on the use of the Hansen Sensei® remote navigation system for the ablation of AF. Of these studies, two only reported on the potential for adverse events associated with the use of the remote navigation system rather than the effectiveness of the system (Rillig et al 2010a; Rillig et al 2010b). Of the remaining six studies, three studies reported adverse events associated with the system, whilst the remaining three studies explicitly stated that no adverse events occurred during ablation performed with the remote navigation system (Table 1).

Most studies included for assessment reported on the fluoroscopy time, with the inference that a reduced fluoroscopy time would result in reduced radiation exposure for both patient and operator. This outcome has been included in the effectiveness section following this safety section (Table 2). Levels of radiation were reported by four of the eight included studies, two of which reported on radiation exposure of the operator (Steven et al 2010 and Saliba et

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4 Surgical puncture of the pericardium especially to aspirate pericardial fluid
al 2008) and two reported on patient exposure (Kautzner et al 2009 and Kanagaratnam et al 2008). Most of these studies reported radiation levels in different units, which were then converted to the more conventional mGy.m² by the evaluators to enable comparison.

The comparative study by Kautzner et al (2009) reported a significant decrease in radiation dose received by patients in the RNS ablation group compared to those in the manual ablation group (1.1 ± 0.596 vs 3.05 ± 2.03 mGy.m², p< 0.001). The small comparative study by Kanagaratnam et al (2008) reported markedly higher radiation exposure levels for patients, however the levels were similar for those treated for AF manually or with RNS (6.6 ± 5.9 vs 8.7 ± 7.7 mGy.m²).

The RCT conducted by Steven et al (2010) reported a significant decrease in the radiation dose received by the operator conducting RNS when compared to that received during manual procedures (0.71 ± 0.31 vs 1.9 ± 0.69 mGy.m², p< 0.001). The earlier RCT conducted by Steven et al (2008) did not report the radiation dose received by the operator but did report a significant decrease in the amount of time the operator was exposed to radiation in the RNS group compared to the manual group (1.8 ± 1.1 vs 8.2 ± 4.6 minutes, p= 0.001), which was markedly less time that that reported in the later study (7.0 ± 2.1 vs 22 ± 6.5, p<0.001). Although, the small case series by Saliba et al (2008) measured radiation dose received by the operator of the remote system, the measurements were reported in micro-sieverts which is difficult to convert to mGy.m² for comparison. Due to space restrictions in the electrophysiology laboratory during this study, the remote system was placed within the laboratory but distant (3-4 m) from the patient and fluoroscope, not in a separate office. Radiation exposure of staff at the workstation was significantly lower (p<0.05) than that measured by dosimeters of staff at the procedure table. The radiation dose received by the patient is likely to be higher than the 149 micro-sieverts recorded by the staff in the theatre.

What is unclear from these studies is whether or not the reported radiation doses for patients or the operators are clinically significant, especially in terms of a cumulative dose. It is clear that, in most cases, RNS does result in reduced radiation exposure when compared to manual ablation. However, it should be noted that for three of the studies reporting radiation exposure, the standard deviation of the reported values were large indicating considerable variation in the amount of exposure. Operators would be monitored for excessive radiation exposure by personal film badge dosimeters and levels of exposure would

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5 Units were reported in the paper erroneously as mGy/m². After contact with the authors the units were confirmed as µGy.m²

6 Coverted values mGy.m² = milli-Gray.m²
have to comply with radiation safety legislation. However, cumulative doses for patients are less well regulated. Patients and clinicians should be aware of any other potential procedures involving high levels of ionising radiation, including CT scans.

When considering the adverse events involved with the conduction of the RNS procedure, the large, well designed study by Di Base et al (2009) reported no significant difference between the rate of adverse events occurring in the remote navigation (3/193, 1.6%) and manual ablation (2/197, 1.02%) arms ($p=0.68$) (level II intervention evidence). Although these adverse events were considered serious (pericardial tamponade and perforation), all patients were successfully treated without further sequelae. Higher rates of adverse events were reported in the comparative study by Kanagaratnam et al (2008) (10%) and the case series by Saliba et al (2008) (5%), however both of these studies were small. Neither study stated whether or not the adverse events occurred in the “learning curve” phase of the use of the remote navigation system.

In two separate case series, Rillig et al (2010) reported on the incidence of iatrogenic septal defect and the incidence of oesophageal lesions, which may be caused by an increase in temperature during the ablation procedure. Iatrogenic septal defects may be caused by the use of the larger catheter to gain access to the left atrium and may lead to an increased risk of thromboembolisms. Although a large proportion of the patients experienced an iatrogenic septal defect (38/40, 95%), no thromboembolic events were reported and the majority of defects had healed by the end of the 6-month follow-up (30/38, 78.9%). An increase in oesophageal temperature during ablation has been associated with oesophageal wall injury which may lead to the development of serious adverse events including atrio-oesophageal fistulas. The majority of patients who successfully had an oesophageal probe inserted recorded an increase in oesophageal temperature above 39°C (76%). Of the patients who consented to an endoscopy a small proportion experienced an oesophageal lesion (14%), all of which healed within two weeks. Of interest is that oesophageal lesions occurred in those patients with a significantly higher body mass index.
Table 1  Adverse events associated with the use of the Hansen Sensei® for AF ablation

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention level of evidence</th>
<th>Study design</th>
<th>Population</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steven et al</td>
<td>II</td>
<td>RCT</td>
<td>Patients randomised (blind allocation) to manual ablation (n=30) or robotic navigation (n=30).</td>
<td>Mean operator radiation exposure (cGy cm²)</td>
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<tr>
<td>2010 Germany</td>
<td></td>
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<td>60 consecutive patients, mean age 62 ± 7.6 years, with symptomatic, drug refractory paroxysmal AF. Mean duration of AF 6.5 ± 4 years and episode duration of 14.5 ± 12.5 hours. Mean left atrial diameter 39 ± 4 mm. Structural heart disease n=7 (12%). 3D mapping with Ensite™ NavX™ Manual and RNS ablation performed using Celsius Thermocool saline irrigated catheter, radiofrequency power maximum 30 W RNS ablation catheter housed inside the Artisan steerable catheter.</td>
<td>Manual 1,899 ± 686 RNS 707 ± 313 p &lt; 0.001</td>
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<tr>
<td>Di Biase et al</td>
<td>II</td>
<td>RCT</td>
<td>Patients sequentially assigned to RNS (n=193) or manual ablation (n=197).</td>
<td>RNS patients 3/193 (1.6%) experienced adverse events. Of these 2/3 (66.7%) pericardial tamponade treated with pericardiocentesis. One perforation case occurred during the manual transeptal procedure. 1/3 (33.3%) haematoma of the groin Manual patients 2/197 (1.02%) experienced adverse events. Of these 1/2 (50%) pericardial tamponade treated with pericardiocentesis. 1/2 (50%) haematoma of the groin</td>
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<tr>
<td>Reference</td>
<td>Country</td>
<td>Type</td>
<td>Study Description</td>
<td>Results</td>
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<td>Kanagaratnam et al 2008 USA</td>
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<td>III-2</td>
<td>Comparative study</td>
<td>20 consecutive adult patients. 10 patients treated with manual ablation (no information given regarding age and symptoms). 10 patients, mean age 58.2 ± 12 years. AF n=7, AFL n=2, treatment for accessory pathway defect n=1. Mapping conducted using conventional (n=3), CARTO (n=2) and NaxX™ (n=5). 1/10 (10%) pericardial effusion (&lt;1 cm) measured 24 hrs post-procedure. Discharged without sequelae.</td>
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<td>Mean patient radiation dose (cGy cm²) (range)</td>
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<td>Manual AF 6,636 ± 5,867 (1,776-19,489)</td>
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<td>AFL 1,369 ± 1,108 (189-3,596)</td>
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<td>APD 2,899 ± 3,224 (219–11,055)</td>
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<td>RNS AF 8,732 ± 7,683 (779-24,667)</td>
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<td>AFL 4,712 ± 5,191 (1,042-8,383)</td>
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<td>APD 2,262</td>
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<td>Converted units (mGy.m²)</td>
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<td>Manual AF 6.6 ± 5.9 (1.8 - 19.5)</td>
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<td>AFL 1.4 ± 1.1 (0.19 – 3.6)</td>
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<td>APD 2.9 ± 3.2 (0.22 – 11.06)</td>
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<td>RNS AF 8.7 ± 7.7 (0.78- 24.7)</td>
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<td>AFL 4.7 ± 5.2 (1.04 – 8.4)</td>
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<td>APD 2.3</td>
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<tr>
<td>Kautzner et al 2009 Czech Republic</td>
<td></td>
<td>III-2</td>
<td>Comparative study without concurrent controls</td>
<td>38 adult patients, mean age 55 ± 9 years, with symptomatic, drug refractory paroxysmal AF. 22 patients underwent RNS and 16 patients underwent manual ablation. 3D mapping with Ensite™ NavX™ Manual and RNS ablation performed using Celcius Thermocool saline irrigated catheter, RF power maximum 35 W for manual ablation and 25 W for RNS. RNS ablation catheter housed inside the Artisan steerable catheter. Mean follow-up for manual ablation group 9 ± 3 months and 5 ± 1 month in the RNS group.</td>
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<td>Manual 3,048 ± 2,029</td>
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<td>RNS 1,119 ± 596</td>
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<td>Converted units (mGy.m²)</td>
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<td>Manual 3.05 ± 2.03</td>
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<td>RNS 1.12 ± 0.596</td>
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<td>Reference</td>
<td>Type</td>
<td>Study Design</td>
<td>Participants</td>
<td>Outcomes</td>
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<tr>
<td>Rillig et al 2010b</td>
<td>IV</td>
<td>Prospective case series</td>
<td>40 patients, mean age 60.3 ± 9.4 years, with drug refractory paroxysmal (n=22) or persistent (n=18) AF. 3.5 mm Thermocool® Navistar RNS ablation catheter housed inside the Artisan steerable catheter.</td>
<td>Detection of iatrogenic atrial septal defect Post-ablation 38/40 (95%) Mean diameter of 3.45 ± 1.5 mm Range 1-6 mm 3-month follow up 19/38 (50%) Mean diameter of 2.1 ± 1.22 mm Range 1-4 mm 6-month follow up 8/38 (21.1%) Mean diameter of 1.3 ± 0.6 mm Range 0.5-2 mm</td>
</tr>
<tr>
<td>Rillig et al 2010a</td>
<td>IV</td>
<td>Prospective case series</td>
<td>73 consecutive adult patients with drug refractory AF. The placement of an oesophageal probe was possible in 58/73 (79.5%) of these patients, with paroxysmal (n=38) or persistent (n=20) AF, mean age 58.6 ± 10.1 years. Consent for post-ablation endoscopy given in 42/58 (72.4%) patients. 3D mapping withNavX. 3.5 mm Thermocool® Navistar RNS ablation catheter housed inside the Artisan steerable catheter. RF power 25-30 W with a maximum temperature of 43°C.</td>
<td>58/73 (79.5%) successfully had an oesophageal temperature probe inserted Mean baseline temperature 36.9 ± 0.4°C Mean maximum temperature 40.3 ± 1.1°C A rise in temperature &gt;39°C was observed in 44/58 (75.9%) of patients Endoscopy 6/42 (14.3%) patients had an oesophageal lesion, all of which healed at end of 2 week follow-up BMI of patients with lesion was significantly higher than in those without BMI Lesion 29.0 ± 5.8 No lesion 24.1 ± 2.0 p = 0.047</td>
</tr>
<tr>
<td>Saliba et al 2008</td>
<td>IV</td>
<td>Prospective case series</td>
<td>40 adult patients, mean age 57 ± 20 years with symptomatic AF for ≥3 months, refractory to at least one anti-arrhythmic medication. Mean duration of AF 48 ± 12 months. Mean left atrial size 4.1 ± 0.8 cm. 23 patients with concomitant AFL. Paroxysmal AF n=29, persistent AF n=11. 3D mapping using CARTO and ablation of the right atrium using the Navistar thermocool catheter housed inside the Artisan steerable catheter. RF power 30 W, maximum temperature 45°C.</td>
<td>2/40 (5%) developed pericardial tamponade, both required pericardiocentesis. 1/40 (2.5%) procedure aborted after manual transeptal Average radiation dose Staff at remote work station 13 micro-sieverts Staff at procedure table 149 micro-sieverts, p&lt;0.05</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation, AFL = atrial flutter, W = watts, RCT = randomised controlled trial, RNS = remote navigation system, RF = radiofrequency, BMI = body mass index
Effectiveness

*Hansen Sensei® remote navigation system*

Of the eight identified studies that used the Hansen Sensei®-X for atrial fibrillation ablation, six reported on effectiveness outcomes (Table 2). All of the included studies reported on procedure time and fluoroscopy time as an outcome.

Immediate post-ablation procedure success, defined by complete pulmonary vein isolation, was reported by the three RCTs included for assessment (level II intervention evidence). Di Biase et al (2009) and Steven et al (2010) reported 100 per cent success rates for patients who underwent manual and RNS ablation. The proportion of patients free from symptoms of AF without anti-arrhythmic medication was reduced at 6-12 month follow-up in both of these studies but remained similar in both the RNS and manual groups at approximately 70 to 76 per cent. However, the smaller, earlier study by Steven et al (2008) reported immediate bidirectional block in 88 and 48 per cent of patients who underwent RNS and manual ablation for atrial flutter, respectively. The comparative study by Kautzner et al (2009) also reported good rates of freedom from AF symptoms at 5-9 month follow-up in both the manual (81%) and the RNS (91%) groups.

The largest study by Di Biase et al (2009) reported no significant difference in procedure time between the manual and RNS groups, as did the later RCT by Steven et al (2010). However, conflicting results were reported by the earlier RCT by Steven et al (2008), where the RNS procedure took a significantly longer time ($p = 0.04$), and the good comparative study by Kautzner et al (2009), where manual ablation took a significantly longer time ($p = 0.007$).

The learning curve associated with the use of the Hansen remote technology was reported by the three well designed randomised controlled trials included for assessment (level II intervention evidence). Steven et al (2008) reported the difference in learning curve when using the remote navigation system (RNS). There was a significant reduction in procedure time between the first and last 10 patients treated in the RNS ($105.3 \pm 34.8$ vs $60.6 \pm 6.3$ minutes, $p=0.003$), which was not apparent in the manual group, indicating a short learning curve for remote navigation. In addition, there was a great deal of variation, as demonstrated by the large standard deviation, in the procedure time for the first 10 patients. A similar result was observed by Di Biase et al (2009), who reported that the first 50 RNS procedures took significantly longer compared to manual ablation ($3.05 \pm 0.65$ hours vs $2.75 \pm 0.69$ hours, $p=0.041$), whereas overall there was no difference in procedure time between the two groups ($p = 0.716$). The later study conducted by Steven et al (2010) did not note a
difference in procedure time between the manual and RNS arms, indicating operator familiarity with the remote navigation technique.

Four comparative studies reported a significant decrease in fluoroscopy time using RNS compared to manual ablation.

It should also be noted that a standard protocol for AF ablation was not used in all studies. Maximum radiofrequency power used during ablation varied from 25 to 45 watts, however the maximum temperature remained reasonably constant at 41-45°C.

Table 2  The use of the Hansen Sensei® for atrial fibrillation ablation

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention level of evidence</th>
<th>Study design</th>
<th>Population</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Di Biase et al 2009 USA and Italy</td>
<td>II</td>
<td>RCT Patients sequentially assigned to RNS (n=193) or manual ablation (n=197).</td>
<td>390 consecutive adult patients, mean age 62 ± 11 years, with symptomatic, drug refractory AF (paroxysmal AF n=262, persistent AF n=110, long-standing persistent AF n=17). Mean left atrial diameter = 43.1 ± 8.0 mm. 3D mapping using CARTO or EnSite™. Manual and RNS ablation performed using Celsius Thermocool saline irrigated catheter, RF power maximum 45 W and 41°C. RNS ablation catheter housed inside the Artisan steerable catheter. Both manual (n=197) and RNS (n=193) procedures performed by two operators in equal numbers. All patients discharged on warfarin for 6 months.</td>
<td>Procedure outcome: Pulmonary vein isolation  RNS 193/193 (100%) Manual 197/197 (100%) AF free at follow-up (14.1 ± 1.3 months) Without anti-arrhythmic drugs RNS 139/193 (72.0%) Manual 138/197 (70.1%) p=0.668 With previously ineffective anti-arrhythmic drugs RNS 164/193 (85.0%) Manual 159/197 (80.7%) p=0.264 Procedure (RNS vs manual) had no effect on AF recurrence HR 1.10, 95% CI [0.57, 2.10] p= 0.786 Mean procedure time (hrs) Manual 3.1 ± 0.8 RNS 3.1 ± 1.1 p=0.716 Learning curve Mean procedure time (hrs) First 50 patients RNS 3.05 ± 0.65 50 2.75 ± 0.69 p = 0.041 Mean fluoroscopy time (mins) Manual 58 ± 20 RNS 49 ± 24 p &lt; 0.001</td>
</tr>
</tbody>
</table>
Steven et al 2008 Germany

RCT
Patients randomised to manual ablation (n=25) or robotic navigation (n=25).

50 consecutive patients, mean age 65.7 ± 9.3 years, with recurrent or persistent AFL with mean duration of 23.5 months (range 2-80). Mean left atrial diameter = 46.4 ± 7.8 mm. Structural heart disease n=19 (47.5%) and n=18 (45%) history AF. Manual ablation (n=25) performed using Celcius Thermocool saline irrigated catheter, RF power maximum 38 W and 48°C. Remote ablation (n=25) performed using thermocool catheter, radiofrequency power maximum 33 W.

RNS learning curve: First 10 patients reported as Group 1 and the remaining 15 patients Group 2.

Procedure outcome: bidirectional isthmus block
Immediate bidirectional block post AFL termination
RNS 22/25 (88%)
Manual 12/25 (48%)

p = 0.03

Mean procedure time (mins)
RNS 58.4 ± 17.7
Manual 79.4 ± 30.6

p= 0.04

Mean RF duration (mins)
RNS 496.4 ± 213.9
Manual 321.7 ± 214.6

p= 0.006

Mean fluoroscopy time (mins)
RNS 8.2 ± 4.6
Manual 5.8 ± 3.6

p= 0.038

Mean operator radiation exposure time (mins)
RNS 8.2 ± 4.6
Manual 1.9 ± 1.1

p= 0.001

Mean preparation time (mins)
RNS 105.3 ± 34.8
Manual 60.6 ± 6.3

p = 0.003

Learning curve
Mean procedure time (mins)
Group 1 105.3 ± 34.8
Group 2 60.6 ± 6.3

p = 0.003

Steven et al 2010 Germany

RCT
Patients randomised (blind allocation) to manual ablation (n=30) or robotic navigation (n=30).

60 consecutive patients, mean age 62 ± 7.6 years, with symptomatic, drug refractory paroxysmal AF. Mean duration of AF 6.5 ± 4 years and episode duration of 14.5 ± 12.5 hours. Mean left atrial diameter 39 ± 4 mm. Structural heart disease n=7 (12%). 3D mapping with Ensite™ NavX™ Manual and RNS ablation performed using Celcius Thermocool saline irrigated catheter, radiofrequency power maximum 30 W RNS ablation catheter housed inside the Artisan steerable catheter.

Procedure outcome: Pulmonary vein isolation
RNS 30/30 (100%)
Manual 30/30 (100%)

Mean procedure time (mins)
RNS 134 ± 12
Manual 156 ± 44.4

p=0.099

Mean fluoroscopy time (mins)
RNS 22 ± 6.5
Manual 9 ± 3.4

p < 0.001

Mean fluoroscopy time during preparation (mins)
RNS 6.0 ± 1.9
Manual 6.0 ± 2.1

p=0.595

Mean fluoroscopy time during...
<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Study Type</th>
<th>Patients Details</th>
<th>Procedure Details</th>
<th>Outcome Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kanagaratnam et al 2008 USA</td>
<td>III-2</td>
<td>Comparative study</td>
<td>20 consecutive adult patients. 10 patients treated with manual ablation (no information given regarding age and symptoms). 10 patients, mean age 58.2 ± 12 years. AF n=7, AFL n=2, treatment for accessory pathway defect n=1. Mapping conducted using conventional (n=3), CARTO (n=2) and NaxX™ (n=5).</td>
<td>Mean procedure time (mins) (range)</td>
<td>Manual AF 17.0 ± 6.3 (range) RNS 3.0 ± 2.4 p &lt; 0.001</td>
</tr>
<tr>
<td>Kautzner et al 2009 Czech Republic</td>
<td>III-2</td>
<td>Comparative study without concurrent controls</td>
<td>38 adult patients, mean age 55 ± 9 years, with symptomatic, drug refractory paroxysmal AF. 22 patients underwent RNS ablation and 16 patients underwent manual ablation. 3D mapping with Ensite™ NavX™ Manual and RNS ablation performed using Celsius Thermocool saline irrigated catheter, RF power maximum 35 W for manual ablation and 25 W for RNS. RNS ablation catheter housed inside the Artisan steerable catheter. Mean follow-up for manual ablation group 9 ± 3 months and 5 ± 1 month in the RNS group.</td>
<td>Mean procedure time (mins) (range)</td>
<td>Manual AF 61.4 ± 31 (24-121) AFL 23 ± 13.3 (7-49) APD 22.9 ± 12.2 (9-44) RNS AF 55.3 ± 31.2 (13.4-116) AFL 32.2 ± 17.4 (19.9-44.5) APD 41.7</td>
</tr>
</tbody>
</table>
Saliba et al 2008 Multicentre study

Prospective case series

40 adult patients, mean age 57 ± 20 years with symptomatic AF for >3 months, refractory to at least one anti-arrhythmic medication. Mean duration of AF 48 ± 12 months. Mean left atrial size 4.1 ± 0.8 cm. 23 patients with concomitant AFL. Paroxysmal AF n=29, persistent AF n=11. 3D mapping using CARTO and ablation of the right atrium using the Navistar thermocool catheter housed inside the Artisan steerable catheter. RF power 30 W, maximum temperature 45°C. Patients all received intravenous heparin.

Procedure outcome: all pulmonary veins including the superior vena cava ablated

12-month follow-up
34/40 (85%) AF free and not taking anti-arrhythmic drugs
5/40 (12.5%) AF free but taking previously ineffective anti-arrhythmic drugs
1/40 (2.5%) procedure aborted after manual trans-septal

Mean procedure time (mins)
All 163 ± 88
AF 189 ± 88
AFL 126 ± 56

Mean ablation time (mins)
All 89.6 ± 43
AF 106 ± 25
AFL 56 ± 54

Mean fluoroscopy time (mins)
All 64 ± 33
AF 83 ± 15
AFL 37 ± 35

AF = atrial fibrillation, AFL = atrial flutter, W = watts, RCT = randomised controlled trial, RF = radiofrequency, RNS = robotic navigation system, PV = pulmonary vein, cGy = centi-Gray units (the unit of absorbed radiation dose), APD = accessory pathway defect

In summary, the Hansen Sensei® remote navigation system appears to be as effective as manual ablation for atrial fibrillation, with similar rates of freedom from symptoms reported in all but one study. Low rates of adverse events were reported in both groups and reduced radiation exposure for patients and the operator were reported by the majority of studies which reported this as an outcome. All studies reported a significant decrease in fluoroscopy time, which would correlate with a corresponding decrease in radiation exposure and dose to the patient and operator alike. Conflicting results were reported regarding procedure time, however the largest comparative study reported no difference between the two techniques for this outcome.

Safety

Sterotaxis Niobe® remote magnetic navigation system

There are no MAUDE database listings for the Stereotaxis Niobe® navigation system to date (FDA 2010).

There were seven papers included for assessment that reported on the use of the Niobe® remote navigation system for the ablation of AF. Of these studies, four reported adverse events associated with the use of system, whilst the remaining two studies explicitly stated that no adverse events occurred during the ablation procedure (Table 3).
Only one study reported on the level of radiation exposure to the patient. Mean radiation exposure was significantly less in the RNS ablation group compared to the manual group (3.3 vs 4.3 mGy.m\(^2\), \(p = 0.032\)). It should be noted that wide ranges for these variables were reported in both the RNS and manual groups (level II intervention evidence).

Low rates of adverse events were reported by the included studies, ranging from 2.2 to five per cent. High rates of charring\(^7\) were reported by Arya et al (19.2%) and Chun et al (30.4%), however this was not associated with further sequelae (level III-3 and IV intervention evidence). Chun et al (2010) reported on their experiences in a case series using the Niobe\(^{®}\) RNS, with the first group of patients (n=28) undergoing ablation with the first generation Thermocool\(^{®}\) Navistar RMT catheter (Biosense Webster) and the remaining 28 patients with the second generation catheter of the same name (level IV interventional evidence). Although the second generation catheter was the same size (3.5 mm) as the first generation, the internal lumen was increased to improve the uniformity of irrigation flow. In addition, the thermal conductivity was maximised and the location of the irrigation port was moved. These changes to the ablation catheter appear to be effective as adverse events were only reported in patients who underwent ablation with the first generation catheter, however this could also be associated with learning curve. In the well designed study by Vollmann et al (2009), only one adverse event, significant local haemorrhage, was reported in the manual ablation arm, with none occurring in the remote navigation arm (level II intervention evidence).

\(^7\) Charring and desiccation may occur during ablation, changing the electrical conductivity of blood and tissue, causing an increase in the overall impedance of the electrical heating circuit and thus a diminution in the power delivered to the tissue. Charring may be problematic due to the possibility that the char may dislodge from the electrode and enter the blood stream causing serious adverse effects for the patient.
Table 3  Adverse events associated with the use of the Stereotaxis Niobe® for AF ablation

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention level of evidence</th>
<th>Study design</th>
<th>Population</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vollmann et al 2009 Germany</td>
<td>II</td>
<td>RCT with randomly assigned blocks of 10 patients.</td>
<td>90 adult patients with ≥ 1 episode CTI dependent AFL. Patients randomised to manual ablation with Celsius catheter (n=45), mean age 68 ± 9 years or RNS with the Celsius Navistar catheter (n=45), mean age 69 ± 8 years. Radiofrequency power maximum 70 W with a target temperature of 60°C.</td>
<td>RNS ablation No reported adverse events Manual ablation 1/45 (2.2%) developed significant local haemorrhage post procedure Mean patient radiation exposure, range (µGy m²) RNS 3,274, 2,045 to 5,025 Manual 4,304, 3,435 to 5,862 p = 0.032 Converted units (mGy.m²) RNS 3.3, 2.05 to 5.03 Manual 4.3, 3.4 to 5.9 p = 0.032</td>
</tr>
<tr>
<td>Arya et al 2008 Germany</td>
<td>III-3</td>
<td>Comparative study with historical controls</td>
<td>26 consecutive adult patients, mean age 64.3 ± 9.0 years, with AFL. Compared to 40 historical controls (no data given), 3D mapping with CARTO and RNS ablation performed using the Navistar catheter. RF power 70 W and maximum temperature 70°C. Learning curve: First 10 patients reported as Group 1 and the remaining 15 patients Group 2.</td>
<td>5/26 (19.2%) reported significant ablation tip charring with no sequelae</td>
</tr>
<tr>
<td>Kim et al 2008 USA</td>
<td>III-3</td>
<td>Retrospective comparative study without concurrent controls</td>
<td>721 consecutive patients. RNS performed in 127 patients and manual ablation in 594 patients. Results presented only for patients with AF, AFLT, AFLA, AT, AVNRT, AVRT, RVOT</td>
<td>2/91 (2.2%) cases tamponade following manual ablation for AF No adverse events reported when RNS was used for ablation.</td>
</tr>
</tbody>
</table>
Chun et al 2010 Germany

56 adult patients, mean age 63 years (range 24-78 years) with drug refractory paroxysmal (n=37) or persistent (n=19) AF. 3D mapping with CARTO and RNS ablation performed using the Thermocool® Navistar catheter. RF power 40 W and maximum temperature 43°C. All adverse events occurred in patients treated with the first generation Thermocool® catheter. 17/56 (30.4%) reported significant ablation tip charring with no sequelae 1/56 (1.8%) non-ST segment elevation myocardial infarction due to embolic occlusion of the distal left anterior descending artery on day 7 1/56 (1.8%) transient ischaemic attack day 14, no thromboembolism and neurological symptoms normalised 1/56 (1.8%) right inferior asymptomatic pulmonary vein stenosis

Effectiveness

Sterotaxis Niobe® remote magnetic navigation system

A large number of studies were identified that used the Stereotaxis Niobe® remote magnetic navigation system for indications other than atrial fibrillation. Due to the time constraints placed on the writing of this horizon scanning report only those studies reporting on the use of the Niobe® for AF or AFL ablation were included. Excluded studies included those which used the Niobe® for percutaneous coronary interventions (PCI): a crossover RCT where 111 consecutive patients underwent a percutaneous coronary intervention (PCI) using both conventional and magnetic guide-wires (Ramcharitar et al 2008); a multicentre case series of 157 patients who underwent PCI using only magnetic guide-wires (Krause et al 2009); a study of 44 patients with a single discrete stenosis who underwent PCI using magnetic guide-wires compared to 44 historical controls who underwent conventional PCI (Patterson et al 2009); and a case series of 30 consecutive patients undergoing PCI who were randomised to either 2D guidance or 3D angioscopy using the Niobe® (Schneider et al 2008). In addition, one study reported on a case series of 15 patients undergoing PCI with the Niobe® using images obtained with computed tomography co-registered on real-time fluoroscopy images (Ramcharitar et al 2009). A number of studies reported on the use of the Niobe® for the treatment of ventricular tachycardias and arrhythmias: a RCT of patients with supraventricular arrhythmias needing ablation for atrioventricular nodal re-entry or accessory pathway who were randomised to magnetic guided (n=56) or manual (n=15 ablation) (Wood et al 2008); a case
series of 30 patients with supraventricular tachycardia (Xu et al 2009); a case-control study of patients with ventricular arrhythmia comparing ablation with the Niobe® (n=110) to manual ablation (n=92) (Di Biase et al 2010); and a study of 26 patients with atrioventricular nodal re-entrant tachycardia who underwent magnetically guided ablation compared to 11 historical controls who underwent conventional manual ablation (Ricard et al 2010). Of interest is the RCT conducted in the Netherlands in a paediatric population (mean age 12.2 ± 3.2 years) treated for several types of tachycardias. Patients were randomised to either magnetic (n=29) or manual (n=29) ablation. No complications or adverse events were reported. When the groups were considered as a whole, there was no significant difference in fluoroscopy time between the two groups. However, when only children <10 years were considered, there was a significant decrease in fluoroscopy time in the RNS group (n=11) compared to the manual group (n=8) (13 ± 7 vs 31 ± 28 minutes, p=0.01). This finding may be of importance for developing children and may make RNS a more attractive option than manual ablation (Schwagten et al 2010). The same research group reported on the earlier results of a case series of children (n=11) with complex arrhythmias and adults (n=12) with congenital heart disease undergoing RNS (Schwagten et al 2009) (level IV intervention evidence). In a small case series of 22 patients with congenital heart disease, the Niobe® was mainly used for mapping purposes with only seven of these patients requiring ablation with the system (Wu et al 2010).

Further evaluation of the effectiveness of the Niobe® for indications other than atrial fibrillation may be warranted.

**Sterotaxis Niobe® remote magnetic navigation system for atrial fibrillation**

A lower level of evidence was available for the assessment of the Niobe®, with only two well-designed prospective comparative studies included for evaluation. Three studies compared historical controls to current cases and two were non-comparative case series.

Six of the seven studies included for assessment reported on the success of the ablation procedure (Table 4). The well designed study for atrial flutter by Vollmann et al (2009), reported no difference in rates of immediate post-ablation cavotricuspid isthmus blockage between patients treated with RNS or manual ablation (84.4% vs 91.1%, p = 0.52) (level II intervention evidence). However, there was a higher, non-significant, proportion of patients with freedom from symptoms of atrial flutter in the manual ablation group at 6-month follow-up compared to RNS patients (88.9% vs 73.3%, p =0.063). Katsiyiannis et al (2008) also reported good procedural outcomes for patients undergoing both manual and RNS ablation (level III-2 intervention evidence). Complete pulmonary vein isolation was achieved in 100 per cent of both RNS
and manual ablation patients and freedom from symptoms of AF were not significantly different at 12-month follow-up (RNS = 80%, manual = 75%). Procedural success rates for AF or AFL ablation varied from 93 to 100 per cent in the lower level evidence studies. The lowest overall rate of ablation was 81 per cent reported by Latcu et al (2009), however this was a mixed patient group of seven indications, including atrial tachycardia, atrioventricular nodal re-entrant tachycardia and atrioventricular re-entrant tachycardia as well as AF and AFL patients. The study with the longest follow-up (mean 426 ± 213 days), a case series of 56 patients, reported 70 per cent of patients had freedom from symptoms of AF at study end (Chun et al 2010).

Of interest, the well designed study by Vollmann et al (2009) reported a significantly longer procedure and ablation time for remote navigation compared to manual navigation (113.5 ± 34.8 vs 77.2 ± 24.1 minutes, \( p < 0.0001 \) and 55 vs 17 minutes, \( p < 0.0001 \), respectively). However, mean radiation exposure (3,274 vs 4,304 µGy m², \( p = 0.032 \)) and mean fluoroscopy time (10.6 vs 15 minutes, \( p = 0.043 \)) was significantly reduced in the remote navigation group compared to the manual group. It should be noted that wide ranges for all these variables, in both the RNS and manual groups, were reported (level II intervention evidence). The other good comparative study by Katsiyiannis et al (2008) reported significantly less procedure time for patients in the RNS group compared to the manual ablation group (109 vs 279 minutes, \( p < 0.001 \)) as well as a significantly reduced fluoroscopy time (18.5 vs 58.6 minutes, \( p < 0.001 \)) (level III-2 intervention evidence).

As with the Hansen system, several studies reported on the learning curve associated with the use of the remote navigation Niobe® system. In the well designed RCT conducted by Vollmann et al (2009), procedure time did not decrease with an increasing familiarity with the technique (level II intervention evidence). In this study the mean procedure time for the first 22 patients was 120 ± 35 minutes, compared to 107 ± 34 minutes for the final 23 patients (difference between the means = -13 minutes, 95% CI [-7.8, 33.8], \( p = 0.21 \)). However, the retrospective comparative study by Kim et al (2008) reported on the learning curve for AF ablation using the Niobe® system (level III-3 intervention evidence) and found that procedure time decreased with increased operator experience. Although there was a high degree of variation, both fluoroscopy time and procedure time decreased with time, as demonstrated by the negative slope of the linear regression (\( r = -0.530 \) and -0.192, respectively). A similar reduction was not observed for the manual ablation of AF with fluoroscopy time remaining constant with a flat linear regression slope (\( r = 0.001 \)) and procedure time increasing over time with a positive slope (\( r = 0.250 \)). The mean fluoroscopy and procedure time for remote navigation AF ablation was 60 and 368 minutes, respectively, however an analysis of the last
25 cases indicated a decrease in both procedure (361 minutes) and fluoroscopy time (46 minutes). The small case series by Arya et al (2008) also reported a significant decrease in fluoroscopy time ($p = 0.014$) and procedure time ($p = 0.0001$) with an increase in operator experience.

**Table 4 The use of the Stereotaxis Niobe® for atrial fibrillation ablation**

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention level of evidence</th>
<th>Study design</th>
<th>Population</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Vollmann et al 2009    | II                            | RCT with randomly assigned blocks of 10 patients. | 90 adult patients with $\geq 1$ episode CTI dependent AFL. Patients randomised to manual ablation with Celsius catheter (n=45), mean age 68 ± 9 years or RNS with the Celsius Navistar catheter (n=45), mean age 69 ± 8 years. Radiofrequency power maximum 70 W with a target temperature of 60°C. | **Procedure outcome:**
|                         |                               |                                                  |                                                                             | **Acute complete CTI block**
|                         |                               |                                                  |                                                                             | 38/45 (84.4%) RNS patients
|                         |                               |                                                  |                                                                             | 41/45 (91.1%) manual patients
|                         |                               |                                                  |                                                                             | $p=0.52$
|                         |                               |                                                  |                                                                             | Manual ablation was used for the 7 RNS patients who failed to achieve CTI block. All were successful.
|                         |                               |                                                  |                                                                             | **Long-term freedom from AFL at 6-month follow-up**
|                         |                               |                                                  |                                                                             | 33/45 (73.3%) RNS patients
|                         |                               |                                                  |                                                                             | 40/45 (88.9%) manual patients
|                         |                               |                                                  |                                                                             | $p=0.063$
|                         |                               |                                                  |                                                                             | **Procedure duration (mins)**
|                         |                               |                                                  |                                                                             | RNS 113.5 ± 34.8
|                         |                               |                                                  |                                                                             | Man 77.2 ± 24.1
|                         |                               |                                                  |                                                                             | Difference between the means 36.3 mins, 95% CI [23.7, 48.9] $p<0.0001$
|                         |                               |                                                  |                                                                             | **RF application duration (mins)**
|                         |                               |                                                  |                                                                             | RNS 17.1, range 8.6-25.1
|                         |                               |                                                  |                                                                             | Man 7.5, range 3.6-10.9
|                         |                               |                                                  |                                                                             | $p<0.0001$
|                         |                               |                                                  |                                                                             | **Ablation time, range (mins)**
|                         |                               |                                                  |                                                                             | RNS 55, 28 to 76
|                         |                               |                                                  |                                                                             | Man 17, 7 to 31
|                         |                               |                                                  |                                                                             | $p<0.0001$
|                         |                               |                                                  |                                                                             | **Mean fluoroscopy time, range (mins)**
|                         |                               |                                                  |                                                                             | RNS 10.6, 7.6 to 19.9
|                         |                               |                                                  |                                                                             | Man 15.0, 11.5 to 23.1
|                         |                               |                                                  |                                                                             | $p = 0.043$
<p>|                         |                               |                                                  |                                                                             | Overall the proportion of patients with paroxysmal or persistent AF increased from 40% at baseline to 62% at 6-month follow-up, NS |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Study Design</th>
<th>Patients</th>
<th>Procedure Outcome</th>
<th>Procedure Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Katsiyiannis et al 2008 USA</td>
<td></td>
<td>Prospective comparative study with concurrent controls</td>
<td>40 consecutive patients with AF. 20 patients (persistent AF n=6, paroxysmal AF n=14) underwent manual ablation with Blazer catheter, RF power 45 W and maximum temperature of 55°C. 20 patients (persistent AF n=7, paroxysmal AF n=13) underwent RNS performed with Celsius catheter, RF power 30 W and a maximum temperature of 55°C. Both patient groups underwent 3D mapping with NavX.</td>
<td>Procedure outcome: PV isolation and complete wide area circumferential ablation 20/20 (100%) RNS patients 20/20 (100%) manual patients</td>
<td>Mean procedure time (mins) RNS 209 ± 56 Manual 279 ± 60 p&lt; 0.001 Mean fluoroscopy time (mins) RNS 19.5 ± 9.8 Manual 58.6 ± 21 p&lt; 0.001 Freedom from AF at 12 months RNS 16/20 (80.0%) Manual 15/20 (75.0%) Additional ablation procedures were required for AFLA in both the manual group (n=2) and the RNS group (n=3)</td>
</tr>
<tr>
<td>Arya et al 2008 Germany</td>
<td></td>
<td>Comparative study with historical controls</td>
<td>26 consecutive adult patients, mean age 64.3 ± 9.0 years, with AFL. Compared to 40 historical controls (no data given). 3D mapping with CARTO and RNS ablation performed using the Navistar catheter. RF power 70 W and maximum temperature 70°C. Learning curve: First 10 patients reported as Group 1 and the remaining 15 patients Group 2.</td>
<td>1/26 (3.8%) the RNS magnets could not be moved from the parking position and manual ablation was performed. Procedure outcome: Termination of AFL 25/25 (100%)</td>
<td>Mean procedure time (mins), range All 53, 30 to 130 Group 1 80, 57 to 130 Group 2 45, 30 to 70 p = 0.0001 Mean fluoroscopy time (mins), range All 7.5, 3.2 to 20.8 Group 1 11, 5.4 to 20.8 Group 2 7.2, 3.2 to 12.2 p = 0.014 Mean ablation time (mins), range All 25, 12 to 78 Group 1 31, 20 to 78 Group 2 20, 12 to 40 p = 0.002 Mean RF time (seconds), range All 614, 262 to 1.728 Group 1 628, 405 to 1.547 Group 2 613, 262 to 1.728 p = 0.313 Historical control comparison Mean procedure time (mins), range RNS 53, 30 to 130 Manual 45, 30 to 110 p = 0.12 Mean fluoroscopy time (mins), range RNS 19.5, 9.8 to 21.8 Manual 58.6, 21 to 121.6 p = 0.001</td>
</tr>
</tbody>
</table>
Kim et al 2008  
III-3  
Retrospective comparative study without concurrent controls

<table>
<thead>
<tr>
<th>Range</th>
<th>Manual</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNS</td>
<td>14.3, 4.0 to 45.3</td>
</tr>
<tr>
<td>Manual</td>
<td>14.3, 4.0 to 45.3</td>
</tr>
</tbody>
</table>

Mean fluoroscopy time (mins)

<table>
<thead>
<tr>
<th>Range</th>
<th>Manual</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNS</td>
<td>51 ± 34</td>
</tr>
<tr>
<td>Manual</td>
<td>51 ± 34</td>
</tr>
</tbody>
</table>

p < 0.0001

Mean procedure time (mins) (n)

<table>
<thead>
<tr>
<th>Range</th>
<th>Manual</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNS</td>
<td>243 ± 95</td>
</tr>
<tr>
<td>Manual</td>
<td>243 ± 95</td>
</tr>
</tbody>
</table>

p < 0.001

721 consecutive patients. RNS performed in 127 patients and manual ablation in 594 patients. Results presented only for patients with AF, AFLT, AFA, AT, AVNRT, AVRT, RVOT.
## Comparative study with historical controls

40 adult patients, median age 57 years (range 28-75 years) with drug refractory paroxysmal (n=25) or persistent (n=15) AF, with median duration of symptoms of 46.5 months, range 12-286 months. 28 matched historical controls, median age 57 years (range 31-75 years). 3D mapping with CARTO and RNS ablation performed using the 4mm Navistar RMT catheter. RF power 50 W and maximum temperature 65°C.

### Learning curve:
First 12 patients reported as Group 1 and the remaining 28 patients Group 2. Historical controls compared to Group 2 only.

### Procedure outcome
38/40 (95%) successful RNS ablation
The 2 patients then underwent successful manual ablation
The first 3 procedures were difficult with the operator finding it difficult to position the catheter.

#### Median procedure time (mins), range

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>152.5 (90 to 380)</td>
</tr>
<tr>
<td>Group 1</td>
<td>192.5 (92 to 380)</td>
</tr>
<tr>
<td>Group 2</td>
<td>148 (90 to 209)</td>
</tr>
</tbody>
</table>

#### Median fluoroscopy time (mins), range

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>32.3 (21.8 to 81.4)</td>
</tr>
<tr>
<td>Group 1</td>
<td>34.5 (22.4 to 81.4)</td>
</tr>
<tr>
<td>Group 2</td>
<td>30.3 (21.8 to 60.4)</td>
</tr>
</tbody>
</table>

#### Median ablation time (mins), range

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>49.5 (17 to 154)</td>
</tr>
<tr>
<td>Group 1</td>
<td>70 (33 to 154)</td>
</tr>
<tr>
<td>Group 2</td>
<td>49 (17 to 72)</td>
</tr>
</tbody>
</table>

### Historical control comparison

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2</td>
<td>148 (90 to 209)</td>
</tr>
<tr>
<td>Manual</td>
<td>110 (45 to 150)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

#### Median fluoroscopy time (mins), range

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2</td>
<td>30.3 (21.8 to 60.4)</td>
</tr>
<tr>
<td>Manual</td>
<td>30.3 (20 to 59)</td>
</tr>
<tr>
<td>p</td>
<td>0.352</td>
</tr>
</tbody>
</table>

#### Median ablation time (mins), range

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2</td>
<td>49 (17 to 72)</td>
</tr>
<tr>
<td>Manual</td>
<td>57.5 (30 to 86)</td>
</tr>
<tr>
<td>p</td>
<td>0.04</td>
</tr>
</tbody>
</table>

---

### Pappone et al 2006 Italy

<table>
<thead>
<tr>
<th>AVNRT (n)</th>
<th>Man (149)</th>
<th>p = 0.978</th>
<th>204 ± 56</th>
<th>203 ± 61</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVRT (n)</td>
<td>Man (80)</td>
<td>p = 0.270</td>
<td>326 ± 119</td>
<td>283 ± 106</td>
</tr>
<tr>
<td>RVOT (n)</td>
<td>Man (22)</td>
<td>p = 0.284</td>
<td>206 ± 71</td>
<td>238 ± 98</td>
</tr>
</tbody>
</table>
### Latcu et al 2009

**Monaco**

<table>
<thead>
<tr>
<th>IV</th>
<th>Case series</th>
<th>84 patients, mean age 54 ± 17 years (range 12-90 years), with paroxysmal AF (n=3), AFLT (n=15), AVNRT (n=7), AT (n=3), VT (n=7) and accessory pathway (n=12). RNS ablation catheters used Navistar RMT, Navistar RMT DS and Navistar thermocool®.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Procedure success</td>
<td>68/84 (81.0%)</td>
</tr>
<tr>
<td></td>
<td>AVNRT</td>
<td>36/37 (97.3%)</td>
</tr>
<tr>
<td></td>
<td>AT</td>
<td>3/3 (100%)</td>
</tr>
<tr>
<td></td>
<td>VT</td>
<td>6/7 (85.7%)</td>
</tr>
<tr>
<td></td>
<td>AP</td>
<td>8/12 (66.7%)</td>
</tr>
<tr>
<td></td>
<td>AFLT</td>
<td>8/15 (53.3%)</td>
</tr>
<tr>
<td></td>
<td>AFLA</td>
<td>4/7 (57.1%)</td>
</tr>
<tr>
<td></td>
<td>AF</td>
<td>3/3 (100%)</td>
</tr>
</tbody>
</table>

Of the 16 failed patients, 13 (81.3%) were successfully treated with manual ablation.

- **Mean fluoroscopy time**: 14 ± 11 minutes
- **Mean operator exposure time**: 1.5 ± 0.6 minutes
- **Mean procedure time**: 169 ± 72 minutes

### Chun et al 2010

**Germany**

<table>
<thead>
<tr>
<th>IV</th>
<th>Case series</th>
<th>56 adult patients, mean age 63 years (range 24-78 years) with drug refractory paroxysmal (n=37) or persistent (n=19) AF. 3D mapping with CARTO and RNS ablation performed using the Thermocool® Navistar catheter. RF power 40 W and maximum temperature 43°C.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Procedure outcome: PV isolation</td>
<td>52/56 (92.9%)</td>
</tr>
<tr>
<td></td>
<td>4/56 (7.1%) underwent manual ablation successfully</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean procedure time</td>
<td>315 mins (range 125-550)</td>
</tr>
<tr>
<td></td>
<td>Mean fluoroscopy time</td>
<td>19 mins (range 8-39)</td>
</tr>
<tr>
<td></td>
<td>Mean fluoroscopy time from control room</td>
<td>6 mins (range 2-14), resulting in a 31% decrease in exposure for the operator</td>
</tr>
<tr>
<td></td>
<td>At follow-up (426 ± 213 days)</td>
<td>Only 50 patients had completed follow-up at this stage</td>
</tr>
<tr>
<td></td>
<td>35/50 (70%) were in sinus rhythm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12/50 (24%) underwent further ablation procedure</td>
<td></td>
</tr>
</tbody>
</table>

In summary, the Niobe® remote navigation system appears to be effective at ablating symptoms of atrial fibrillation and atrial flutter with procedural success rates ranging from 93 to 100 per cent. Of those studies that reported long-term follow-up, sustained levels of freedom from symptoms were reported in 70-80 per cent of patients. Comparative studies reported reduced fluoroscopy time for patients undergoing RNS ablation, indicating less radiation exposure not only to patients but also to the clinical staff involved with conducting the procedure.
Potential cost impact

Cost Analysis

No cost-effectiveness studies on either the Niobe® or Sensei® remote navigation systems were identified for inclusion in this assessment. Due to the nature of the results of this assessment, that is the main health outcome is in terms of reduced radiation exposure to the patient but especially the clinician, a cost-consequences analysis may be the more appropriate economic analysis to conduct.

Manual or remote navigation techniques require mapping studies of the heart’s anatomy to be conducted. The same mapping systems can be used for both manual and RNS techniques, with most electrophysiological laboratories opting for the EnSite™ NavX™ (St Jude Medical Inc., USA) or the CARTO (Biosense Webster Inc., USA) three dimensional systems. These 3D-mapping systems cost approximately A$250,000. The Niobe® is only compatible with the CARTO mapping system (personal communication Devices Australia).

The Hansen Sensei® remote navigation system currently costs approximately A$1.2 million, however this initial outlay includes the training of clinical personnel in the use of the system and continued company support for the first 20 cases. The lifespan of the system as a whole has yet to be ascertained, however the robotic catheter arm has a lifespan of 300 operating hours and is then replaced under warrantee. Other costs associated with the purchase of the Hansen system include the radiofrequency receiving patches placed on the patient, which cost approximately A$2,500. Additional costs include the purchase of the single-use steerable Artisan™ catheter sheaf, which can only be used with the Hansen system and costs approximately A$3,000. The single-use only ablation catheters which fit inside the Artisan™ cost approximately A$1,600. It has been estimated that the cost per remote navigation system procedure is $1-2,000 more than that performed manually depending on the consumables used, however a full cost-effectiveness analysis may place a value of reduced procedure and fluoroscopy time (personal communication St Jude Medical).

The Niobe® remote navigation system currently costs approximately US$1.25 million, with the initial outlay including training costs of clinical personnel in the use of the system and continued company support for clinicians throughout the learning curve of between 50-75 cases. This price excludes the cost of the 3D mapping system, but an additional US$250,000 is required to purchase the integrated information system, the Odyssey. The Niobe® system requires that the operating room have magnetic shielding installed, and the degree of shielding will depend on the functionality of adjoining rooms, that is, more
shielding would be required if the electrophysiology laboratory was housed next to an MRI facility. Typically shielding would cost between US$30 – 60,000 depending on the location relative to other magnetic fields in the hospital. Currently the Biosense Webster RMT catheters are the only ones that can be used with the Niobe® system. These single use catheters cost approximately A$3-3,500 each (personal communication Devices Australia).

Currently ablation procedures using the remote navigation systems are being conducted in a private hospital setting using the Medicare Benefit Schedule item number 38290 for the “ablation of arrhythmia circuits or foci, or isolation procedure involving both atrial chambers and including curative procedures for atrial fibrillation” which has a fee of $2,525. Cardiac mapping with the 3D system is not covered by a separate MBS item number. If this procedure is conducted in a private hospital some of the costs of mapping may be borne by the patient or their health insurance company.

An Australian report commissioned by the National Stroke Foundation in 2010 estimated the costs to the Australian economy resulting from atrial fibrillation, including medical costs, care for patients with a long-term disability and loss of productive output to be $1.25 billion for the year 2008-09. A significant proportion of these costs (64% or $797 million) relate to the sequelae of AF, including stroke and heart failure. Although many of these events may be avoided through early detection, AF is often asymptomatic with approximately 30 per cent of cases diagnosed serendipitously when patients are hospitalised for reasons other than AF. If the prevalence of people living with AF in the population increases by 1.2 to 1.5 per cent, total annual health-care costs for AF have been estimated to increase accordingly by $84 to $352 million (PricewaterhouseCoopers 2010).

A recent reported conducted in New Zealand also found that the projected increase in the prevalence of AF will add greatly to health care costs in New Zealand. The report quotes figures from a study conducted in the United Kingdom where costs associated with AF accounted for 0.62 per cent of total National Health Service (NHS) expenditure in 1995 which included hospitalisations, drug prescriptions and long-term nursing home care after hospital admission. By the year 2000, the direct cost of health care for people with AF had risen to 0.97% of total NHS expenditure. As in Australia, most costs associated with AF are due to stroke and heart failure, with the life-time cost of one stroke estimated to cost NZ$50,000. It is estimated that only 32 per cent of patients who could benefit from preventative anti-coagulant therapy are currently taking it. By increasing the proportion of people with AF taking anticoagulant therapy from 32 to 50 per cent, approximately 200 strokes per year in New Zealand could be prevented, with a cost saving of around NZ$10 million per year (NZGG 2005).
Ethical considerations

The Hansen Sensei® and Niobe® remote navigation systems are, in some ways, ethically uncontroversial. They would replace existing treatment regimes with new regimes that are as effective as the old, they can be provided in the same institutional settings, and they rely on similar patterns of training for operators as have been developed in the past for previous treatments. The key ethical question that remains is whether the reductions in fluoroscopy time that they offer are of clinical relevance for patients and operators. There are two ethical concepts that are relevant to addressing this question but, in this instance, neither provide a clear answer.

The precautionary principle

One problem with innovative technologies is that the risks associated with these technologies are rarely understood at the outset. This problem has been well illustrated, over a long timeframe, with respect to the effects of radiation exposure for both patients and operators in clinical investigations and treatments.

The precautionary principle has been developed in response to this problem. The precautionary principle, in its simplest form, encompasses the notion that we should not introduce new technologies unless we are convinced that they are safe both for humans and the environment. The corollary is that, whenever possible, we ought to minimise exposure to technologies, such as radiation, which have been shown to have adverse effects on human health and wellbeing. One of the basic concepts in the precautionary principle is the idea that the responsibility for proof of safety lies with those who would expose people, in this case patients and clinicians, to higher risk.

If the precautionary principle is applied to the Hansen Sensei® and Niobe® remote navigation systems, the immediate conclusion might that these technologies should be adopted forthwith, because they reduce fluoroscopy time, with the inference that a reduced fluoroscopy time will result in reduced radiation exposure for both patient and operator. On this view, any reduction in radiation exposure is a good thing and should be promoted whenever possible.

The difficulty with the precautionary principle in this context is deciding whether or not the reported reductions in radiation doses for patients or the operators actually are clinically significant, especially in terms of a cumulative dose. Put another way, critics of these remote-controlled navigation systems might argue that, since they do not appear to offer clinically relevant
reductions in radiation, the precautionary principle does not apply. Instead, uptake of these devices should be determined by other ethical principles.

*The principle of justice*

Focusing on justice generally means asking question such as:

- is the use of the technology limited to major metropolitan areas?
- what provisions will need to be made for access in rural and remote areas?
- Are there likely to be gender differences in access to the technology?

With respect to the Hansen Sensei® and Niobe® remote navigation systems, these questions are really not relevant, since diffusion of the technology is likely to lead to the same pattern of service availability as alternative existing treatments.

A second aspect of justice and fairness directs attention toward cost-effectiveness. Simply put, are these technologies worth the investment, if other health care services and technologies will have to be foregone to fund them? To answer these questions, information about the cost-effectiveness of these systems is required but, as noted above, such information is scant.
Training and accreditation

Training

The Cardiac Society of Australia and New Zealand have recently issued training guidelines for cardiologists wishing to practice clinical cardiac electrophysiology. Training programmes in cardiac electrophysiology must be part of a cardiology training programme suitable for advanced training in cardiology with Royal Australasian College of Physicians accreditation. In the Australasian setting, practising electrophysiology clinicians have expertise in the area of cardiac pacing and defibrillator therapy. The CSANZ guidelines are based on guidelines produced by the American College of Cardiology and the American Heart Association for the Training in Specialised Electrophysiology, Cardiac Pacing, and Arrhythmia Management (Naccarelli et al 2008), but have been modified for the Australian setting. Trainees should have knowledge and experience in the diagnosis and treatment of brady and tachyarrhythmias, including an understanding of pharmacological therapy for cardiac arrhythmias, the use and interpretation of non-invasive tests in the diagnosis of arrhythmias (ECG, ambulatory cardiac monitoring, exercise testing for arrhythmia assessment, tilt table testing), the role of catheter ablation in the treatment of cardiac arrhythmias including the potential complications of these procedures and the role of cardiac pacemaker, ICD and resynchronisation therapy. The CSANZ guidelines refer to the two tables (Table 5, Table 6) contained in the American Heart Association guidelines which summarise the desired technical and cognitive skills expected from training. It is recommended that institutions that provide training in cardiac electrophysiology should have at least one fully trained and active cardiac electrophysiologist who performs a minimum of 100 and preferably 150 electrophysiology procedures (including at least 100 ablations) per year. In addition minimum requirements for cardiac implantable electrical devices should be met. Institutions should regularly audit to review morbidity and mortality data. Each trainee should actively participate in and analyse 150 diagnostic electrophysiology procedures, with at least 50 of these as the primary operator. As not all centres will perform all types of electrophysiology procedures, additional training may be required for complex procedures such as the curative ablation for atrial fibrillation and ablation of ventricular tachycardia in other centres. To assure maintenance of competency, it is recommended that the physician should perform at least 50 electrophysiology procedures per year, of which at least 30 should be radiofrequency ablation procedure (Thomas 2010).
Table 5  Cardiac arrhythmia and electrophysiology curriculum training summary (Naccarelli et al 2008)

<table>
<thead>
<tr>
<th>Level</th>
<th>Level curriculum/skills</th>
<th>Time requirement</th>
<th>Optional training in device implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cardiac arrhythmia and electrophysiology core</td>
<td>2 months (in addition to Task Force 2 training requirements)</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Advanced non invasive arrhythmia management</td>
<td>6 months</td>
<td>Yes: In addition to 6 months of non-invasive emphasis, another 6 months for a total of 12 months is required for pacemaker implantation training</td>
</tr>
<tr>
<td>3</td>
<td>Clinical invasive cardiac electrophysiology</td>
<td>1–2 years (12–24 months)</td>
<td>Yes: A total of 1 year beyond the 3-year cardiology training program is required. If surgical aspects of CIED implantation are desired, a total of 12 months will need to be devoted to this discipline.</td>
</tr>
</tbody>
</table>

Table 6  Core cardiac arrhythmia and electrophysiology curriculum training (Naccarelli et al 2008)

<table>
<thead>
<tr>
<th>Level</th>
<th>Minimal number of procedures</th>
<th>Cumulative duration of training (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10 temporary pacemakers</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>10 cardioversions</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>100 cardiac implantable electrical device interrogations/programming</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>150 EP cases</td>
<td>12-24</td>
</tr>
<tr>
<td></td>
<td>75 ablations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30–50 atrial fibrillation ablations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 trans-septal procedures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>75 CIEDs (25 ICD, 25 dual-chamber devices, 25 CRT devices)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30 CIED revisions/replacements</td>
<td></td>
</tr>
<tr>
<td></td>
<td>200 CIED interrogations/programming</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(100 ICDs, 100 pacemakers)</td>
<td></td>
</tr>
</tbody>
</table>

CIED = cardiac implantable electrical device, ICD = implantable cardioverter defibrillator, CRT = cardiac resynchronising therapy, EP = electrophysiology

Training for the Hansen Sensei® is included in the price of the system.
Training is conducted by Hansen in the United States (California or Texas) and consists of a one-day theoretical instruction followed by practical
experience which is usually conducted in a two-day time frame. Cardiologists already versed in ablation and mapping techniques first train on a Hansen simulator and then proceed to using the system on porcine cases. They are then required to observe a number of mapping and ablation procedures in humans before using the system, under supervision, on a number of consecutive patients. Although Hansen would support training in other centres, namely Adelaide which has at least four personnel trained, for the foreseeable future training will remain in the United States. Once a system is installed in a centre, Hansen Medical send an observer to monitor the first 10 conducted cases. It is estimated that the learning curve associated with proficient use of the Sensei® system is 20 cases (personal communication St Jude Medical Australia).

Similar measures are taken with clinical training for the Niobe® system by Stereotaxis Inc. The main training takes place in St Louis, USA and clinicians (usually 2-3) are also matched to a centre that performs ablative procedures in a similar manner to their institution to receive further training. A set number of hours are spent training clinicians on phantom hearts, then in observing live patient cases before finally performing cases alongside the training clinicians. Once a system is installed in an Australian centre, clinical observation by Stereotaxis personnel is ongoing. It is estimated that the learning curve associated with proficient use of the Niobe® system is 50 cases Magnetic safety training is also provided ongoing to the clinicians and ancillary staff (personal communication Device Technologies Australia).

Clinical Guidelines

The 2001 Guidelines for management of patients with chronic heart failure in Australia recommend that for patients with heart failure or cardiac arrhythmia that “Efforts should be made to restore and maintain sinus rhythm in patients with atrial fibrillation. This may require episodic electrical cardioversion while patients are anti-coagulated with warfarin. If sinus rhythm cannot be maintained for prolonged periods, therapy should be directed at controlling the ventricular response rate (with digoxin, β-blockers or amiodarone) and reducing thromboembolic risk by anticoagulation with warfarin.” (Krum 2001). The updated 2006 Guidelines for the prevention, detection and management of people with chronic heart failure in Australia recommend “long-term anticoagulation therapy (ie, warfarin) in patients with chronic atrial fibrillation” (Krum et al 2006). In 2001 the National Blood Pressure Advisory Committee of the National Heart Foundation issued a position statement on Non-valvular atrial fibrillation and stroke prevention, which outlines which discusses cardioversion and pharmaceutical options for patients with AF, with a view to stroke prevention (Hankey 2001).
The New Zealand cardiovascular guidelines state that “A new diagnosis of atrial fibrillation will be suspected after detecting an irregular pulse or irregular heart rhythm and an ECG should be performed to confirm AF. All people presenting with AF or atrial flutter for the first time should have the following investigations: history and clinical examination, ECG, transthoracic echocardiogram blood tests – thyroid function, renal function (creatinine), INR (pre-warfarin) (NZGG 2009).” The New Zealand Guidelines Group has also produced a guideline for The Management of People with Atrial Fibrillation and Flutter. This document discusses appropriate treatment options for patients with AF including cardioversion and pharmaceutical options. In addition it discusses the prevention of AF with ablation therapy. Atrioventricular nodal ablation or permanent pacemaker implantation is recommended if drug therapy is ineffective (pg 108, Level B\textsuperscript{8} evidence). In addition, patients with lone or predominant atrial flutter should be referred for electrophysiological review and consideration of radiofrequency ablation (pg 110 Level A evidence) (NZGG 2005).

\textsuperscript{8} Recommendation Level A: The recommendation is supported by GOOD evidence (where there is a number of studies that are valid, consistent, applicable and clinically relevant). Recommendation Level B: The recommendation is supported by FAIR evidence (based on studies that are valid, but there are some concerns about the volume, consistency, applicability and clinical relevance of the evidence that may cause some uncertainty but are not likely to be overturned by other evidence) pg 125 NZGG (2005).
Limitations of the assessment

Methodological issues and the relevance or currency of information provided over time are paramount in any assessment carried out in the early life of a technology.

Horizon Scanning forms an integral component of Health Technology Assessment. However, it is a specialised and quite distinct activity conducted for an entirely different purpose. The rapid evolution of technological advances can in some cases overtake the speed at which trials or other reviews are conducted. In many cases, by the time a study or review has been completed, the technology may have evolved to a higher level leaving the technology under investigation obsolete and replaced.

An Horizon Scanning Report maintains a predictive or speculative focus, often based on low level evidence, and is aimed at informing policy and decision makers. It is not a definitive assessment of the safety, effectiveness, ethical considerations and cost effectiveness of a technology.

In the context of a rapidly evolving technology, an Horizon Scanning Report is a ‘state of play’ assessment that presents a trade-off between the value of early, uncertain information, versus the value of certain, but late information that may be of limited relevance to policy and decision makers.

This report provides an assessment of the current state of development of remote-controlled catheter navigation systems, its present and potential use in the Australian public health system, and future implications for the use of this technology.

Search strategy used for the report

The medical literature (Table 8) was searched utilising the search terms outlined in Table 7 to identify relevant studies and reviews, until August 2010. In addition, major international health assessment databases were searched.

<table>
<thead>
<tr>
<th>Search terms utilised</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MeSH</strong></td>
</tr>
<tr>
<td>Catheter Ablation OR Robotics OR Magnetics</td>
</tr>
<tr>
<td><strong>Text words</strong></td>
</tr>
<tr>
<td>(remote OR robotic OR niobe OR sensei OR stereotaxis OR Hansen) AND (catheter AND navigation AND system*)</td>
</tr>
<tr>
<td><strong>Limits</strong></td>
</tr>
<tr>
<td>English, human</td>
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Table 8  Literature sources utilised in assessment

<table>
<thead>
<tr>
<th>Source</th>
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<tr>
<td><strong>Electronic databases</strong></td>
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<td>AustHealth</td>
<td>University library</td>
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<tr>
<td>Australian Medical Index</td>
<td>University library</td>
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<tr>
<td>Australian Public Affairs Information Service (APAIS) - Health</td>
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<td>Cinahl</td>
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<tr>
<td>Cochrane Library – including, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Database, the NHS Economic Evaluation Database</td>
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<td>Current Contents</td>
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<tr>
<td>Embase</td>
<td>Personal subscription</td>
</tr>
<tr>
<td>Pre-Medline and Medline</td>
<td>University library</td>
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<td>University library</td>
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<td>PsycInfo</td>
<td>University library</td>
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<td>Web of Science – Science Citation Index Expanded</td>
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<td><strong>Internet</strong></td>
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<tr>
<td>Current Controlled Trials metaRegister</td>
<td><a href="http://controlled-trials.com/">http://controlled-trials.com/</a></td>
</tr>
<tr>
<td>Health Technology Assessment international</td>
<td><a href="http://www.htai.org">http://www.htai.org</a></td>
</tr>
<tr>
<td>International Network for Agencies for Health Technology Assessment</td>
<td><a href="http://www.inahta.org/">http://www.inahta.org/</a></td>
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<td>Trip database</td>
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<tr>
<td>U.K. National Research Register</td>
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</tr>
</tbody>
</table>

**Availability and level of evidence**

A total of 470 potential studies were downloaded into Endnote. Once duplicates were removed, 161 references were assessed for relevance. Of these, 123 were considered to be germane to remote catheter navigation systems and their abstracts were assessed accordingly. A number of case reports were identified. In a systematic review these would be included to assess the safety of the technology, however, due to the time constraints placed on writing a horizon scanning report, these were not included. A prioritising summary on the use of the Niobe® system was published in 2005 and was
updated in 2006 and 2007. Therefore only studies published post-2006 and those not included in the original summaries were considered for inclusion. This strategy would not exclude any published studies on the Hansen Sensei system as this system only came into use post-2007. A total of 78 references had their abstracts appraised and of these, 48 had a full text version available, however, a number of these papers were reviews describing the use of remote navigation systems. A total of 15 studies were included for assessment, seven of which described the use of the Niobe® navigation system and eight the use of the Hansen system (see Appendix B for study profiles). Of those studies describing the use of the Hansen system, two reported only on safety outcomes associated with the use of the system rather than the effectiveness of the system (Rillig et al 2010a; Rillig et al 2010b) (level IV intervention evidence). Of the remaining six studies there were three randomised controlled trials (level II intervention evidence), two level III-2 intervention evidence studies and one case series (level IV intervention evidence). Adverse events associated with the use of the remote navigation system were reported in three of these studies. Of the seven studies describing the use of the Niobe® system, there was one randomised controlled trial (level II intervention evidence), one level III-2, three level III-3 intervention evidence studies and two case series (level IV intervention evidence). Of these, four studies reported adverse events associated with the use of the Niobe® system.

Sources of further information

A prospective randomised trial of the Hansen system for introducing and positioning the Biosense ThermoCool Catheter for the treatment of adult patients with atrial fibrillation is currently recruiting (ClinicalTrials.gov Identifier NCT01122173). The study is being conducted on behalf of Hansen Medical Inc by the Texas Cardiac Arrhythmia Institute at St. David's Medical Center, Austin, Texas. As previously mentioned, the Hansen Sensei® System has received FDA clearance as a robotic delivery system to facilitate manipulation, positioning and control of catheters used to collect electrophysiological data but has not been approved for use in ablation treatment. This trial will compare the safety and effectiveness of the ablation procedure when the ThermoCool catheter is delivered manually or robotically using the Hansen system. Primary outcomes measures include: major adverse events within seven days of the procedure; the presence or absence of symptoms of atrial fibrillation (from days 91-365) and an absence of oesophageal injury or pulmonary vein stenosis up to day 365. The trial is aiming to enrol 300 patients and expects to be finalised by December 2010.
Asklepios proresearch (Hamburg, Germany) are currently conducting a randomised controlled trial (RCT) in conjunction with Hansen Medical Inc and St Jude Medical (ClinicalTrials.gov Identifier NCT00982475). This RCT aims to compare manual and robotic catheter ablation in patients aged 30-75 years with drug-refractory atrial fibrillation. This trial is currently recruiting patients (number not stipulated) and expects to be completed in September 2011.

St Barts Hospital in London commenced an RCT in 2008 (ClinicalTrials.gov Identifier NCT01037296). Patients (n=100) with atrial fibrillation underwent ablation either manually or with the Hansen system robotic navigation. The trial is no longer recruiting, however data analysis is ongoing.

A 2006 multicentre RCT (USA), conducted in conjunction with Stereotaxis, compared the use of magnetic to manual navigation for the placement of an over-the-wire, left ventricle lead at a specific target site (ClinicalTrials.gov Identifier NCT00370474). This study was terminated in June 2007 as the study protocol had become obsolete. Another multicentre RCT (USA, Italy and Canada), conducted in conjunction with Stereotaxis, randomised patients to receive a conventionally-placed or magnetically-placed left ventricular lead. This 2006 trial aimed to recruit 100 patients who were symptomatic for congestive heart failure. The trial was terminated in 2008 due to insufficient enrolment (ClinicalTrials.gov Identifier NCT00370526).

A small RCT (n=15) is currently being conducted by the New York Presbyterian Hospital-Columbia Medical Center, in conjunction with Stereotaxis (ClinicalTrials.gov Identifier NCT00994331). Vectors acquired using the computed tomography (CT) co-registration feature of Navigant™ were used to provide navigation during percutaneous coronary intervention (PCI). It is hoped that this approach would reduce the amount of contrast used during complex PCI procedures. Three patient groups (n=5) undergoing a non surgical procedure to open blocked coronary arteries are being compared: CT co-registration with magnetically navigated PCI, angiographic co-registration with magnetically navigated PCI and standard angiography with conventional PCI. This study is no longer recruiting patients but is currently ongoing.
Conclusions

A normal heart in sinus rhythm contracts 60 to 100 times per minute. Electrical signals, which emanate from the sinus node, initiates contraction of the atria. Abnormal electrical signals, originating from the pulmonary veins, cause the muscle fibres in the atria to contract out of time, resulting in atrial fibrillation (AF). Symptoms of AF include an irregular pulse, fatigue, exercise intolerance, dizziness, fainting and general weakness. Atrial fibrillation may occur as a one-off episode, or may be paroxysmal or persistent. The most common causes of atrial fibrillation include long-term high blood pressure, coronary heart disease, valvular heart disease and, less commonly, hyperthyroidism (NHF 2008). A number of treatment options are available for AF depending on the severity of the symptoms including medication, cardioversion or ablation procedures. Catheter ablation is rarely used as a first-line treatment option for atrial fibrillation. The primary indication for catheter ablation is the persistence of atrial fibrillation which is refractory to anti-arrhythmic medication (Calkins et al 2007; Darge et al 2009).

Atrial fibrillation is the most common sustained cardiac rhythm disturbance, affecting approximately two per cent of the population. The prevalence of AF increases with age with approximately five per cent of individuals aged over 65 years affected. Haemodynamic impairment and thromboembolic events related to AF result in significant morbidity, mortality and cost. In people aged over 65 years with untreated AF the risk of experiencing a stroke is approximately one in 20, which is five to six times higher than in those without AF. The risk of stroke increases in individuals with AF and other co-morbidities, including diabetes and high blood pressure (NHF 2008). In Australia, during the period 2007-08 there were 47,164 public hospital separations for atrial fibrillation and flutter, representing 145,200 patient days with an average length of stay of 3.1 days. The majority of these cases (76%) occurred in patients aged 60 years and over (AIHW 2010b).

A number of options are available for the treatment of atrial fibrillation depending on the severity of the symptoms, including medication, cardioversion or ablation procedures. Most patients diagnosed with AF will be prescribed an anticoagulant, either aspirin or warfarin, to prevent clot formation. Patients may also be prescribed medication which aims to slow the heart rate or anti-arrhythmic drugs which aim to maintain a normal heart rhythm, achieving pharmacological cardioversion. Electrical cardioversion involves the application of an electrical “shock” to the heart via external defibrillator pads placed on the chest. Patients with AF for whom cardioversion has failed or medication is not a suitable option may undergo an
Patients with AF for whom other treatment options have failed or are not a suitable option may undergo an ablation procedure in an electrophysiological laboratory to isolate the abnormal AF electrical signal, restoring normal heart rhythm. Ablation involves the electrical isolation of the heart tissue which is contributing to the arrhythmia by the creation of insulation lesion lines. There are two types of ablation procedures: catheter and surgical ablation (NHF 2008). Adverse events associated with catheter ablation include thromboembolism, perforation and thermal injury to adjacent tissue. Cardiac tamponade may occur due to the need of systemic anticoagulation. Pulmonary vein stenosis is also common and may be caused by thermal injury to the pulmonary vein musculature. A rare complication is atrio-oesophageal fistula formation, which carries a 50 per cent risk of mortality (Calkins et al 2007; Darge et al 2009).

During catheter ablation, a catheter, with an electrode at the tip, is inserted into a blood vessel in the leg and guided up to the heart. The heart is first “mapped” by the cardiologist using 3D-cardiovascular mapping systems to elucidate the region of abnormal cardiac arrhythmia and the potential source of atrial fibrillation. Once the region of interest has been identified, the tip of the catheter emits radiofrequency waves to burn a small area of tissue and inactivate the electrical signal. During manual catheter ablation the physician manually manipulates the catheters through the heart using direct visual feedback from fluoroscopic images taken in real time. Manual ablation exposes the physician and patient to high levels of ionising radiation (Beyar 2010). Robotic systems such as the Niobe® and the Sensei® do these three steps; guidance, mapping and ablation, remotely, exposing the physician to markedly reduced levels of radiation (NHF 2008).

The Sensei® X and the Niobe® consist of an operating console that can be located outside the operating room, reducing radiation exposure to the majority of the attending medical staff. The console features a work station with either a joystick or a computer mouse used to guide the ablation catheter, and multiple screens alongside each other to visualise the electrogram generated throughout the ablation procedure, the 3D constructed image, which can be rotated in any plane, and fluoroscopic images of the heart (Dewire & Calkins 2010).

The Sensei® operates using an electromechanical “master-slave” system. The robotic catheter control system steers the ablation catheter within the heart via a pull-wire mechanism, with its movements controlled by the robot arm or the “slave” system, which is fixed at the patient’s table. The “slave” receives input
from the “master” that transmits the operator’s three-dimensional movements using the joy stick, moving the catheters in the heart according to the images generated by the mapping system (Ernst 2008). The Sensei® uses the steerable Artisan™ ablation catheter, which at 14 French is considerably larger than those used in conventional manual ablation (8 Fr), and as such has caused some concern with regard to post-operative bleeding events. When ablation begins only the steerable catheter is moved using the Sensei®, with the remaining catheters moved into the four pulmonary veins manually under fluoroscopic guidance. To prevent perforation, the Sensei® has a built-in pressure sensor which continuously measures the force applied by the catheter and alerts the operator both visually and physically to pressures that exceed a set threshold.

The Niobe® uses a magnetic field to guide catheters with magnetic tips. The Niobe® consists of two, large permanent magnets which are placed on either side of the patient and emit a uniform low-intensity magnetic field (0.10 Tesla) (Ganji et al 2009; Schmidt et al 2008). As such, an electrophysiology laboratory equipped with the Niobe® system must be custom made with magnetic shielding and all of its equipment must be magnetic field compatible. Catheters used in the Niobe® system do not need to be sheathed and are therefore smaller and more flexible in comparison to those used with the Sensei® (Burkhardt & Natale 2009). The magnetic ablation catheter aligns parallel to the external magnetic field and is navigated through the heart by changing the orientation of the outer magnets to each other and thus changing the orientation of the magnetic field, which is controlled by a computer interface system. Changes in the magnetic field deflect and move the ablation catheter allowing for small movements (1° and 1mm).

There are two remote navigation systems installed in Australia: the Sensei® X is currently installed at Flinders Private Hospital, South Australia and there is one Niobe® system installed at the Westmead Hospital, New South Wales. The Niobe® at Westmead Hospital is currently being used to treat patients with ventricular tachycardia, atrioventricular nodal re-entrant tachycardia as well atrial fibrillation, in addition to performing percutaneous coronary interventions.

There are at least two other robotic catheter navigation systems in development: the CorPath® 200 System (Corindus Inc, USA) and the Amigo™ (Catheter Robotics Inc, USA).

Hansen Sensei® remote navigation system

Eight studies describing the use of the Hansen Sensei® for the ablation of AF were included for assessment. Of these studies, two case series reported only on the potential for adverse events, specifically the incidence of iatrogenic
septal defect and oesophageal lesions associated with the use of the remote navigation system, rather than the effectiveness of the system itself (Rillig et al 2010a; Rillig et al 2010b). Iatrogenic septal defects, caused by an increase in temperature during the ablation procedure, may lead to an increased risk of thromboembolisms. A large proportion of the patients experienced an iatrogenic septal defect (38/40, 95%), however no thromboembolic events were reported and the majority of defects had healed by the end of the 6-month follow-up (79%). Of the patients who consented to an endoscopy, a small proportion (14%) experienced an oesophageal lesion, which may lead to the development of serious adverse events including atrio-oesophageal fistulas. All reported lesions healed within two weeks with no sequelae.

Of the remaining six studies, three studies reported adverse events associated with the system, whilst the remaining three studies explicitly stated that no adverse events occurred during ablation performed with the remote navigation system Table 1. Serious adverse events (pericardial tamponade and perforation) were reported at a rate of fewer than two per cent in both arms of the large RCT that compared manual and RNS ablation (Di Base et al 2009). Although these adverse events were considered serious, all patients were successfully treated without further sequelae. Pericardial effusion and pericardial tamponade were reported in other studies, and although the rates of adverse events appeared high (5 and 10%), the studies were only small and the adverse events occurred in one and two patients, respectively. Neither study stated whether or not the adverse events occurred in the “learning curve” phase of the use of the remote navigation system.

Levels of radiation were reported by four of the eight included studies. The two comparative studies that described patient exposure to radiation reported quite different results. Kautzner et al (2009) reported a significant decrease in radiation dose received by patients in the RNS ablation group compared to those in the manual ablation group (1.1 ± 0.596 vs 3.05 ± 2.03 mGy.m², p < 0.001), however Kanagaratnam et al (2008) reported markedly higher levels of radiation exposure than Kautzner for both groups but with no difference between the two groups (6.6 ± 5.9 vs 8.7 ± 7.7 mGy.m²). A significant decrease in the radiation dose received by the operator conducting RNS, compared to that received during manual procedures (0.71 ± 0.31 vs 1.9 ± 0.69 mGy.m², p < 0.001) was reported by the RCT conducted by Steven et al (2010). It is unclear from these studies whether or not the reported radiation doses for patients or the operators are significant in terms of a cumulative dose. It should also be noted that the radiation exposure values reported in these studies had large standard deviations indicating considerable variation in the amount of exposure.
Of the eight identified studies that used the Hansen Sensei®X for the ablation of atrial fibrillation or atrial flutter, only four studies reported on post-ablation procedure success, defined by complete pulmonary vein isolation. In two RCTs, 100 per cent of patients were free from symptoms of AF without anti-arrhythmic medication in both the manual and the RNS groups immediately post-procedure (Di Biase et al 2009 and Steven et al 2010), however this rate decreased in both groups at 6-12 month follow-up to 70-76 per cent. A significant difference in immediate bidirectional block was reported in the RCT by Steven et al (2008) between patients who underwent RNS (88%) and manual ablation (48%) for atrial flutter (p = 0.03). The comparative study by Kautzner et al (2009) also reported good rates of freedom from AF symptoms maintained at 5-9 month follow-up in both the manual (81%) and the RNS (91%) groups.

Six of the included studies reported procedure and fluoroscopy time. Some studies reported no significant difference in procedure time between the manual and RNS groups for AF ablation (Di Biase et al 2009 and Steven et al 2010), whilst others reported that RNS took significantly longer for ablation of atrial flutter (p = 0.04) or that manual ablation took a significantly longer time (p = 0.007) (Kautzner et al 2009). Two of the included studies reported on the learning curve involved with the use of the remote navigation systems, with the first set of RNS patients taking a significantly longer time than patients treated later, indicating that it took at least 10 patients for operator familiarity with the remote navigation technique (Steven et al 2008 and Di Biase et al 2009). Four comparative studies reported a significant decrease in fluoroscopy time using RNS compared to manual ablation.

**Sterotaxis Niobe® remote magnetic navigation system**

There were seven papers included for assessment that reported on the use of the Niobe® remote navigation system for the ablation of AF. Of these studies, four reported adverse events associated with the use of system, whilst the remaining two studies explicitly stated that no adverse events occurred during the ablation procedure.

Only one study reported on the level of radiation exposure to the patient (Vollmann et al 2009). Mean radiation exposure was significantly less in the RNS ablation group compared to the manual group (3.3 vs 4.3 mGy.m², p = 0.032). It should be noted that wide ranges for these variables were reported in both the RNS and manual groups.

Low rates of adverse events were reported by the included studies, ranging from 2.2 to five per cent. In the well designed study by Vollmann et al (2009), only one adverse event, significant local haemorrhage, was reported in the manual ablation arm, with none occurring in the remote navigation arm.
A lower level of evidence was available for the assessment of the effectiveness of the Niobe®, with only two well-designed prospective comparative studies included for evaluation. The remaining studies compared historical controls to current cases or were non-comparative case series.

Six of the seven studies included for assessment reported on the success of the ablation procedure. The RCT conducted by Vollmann et al (2009) reported no difference in rates of immediate freedom from symptoms of atrial flutter post-ablation between patients treated with RNS or manual ablation (84.4% vs 91.1%, \( p = 0.52 \)). At 6-month follow-up the majority of these patients were still symptom-free and there was still no difference the two groups (73.3% vs 88.9%, \( p = 0.063 \)). Similar results were reported by the comparative study by Katsiyiannis et al (2008) with 100 per cent of patients symptom-free immediately post-ablation, which was maintained at 12-month follow-up in 80 and 75 per cent of patients treated with RNS and manual ablation, respectively. Procedural success rates for AF or AFL ablation varied from 93 to 100 per cent in the lower level evidence studies. A case series of 56 patients had the longest follow-up (mean 426 ± 213 days) and reported 70 per cent of patients with AF were symptom-free at study end (Chun et al 2010).

The two comparative studies reported different results for length of procedure time. The RCT by Vollmann et al (2009) reported a significantly longer procedure time for remote navigation compared to manual navigation (113.5 ± 34.8 vs 77.2 ± 24.1 minutes, \( p <0.0001 \)). However the comparative study by Katsiyiannis et al (2008) reported significantly less procedure time for patients in the RNS group compared to the manual ablation group (109 vs 279 minutes, \( p < 0.001 \)). Both studies reported significantly less fluoroscopy time. A learning curve was reported by two poorer quality studies (Kim et al 2008 and Arya et al 2008), that is a decrease in procedure time correlated with increased operator experience, however the RCT by Vollmann et al (2009) found no correlation between procedure time and experience with the system.

No cost-effectiveness studies on either the Niobe® or Sensei® remote navigation systems were identified for inclusion in this assessment, however a cost-consequences analysis may be the more appropriate economic analysis to conduct. The main health outcome when using remote navigation systems is reduced radiation exposure to the patient and especially, the clinician. The included studies refer to surrogate outcomes of length of exposure (as a measure of dose) but do not provide evidence of how this reduction translates into a health benefit. We have sought this evidence elsewhere but have not been successful. Thus it is not possible to assess the health consequences of the capital investment in excess of $1 million combined with the ongoing maintenance costs.
Total costs of the two systems, excluding the price of the 3D mapping systems and the integrated information systems that both require, are approximately A$1.2 million for the Hansen and US$1.3 million for the Niobe®. Additional costs and disposables for the Hansen include radiofrequency receiving patches $2,500, single-use steerable Artisan™ catheter sheaf $3,000 and single-use only ablation catheters $1,600. Currently only the Biosense Webster RMT single use catheters can be used with the Niobe® system which cost A$3-3,500 each.

Training guidelines for cardiologists wishing to practice clinical cardiac electrophysiology have recently been issued by The Cardiac Society of Australia and New Zealand in accordance with the guidelines produced by the American Heart Association. Each trainee should actively participate in and analyse 150 diagnostic electrophysiology procedures, with at least 50 of these as the primary operator. To assure maintenance of competency, it is recommended that the physician should perform at least 50 electrophysiology procedures per year, of which at least 30 should be radiofrequency ablation procedure (Thomas 2010). Training is provided by the companies for both the Hansen Sensei® and the Niobe® and support is ongoing once the systems are installed.

The Hansen Sensei® and Niobe® remote navigation systems are, in some ways, ethically uncontroversial. They would replace existing treatment regimes with new regimes that are as effective as the old, they can be provided in the same institutional settings, and they rely on similar patterns of training for operators as have been developed in the past for previous treatments. The key ethical question that remains is whether the reductions in fluoroscopy time that they offer are of clinical relevance for patients and operators.

In summary, both the Hansen Sensei® and Niobe® remote navigation systems appear to be as effective as manual ablation for atrial fibrillation and atrial flutter. Few adverse events were reported in both groups and reduced radiation exposure for patients and the operator were reported by the majority of studies which reported this as an outcome. All studies reported a significant decrease in fluoroscopy time, which would correlate with a corresponding decrease in radiation exposure and dose to the patient and operator alike. Although conflicting results were reported regarding procedure time, with some studies reporting an increase, a decrease or no difference in procedure time with the RNS systems, most studies reported that these differences could be explained by the learning curve associated with the use of the RNS system. Immediate success rates of the procedure, indicated by freedom from symptoms, were similar for both systems, ranging from 88-100 per cent, which was sustained at 5-12 month follow-up in 70-91 per cent of patients.
## Appendix A: Levels of evidence (Merlin et al 2009)

<table>
<thead>
<tr>
<th>Level</th>
<th>Intervention</th>
<th>Diagnostic accuracy</th>
<th>Prognosis</th>
<th>Aetiology</th>
<th>Screening Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A systematic review of level II studies</td>
<td>A systematic review of level II studies</td>
<td>A systematic review of level II studies</td>
<td>A systematic review of level II studies</td>
<td>A systematic review of level II studies</td>
</tr>
<tr>
<td>II</td>
<td>A randomised controlled trial</td>
<td>A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive persons with a defined clinical presentation</td>
<td>A prospective cohort study</td>
<td>A prospective cohort study</td>
<td>A randomised controlled trial</td>
</tr>
<tr>
<td>III-1</td>
<td>A pseudorandomised controlled trial (i.e. alternate allocation or some other method)</td>
<td>A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive persons with a defined clinical presentation</td>
<td>All or none</td>
<td>All or none</td>
<td>A pseudorandomised controlled trial (i.e. alternate allocation or some other method)</td>
</tr>
<tr>
<td>III-2</td>
<td>A comparative study with concurrent controls: - Non-randomised, experimental trial - Cohort study - Case-control study - Interrupted time series with a control group</td>
<td>A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence</td>
<td>Analysis of prognostic factors amongst persons in a single arm of a randomised controlled trial</td>
<td>A retrospective cohort study</td>
<td>A comparative study with concurrent controls: - Non-randomised, experimental trial - Cohort study - Case-control study</td>
</tr>
<tr>
<td>III-3</td>
<td>A comparative study without concurrent controls: - Historical control study - Two or more single arm studies - Interrupted time series without a parallel control group</td>
<td>Diagnostic case-control study</td>
<td>A retrospective cohort study</td>
<td>A case-control study</td>
<td>A comparative study without concurrent controls: - Historical control study - Two or more single arm studies</td>
</tr>
<tr>
<td>IV</td>
<td>Case series with either post-test or pre-test/post-test outcomes</td>
<td>Study of diagnostic yield (no reference standard)</td>
<td>Case series, or cohort study of persons at different stages of disease</td>
<td>A cross-sectional study or case series</td>
<td>Case series</td>
</tr>
</tbody>
</table>

### Table notes

1. Level I studies are systematic reviews of level II studies.
2. Level II studies are based on diagnostic accuracy.
3. Level III-1 studies are based on prognostic factors.
4. Level III-2 studies are based on a comparison with a reference standard.
5. Level III-3 studies are based on case series.
6. Level IV studies are based on cross-sectional studies.

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Remote-controlled catheter navigation systems: November 2010
Definitions of these study designs are provided on pages 7-8. How to use the evidence: assessment and application of scientific evidence (NHMRC 2000).

The dimensions of evidence apply only to studies of diagnostic accuracy. To assess the effectiveness of a diagnostic test there also needs to be a consideration of the impact of the test on patient management and health outcomes (Sackett & Haynes 2002; MSAC 2005).

If it is possible and/or ethical to determine a causal relationship using experimental evidence, then the ‘Intervention’ hierarchy of evidence should be utilised. If it is only possible and/or ethical to determine a causal relationship using observational evidence (ie. cannot allocate groups to a potential harmful exposure, such as nuclear radiation), then the ‘Aetiology’ hierarchy of evidence should be utilised.

A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence. Systematic reviews of level II evidence provide more data than the individual studies and any meta-analyses will increase the precision of the overall results, reducing the likelihood that the results are affected by chance. Systematic reviews of lower level evidence present results of likely poorer internal validity and thus are rated on the likelihood that the results have been affected by bias, rather than whether the systematic review itself is of good quality. Systematic review quality should be assessed separately. A systematic review should consist of at least two studies. In systematic reviews that include different study designs, the overall level of evidence should relate to each individual outcome/result, as different studies (and study designs) might contribute to each different outcome.

The validity of the reference standard should be determined in the context of the disease under review. Criteria for determining the validity of the reference standard should be pre-specified. This can include the choice of the reference standard(s) and its timing in relation to the index test. The validity of the reference standard can be determined through quality appraisal of the study (Whiting et al 2003).

Well-designed population based case-control studies (eg. population based screening studies where test accuracy is assessed on all cases, with a random sample of controls) do capture a population with a representative spectrum of disease and thus fulfill the requirements for a valid assembly of patients. However, in some cases the population assembled is not representative of the use of the test in practice. In diagnostic case-control studies a selected sample of patients already known to have the disease are compared with a separate group of normal/healthy people known to be free of the disease. In this situation patients with borderline or mild expressions of the disease, and conditions mimicking the disease are excluded, which can lead to exaggeration of both sensitivity and specificity. This is called spectrum bias or spectrum effect because the spectrum of study participants will not be representative of patients seen in practice (Mulherin & Miller 2002).

At study inception the cohort is either non-diseased or all at the same stage of the disease. A randomised controlled trial with persons either non-diseased or at the same stage of the disease in both arms of the trial would also meet the criterion for level of evidence.

All or none of the people with the risk factor(s) experience the outcome; and the data arises from an unselected or representative case series which provides an unbiased representation of the prognostic effect. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of smallpox after large-scale vaccination.

This also includes controlled before-and-after (pre-test/post-test) studies, as well as adjusted indirect comparisons (ie. utilise A vs B and B vs C, to determine A vs C with statistical adjustment for B).

Comparing single arm studies ie. case series from two studies. This would also include unadjusted indirect comparisons (ie. utilise A vs B and B vs C, to determine A vs C but where there is no statistical adjustment for B).

Studies of diagnostic yield provide the yield of diagnosed patients, as determined by an index test, without confirmation of the accuracy of this diagnosis by a reference standard. These may be the only alternative when there is no reliable reference standard.

**Note A:** Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials: physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.

**Note B:** When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question eg. level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence.

**Source:** Hierarchies adapted and modified from: Phillips et al 2001; NHMRC 1999; Lijmer et al 1999; Bandolier editorial 1999)
## Appendix B: Profiles of studies

<table>
<thead>
<tr>
<th>Intervention level of evidence</th>
<th>Study</th>
<th>Location</th>
<th>Study design</th>
<th>Study population</th>
<th>Outcome assessed</th>
<th>Length of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hansen Sensei® remote navigation system</strong></td>
<td>Hansen Sensei® remote navigation system</td>
<td>Austin, USA and Foggia, Italy</td>
<td>RCT Patients sequentially assigned to RNS (n=193) or manual ablation (n=197).</td>
<td>390 consecutive adult patients, mean age 62 ± 11 years, with symptomatic, drug refractory AF (paroxysmal AF n=262, persistent AF n=110, long-standing persistent AF n=17). Mean left atrial diameter = 43.1 ± 8.0 mm. 3D mapping using CARTO or EnSite™. Manual and RNS ablation performed using Celsius Thermocoool saline irrigated catheter, RF power maximum 45 W and 41°C. RNS ablation catheter housed inside the Artisan steerable catheter. Both manual (n=197) and RNS (n=193) procedures performed by two operators in equal numbers. All patients discharged on warfarin for 6 months.</td>
<td>Pulmonary vein isolation, freedom from AF, radiation exposure, procedure time and learning curve. 7-day Holter monitor obtained at 3, 6, 9 and 12 months.</td>
<td>12 months</td>
</tr>
</tbody>
</table>

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### III-3

| Kautner, J., Peichl, P., Čihák, R., Wichterle, D., Mičochová, H. (2009) | Prague, Czech Republic | Comparative study without concurrent controls | 38 adult patients, mean age 55 ± 9 years, with symptomatic, drug refractory paroxysmal AF. 22 patients underwent RNS AF ablation and 16 patients underwent manual ablation. 3D mapping with Ensite™ NavX™ Manual and RNS ablation performed using Celcius Thermocool saline irrigated catheter, radiofrequency power maximum 35 W for manual ablation and 25 W for RNS. RNS ablation catheter housed inside the Artisan steerable catheter. | Freedom from AF, radiation exposure and procedure time. | Mean follow-up for manual ablation group 9 ± 3 months and 5 ± 1 month in the RNS group. |

### IV

<p>| Rillig, A., Meyerfeldt, U., Birkemeyer, R. West, S., Sauer, B.M., Staritz, M. Jung, W. (2010) | Villingen-Schwenningen, Germany | Prospective case series | 73 consecutive adult patients with drug refractory AF. The placement of an oesophageal probe was possible in 58/73 (79.5%) of these patients, with paroxysmal (n=38) or persistent (n=20) AF, mean age 58.6 | Oesophageal temperature during ablation and presence of oesophageal lesion post-ablation. | 2 weeks |</p>
<table>
<thead>
<tr>
<th>IV</th>
<th>Rillig, A. Meyerfeldt, U. Kunze, M. Birkemeyer, R. Miljak, T. Jäckle, S. Hajredini, B. Treusch, F. Jung, W. (2010)</th>
<th>Villingen-Schwenningen, Germany</th>
<th>Prospective case series</th>
<th>40 adult patients, mean age 60.3 ± 9.4 years, with drug refractory paroxysmal (n=22) or persistent (n=18) AF. 3.5 mm Thermocool® Navistar RNS ablation catheter housed inside the Artisan steerable catheter. RF power 25-30 W with a maximum temperature of 43°C.</th>
<th>Presence of iatrogenic atrial septal defect</th>
<th>3 and 6 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>Saliba, W. Reddy, V.Y. Wazni, O. Cummings, J.E. Burkhardt, J.D. Haissagure, M. Kautzner, J. Peicht, P. Neuzil, P. Schibgilla, V. Noelker, G. Brachmann, J. Di Biase, L. Barrett, C. Jais, P. Natale, A. (2008)</td>
<td>Multicentre: Cleveland, Boston, Palo Alto and Austin USA, Bordeaux, France, Prague, Czech Republic, Coburg, Germany and Foggia, Italy.</td>
<td>Prospective case series</td>
<td>40 adult patients, mean age 57 ± 20 years with symptomatic AF for ≥3 months, refractory to at least one anti-arrhythmic medication. Mean duration of AF 48 ± 12 months. Mean left atrial size 4.1 ± 0.8 cm. 23 patients with concomitant AFL. Paroxysmal AF n=29, persistent AF n=11. 3D mapping using CARTO and ablation of the right atrium using the Freedom from AF and AFL, radiation exposure and procedure time.</td>
<td>12 months</td>
<td></td>
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</tbody>
</table>
II

| Steven, D. Rostock, T. Servatius, H. Hoffmann, B. Drewitz, I. Müllerlelle, K. Meinertz, T. Willems, S. (2008) | Hamburg, Germany | RCT Patients randomised to manual ablation (n=25) or robotic navigation (n=25). | 50 consecutive patients, mean age 65.7 ± 9.3 years, with recurrent or persistent AFL with mean duration of 23.5 months (range 2-80). Mean left atrial diameter = 46.4 ± 7.8 mm. Structural heart disease n=19 (47.5%) and n=18 (45%) history AF. Manual ablation performed using Celsius Thermocool saline irrigated catheter, radiofrequency power maximum 38 W and 48°C. Remote ablation performed using Thermocool catheter, radiofrequency power maximum 33 W. | Bidirectional isthmus block, freedom from AFL, radiation exposure and procedure time. | 7.0 ± 1.6 months |

II

| Steven, D. Servatius, H. Rostock, T. Hoffmann, B. Drewitz, I. Müllerlelle, K. Sultan, A. Ali Aydin, M. Meinertz, T. Willems, S. (2010) | Hamburg, Germany | RCT Patients randomised (blind allocation) to manual ablation (n=30) or robotic navigation (n=30). | 60 consecutive patients, mean age 62 ± 7.6 years, with symptomatic, drug refractory paroxysmal AF. Mean duration of AF 6.5 ± 4 years and episode duration of 14.5 ± 12.5 | Pulmonary vein isolation, freedom from AF, radiation exposure and procedure time. | 1, 3 and 6 months |
Mean left atrial diameter 39 ± 4 mm. Structural heart disease n=7 (12%).

3D mapping with Ensite™ NavX™ Manual and RNS ablation performed using Celsius Thermocool saline irrigated catheter, radiofrequency power maximum 30 W RNS ablation catheter housed inside the Artisan steerable catheter.

### Stereotaxis Niobe® remote magnetic navigation system

<table>
<thead>
<tr>
<th>III-3</th>
<th>Chun, K.R.J. Wissner, E. Koektuerk, B. Konstantinidou, M. Schmidt, B. Zem, T. Metzner, A. Tilz, R. Boczer, S.</th>
<th>Leipzig, Germany</th>
<th>Comparative study with historical controls</th>
<th>26 consecutive adult patients, mean age 64.3 ± 9.0 years, with AFL. Compared to 40 historical controls (no data given). 3D mapping with CARTO and RNS ablation performed using the Navistar catheter. RF power 70 W and maximum temperature 70°C. <strong>Learning curve:</strong> First 10 patients reported as Group 1 and the remaining 15 patients Group 2.</th>
<th>Termination of AFL, procedure time, RF time, fluoroscopy time and learning curve.</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>Chun, K.R.J. Wissner, E. Koektuerk, B. Konstantinidou, M. Schmidt, B. Zem, T. Metzner, A. Tilz, R. Boczer, S.</td>
<td>Hamburg, Germany</td>
<td>Case series</td>
<td>56 adult patients, mean age 63 years (range 24-78 years) with drug refractory paroxysmal (n=37) or persistent (n=19) AF. 3D PV isolation, recurrence of anti-arrhythmic drug use and procedure time.</td>
<td>1, 3, 6, 9, 12, 18 and 24 months</td>
<td>1, 3, 6, 9, 12, 18 and 24 months</td>
</tr>
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<td>III-2</td>
<td>Katsiyiannis, W.T. Melby, D.P. Matelski, J.L. Ervin, V.L. Laverence, K.L. Gomick, C.C. (2008)</td>
<td>Minnesota, USA</td>
<td>Prospective comparative study with concurrent controls</td>
<td>40 consecutive patients with AF. 20 patients (persistent AF n=6, paroxysmal AF n=14) underwent manual ablation with Blazer catheter, RF power 45 W and maximum temperature of 55°C. 20 patients (persistent AF n=7, paroxysmal AF n=13) underwent RNS performed with Celsius catheter, RF power 30 W and a maximum temperature of 55°C. Both patient groups underwent 3D mapping with NavX.</td>
<td>Wide area circumferential ablation, PV entrance block and freedom from AF.</td>
<td>2, 6 and 12 months</td>
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<td>IV</td>
<td>Latcu, D.G. Ricard, P. Zarqane, N. Yaici, K. Rinaldi, J.-P. Malusski, A. Saoudi, N. (2009)</td>
<td>Monaco</td>
<td>Case series</td>
<td>84 patients, mean age 54 ± 17 years (range 12-90 years), with paroxysmal AF (n=3), AFLT (n=15), AFLA (n=7), AT (n=3), AVNRT (n=37), VT (n=7) and accessory pathway (n=12). RNS ablation catheters used Navistar RMT, Navistar RMT DS and Navistar thermocool®.</td>
<td>Elimination of arrhythmia, procedure time</td>
<td>Mean 2.5 months</td>
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<tr>
<td>III-3</td>
<td>Pappone, C. Vicedomini, G. Manguso, F. Gugliotta, F. Mazzone, P. Gulletta, S. Sora, N. Sala, S. Marzi, A. Augello, G. Livolsi, L. Santagostino, A. Santinelli, V. (2006)</td>
<td>Milan, Italy</td>
<td>Comparativ e study with historical controls</td>
<td>40 adult patients, median age 57 years (range 28-75 years) with drug refractory paroxysmal (n=25) or persistent (n=15) AF, with median duration of symptoms of 46.5 months, range 12-286 months. 28 matched historical controls, median age 57 years (range 31-75 years). 3D mapping with CARTO and RNS ablation performed using the 4mm Navistar RMT catheter. RF power 50 W and maximum temperature 65°C. <strong>Learning curve:</strong> First 12 patients reported as Group 1 and the remaining 28 patients Group 2.</td>
<td>Procedure success, procedure time and learning curve.</td>
<td>N/A</td>
</tr>
</tbody>
</table>
II

| Vollman, D. Lüthje, L. Seegers, J. Hasenfuss, G. Zabel, M. (2009) | Göttingen, Germany | RCT with randomly assigned blocks of 10 patients. | 90 adult patients with ≥1 episode CTI dependent AFL. Patients randomised to manual ablation with Celsius catheter (n=45), mean age 68 ± 9 years or RNS with the Celsius Navistar catheter (n=45), mean age 69 ± 8 years. Radiofrequency power maximum 70 W with a target temperature of 60°C. | Fluoroscopy time, procedure duration, acute success (complete bidirectional CTI block) and learning curve. | 3 and 6 months |

AF = atrial fibrillation, AFL, atrial flutter, W = watts, RCT = randomised controlled trial, RNS = remote navigation system, PV = pulmonary vein, N/A = not applicable, CTI = cavotricuspid isthmus, AFLT = typical atrial flutter, AFLA = atypical atrial flutter, AT = atrial tachycardia, AVNRT = atrioventricular nodal re-entrant tachycardia, AVRT = atrioventricular re-entrant tachycardia, RVOT = right ventricular outflow tract, VT = ventricular tachycardia
Appendix C: Glossary

Atrial fibrillation: very rapid uncoordinated contractions of the atria of the heart resulting in a lack of synchronism between heartbeat and pulse beat—called also auricular fibrillation. Abbreviation VF, V-fib.

Arrhythmia: an alteration in rhythm of the heartbeat either in time or force.

Coronary heart disease: reduced blood flow to the heart caused by clogging of the arteries.

Coronary artery bypass graft (CABG): surgical procedure using blood vessel grafts to bypass blockages in the coronary arteries and restore adequate blood flow to the heart muscle.

Echocardiography: the use of ultrasound to examine and measure the structure and functioning of the heart and to diagnose abnormalities and disease.

Electrocardiogram (ECG): a recording of the changes of electrical potential occurring during the heartbeat used in diagnosing abnormalities of heart action.

High blood pressure/hypertension: the World Health Organization defines high blood pressure as: a systolic blood pressure ≥140 mmHg or a diastolic blood pressure ≥90 mmHg.

Paroxysmal atrial fibrillation (PAF): atrial fibrillation that spontaneously reverts to normal sinus rhythm without a cardioversion procedure or therapy, but tends to recur intermittently.

 Permanent atrial fibrillation (AF): AF that is known to be unresponsive to cardioversion therapy, ie, cannot be converted to normal sinus rhythm by either electrical or pharmacological means. Permanent AF also includes cases of long-standing AF (eg, greater than one year) in which cardioversion has not been indicated or attempted.

Persistent atrial fibrillation: atrial fibrillation that does not spontaneously revert to normal sinus rhythm, but can be converted by either electrical or pharmacological cardioversion therapy.

Thrombosis: clotting of blood, with the term usually applied to clotting within a blood vessel due to disease, as in a heart attack or stroke.

Valvular heart disease: problems with the valves of the heart that keep blood flowing in the right direction.

Hyperthyroidism: an over-active thyroid gland.

Ventricular fibrillation: very rapid uncoordinated fluttering contractions of the ventricles of the heart resulting in loss of synchronization between heartbeat and pulse beat—abbreviation VF, V-fib.
Appendix D: HTA internet sites

AUSTRALIA

- Centre for Clinical Effectiveness, Monash University
  http://www.mihsr.monash.org/cce/

- Health Economics Unit, Monash University
  http://www.buseco.monash.edu.au/centres/che/

AUSTRIA

- Institute of Technology Assessment / HTA unit
  http://www.oear.at/ita/welcome.htm

CANADA


- Alberta Heritage Foundation for Medical Research (AHFMR)
  http://www.ahfmr.ab.ca/publications.html
  http://www.albertainnovates.ca/

- Canadian Agency for Drugs and Technology in Health (CADTH)
  http://www.cadth.ca/index.php/en/

- Canadian Health Services Research Foundation
  http://www.ehrs.ca/about/index_e.php

- Centre for Health Economics and Policy Analysis (CHEPA), McMaster University http://www.chepa.org

- Centre for Health Services and Policy Research (CHSPR), University of British Columbia http://www.chspr.ubc.ca

- Health Utilities Index (HUI)
  http://www.fhs.mcmaster.ca/hug/index.htm

- Institute for Clinical and Evaluative Studies (ICES)
  http://www.ices.on.ca

DENMARK

- Danish Institute for Health Technology Assessment (DIHTA)
  http://www.dihta.dk/publikationer/index_uk.asp
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- Danish Institute for Health Services Research (DSI)  
  [http://www.dsi.dk/frz_about.htm](http://www.dsi.dk/frz_about.htm)

**FINLAND**
- FINOHTA  [http://www.stakes.fi/finohta/e/](http://www.stakes.fi/finohta/e/)

**FRANCE**

**GERMANY**
- German Institute for Medical Documentation and Information (DIMDI) / HTA  [http://www.dimdi.de/dynamic/en/](http://www.dimdi.de/dynamic/en/)

**THE NETHERLANDS**
- Health Council of the Netherlands Gezondheidsraad  

**NEW ZEALAND**
- New Zealand Health Technology Assessment (NZHTA)  
  [http://nzhta.chmeds.ac.nz/](http://nzhta.chmeds.ac.nz/)

**NORWAY**
- Norwegian Centre for Health Technology Assessment (SMM)  
  [http://www.kunnskapssenteret.no/](http://www.kunnskapssenteret.no/)

**SPAIN**
- Agencia de Evaluación de Tecnologías Sanitarias, Instituto de Salud “Carlos III”/Health Technology Assessment Agency (AETS)  

- Catalan Agency for Health Technology Assessment (CAHTA)  

**SWEDEN**
- Swedish Council on Technology Assessment in Health Care (SBU)  

- Center for Medical Health Technology Assessment  
  [http://www.cmt.liu.se/?l=sv](http://www.cmt.liu.se/?l=sv)
SWITZERLAND

- Swiss Network on Health Technology Assessment (SNHTA)
  http://www.snhta.ch/

UNITED KINGDOM

- NHS Quality Improvement Scotland
  http://www.nhshealthquality.org/nhsqis/qis_display_home.jsp?pConten
  tID=43&p_applic=CCC&pElementID=140&pMenuID=140&p_service=Content.show&

- National Health Service Health Technology Assessment (UK) / 
  National Coordinating Centre for Health Technology Assessment 
  (NCCHTA) http://www.ncchta.org/

- University of York NHS Centre for Reviews and Dissemination (NHS 
  CRD) http://www.york.ac.uk/inst/crd/

- National Institute for Clinical Excellence (NICE)
  http://www.nice.org.uk/

UNITED STATES

- Agency for Healthcare Research and Quality (AHRQ)
  http://www.ahrq.gov/clinic/techix.htm

- Harvard School of Public Health – Cost-Utility Analysis Registry
  http://www.tufts-nemc.org/cearegistry/index.html

- U.S. Blue Cross/ Blue Shield Association Technology Evaluation 
  Center (TEC) http://www.bcbs.com/tec/index.html
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Phillips, B., Ball, C. et al (2001). Levels of Evidence and Grades of Recommendations [Internet]. Centre for Evidence-Based Medicine, Oxford,


