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Prioritising Summary

Circumferential pulmonary vein ablation

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PRIORITISING SUMMARY

REGISTER ID: **S000073**

NAME OF TECHNOLOGY: **CIRCUMFERENTIAL PULMONARY VEIN ABLATION**

PURPOSE AND TARGET GROUP: **FOR THE RELIEF OF SYMPTOMS IN PATIENTS SUFFERING ATRIAL FIBRILLATION**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- ☐ Yet to emerge
- ☐ Experimental
- ☑ Investigational
- ☐ Nearly established
- ☐ Established
- ☐ Established *but* changed indication or modification of technique
- ☐ Should be taken out of use

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- ☐ Yes
- ☑ No
- ☐ Not applicable

ARTG numbers

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Australia	✓		
China	✓		
Denmark	✓		
Japan	✓		
United Kingdom	✓		
United States	✓		

IMPACT SUMMARY:

Circumferential pulmonary vein ablation is an alternative to other types of ablation therapies, such as segmental and linear, for the treatment of atrial fibrillation. The Navi-star™ open irrigated-tip ablation catheter (ThermoCool®, Biosense Webster, Inc., Diamond Bar, California, USA), Celsius™ irrigated tip catheter (ThermoCool®, Biosense Webster, Inc., Diamond Bar, California, USA) and the Lasso (Biosense Webster, Inc, Diamond Bar, California, USA) mapping catheter are three products used internationally currently listed on the ARTG.

BACKGROUND

The heart is a highly organised and intricate component of anatomy. It normally beats about 100,000 times a day at a rate of 60 to 100 beats per minute. This is controlled by a steady flow of electrical impulses originating from highly specialised cells (sinus node) in the upper right chamber of the heart (the right atrium). Such impulses translate a signal that encourage the upper chambers of the heart to contract pushing oxygen-rich blood into the lower chambers of the heart (the ventricles). The ventricles, on receiving signal from the atrium, contract forcing oxygenated blood out into the body.

In some situations, however, the flow of electrical impulses varies from normal. The sinus node may discharge signals too rapidly or excessively. On the other hand, signals can bounce around the chambers of the heart rather than flowing in a regular fashion. Such variation translates as a fast or irregular heartbeat, rhythm disturbances called arrythmias. Atrial fibrillation is one example of an arrhythmia caused by the misfiring of the sinus node in the right atrium. Symptoms of atrial fibrillation include:

- palpitations
- rapid heart rate
- shortness of breath
- chest pain
- dizziness
- lightheadedness; and
- fainting (American Heart Association 2007)

It is not fully understood as to what causes atrial fibrillation, however one theory includes the “rotor” hypothesis. This hypothesis suggests that uncontrolled, rapid, irregular contractions are maintained by signals originating from a rotating bar or ‘rotor’ situated near the pulmonary vein-left atrium junction (Jalife 2003). Despite uncertainty regarding the exact cause of atrial fibrillation, risk factors include:

- a history of congestive heart failure
- valvular heart disease and stroke
- left atrial enlargement
- abnormal mitral or aortic valve function
- treated systemic hypertension
- advanced age; and
- obesity (Olgin and Zipes 2007)

If atrial fibrillation is untreated, the excessively active heart muscle can weaken and stretch out making it much harder for the atria to contract. This may lead to the pooling of blood, which increases the risk of stroke and congestive heart failure. Therefore treatment is highly necessary and is usually focused on four important aspects: treating risk factors, controlling ventricular rate, preventing recurrences and preventing blood vessel blockage by clots (thromboembolic episodes) (Olgin and Zipes 2007; AFFIRM 2003).

The standard non-surgical treatment for atrial fibrillation involves using pharmacological agents, most commonly ß-adrenergic blockers or calcium channel blockers, to control the rate of atrial fibrillation and antiarrhythmic agents, such as lidocaine and flecainide, to restore and maintain the sinus rhythm (Prystowsky and

Katz 2007). Anti-coagulation agents are also administered to reduce the risk of thromboembolism (Prytowsky and Katz 2007).

The standard treatment for atrial fibrillation refractory to pharmacological management is surgery using the Cox/ Maze III technique. This technique traditionally is carried out by operating on an open chest to make numerous atrial incisions forming a maze-like pattern. The resulting scar tissue then provides a conduction block that interrupts the excessive and irregular electrical impulses travelling through the atria. The Cox/ Maze III technique is not commonly undertaken as a stand alone operation but in conjunction with other open heart procedures, often dealing with the risk factors of atrial fibrillation (for example, mitral valve surgery). Catheter ablation, also termed radiofrequency ablation, differs from the Cox/Maze III procedure, especially in surgical technique. Instead of operating through the thoracic cavity, a catheter is fed through a remote vessel (often the femoral vein in the upper leg) and thread up to the heart where radiofrequency heat is used to sear particular anatomical points. This results in the block of irregular signals through the heart, particularly the atrium.

There are four main catheter ablation approaches that have been trialled since the mid 1990s for treating atrial fibrillation (Marine et al 2005). These are:

- Linear Ablation
- Focal Ablation
- The Segmental Ostial Approach; and
- The Circumferential Approach.

These ablation approaches can use various different energy sources including laser, cryoablation and radiofrequency ablation. The overall aim of catheter ablation is to make a full thickness lesion safely and reliably, something that is dependent on a catheter that can deliver to the appropriate location.

Linear ablation involves ablation lines being constructed in a linear fashion between the pulmonary veins and other areas of the atrium. Linear ablation has had various problems associated with it including pericardial effusion, pulmonary embolus, inferior myocardial infarction, pulmonary vein thrombosis and transient ischemic attack.

When compared to focal ablation, ablation of specific foci or points, results were significantly improved in the foci condition (Marine et al 2005). By targeting specific points within the atria or at the pulmonary veins or vena cava the irregularity associated with atrial fibrillation was reduced (Marine et al 2005). However, focal ablation requires observation of premature atrial beats during the ablation procedure limiting it to patients with frequent spontaneous or inducible atrial premature beats.

The segmental ostial approach became the next progression from the limited focal ablation. Discrete connections between the pulmonary vein musculature and left atrial musculature allowed investigators to target such connections with catheters shaped into ring or baskets. It was found that by ablating and isolating such connections had the advantage of treating all points within the vein at the same time and thus avoiding the need to target these points individually. Although the segmental ostial approach has moderate benefit and certainly more benefit than the first two methods, there still remains some complications such as pulmonary vein stenosis, stroke, cardiac tamponade and mitral valve injury. Due to this the circumferential pulmonary vein ablation approach has been trialled based on the Pappone method (Pappone et al 2000).

In 2000, Pappone and colleagues reported a method of treating atrial fibrillation through circumferential radiofrequency ablation of the openings in the heart wall where the pulmonary veins attach to the heart (Pappone et al. 2000). Patients were mapped using a nonfluoroscopic navigation system (CARTO; Bioscience Webster, Diamond Bar, California, United States), followed by placement of a navigator catheter into each pulmonary vein, with a minimum of 50 points mapped. Radiofrequency pulses were delivered until a conduction block surrounding the outside of each pulmonary vein was established. Remapping then took place and patients were monitored for at least 48 hours with follow up at week one and then monthly or on symptom recurrence. As previously mentioned, radiofrequency ablation is the most commonly used energy source particularly in circumferential pulmonary vein ablation. Circumferential pulmonary vein ablation, despite being in the investigational stage, is comparable to segmental ostial ablation and as such the comparison, between these two approaches, is the subject of this summary.

CLINICAL NEED AND BURDEN OF DISEASE

Between April 1998 and May 1999 there were 589,000 cases of atrial fibrillation reported in Australia, including 36,000 new cases of atrial fibrillation diagnosed in general practice (Senes and Britt 2001). As data relating to atrial fibrillation is usually grouped under the more general heading of cardiovascular disease, these prevalence data were the most up to date that could be found. With an Australian population of 19 million in 1999, these data translate to 3.1% of the Australian population being reported cases and 0.2% of the Australian population being diagnosed as new cases in general practice. Patients with atrial fibrillation were predominantly male and aged 75 years or older, with hypertension, heart failure and diabetes being the most common co-existing problems. Between 2004 and 2005, 122,193 hospital patient days were attributed to atrial fibrillation with the average length of stay being 3.2 days (AIHW 2006). One study, the Framingham study found that there was a 15% overall prevalence of atrial fibrillation among stroke case (Wolf et al 1997).

There were no Australian reports on the number of ablations on the pulmonary veins, however the number of ablations of arrhythmia circuit or focus involving one atrial chamber was 526 for the year 2004 to 2005 (AIHW 2006).

DIFFUSION

The Navi-Star catheter, the Celsius catheter and the Lasso circular mapping catheter have all received approval from the FDA. Both the Navistar and Celsius catheters have received premarket approval status as of 11 August 2006 (P030031) and are not to be used in patients that 1) have a clot inside the heart or 2) have an infection in the blood. The Lasso circular mapping catheter has 510(k) approval as of 31 August 2000 (K002333) and is limited to class (II) only and not class (II) (special controls) or class III (premarket approval). These catheters are the only catheter ablation devices listed on the Australian Register of Therapeutic Goods (ARTG).

The Lasso mapping catheter is designed to measure electrical signals within the heart and determine where the impulses arise, whereas the NaviStar and Celsius devices are designed to administer radiofrequency energy to the anatomy of the upper chambers of the heart.

Another component of the device is the CARTO system, which provides a three-dimensional depiction of the heart and reduces the need for excessive radiation.

COMPARATORS

Comparators to circumferential pulmonary vein ablation:

- COX/ MAZE III Procedure
- Alternative Ablation techniques:
    - Segmental pulmonary vein ablation (SPVA)
    - Linear Ablation
    - Focal Ablation
    - Hybrid Approaches (Circumferential Pulmonary Vein Ablation with ‘roof’ line or ‘mitral’ line ablation as well)

SAFETY AND EFFECTIVENESS ISSUES

In the present summary, studies reporting on circumferential pulmonary vein ablation in respect to other ablation techniques, namely the segmental approach, mainly use the Lasso mapping catheter for the initial mapping of the pulmonary veins and left atrium. The Navi-Star or Celsius Thermacool 3.5 mm, 4 mm or 8 mm tip irrigated catheters are used in the four included randomised controlled trials.

Karch et al. (2005) randomly assigned 100 patients to undergo CPVA or SPVA for atrial fibrillation. The mean duration of atrial fibrillation for patients undergoing CPVA was 5 years (range: 3 to 7 years) and 4 years for patients receiving SPVA (range: 2 to 7 years), with each group having the same mean number of episodes per month. The geometry of the left atrium was reconstructed using the CARTO electroanatomic mapping system and radiofrequency current was applied using the 8 mm tip ThermoCool catheter (maximum temperature 55°C; power 50 to 70 Watts) and/or the 4 mm cooled tip catheter (maximum temperature 48°C, power 35 to 50 Watts). This study included a six month follow-up period with assessments at one, three and six months.

Bauer et al (2006) explored the effect of circumferential and segmental pulmonary vein ablation on autonomic function in terms of acceleration and deceleration-related modulations of heart rate and compared between the two groups. This study was a substudy of that conducted by Karch and colleagues (2005), with one hundred patients randomly assigned to each intervention.

Oral et al. (2003) randomly assigned 80 patients to pulmonary vein isolation by segmental ostial ablation (SOA group) or CPVA. There were three patients with structural heart disease in the SOA group and one in the left atrial ablation group, however this was not statistically significant ($p = 0.6$). Mapping took place in both groups with a temperature-controlled 4 mm tip deflectable catheter (EP Technologies, Inc., San Jose, California, United States) in the SOA group and an 8 mm tip deflectable Navistar catheter in the left atrial ablation group. Radiofrequency energy in the SOA group was delivered at 52°C (maximum output 35 Watts) for 20 to 45 seconds at each ostial site, whereas the temperature and power was slightly higher (55°C, maximum power 60 Watts) for a period of greater than 20 seconds for the circumferential ablation (LAA group). Patients were assessed between four and six weeks and then three and six months with a mean follow-up of 164 ± 100 days.

Liu et al. (2006b) compared segmental pulmonary vein ablation with isolation (SPVI) to circumferential pulmonary vein ablation with the endpoint of pulmonary vein isolation, also called circumferential pulmonary vein isolation (CPVI). One hundred and ten patients with comparable baseline characteristics were randomly assigned to undergo either SPVI or CPVI. Segmental pulmonary vein isolation was achieved by circumferential pulmonary vein mapping and dissociation of the pulmonary vein potentials with a Lasso catheter. The ablation progressed with linear ablation along the "roof" line initially and then along the "mitral isthmus" line if atrial fibrillation was refractory to preliminary ablation. Ablation was performed using a 4 mm irrigated tip Celsius ThermaCool catheter at a target temperature of 43°C (power output 30 Watts) for 30 seconds at each point, whereas the circumferential pulmonary vein isolation approach used a 3.5 mm Navistar irrigated tip ablation catheter. Patients were discharged under anticoagulation treatment and anti-arrhythmic drugs were administered routinely for the first two months. Follow up occurred at two weeks and then at one, three, six and nine months after ablation.

a) Safety

Although Karch et al. (2005) reported no instances of pericardial tamponade, there were 22 cases of pericardial effusion after CPVA and five after SPVA ($p < 0.01$). One patient in each treatment group experienced a transient ischaemic attack. One stroke with a persistent sensorimotor defect also became evident after CPVA. Fewer patients experienced pulmonary vein stenosis in the CPVA group, compared to the SPVA group (3 versus 6 patients), but this difference was not statistically significant.

In Oral et al. (2003), one patient in the CPVA group developed left atrial flutter, however additional ablation in the mitral isthmus abolished this flutter. No further safety outcomes were reported.

Three patients from the SPVI group in Liu et al. (2006b) developed subcutaneous haematoma, compared to four patients from the CPVI group. One patient from the SPVI group required a blood transfusion. Both the SPVI and CPVI groups had a patient exhibiting an asymptomatic right superior pulmonary vein stenosis.

b) Effectiveness

The mean procedure times in Karch et al. (2005) were 284 minutes (CPVA group) and 256 minutes (SPVA group) ($p = 0.02$), including total ablation times of 72 minutes and 52 minutes for CPVA and SPVA respectively ($p < 0.001$). During the six-month follow-up 27 CPVA patients (54%) and 41 SPVA patients (82%) ($p < 0.01$) were free of arrhythmia-related symptoms. Results of seven-day Holter monitoring at six month follow-up showed that 21 patients (42%) after CPVA and 33 patients (66%) after SPVA were in sinus rhythm ($p = 0.02$). This study found that 28% (8/29) of patients in the CPVA group and 47% (8/17) in the SPVA group with documented recurrence of atrial tachyarrhythmia were free of arrhythmia symptoms during the six month follow-up. After CPVA atypical atrial flutter was observed in nine patients, whereas after SPVA it was observed in one patient ($p < 0.01$)

After being exposed to the same ablation conditions as in Karch (2005), deceleration capacity, in the circumferential pulmonary vein ablation group, decreased by 42% ($p < 0.00001$) (Bauer, 2006). In the segmental pulmonary vein ablation group, deceleration capacity decreased by 41% ($p < 0.00001$). Effects of pulmonary vein ablation on acceleration capacity were similar to those on deceleration capacity decreasing by 31% ($p < 0.00001$) in the circumferential pulmonary vein ablation group. Acceleration capacity in the segmental pulmonary vein ablation group decreased significantly ($p < 0.004$). Both deceleration and acceleration capacity returned to baseline values within one month in the segmental pulmonary vein ablation group whereas both capacities were present in circumferential pulmonary vein ablation group for at least a year (p = .001) (Bauer 2006).

The primary outcome for Oral et al. (2003) was freedom from paroxysmal atrial fibrillation after a single ablation procedure. Of the patients who underwent CPVA, 88% were free of paroxysmal atrial fibrillation at six months, whereas this figure reached 67% in the SOA group (p = 0.01). The mean duration of radiofrequency energy required to encircle the left and right-sided pulmonary veins in the CPVA group was 22 ± 8 minutes and 18 ± 8 minutes, respectively, whereas for the SOA group it took 18 ± 9 minutes per patient. The mean total duration of the procedure for the CPVA group was 149 ± 33 minutes, compared with 156 ± 45 minutes for the SOA group (p = 0.7).

After the first ablation procedure in Liu et al. (2006), atrial tachyarrhythmia occurred in 41.8% (23/55) of patients in the stepwise SPVI group and in 36.4% (20/55) in the CPVI group (p = 0.69). Atrial fibrillation constituted the majority of the cases of atrial tachyarrhythmia in the SPVI group (65.2%; 15/23 patients), whereas it constituted the minority of cases in the CPVI group (34.8%; 8/23 patients). Late recurrence of atrial fibrillation was detected in one patient in the SPVI group five months after the first procedure and in one patient from the CPVI group six months after the first procedure. Overall, successful clinical outcome was achieved in 83.6% patients (46/55) from the CPVI group and in 78.2% patients (43/55) from the stepwise SPVI group (p = 0.63). Mean total procedure time for the SPVI approach (219 ± 67 minutes) was significantly longer (p = 0.003) than for the CPVI approach (181 ± 66 minutes) (p = 0.03). The ablation time was comparable for SPVI relative to CPVI, with a duration of 63 ± 15 minutes and 59 ± 9 minutes, respectively (p = 0.09).

COST IMPACT

The cost of performing circumferential radiofrequency pulmonary vein ablation for atrial fibrillation was estimated to range from $18,498 to $24,199 (calculated using current exchange rate of 1 Canadian Dollar to 1.14 Australian dollars) (Khaykin et al 2007). A possible breakdown of relevant costs is included below:

Table 1: Cost of Devices (in Australian Dollars)

	Low	Medium	High
Navistar Catheters (8mm)	4601.34	4909.99	5678.71
Celsius Catheter (8mm)	892.50	1040.36	1350.40
LASSO Catheter	2086.40	2596.49	3017.67

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified from the retrieved material.

Other Issues

No issues were identified from the retrieved material.

HealthPACT Action

Based on the evidence suggesting that CPVA does not appear to offer a clear clinical advantage over SPVA, CPVA will be archived.

List of Studies Included

Total number of studies	4
Level II Intervention	4

Search Criteria to be Used:

Circumferential
Pulmonary Vein
Ablation
Atrial Fibrillation
Catheter ablation

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