Australian Government

Department of Health and Ageing

Australia and New Zealand Horizon Scanning Network

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AN INITIATIVE OF THE NATIONAL, STATE AND TERRITORY GOVERNMENTS OF AUSTRALIA AND THE GOVERNMENT OF NEW ZEALAND

Horizon Scanning Technology

Prioritising Summary

Excimer laser assisted nonocclusive anastomosis

May 2007

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.

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PRIORITISING SUMMARY

REGISTER ID: **S000036**

NAME OF TECHNOLOGY: **EXCIMER LASER-ASSISTED NONOCCLUSIVE ANASTOMOSIS (ELANA) FOR EXTRACRANIAL-TO-INTRACRANIAL AND INTRACRANIAL-TO-EXTRACRANIAL BYPASS**

PURPOSE AND TARGET GROUP: **FOR INTRACRANIAL BYPASS SURGERY, PRIMARILY FOR TREATING GIANT ANEURYSMS OF THE INTRACRANIAL CIRCULATION AND CEREBRAL ATHEROSCLEROSIS**

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 — ARTG number **N/A**
- ☑ No
- ☐ Not applicable

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
The Netherlands	✓		

IMPACT SUMMARY:

The conventional extracranial-to-intracranial bypass procedures used to treat large intracranial aneurysms or severe cerebral atherosclerosis require temporary occlusion of the main arteries (internal carotid artery and/or its major branches), which can lead to brain damage or death. The ELANA technique may potentially eliminate the need for temporary occlusion and, therefore, reduce the risk of cerebral ischaemia in the select group of patients requiring such treatment. This prioritising summary examines the evidence currently available on the safety and effectiveness of the ELANA technique.

BACKGROUND

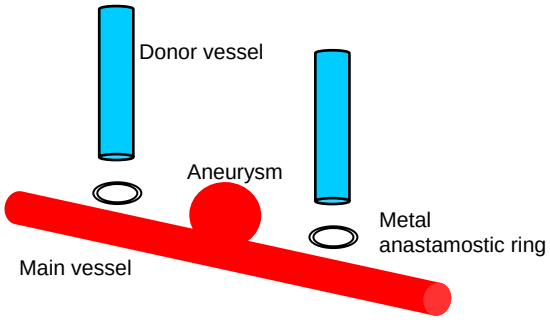
An aneurysm is an abnormal localised dilation of a blood vessel. Aneurysms commonly occur in arteries that supply blood to the brain. In some patients, selective obliteration of an intracranial aneurysm is not always feasible because of its size, location or shape (Brilstra et al. 2002). Giant aneurysms (>25 mm), in particular, are often difficult to treat and are associated with rupture, re-bleed and death rates ranging from 20% to 70% at 5 years. In approximately 80% of cases, large aneurysms of the internal carotid artery can be treated by sacrificing the artery (known as the parent vessel). Collateral flow from surrounding vessels can provide sufficient blood to the area affected by vessel sacrifice in the majority of patients. However in some individuals, vessel sacrifice is not an acceptable treatment option owing to underdeveloped or absent collateral arteries. In these patients, complete blockage or sacrifice of the parent vessel could lead to cerebral ischaemia, which can result in unconsciousness, brain damage or death.

In this situation, an extracranial-to-intracranial (EC-IC) bypass is constructed with a superficial temporal or middle cerebral artery to provide the necessary blood flow once the internal carotid artery is sacrificed. The parent artery is temporarily occluded in order to complete the anastomosis, but this exposes the patient to the risk of intraoperative cerebral ischemia (Langer and Vajkoczy 2005). Despite the use of brain protective measures, perioperative stroke occurs in 9.5% of patients undergoing this procedure (van der Zwan et al. 2001).

The ELANA (excimer laser-assisted nonocclusive anastomosis) technique enables the surgeon to construct an EC-IC or intracranial-to-intracranial (IC-IC) bypass without occluding the recipient artery, thus eliminating the possibility of intraoperative cerebral ischemia. The technique involves attaching an anastomotic ring to the recipient artery. A donor vessel is grafted to the recipient artery around the ring using conventional microsurgical techniques. A laser suction catheter is then passed down the lumen of the open donor vessel and placed against the side wall of the donor vessel that is aligned with the anastomosis site. The donor recipient vessel wall is then sucked into the catheter and the laser cuts through both the donor and recipient vessel walls. The suction keeps the small vessel flap in contact with the catheter, thus preventing it from migrating into the lumen of the recipient vessel. Back bleeding through the anastomosis site is controlled by applying a temporary aneurysm clip to the donor vessel. After the catheter is withdrawn, the proximal donor lumen is sewn end-to-end to a second portion of donor vessel that is attached to the extracranial donor artery and the aneurysm clips are removed (Brilstra et al. 2002; Langer and Vajkoczy 2005). The ELANA technique can also be used to treat occlusive diseases such as cerebral artherosclerosis. However, the technique is only useful in the relatively small group of patients for whom vessel sacrifice is not a viable treatment option.

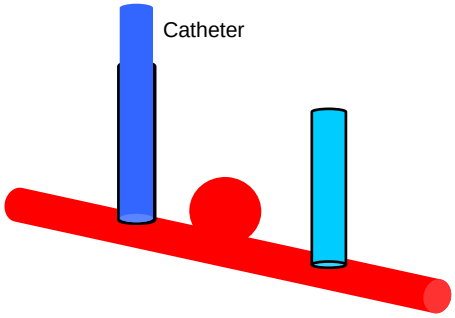
Figure 1: ELANA technique

A)



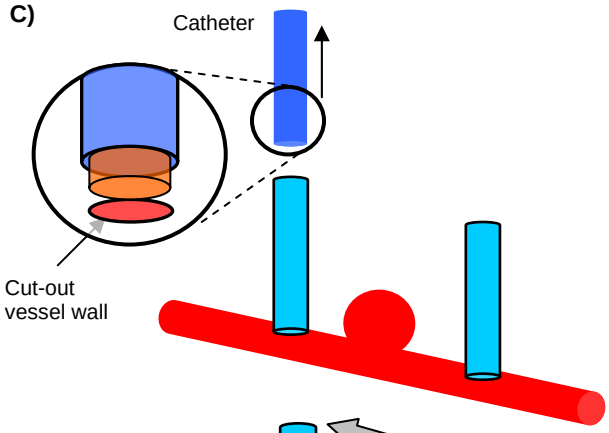
The main blood vessel/recipient artery is not occluded with clips. The donor vessels are sutured to the main vessel with a metal anastamostic ring. No incisions are made on the main vessel.

B)



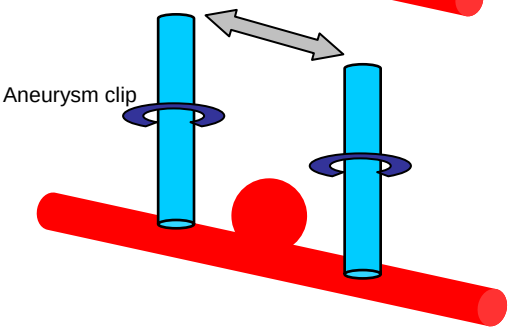
The laser suction catheter is passed down the lumen of the donor vessel and is placed against the side wall of the donor vessel. The vacuum pump is activated and the catheter sucks the wall of the main vessel against the catheter. The laser is then activated and proceeds to cut a hole in the wall of the main/recipient vessel.

C)



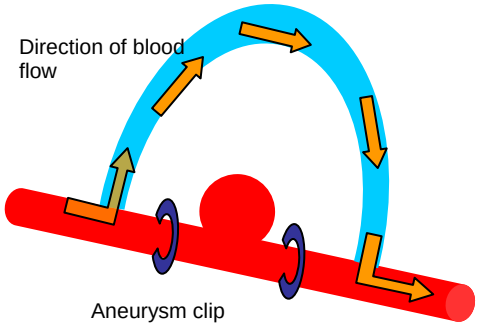
With the vacuum still activated (to ensure that the cut-out vessel wall does not migrate into the main vessel), the catheter is retracted from the donor vessel. As the catheter is retracted, blood will flow into the donor vessel. This backbleeding is controlled by temporarily occluding the donor vessel with the use of an aneurysm clip.

D)



After performing the same procedure on the other donor vessel, the proximal ends of both donor vessels are sutured together.

E)



The aneurysm clips are removed from both donor vessels, therefore completing the bypass. The aneurysm is then taken out of the circulation.

CLINICAL NEED AND BURDEN OF DISEASE

The annual incidence of aneurysmal subarachnoid haemorrhage in the United States exceeds 30,000 people, of whom 10% to 15% will die before reaching hospital and 50% will die within the first 30 days of rupture. For those who survive, about half will suffer some form of permanent neurological deficit (Brain Aneurysm Resources 2007). A systematic review by Rinkel et al. (1997) found that unruptured intracranial aneurysms occur in 4% to 6% of the general population.

There are approximately 40,000 to 48,000 stroke events annually in Australia, and intracranial cerebral atherosclerosis accounts for approximately 8% to 10% of them (AIHW 2005; Higashida et al. 2005). In patients with intracranial atherosclerosis, the annual risk of stroke from all causes ranges from 4% to over 13% (Higashida et al. 2005).

DIFFUSION

The ELANA technique is currently being trialled in the Netherlands and has been used in approximately 300 patients worldwide (BBC News 2007). The technique was first utilised in the United States (December 2006) to successfully treat a young man suffering from a giant cerebral aneurysm. At the same time, an independent group of researchers in the United Kingdom performed the technique in four patients with cerebral aneurysms or brain tumours (Elana bv 2007).

COMPARATORS

Other treatment options for cerebral aneurysms and occlusive diseases are:

- craniotomy and open repair for cerebral aneurysms;
- direct coiling or clipping of cerebral aneurysms;
- conventional EC-IC bypass;
- intracranial stents/angioplasty for cerebral atherosclerosis.

SAFETY AND EFFECTIVENESS ISSUES

Safety

The largest case series study, representing 40 patients, was conducted by Tulleken et al. (1997) in the Netherlands. One patient with severe atherosclerosis and an occlusion of the internal carotid artery experienced spontaneous dehiscence at the anastomosis site, the repair of which required temporary occlusion of the intracranial internal carotid artery that resulted in serious neurological sequelae. In three other patients, the flap from the recipient artery wall at the anastomosis site was not recovered. Since this could potentially block a vessel in another part of the body, a distal anastomosis using a cortical branch of the middle cerebral artery was constructed with a conventional end-to-side anastomosis technique instead. The authors stated that a fault in the design of the laser catheter was the likely reason for it failing to punch out a full-thickness portion of the recipient arterial wall at the anastomosis site in two of these three patients (Tulleken et al. 1997).

The case series by van Doormaal et al. (2006) studied 34 patients with giant intracranial aneurysms of the internal carotid artery proximal to its bifurcation who were treated with the ELANA technique. Two patients (6%) experienced a fatal complication and seven patients (21%) experienced non-fatal complications. The first patient died of an air embolus originating from the central line 1 day after surgery, while the second patient died from a ruptured internal carotid artery aneurysm 2 days post-surgery. The non-fatal complications observed were: intraoperative ischaemia (1 patient, 3%), postoperative ischaemia (3 patients, 9%), aneurysm bleed (2 patients, 6%) and cranial nerve palsy (2 patients, 6%). The authors

reported that in five patients, the artery wall flap was not retrieved after laser activation. However, all five ELANA anastamoses were still used for bypass construction because vigorous backflow was noted after laser catheter withdrawal. One of these patients experienced ischaemia, most likely due to a large blood clot that formed in the aneurysm. In five patients where the internal carotid artery was left open during the bypass operation, a clot formed in the bypass after the procedure, which necessitated the construction of a second bypass (van Doormaal et al. 2006).

In the study by Klijn et al. (2002), 27% (4/15) of patients who underwent the ELANA technique for symptomatic carotid artery occlusion experienced complications during the operation (3 cases of ipsilateral ischemic strokes; 1 patient died of myocardial infarction). One patient suffered a severely disabling stroke (Rankin grade 4) 11 days after the operation, while two additional patients suffered moderately disabling stroke (Rankin grade 3) immediately after the operation. The investigators reported that the median follow-up of the 14 patients who survived the postoperative period was 27 months. Of the 11 patients who did not experience any perioperative complications, one died 17 months after surgery from a brainstem stroke, while another patient suffered a new stroke ipsilateral to the carotid artery occlusion 10 months post-surgery (Klijn et al. 2002).

Effectiveness

Of the 35 patients who successfully underwent the ELANA technique in the study by Tulleken et al. (1997), 92% had patent anastomoses over a follow-up period ranging from 4 weeks to 4 years. Blood flow was measured in the bypass graft of seven patients who had an internal carotid artery occlusion and found to be between 120 and 190 mL/minute (mean normal internal carotid artery flow: 250 ml/minute).

van Doormaal et al. (2006) reported that in the short-term (mean: 24 days, range: 8-59 days), 71% of patients (24/34) had favourable[1] outcomes and 10 patients (19%) had unfavourable[2] outcomes. Two of the latter patients died (6%). Long-term (mean: 3.3 years, range: 0.6-5.6 years) results showed that 25/34 patients (74%) had favourable outcomes (16 patients had identical modified Rankin Scale [mRS] scores, 9 patients had improved postoperative mRS scores), while 7/34 patients (21%) had unfavourable outcomes. Two patients were lost to follow-up. Overall, the proportion of patients who were dependent remained unchanged after surgery. Of the 27 patient with cranial nerve compression before surgery, symptoms were completely resolved in 10 patients (37%) after surgery.

The study by van der Zwan et al. (2001) quantified the blood flow within the bypass of 34 patients (26 patients with giant cerebral aneurysms, 8 patients with occlusive disease of the internal carotid artery) treated with the ELANA EC-IC technique. Postoperative magnetic resonance angiography was performed in 14/26 cerebral aneurysm patients (after ligation or balloon occlusion of the internal carotid artery) and revealed a mean flow in the bypass of 158 mL/minute. In patients with occlusive disease (n = 8), the mean postoperative flow was 130 mL/minute. The authors noted that conventional bypass techniques usually result in blood flows of approximately 25 mL/minute (van der Zwan et al. 2001).

COST IMPACT

The Elana Arteriotomy System costs approximately US$500,000 (New York Times 2006). The cost of the entire procedure is unknown.

[1] Favourable outcomes: modified Rankin Scale (mRS) score equal to or higher than preoperative mRS.
[2] Unfavourable outcomes: mRS less than preoperative mRS.

The Medicare Benefits Schedule reimbursement fees for procedures to treat intracranial aneurysms are listed in Table 1. Note that the number of claims presented below understates the total number of cerebral aneurysms in Australia and that only a small proportion of these claims could possibly have been treated with the ELANA technique.

Table 1 Medical Benefits Schedule of procedure related to the treatment of cerebral aneurysms (Department of Health and Aging 2007)

Category	Item Number	Benefit (AUD)	Number of Claims (July 2006 to February 2007)
Replacement by graft of vein or synthetic material for aneurysm of common or internal carotid artery, or both.	33100	$1269.15	7
Aneurysm of major artery, replacement by graft.	33172	$1129.60	19
Endovascular occlusion with detachable coils, and assisted coiling if performed, with parent artery preservation for intracranial aneurysm, ruptured or unruptured.	35412	$2525.05	20
Aneurysm, clipping or reinforcement of sac.	39800	$2525.05	239
Intracranial proximal artery clipping of aneurysm, or arteriovenous malformation.	39806	$1136.20	2
Ligation of cervical vessel or vessels, intracranial aneurysm or arteriovenous fistula.	39812	$558.25	6

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified from the retrieved material.

OTHER ISSUES

Elana bv (The Netherlands) is currently working on a sutureless technique (SELANA), which is essentially an addition to the current ELANA procedure, that will substantially reduce surgical time. Instead of suturing the bypass graft to the recipient vessel wall, a small spring-like device is attached to the end of the bypass graft so that it can be fastened without the use of sutures. The vessel wall is removed in the same way as the current ELANA technique (Elana bv 2007).

HEALTH PACT CONCLUSION

Based on the results of this selection of case series, the ELANA technique appears to carry a substantial amount of risk. However, it is unclear if the risk observed is related only to the procedure itself but also due to the selection of patients. The study by Tulleken et al. (1997) highlights that device failure may occur, and under certain circumstances these malfunctions may contribute to peripheral embolisation. The encouraging results observed (flow rates etc.) in the included case series studies should be interpreted with caution, comparative studies are required before this technique can be adopted as a suitable alternative to conventional bypass surgery. It is recommended that the ELANA technique be monitored for future developments.

SOURCES OF FURTHER INFORMATION:

Vega C, Kwoon JV, Lavine SD. Intracranial aneurysms: current evidence and clinical practice. *American Family Physician* 2002; 66**(2)**: 601-608.

LIST OF STUDIES INCLUDED

Total number of studies	4
Level IV intervention evidence	4

SEARCH CRITERIA TO BE USED:

Cerebral revascularization/methods*
Cerebral revascularization/instrumentation
Anastomosis, Surgical/methods*
Intracranial aneurysm/surgery*
Excimer laser assisted nonocclusive anastomosis
ELANA

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Brain Aneurysm Resources. Last updated 2007. www.brainaneurysm.com [Accessed March 2007].

Brilstra EH, Rinkel GJE, Klijin CJM, van der Zwan A, Algra A, Lo RTH, Tulleken CAF. Excimer laser-assisted bypass in aneurysm treatment: short-term outcomes. *Journal of Neurosurgery* 2002; 97**(5)**: 1029-1035.

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Higashida RT, Meyers PM, Connors JJ, Sacks D, Strother CM, Barr JD, Wojak JC, Duckwiler GR. Intracranial angioplasty and stenting for cerebral atherosclerosis: A position statement of the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology, and the American Society of Neuroradiology. *Journal of Vascular and Interventional Radiology* 2005;16**(10)**: 1281-1285.

Klijn CJM, Kappelle LJ, van der Zwan A, van Gijn J, Tulleken CAF. Excimer laser-assisted high-flow extracranial/intracranial bypass in patients with symptomatic carotid artery occlusion at high risk of recurrent cerebral ischemia: Safety and long-term outcome. *Stroke* 2002; 33**(10)**: 2451-2458.

Langer DJ and Vajkoczy P. ELANA: Excimer laser-assisted nonocclusive anastomosis for extracranial-to-intracranial and intracranial-to-intracranial bypass: a review. *Skull Base: An Interdisciplinary Approach* 2005; 15**(3)**: 191-205.

New York Times. With lasers and daring, doctors race to save a young man's brain. Last updated 2006. http://www.nytimes.com/2006/12/19/health/19brai.html?ex=1324184400&en=3280ea62e1a8c80d&ei=5088&partner=rssnyt&emc=rss [Accessed March 2007].

Rinkel GJ, Djibuti M, Algra A, van Gijin J. Prevalence and risk of rupture of intracranial aneurysms: a systematic review. *Stroke* 1997; 29**(1)**: 251-256.

Tulleken CAF, Verdaasdonk RM, Beck HJM. Nonocclusive excimer laser-assisted end-to-side anastomosis. *Annals of Thoracic Surgery* 1997; 63**(S6)**: S138-S142.

van der Zwan, Tulleken CAF, Hillen B. Flow quantification of the non-occlusive excimer laser-assisted EC-IC bypass. *Acta Neurochirurgica* 2001; 143**(7)**: 647-654.

van Doormaal TPC, van der Zwan A, Verweij BH, Langer DJ, Tulleken CAF. Treatment of giant and large internal carotid artery aneurysms with a high-flow replacement bypass using the excimer laser-assisted nonocclusive anastomosis technique. *Operative Neurosurgery* 2006; 59**(4)**: 329-335.