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# Horizon Scanning Technology Prioritising Summary

## Percutaneous Left Atrial Appendage Transcatheter Occlusion (PLAATO) System

July 2005

(Updated June 2006)



**ASERNIP(S)**

**Australian  
Safety  
and Efficacy  
Register  
of New  
Interventional  
Procedures -  
Surgical**



**Royal Australasian  
College of Surgeons**



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The production of this Horizon scanning prioritising summary was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

This Horizon scanning prioritising summary was prepared by staff from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S).

**Name of Technology:**

Percutaneous Left Atrial Appendage Transcatheter Occlusion (PLAATO) System

**Purpose and Target Group:**

The PLAATO system (ev3 Inc., Plymouth, Minnesota) was developed to prevent thromboembolism in patients with atrial fibrillation (AF) and consists of an implant and a delivery catheter. The implant is a self-expanding nitinol cage covered with an occlusive expanded polytetrafluoroethylene membrane. It occludes the orifice of the left atrial appendage, a section of the heart which has been identified as playing a significant role in cardioembolism in atrial fibrillation, a major cause of stroke (Blackshear *et al.* 1996).

**Stage of Development (in Australia):** Not yet emerged in Australia

- Experimental
- Investigational
- Nearly established
- Established
- Established but changed indication or modification of technique
- Should be taken out of use

The PLAATO system is not listed or registered in the Australian Register of Therapeutic Goods (ARTG).

**International Utilisation:**

COUNTRY	LEVEL OF USE		
	Trials underway	Limited use	Widely diffused
Europe	✓		
United States	✓		
Canada	✓		

**Impact Summary:*****Background***

Atrial fibrillation (AF) is the most common form of cardiac arrhythmia, with approximately 2.2 million individuals in the United States affected by this condition. In the past, AF has been considered a relatively benign condition by the medical community, however, numerous studies have indicated that non-rheumatic AF is strongly linked to systemic embolism and stroke (Wolf *et al.* 1997). With AF, patients have a five-fold increase in the risk of stroke (Wolf *et al.* 1978). In addition to this, the Framingham study revealed that there was a 15% overall prevalence of atrial fibrillation among stroke cases (Wolf *et al.* 1997). Echocardiographic, surgical and post-mortem



studies have now demonstrated that 90% to 100% of thrombi form in the left atrial appendage (LAA) in non-rheumatic AF patients (Sievert *et al.* 2002). Hence, there is a considerable chance that the LAA plays a significant role in the occurrence of stroke in AF patients. Based on these findings, LAA occlusion/obliteration has been investigated as a potential treatment for thromboembolic stroke (Blackshear *et al.* 1996). Obliteration of the LAA is now a common practice during the Maze III procedure, mitral valve surgery and coronary artery bypass graft surgery (Blackshear *et al.* 1996) as a step to reduce stroke incidence. However to perform these invasive procedures solely to occlude the LAA is not advisable.

Pharmacological approaches to prevent stroke involve the use of drugs such as warfarin, antithrombins (e.g. ximelagatran) and antiplatelet medications (eg. aspirin). Anticoagulation therapy using the drug, warfarin, is currently the gold-standard treatment for the prevention of stroke (Sievert *et al.* 2002) and has been reported to reduce the risk of thromboembolic events by 70% (Ostermayer *et al.* 2003). However, the use of warfarin is associated with several disadvantages; warfarin has a narrow therapeutic index, which means the dosage range for effective and safe warfarin treatment is small. An overdose of warfarin could lead to haemorrhaging, whereas an insufficient dose of warfarin could lead to the formation of a life-threatening blood clot. To further compound this disadvantage, warfarin reacts with a large number of drugs and may lead to adverse drug interactions. Additionally, warfarin treatment is not effective in some patients due to long-term contraindications.

Percutaneous left atrial appendage transcatheter occlusion (PLAATO) via transseptal catheterisation was developed with the aim of reducing the incidence of stroke in high risk AF patients who are contraindicated to warfarin treatment.

### ***Clinical Need and Burden of Disease***

Annually, 15 million people worldwide suffer a stroke (<http://www.who.int>). Of these, 5 million will die and another 5 million will be left permanently disabled. The American Heart Association estimates that stroke alone will cost a total of US\$53.6 billion a year in the United States. The average cost per patient for the first 90 days after a stroke was US\$15,000 in 2001 (<http://www.who.int>).

In Australia, there are approximately 40 000 stroke events every year, and it is estimated that 120 000-220 000 individuals will have a stroke at some time of their lives. Stroke is the cause of 25% of all chronic disabilities and the second single most common cause of death among Australians in 2002, accounting for 12 533 deaths or 9.4% of all deaths (Australian Institute of Health and Welfare, 2002).



## ***Estimated Speed, Geographic and Practitioner Use, Patterns of Diffusion in the Health System***

PLAATO was developed by Appriva Medical Inc., Germany (currently owned by ev3 Inc.). Clinical trials have been conducted in Europe, Canada and the United States, where over 200 patients have been treated with this device. In May 2002, Appriva Medical Inc. received the CE mark approval for the PLAATO™ LAA Occlusion System in Europe. Currently, a non-randomised multicentre trial involving approximately 300 patients is being conducted in Europe, Canada and the U.S. (<http://www.theheart.org>).

### ***Existing Comparators***

- LAPTONI (Thoracoscopic Left Appendage, Total Obliteration, No cardiac Invasion) procedure

The LAPTONI procedure was used by Blackshear *et al.* (2003) to occlude the LAA in 15 AF patients with high risk of stroke. This procedure involves the use of a thoracoscope and a loop snare/stapler to occlude the LAA.

- Amplatzer septal occluder (AGA Medical Corp., Golden Valley, MN)

The Amplatzer septal occluder (ASO) device is indicated for the occlusion of atrial septal defects (ASD) in the secundum position. It is also indicated in patients who have undergone a fenestrated Fontan procedure and who now require closure of the fenestration (<http://www.amplatzer.com>). It has been trialled to occlude the LAA and hence can function similarly to the PLAATO procedure (Meier *et al.* 2003). This technique appears to involve a more simple approach than the PLAATO procedure; however its effectiveness with regards to LAA occlusion has not been studied extensively.

- Surgical removal of the LAA

### ***Estimated Cost Impact***

The costs associated with this new product are not available. The cost of surgery for the Amplatzer device to achieve LAA occlusion was also unavailable. However, the cost for surgery using of the Amplatzer septal occluder for ASD was estimated to be about AUD\$10 000 (Hughes *et al.* 2002), which includes the cost of the theatre/catheter laboratory, anaesthetic, and the Amplatzer septal occluder. The reimbursement fees as stated by the Medicare Benefits Schedule for ASD closure with a septal device by transcatheter approach is \$774.05 (Item number 38743), which was introduced in November 2004. According to the HIC, there has been one claim to Medicare for ASD closure with septal occluder or other similar device to date (<http://www.hic.gov.au>).

### ***Efficacy and Safety Issues***



## List of Studies Found

Total number of studies	4
Case series studies	3
Case reports	1

The studies included in this summary are highlighted in bold in the reference list.

Safety and efficacy data from three case series studies and one case report have been selected for inclusion in this summary. All studies on PLAATO were included due to limited literature on this procedure.

In the study by Sievert *et al.* (2002), LAA occlusion was successful in all 15 patients. Similarly, Omran *et al.* (2003) and Nakai *et al.* (2003) had successful occlusion in all patients (n=9 and n=1 respectively). Both Sievert *et al.* (2002) and Omran *et al.* (2003) reported that reimplantation was required in 4/15 (27%) and 2/9 (22%) patients, respectively, due to incompatible size of the implant leading to incomplete closure of the LAA. Reimplantation was uneventful in all patients.

Several minor complications were noted during the implantation procedure. Sievert *et al.* (2002) reported that one patient (1/15, 6.7%) experienced haemopericardium during LAA access, with the appendage being successfully occluded 4 weeks later. Omran *et al.* (2003) reported minor postprocedural pericardial effusion in 1/9 (11%) patient and a small postprocedural atrial septal defect (ASD) due to transseptal puncture occurred in another patient (1/9, 11%). Both defects were resolved during follow-up. The case report by Nakai *et al.* (2003) on a 62-year-old patient did not report any complications during the implantation procedure.

During follow-up, no evidence of perforation, device embolization, or interference with surrounding structures such as pulmonary vein flow or mitral valve function was noted by Nakai *et al.* (2003) using transesophageal echocardiography (TEE) and colour Doppler. Likewise, both Sievert *et al.* (2002) and Omran *et al.* (2003) did not observe any evidence of embolic events during follow-up. In all three studies, the device did not dislodge and appeared stable throughout the duration of follow-up.

The study by Hanna *et al.* (2004) evaluated the effect of PLAATO on the anatomic and haemodynamic properties of the mitral valve (MV) and left upper pulmonary vein (LUPV). Of the 11 patients who completed six months of follow-up after successful LAA occlusion, LUPV diameter, peak systolic flow velocity and diastolic flow velocity did not differ significantly during follow-up. Additionally, left atrial size, mitral regurgitation severity and MV peak E-wave velocities did not vary significantly with baseline readings. The data indicates that implantation of the PLAATO device in the neck of the LAA does not result in any detrimental anatomical or physiological alterations to adjacent structures at six months post-implantation.



## 2006 update

### Safety and efficacy

A search of relevant databases, online journals and the Internet was conducted in May 2006, following the recommendation in July 2005 that PLAATO be monitored for assessment in 12 months time. Four new sources of evidence on the safety and efficacy of this intervention have been located in the literature.

<b>Total number of studies</b>	4
<b>Case series</b>	1
<b>Case report</b>	3

Left atrial appendage (LAA) occlusion utilizing the PLAATO system was evaluated in a prospective, multicentre trial involving 111 patients with successful LAA occlusion in 108/111 (97.3%) patients. Three patients did not receive the PLAATO device due to the presence of a left atrial thrombus (n=1), vessel perforation of the right femoral artery (n=1) and a cardiac tamponade after trans-septal puncture (n=1). Of the 108 patients who has successful LAA occlusion with PLAATO, 100 (92.6%) received aspirin and 82 (75.9%) received clopidogrel after the procedure. One (0.9%) patient experienced two major adverse events (MAE) within 30 days post-procedure. This patient was one of the three patients who did not receive the PLAATO device and suffered from cardiac tamponade and finally neurological death after hospitalisation. At 6 months post-procedure, 97.9% of patients were free from major adverse events and/or mobile left atrial thrombus. Two patients died before the 6 month follow-up, one being the previously mentioned patient with two MAEs and the other experienced an ischemic stroke 173 days post-procedure. With regards to device performance, implantation and treatment was successful in 108 of 113 procedures (95.6%) (in 111 patients) with no complications during recapture and retrieval. 'Trace leak' or 'absent leak' was identified in 94/108 (87%) implanted devices after LAA occlusion while 14/108 (13%) patients had a 'mild leak'. Echocardiographic results immediately after the procedure revealed that 86/88 (97.7%) patients with assessable transesophageal echocardiogram (TEE) had successful occlusion of the LAA. At 1 month, 60/60 (100%) patients had successful LAA occlusion while at 6 months, 49/50 (98%) patients had complete LAA occlusion. Echocardiography did not reveal any mobile thrombus, disruption of mitral valve function or pulmonary vein inflow in any patient. Two (2/111, 1.8%) patients experienced stroke 173 and 215 days post-procedure respectively, TEE at 1 and 6 month follow-up did not reveal any device migration or thrombogenic layer on the device surface. Three transient ischemic



attacks occurred in 2 patients, thus resulting in an annual stroke rate of 2.2%. The authors reported a total of 6/111 (5.4%) deaths, none of which were related to the device or procedure. On the basis of patient's CHADS<sub>2</sub> score (2.5 points), the estimated annual stroke rate for this patient population was 6.3%, this translates to a relative stroke reduction of 65% assuming the patients were taking aspirin prior to implantation.

Post-mortem analysis of a PLAATO patient (Omran *et al.* 2005) who died one year after implantation revealed no thrombus on the device, indicating that the device was not responsible for patient death. The atrial surface of the device was completely covered by a neo-endothelium, including the area of the hub where the device was connected to the delivery sheath. The autopsy revealed that the PLAATO device was rotated slightly off-axis of the left atrial appendage. However this was not due to device migration as surgical records revealed that the off-axis position was appreciated during implantation and was unavoidable due to the angulated appendage. Anchors of the PLAATO device provided adequate hold to retain the device in its original position and did not penetrate the left atrial appendage. Overall, the authors concluded that the device remained stable and completely occluded the left atrial appendage one year post-implantation, lending support that the device was not responsible for the patient's death (Omran *et al.* 2005).

The remaining two studies are case reports and were not included in this update as the articles were not retrievable. These case reports (Mohrs *et al.* 2006, Mohrs *et al.* 2006b), are imaging studies utilizing computed tomography or contrast enhanced magnetic resonance imaging. Abstracts for these articles were not available.

### **2006 Recommendation**

The latest studies indicate that percutaneous left atrial appendage occlusion can be performed with the PLAATO system with acceptable risks. Despite promising results, no randomized controlled trials have been conducted at the time of writing and the long-term efficacy of PLAATO remains unknown. Due to the limited evidence available, it is therefore recommended that the following be conducted:

- |  |  |
|--|--|
| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input checked="" type="checkbox"/> Monitor      | <input type="checkbox"/> Archive                           |



## References

Omran H, Schmidt H, Hardung D, Hammerstingl C, von der Recke G, Haas S, Buttner R, Luderitz B. Post mortem analysis of a left atrial appendage occlusion device (PLAATO) in a patient with permanent atrial fibrillation. *Journal of Interventional Cardiac Electrophysiology* 2005;14(1): 17-20.

Ostermayer SH, Reisman M, Kramer PH, Matthews RV, Gray WA, Block PC, Omran H, Bartorelli AL, Della Bella P, Di Mario C, Pappone C, Casale PN, Moses JW, Poppas A, Williams DO, Meier B, Skanes A, Tiersten PS, Lesh MD, Nakai T, Bayard Y, Billinger K, Trepels T, Krumdordf U, Sievert H. Percutaneous left atrial appendage transcatheter occlusion (PLAATO system) to prevent stroke in high-risk patients with non-rheumatic atrial fibrillation: results from the international multi-center feasibility trials. *Journal of the American College of Cardiology* 2005;46(1): 9-14.

Mohrs OK, Ruebesam D, Peters J. Images in cardiology. Computed tomography in a patient after percutaneous left atrial appendage transcatheter occlusion (PLAATO). *Heart* 2006;92(2): 486.

Mohrs OK, Schraeder R, Petersen SE, Scherer D, Nowak B, Kauczor HU, Voigtlaender T. Percutaneous left atrial appendage transcatheter occlusion (PLAATO): planning and follow-up using contrast-enhanced MRI. *American Journal of Roentgenology* 2006;186(2): 361-364.

## Ethical Issues

No issues were identified from the retrieved material.

## Cultural or Religious Considerations

No issues were identified from the retrieved material.

## Other Issues

It should be noted that all the published papers on the PLAATO procedure have been conducted by the same research group. Additionally, all patients who underwent the PLAATO procedure were placed on an oral anticoagulant treatment post-operation; this may confound the actual efficacy of the PLAATO procedure.

## HealthPACT recommendation:

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|--|--|
| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input checked="" type="checkbox"/> Monitor      | <input type="checkbox"/> Archive                           |



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Hughes ML, Maskell G, Goh TH, Wilkinson JL. Prospective comparison of costs and short term health outcomes of surgical versus device closure of atrial septal defect in children. *Heart* 2002, **88**: 67-70.

Meier B, Palacios I, Windecker S, Rotter M, Cao QL, Keane D, Ruiz CE, Hijazi ZM. Transcatheter left atrial appendage occlusion with Amplatzer devices to obviate anticoagulation in patients with atrial fibrillation. *Catheterization and Cardiovascular Interventions* 2003, **60**(3): 417-422.

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Odell JA, Blackshear JL, Davies E, Byrne W J, Kollmorgen C F, Edwards WD, & Orszulak TA. Thoracoscopic obliteration of the left atrial appendage: potential for stroke reduction? *Annals of Thoracic Surgery* 1996, **61**(2): 565-569.

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Ostermayer S, Reschke M, Billinger K, Trepels T, Buschek F, Bayard Y, Sievert H. Percutaneous closure of the left atrial appendage. *Journal of Interventional Cardiology* 2003, **16**(6): 553-556.

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Wolf PA, Dawber TR, Thomas HE Jr, Kannel WB. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: the Framingham study. *Neurology* 1978, **28**(10): 973-977.



Wolf PA and Singer DE. Preventing stroke in atrial fibrillation. *American Family Physician* 1997, **56**(9): 2242-2252.

### Sources of Further Information:

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### Search Criteria:

A search of MEDLINE, PubMed and Cochrane Library, Current Controlled Trials metaRegister, UK National Research Register, International Network for Agencies for Health Technology Assessments, relevant online journals and the Internet was conducted in February 2005.

Search terms used were: 'PLAATO', 'Percutaneous left atrial appendage transcatheter occlusion', 'cardioembolic stroke prevention', and 'atrial fibrillation'.

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This Horizon Scanning Prioritising Summary was prepared by Mr Irving Lee from the NET-S Project, ASERNIP-S for the Health Policy Advisory Committee on Technology (HealthPACT), on behalf of the Medical Services Advisory Committee (MSAC) and the Australian Health Ministers' Advisory Council (AHMAC)