The ELANA technique:

Applicability in Experimental and Clinical Settings

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The ELANA technique: Applicability in Experimental and Clinical Settings
Thesis Utrecht University

ISBN-10: 90-9019-945-4
ISBN-13: 97-8909-019-945-0

Cover: 3D reconstruction, angiography and photograph of a patient with an ELANA anastomosis to the basilar artery. Also various scanning electron microscopic images of ELANA anastomoses. Coverdesign, bookdesign, and typesetting: H.J.N. Streefkerk. Photos and images: H.J.N. Streefkerk and C. Timmers. 3D Reconstructions: H.J.N. Streefkerk. Printed by: Drukkerij Graficolor, Nijmegen

The ELANA technique:
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De ELANA techniek:

Applicatie in Experimentele en Klinische Situaties

(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van docotor

aan de Universiteit Utrecht

op gezag van de Rector Magnificus, Prof. dr. W.H. Gispen,

ingevolge het besluit van het College voor Promoties

in het openbaar te verdedigen

op dinsdag 25 oktober 2005 des ochtends te 10:30 uur

door

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We gratefully acknowledge financial support for this research by
the Hersenstichting Nederland.

Publication of this thesis was financially supported by
ELANA B.V.
and Spectranetics International.

Printing of this thesis was further financially supported by
Carl Zeiss B.V.,
B.Braun Medical B.V.,
Gyrus Medical B.V.,
and Medtronics B.V.

Aan Aimée en Anton

Contents

List of Abbreviations

A1 / A2	First or second branch of the anterior cerebral artery
A3 / Acx	Third or cortical branch of the anterior cerebral artery
ACA	Anterior cerebral artery
AComA	Anterior communicating artery
AICA	Anterior inferior cerebellar artery
BA	Basilar artery
BA top	Top of the basilar artery (bifurcation)
BA trunk	Trunk of the basilar artery (between vertebral artery junction and the superior cerebellar artery)
BA-VA	Junction of the VAs into the basilar artery
BTO	Balloon test occlusion
CBF	Cerebral blood flow
CT	Computed tomography
CTA	Computed tomographic angiography
E-E / E2E	End-to-end anastomosis
E-S / E2S	End-to-side anastomosis
EA	Epigastric artery
ECA	External carotid artery
EC-IC	Extracranial-to-intracranial
ELANA	Excimer Laser-Assisted Non-occlusive Anastomosis
EpigA	Epigastric artery
ICA	Internal carotid artery
IC-IC	Intracranial-to-intracranial
IOA	Intraoperative angiography
M1 / M2	First or second branch of the middle cerebral artery
M3 / Mcx	Third or cortical branch of the middle cerebral artery
MCA	Middle cerebral artery
MRA	Magnetic resonance angiography
MRF	Magnetic resonance flowmetry
MRI	Magnetic resonance imaging
OA / OccipA	Occipital artery
OEF	Oxygen extraction fraction
OM image	Operation Microscopic image
OphthA	Ophthalmic artery
P1 / P2	First or second branch of the posterior cerebral artery

PCA	Posterior cerebral artery
PComA	Posterior communicating artery
PET	Positron emission tomography
PICA	Posterior inferior cerebellar artery
PTA	Posterior temporal artery
RA	Radial artery
rCBF	Regional cerebral blood flow
SCA	Superior cerebellar artery
SEM image	Scanning Electron Microscopic image
SEP	Somatosensory evoked potential
SPECT	Single proton emission computed tomography
S-S / S2S	Side-to-side anastomosis
STA	Superficial temporal artery
SubclA	Subclavian artery
SVG	Saphenous vein graft
TCD	Transcranial doppler
ThyrA	Thyroid artery (superior)
TIA	Transient ischemic attack
TOF	Time of flight (MR technique)
USF	Ultrasound flowmetry
VA	Vertebral artery
VBA	Vertebrobasilar aneurysm

Part I

Background Information

Preface

The ELANA technique is an arterial anastomosis technique which allows for a complete end-to-side anastomosis to a cerebral artery without occluding that recipient artery (see Figure1.). First a graft with a platinum ring in its distal end is stitched onto the wall of the recipient (see Figure1.a and b). Then a laser catheter is inserted inside the graft so that the tip touches the wall of the recipient artery within the platinum ring (see Figure1.c). Vacuum suction is activated within the laser catheter, ensuring a firm fixation of the laser fibres to the wall of the recipient artery (see Figure 1.d). When the laser is activated, a hole is burned in the wall, effectively creating the anastomosis (see Figure1.e). Upon retraction of the laser catheter, the punched-out portion of arterial wall is also withdrawn with the catheter because of the continued vacuum suction (see Figure1.f). Attaching the free end of the graft with another graft will complete the bypass procedure.

In order to give the reader more background information on cerebral revascularization, we have described the anatomy of the cerebral arteries in chapter 1. Chapter 2 discusses the possible indications for bypass surgery. In the next chapter (3), the various diagnistic and surgical procedures have been described. Chapter 4 gives an introduction to in vitro and in vivo evaluation. The studies described in the remaining chapters in this thesis all concern the application of the ELANA technique in in vitro experimental settings, in animal experimental settings, and in clinical patient settings.

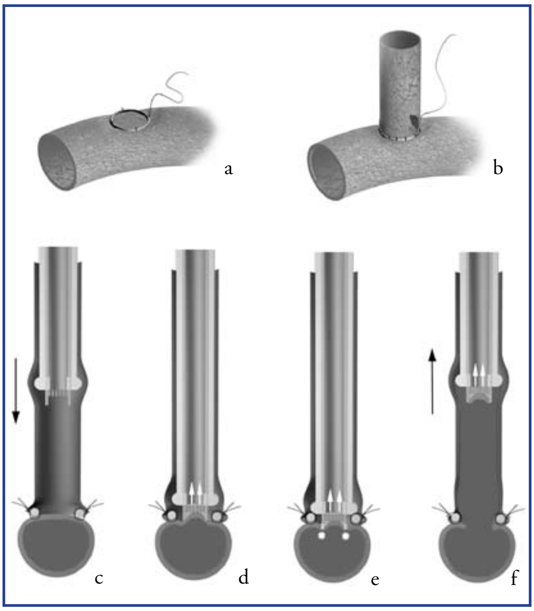


Figure 1.
Theory of the ELANA technique. A platinum ring with a diameter of 2.6, 2.8, or 3.0 mm is stitched onto the wall of the recipient artery (a). Both median stitches are placed very superficially, only passing the adventitial and medial layers of the recipient. However, the 2 lateral stitches are placed deeply, fully passing the wall of the recipient artery. Then the bypass graft is stitched onto the wall of the recipient using the platinum ring as a guide (b). All 8 stitches are placed very superficially, only passing the adventitial and medial layers. An excimer laser catheter is introduced into the open end of the bypass graft (c). When the tip of the catheter touches the wall of the recipient artery within the platinum ring and within the bypass graft, vacuum suction through the catheter is activated, ensuring a firm contact of the laser fibres with the wall of the recipient artery (d). After 2 minutes of vacuum suction, the excimer laser is activated, and a small flap of arterial wall is punched out (e). When the catheter is withdrawn, the punched-out flap of arterial wall is also withdrawn due to the continuous vacuum suction through the laser catheter (f). To prevent excessive backbleeding through the open end of the bypass graft, the graft is filled with a heparine-saline solution, and a temporary hemoclip is placed over the bypass graft. This part of the bypass is then completed.

Aim of this thesis

The aim of this thesis is: to investigate the technical and clinical applicability of the ELANA technique in order to analyse the creation of successful non-occlusive intra-cranial anastomoses. In order to confirm the hypothesis that the ELANA technique is a safe and easy method to create intracranial anastomoses, we formulated several criteria with which the ELANA technique should comply.

1. Anastomoses made with the ELANA technique should be easy to create in experimental settings as well as in clinical settings.

2. Anastomoses made with the ELANA technique should re-endothelialize as well as conventionally sutured anastomoses in experimental settings as well as in clinical settings.

3. The ELANA technique should enable surgeons to create a bypass to otherwise inaccessible cerebral arteries in a safe way.

The above mentioned criteria should be refined. The first criterion comprises the actual ELANA technique itself. The ELANA technique should allow for reproducable results in standardized experimental settings. In chapter 5, we describe the development of a suitable in-vivo model in which the ELANA technique can be studied.

We studied the re-endothelialization of the ELANA technique in pigs, which has been described in chapter 6. In chapter 7, a description of the re-endothelialization in patients is given. In this chapter, we also compare these results with those obtained from the pig study.

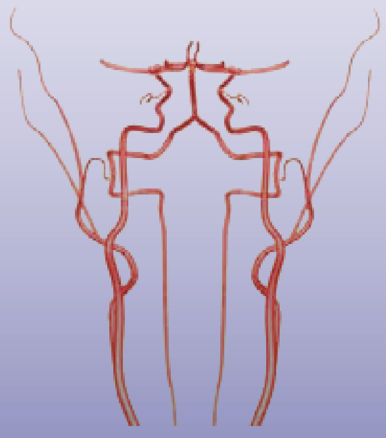
The ELANA technique has now been used in a large number of patients. Chapter 8 gives a detailed description of the application of the technique in a patient with poor posterior circulation circulation. Chapters 9 and 10 describe the application in two patients with very difficult basilar artery aneurysms. The following chapter (11) then summarizes the application and clinical results in 42 patients with giant intracranial aneurysms. Most of these patients received an intracranial-to-intracranial bypass.

We discuss the impact and relevance of the results in chapter 12. The conclusions of these investigations have been summarized in chapter 13. The last chapter (14) concerns future aspects.

In the appendices, a small study on the vacuum suction system is described, a list of the patients studied in chapter 11 is given, as well as the references.

Chapter 1

Anatomy & History of Cerebral Revascularization



Anatomy of the Cerebral Arteries

In this part, we give a short overview of the anatomy of the cerebral arteries. We pay special attention to the locations that are important for bypass surgery.

Arterial blood is pumped from the heart into the aortic arch. Typically, there are 3 branches of the arch of the aorta. As the aortic arch usually is directed from right to left, the rightmost of these branches is the brachiocephalic trunk, the middle branch forms the left common carotid artery, and the leftmost branch is the left subclavian artery. The brachiocephalic trunk gives rise to the right subclavian artery, which supplies the right arm with oxygenated blood, and the right common carotid artery. The right subclavian artery also supplies the right vertebral artery. The left subclavian artery supplies the left arm. A branch of the left subclavian artery is the left vertebral artery. The common carotid arteries and the vertebral arteries are the main blood supply to the head and neck (see Figure 1.1.).

A global (vascular) division can be made into front-side (anterior) and back-side (posterior) blood vessels. At the posterior side, the vertebral arteries follow a traject through the round holes in the vertebrae (foramina rotundum) upwards into the posterior part of the skull. At the anterior side, again a division can be made into outside (external) and inside (internal) of the skull. Both common carotid arteries divide into the external carotid arteries (ECAs) and the internal carotid arteries (ICAs) (see Figure 1.2.). Almost all structures in the neck and on the outside of the skull are supplied by (branches of) the external carotid arteries (the exceptions being the ethmoidal arteries supplying the nasal septum and the ethmoidal cells, and the other collateral branches of the ophthalmic arteries with the angular artery of the face). The internal carotid arteries do not have any branches in the neck. Instead, the first branches can be found only after entering the base of the skull, where they give rise to the ophthalmic arteries (OphthAs), to supply the eyes and the surrounding structures with blood (see Figure 1.3.).

Among the many branches of the external carotid artery (ECA) to the structures in the neck and the external part of the head, the facial artery can be of importance, as this artery can form a natural supply of extra blood to the internal system. As the third of fourth branch of the ECA, the facial artery and its end branches supply many parts of the face, including the external parts of the eyes. Here, the angular artery meets (anastomoses) with the ophthalmic artery, which is the first branch of the internal carotid artery. Thus, this is a pathway (ophthalmic anastomosis) where blood can flow from the internal circulation to the external circulation, or the other way around.

Previous page:
3D reconstruction of the circle of Willis and the relation with some branches of the external carotid artery.

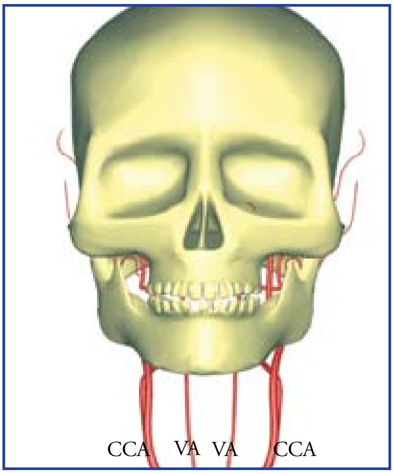


Figure 1.1.
Bloodvessels in the neck related to the skull. Frontal view. Observe the 2 vertebral arteries (VA) in the midline, and the 2 common carotid arteries (CCA) on the outside.

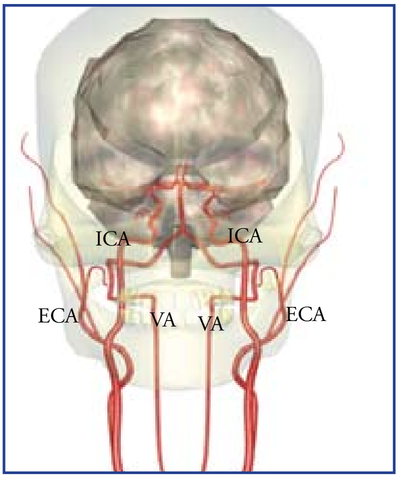


Figure 1.2.
Cerebral bloodvessels in relationship to the brain. Frontal view. Observe some of the extracranial branches of the external carotid artery (ECA), and the junction of the 2 vertebral arteries (VA) at the base of the brain stem.

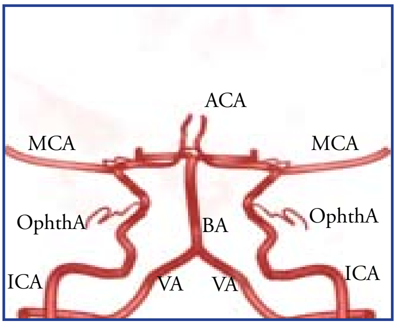


Figure 1.3.
Cerebral bloodvessels at the base of the brain. Frontal view (enlarged view of figure 1.2.). The ophthalmic artery (OphthA) is the first branch of the internal carotid artery (ICA). Inside the skull, the ICA divides into the middle cerebral artery (MCA) and the anterior cererbral artery (ACA). Also, both vertebral arteries (VA) conjunct and form the basilar artery (BA).

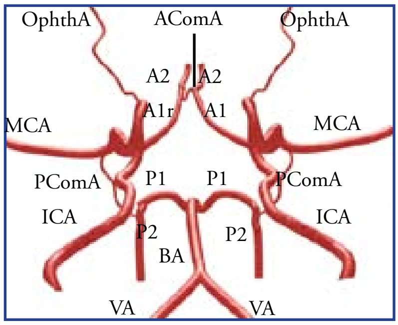


Figure 1.4.
Cerebral bloodvessels at the base of the brain. View from below. Observe the anterior communicating artery (AComA) between both anterior cerebral arteries. Also, observe both posterior communicating arteries (PComA) between the posterior cerebral arteries and the internal carotid arteries (ICA) just before the bifurcation of the middle cerebral artery (MCA) and the first segment of the anterior cerebral artery (A1).

The internal carotid artery rises from the neck and enters the skull. Here, the ophthalmic artery is the first branch of the internal carotid artery. The internal carotid artery then enters the intracranial space. A second branch of the internal carotid artery is the posterior communicating artery. This small artery is one of two communicating arteries (one on each side) from the anterior circulation to the posterior circulation. The internal carotid artery then branches into the first (A1 or pre-communicating) part of the anterior cerebral artery and the first segment (M1) of the middle cerebral artery (see Figure 1.4.). The first part of the anterior cerebral artery is also called "pre-communicating" as this part is located before the first branch, which is the anterior communicating artery which connects both anterior cerebral arteries with each other. The segments directly after the anterior communicating artery are denominated as post-communicating or A2. Following the next branching the anterior cerebral artery is then at its A3 segments. A similar denomination is used for the middle cerebral artery. However, this artery lacks a branch with a communicating artery. Therefore the denomination is simply M1 for the first segment. After the first bi- or trifurcation, the next segments are the M2 segments. The next branching accordingly changes the denomination to M3, and so forth. Branches which are located at the cortex obtain the suffix "cortical" even though they may be M2 or M5 segments.

History of Cerebral Revascularization

Vascular Anastomoses

The first description of a vascular anastomosis was published more than 120 years ago in *The Military Medical Journal* in Russian by Eck.[98] Effectively, he described the side-to-side (S-S) anastomosis of the hepatic vein to the inferior caval vein, later known as the Eck Fistula (see Figure 1.5.). The operations were performed in the animal laboratory on eight dogs. Of these experimental animals, seven died within the first week. The eighth dog lived for more than 2 months, but ran away. Patency of the fistula was not established, but Eck still recommended application to man! When Pavlov used this procedure for his Eck Fistula dogs, investigating "meat intoxication",[327] he stated that: "although it requires no extraordinary skill, it does demand the uninterrupted attention of the operator and is, therefore, rather exhausting." Note that this procedure involved suturing of 1 cm diameter vessels with an incision in both vessels of 1 cm during the 19th century with the equipment of that century. In 1904 Pavlov received the Nobel Prize for his work on the physiology of digestion. Carrel was awarded the Nobel Prize in 1912 for his now famous work on the suturing of blood vessels and transplantation of

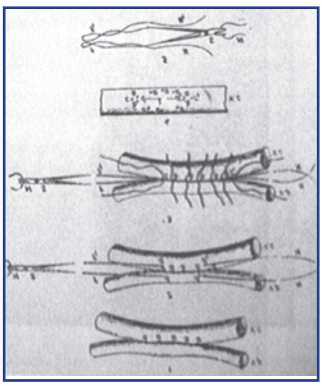


Figure 1.5.
Eck's Fistula. Essentially, this is a side-to-side anastomosis of the hepatic vein to the inferior caval vein, Eck invented special scissors with sutures attached to the sharp endings. Using interupted sutures the vessel walls were sutured together. The special scissors were then used to cut the remaining wall between both vessels. This procedure was performed in 8 dogs. Seven died, and one ran away. However, this is the first non-occlusive anastomosis which has been described in litature. Carrel published on Eck's Fistula a decade later. The first thing Carrel described on this technique was temporary occlusion of both vessels to ensure a blood free operation area.

organs, which he performed together with Guthrie.[59] The article describes the use of very fine suture material and the technique of triangulation, which permits an anastomosis to be accomplished with little decrease in the diameter of the vessel, with apposition of the endothelium, and with relative technical ease. It is noteworthy, that he also published an improved and more simpler technique of the Eck Fistula.[61] Cushing, after having visited Carrel's laboratory as early as 1905, included the improved Eck Fistula in his student teaching course "Performance of an Eck Fistula".[182]

Cerebral Revascularization

Cerebral revascularization started around 1939, when German and Taffel described a procedure called encephalomyosynangiosis, covering the cerebral cortex with a vasculated muscle flap.[116] The theoretical basis for vascular bypass surgery was provided by Fisher in 1951.[109] Two case reports supported that theory; In 1939, Pool and Potts performed a superficial temporal artery (STA)-to-distal anterior cerebral artery (ACA) shunt using a plastic tube inserted into the STA.[225] Ten days after operation, arteriography showed that the tube was clotted. The patient was fine and at full-time work 12 years later. Woringer and Kunlin published in 1965 on a common carotid artery (CCA)-to-intracranial internal carotid artery (ICA) bypass using a saphenous vein graft (SVG).[340] The patient died, but autopsy revealed the graft to be patent. It was not until the arrival of the operating microscope that small vessel anastomoses became generally feasible. In 1961, Jacobson and Suarez described the technique to make an anastomosis of blood vessels (with a diameter of 2 mm) using the operating microscope, while working in the laboratory of Donaghy.[161] In 1967, Yasargil, who had worked in the same laboratory, performed the first extracranial-to-intracranial (EC/IC) bypass in man, using an anastomosis between the superficial temporal artery (STA) and the middle cerebral artery (MCA) (cortical branch),[344] after performing the first experimental STA-MCA bypass in dogs.[342]

The EC/IC Bypass Study

The interest of neurosurgeons in this technique was reflected in the organization of the First International Meeting on Microsurgical Anastomosis for cerebral ischemia in 1973.[311] Most of those early patient series were nonrandomized and poorly controlled. Therefore, in 1977, The International Cooperative Study of Extracranial-Intracranial Arterial Anastomosis (EC-IC Bypass Study) was initiated to perform a prospective randomized trial to compare medical management (aspirin treatment) with combined surgical and medical treatment of intracranial vascular disease.[11] In March 1980, one of the problems encountered was that every participating centre truly had to attempt to randomise all eligible patients. If a number of centres operated on less complicated patients and submitted only the more serious cases for randomisation, the outcome would look less favourable.[39] In 1985, the EC-IC Bypass Study reported on the 5-year clinical outcome.[289, 290] The study failed to confirm the hypothesis that STA-MCA anastomosis in combination with medical treatment was more effective than medical treatment alone in preventing stroke or stroke-related deaths for all groups studied.[289] Since this publication, use of this procedure has been greatly reduced. However, in September 1986, Ausman and Diaz,[15] and in October 1986, Awad and Spetzler found some potential sources of bias that they thought to have affected the study.[29] At least two groups of patients were not specifically addressed in the study: Those failing the best medical treatment and those with clearly documented hemodynamic compromise. The first group was not included. The second group was included, but not isolated. Both groups may benefit the most from revascularization surgery compared to medical therapy. Also, observational bias in neurologist and patient, "randomisation-to-treatment" bias because of pre-operative clinical differences between the groups, and pre-randomization bias was observed by Awad and Spetzler. The latter, already discussed by Barnett and McCormick in 1980,[38] was considered a more serious problem because the fraction of eligible patients within each centre, who where actually entered in the study, could not be verified. Awad and Spetzler pointed out the difference in understanding of the pathofysiology between the initiation of the study in 1977 and 1986. As the approach to different lesions changed during the study, different patients were considered eligible.

In March 1987, three special reports appeared in the New England Journal discussing the EC/IC Bypass Study.[40, 119, 278] In the first special report, Sundt reported to have contacted with many centres by phone. He found two main problems: high patency rates achieved by small contributing centres, and the relatively small number of symptomatic patients.[278] As small contributing centres would treat fewer patients, the patency rate should be expected to be lower. The second paper was a report of the committee appointed by the AANS to examine the Study.[119] They had investigated why so many patients were operated upon outside the trial and how many of them would have been eligible. The committee concluded that EC/IC bypass surgery may still benefit stroke patients because the EC/IC Bypass Study population may not have been representative for the population at risk. In answer to the other special reports, Barnett reported that it was the quality of the data and not the quantity that counts because it is not necessary to include all eligible patients in a trial to observe an effect.[40] In spring 1986, another attempt had been made to verify the accuracy of the information, using the same approach as Sundt had performed as mentioned in the special report. Responses were received from 84% of the participants. Barnett concluded, while adding some more information concerning eligibility, that if a subgroup existed who would benefit from surgery, it would have been identified in the trial, given the available information at that time.

In 1996 Surgical Neurology surveyed neurosurgeons and neurologists about the value of EC/IC bypass surgery, 10 years after the Bypass Study.[58] Confronted with a hypothetical patient with TIA's, ICA occlusion and compromised collateral circulation, 12 centres were asked for their opinion concerning cerebral bypass surgery and about the hypothetical case. Six of them were absolutely positive regarding surgery in this case. The others were negative or not sure. Low frequencies of bypass procedures were reported when bypass surgery was indicated, varying from several to once a year.

Technical advancements

Despite the EC/IC Bypass Study, technical developments and clinical applications in cerebral revascularization progressed all through the seventies, eighties, and nineties. The donor vessels that have been used now include the common carotid artery (CCA) as reported in 1984,[56] extracranial internal carotid artery (ICA) in 1985,[309] and intracranial ICA in 2002.[297] Also the vertebral artery (VA) has been used as donor vessel.[132] All afferent cerebral arteries have been used as donor vessel, including the first segment of the anterior cerebral artery (ACA A_1),[297] the first segment of the MCA M_1, and the first segment of the PCA P_1.[313] For EC/IC bypass procedures the external carotid artery (ECA) [74], and the STA,[344, 345] have been used most often as donor vessel. The occipital artery (OA) has been used since 1976,[173] and the subclavian artery (SubclA) since 1980.[266] For recipient vessel branches of the MCA has been used since the beginning of 1967.[344] Also, the intracranial ICA in 1971,[199] posterior inferior cerebellar artery (PICA) in 1976,[173] VA in 1977,[74] superior cerebellar artery (SCA) in 1979,[23] anterior inferior cerebellar artery (AICA) in 1981,[18] posterior cerebral artery (PCA) in 1982,[149] intracranial ICA in 1993,[305] ACA,[297] and even the basilar artery (BA) in 1998,[246] have been used as recipient vessel. Considering grafts, Lougheed was the first to report on a case with a saphenous vein bypass graft (SVG).[199] As bypass graft the epigastric artery (EA),[305] and the radial artery (RA) have been reported.[154]

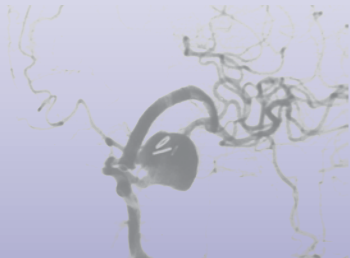
Conclusion

The revascularization techniques of the brain, which looked so very promising in the laboratory and on individual cases, did not succeed in convincing the medical community of its usefulness in decreasing the risk of stroke in certain patients and the International EC/IC Bypass Study proved the procedure to be ineffective in this respect. As was proven by the many case reports and applicability studies the main problem was not in the technique itself, for the EC/IC Bypass Study carried a patency rate of 95%. Also, there has never been any real doubt of its usefulness in aneurysm or skull base tumour surgery, and it is quite improbable that we need a similar trial to prove these points. So, next to aneurysm surgery, skull base tumour surgery, and posterior circulation enhancement (as vertebrobasilar occlusive disease was not included in the EC/IC Bypass Study), the question remains which patients with symptoms of cerebral ischemia should be treated with bypass surgery. The introduction of advanced diagnostic methods has given new hope in the search for a patient subgroup eligible for revascularization. However, the only way to demonstrate the efficacy of any type of bypass using any diagnostic means is by a new randomised clinical trial.

The impact of the EC-IC Bypass Study has been dramatic. The numbers of patients with symptoms of cerebral ischemia referred for bypass operation have been reduced to zero in most neurosurgical clinics. Although intuitively, one would expect that improvement of cerebral blood flow would reduce progression of ischemic symptoms as compared to medical treatment, the EC-IC Bypass Study proved this to be wrong. However, maintaining cerebral blood

Chapter 2

Possible Indications for Revascularization



Cerebral revascularization

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Adv Tech Stand Neurosurg. 2003;28:145-225. Review.

Possible Indications for Cerebral Revascularization

Possible indications for bypass surgery include low-flow syndromes, vasospasm,[42] amaurosis fugax after ICA occlusion,[180] giant cell arteritis,[156] mycotic aneurysms[100], and multi-infarct dementia.[208] Bypass surgery may also be considered in selected cases of cerebral ischemia resulting from cervical or intracranial dissection or trauma. In general when permanent or transient occlusion of an injured ICA is necessary, revascularization can be indicated.[117] Bypass surgery is usually preferred over omentum or temporalis muscle transposition, except when there is no usable donor artery of sufficient caliber or when, as in moya-moya disease, none of the vessels distal to the lesion is large enough to accept a bypass graft. Although many reports have been written on Moya-Moya disease, we do not cover Moya-Moya disease in this review. We want to refer to the excellent reviews of Moya-Moya disease which appeared in 1997 in Clin Neurol Neurosurg 99 supplement 2.[67]

Symptomatic Cerebral Ischemia

Considering atherosclerotic carotid disease, two-third of the cerebral infarctions is probably due to embolism, and one-third to distal insufficiency.[63] Most emboli are originating from carotid artery stenosis or ulcerated plaques. Clinical symptoms depend on the major cerebral artery territories into which the emboli become stuck. The result is an embolic stroke, which is more severe, and less frequently preceded by TIAs than non-embolic strokes. Non-embolic stroke most often is caused by decreased vascular perfusion because of severe stenosis or occlusion of the cerebropetal arteries. First affected are the territories located furthest from the site of occlusion. The resulting "watershed" or "border zone" – infarct has been well documented.[314] Five sources of collateral supply have been described. We believe that the circle of Willis was "constructed" to counter such problems, giving alternative blood supply from the contralateral ICA through the anterior communicating artery, and from the BA through the PComA. In healthy volunteers, we have performed test occlusions of the ICA under MR volume flow monitoring of the ICAs and BA. We have observed that also the flow through the contralateral posterior communicating artery may reverse, suggesting collateral flow through the contralateral posterior communicating artery, through both P_1 segments and through the ipsilateral posterior communicating artery to the ipsilateral carotid territory, as both contralateral ICA and BA fully compensated for the lack of flow, without reversing the flow in the ipsilateral A_1. Other collaterals include the ECA – ophthalmic artery system, and the leptomeningeal anastomosis system between the cortical branches of the PCA, MCA, and ACA.[312]

Previous page
Intracranial-to-Intracranial bypass from the M1 segment of the middle cerebral artery to a M2/3 segment of the same artery in order to remove a giant M1 aneurysm from the circulation. Postoperatively, the aneurysm was successfully coiled by an endovascular operation, with preservation of flow in the vascular region distally of the aneurysm, due to the bypass.

The presence of such collaterals usually means the absence of an AComA. Reperfusion can be critical in the recovery process of ischemic tissue. If reperfusion occurs within 3-4 hours, the amount of permanent damage decreases.[164] Ischemia leads to vasodilatation and loss of autoregulation, resulting in an increase of regional blood flow in the area around the ischemic focus. This reactive hyperemia may result in worsening of vasogenic edema or even hemorrhage in the ischemic tissue. The autoregulation process ensures that in normal conditions the cerebral blood flow is independent of cerebral perfusion pressure. In healthy subjects the upper and lower limits of autoregulation are 140 and 65 mmHg.[137] Without autoregulation the cerebral blood flow is completely dependent on the systemic pressure. In patients with severe stenosis or occlusions of the major cerebral vessels, lack of autoregulation may indicate hypoperfusion of the brain, despite maximum dilatation of the vessels as the autoregulation process has reached its outer limits. The idea of cerebral revascularization for patients with symptoms of cerebral ischemia is, of course, to counter the hypoperfusion, decrease the symptoms and prevent further ischemia-related complications.

Anterior Circulation

The EC/IC Bypass Study (again)

The EC/IC Bypass Study was the first randomized trial concerning a surgical procedure. Its primary objective was to determine whether the standard STA-MCA (cortical branch) anastomosis procedure could reduce, despite perioperative stroke and death, subsequent events of stroke and stroke-related death among patients with symptomatic, surgically-inaccessible (to endarterectomy) atherosclerotic stenosis or occlusion of the ICAs or MCAs.[11, 290] Patient eligibility was very well defined with clinical and radiological inclusion criteria. Patients had to have experienced within three months prior to entry TIAs or a minor completed stroke in the carotid system, and a demonstrated MCA or ICA stenosis or occlusion. For a false-positive risk of 5%, a false-negative risk of 10%, and a net surgical benefit of 33% reduction of fatal and non-fatal stroke, a minimum sample size of 442 patients was calculated. Seventy-one centres from all over the world entered a total of 1495 patients. One-hundred and eighteen failed to meet the entry criteria and were excluded, leaving 1377 eligible patients, of whom 714 were randomized to medical treatment alone and 663 to STA-MCA bypass surgery together with medical treatment. No patients were withdrawn and only one patient was lost to follow-up. Both medical and surgical groups were well matched considering entry characteristics, radiological lesions, neurological examination, risk factors and sex. The methodological characteristics have been applauded and cited as a standard for future studies.[223] And indeed the critique on the EC/IC Bypass Study did not comprise its general methodology. So, general agreement has been achieved on the fact that the Study proved STA-MCA bypass surgery + medical treatment to be less effective than medical treatment alone in reducing stroke in the patient group that was investigated.

The Study was performed with the knowledge and technological means of that time. Looking back with the current knowledge and with the ongoing discussion on embolic or hemodynamic causes of stroke, we would definitively have narrowed the entry characteristics. Patients in whom low rCBF may be the cause of their TIAs, or with a decreased perfusion pressure distal to a carotid stenosis, could form a subgroup which may benefit from standard STA-MCA bypass surgery.[6, 85, 125] Clinical stroke scales and general outcome scales should determine whether the increase in regional and vascular blood flow, measured with PET, SPECT, functional MR, or MR Flow correlates with neurologic status.[58]

Aside from the large EC/IC Bypass Study, a lot of other studies have reported on the results of STA-MCA anastomosis for intracranial ICA occlusion or severe, inaccessible, stenosis of the ICA. Most of them only demonstrate the applicability of a certain diagnostic method like rCBF measurements or even the applicability of the bypass procedure itself. Several case reports concerning the effect of STA-MCA anastomosis for ICA occlusions on motor activity, oculopathy and retinopathy have been made public.

Searching the subgroup

After the negative results of the EC/IC Bypass Study, few researchers went on searching for the subgroup of patients with occlusive anterior circulation lesions. Among the most prominent was Sundt who reported in 1985 on 415 bypass procedures for occlusive disease of the carotid system.[286] Within the first 30 days post-operatively, the mortality was 1%, and a 4% development of a new neurologic deficit not present before the operation. In the follow-up strokes always occurred on the side of the vascular lesion in patients with siphon stenosis, MCA stenosis / occlusion. In the largest group of patients-those with an ICA occlusion-a third of the strokes during follow-up occurred on the side opposite the operative procedure. Treated were medically managed patients with persistent ischemic symptoms who were not, because of the location of the occlusive lesions, candidates for a carotid endarterectomy.

Many studies concerning regional cerebral blood flow have been performed. For instance, Vorstrup published in 1986 the results of a ^{133}Xe rCBF acetazolamide induced vasodilatory stress study in 18 patients before and 18 months after EC/IC bypass surgery.[323] His aim was to identify pre-operatively the patients having a reduced CBF due to a compromised collateral circulation. Indeed in half of the patients a limited vasodilatory response ipsilateral to the ICA occlusion was observed, identifying a subgroup of hemodynamically threatened patients. A similar study was reported by Schmiedek in 1994.[241] He concluded that for patients, who have a hemodynamic cerebral ischemia and a severely impaired cerebrovascular reserve capacity, a standard STA-MCA bypass procedure may be the only effective treatment. Especially, in cases when anticoagulation therapy has failed.

At present, still no precise description can be given for the subgroup of patients with anterior circulation occlusions or stenoses who would benefit from EC/IC bypass surgery. The only way to investigate the efficacy of any type of bypass for this subgroup is by a new randomized clinical trial. Grubb and Powers recently published an extensive review on the risk of stroke and the current CBF measurements in patients with symptomatic carotid occlusion.[96, 125] We want to refer to that excellent publication for a review of rCBF measurements performed for revascularization procedures. They concluded that patients with symptomatic carotid occlusion and stage 2 (increased oxygen extraction fraction [OEF]) impairment of cerebral hemodynamics can now be identified using PET scan techniques. It is this group of patients that may benefit the most of EC-IC bypass surgery, and they recommend a new trial of bypass surgery. A new American EC/IC bypass trial has recently started using indications as described by Grubb and Powers.[6, 125]

Posterior Circulation

Vertebrobasilar insufficiency may be caused by a variety of intracranial or extracranial lesions. Stenoses or occlusions of the SubclA, VA, or BA may give rise to TIAs and a complete spectrum of vertebrobasilar insufficiency symptoms like dizziness, vertigo and diplopia. An alternative for anticoagulation therapy may be in the form of revascularization surgery. In conjunction to endarterectomy, repositioning and bypass surgery can be necessary. Depending on the location of the lesion, different donor and recipient vessels can and have been used. The value of prophylactic VA reconstruction or posterior revascularization needed a long time to be established. It must be stressed, though, that the EC/IC Bypass Study did not include posterior circulation lesions, and that the results thus cannot be applied to posterior revascularization procedures. For a very comprehensive review on vertebrobasilar insufficiency, we want to refer to a publication by Ausman in 1985.[28] Some very demanding techniques have been developed for these posterior circulation lesions.

Case Reports

In 1966, Clark and Perry reported on carotid vertebral anastomosis as a technique for repair of the subclavian steal syndrome.[71] In 1976, Ausman reported on OA-PICA bypass surgery for vertebral basilar occlusive disease, followed by VA-PICA bypass using a radial artery graft in 1978.[25] Since then, OA-PICA anastomosis has been an important surgical alternative for the treatment of vertebrobasilar insufficiency. Also in 1976 and 1977, Khodadad reported independent on OA-PICA bypass procedures for multiple extracranial artery occlusions.[173] Ausman reported STA-SCA anastomosis in 1979.[23] This kind of STA-SCA anastomosis has been most commonly used for rostral brain stem ischemia. Corkill was the first to use the VA as recipient vessel in an ECA-VA anastomosis in 1977.[74] Others have used the VA as recipient vessel using as donor vessel the ECA,[228] SubclA,[47, 87] CCA,[56, 87] and the OA.[264] Sundt reported in 1981 two patients who were treated with posterior circulation surgery.[279] One of them showed diffuse BA atherosclerosis on angiography. The left PCA was supplied by the BA. The right PCA was supplied by the right ICA, where no connection to the BA existed. An anastomosis was made between the right PCA and the right SCA, supplying the BA and the left PCA with excellent blood flow.

In a technical report, Hopkins reported in 1982 a patient with bilateral VA occlusion and large SCA who was treated with STA-SCA anastomosis.[149] He stated that indications should include both clinical and angiographic evidence of upper brain stem ischemia. In 1983, Eguchi described a case treated with a double EC/IC bypass using an ECA-MCA M_2 bypass and a ECA-PCA P_3 bypass with interposed saphenous vein grafts.[99] In 1988, Ausman, performed a remarkable tandem bypass by anastomosing the OA to the PICA side-to-side (S-S), and the distal OA to the AICA with an E-S anastomosis to treat a patient who had both VA occluded.[27] Recently, Nagasawa reported two cases in which the posterior temporal artery (PTA) was used as recipient artery to resupply the rostral brain stem. The PTA is a branch of the PCA, so the PCA, BA and SCA were resupplied via the PCA.[215] Recently, we reported a case of A_1-P_1 anastomosis, effectively creating a new PComA.[297]

Clinical Series

In 1981, Berguer and Bauer reported on 14 patients with VA reconstructions using bypasses and reimplantations.[47] All patients but one were relieved of their incapacitating symptoms. Two years later, Berguer and Feldman reviewed 35 VA reconstructions.[48] In 1981, Ausman reported on stenoses of the BA and VA distal to the PICA, treated with OA-AICA bypass surgery.[18] He divided vertebrobasilar lesions into proximal to the PICA and distal to the PICA. He also presented a technical note in which STA-proximal SCA anastomosis was described. In 1982, a series of 8 patients with BA stenosis was reported by Ausman treated with the same procedure.[19]

Pritz reported in 1981 on four types of surgical procedures: proximal VA-CCA repositioning, ECA-mid-cervical VA anastomosis, ECA-distal VA anastomosis, and OA-PICA anastomosis.[228] He also reviewed the literature concerning surgical approaches to the VA. In 1982, Sundt reported his initial experience with ECA-proximal PCA interposition vein grafts for 13 patients with occlusive disease of the BA and one patient with a non-clippable VA aneurysm.[283] Roski reported also in 1982 on 14 patients with OA-PICA anastomosis.[237] Three patients had such sever orthostatic cerebral ischemia, that ambulation was almost impossible. Almost all patients had symptomatic improvements, 8 of them being asymptomatic in follow-up.

Diaz reviewed his experience with 55 patients with vertebrobasilar insufficiency and VA stenosis or occlusion.[87] In 1984, forty-eight patients had been treated with transposition of the VA to the CCA. Of these, 30 underwent transposition alone, and 18 had an associated CCA endarterectomy performed. Seven underwent a VA endarterectomy before transposition. Two patients had saphenous vein grafts, one from the SubclA and one from the CCA to the VA. In two patients the VA was transposed to the thyrocervical trunk, and in a third to the SubclA. The decision to proceed with the reconstruction of the VA was based on the severity of the bilateral VA lesions. Diaz extensively reviewed the literature on the reconstruction of the proximal VA, including the many articles on VA-CCA transpositions

In 1987, Spetzler published on the treatment of extracranial vertebrobasilar disease.[264] The report reviewed his experience with VA-CCA transposition, VA endarterectomy and ECA-VA bypass in 40 patients. He continued with the discussion of 45 patients with intracranial vertebrobasilar disease. In 1990, Ausman produced the results of a very large series of revascularization procedures for vertebrobasilar insufficiency, operating on 83 patients with 85 bypasses to the posterior circulation.[22]

Intracranial aneurysms

The ideal treatment of intracranial aneurysms should eliminate the aneurysm from the circulation while preserving blood flow through parent and branch vessels. This is usually best accomplished by direct clip placement around the aneurysm neck or complete coiling of the aneurysm. Some aneurysms may be unclippable because of their size (giant), shape (fusiform), location (intracavernous), content (thrombus inside), wall (calcifications or plaques). Aneurysms, which the interventional neuroradiologists also find impossible to coil because of many of the reasons mentioned above, are indicated for revascularization procedures with hunterian ligation as recommended by Drake.[94] In their extensive review on revascularization and aneurysm surgery in 1985, Spetzler and Carter still recommended the use of the Selverstone clamp to gradually occlude the ICA in cases of bypass surgery for ICA aneurysms.[262] With the advances in endovascular techniques, this has changed into the more elegant method of endovascular occlusion of the ICA during the days after a bypass procedure.[300] Less frequently, an aneurysm can be coiled after revascularization.

Presently, there are two approaches for revascularization. The selective approach favors revascularization in patients who do not tolerate BTO. Patients with an inadequate cerebrovascular reserve are selected for revascularization. In the universal approach, all patients who will undergo ligation of the parent vessel are selected for revascularization. Sekhar developed a protocol based on the BTO, in which patients with moderate and high risk of stroke are selected for revascularization. Patients with low risk would therefore not receive a possibly unnecessary bypass. However, with the universal approach the patients in the moderate and high risk group would be treated with bypass surgery without the added risk of the BTO. Lawton reviewed the risks of BTO and the selective approach versus the risks of the universal approach.[188] He reported to have found risks of immediate ischemic complications of 2- 22% in literature. Also, he pointed out the risk of delayed ischemic complications, which is probably underestimated, and the risk of de novo formation of aneurysms of the occluded vessel or enlarging of the existent aneurysm. However, he found the universal approach to carry an acute stroke risk of 7 to 10% and a small delayed stroke risk from graft failure, which led him to commend the universal approach. In conventional anastomosis techniques, the risk of immediate or delayed stroke is directly influenced by the occlusion time needed for the distal anastomosis. Using the ELANA technique, we cannot eliminate the need for a test occlusion. However, we find the balance now even more in favor of the universal approach.

Proximal Ligation of Parent Vessels

Proximal balloon ligation in aneurysm treatment has been performed since the late seventies.[110] However, in 1986 McGrail was the first to report occlusion of the ICA after standard STA-MCA bypass using detachable intraluminal balloons.[203] Since then our group indeed prefers to have ligation of vessels performed by the interventional neuroradiologist with intraluminal balloons. The first series with detachable balloons was reported one year later by Fox.[110] The actual balloon catheter procedure is performed with the patient awake and under local anesthesia using femoral artery catheterization. The balloon catheter is introduced into the introducer catheter and placed in the artery at a level below the to-be-occluded site. The balloon is inflated and the patient is carefully monitored for at least 15 minutes to determine hemodynamic tolerance. If occlusion is tolerated, the balloon is detached, and a second balloon is placed below the first one as a fail-safe mechanism. If the test is not tolerated, the balloon is deflated and removed, resulting in immediate reversal of neurological deficit. When the patient does not show any neurological deficit, but the interventional radiologist notices a delay of venous outflow at the side of the balloon-occlusion, the balloon is deflated and the procedure is cancelled, because the chance of a stroke may be very high.[316]

Using the universal approach gives us the opportunity to test the patency of the bypass prior to, and not after, the occlusion of the ICA. During the balloon occlusion by the interventional radiologist tolerance of ICA occlusion is easily verified by simply asking the patient. Exclusion of the aneurysm also can be verified immediately.

Proximal Ligation and Revascularization

Anterior Circulation

Case Reports

Yasargil first reported the use of standard STA-MCA anastomosis for maintaining flow in an electively ligated MCA in the management of an aneurysm.[344] Several reports followed. Spetzler also performed STA-MCA anastomosis in patients with anterior circulation aneurysms.[265] Ausman was the first to report CCA-MCA bypass anastomosis with gradual occlusion of the distal CCA because of an ICA aneurysm extending into the CCA bifurcation.[26] A saphenous graft was connected with an E-S anastomosis to the CCA and with a standard E-S anastomosis to a cortical branch of the MCA. The patient was discharged without complications after the second operation, in which the completely occluded CCA and the aneurysm were resected. Dolenc reported three cases of direct reconstruction of the ICA in the treatment of cavernous ICA aneurysms via extensive cavernous sinus surgery.[88] In one case, the ICA remained patent and the patient resumed his previous job. The two other patients died of non-bypass related causes.

Clinical Series

Hopkins treated 11 patients with good results.[150] Another series of patients treated with standard STA-MCA bypass surgery was reported in 1980 by Gelber and Sundt.[114] Six patients with intracavernous aneurysms, one patient with a high petrous aneurysm, one patient with an aneurysm arising from the bifurcation, and two patients with carotid-ophthalmic aneurysms were studied with pre-operative and post-operative rCBF (Xe^{-133}) techniques. Post-operative angiograms showed all but one bypass to be patent, for in one patient the angiogram was not obtained for family financial reasons. Despite the high patency rate, three patients suffered from ischemic complications after ligation of the ICA. Similar studies have been published with varying results. Spetzler reported standard STA-MCA bypass surgery in 13 patients with ICA aneurysms, also in 1980.[268] All bypasses were patent, and, post-operatively, no patients experienced immediate or delayed ischemic complications.

Five patients with intracavernous ICA aneurysms were reported by Silvani in 1985 to be treated with standard STA-MCA bypass surgery and Selverstone clamp occlusion of the ICA.[256] All bypasses remained patent. One patient completely recovered, three patients improved, but one patient died four days after complete ICA clamp occlusion. Sundt reviewed in 1986 the results and operative techniques for 19 patients with 20 distal extracranial ICA aneurysms. Five patients were treated with direct E-E ICA anastomosis after resection of the aneurysm. Seven were treated with an interposition vein graft, and four with a standard STA-MCA bypass. All patients but one had excellent long-term follow-up results.[280] De Jong published a series of 26 patients treated with EC/IC bypass and selective ligation of the parent artery.[81] In 11 patients, ligation was not necessary because the aneurysm could be clipped while the bypass only existed as backup, with excellent outcome. Ten patients tolerated the intra-operative ligation without clinical or EEG disturbances, with excellent outcome. Five patients remained symptomatic, however some improved remarkably. In 1990, Serbinenko described nine patients treated for ICA aneurysms using EC/IC bypass surgery and balloon occlusion.[254] All but one patient showed considerable clinical improvements. In the same year, Sekhar published on 6 patients with cavernous ICA aneurysms treated with petrous-supraclinoid ICA bypass with a saphenous graft.[250] It is important to note that the time required performing anastomosis ranged from 60 to 120 minutes. However, in one case the ICA was occluded for 5 hours because of thrombosis at the proximal anastomotic end of the graft. The anastomosis was reconstructed with good result. Spetzler reported the same procedure in 18 patients also in 1990.[263] Clinical outcome was improved in 16 patients, the other two remained stable. Patency was achieved for all but one patient, who showed no deficits from her occluded bypass. In 1994, a special protocol for patients with ICA aneurysms treated with STA-MCA bypass was described by Barnett for 7 patients.[37] All patients presented with nerve paresis (III, IV, VI). Three patients achieved full recovery, four improved with symptoms remaining. In 1996, Lawton described a series of 63 aneurysms in 61 patients treated with revascularization techniques.[188] Fifty-seven patients (93%) had a moderate to good outcome with a patency rate of 95%.

Six patients with intracavernous aneurysms, 2 with carotid-ophthalmic aneurysms and 1 with a large PComA aneurysm were treated with STA-MCA and ECA-SVG-MCA bypass surgery by Hacein-Bey in 1997, because the patients did not tolerate the ICA test occlusion.[131] Post-operatively all patients showed clinical improvement despite an occluded STA-MCA bypass in one patient. Recently, Sekhar published on 133 patients, of whom 100 (73%) had a good clinical outcome after a revascularization procedure.[248]

Posterior Circulation

Depending on the site of the aneurysm, bypasses have been made from and to several arteries of the vertebral-basilar circulation. The PCA has frequently been used as a recipient vessel, especially for PCA aneurysms. Sundt reported in 1981, a case of SCA-distal PCA anastomosis after resection of a giant PCA aneurysm.[279] Hopkins reported in 1983 combined use of EC/IC bypass and BA ligation for giant BA aneurysms.[148] End-to-side anastomosis between the STA and the PCA was performed twice and the BA was ligated using a Drake-style tourniquet by passing 2-0 Prolene around the BA at the origin of the aneurysm proximal to the PCAs. In 1984, Heros and Ameri operated on a similar case but used a saphenous vein between the ECA and the PCA.[142] The patient died from rupture of the aneurysm just before the planned occlusion of the BA. In 1992, Wakui performed ECA-P_2 anastomosis using a radial artery graft for treatment of a VA aneurysm.[325] Graft patency was confirmed using Doppler US. Vishteh reported two cases of OA-distal PCA anastomosis followed by coil occlusion of a VA aneurysm and a PICA aneurysm. Bypass to PICA for aneurysm surgery came only recently into view. In order to trap a VA aneurysm, Ausman described a PICA to PICA anastomosis in 1990.[21] Proximal VA ligation was achieved, after which the aneurysm filled from the opposite vertebrobasilar junction. End-to-end anastomosis of both PICAs ensured trapping of the aneurysm. Khayata reported another PICA-PICA anastomosis, in 1994, in a 5 year old boy with a VA-PICA aneurysm.[172] Hamada reported also in 1996 the reconstruction of the PICA in the treatment of giant aneurysms of the VA and the PICA.[136]

Hadley published on OA to VA bypass surgery in 1985 for a pseudoaneurysm of the distal VA.[133] In 1986, Sundt described the use of saphenous bypass grafts for giant aneurysms in the posterior circulation.[284] Lee and Sekhar operated on 3 patients with aneurysms of the MCA and VA using total excision, interposition of the STA and arterial reimplantations in 1996.[195] Guided by 3D CT angiography and repeated cerebral angiography, patent revascularization was performed and confirmed by Doppler US. Next to the technical difficulties, the disadvantage of prolonged temporary occlusion was considered and reviewed in the literature. Direct attack of the BA was reported in 1998, by Sekhar when he interposed a saphenous vein graft between the ICA and the BA using a special hypothermic circulatory arrest technique in a 15 year old female with a giant BA aneurysm just distal to the origin of the PICA and just proximal to the origin of both AICAs.[246] After the failure of an initial ICA-PCA saphenous graft anastomosis, optimal flow to the BA was achieved using the ICA-BA revascularization. It is noteworthy that this operation took three days, of which the patient was under deep narcosis during the nights also. In a comment, Spetzler and David report that they might have preferred a bypass to the superior cerebellar or PCA. Dr. Heros appraised the anastomosis to the BA, which he considered impossible before. Hypothermic techniques were used further by Sullivan,[277] Sekhar in 1999,[244] and Kawaguchi and Sekhar in 2000.[171] Recently, we reported the successful use of the ELANA technique in the creation of an EC-IC bypass to the BA (see Chapter 10).[271]

Other Vascular Lesions

Arterial Dissections

Morgan reported bypass surgery for carotid or vertebral artery dissections in 6 patients after the initial reports by Gratzl in 1973.[124, 210] Aim of the bypass was high flow and avoidance of an abnormal watershed area. Five grafts were proximally anastomosed to the CCA and distally with an E-E anastomosis to the ICA proximal of the PComA and two grafts were distally anastomosed to the VA. Morgan stated that their six patients formed a subgroup with a high risk of stroke in which a prophylaxis may be provided in the form of an EC/IC bypass. Sundt operated in 1986 on 9 ICA dissections using ICA E-E anastomoses, venous grafts, and conventional EC/IC bypasses.[284] In 1996, Alimi reported 6 cases of venous graft restoration of the ICA in the skull base after blunt injury to the ICA.[10]

Blunt injury may cause a false aneurysm, stenosis or a dissection, leading to neurologic deficit. Vishteh reported in 1998 a long term study of 13 patients who underwent revascularization surgery for symptomatic traumatic ICA dissection.[321] STA-MCA bypass, cervical-to-petrous ICA bypass, cervical-to-MCA M_2 bypass and petrous-to-supraclinoid ICA bypass was performed under Doppler ultrasound. Vishteh stated that revascularization is a treatment option for patients with systemic traumatic injuries, contraindicating anticoagulation and for patients who continue to have neurological ischemic deficits. Samson and Horowitz commented on this article pointing out the difficulty to determine the need for high flow bypasses as opposed to low flow (STA-MCA) bypasses without the use of CBF evaluation.

Venous reconstruction

Reconstruction of venous structures is not considered cerebral revascularization. But the authors want to mention some interesting surgical procedures. In 1980, Sindou reported the insertion of a bypass graft between the right transverse sinus and the superficial jugular vein to re-establish intracranial venous circulation after occlusions of the intracranial sinuses.[257] Sekhar reported SVG bypass of the sigmoid sinus and jugular bulb during the removal of glomus jugulare tumours in 1997.[251] Reconstruction of the vein of Labbé was reported by Morita in 1998.[211]

Revascularization Procedures in Children

Too often a young patient presenting with subarachnoidal haemorrhage has not been correctly diagnosed, missing aneurysms in the differential diagnosis. With current microsurgical and neuroanesthesia techniques, excellent results can be achieved in those patients. Meyer reported on 4 bypass procedures and 2 direct excisions with E-E anastomosis in 23 patients under the age of 18 in 1989.[207] In 1988, Ausman reported a special survey on cerebrovascular occlusive disease in 8 children treated with STA-MCA bypass with good result.[20] In 1990, Guha published on a 7 year old patient with multiple aneurysms of the petrous-cavernous ICA and the VA-BA junction.[127] Prophylactic ligation of the ICA posed a considerable risk. Among the alternatives for treatment, an initial STA-MCA bypass and ICA ligation would possibly have increased the risk of rupture of an aneurysm of the posterior circulation. The child was elected to be treated conservatively.

Cranial base tumors

Involvement of the ICA or VA may require resection of part of these vessels along with tumor resection, either because the tumor cannot be dissected free in case of benign tumors, or with malignant tumors it may be necessary to resect part of the vessel if the tumor is not safely resectable and thus leave a small rim of tumor attached to the vessel.

In their review in 1999, Sekhar and Kalavakonda describe the approach to patients with tumours.[247] They changed the philosophy to include grafting from young patients or patients who failed BTO to any patient for whom the vessel needed to be resected during tumour resection. For patients with benign tumours or chordomas, grafting was performed for patients of <60 years when the artery was encased by tumour and could not be dissected free at surgery. Arterial resection and replacement were also performed for a number of patients with recurrent tumours (after previous surgery and/ or radiotherapy), in attempts to eradicate the tumours. Indications for vascular resection included: Tumour encasement of the artery or exposure of the carotid artery to the nasopharynx after tumour removal.

Conley was the first to consider vein grafts to the carotid arteries in the treatment of tumours of the neck.[73] STA-MCA anastomosis for the treatment of skull base tumours was first reported in 1984 by Moritake.[212] The use of the Ultrasonic Doppler Flow meter showed the expected increase in flow after ligation of the parent vessel. Urken reported ICA reconstruction using an autogenous vein in 1985.[309] As Sekhar reported in 1986, almost all skull base tumours may be located around a major cerebral vessel.[249] He reported on the exposure and management of the petrous and upper cervical ICA in 29 patients, 27 of whom had a cranial base tumour. In four cases ICA reconstruction using a venous graft was considered necessary, and although three remained with a mild disability all had a good outcome.

In 1990, Miyazaki treated 2 patients with high-cervical paraganglioma using ICA reconstruction with a interposed SVG with excellent results.[209] In 1992, Sen and Sekhar published on direct vein graft reconstruction of the ICA in 30 patients, with 27 patients having a tumour involving the petrous or cavernous ICA.[252] They extensively review the literature on vein graft reconstruction of the ICA, risk of ICA ligation and discuss the options for revascularization. Lawton recommended in 1995, that the ICA should not be considered a limitation to radical tumour resection, because the ICA can be safely reconstructed with an appropriate bypass procedure.[189] One such procedure is the Excimer Laser-Assisted Non-occlusive Anastomosis technique (ELANA) as reported by Graamans and Tulleken in 1998 for the removal of a large nasopharyngeal angiofibroma which encased and was supplied by the ICA.[123] A case report by Kinugasa in 1993 mentioned a special technique of STA graft between ACA A2 – A3 segment after excision of a neuroblastoma with the A2 segments of both ACAs.[176]

Chapter 3

Diagnostic and Surgical Procedures

Cerebral revascularization

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Adv Tech Stand Neurosurg. 2003;28:145-225. Review.

Diagnostic and Surgical Procedures

In his monograph on the EC/IC bypass operation in 1979, Kletter stated that in the literature neurological examination was taken for granted, and thus rarely specifically mentioned.[177] At the time of this writing that statement still holds. Although almost every author mentions improvement or decline of mental status, most of them do not state the type of neuropsychological examination performed. Very few trials are based only on neurological or neuropsychological data. In 1982, Binder studied the neuropsychological effect of EC/IC bypass on 19 patients with a history of TIAs or stroke observing benefit from surgery in most patients.[50] In 1984, Drinkwater reported a 38 patients study using the Halstead-Reitan neuropsychological tests in order to compare the results with the outcome of the study by Perry in 1975,[222] on 20 patients undergoing carotid endarterectomy.[96] Because of the lack of control group, the only strong conclusion to be made was that, in terms of cerebral function, EC/IC bypass (STA-MCA) is less successful than endarterectomy.

Angiography

Selective 4-vessel angiograms are performed pre- and post-operatively to assess the anatomy and collateral circulation and to confirm the patency of the bypass. Angiography is still the gold standard. Visualizing the luminal morphology from the aortic arch to the smallest cortical branches of the intracranial vessels, both site and cause of a vascular lesion can be demonstrated.

Sekhar and Kalavakonda recommend the use of CBF studies with or without BTO to establish the need for a bypass procedure in patients with symptoms of cerebral ischemia. We routinely perform a balloon test occlusion to assess collateral circulation with angiographic control. A balloon catheter is introduced by the neuroradiologists into the femoral artery into the ICA. With the patient fully conscious, the balloon is inflated to occlude the ICA for 15 minutes, which is documented angiographically. If the patient remains asymptomatic for 15 minutes, and the venous outflow does not become asymmetric, we conclude that he has well developed collaterals.[316] We do not perform the BTO of the cervical VA, as we prefer 4-vessel angiography there only. Other studies may be of value, including TCD and EEG. Some would recommend psychological testing, especially in patients showing dementia from cerebrovascular disease.

Transcranial Doppler Flow Velocity

Transcranial Doppler (TCD) was developed by Aaslid and first described in 1982.[3] This was the first non-invasive method to view the cerebropetal arteries real-time. We have specialized technicians working full-time with the TCD instrument, as TCD requires a significant under-

Previous page:
Intraoperative image of professor Tulleken during a cerebral revascularization procedure.

Transcranial Doppler
The system consists of a 2MHz pulse-wave Doppler probe that has to be directed towards the target blood vessel through an "acoustic window" in the skull, where the density of the bone is thin enough to permit the ultrasound penetration. Usually the transtemporal approach permits the technician to observe the circle of Willis from a lateral view. Towards the observer, the M1 can be seen, as well as the intracranial ICA, the A1, the P1, the anterior communicating and the posterior communicating artery. Once the targeted vessel has been found, using a spectral analyzer will display the direction of flow, the peak velocity, mean velocity, and the beam depth.

standing of the normal and variant anatomy of the circle of Willis. However, even with these highly experienced people the velocity flow measurements in the same person have a deviation of 10%. Also, up to 15% of patients are very difficult to measure as they have inaccessible acoustic windows. In 1986, Sundt estimated volume flow by determination of the diameter of the graft on angiography.[284] Nagasawa estimated the volume flow of the posterior circulation in 2000.[214] As flow estimation using TCD and angiography has not been validated yet, the use of TCD is still restricted to the observation of patency, and observing the velocity of the blood flow.

Magnetic Resonance Flow Quantification

A new non-invasive technique for quantitative flow measurements is with magnetic resonance techniques (MR). With MR, randomly oriented tissue protons are aligned by a powerful, uniform magnetic field, (in our Hospital this field is generated by a 1.5 Tesla Philips System, soon to be replaced by a 3 Tesla System) producing an equilibrium "magnetization" of the tissue. This magnetization is then excited by properly tuned radio-frequency (RF) pulses. As the nuclei recover to equilibrium, the produced RF signals are proportional to the magnitude of the initial alignment. The contrast between tissues develops as a result of the different rates at which nuclei relax with the magnetic field. The positions of the protons are localized during this process by a sophisticated way of encoding the phase and frequency of the protons with spatially dependent magnetic fields, called gradients. The signals are measured, or read out, after a user-determined time has elapsed from the initial RF excitation. The signal is transformed into an image by the computer using a mathematical process called the Fourier transformation. Using MR techniques, moving blood can be detected.

Magentic Resonance Flow Quantification
There are two major mechanisms by which moving blood affects the MR signal. These are "Time-of-flight effect" and "Phase contrast effect". Both can be used to generate MR angiograms, but only the Phase effect is used in quantitative flowmetry. Phase-contrast angiographic (PCA) flowmetry is based on the principle that the phases of moving spins develop a phase shift as they move through a magnetic field in the presence of a bipolar opposing gradient. Stationary spins develop no phase shift, whereas spins moving along the direction of the gradients do develop a phase shift. The amount of phase shift is related to the flow velocity. The Phase shift – flow velocity relation is used to calculate volume flow by multiplying the average velocity (cm/s) with the pixel area (cm^2), after which the volume flow rate through the pixel is obtained in ml per second (ml/sec). By summing the flow in the pixels that cover a blood vessel the total volume flow rate in that vessel is obtained. In previous phantom and patient studies in the University Hospital Utrecht, MR flow measurements using PCA techniques (MRF) has been proven to produce reliable and reproducible results in volume flow measurements. These measurements correlated well with flow rates determined by Ultrasound flowmetry techniques.[52]

Singer and Crooks used phase difference MRI techniques in men in 1983.[258] In phantom studies by Bakker in 1995, MRF has been proven to produce reliable and reproducible results in volume flow measurements.[32] These measurements correlated well with flow rates determined with USF, as studied by Bosman in 1996.[52] In a study by van Everdingen in 1997 for the Dutch EC/IC Bypass Study Group, fifty-four patients with TIA's or minor ischemic neurological deficits and ICA occlusion, and 16 control subjects underwent MRF through the CCA, BA, ICA and MCA.[315] In the control subjects, no significant differences in flow were found between the left and right ECA, ICA, or MCA. In patients with symptomatic unilateral ICA occlusion, flow in the contralateral ICA and in the BA was increased, but flow in both MCA's was decreased. The contralateral ICA appeared to be the main collateral artery, and together with the BA the flow compensation of the ICA was sufficient to keep total cerebropetal flow within normal limits. A lot of research is being done to increase the resolution of MRF so that smaller vessels can be assessed.

Cerebral Blood Flow Measurements

Many regional cerebral blood flow measurements have been performed, both to assess the applicability of such measurements in bypass surgery, and to find that special group of patients who need such an operation. Current techniques in evaluating flow are intermittent, and presume constant CBF over the clearance time. These comprise inhalation or injected radioactive Xe133 washout, stable Xenon CT, SPECT and PET scanning. Normal mean whole brain CBF values range from 50 to 55 ml/100g per minute.

Determining rCBF by Inhalation or injected Xe133 washout is based on the principle that the rate of uptake of the gas is proportional to the blood flow in tissue. The washout of the gas can then be detected by sensors placed over the skull and the speed of the washout is related to the amount of blood flow. Most systems use multiple sensors over each hemisphere; however, it is possible to use this technique at the bedside. Already in 1976, Schmiedek published the first large series (110 patients, of whom 53 were treated with STA-MCA anastomosis) to study the applicability of Xe133 rCBF in the selection of patients.[124] Similar studies were carried out.[82, 83, 186, 287, 324, 349] Also, several studies with Xe133 and autoregulation manipulation have been carried out.[12] The lack of CO2 reactivity could point to a subgroup of patients.[51, 135] However, although these publications all found various relations between rCBF and clinical outcome, it remained very difficult to select patients based on Xe133 rCBF techniques.

Stable Xenon CT involves inhalation of non-radioactive Xenon as a contrast agent, providing information about tissue perfusion in correlation with CT images, which are enhanced by the Xenon. The inhalation of gas has specific side-effects, including anaesthesia, sedation and alterations in respiratory rate. Yonas confirmed in 1985 the applicability of this technique for bypass surgery.[347] A similar applicability study was performed by Beristain in 1996.[49]

Single photon emission computed tomography (SPECT) is a non-invasive method using radiopharmaceuticals or radioactive gases which are extracted from the blood into the brain. The regional emission of photons can be monitored with detectors or gamma cameras. The main disadvantage is that SPECT only gives qualitative information of rCBF.[216, 292] As with Stable Xenon CT, only the applicability of SPECT has been proven. Like with Xenon inhalation studies, autoregulation has also been assessed using SPECT, in the search for eligible patients. Applicability for bypass surgery was confirmed, however, without a clear definition of which patients would benefit from bypass surgery.[43, 138]

Positron emission tomography was developed to observe rCBF in 3 dimensions, using inert, stable compounds like labelled water, labelled CO2, or labelled methane, based on the same principle as Xenon inhalation or SPECT techniques. However, PET scans are very costly because the labelling of the compounds requires a cyclotron. Many different results have been published, proving applicability of PET,[41, 227] benefit of bypass surgery,[238] no results, and even worsening of oxygen extraction after bypass surgery.[192] Post-operative fall of CBV was observed in a study of 12 patients by Gibbs.[118] He found that CBF is rarely increased after standard STA-MCA bypass surgery, however, post-operative fall of total cerebral blood volume (CBV) is consistent with improvement of cerebral perfusion pressure (CPP). Improvement of CPP is important as patients with "misery" perfusion syndrome (inadequate perfusion relative to the oxygen requirements) may form the long-searched-for group of patients eligible for cerebral bypass surgery.[41] This was confirmed in a larger study (29 patients) by Powers in 1989.[226]

Thermal diffusion flowmetry is based on the principle of applying a thermal gradient directly to the cerebral cortex. Heat is conducted from the heating element by the blood flow in the cortical capillary bed. The amount of energy necessary to keep the heating element at a constant temperature is related to the blood flow. Carter evaluated cortical blood flow, in 1984, using a thermal diffusion flow probe in 25 EC/IC bypass operations.[62] The probe consisted of a Peltier stack which created a thermal gradient between two gold plates. The temperature difference was recorded and this has been shown to correlate with cortical blood flow measured with Xe_{133} clearance. This technique measured grey matter flow or the fast component of Xe_{133} clearance. This is much more variable than whole brain flow. During temporary occlusion of the cortical vessel, no significant changes in cortical blood flow were identified, most likely due to extensive collateral cortical vessels. Carter concluded that EC/IC bypass acutely increases cortical flow in regions of reduced flow, that the increase is not adequate to provide normal flow to ischemic areas, and that a wide variability of rCBF exists between patients and within the same operative field in patients with cerebral ischemia.

In 1996, Mendelowitsch confirmed the applicability of microdialysis in a study on 9 patients with an aneurysm to monitor metabolism in the cerebral cortex during EC/IC bypass operation. Changes of levels in the extracellular fluid (ECF) of various parameters can be monitored continuously, including pH, glucose, lactate, glutamate and some antioxidants. Although increased metabolic levels were observed, significance remained to be investigated due to the small sample size.[204, 205]

Pre-operative selection of vessels

We have classified cerebral revascularization procedures into direct reconstruction of blood vessels and indirect revascularization as reported by Sekhar and Kalavakonda in 1999. However, because of the large variety of forms of EC-IC bypass that have become possible, we decided to let go of the classification of EC-IC bypass procedures in low-flow, moderate-flow, and high-flow bypass procedures. Depending on the selected donor vessel, recipient vessel, and graft the expected and observed flow through an EC-IC bypass may result in everything from low to high.

Direct reconstruction by end-to-end anastomosis or graft interposition

Direct reconstruction is usually performed for unexpected vascular injuries during aneurysm or tumor surgery. In such cases it is clear that the injured vessel needs to be reconstructed. However, several vascular groups use direct reconstruction of the ICA to treat cervical or cavernous aneurysms.[9] We do not have a lot of experience in these reconstruction procedures, because we would make a prophylactic bypass before attacking an aneurysm or tumor that might give problems. Using the ELANA technique, we are able to make such a bypass without occluding any blood vessels, thus preventing any ischemic problems. After that, we proceed in treating the aneurysm or tumor surgically or with endovascular techniques.

Indirect revascularization by anastomosis or graft

It is important to observe the presence of collaterals by performing a balloon test occlusion of the ICA. If indeed some collaterals are present or only distal / cortical branches are available for recipient artery, then a distal branch of the ECA can be used in order to prevent a flow discrepancy between donor artery and recipient vessel. We used the distal STA or the OA when performing revascularization without a venous graft. The selection of the recipient vessel is, of course, completely dependent on the pathology. Pre-operatively, we select the recipient vessel using the angiograms and intra-operatively on site. For most revascularization procedures, we tend to use a high flow donor vessel. With conventional techniques, the ECA has been used frequently. End-to-side anastomosis to the ECA ensures high flow through the bypass, especially when treating an intracavernous aneurysm. The distal branches, like the STA or the OA, usually will facilitate a moderate flow, which, in time, may result in high flow because of the adaptation to the increased blood flow. However, for some intracranial aneurysms, and posterior circulation ischemia we have used the paraclinioid ICA, the ICA bifurcation, the proximal ACA A1 segment, or the proximal M1 segment as donor vessel, to ensure sufficient flow. The risk of ischemic complications, due to making an anastomosis with these major vessels, is virtually non-existent, because of the ELANA technique. It is obvious that, when treating an intracavernous aneurysm with hunterian ligation, the recipient anastomosis site should be as proximal as possible, to ensure a flow which can compensate for the flow through the ICA. We found that the ICA distally from the aneurysm is the best recipient vessel in procedures, when the ELANA technique can be used.

Selection of graft

The main advantage of using the great saphenous vein as graft (SVG) is its greater length. Especially, when performing ECA-to-intracranial vessel procedures, harvesting a length of 40 cm is not unusual. This is simply not possible when using the radial artery. The larger diameter (3-4 mm) of the SVG also brings higher flows than observed with the radial artery (2-3 mm diameter). We seldom use the radial artery (RA). When we harvest the great saphenous vein, we take great care to ligate every side branch and to closure of the wound. Thus far, we have not observed any problems whatsoever. In cases of vertebral basilar circulation insufficiency, Ausman stated that the best revascularization procedure is one that provides the widest channel of flow.[16] Also, revascularization should be done distal to the stenotic or occluding lesion. The OA-PICA bypass was the first posterior circulation bypass procedure performed, in order to provide additional circulation to a compromised posterior circulation. Usually, this procedure is performed to treat patients with angiographically proven VA stenosis or occlusions. Depending on the stenotic or occluded vessel, different recipient vessels have been used in the posterior circulation and a vein graft can be used to achieve higher flows. The radial artery (RA) is more suited for short low flow bypass surgery because less turbulence is created. The main disadvantage is vasospasm, which can be solved using the “pressure distension technique”.[248] We also like the firmer consistency of the RA when handling it during the anastomosis procedure.

Surgical procedures

Anesthesia and intra-operative monitoring.

Neuroanesthesia should emphasize brain relaxation, fluid hemostasis, and adequate oxygenation.[248] Pre-medication for surgery includes sedation. Prophylactic antibiotic should be used, which is started just before surgery and continued post-operatively for 48 hours. Like others, we also use Mannitol when the intracranial pressure is elevated.

Hypothermic techniques

Sekhar reported on extensive hypothermic and cardiac arrest techniques when occlusion of the ICA was necessary.[277] The use of the ELANA technique has eliminated the need for such strategies for us, and therefore our anesthetists do not have any experience with such procedures in combination with cerebral revascularization. However, it is a great help to have specialized vascular neuro-anesthetists working in close cooperation with the vascular neurosurgeon. Also Sekhar recommends administering 1000 to 2000 units of heparin intravenously before vascular occlusion. The ELANA technique does not give rise to immediate thrombus forming, so we usually only administer Heparin locally. However, directly after the completion of the bypass, we give the patient 500 to 1000 units Heparin intravenously. We do not maintain the patient on Heparin for a week, like Sekhar and Kalavakonda, but we do maintain them on anti-thrombotic agents like aspirin for at least 2 weeks.[277]

Intra-operative angiography

The use of intra-operative angiography has been propagated since 1992 by Sekhar during bypass surgery.[252] This allows the recognition, exact location and immediate correction of graft-related problems. The neuroradiologist places a femoral artery sheath at the beginning of the operation. Arteriograms are obtained after the grafting procedure and observed using different views. Although the speed of blood flow can be observed, no exact flow measurements through the blood vessel can be performed. However, there is no doubt that intra-operative angiography indeed is a big help during bypass surgery so intra-operative angiography for revascularization is still an item on our wishing list.

Doppler and Ultrasound techniques

In 1980, Moritake used TCD to assess pre-, intra-, and post-operative hemodynamics in 24 STA-MCA anastomoses. Patency of blood vessels was very easily observable, non-invasive and in real-time. The main disadvantage is that only flow velocity, and not volume flow, can be measured. We recommend the use of a micro-Doppler intra-operatively, because it provides a quick and non-invasive qualitative flow measurement. However, for intra-operative flow measurements, we use the Ultrasound Flow (USF) meter (Transonic Systems, Inc, Ithaca, NY). This device for flow rate measurements was introduced in 1995 for use with haemodialysis patients. The benefits of a direct method of flow measuring during cerebral bypass surgery were quickly understood by Dr. van der Zwan.[313] It consists of two parts: a bench-top electronic flow detection unit and volume flow sensing probes. The latter comes in two styles of which the perivascular flow probe is used here. The flow recording system uses an ultrasonic transit-time principle to sense liquid volume flow in vessels largely independent of flow velocity, turbulence and hematocrit. Charbel published the various techniques of USF in neurosurgery in 1998.[65, 66] As

Ultrasound Flow Measurements
A flow probe consists of two ultrasonic transducers and a fixed reflector. The transducers are positioned on one side of the vessel and the reflector is positioned between the two transducers on the opposite side of the vessel. The flow meter directs a flow probe through the following cycles: An electrical excitation causes the downstream transducer to emit a plane wave of ultrasound. This ultrasonic wave intersects the vessel in the upstream direction, then bounces off the "acoustic reflector" and again intersects the vessel and is received by the upstream transducer where it is converted into electrical signals. From these signals, the flow meter then derives an accurate measure of the "transit time". The same transmit-receive sequence of the upstream cycle is repeated, but with the transmitting and receiving functions of the transducers reversed so that the flow under study is bisected by an ultrasonic wave in the downstream direction. Again, the flow meter derives an accurate measure of transit time. The difference of transit times is a measure of volume flow rather than velocity. One ray of the ultrasonic beam undergoes a phase shift in transit time proportional to the average velocity of the liquid times the path length over which this velocity is encountered. With wide-beam ultrasonic illumination, the receiving transducer adds these products over the vessel's full width and yields volume flow (mean velocity mm/min * mm^2 = ml/min).

Figure 3.1.
Setup of our operation room. At the head of the patient the neurosurgeon is standing or sitting (most right in the figure). On his right hand he has the assisting neurosurgeon. The surgeon, who is harvesting the graft (most left in the figure), is on the right side of the assisting nurse, so she can offer service to all. The sterile field ends on the right side of the surgeon working at the leg. Next to him, the anaesthesists are working, located at the feet of the patient. They often need to walk to the head of the patient to observe him more closely.

the invasive nature of USF makes obtaining standard flow values of intracerebral arteries quite difficult, its main use is restricted to intra-operative flowmetry in patients. However, the possibility to quantify the blood flow is of great help in the evaluation of the bypass. The perivascular flow probes are designed to measure instantaneous and average volume flow in exposed vessels. In 1996 Bosman described the in vivo validation of this new flowmetry technique.[52] They found a mean coefficient of variation of 13.4 +/- 6.8%

Operative position and approaches

In our operating room, we have the anesthetists sitting at the feet of the patient. The surgeon is positioned at the head of the patient with the assisting surgeon on his right hand side (see Figure 3.1.). The operating nurse is standing right next to the assistant, in a position to help both the surgeons at the head of the patient as well as the surgeons who harvest the vein from the leg. The operation microscope (Zeiss) is positioned on the left side of the patient and can be used for the intracranial procedures and for the procedures in the neck. The patient lies on his back with his head turned to the contralateral side, so that the side of the bypass is easily accessible. The hair is shaved and both the STA and the OA are palpated. We usually also include the part of the neck into the sterile field, in case a really high flow is needed. The patient is placed in a four-point head fixation system. After extensive preparation and draping with iodine the skin incision is made just posterior alongside the STA. In cases of STA-MCA cortical branch bypass procedures, the STA is dissected free. The temporalis muscle and fascia are incised for the craniotomy. A small craniotomy of 3-4 cm is made. The dura is opened and held back with some dural tack-up stitches. After careful inspection of the cortex a recipient vessel of sufficient size (at least 1 mm in diameter and with a length of at least 7 mm) is chosen and prepared for anastomosis. In our cases we perform the ELANA technique on the proximal cerebral arteries. Therefore we need a craniotomy for a pterional approach. The skin incision can be elongated to reach into the neck for the anastomosis with the ECA. We prefer not to tunnel a high flow bypass because we want to be able to visually inspect the whole bypass tract. Using a standard pterional approach the intracranial ICA is exposed. For posterior revascularization procedures different positions have been described. Ausman reported that he prefers the patient horizontally and in the three-quarter prone position, allowing for the surgeon to use the microscope, avoiding intra-operative hypotension, and because it is more convenient for the patient.[16]

Graft preparation

The saphenous vein is harvested from the lower limb from the ankle upward to the thigh. External rotation from the hip facilitates the approach. Just anterior of the medial malleolus an incision is made and the saphenous vein can be exposed with a longitudinal incision. The vein is harvested with as little manipulation as possible to avoid vascular injury and potential thrombosis. We ligate every side branch, tiny branches are coagulated and large ones are clipped, while working upward until we have exposed a length of about 40 cm. Distal insertion of a small catheter and gently flushing with heparin solution into the vein in the flow direction while the vein is still in situ and with a temporary clamp proximal, helps finding all side branches. It is recommended by Sundt to mark the vein with a marker superficially before dissection to avoid later torsion.[76] A mini vascular loop can be used for control and gentle elevation. We take the vein out and flush the lumen with heparin solution without distending it too much. Any leaks are repaired with a suture 8/0 Prolene. Careful note is made of the flow direction and a marker is place at the distal end. We preserve the vein in heparin solution until it is needed.

Using Papaverin or not

Sekhar and Kalavakonda report covering of the vein with cottonoids soaked in papaverin to relieve spasm of the vein.[248] Also, they administer methylprednison intravenously to protect the venous endothelium from the arterial blood flow. We do not perform such actions and have not seen any problems. The wound is closed using Vicryl 2/0 or 3/0 subcutaneously and staples to close the skin, leaving a suction-drain to prevent hematoma formation. One team of surgeons may harvest the vein graft while the other team is opening the craniotomy or the neck-dissection. Veins stored in heparinized electrolyte solution demonstrated a normal relaxed appearance, in contrast to veins soaked in autologous heparinized blood.[64] Gundry stated in 1980 that cooling of the venous graft should be avoided.[129] Distension with pressures higher than 100 mm Hg, by injecting saline into the occluded vessel, will also not benefit the graft. Catinella observed that the vein wall is extremely sensitive to dissection, manipulation, or introduction of fixative solutions and reacts to such stimuli with severe contraction, resulting not only in a diminished luminal diameter, but also protrusion of endothelial cells into the lumen.[64] In the discussion following the article, Page comments that he and his associates drop the venous graft in a papaverin solution, and use the blood-papaverin medium to distend the vein. In response to Page's comment, Catinella reported that in the operating room, they prepare a heparin and papaverin solution and allow the formed precipitate to settle to the bottom. Following this, aliquots of the solution are drawn up in syringes without disturbing the precipitate. The solution is then transferred to a basin in which the vein will be placed prior to its grafting. Gundry reported also that prevention of smooth muscle spasm by the use of papaverin is advantageous for preservation of endothelium.[129] He recommended that, when distended, the vein should be between 6 and 9 mm in diameter. Still, the optimal solution for distension as well as storage of the vein before insertion is much debated.

Distension and Spasm of the vein

After harvesting, the vein can be distended with cold heparinized saline utilising the Shiley balloon-distension system.[284] This system has a balloon that inflates at 200 mm Hg and thus prevents over-distension and fracture of the vein wall. In 1990, Puca published a technical note on dilatation of autologous vein grafts.[229] For preparation of the graft he immediately cannulated the vein at its distal end after harvesting and connected it to the high-pressure line of an arterial pressure transducer. The proximal end is occluded. The vein is hydrostatically distended using normal heparinized saline at room temperature at a constant pressure of 80 to 100 mm Hg, approximating mean arterial pressure. In a technical note, in 1997, David reported on a reversed-flow SVG.[79] He used the Lemaitre valvulotome to excise the valves and allow reversed flow in the graft. Reversing the orientation allows the large end to be anastomosed proximally and the narrow end distally, giving a more proportionally distal anastomosis. This procedure was used successfully in 5 patients. Although the use of the valvulotome may induce endothelial damage, David stated that no discernible endothelial difference can be observed in experiments in dogs. He did, however, stress the necessity for gentle handling of the vein.

Donor vessel preparation

The donor vessel in EC-IC bypass procedures usually is the ECA, or one of its branches, like the STA or the OA. When using the STA or the OA the vessel is sectioned at its distal portion. The amount of bleeding is observed to have an idea of the flow. A temporary clip is placed on the vessel. The end of the vessel is exposed. If a venous graft will be used than using a fish-mouth form or an oblique cut the vessel lumen size can be adjusted to the graft size. In direct revascularization by anastomosis procedures the end of the donor vessel can be cut obliquely in order to facilitate the end-to-side anastomosis with the recipient vessel.

Recipient vessel preparation

The recipient vessel is isolated and exposed using sharp dissection. The anastomosis site is checked for perforating vessels. These should not be accidentally occluded. In cases of cortical branch anastomosis, the cortex may be protected using a colored background material of Silastic or other plastic. The vessel is kept intact until the anastomosis is to be performed. Temporary clips are placed on both sides of the anastomosis site. In case of an end-to-end (E-E) anastomosis procedure, the end is denuded of adventitial layer. For end-to-side (E-S) anastomosis an incision is made for approximately 1.5 times the diameter of the graft. The recipient vessel is irrigated with a heparin solution.

Revascularization using an End-to-Side technique

In cases of STA-MCA anastomosis procedures an arteriotomy is made in the cortical MCA branch between the clips, using fine curved scissors. An intimal flap or irregular cut should be avoided, and it is better to make the initial arteriotomy too short rather than too long. Irrigation with heparin solution is carried out. The first stitch is placed at the distal end of the arteriotomy so that, when there is a mismatch, either the arteriotomy or the end of the donor can be enlarged in the proximal direction. If necessary the arteriotomy is extended to match the donor vessel. If there is no space for this, then the donor vessel can be cut in a fish-mouth fashion to match the arteriotomy. The second stitch is placed. We prefer to start with suturing the back wall with interrupted sutures, so that we can easily detect a stitch that accidentally was placed through both walls. The front wall is next, so the donor vessel is flipped over to the other side. After careful examination of the interior the front wall is sutured in a similar way, leaving one suture unknotted. Using irrigation through the remaining hole, the suture lines are then checked for leakages, which can be closed with interrupted stitches. The clips of the recipient vessel are temporarily removed, so that the air disappears from the anastomosis. Then the last suture is completed. After that the clip on the donor artery can be removed.

In cases of EC-IC bypass procedures using a graft, the distal anastomosis is performed first. Depending on the recipient vessel an end-to-side anastomosis is made using the same technique as mentioned above. Because a venous graft usually is larger in diameter (3-4mm), the arteriotomy should also be longer (5-6mm) to match the vein. If a cortical branch is used as recipient we would recommend using interrupted 10/0 Prolene sutures. However, for larger recipient vessels 9/0 or even 8/0 Prolene can be more useful. When the anastomosis is completed, the graft is filled with heparin solution, and a temporary clip is placed on the graft. Then the clips on the recipient artery are removed and the anastomosis is observed to confirm the quality of the anastomosis. Any leaks can be solved with extra interrupted sutures. As the microsurgical techniques became more advanced, also intracranial-to-intracranial bypass procedures were developed and performed. The more progressive forms of anastomosis techniques require a lot of microsurgical skill and experience for the available working space is small. This is especially the case for posterior circulation revascularization.

Intra-operative complications

Catinella reported on the factors that influence patency of coronary artery bypass vein grafts in 1982.[64] In 1985, Whisnant reported on the long-term mortality and stroke morbidity after STA-MCA bypass surgery.[332] He concluded that a patient who has had a single focal ischemic event and a subsequent confirmation of ICA occlusion is not at a great enough risk for the occurrence of stroke to justify a bypass operation unless angiography suggest a precarious collateral circulation. The 30-day combined mortality and stroke morbidity was 5% among experienced surgeons. Sundt reported in 1986 on 132 bypass graft procedures.[284] Complications varied from graft occlusions, deficits from temporarily occluded recipient vessels, stroke from occlusion of bypassed vessels, subdural hygromas, to intracerebral haemorrhages, intracerebral hematomas, subdural hematomas and myocardial infarction. Most of the graft occlusions occurred early and were related to technical problems. Among the strokes, two major strokes occurred from M_1 occlusion. Since then, they preferred placing the distal anastomosis to the M_2 segment. Sundt and Sundt published a review article on the preparation of vein bypass grafts in 1987, extensively reviewing the experience in cardiovascular and peripheral vascular surgery.[285] They classified graft occlusion in early graft thrombosis within 30 days after surgery, subacute graft occlusion within the first 1 to 2 years, and late occlusion 5 or more years postoperatively. In 1999, Sekhar reported his experience with 102 bypasses in 101 patients.[244] They classified graft problems anatomically in general problems, proximal end problems, tunnel-related problems, and distal end problems. The principles of preparation of bypass grafts, and the prevention of complications of revascularization have some overlap.

Post-operative complications

Early Graft thrombosis

Early graft occlusion is almost invariably due to thrombosis. The study by Chesebro in 1982 reports the improvement of patency in a group of patients treated with dipyridamole plus aspirin in a trial comparing dipyridamole plus aspirin to a placebo in 407 patients with coronary bypass grafts.[69, 70] After a short overview of normal venous histology, Sundt and Sundt discussed early graft thrombosis of which loss of intimal layer, slow graft flow and host coagulability seem the most important factors.[285] Sundt and Sundt stated that intimal desquamation of the graft may be considered as secondary to shear after harvesting and after transplantation to an arterial environment. They continued with the discussion of subacute graft occlusion, pointing to intimal hyperplasia and medial fibrosis, valve fibrosis, aneurismal dilatation, clamp stenosis, suture stenosis as identifiable factors. Catinella reported in their study that veins were routinely removed by a senior surgeon with a minimum of trauma.[64] No-touch harvesting technique is also propagated by Gundry in 1982.

Late Occlusion

Chesebro reported in 1984 the results of a 407 patients trial concentrating on late occlusion of coronary artery bypasses.[70] The results show that dipyridamole and aspirin continue to be effective in preventing vein-graft occlusion late after operation. In 1995, Regli reviewed 201 patients with 202 long venous grafts for cerebral revascularization.[233] They summarise the technical factors contributing to venous bypass graft occlusion classifying them into: Endothelial damage, slow flow, anastomosis obstruction and recipient vessel-related runoff.

Tunnel related problems

To prevent narrowing in the tunnel, compression, torsion, and/or kinking of the graft, Sundt used a normal French argyle trocar catheter to guide the distended vein graft through the tunnel. Torsion is described by Bergamini as a technical error in in situ venous bypass surgery.[34, 46] In 5 of 179 bypasses the graft was occluded due to torsion, but that amount decreased to zero with the increase of the surgeon's experience. In a technical note, Okada reported a retro auricular subcutaneous Dacron tunnel for EC/IC bypass graft.[219] This method has been applied in 15 EC/IC bypass procedures with vein grafts, and all bypasses were demonstrated to be patent. We now prefer to open the skin for the complete length of the bypass, that is from the neck up to the skull. This gives us visual control over the bypass when we open the clips and the bypass is filling with blood. Any kinking or torsion is easily detected. Careful closure of the skin over the bypass under control of the ultrasound flow meter guarantees that we do not occlude the bypass.

Cerebral ischemia

Heros reported in 1983 a case of embolic stroke after ICA occlusion with STA-MCA bypass for treatment of a giant paraclinoid aneurysm.[143] Post-operatively, the patient became hemiplegic. Angiography revealed no filling of the ACA complex, indicating embolic occlusion of the ACA complex, because it had previously filled from both sides. Heros discussed that administration of anticoagulants may have avoided embolic problems. Earlier, Hopkins and Grand in 1979,[150] Ferguson and Drake in 1980,[106] Diaz in 1982, and Spetzler and Carter in 1985,[262] reported ischemic complications after EC/IC bypass surgery for aneurysm treatment.

Diaz discussed that, even for patent anastomoses, it takes time for the cerebral hemodynamics to accommodate to the new route of flow. If sufficient time is allowed for the bypass to expand, in some cases the STA will expand 2 or 3 times. Anastomosis of the saphenous vein may produce a greater amount of flow, but even in these cases, potential for ischemic complication exists because the recipient MCA branch may also require time to expand. They concluded that ICA occlusion using a Selverstone clamp accompanied by STA-MCA anastomosis should be performed gradually over 7 to 10 days to decrease ischemic complications. Administration of antiplatelet agents is recommended and now standard. However, ischemic complications have been reported in many reports on cerebral bypass procedures. Although Sekhar reported that with good operative technique and a short anastomotic time the risk of ischemic injury is low, rates of perioperative stroke is still 9,5%.[247]

Rupture of aneurysms in aneurysm surgery.

In preparation for a direct surgical approach to a giant MCA aneurysm, Scott reported rupture after STA-MCA anastomosis in 1982.[242] It is possible that the bypass, by increasing blood flow through the MCA branches, increased turbulence adjacent to the mouth of the aneurysm, leading to its rupture. In the comments, Samson replies that his policy was to perform the bypass and eradicate the aneurysm at the same operative sitting. Only in cases in which proximal occlusion or permanent trapping have been demonstrated two-staged procedures were opted. Ferguson also states that there is no reason for undue delay in treating the aneurysm itself after bypass surgery.[107] This was years before the publication of the spontaneous occlusion of aneurysms after EC/IC bypass in 1999 by Cantore.[57]

In 1984, Heros and Ameri operated on a patient with a giant BA aneurysm and used a saphenous vein between the ECA and the PCA.[142] The patient died from rupture of the aneurysm just before the planned occlusion of the BA. Heros and Ameri believe that the different hemodynamics brought about by the vein graft were partially responsible for the rupture. Given the same situation again, they would occlude the BA acutely after making sure of adequate flow through the vein graft. No undue delay of performing occlusion of the supply artery of the aneurysm is also supported by W Houdek described in 1986 the possible therapeutic consequences of detection of an MCA aneurysm after performing an EC/IC bypass operation.[153] Direct intervention, conservative non-surgical therapy or ligation of the parent artery were possible alternatives. As the aneurysm was asymptomatic, conservative therapy was applied.

General neurosurgical complications.

A lot of reported complications are related to surgery itself. Myocardial infarction, pulmonary embolus, subdural hematoma are not especially related to revascularization. Kletter wrote in his monograph, in 1979, that surgical risk of STA-MCA bypass surgery is relatively low, although anaesthesia itself represents a certain risk. Also, in the treatment of patients with symptoms of cerebral ischemia the majority of patients have a general sclerotic disease, leading to increasing mortality and morbidity.

Part II

In Vivo Evaluation

Chapter 4

Introduction to In Vitro and In Vivo Evaluation

Cerebral revascularization
H.J.N. Streefkerk, A. van der Zwan, R.M. Verdaasdonk, H.J. Mansvelt Beck, C.A.F. Tulleken
Adv Tech Stand Neurosurg. 2003;28:145-225. Review.

Introduction to in vitro and in vivo evaluation

Microvascular surgery is still and will remain a highly specialized technique, also among the other disciplines like reconstructive surgery, cardiovascular surgery and hand surgery. The pioneers of cerebral revascularization all started in the laboratory. Yasargil recommended that trainees should spend at least 3 months learning microsurgical skills in the laboratory before proceeding to neurosurgery.[344] The effect of training is well known even among gynecologic infertility surgeons as Oelsner demonstrated the progress of training by asking an inexperienced surgeon to make anastomosis of rabbit fallopian tubes.[218] Three weeks after microsurgical reanastomosis the rabbits were mated. Ten to 14 days later the number of corpora lutea was counted and a pregnancy rate was calculated as measure of successful anastomoses. The first ten anastomoses resulted in a 30% pregnancy rate. The 50th to 60th anastomoses resulted in a 70% pregnancy rate, and after the 100th anastomosis the pregnancy rate was 100% over the last 30 anastomoses.

Experimental Anastomoses

Laboratory exercises for revascularization of the brain have been promoted by neurosurgeons even before Yasargil published the results of the STA-MCA bypass in the dog.[342] The year before, Khodadad and Lougheed reported on the operating microscope in end-to-end anastomosis surgery in the dog.[174] Albanese proposed some experimental models for arterial anastomoses in 1975.[8] Rosenbaum and Sundt stated that an anastomosis of the CCA of the rat proved an excellent model of the human operation.[236] Concerned about the difficulties in STA-MCA anastomosis procedures, Kletter described in 1979 that end-to-end (E-E) anastomoses of vessels with a diameter of 1mm or less required thorough training.[177] He explained the clamping, severing and reconnection of the CCA of the rat, using the "classical technique" of applying two corner sutures at an angle of 180 degrees and then suturing the anterior and posterior walls (as described by Carrel and Yasargil). He also described E-S anastomosis of the CCA to the contralateral CCA of the rat, and thought that STA-MCA anastomosis in dogs would also be good training.

Laboratory Procedures

Sekhar and Kalavakonda recently described neurosurgical training for revascularization procedures.[248] Obviously a surgeon should not have a significant physiological tremor, although we have seen some trainees in our laboratory who overcame this problem. Laboratory experiments and cadaver experiments are obligatory. The next step, treating patients should first be performed in a patient with a low risk of stroke, and with the patient's knowledge regarding the inexperience of the surgeon. This requires a measure of honesty and self-knowledge,[54] also discussed by Hernesniemi.[141] Even after extensive learning of the textbooks on anatomy and successful laboratory training the surgical statistics will be harsh on inexperienced surgeons.[141]

Figure 4.1.
The blood vessel holder for in vitro microsurgical training. Originally developed as a tool for holding blood vessels when applying outside forces to it (see Chapter 5), the training characteristics were quickly recognized. This second generation model has been developed especially for training purposes. Using separate tubes and a water reservoir a full scale blood vessel model with intraluminal flow can be created for trainees to practice conventional end-to-end, end-to-side, and even side-to-side anastomoses, and of course the ELANA technique.

Figure 4.2.
The blood vessel is connected to the tubes. Using 3/0 Prolene sutures the blood vessel is tightly fixated to the hollow tubes.

Figure 4.3.
The tubes are gently laid within the blood vessel holder. to enhance the difficulty level, a trestle with a hole can be placed over the setup. The height of the trestle is adjustable (6-10 cm above the blood vessel).

A complete rehearsal of the necessary equipment and instruments is beyond the scope of this review. For more details we want to refer to the excellent publication by Yonekawa in 1999 in *Operative Techniques in Neurosurgery.*[348]

In Vitro Model Training

In order to reduce the amount of experimental animals used for training, we introduced an in vitro setup in the laboratory (see Chapter 5.). We prefer to use the abdominal aortas of rabbits, which have been killed in a rabbit facility for food production. The aorta was excised with ligation of every side branch using a 7/0 or 8/0 Prolene suture. Before excision 2 marker sutures (8/0 Prolene) were placed in the wall of the aorta at a distance of exactly 60 mm of each other. The vessel was then excised with on both sides at least 6 mm extra, and preserved in medium (Dulbecco's Mod Eagle Medium with 0.11G/L NA Pyr and Pyridoxine). We have developed a model (see Figure 4.1.) in which the blood vessel can be placed and we can apply intraluminal pressure, so that the circumstances are comparable to the in vivo setting. We prefer to use this setup instead of starting training on plastic tubes, because it is much easier to check the anastomoses and because the vascular material has the same consistency and feel as in in vivo experiments.

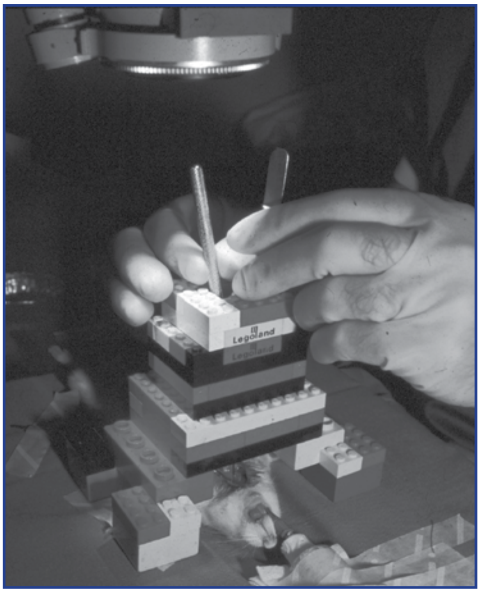


Figure 4.4.
The senior author (CAFT) has been working in the experimental animal laboraty for more than 20 years. Initially starting with a low difficulty level, skills have been obtained over the years using very specialized equipment (like Lego).

The blood vessel holder consists of several parts. Two tubes with adjusted ends to hold the vessel are placed on a moving metal frame so that the vessel is easily connected between the tubes (see Figure 4.2.). A single 3/0 Prolene will hold the vessel in place. Then the tubes are gently removed from the metal frame and placed inside the white tube holder (see Figure 4.3). In this setup, inexperienced trainees start with cutting the aorta in half and then making an E-E anastomosis with the use of the operating microscope. We prefer to use 8/0 or 9/0 Prolene, first for an interrupted E-E anastomosis, later for a running anastomosis. Also E-S anastomoses, both with interrupted as well as with running sutures can be learned. The next stage is to enhance the difficulty, so a trestle is put over the vessel holder (see Figure 4.3.). The trestle contains a hole of approximately 4 cm in diameter and can be adjusted in height, varying from 6 to 10 cm above the blood vessel. The advantages over animal experiments and cadaver training are clear. Trainees can still work with vessel structures, learning the structure and properties of the material and learning the use of the micro-instruments, without the need for anesthetics, living animals, or a fully equipped operating room.

In Vivo Model Training on the Rat

After excelling with the in vitro setup, trainees should proceed to experiments on living rats. After the rat is anesthetized trainees start with tracheotomy, dissecting the CCAs and making E-E anastomoses, followed by dissecting and re-anastomosing the femoral arteries and vena cava. Both E-E and E-S anastomoses can be trained on vessels with a diameter of 1 to 3 mm, commencing with the larger vessels, using 8/0 to 11/0 Prolene sutures. A similar trestle or anything like mentioned above can be placed over the rat in order to increase the degree of difficulty (see Figure 4.4.).

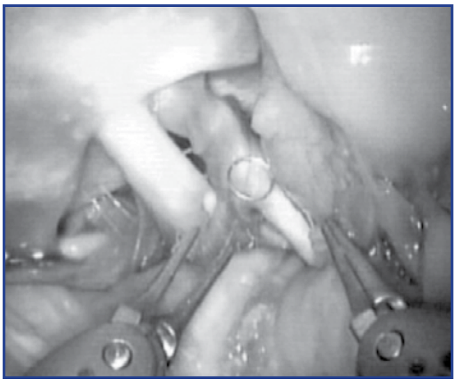


Figure 4.5.
Pilot study with the Da Vinci telemanipulation system. A platinum ring with a diameter of 2.8 mm was stitched onto the wall of the supraclinoid ICA in a cadaver. A saphenous vein graft was stitched onto the wall of the ICA using hte platinurm ring as guide.

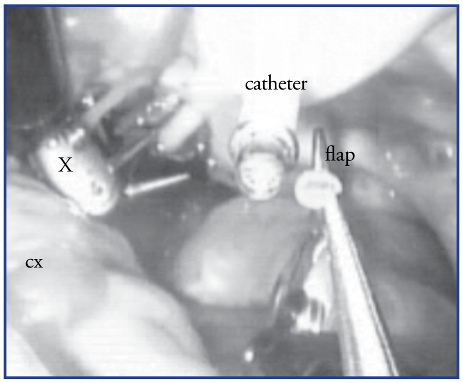


Figure 4.6.
After the laser procedure the catheter was withdrawn. A very nice punched-out disc of ICA wall (flap) was visible on the tip of the cathter. Note that the relatively large "microsurgical" instruments of the Da Vinci (X) are brushing the temporal cortex (cx).

Cadaver Training

Anatomical studies remain the basis of surgery. Before engaging in difficult posterior fossa surgery, Shrontz performed a study to find and evaluate the best sites at which to perform bypass procedures.[255] They found the pretonsillar segment of the PICA, the second portion of the AICA, the perimesencephalic segment of the SCA, and the perimesencephalic part of the PCA to be best suited as recipient vessel, based on outer diameter, degree of mobility, least number of branches, and frequency of occurrence. It was because of cadaver training that Drake found the explanation to the sudden deaths after ligation of basilar bifurcation aneurysms.[95] Injury or occlusion of the microscopic small thalamoperforating branches which may arise from the back of the BA leads to a deep coma with quadriparesis. A beautiful example of cadaver training was reported in 1990 when Al Mefty performed an excellent cadaver study on direct ICA reconstruction techniques.[7] Three types of "shunts" were explored. The external intrapetrous-supraclinoid shunt, the internal intrapetrous-supraclinoid shunt and the cervical carotid-supraclinoid shunt. However, this was long after the first demonstration of the feasibility of such procedures by Sekhar in 1987 also in cadavers.[245]

Recently we performed a pilot experiment on cadavers (Tulleken & Streefkerk, unpublished). Enchanted by the da Vinci telemanipulation system (Intuitive Surgical, Mountain View, Calif), usually misnamed as "robot", we tried to apply this system inside the skull. An enlarged pterional approach was used to expose the ICA bifurcation (see Figure 4.5.). With a suture 3/0 Prolene both the M_1 and A_1 were ligated. A red glycerin solution was injected into the proximal ICA, creating an illusion of intraluminal pressure. With the Master Slave system, we tried and succeeded in performing the ELANA technique, which resulted in a very nice non-occlusive anastomosis of a venous graft with the intracranial ICA and a beautiful punched-out disc of carotid wall (see Figure 4.6.). However, when we observed the temporal lobe, it became obvious that the Intuitive Instruments are quite large, because parts of the cortex had been brushed away. Therefore, we concluded that if we want to use the Intuitive telemanipulation system in neurosurgical applications, the instruments need to be refined and miniaturized. It will be necessary to adjust the movements of the instruments in such a way that certain damaging movements are not possible. However, after 10 minutes of training, the senior author (CAFT) was able to make anastomoses with almost the same ease as with normal microsurgical instruments.

Learning the ELANA technique

Using the above mentioned in vitro setup a rabbit abdominal aorta of 3 mm in diameter is placed in the blood vessel holder. The vessel is stretched to its normal length and intraluminal pressure is applied to a level of 50 mmHg and any leaks are closed with a suture of 9/0 Prolene. The trestle is placed on top of the blood vessel holder at a height of 6 cm above the blood vessel (see Figure 4.3.). Using the microscope a platinum ring with a diameter of 2.8 mm is stitched onto the wall of the vessel with 4 sutures 9/0 Prolene. The first stitch is placed in the median of the vessel, around the platinum ring. The second stitch is also placed in the median of the vessel, however at 180 degrees along the platinum ring, with the bite slightly aside of the platinum ring, which causes a bit of accumulation of arterial wall inside the platinum ring. The third stitch is placed at 90 degrees lateral of the vessel, causing the platinum ring to tilt. With the fourth ring, placed at 270 degrees, the ring is firmly attached to the wall of the recipient vessel, creating a flat surface within the platinum ring. The next step is attaching the graft, usually the greater saphenous vein from cadavers, to the platinum ring and the recipient vessel. We like to use 8 interrupted sutures 9/0 Prolene, with the bite slightly aside from the platinum ring, penetrating the wall of the recipient vessel only superficially, coming out exactly inside the platinum ring, and passing completely from inside to outside the graft wall. Then the graft is filled with heparin solution to observe any leaks, which can be countered with an extra suture. The excimer laser catheter is then introduced into the graft so that the tip of the catheter is firmly placed against the wall of the recipient artery, within the platinum ring. Vacuum suction is applied for 2 minutes, after which the laser is activated. The catheter is then withdrawn, and, if all went well, a punched-out flap is located inside the laser fibre configuration at the tip of the laser catheter. The graft is cut just above the anastomosis, so the inside of the anastomosis can be observed. Afterwards a clip is placed on the graft, allowing the trainee to continue making anastomoses on another site of the vessel.

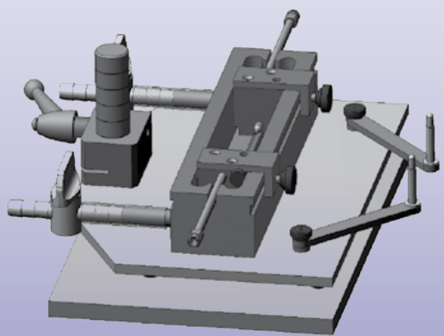
In Vivo Model Training on the Rabbit

The experimental procedure described here has been performed in our laboratory for more than 10 years. The experiments are performed on rabbits (New Zealand White) under general anesthesia (halothane). A median incision is made in the neck. The jugular vein is exposed and excised for a length of 4 cm. We preserve this graft in a heparin solution. Using a median laporotomy, the peritoneal layers are cut, and the intestines are gently pushed aside. We prefer to cover them in some water drenched cottonoids. The operation area is enlarged with retractors, and the abdominal aorta is exposed over a length of 3-4 cm. Usually we use the operation microscope for the sharp exposure. A platinum ring with a diameter of 2.8 mm is stitched distally onto the wall of the abdominal aorta in a similar way as described in the in vitro model training, using 4 sutures 9/0 Prolene. The graft is checked for valves, and placed in the right direction. The graft is attached to the aorta and the platinum ring as described before, with the flow direction towards the aorta, using 8 to 12 interrupted sutures 9/0 Prolene. The excimer laser catheter is then introduced into the graft and pushed up until the tip touches the wall of the aorta, inside the platinum ring. Vacuum suction is activated for 2 minutes to ensure a firm contact of the laser fibres to the wall of the aorta. The laser is then activated for 5 seconds, punching out a full-thickness disc of arterial wall with a diameter similar to the diameter of the catheter tip (2.2 mm). The catheter is withdrawn, and since the high vacuum is continued, the disc of arterial wall stays attached to the laser tip until it is removed. Profuse back bleeding from the graft is observed, and a temporary clip is applied to the graft to stop the bleeding. The graft is then cut and the separate end is connected to the aorta proximally of the laser anastomosis, using a conventional E-S anastomosis with a running suture 8/0 Prolene or interrupted sutures 9/0 Prolene. The free ends are cut obliquely and connected using a conventional E-E anastomosis with interrupted or running sutures 8/0 or 9/0 Prolene. When all clips are removed the bypass should have a low competitive flow (15 ml/min). After occluding the aorta in between the anastomoses, the flow will increase to more than 30 ml/min (normal flow through the rabbit aorta is 35-55 ml/min).

In non-survival experiments it is very well possible to make several anastomoses, so that the ELANA technique can be practiced. With four or even five anastomoses on the same aorta the learning curve is already obvious. We have welcomed several neurosurgeons in our laboratory who were willing to master the technique both with in vitro experiments as well as with in vivo experiments. After finishing their laboratory course with our group they will continue to hone their skills in their own laboratories before proceeding on patients. However, obtaining the necessary skills for cerebral revascularization is only part of the story. Ultimately we will have to face the patient. And for some patients we still do not know whether bypass surgery will be the best treatment for them.

Chapter 5

The ELANA Practice Model



Accepted for publication
Neurosurgery

The ELANA Practice Model

Abstract

Summary

In order to practice microsurgical skills several experimental models are available which diminish the need for experimental animals. We defined criteria with which such models should comply, and we tested whether the models described in literature, as well as our own practice model, comply with these criteria.

Methods

We defined the criteria to which these should comply and we performed a literature search on microvascular practice models. During the development of the Excimer laser-assisted non-occlusive anastomosis (ELANA) technique, we designed our own ELANA practice model (EPM) according to those criteria and we compared that model to the models described in the literature.

Results

All practice models could be categorized into three groups: beginner, moderate, and advanced. Our EPM complies with almost all criteria defined in the beginner- and moderate groups, and has much in common with the models which are categorized in the advanced group.

Conclusion

Considering the methods to learn microvascular surgical techniques, the EPM can be used for a very long time before the need for living animals arises. This last aspect remains an inescapable condition for practicing microsurgical skills. However, using the EPM or another practice model, the amount of experimental animals can be drastically reduced.

Previous page.
3D building plan of the ELANA Practice Model version 3.

Objective

Microvascular training

The pioneers of cerebral revascularization procedures all started in the laboratory. Jacobson and Suarez introduced the operating microscope into the animal laboratory in 1960.[161] Quite soon after that, they published on the first microvascular anastomosis made in the rat. Not only did they describe the use of the operating microscope, they also elaborated on the enhancement of surgical skills. Among others, Yasargil recommended that trainees should spend at least 3 months learning microsurgical skills in the laboratory before proceeding to neurosurgery.[344] Since then, many rats,[348] rabbits,[165, 175] cats,[302] dogs,[174] and other experimental animals have been used to hone surgeon's skills in the laboratory, and even at home.[163] At present, practice sessions in the animal laboratory are an obligatory part of neurosurgical training.

The last years, the attitude towards animal experiments has changed. This has resulted in an increase of (in vitro) microsurgical models which may replace the use of experimental animals. During the development of the Excimer laser-assisted non-occlusive anastomosis (ELANA) technique, we found ourselves looking for a suitable and reproducible microvascular model in order to learn and practice the ELANA technique as well as creating a standardized environment to investigate enhancements of the ELANA technique.

The ELANA Practice Model

Long before the first publication on the ELANA technique, our research group has been working on the development and enhancement of non-occlusive anastomoses.[293, 296, 301, 302] As mentioned above, the need arose to obtain a standardized microvascular model. In order to reduce the amount of experimental animals the model should be an in vitro model. Four years ago we developed the first version of the ELANA Practice Model (EPM v1, see Figure 5.1.). The EPM

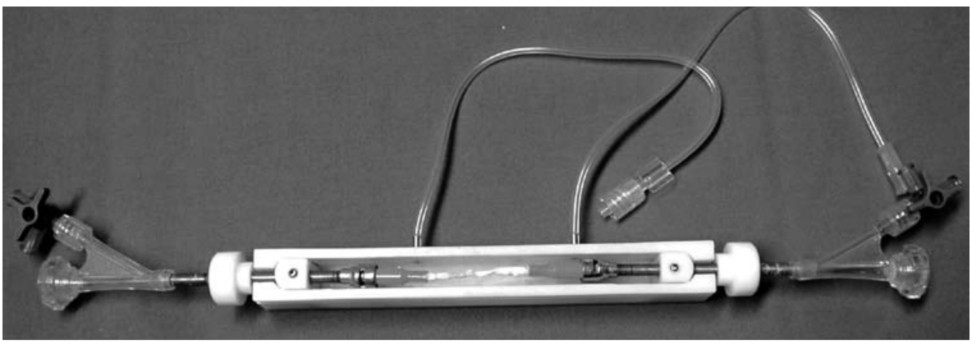


Figure 5.1.
The first ELANA practice model. The blood vessel is attached to two metal tubes, which can be attached to a small white box. The lumen within the tubes is wide enough to allow endovascular scopes to enter the bloodvessel for intraluminal evaluation of anasotmoses. Intraluminal pressure can be realised by attaching the tubes with a flow system.

v1 was really a very simple model. It was possible to fixate a bloodvessel between two pipes in such a way that intraluminal pressure, using any fluid, could be realized. We appreciated the research functions it offered; however, its training characteristics were quickly recognized. We then proceeded to develop a second version (EPM v2) which would be suitable for training microvascular techniques. The same principle was used as in the EPM v1; a bloodvessel is fixated between two hollow tubes. These tubes, together with the bloodvessel, are fixated within a box. For training purposes a trestle with a trephination like hole can be placed over the box. The height of the trestle can be adjusted to increase the level of difficulty. The EPM v2 has been used for quite some time in our experimental laboratory for the training of the ELANA technique and has extensively been described elsewhere.[273] Thanks to the comments of the neurosurgeons and neurosurgical residents who have been using the EPM v2, we were able to define most of the criteria with which a good training device should comply. We tried to incorporate these ideas in our most recent version of the EPM (v3). The objective of this paper is to present the EPM v3 and to compare this training device with models described in the literature.

Materials and Methods

EPM version 3

The EPM v3 has been designed using computer aided designing tools to allow a trainee to work with bloodvessels with a variable diameter (1,00 – 10 mm), a variable intraluminal pressure (0 – 500 mmHg) which can be created using any kind of fluid flowing through the bloodvessel, and with an adjustable level of difficulty. The EPM v3 consists of a gray box with a lumen of 100 x 20 mm. Within this lumen, a bloodvessel can be fixated between two small tubes, using 2 sutures 3-0 Prolene.The bloodvessel can be stretched by moving the fixation tubes in opposite directions within the gray box, and fixating them in such a position that the original length of the bloodvessel has been realized, which is necessary for training the ELANA technique. Intraluminal pressure can be applied by activating a flow system through the fixation tubes and thus through the bloodvessel using any kind of fluid. On top of the gray box, a translucent table can be positioned which contains a small hole through which the trainee can work (see opposite page). The position of the gray box can be adjusted to create a superficial or deep operation area.

Blood vessels

We prefer to use the abdominal aortas of rabbits, which have been killed in a rabbit facility for food production (see Figure 5.2.). The abdominal aorta of the rabbit has a diameter between 2,0 – 4,0 mm. After exposing the aorta (see Figure 5.3.), two marker sutures (8-0 Prolene) are placed in the wall of the vessel at a distance of 60 mm of each other. The aorta is then excised over a length of 8 cm, including the two marker sutures, and preserved in medium (Dulbecco's Mod Eagle Medium with 0,11 G/L NA Pyr and Pyridoxine). We then preserve each aorta in


SONY

Figure 5.2.
In order to minimize the amount of rabbits, which have to suffer from medical experiments, we obtain our blood vessels from a rabbit meat facility. This facility produces rabbit meat, so the vessels can be obtained from freshly killed rabbits.

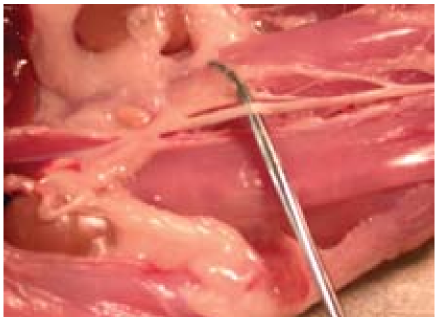


Figure 5.3.
We prefer to use the abdominal aorta of the rabbit. Directly after the rabbit has been killed, the intestines are removed, and the retroperitoneal aorta con easily be excised. After exposure, two marker sutures are placed in the aorta over a length of 8 cm. Then the aorta is excised.

the freezer at -4 degrees Celsius. After defrosting the vessel can be fixated in the EPM v3, using the 2 marker sutures to stretch the vessel to its original length if necessary (for training the ELANA technique).

Literature

A literature search was performed using the following keywords alone and in combination: "microsurgery, microvascular, in vitro, model, non animal, exercises, training". All references were then investigated and summarized. We defined various criteria and categorized them according to the following groups: (I.) learning basic microvascular principles, (II.) simulating the clinical situation as well as possible, (III.) possibilities to evaluate microvascular anastomoses, and (IV.) ease of use of the practice model. The practice models were also divided into 3 stages; (1.)Beginner, (2.) Average, and (3.) Advanced, according to their supposed purpose. All models, including the EPM v3 where evaluated each in their own group, using these criteria.

Criteria

Group I. Learning basic microvascular principles

We have summarized the criteria in table 1. In order to learn microvascular skills, the trainee should learn how to make a stitch (criterion 1), how to tie knots (criterion 2), how to repair a longitudinal vascular incision (criterion 3), and how to make a conventional end-to-side anastomosis (criterion 4). Along the way, the trainee will learn to correctly handle both micro instruments as well as the operation microscope, which is a requisite for all models (except the virtual reality model). A learning trajectory can be created by increasing the level of difficulty, like using a variable operation area, or a deeper level of the operation area (criterion 5).

Table 5.1. Criteria

Group I.	Group II.	Group III.	Group IV.
1. Stitching	8. Living animal model	14. Patency observation	17. Always available
2. Tying knots	9. Real bloodvessels	15. Leakage observation	18. Operational < 15 minutes
3. Incision repair	10. Intraluminal pressure	16. Flow system	19. Standardized quality
4. E2E anastomosis	11. Bleeding simulation		20. Maintenance free
5. Deep operation area	12. Variable diameter		21. Preservation > 6 months
6. Placing a hemo clip	13. Variable vessel wall		22. No risk of infection
7. Correcting misplaced sutures			

Table 5.2. Group I. Learning Basic Microvascular Principles

Model	1. Stitching	2. Tying knots	3. Incision repair	4. End-to-End Anastomoses	5. Deep operation area	6. Placing a hemo clip	7. Correcting misplaced sutures
Stage 1. Beginner							
Latex glove [75, 105, 111, 128, 194, 232, 234, 310]	+	+	+	-	-	-	-
Dexter [261]	+	+	-	-	-	-	-
Surgical gauze [84]	+	+	-	-	-	-	-
Foliage leaf [170]	+	+	+	-	-	-	-
Stage 2. Average							
Avulsed skin [122]	+	+	+	+	-	+	+
Ex-vivo animal [36, 121, 175, 269, 275]	+	+	+	+	-	+	+
Microvascular simulator [201, 253]	+	+	+	+	-	+	+
Humane placenta [30, 328]	+	+	+	+	-	+	+
Practice rat [329]	+	+	+	+	-	+	+
PVC rat [234]	+	+	+	+	-	+	+
Synthetic bloodvessel [111, 152, 183]	+	+	+	+	-	+	+
EPM v3	+	+	+	+	+	+	+
Stage 3. Advanced							
Living rabbit [77, 134, 165, 175, 218, 338]	+	+	+	+	-	+	+
Living rat [86, 130, 206, 206, 236, 276, 293, 351]	+	+	+	+	- / +*	+	+
Virtual reality [102, 217]	+	+	+	+	+	+	+
Cadaver [4]	+	+	+	+	+	+	+

+ Possible
- Not possible
+* Possible in the Skull Cast Model described by Menovsky[206]

Table 5.3. Group II. Simulating the Clinical Situation

Model	8. Living animal model	9. Real bloodvessels	10. Intraluminal pressure	11. Bleeding simulation	12. Variable vessel diameter	13. Variable vessel wall
Stage 1. Beginner						
Latex glove [75, 105, 111, 128, 194, 232, 234, 310]	-	-	-	-	-	-
Dexter [261]	-	-	-	-	-	-
Surgical gauze [84]	-	-	-	-	-	-
Foliage leaf [170]	-	-	-	-	-	-
Stage 2. Average						
Avulsed skin [122]	-	+	-	-	+	+
Ex-vivo animal [36, 121, 175, 269, 275]	-	+	-	-	+	+
Microvascular simulator [201, 253]	-	+	+	+	+	+
Humane placenta [30, 328]	-	+	- / +*	- / +*	+	+
Practice rat [329]	-	-	-	+	+	-
PVC rat [234]	-	-	-	-	+	-
Synthetic bloodvessel [111, 152, 183]	-	-	-	- / +**	+	-
EPM v3	-	+	+	+	+	+
Stage 3. Advanced						
Living rabbit [77, 134, 165, 175, 218, 338]	+	+	+	+	+	+
Living rat [86, 130, 206, 206, 236, 276, 293, 351]	+	+	+	+	+	+
Virtual reality [102, 217]	-	+	+	+	+	+
Cadaver [4]	-	+	+	+	+	+

+ Possible
- Not Possible
+* Possible with dynamic artificial circulation as described by Waterhouse.[328]
+** Possible in the model described by Hosnuter.[152]

Further, the trainee should be able to counter some complications like a bleeding by placing a hemo clip (criterion 6) and he and should be able to correct a misplaced suture (criterion 7).

Group II. Approaching the clinical situation

Of course, training in a living animal model (criterion 8) will approach the clinical situation best. However, several more stages of clinical similarity can be performed in a model. With the

Table 5.4. Group III. Evaluating the results

Model	14. Patency observation	15. Leakage observation	16. Flow system
Stage 1. Beginner			
Latex glove [75, 105, 111, 128, 194, 232, 234, 310]	-	-	-
Dexter [261]	-	-	-
Surgical gauze [84]	-	-	-
Foliage leaf [170]	-	-	-
Stage 2. Average			
Avulsed skin [122]	-	-	-
Ex-vivo animal [36, 121, 175, 269, 275]	- / +*	- / +*	- / +*
Microvascular simulator [201, 253]	+	+	+
Humane placenta [30, 328]	- / +**	- / +**	- / +**
Practice rat [329]	-	+	-
PVC rat [234]	-	-	-
EPM v3	+	+	+
Stage 3. Advanced			
Synthetic bloodvessel [111, 152, 183]	- / +***	- / +***	- / +***
Living rabbit [77, 134, 165, 175, 218, 338]	+	+	+
Living rat [86, 130, 206, 206, 236, 276, 293, 351]	+	+	+
Virtual reality [102, 217]	+	+	+
Cadaver [4]	+	+	+

+ Possible
- Not possible
+* Possible in the perfusion models by Steffens,[269] and Kim.[175]
+** Possible with dynamic artificail circulation as described by Waterhouse.[328]
+*** Possible in hte model described by Hosnuter.[152]

use of real blood vessels (criterion 9) tissue dissection and adventitial stripping can be practiced in a crude way. Using the application of intraluminal pressure (criterion 10) it is possible to simulate a bleeding (criterion 11). Also, the possibility to use bloodvessels with various diameters (criterion 12) and various vessel walls (criterion 13) is advantageous in gaining a wider experience.

Group III. Evaluating the results

We considered the immediate postoperative patency (criterion 14) and the absence of leakage (criterion 15) to be the most important factor in evaluating the anastomoses. Intraluminal pressure is sufficient to examine any leakages; however it is insufficient to prove patency. A complete flow system would be ideal (criterion 16).

Table 5.5. Group IV. Ease of Use

Model	17. Always available	18. Operational < 15 min	19. Standardized quality	20. Maintenance free	21. Preservation > 6 months	22. No risk of infection
Stage 1. Beginner						
Latex glove [75, 105, 111, 128, 194, 232, 234, 310]	+	+	+	+	+	+
Dexter [261]	+	+	+	+	+	+
Surgical gauze [84]	+	+	+	+	+	+
Foliage leaf [170]	+	+	+	-*	+	+
Stage 2. Average						
Avulsed skin [122]	+	+	-	-	-	-
Ex-vivo animal [36, 121, 175, 269, 275]	+	+	+	-	-	-
Microvascular simulator [201, 253]	+	+	+	+	+	+
Humane placenta [30, 328]	-	+	-	-	-	-
Practice rat [329]	+	+	+	+	+	+
PVC rat [234]	+	+	+	+	+	+
Synthetic bloodvessel [111, 152, 183]	+	+	+	+	+	+
EPM v3	+	+	+	+	+	-
Stage 3. Advanced						
Living rabbit [77, 134, 165, 175, 218, 338]	-	-	-	-	-	-
Living rat [86, 130, 206, 206, 236, 276, 293, 351]	-	-	-	-	-	-
Virtual reality [102, 217]	+	+	+	+	+	+
Cadaver [4]	-	-	-	-	+	-

+ Possible
- Not possible
-* Some maintenance is required to keep the plants alive

Group IV. Ease of use

It is advantageous to have the model available all times (criterion 17), and within 15 minutes (criterion 18). The model should always have roughly the same quality (criterion 19) and should need no maintenance (criterion 20) over an extended period longer than 6 months (criterion 21). Lastly, we considered the risk of infection of the trainee by the model to be disadvantageous (criterion 22).

Results

The results have been summarized in tables 2 to 5. We found many publications with a description of a microsurgical practice model. All models except the Virtual Reality model require the use of the operating microscope and micro instrumentation. In the Beginner stage (Stage 1.) several models describe a latex hand shoe or another artificial product which has been fixated on a box or a card.[75, 105, 111, 128, 194, 232, 234, 310] The latex can be put under tension, on which simple stitching and tying can be practiced. In order to make the practice more difficult, similar techniques can be performed on a foliage leaf instead of on latex.[170] As the leaf is ruptured very easily, stitching can be very difficult. Similar exercises can be performed on a surgical gauze.[84] Another approach to learning how to handle microsurgical instruments and sutures is the Dexter.[261] This model contains several beads through which the trainee should pass a suture. Progress of the trainee can be evaluated by measuring the time. To increase the difficulty a different trajectory can be chosen which includes multiple planes of view.

The second stage "Average" is the stage with the models which try to emulate the experimental animal as close as possible. The "Avulsed skin" model has been developed by plastic surgeons.[122] Clinically discontinued humane skin flaps can be used to practice dissection and anastomoses. Several animal parts, usually originating from other animal experiments, have been described as a suitable practice model. These include rats (vessels in the body,[36] legs,[5] as well as in the tail.[36, 351]) rabbits (body vessels,[77, 165, 175, 218] and ears [134]), chicken (body [121] and leg [275]), and pigs (heart [111] and legs [269]). Other discontinued humane parts models include the human placenta.[30, 328] The EPM v3 also uses ex vivo animal material in the form of rabbit aortas. Intraluminal pressure can be created in models with a flow system. These models include the EPM v3, the Microvascular simulator,[201, 253] and the Practice rat.[329] The PVC rat is an example of a model using non-perfused artificial bloodvessels, [234] similar to using silicon bloodvessels,[111, 152] or Gore-tex vessels.[183]

Stage 3. (Advanced) includes living animal models and a cadaver model. In these models either the circulation is kept intact, as in the living animal models, or a flow system has been added which creates intravascular flow. Evaluating anastomoses on patency or leakages is very well possible. Also, in a humane cadaver model it is quite easy to realize a neurosurgical trephination to simulate the clinical situation. However, Menovsky described a human skull cast which can be placed over a living rat, thus recreating a humane neurosurgical situation.[206]

Discussion and Conclusion

We have tried to evaluate the various practice models described in the literature by defining criteria. The importance of these criteria will differ along with the purpose of the training. An ideal microsurgical training should be cheap, always available, it should not be necessary to use any living animals; however, it should closely simulate a clinical situation. During the training it should be possible to practice basic skills, average skills, and advanced skills in the same model. Unfortunately, no model exists which combines all these characteristics. Basic skills can be learned on every Stage 1. model, which are very cheap, always available, and easy to access. We do not consider it justifiable to use animals from the beginning when training on suturing techniques. Starting on a latex glove and proceeding to a foliage leaf is a nice and cheap way to learn how to handle the microscope and the instrumentation. However, as we have the EPM v3 in our laboratory we prefer to use that, so that the progression of the trainee is easily observed in a standardized situation. The immediate satisfaction of being able to repair a longitudinal incision in a real bloodvessel, which is the real thing, adds to the "microsurgical experience" and makes the course not only practical but also a lot of fun. Still, we had fun working with the surgical gauze and the foliage leaf. Also, we compared our skills on a self made Dexter model. This last model is not suitable for learning to tie knots or make stitches, but it strains the trainee's 3D capabilities.

Average skills can be honed on bloodvessels using the Stage 2. models, among which we prefer those models which use real bloodvessels. Some of these use the legs or even a complete chicken bought at the butcher's. In the Netherlands this is not allowed. The use of humane placenta's carries the risk of infection, so it should also be avoided.[185] Advanced skills can be learned best in a living animal as described in the third group. However, many of these skills can be practiced on any of the ex-vivo real bloodvessel models, including the EPM v3, thus reducing the amount of animals necessary to complete the training. Only for specific neurosurgical procedure training would we recommend Aboud's human cadaver model with vascular filling.[4] We have presented a similar, however, more simple cadaver model when we experimented with the Da Vinci telemanipulation system for intracranial uses.[273] At that time we were unaware of Aboud's publication. The use of human cadavers with vascular filling has also been applied to improve endovascular skills throughout the main large human arteries.[113] Advanced methods to evaluate the skills of the trainee have not been included in the criteria that we have used, aside from the obvious patency and leakages observations. We consider patency and leakage to be the most important factors, and the time necessary to complete an anastomosis can be measured in every model. Some authors consider an anastomosis to be patent only after 1 week postoperatively.[157] We did not consider this as this factor obviously can only be determined in living animals.

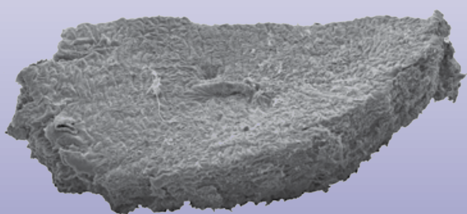
Although talent probably plays a large role in acquiring microsurgical skills, practicing will definitely result in a higher patency rate and less technical errors. The EPM v3 complies with almost all criteria in the beginner and average groups, and it can simulate quite nicely the living animal models in the advanced stage. We conclude that the EPM v3 allows for a good practice model, as the number of animals needed decreases.

Acknowledgements.

We gratefully acknowledge the support of Ed Duivenman and Liesbeth Jansen† of the department of Biomedical Engineering in designing and building the ELANA Practice Models versions 2 and 3.

Part III

Re-endothelialization

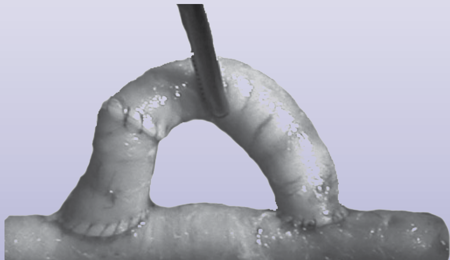


Previous page
Scanning Electron Microscopic image of a punched-out portion of arterial wall immediately after the laser ablation procedure in a patient treated for a giant intracranial aneurysm.

Next page
Intraoperative photo of a bypass which has been created by using the ELANA technique for the proximal (right) anastomosis, and a conventional end-to-side anastomosis technique for the distal anastomosis (left). Both free ends of the graft have been connected using a conventional end-to-end anastomosis.

Chapter 6

Re-endothelialization in Pigs



Long-term Re-endothelialization of ELANA Anastomoses versus Conventionally Sutured Anastmoses in Pigs

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J Neurosurg 103:328-336, 2005

The ELANA Technique: Long-term Re-endothelialization of ELANA Anastomoses versus Conventionally Sutured Anastomoses in Pigs

Abstract

Objective

The excimer laser-assisted non-occlusive anastomosis (ELANA) technique involves a platinum ring and intima-adventitia apposition with a rim of medial and adventitial layers exposed to the blood stream, in contrast to conventional anastomosis techniques. We assessed the re-endothelialisation of the ELANA anastomoses versus conventional anastomoses on the carotid arteries in pigs using scanning electron microscopy.

Methods and Materials

In 28 pigs a bypass with one ELANA and one conventional anastomosis was made on the left common carotid artery (CCA) using the right CCA as graft (56 end-to-side anastomoses). All patent end-to-side anastomoses were evaluated intra-operatively with the ultrasound flow meter and post-operatively using scanning electron microscopy at 2 weeks, at 2 months, at 3 months, and at 6 months.

Results

Twenty-four of 28 bypasses (48 of 56 end-to-side anastomoses) were fully patent at time of evaluation. On scanning electron microscopic evaluation of the patent bypasses, all 48 patent anastomoses showed complete re-endothelialisation, including all 24 ELANA anastomoses in which the endothelium covered the rim and the laser ablated edge completely. No endothelial differences were observed between conventional End-to-Side anastomoses and ELANA anastomoses, aside from the obvious anatomical differences (like the platinum ring which had been completely covered with endothelium). At 6 months, remodelling of the ELANA anastomoses was observed, leaving the ring as the most narrow part of the anastomosis, covered with a layer of endothelium.

Conclusions

In long-term experiments ELANA anastomoses will re-endothelialize comparable with conventional anastomoses. Considering the non-occlusive and high-flow characteristics of the ELANA technique we prefer to use the ELANA technique in cerebral revascularization procedures.

Introduction

The techniques for cerebral revascularization procedures have advanced ever since Yasargil made the first extracranial-to-intracranial (EC-IC) bypass in a patient, despite the negative outcome of the EC-IC Bypass trial in 1985.[1, 2] Currently, most cerebrovascular surgeons have had experience in anastomosing cerebral vessels. However, assessing the major cerebral vessels carries the risk of temporary ischemia of the cerebral region supplied by these arteries, during the temporary occlusion necessary for conventional anastomosis techniques.

These techniques were first outlined by Carrel in 1902, and his postulations have been held in high esteem by every vascular surgical discipline ever since.[59, 60] He stressed the importance of perfect intima-intima apposition within anastomoses. However, the ELANA technique consists of intima-adventitia apposition and brings the use of a platinum ring which is also exposed to the blood stream. Also, the use of the excimer laser creates a rim of medial and adventitial layers, which are exposed to the blood stream. In earlier experiments we observed that both disputed characteristics do not seem to inhibit the short term re-endothelialization of ELANA anastomoses.[273, 313, 338] These findings were confirmed in similar intima-adventitia apposition experiments.[55, 139] However, little is known about the long term results of media-adventitia exposition or the exposition of the platinum ring to the blood stream.

The main purpose of this study was to investigate the long term re-endothelialization of these ELANA anastomoses as compared to conventional End-to-Side anastomoses under high flow circumstances with special attention to the rim of medial and adventitial layers and the platinum ring, both of which are exposed to the blood stream. We therefore developed a porcine model in which a bypass was made, consisting of the right common carotid artery (CCA) transplanted onto the left CCA, using both an ELANA E-S anastomosis and a conventional E-S anastomosis. The re-endothelialization of both anastomoses was observed using the scanning electron microscope (SEM).

Materials and Methods

Animals

We used twenty-eight Dutch female Landrace pigs (weighting 25-30 kg). The animals were fed a normal diet and received humane care in compliance with the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources, National Research Council. This study was approved by the Animal Experimentation Committee of the Utrecht University. All animals received 160 mg of acetylsalicylic acid orally 1 day before surgical intervention. Postoperatively, this was continued in a dose of 80 mg per day until termination.

Anaesthesia

Anaesthesia was induced with ketamine (10 mg/kg) intramuscularly. Each animal received thiopentalnatrium (4 mg/kg), atropine (1 mg), and antibiotic prophylaxis (500 mg of amoxicillin) through an intravenous line (iv). The animals were intubated and ventilated. Anaesthesia was maintained by supplying a mixture of oxygen and air with 0.5% to 1% halothane added and by a continuous iv infusion of midazolam. Analgesia was obtained with infusion of sufentanil-citrate and muscle relaxation with pancuronium. During the operation, each animal received a continuous infusion of saline solution (300 ml/h). Post-operatively, antibiotic amoxicillin trihydrate was administered, and analgesia was obtained with buprenorphine intramuscularly for 1 day. Each animal was also given a daily 80 mg acetylsalicylic acid per os.

Surgery and Experimental Model

Using a median incision in the neck of approximately 15 cm the right common carotid artery (CCA) was exposed, excised over a length of 10 cm, and preserved in a papaverine-saline (5 mg/ml) solution to prevent spasm. The left femoral artery was exposed, and a sheath for intra-operative angiography was inserted into the femoral artery. The left CCA was exposed over a length of 10 cm. After this, the operating microscope (Zeiss Opmi 6) was used to create the anastomoses.

ELANA anastomosis

The ELANA technique has extensively been described elsewhere.[273, 274, 297, 299, 300] In the pigs the left CCA was exposed, and peri-adventitial tissue was removed, leaving the adventitial layer exposed. Using the ELANA technique one part of the right CCA was attached to the left CCA.

Conventional anastomosis

The adventitial layer of the end of the second part of the right CCA graft was removed. A site was randomly chosen, approximately 15 – 20mm proximally or distally from the ELANA anastomosis site, and was carefully cleaned of peri-adventitial tissue. Vessel loops were then placed around the CCA on both sides of the anastomosis site and tightened to occlude the CCA. A longitudinal incision of 4 mm was made in the CCA at the planned site of the conventional anastomosis between the vessel loops. The right CCA graft was then connected perpendicularly to the left CCA. First a corner suture (8/0 Prolene) was placed. Then a running suture (8/0 Prolene) was used to connect the posterior wall of the anastomosis starting from the 180 degree corner using 4-6 bites to the first corner suture, ensuring good intima-intima apposition. Returning to the anterior wall of the anastomosis with the same suture, using another 4-6 bites, again taking care of good apposition of both intimal layers, until the 180 degree corner was reached, completed the anastomosis. Upon completion the anastomosis was irrigated extensively and filled with heparin-saline solution and a temporary clip was placed on the graft. Then the flow was restored in the CCA by loosening the vessel loops.

Completion of the bypass

Both ends of the CCA graft were then end-to-end connected using a running suture 8/0 Prolene, or 10 – 12 interrupted sutures 8/0 Prolene. Upon completion the bypass was extensively irrigated and filled with heparin-saline solution. Any leaks in the conventional anastomoses were countered with an extra suture 8/0 Prolene. The clip on the proximal graft was opened and any remaining air in the bypass was removed by gently re-opening the E-E anastomosis between two sutures and injection of heparin-saline solution. The clip on the distal graft was removed and the bypass was completed. Then intravenous heparin (5000 units) was administered and a permanent clip was placed on the CCA between both End-to-Side anastomoses.

Animal assignment

Each animal was randomly assigned to one of the following combinations of bypass procedures: (1) distal ELANA anastomosis and proximal conventional anastomosis; (2) proximal ELANA anastomosis and distal conventional anastomosis (in order to look for in- and outflow differences). All bypasses had a conventional E-E anastomosis between both E-S anastomoses. All animals were then randomly assigned to one of the following groups for survival: Group I: 2 weeks survival (n=7); Group II: 2 months survival (n=7), Group III: 3 months survival (n=7); and Group IV: 6 months survival (n=7). All animals were evaluated intra-operatively, during post-operative follow-up, and at the time of termination.

Intra-operative evaluation

Flow through the CCA was measured with an Ultrasound Flow Meter (USF meter) using a calibrated transit time flow probe (3S) connected to a flow meter (model T208: Transonic Systems, Inc, Ithaca, NY). After completion of the bypass and stabilization of flow (<15 min after completion), mean bypass flow was measured and recorded at a mean blood pressure of 90 mmHg. Intra-operative angiography was also used to look for technical errors, to confirm patency of the bypass, and to detect and counter vasospasm (with local administration of papaverine solution).

Post-operative evaluation

All patent bypasses were perfused with heparine-saline solution to prevent any post-mortem coagulation, and then excised. Immediately after excision, all End-to-Side anastomoses were excised, photos were taken using the operating microscope (OM), and the specimens were longitudinally cut to enable evaluation using the scanning electron microscope (SEM).

Scanning Electron Microscopy

Examination with a scanning electron microscope (SEM: Philips XL30LAB) was performed after fixation with a 2% glutaraldehyde solution buffered in 0.1 M purified phosphate buffer for 1 hour. Fixation was completed after the specimens were left in 1% buffered osmium tetroxide for one hour. After fixation, the specimens were dehydrated in a graded series (50%, 70%, 90%, 100%) of ethanol and dried in liquid CO2 using the critical point method. The specimens were then fixed on scan tubs and covered with a thin layer of gold by sputter processing to enhance the image quality.

Results

Surgical results

All 56 end-to-side anastomoses (28 bypasses) were performed by one investigator (HJNS). Long term evaluation after termination was not obtained in 4 animals (8 anastomoses). In one pig we failed to check the flow in the left CCA, which turned out to be hypoplastic (<1.5 mm in diameter over a length of 3 cm distally of the bypass). Removing the right CCA proved to be fatal within 60 minutes, almost immediately after completion of the bypass. This animal was then terminated while still under anaesthesia. In all other pigs a high flow in the left CCA was observed using the USF meter before excising the right CCA. Another animal died because of severe thrombus formation distal of the conventional E-S anastomosis, 30 minutes after completion of this anastomosis. Although we managed to complete an ELANA anastomosis proximally of the E-S anastomosis, initial flow through the bypass was 45 ml/min, and decreased to 0 ml/min within 1½ hours. This animal was terminated while still under anaesthesia. Two other animals survived in their assigned groups and suffered from mild ischemic symptoms (red hanging eye on the left side). On termination both bypasses were found to be occluded.

Temporary occlusion time for conventional E-S anastomosis (n=28) was measured from placement of the first temporary clip or vessel loop around the recipient artery to removal of the last temporary clip or vessel loop from the recipient, with restoration of flow. For all animals the mean temporary occlusion time was 25.8 ± 12.6 minutes. Mean results for each group were: I. 24.0 ± 8.2 minutes, II. 32.1 ± 13.5 minutes, III. 27.5 ± 17.5 minutes, IV. 18.3 ± 4.1 minutes. No significant differences between the groups could be found. Every conventional anastomosis was evaluated for leakage and the necessity of placing extra stitches to control the bleeding. There was minor leakage in 11 anastomoses and abundant bleeding in 2. In all cases bleeding was effectively countered with 1 or 2 stitches. Surgery time for ELANA anastomosis was estimated from placement of the first stitch in order to attach the platinum ring to the common carotid artery to the application of the temporary clip around the graft after the laser ablation process. For all animals the mean surgery time was 45.2 ± 9.3 minutes. Mean results for each group were: I. 45.0 ± 9.4 minutes, II. 47.1 ± 8.6 minutes, III. 44.2 ± 7.4 minutes, IV. 44.2 ± 13.2 minutes. Again no significant differences between the groups could be found. Every ELANA anastomosis was evaluated for leakage and the necessity of placing extra stitches to control the bleeding. There was minor leakage in 14 anastomoses, which did not need any counter measurements, and abundant bleeding in 1. In that case the bleeding was effectively countered with 1 extra stitch.

Follow-up

The schedule of termination was completed by 26 animals. In two pigs the bypass was occluded; one at 4 weeks, the other after 6 months (total patency rate of 92%). In the first bypass a posterior-anterior suture was found in the End-to-End anastomosis. The other bypass showed occluded anastomoses and extensive neo-angiogenesis aside of the bypass within a large fibrotic area. In the CCA proximal of this part a flow could be observed of 20 ml/min. Two other pigs developed a sterile inguinal cyst at the location where we had inserted the Seldinger-catheter for intra-operative angiography. Both bypasses were patent. All animals were weighted (n=24). Mean initial weight was 31.4 ± 4.3 kg. At 4 weeks (Group I), the mean weight of the animals was 38.6 ± 2.3 kg, at 2 months (Group II) it had increased to 72.4 ± 12.3 kg, at 3 months (Group III) to 77.7 ± 6.2 kg, and at 6 months (Group IV) to 112.3 ± 26.6 kg. The mean flow at termination through the bypass was in Group I: 155.2 ± 33.7 ml/min, in Group II: 173.6 ± 46.4 ml/min, in Group III: 165.2 ± 39.7 ml/min, and in Group IV: 169.2 ± 45.3 ml/min. All measured flows were considered optimal, and no significant differences could be found between the groups.

Morphological Results

Group I (n=7, 2 weeks survival)

One pig in which the bypass was found to be occluded was not included in this group. In the other six animals we observed nice re-endothelialization of all anastomoses, both using the operating microscope (OM) as well as with the scanning electron microscope (SEM) (see Figure 6.1. for a representative image of a conventional anastomosis and an ELANA anastomosis after 2 weeks). On OM the ELANA anastomoses appeared more symmetrical than the conventional anastomoses. In all ELANA anastomoses we observed on SEM a small bulge protruding into the lumen just below (recipient-side) the platinum ring (see Figure 6.1.E), which was absent on the graft-side of the platinum ring, regardless of the direction of blood flow. Both conventional and ELANA anastomoses showed complete re-endothelialization. In all ELANA anastomoses both platinum ring and the rim of medial and adventitial layers were completely covered with endothelium.

Group II (2 months)

In this group, all seven animals survived with a patent bypass, which showed very nice re-endothelialization (see Figure 6.2.). Using the OM the stitches could be seen shining through in all anastomoses, with the platinum ring partially shining through in an all ELANA anastomoses. Again the ELANA anastomoses appeared more symmetrical than the conventional anastomoses. In all ELANA anastomoses the rim had disappeared for at least ½ of the circumference of the anastomosis, and often for ¾ of the circumference (see Figure 6.2.D). Wherever the rim persisted, it was completely covered with endothelium (see Figure 6.3.), which was continuous with the rest of the anastomosis, the platinum ring, the recipient, and the graft. On the

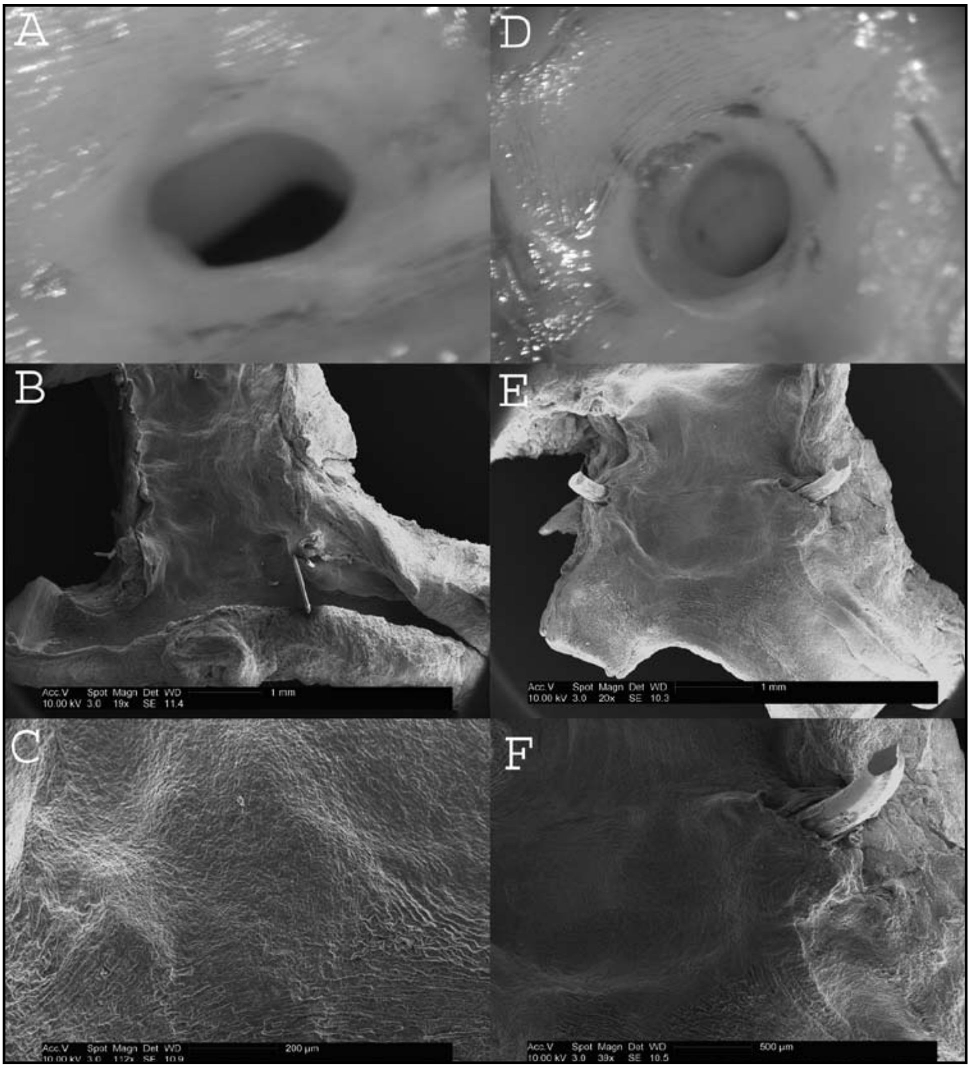


Figure 6.1. Group I (2 weeks survival)
OM image (A) of the inside of a conventional anastomosis after 2 weeks. The recipient artery has been cut open and the point of view is directed inside the graft. SEM image (B) of the same conventional anastomosis, longitudinal view. Some irregular wall deformities are visible within the lumen. The bolt-like structure on the right is an artefact. High magnification detail (C) of the same anastomosis. The endothelial lining of the graft (upper-right side) is completely continuous with the recipient artery (down-left side). OM image (D) of the inside of an ELANA anastomosis after 2 weeks. Similar point of view as (A). Notice that several stay sutures of the ring can be seen shining through. The innermost circle is the lumen of the graft several millimetres away from the anastomosis. Outside this circle, the rim of the real anastomotic site (with the platinum ring shining through) can be observed. SEM image (E) of the same ELANA anastomosis. The platinum ring has been cut in two for the SEM. Both ends of the ring can clearly be seen, as well as a thickening of the endothelium which protrudes into the lumen of the recipient just below the platinum ring. Medial of the platinum ring the rim of medial and adventitial layers is visible. High magnification detail (F) of the ELANA anastomosis. Around the platinum ring there seems to be an accumulation of tissue. However, the endothelial surface is completely continuous; from the graft, covering the platinum ring, covering the rim, to the recipient.

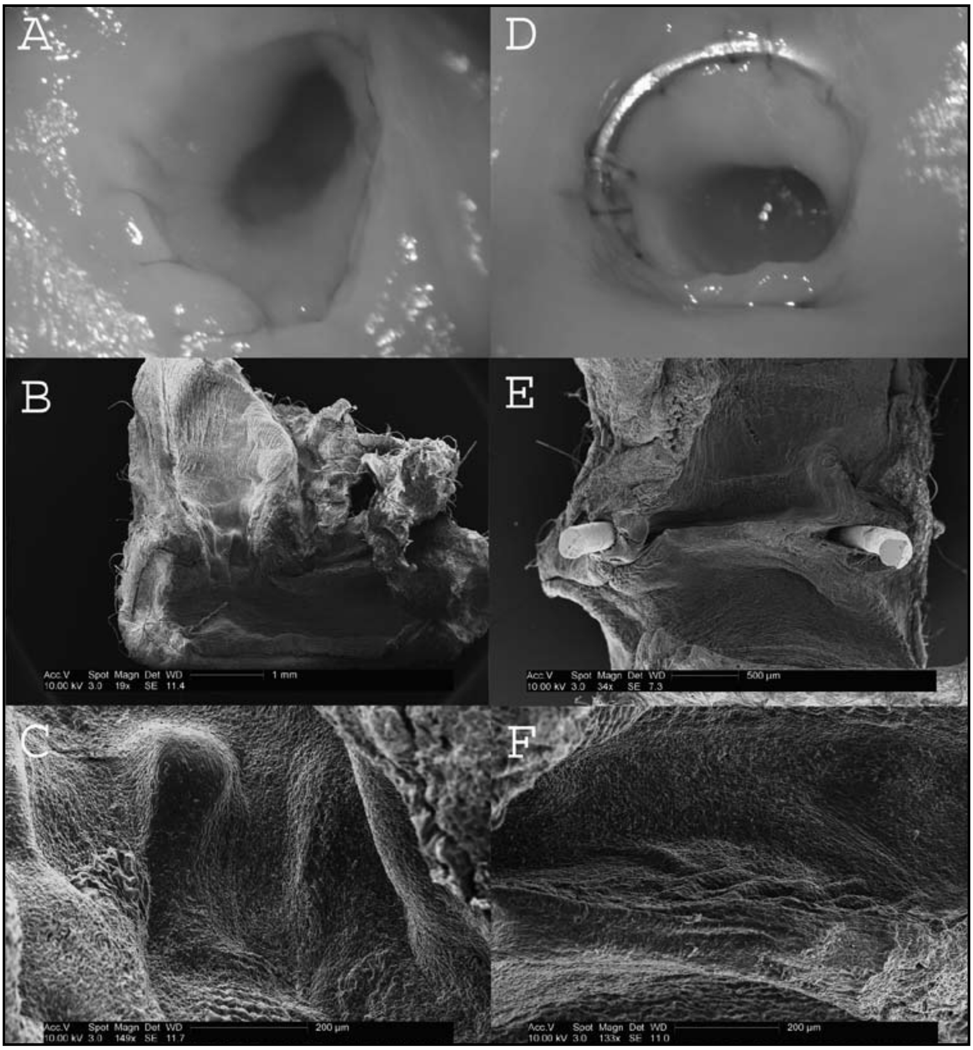


Figure 6.2. Group II (2 months survival)
OM image (A) of a conventional anastomosis after 2 months. Point of view from inside the ricipient, looking through the anastomosis into the graft. The running suture is clearly visible and covered with endothelium. Although the anastomosis is not perfectly round, no irregularities of the anastomosis can be observed. On the longitudinal SEM image (B) of the same conventional anastomosis, the endothelial lining of the graft seems continous with the recipient, despite some folding of the graft wall. A high magnification image (C) of the same anastomosis at the transition of recipient to graft shows that the endothelialisation of the anastomosis seems complete, leaving no trace of any transition between graft and recipient. OM image (D) of an ELANA anastomosis after 2 months with the point of view similar to A. The stay sutures for the ring as well as the sutures fixating the graft onto the recipient around the ring are clearly visible and are covered with a small transparent layer of endothelium. A small part of the rim is visible in the lower-right quadrant. However, this has disappeared in the other three-quarters of the anastomosis. On the longitudinal SEM image (E) of the ELANA anastomosis, the thickening of the vessel wall below the ring as seen in figure 6.1.E is absent. On the top of the ring the endothelial lining can be seen to have become very thin. On high magnification and under a small oblique point of view (F) the ring is completely covered with endothelium, and the upper surface (graft-side) of the ring is covered with several folded layers of endothelium.

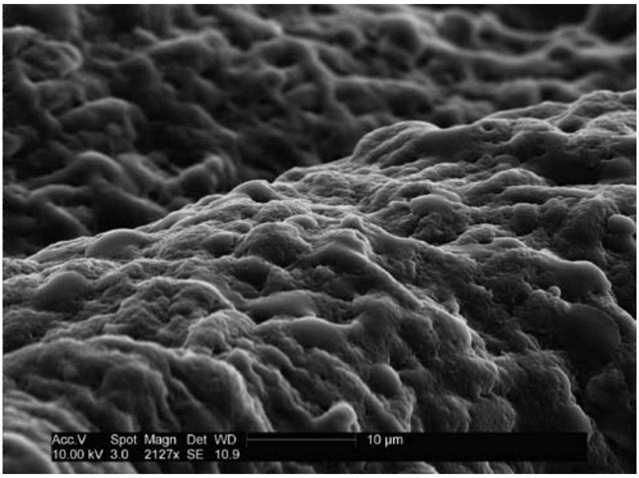


Figure 6.3.
Very high magnification SEM image of the platinum ring in Figure 6.2.(Group II, 2 months survival). This is a close-up of the rim which has been created during the laser ablation process. The excimer laser has been activated from the top side downwards, first passing the adventitial layer, then the medial layer, and finally the intimal layer. Both adventitial and medial layers are indistinguishable and have been covered with endothelial cells in which the protruding nuclei can be seen clearly.

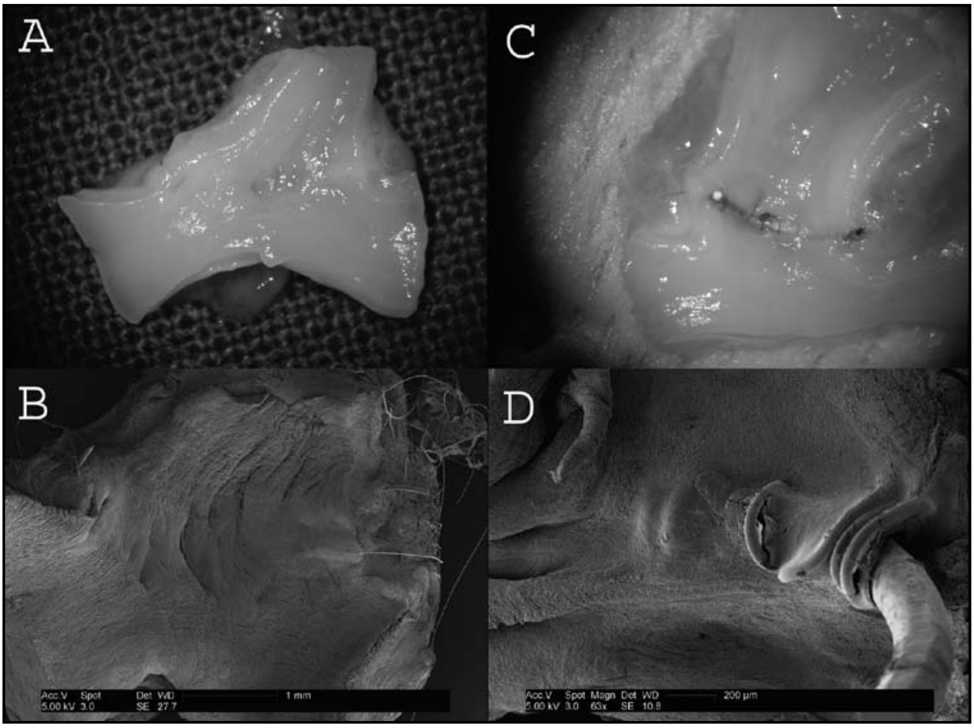


Figure 6.4. Group III (3 months survival)
Longitudinal OM image (A) of a conventional anastomosis after 3 months. Again the running suture can vaguely be seen shining through a layer of endothothelium. The SEM image (B) of the same conventional anastomosis shows that aside from the lumen being somewhat wider this anastomosis is similar to conventional anastomoses at earlier termination moments. Longitudinal OM image (C) of an ELANA anastomosis after 3 months. The ring and the sutures can be seen clearly, covered with a transparent layer of endothelium. The oblique SEM image (D) of the ELANA anastomosis shows that the rim has disappeared and the ring is covered with a very thin lining of endothelium, which consists of a very small layer all around the ring. The 9/0 Prolene sutures are also covered with endothelium. The lumina of both recipient and graft appear to be very wide.

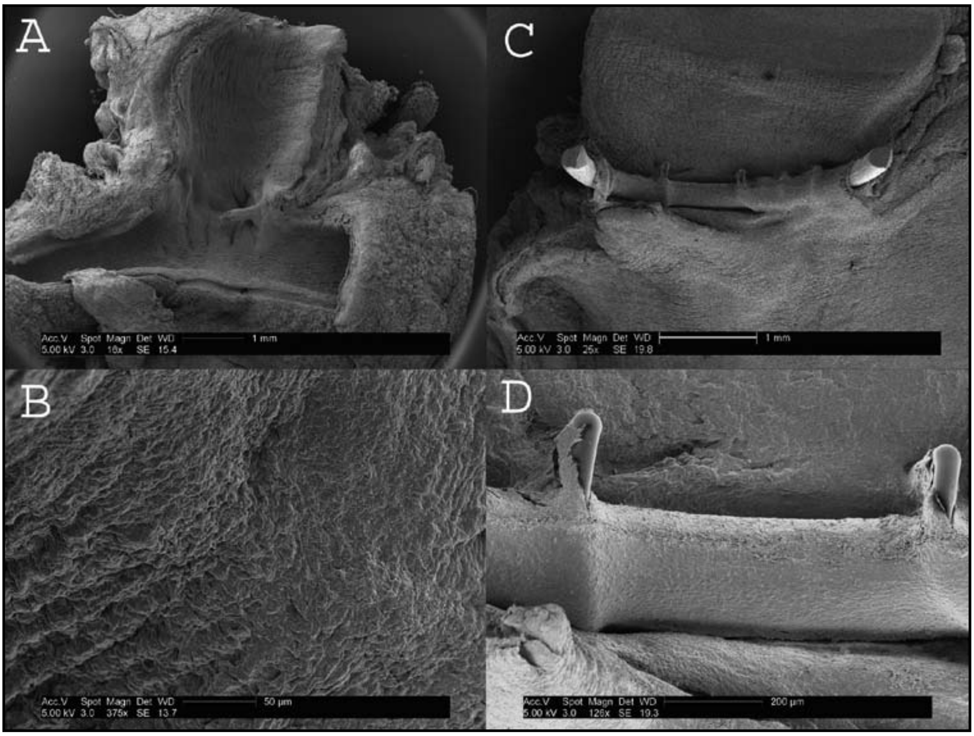


Figure 6.5. Group IV (6 months survival)
Overview SEM image (A) of a conventional anastomosis after 6 months. Here the graft lumen is somewhat wider than the recipient. However, the re-endothelialisation is similar to conventional anastomoses at earlier termination moments. A high resolution SEM image (B) of the conventional anastomosis shows that the transition of graft (upper-right) to common carotid artery (left) is only distinguishable because of the different muscle contraction direction, which creates the grooved surface of the common carotid artery. The endothelial lining is completely uninterrupted.
Overview SEM image (C) of an ELANA anastomosis after 6 months. The laser ablation rim has completely disappeared, leaving the ring covered with a layer of endothelium. This endothelium is entirely continuous from graft, over the ring, to the common carotid artery. The high magnification SEM image (D) of the ELANA anastomosis shows that the platinum ring has been covered completely with endothelial cells. The 9/0 Prolene sutures once were pulled tight around the tissue of the graft, the ring, and the tissue of the common carotid artery, and were pulled free from their endothelial cover during the fixation process.

graft-side the platinum ring is covered with an extremely thin layer of endothelium (see Figure 6.2.D, E).

Group III (3 months)

In this group, all seven animals survived with a patent bypass, which showed very nice re-endothelialization (see Figure 6.4.). Using the OM the stitches could be seen shining through in all anastomoses, with the platinum ring completely shining through in an all ELANA anastomoses. Again the ELANA anastomoses appeared more symmetrical than the conventional anastomoses. In all ELANA anastomoses the rim had disappeared completely, and the platinum ring seems to be the narrowest part of the anastomosis (see Figure 6.4.C). On both graft-side as well as recipient-side the platinum ring is covered with an extremely thin endothelial layer, through which the contours of the 9/0 Prolene sutures can be seen clearly as they have been covered with endothelial as well (see Figure 6.4.D).

Group IV (6 months)

In this group, six out of seven animals survived with a patent bypass, which showed very nice re-endothelialization (see Figure 6.5.). In all ELANA anastomoses the rim had disappeared completely, and the platinum ring seems to be the narrowest part of the anastomosis (see Figure 6.5.C). On both graft-side and recipient-side the platinum ring is covered with an extremely thin layer of endothelium, and again the contours of the 9/0 Prolene sutures are very well visible (see Figure 6.5.D).

Discussion

The main purpose of this study was to investigate the endothelialisation of the platinum ring and the rim of medial and adventitial layers at the ELANA anastomosis site. Our methods include an experimental pig model in order to study a novel anastomosis technique, in which we created high flow circumstances to observe the re-endothelialisation of the anastomoses with special consideration for the above mentioned points.

Experimental Models

In 1968 Yasargil reported the first Extracranial-to-Intracranial (EC-IC) arterial shunting procedure in the dog.[342] Other experimental E-S anastomosis techniques have successfully been applied in rats,[35, 115, 235, 236, 291] rabbits,[196, 231, 301, 305, 338] and pigs.[55, 139] Although we found the rabbit abdominal aorta to be an excellent model for cerebral revascularization techniques,[338] we thought that the necessary laparotomy in this animal was a negative factor for long-term survival. As pigs have been used by our department of experimental cardio-thoracic surgery for some time,[139] we considered the advantage of small neck surgery to be important. Both carotid arteries can be exposed within 10 minutes. However, these porcine CCAs are relatively large compared to human ICAs, and the wall is much thicker (30 – 40 micrometer, compared to human 10 – 20 micrometer). In our experiments with rabbits we could use the same clinical settings for the laser device as we use in human surgery (a total of 200 pulses at a frequency of 40 Hz with Energy of 10mJ). In the pigs we used similar settings, however, with a total of 300 pulses. Any thermal effects to the anastomoses would be more clearly detectable. Still, after two weeks we did not find any thermal effects, which is supported by the results of our earlier experiments in rabbits.[305]

Surgical Techniques

Carrel's triangulation technique is still the basis of conventional E-S anastomosis techniques.[59] After good haemostasis an arteriotomy is made in the recipient artery, and the donor is then connected to the recipient using interrupted or a running sutures. Carrel stated that precise apposition of the endothelial layers was obligatory for a patent anastomosis.[60] Few studies have tried to challenge that statement.[341] And indeed most conventional anastomosis in cardio-thoracic surgery, plastic surgery, vascular surgery, neurosurgery, and fertility surgery are made with careful approximation of the endothelial layers. However, for neurosurgical application of high flow vascular anastomoses a non-occlusive technique is advantageous because of the limited risk of cerebral ischemia. In 1993 the Excimer laser became available in our department.[305] With the help of the platinum ring and the newly designed laser tip we are now able to create high-flow extracranial-to-intracranial and intracranial-to-intracranial bypasses to all major blood vessels in the brain.[123, 178, 179, 181, 273, 297, 299, 300, 303-306, 313]

Clinical Experience

Our clinical experience with the ELANA technique are largely dependent on the indications for bypass surgery. We have applied the ELANA technique in patients who have symptomatic unilateral or bilateral ICA stenosis, inaccessible to endarterectomy, and who suffer from multiple TIAs or progressive stroke, despise optimal anticoagulantia therapy. In a short series we have seen that the complications of the ELANA technique itself are almost non-existent.[179, 180] However, the risk of major intracranial surgery, which includes bypass surgery using the ELANA technique, is large enough for us to only include those patients mentioned above.

There are cases in which a low flow bypass is indicated. In such cases traditional STA-MCA (cortical branch) bypass or OA-PICA bypass would suffice and the ELANA technique would not be useful. In aneurysm surgery we found that giant aneurysms of the cavernous or more distal ICA segments can be well treated using EC/IC bypass surgery, during which the distal anastomosis was made using the ELANA technique in order to prevent temporary ischemia of the brain. Again, we found the complications of the ELANA technique itself to be non-existent.[140, 274, 297, 313] However, again the risk of major intracranial surgery with the ELANA technique is comparable to aneurysm surgery without the ELANA technique (publications in preparation). The ELANA technique has now been used by several other institutions, among which are the University Clinic Mannheim, Germany, the Helsinki University Central Hospital, Helsinki, Finland, and the University Clinic, Bern, Swiss. The Excimer laser, the laser catheters, and the platinum rings (sizes 2.6/2.8/3.0 mm) are commercially available. For more information see www.ELANA.com The authors do not have a financial interest in the production.

Arterial Blood Flow in Pigs

We transplanted the right CCA onto the left CCA. As pigs have a high capacity to form collateral vessels next to the many existing collaterals (rete mirabile), removing one CCA usually is not a problem. One pig died because of the fact that the remaining CCA was hypoplastic. The high amount of collaterals also means that we should not give too much weight to the flow measurements. It is very clear, though, that the flow through the bypass is diminished for $^1/_3$

to ½ of the original flow, because of the many curves and the size of the ELANA anastomosis (lumen diameter is 2.6 – 2.8 mm). However, in 6 months the pigs grew a lot (from 31.4 ± 4.3 kg to 112.3 ± 26.6 kg) and the mean flow through the bypass increased from 144.8 ± 28.9 mol/min with 20.8 ± 41.5 mol/min (16.3 ± 34.0 %) to 169.2 ± 45.3 mol/min.

Re-endothelialisation

In rats, re-endothelialisation in conventional E-S anastomoses has been reported to be completed in 2 weeks as observed by SEM.[35, 115, 291] This was also the case in our early rat experiments with the semi-non-occlusive anastomosis technique.[293] In our rabbit experiments we observed complete re-endothelialisation within 9 days.[338] Testing the applicability of intima-adventitia apposition in high flow conditions in the pig (without the use of the Excimer laser), Heijmen et al reported a patency rate of 100% despite thrombotic phenomena were observed within the first 2 hours.[139] These findings were confirmed in low flow circumstances by Buijsrogge et al in 2002.[55] However, to our knowledge, we are the first to report on the intermediate (3 months) and long-term (6 months) re-endothelialisation on high flow Excimer laser-assisted non-occlusive anastomoses with a rim of medial and adventitial layers, and a platinum ring exposed to the blood stream.

In our pig experiments, we found the re-endothelialisation of all anastomoses to be complete after 2 weeks, including the endothelialisation of the platinum ring. However, below the rim we could observe some hyperplasia of the wall, which has been described in literature, and may be due to medial hyperplasia.[196] We did not observe the rim itself nor any hyperplasia in the anastomoses which survived for 3 months or more.

Conclusions

Our results show that within 2 weeks complete re-endothelialisation of the ELANA anastomoses has been realized. Within three months the rim of medial and adventitial layers has completely disappeared, leaving only a continous endothelial lining. The platinum ring is included in the complete re-endothelialisation after 2 weeks. After three months only a very thin layer of endothelium is covering the parts of the ring which are exposed to the blood stream. We conclude that in long-term experiments in pigs ELANA anastomoses re-endothelialize comparable with conventional anastomoses under high flow circumstances (>100 ml/min). Considering these results, the unique non-occlusive characteristics, and combined with the high-flow capabilities of the ELANA technique, we will continue to use the ELANA technique as the best option in cerebral revascularization procedures for non-coilable and non-clippable giant aneurysms, difficult skull-base tumours, and selected cases with persistent symptoms of cerebral ischemia despite optimal medical treatment.

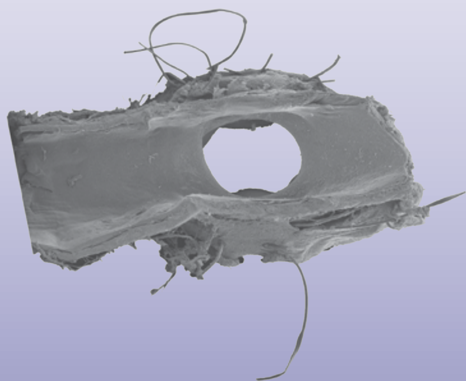
Acknowledgements

Because of their extensive assistance with all the experiments, the authors wish to thank the biotechnical assistants of the Animal Laboratory, especially Hans Vosmeer, Herman Koning, Nico Attevelt, Jannie Visser, and Elly van Zwol, and the rest of the ELANA Research Group, namely J.P. Bremmer and M. Muenker.

Next page
Scanning Electron Microscopic image of an ELANA anastomosis in a human treated for a giant AComA aneurysm. Point of view is from within the P2, looking through the ELANA anastomosis into the bypass graft. Observe the almost completely roundness of the anastomosis.

Chapter 7

Re-endothelialization in Humans



H.J.N. Streefkerk, K.S. Han, J.P. Bremmer, E.L.G.E. Koedam,
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Scanning Electron Microscopic Evaluation of the Re-endothelialization of Intracranial Anastomoses

Abstract

Objective and Importance

Using the ELANA technique, anastomoses can be made without occluding the recipient vessel. However, the medial and adventitial layers of the recipient and a platinum ring are exposed to the blood stream. We evaluated scanning electron microscopic (SEM) images of the anastomoses in four patients with a cerebral bypass.

Presentation and Intervention

Three patients suffered from a giant intracranial aneurysm. One patient had a skull base tumor encasing the internal carotid artery which was supplied by a branch of the external carotid artery. All patients were operated with bypass surgery.

Techniques

All four patients died of causes not directly related to the bypass procedure. At autopsy, the anastomoses were taken out and evaluated using the SEM.

Results

In all ELANA anastomoses older than 4 days, the laser edge was very smooth. Endothelial cells on the laser edge were observed only in case 4 (5 years survival). The platinum ring could only be observed to be partially without covering in case 1 (4 days survival). In all other anastomoses a different suturing technique had been used so that the ring was not exposed to the blood stream.

Conclusion

Re-endothelialization of the platinum ring starts after 4 days, and completes between 31 days and 5 years, after which the anastomoses are wide open, fully round, and with a continuous layer of endothelium covering the inside of the anastomosis. We conclude that the re-endothelialization of ELANA anastomoses in human is likely to occur.

Introduction

The excimer laser-assisted non-occlusive anastomosis (ELANA) technique can be used to make anastomoses to cerebral arteries with a diameter between 2.6 and 3.5 mm, without occluding that recipient artery. We have previously described several successful series and case reports about the use of the ELANA technique for the creation of in the treatment of cerebral ischemia,[179, 180, 297, 298] giant intracranial aneurysms,[274, 313] and skull base tumors.[123] It has been established that ELANA anastomoses allow for quite an amount of blood flow.[140, 313] In the laboratory, we have observed very nice re-endothelialization of ELANA anastomoses in short-term rabbit experiments[339] and in long-term pig experiments (submitted).[272] As most patients treated with the ELANA technique have survived, we have not reported on the human re-endothelialization of ELANA anastomoses before.

The last years, we have been in the process of re-evaluating all data on the ELANA technique. In case of a fatality, we asked the patient's family to allow autopsy on the patient, in order to find out the exact cause of death, and to evaluate the ELANA technique. Only recently we lost a patient to a fatal pneumonia. This patient had been operated upon using the ELANA technique exactly 5 years earlier. From three other families also we got permission to perform an autopsy. Therefore, we are now able to present the re-endothelialization of ELANA anastomoses in 4 patients, who were operated for various indications, and who died from causes not related to bypass surgery. The main objective of this paper is to present the re-endothelialization results, with special attention to the edge of the laser ablated opening in the wall of the recipient artery and to the re-endothelialization of the platinum ring, and to compare these with the short-term and long-term re-endothelialization as observed in pigs at the above-mentioned sites.

Patients and Methods

We present a post-mortem study of 4 patients (see Table 7.1.). Three patients suffered from a giant intracranial aneurysm. One patient had a skull base tumor encasing the internal carotid artery (ICA) and which was extensively supplied by a branch of the external carotid artery (ECA). All patients were operated with bypass surgery, in which one or two anastomoses were made using the ELANA technique.

The ELANA technique

This technique has extensively been described elsewhere.[273, 274, 299, 300, 303-306] In short, a platinum ring with a diameter of 2.6 mm or 2.8 mm is attached to the wall of the recipient artery with 8-0 or 9-0 sutures. The bypass graft is cut in two. One of those parts is then sutured to the wall of the recipient artery, using the ring as guide, taking into account the correct direction of flow. An excimer laser catheter is introduced into the graft so that the tip is touching the wall of the recipient artery within the platinum ring. Vacuum suction is applied through the

Table 7.1. Indications and presentation

	Sex age	Indication	Presentation	CT/MRI-scan	Angiographic details
1	M 36	Giant BA trunk aneurysm	Diplopia, hemiparesis with mild central facial paresis, dysarthria, swallow problems.	Giant, partially thrombosed aneurysm with space-occupying effect to brain stem.	Absent PcomAs.
2	F 63	Giant AComA aneurysm	Hemianopsia. No other neurological deficits	Giant, partially thromobosed aneurysm. Obvious space-occupying effects to optic chiasm.	Filling of Aneurysm by right A1 only.
3	M 57	Giant VA-BA aneurysm	Episodical vertigo and tinnitis. Diplopia, Left facial paresis, swallow dysfunction, dysarthria, distal paresis left arm, left leg.	Very thin layer of brain stem around giant BA aneurysm.	Very thin left PcomA. Right PcomA absent with embryonal right PCA (PCA is continuation of PcomA from ICA)
4	M 40	Skull Base Chemodectoma	Left facial palsy, left vocal cord palsy, hearing loss left, vertigo, tinnitis. No other neurological deficits	Petrosal infiltration with cerebellar and temporal progression	Major supply of ECA to tumor

catheter in order to firmly fixate the laser fibres against the wall of the recipient artery. After 2 minutes of vacuum suction the laser is activated, creating a connection between the blood vessels, and a full-thickness, round part ("flap") of the wall of the recipient is punched out. Due to the continuous vacuum suction, the flap is taken out of the anastomosis together the withdrawal of the catheter. This technique was used either for the proximal anastomosis, the distal anastomosis, or both. After completion of one anastomosis the other part of the graft was used for the second anastomosis. The two open ends were then connected at an angle (to prevent accidental kinking of the graft) using a conventionally sutured end-to-end anastomosis with a 7-0 or 8-0 suture. For each patient the anatomical sites of both anastomoses were noted. In case of an ELANA anastomosis, also the size of the platinum ring, the retrieval of the flap, and the successful connection of both vessels was noted. After completion of the bypass, the flow through the bypass was measured using a Transonic Flow Meter (Transonic Systems Inc, Ithaca, New York) and a 3 mm flow probe.

Case reports (see Tables 7.1. and 7.2.)

Case 1 (We have previously published this case as a separate case report.[274])

This 36 year old male presented with severe headaches, dizziness, and symptoms of dysphasia, eye-movement disorders, a mild central facial paresis, dysarthria, swallow problems, and hemiparesis on the right side. His medical history mentioned a familial thrombopathy and a stroke in 1985 that caused a hemiparesis and dysphasia, which had gradually improved. There were also transient ischemic attacks with dysarthria, and right sided paresis of the facial nerve. Sometimes, his headaches were especially severe when accompanied with diplopia, dizziness,

Table 7.2. Interventions and Outcome

	Interventions					FU	Outcome
	Proximal anastomosis	Distal anastmosis	Graft	Flow	Other		
1	Conv ELANA ICA 2.8 mm flap	Convent SCA	SVG	41 (after ligation)	BA ligation proximal of SCA (intra-op)	4 days	Thromboembolic occlusion of right MCA resulting in fatal stroke.
2	Conv ELANA ICA 2.8 mm flap	Conv ELANA A2 2.6 mm flap	SVG	25 (competitive)	- (Intented A1 ligation was postponed due to bad lung function)	6 days	Direct post-operatively completely oriented and no neurological deficit (hemianopsia not evaluated). After 6 days sudden fatal SAH from the basis of the aneurysm. Bypass pink and pulsating.
3	Adv ELANA ICA 2.8 mm flap	Adv ELANA P1/2 2.6 mm flap	SVG	70 (after ligation)	VA ligation (intra-op)	31 days	Post-operatively similar neurological deficits as pre-operatively. After 3 weeks hydrocephalus. Intracerebral hemorrhage due to EVD insertion. Multiple occlusions of EVDs with re-operation for new EVD. Meningitis. Progressive brain stem compression due to progressive thrombosis of aneurysm. Life support discontinued
4	Conventional ECA	artificial branch ELANA ICA flap 2.8 mm	SVG	95 (competitive)	ECA ligation (intra-op) ICA ligation (post-op) Tumor debulking	5 years	Pneumothorax. Direct post-operatively no neurological deficits. Retired with excellent outcome to full working status. During the year, progressive mild hemiparesis, multiple pneumonias, countered with antibiotics, and hydrocephalus treated with EVD. Re-admission after 5 year with a fatal respiratory insufficiency after pneumonia with aspiration. Last patency evaluation of bypass 2 years post-operatively. Bypass patent on MRI and pulsating nicely.

and vertigo. Angiography and computed tomographic (CT) scans showed a giant, partially thrombosed aneurysm of the basilar artery, located between the anterior inferior cerebellar arteries (AICAs) and the superior cerebellar arteries (SCAs). Both posterior communicating arteries (PComAs) were found to be absent, and a transcranial Doppler-guided (TCD) balloon-test-occlusion (BTO) of the posterior cerebral arteries (PCAs) showed that the patient would not tolerate basilar artery (BA) or vertebral artery (VA) occlusion without revascularization.

In April 2001, an IC-IC bypass was constructed from the left intracranial ICA to the left SCA, after which the BA was ligated with a hemo clip just distally from the aneurysm and proximally of the SCAs. The proximal anastomosis to the ICA was successfully made with the ELANA technique (successful connection with successful retrieval of the flap). A 2.8 mm platinum ring was used for the ELANA anastomosis. Post-operative course was complicated by ischemia in the area of the left middle cerebral artery (MCA) after two days. An angiogram showed the bypass to be open. A repeat CT showed larger hypodens areas on the left side, and midline shift was observed. Treatment was discontinued and the patient died 4 days post-operatively. Considering the patient's familial thrombopathy, and considering the flow direction of the bypass, we found it very unlikely that the severe left MCA stenosis would have been bypass-related. At autopsy, also multiple lung emboli were found, suggesting a systemic thrombogenic cause. Elsewhere, we have extensively described our thoughts on this patient's death.[274] For more details we would like to refer to that publication.

Case 2

A 63 year old female presented with symptoms of hemianopsia on the right side. She had no other neurological deficits. Angiography, CT, and MRI scanning showed a giant, partially thrombosed aneurysm of the anterior communicating artery (AComA) which filled only from the A1 (pre-communicating) segment of the right side. The aneurysm was considered uncoilable without danger to the A2 segments. Also, it was considered unclippable without occluding the AcomA or both A2s.

In January 2002 an IC-IC bypass was made from the intracranial ICA to the right A2 at the genu of the callosal corpus. Both anastomoses were made using the ELANA technique. A 2.8 mm platinum ring was used for the ICA anastomosis. For the A2 anastomosis a smaller (2.6 mm) platinum ring proved a better fit. Direct post-operative state of the patient was excellent, with a maximal Glasgow coma score (GCS), well orientated, and without focal neurological deficits. However, after 6 days, she was walking around, and she suddenly became comatose with an GCS of 3. CT-scanning showed a massive subarachnoid hemorrhage (SAH). At re-operation the brain was very edemous, and was pushed outwards through the trephination hole. On exploration the bypass was found to have a very pink color and was seen to be pulsating very well. The SAH did not originate from the proximal or distal anastomosis. However, continuous bleeding was seen from the basis of the aneurysm. As it was impossible to clip the aneurysm at that moment with such a swollen brain, further interventions were discarded. Treatment was discontinued and the patient died 6 days after bypass surgery.

Case 3

This 57 year old male presented in summer 2000 with several episodes of vertigo and tinnitus. His medical history also mentioned angina pectoris, cardial decompensation based on hypertension, an abdominal aorta aneurysm treated with an aorta-bifurcation prothesis, and hepatic steatosis. In 2001, a giant vertebro-basilar aneurysm (VBA) was observed on CT and angiography. Since then, his symptoms worsened and in October 2002 he was unable to walk, had swallow problems, diplopia, left facial paresis, dysarthria, which was presumably based on progressive brain stem dysfunction due to the mass-effect of the VBA. As he declined so rapidly, bypass surgery was offered in the hope that flow reversal in the aneurysm would slow its rapid growth.

Using a very large fronto-temporal trephination, which ex the lateral orbita, the Sylvian fissure was exposed. The intracranial ICA was seen to be very large and was chosen as proximal anastomosis site. Laterally of the ICA/M1 the posterior fossa was observed with the outlines of the giant aneurysm. Following the oculomotor nerve, the PCA was found. Through this approach the P1/2 segment was considered as a suitable distal anastomosis site. Both anastomoses were made using the ELANA technique. A 2.8 mm platinum ring was used for the proximal anastomosis with the ICA. For the P1/2 anastomosis a 2.6 mm platinum ring was used. In each case a connection was successfully made, and a flap was retrieved. The flow through the bypass (without any vessel occlusion) at that time was about 10 ml/min. Intra-operatively the VA was then occluded with a temporary hemo clip, and the flow through the bypass increased to 70 ml/min. The temporary hemo clip was replaced by a permanent clip. The patient recovered very slowly, and showed neither progression nor regression of his neurological deficits. However, within the period of one month, he developed hydrocephalus 3 times, due to occluding external ventricle drains (EVDs). This was complicated by meningitis and an intraparenchymatous hemorrhage due to the insertion of the second EVD. One month after bypass surgery the patient died due to progressive thrombosis of the aneurysm with fatal brain stem ischemia.

Case 4

A 40 year old male was known with a partially resected (1979 and 1981) chemodectoma which caused a left facial paresis, left vocal cord paresis, and deafness on the left side. After the resection he had been without complaints for more than 15 years. However, the last years he suffered from a progressive facial paresis, vertigo and tinnitus. In 1999, MRI showed a regrowth of the tumor in the petrosal bone with progression in cerebellar direction and temporal. The tumor was extensively supplied by a branch of the external carotid artery (ECA).

A bypass was made from the ECA to the intracranial ICA. The distal anastomosis was made using the ELANA technique with a 2.8 mm platinum ring. The connection was successfully made and a nice flap was retrieved. Before occlusion, the free flow (outflow of the artery into the air) of the ECA was observed to be 800 ml/min. The ECA was then permanently occluded distally from the proximal anastomosis. The flow through the bypass was approximately 95 ml/min. Post-operative clinical state was without complications, and he retired to his home. Several months later bypass patency was confirmed by MR-angiography with a flow of 110 – 210 ml/min. His facial paresis remained stable. He no longer had any complaints about vertigo or tinnitus. In 2001 the patient was re-admitted because of several episodes with severe headache and vomiting. MRI showed the tumor with compression of the brain stem and compression of the fourth ventricle. A ventriculo-peritoneal drain (VPD) was placed without complications, and he returned home. In February 2003, the patient was admitted because of respiratory insufficiency due to aspiration pneumonia. Under optimal antibiotic treatment

Table 7.3. Summary of Results

	Anastomosis	Ring size	Post-op time	Figures LM	Figures SEM	Flow direction	Laser edge	Platinum ring
1	Prox ICA	2.8	4 days	2, 3	4, 5	Outflow	Partially covered with fibrinous layer	Partially covered with fibrinous layer
2	Prox ICA	2.8	6 days	8	11, 12, 13	Outflow	Very smooth Irregularities in crease between graft // edge	Completely covered
	Distal A2	2.6	6 days	9, 10	14, 15	Inflow	Very smooth No irregulari-ties in crease	Completely covered
3	Prox ICA	2.8	31 days	16, 17	20, 21, 22	Outflow	Very smooth Crease not observed	Not observed due to new suturing technique
	Distal P2	2.6	31 days	18, 19	23, 24, 25	Inflow	Very smooth Fibrinous layer Crease not observed	Not observed due to new suturing technique
4	Distal ICA	2.8	5 years	-	26, 27	Outflow	Very smooth Crease disap-peared Endothelial cells visible	Not observed due to old suturing technique

and bronchial lavage, his clinical status improved. However, his pneumonia returned several times, and in May 2003 he died of respiratory insufficiency.

Anastomosis preparation for SEM

After each patient died, permission for autopsy was asked and given in every case. The bypasses were excised, perfused with Dulbecco's medium (modified eagle medium, Life Technologies) and the anastomoses were inspected using the operating microscope. Then the anastomoses were cut longitudinally or transversally and fixated using a 2% glutaraldehyde solution buffered in 0.1 M purified phosphate buffer for one hour. Fixation was completed after the specimens were left in 1% buffered osmium tetroxide for one hour. After fixation, the specimens were dehydrated in a graded series (50%, 70%, 90%, 100%) of ethanol and dried in liquid CO_2 by the critical point method.[320] Before observation in the scanning electron microscope (SEM), the specimens were covered with a thin layer of platinum by sputter processing to enhance the image quality. Using the SEM, specific attention was paid to the anastomosis edge, where the laser had ablated the wall of the recipient artery, and to the platinum ring itself.

Results

In 4 patients, a total of 3 proximal ELANA anastomoses and 3 distal ELANA anastomoses were evaluated. In cases 1 and 2, the anastomoses were cut in two to be able to observe the laser edge in a perpendicular way. In cases 3 and 4 the recipient artery was cut longitudinally in such a way that the integrity of the platinum ring and the surrounding tissue was better

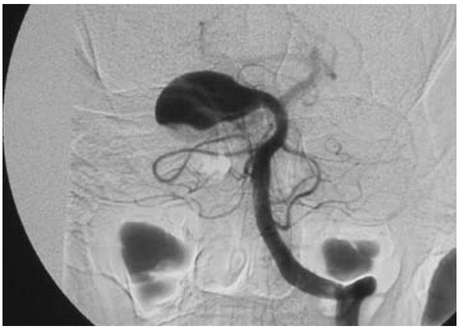


Figure 7.1.
Case 1. AP angiogram of the left VA and the giant fusiform BA aneurysm.

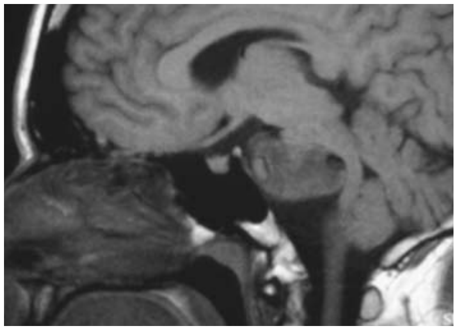


Figure 7.2.
Lateral MR image of the giant BA aneurysm. Observe the mass effect of the aneurysm to the brain stem.

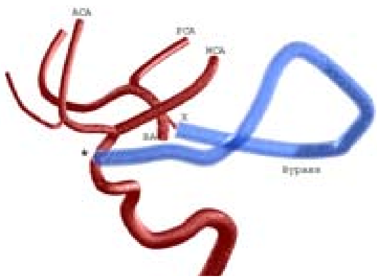


Figure 7.3.
3D reconstruction of the ICA-SCA bypass.

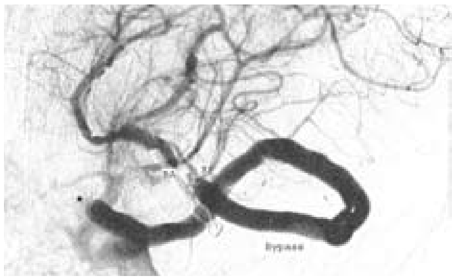


Figure 7.4.
Oblique angiogram of the ICA-SCA bypass.

Figure 7.5.
OM image. Observe the thrombus in the M1 (lower right) and the ELANA anastomosis (left circular).

Figure 7.6.
OM image. Observe that the platinum ring is free of thrombus.

preserved. Although this did not allow for a perfect perpendicular point of view (POV), tilting the specimen proved to be sufficient for good imaging of the laser edge and the covering of the platinum ring.

A summary of the results is given in Table 7.3.

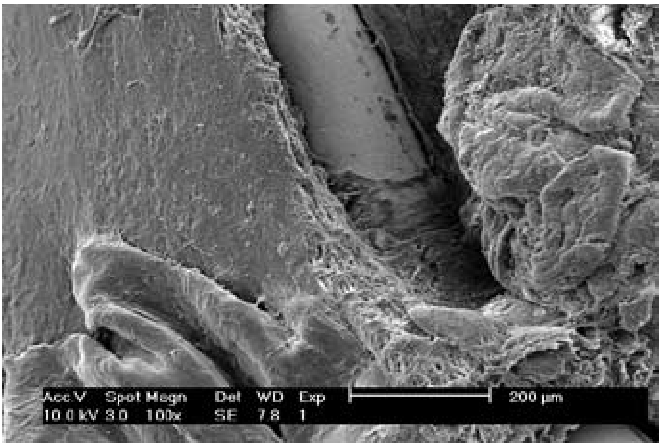


Figure 7.7.
Case 1. SEM image of the inside of the ELANA anastomosis after longitudinal incision of both the ICA, the platinum ring, and the graft (similar to Figure 7.6.). The laser ablated edge of the hole in the ICA can be seen clearly as a sharp edge, located on the left side of the platinum ring. The outline of the ring can also clearly be seen. The ring is partially covered with a fibrinous layer. However, a small part of the ring is not (yet) covered with fibrin. the irregular bulb prominently seen on the right is a corruption of the wall during the fixation procedure (see Figure 7.6.).

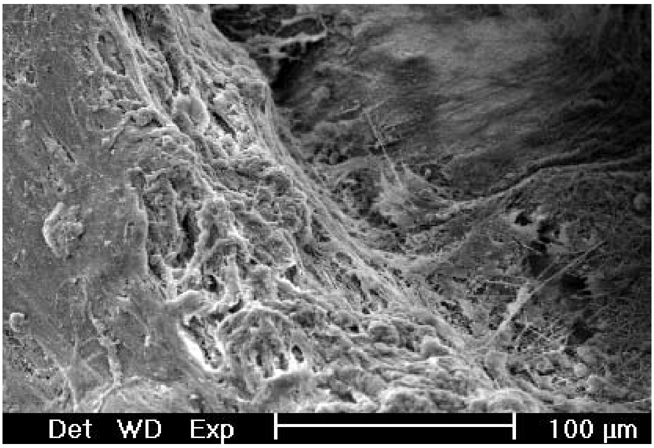


Figure 7.8.
High magnification SEM image of the same anastomosis as in Figure 7.7. The fibrinous layer is continuous with the layer over the laser edge. The edge itself is slightly irregular. Except for the fibrinous layer, no large thrombus is visible on the laser edge. It is not possible to distinguish the different layers in the wall of the ICA.

Case 1

In this patient, an ICA-SCA bypass was created in the treatment of a giant BA aneurysm (see Figure 7.1. to 7.4.). He died 4 days postoperatively, due to a fatal media infarction. At autopsy, the stenosis in the MCA was very obvious (see Figure 7.5.). However, the ELANA anastomosis on the ICA was free of any thrombi (see Figure 7.5. and 7.6.). The SEM images showed the laser edge to be partially covered with a fibrinous layer (see Figure 7.7 and 7.8). Similarly, the platinum ring was covered with a fibrinous layer, which was continuous with the layer on the laser edge. (These images have previously been published.)

Figure 7.9.
Case 2. Overview of the autopsy specimen. The aneurysm is quite obviously visible, quite “giant”, and located at the AComA approximately 2 cm of the ICA bifurcation. The bypass is seen at the right side positioned in a curve with the end-to-end anastomosis at the far right. The ICA is located in the middle, with the ELANA anastomosis already cut open. The ICA bifurcation is approximately 1 cm distally of the ELANA anastomosis. The distal ELANA anastomosis is separately located in the center near the upper end of the bypass.

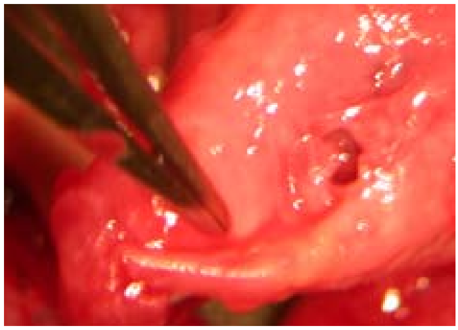


Figure 7.10.
Close-up of the basis of the aneurysm. A hole of 5 mm in diameter was found at the basis, which is likely to be the cause of the fatal SAH.

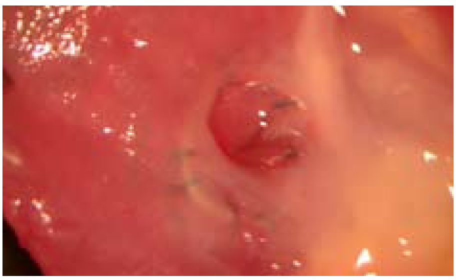


Figure 7.11.
Photo of the proximal ELANA anastomosis on the ICA with the POV from within the opened ICA. Again the platinum ring of 2.8 mm, which is attached to the outside of the ICA, can be seen shining through the wall of the ICA, together with several sutures. The hole in the ICA is clearly off-centered towards the upper part of the image. No obvious signs of thrombus can be observed.

Figure 7.12.
Photo of the distal ELANA anastomosis on the A2 with the POV from the graft into the anastomosis.

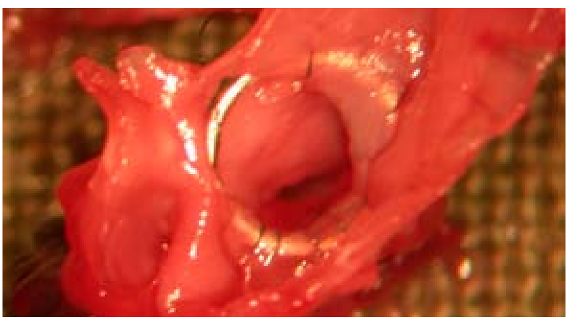


Figure 7.13.
Photo of the same distal A2 anastomosis with the POV from within the A2 into the anastomosis. As the platinum ring has a size of 2.6 mm, the hole looks relatively larger than the hole in the ICA (Figure 7.12.). Again the hole is slightly off-centered. No signs of thrombus can be observed.

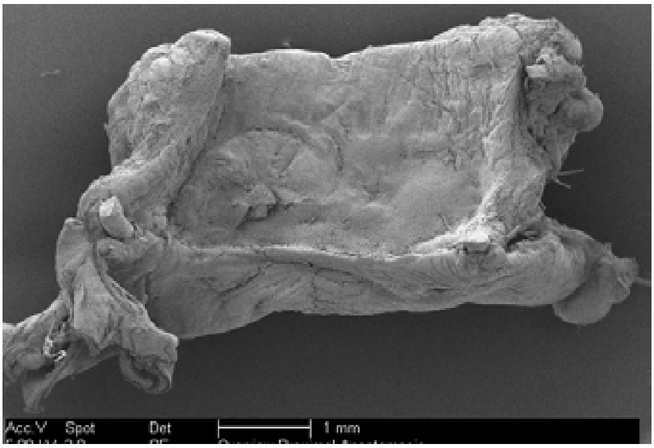


Figure 7.14.
Case 2. SEM of the proximal ELANA anastomosis on the ICA. The anastomosis, including the graft, the ICA, and the platinum ring, was cut longitudinally in two. Both ends of the platinum ring can be seen pointing towards the viewer. The laser edge is visible in between. The bypass graft is located at the upper part of the image. The lumen of the ICA is located at the lower part, with the flow direction in the ICA going from left to right.

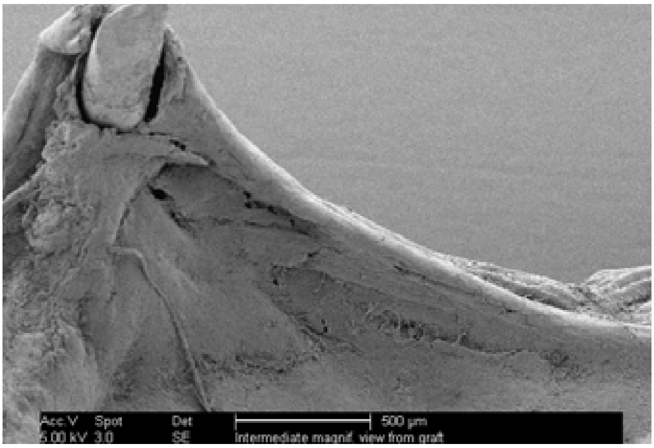


Figure 7.15.
SEM of the same anastomosis as in Figure 7.14. The specimen was turned 180 degrees. The POV is from inside the graft looking at the platinum ring and the laser edge. The laser edge looks very smooth. However, some irregularities can be observed behind the laser edge in the crease between the inside of the graft and the laser edge.

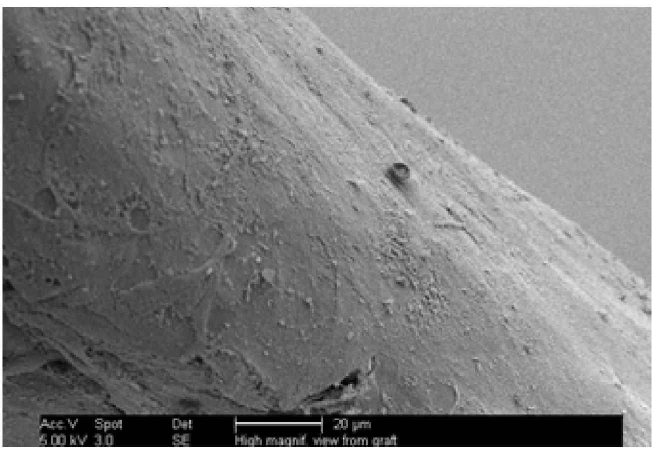


Figure 7.16.
Close-up SEM of the laser edge of the same anastomosis as in Figure 7.14 (proximal anastomosis on the ICA in case 2). The edge looks very smooth. A single red blood cell is seen in the middle. It is not possible to distinguish the different layers in the wall of the ICA.

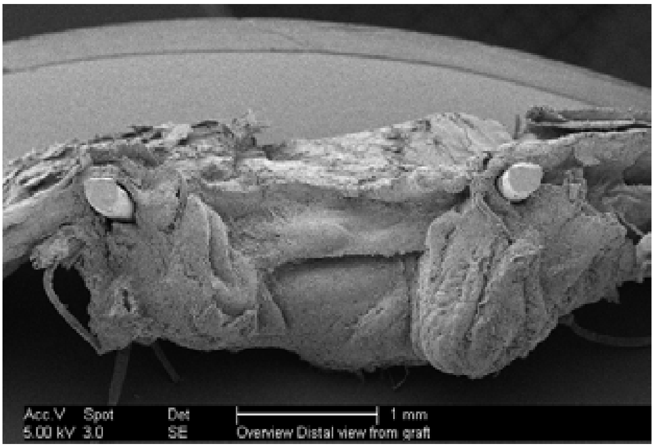


Figure 7.17.
Case 2. SEM overview of the distal anastomosis to the A2. This anastomosis was also cut longitudinally. The bypass graft is located in the lower part of the image. The lumen of the A2 is located in the upper part. The 2.6 mm platinum ring is cut in two and the ends are pointing towards the viewer. The laser edge is visible in between the points of the ring.

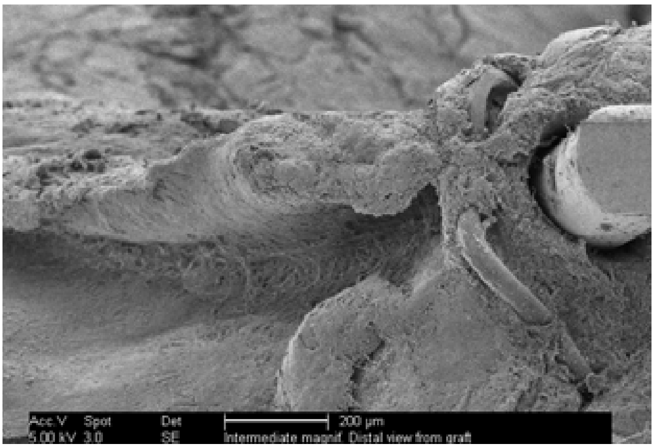


Figure 7.18.
Case 2. SEM close-up of the same anastomosis as in Figure 7.17. from the same POV. The laser edge is completely smooth and continuous with the inside of the graft. The crease between the inside of the graft and the laser edge is very smooth (in contrast to the proximal anastomosis in Figure 7.15.). It is not possible to distinguish the different layers in the wall of the A2.

Case 2

This patient underwent ICA-A2 bypass to treat a giant AComA aneurysm. After 6 days she died of a subarachnoid hemorrhage. At autopsy a large hole in the base of the aneurysm was observed (see Figure 7.9. and 7.10.). The bypass was still patent and no thrombi or other problems were found at the anastomosis sites (see Figure 7.11. to 7.13.). On SEM no parts of either platinum ring were found exposed to the blood stream (see Figure 7.14 to 7.18.). Also, in both anastomoses the laser edge was found to be very smooth. It was not possible to distinguish the different layers in the wall of the recipient artery. No epithelial cells could be observed.

Figure 7.19.
Case 3. Photo of the proximal ELANA (2.8 mm ring) anastomosis to the ICA with the POV from the graft towards and into the anastomosis. In this image, on the left side (near the forceps), the ICA bifurcation is visible. The inside of the anastomosis looks clear of any thrombi. In this patient a different suturing technique was used (see text).

Figure 7.20.
Photo of the proximal ELANA (2.8 mm ring) anastomosis to the ICA with the POV from the graft towards and into the anastomosis (lateral POV of Figure 7.19.). The fold of the graft is visible, which is the result of everting the end of the graft over the platinum ring.

Figure 7.21.
Same anastomosis as in Figure 7.20. However, the POV is from the inside of the ICA into the anastomosis and into the graft. The ICA and the MCA have been cut open in a longitudinal way. From this POV, the anastomosis also looks clear of any thrombi. However, several atherosclerotic plaques can be seen clearly. The anastomosis is placed at a site without plaque. Several sutures can be seen shining through.

Figure 7.22.
Photo of the distal ELANA anastomosis to the P2 (2.6 mm platinum ring) with the POV from the graft into the anastomosis. Notice the difference between the sizes of the P2 in this image with the ICA in Figure 7.19. Also notice the similar size of anastomosis lumen in this image and the ICA anastomosis in Figure 7.19. (even though this photo is taken at a slightly larger magnification).

Figure 7.23.
Photo of the same distal P2 anastomosis as in Figure 18. However, the POV is from within the P2 through the anastomosis into the graft. The platinum ring and several sutures are shining through.

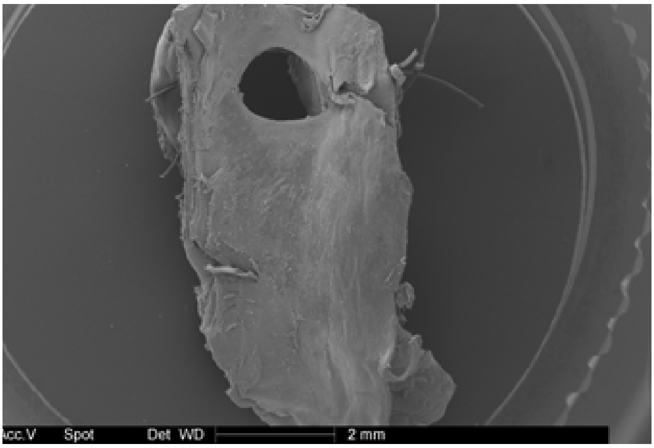


Figure 7.24.
Case 3. SEM overview of the proximal ELANA anastomosis to the ICA. The POV is from within the ICA through the anastomosis into the bypass graft. The rupture of the vessel wall on the upper right is an artifact of the fixation procedure. The lumen of the anastomosis is not perfectly round.

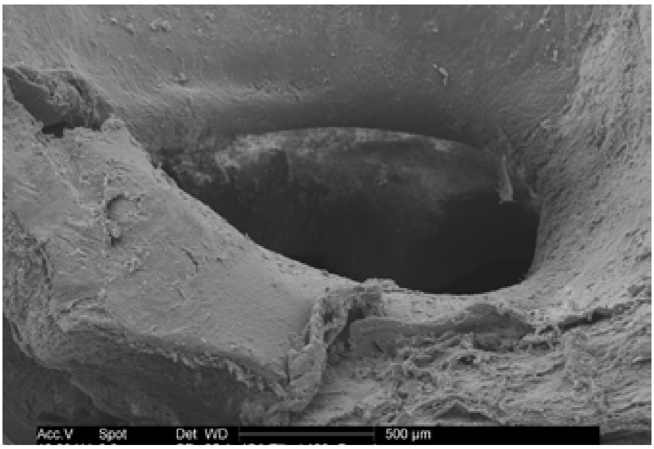


Figure 7.25.
SEM of the same proximal ICA anastomosis as in Figure 7.24.. However, the specimen has been tilted so that the laser edge can be observed from a more perpendicularly POV.

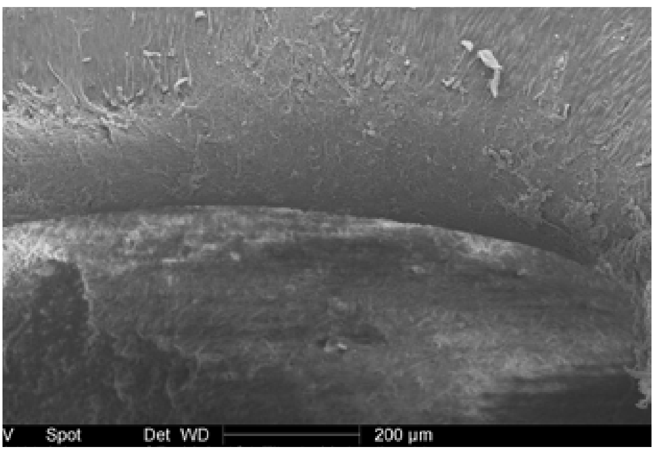


Figure 7.26.
Close-up of the same proximal ICA anastomosis as in Figure 7.25. with the same POV (in case 3). The laser edge is very smooth and continuous with the wall of the ICA. On the right side a very small strand of fibrin is sticking to the inside. The platinum ring is covered completely with endothelium. Due to the POV the crease between the inside of the graft and the edge cannot be observed. It is not possible to distinguish the different layers in the wall of the ICA.

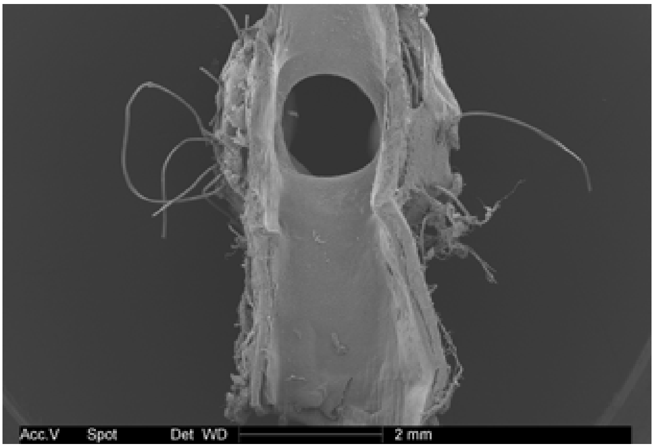


Figure 7.27.
Case 3. SEM overview of the distal P2 anastomosis. The POV is from the inside of the P2 through the anastomosis into the graft. The lumen of the anastomosis looks very large compared to the size of the P2. The lumen is almost perfectly round.

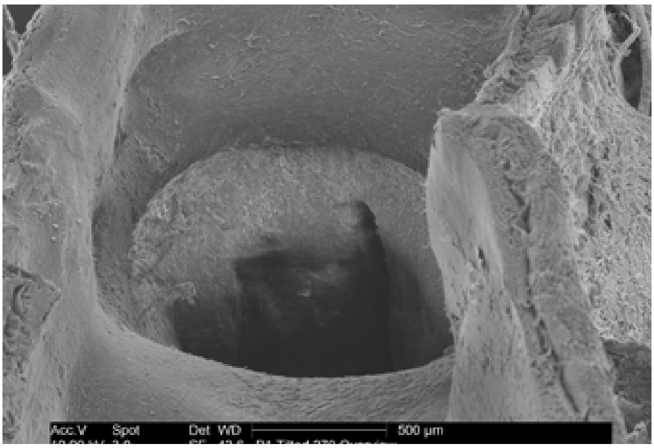


Figure 7.28.
SEM of the same P2 anastomosis as in Figure 7.27.. The specimen has been tilted to give a better view of the laser edge.

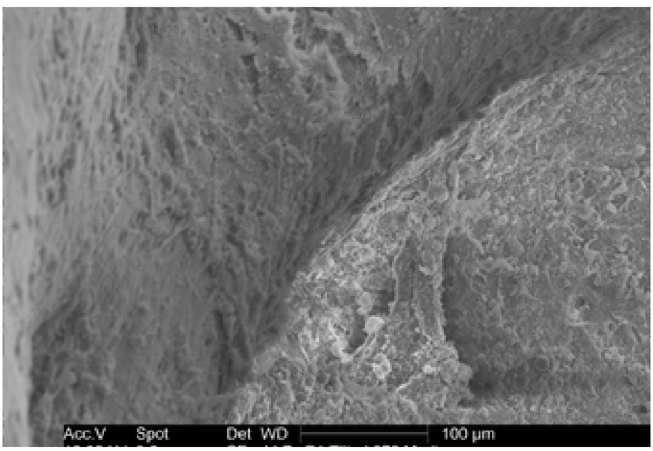


Figure 7.29.
Close-up of the laser edge from the same anastomosis as in Figure 7.27. (distal anastomosis to the P2 in case 3) with the same POV. The laser edge is completely continuous with the wall of the P2, although it seems to be a bit irregularly formed fibrinous layer. No separate layers of media and adventitia can be distinguished.

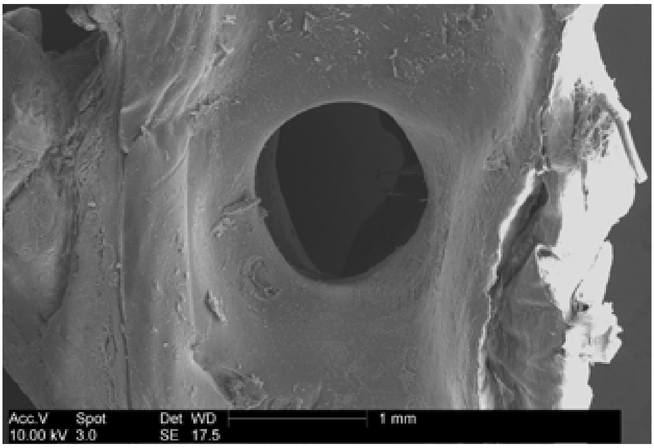


Figure 7.30.
Case 4. SEM of the distal ELANA anastomosis (2.8 mm ring) on the ICA. The POV is from within the ICA through the anastomosis into the bypass graft.

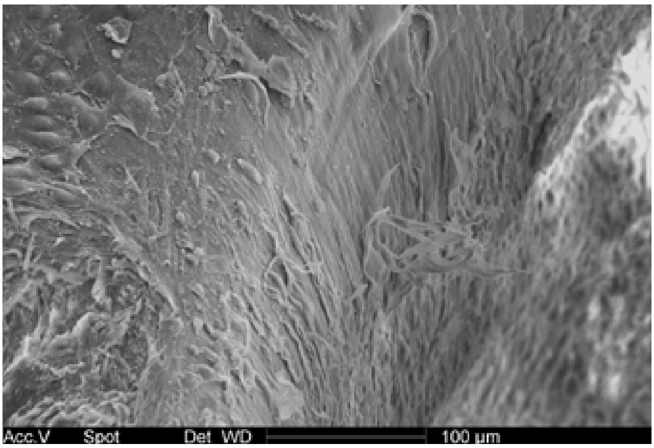


Figure 7.31.
Close-up of the laser edge of the same anastomosis as in Figure 7.30. The endothelial lining of the graft is completely continuous with the wall of the ICA. There is no laser edge as observed in Figure 7.18.(case 2). It is not possible to distinguish the different layers in the wall of the ICA.

Case 3

An ICA-P2 bypass was made in the treatment of a giant VBA. This patient died 31 days after bypass surgery, due to multiple brain stem infarctions caused by the progressive thrombosis of the aneurysm. At autopsy both anastomoses looked completely free of any thrombosis (see Figures 7.19. to 7.23.). In this patient a different suturing technique was used, which prevented the platinum ring from being exposed to the blood stream. Instead of suturing the ring to the wall of the recipient vessel, the ring was pushed over the end of the graft. Then the end of the graft was everted over the platinum ring and fixated with 8 or more sutures. Thus, the platinum ring was completely enclosed in the end of the graft. Then the graft, with the ring, was attached to the wall of the recipient artery. After that the laser procedure was performed in the same way as in the other anastomoses. On SEM (see Figures 7.27. to 7.29.) both laser edges were observed to be very smooth, without any nice endothelial cells, and covered with a thin layer of fibrinous tissue (especially Figure 7.29.).

Case 4

This patient was treated with an ECA-ICA bypass and ICA/ECA occlusion to diminish the flow to a skull base tumor. Five years after bypass surgery he died due to a fatal respiratory insufficiency after multiple pneumonias. On SEM the anastomosis on the ICA was almost perfectly round (see Figure 7.30.). A close-up showed many endothelial cells, continuously arranged over the laser edge and the inside of the bypass graft in the direction of the flow (see Figure 7.31.). No laser edge could be observed. As an old suturing technique was used, which did not expose the ring to the blood stream, the platinum ring was not evaluated.

Discussion

Suturing technique and ring exposure

As the suturing technique changed over time, the platinum ring is was found to be exposed to the blood stream in patients 1 and 2 only. In patient 4 a side branch-assisted suturing technique had been used to connect the ring and the graft to the recipient artery. This evolves the evertion of the end of the graft over the platinum ring, which leaves no part of the ring exposed to the blood stream, and a side branch, through which the laser catheter is introduced to facilitate the laser procedure. In time, this technique was abandoned for the conventional suturing technique, which allows for excellent observation of the ring placement and the graft placement during suturing. First the ring is sutured to the recipient vessel. Then the graft is attached to the wall of the recipient using the ring as guide. This leaves part of the ring exposed to the blood stream. However, the most recent suturing technique is the advanced suturing technique. This technique is reminiscent of the side branch-assisted suturing technique in that the evertion technique is used. However, the side branch is no longer used. Instead the graft is cut in two, and the catheter is introduced into the graft through the open end of the graft. This technique, of course, also does not leave any part of the ring exposed to the blood stream. Therefore, we did not pay attention to the rings in cases 2 and 3. However, in case 1 the process of coverage with fibrinous tissue is in our opinion quite nice (see Figures 7.7. and 7.8.). In case 2, the same suturing technique was used, but no part of either ring is visible anymore (see Figures 7.15. and 7.18.). Whether this may be due to complete coverage of the rings due to progression of the fibrinous layer seen in case 1, or that accidentally no part of the ring was exposed to the blood stream after the suturing, is difficult to tell. As we now use the advanced suturing technique, coverage of the platinum ring may be of lesser importance.

Exposition of the Medial and Adventitial Layers

One hundred years after Carrel, his adage of close intima-intima approximation in the creation of vascular anastomoses still stands. Although his technique facilitates the performance of an anastomosis, and is therefore used by all vascular surgeons, its inherent temporary occlusive design inhibits the assessment of the major cerebral arteries for revascularization procedures. In 1902, Carrel described the principles for creating vascular anastomoses which have hardly

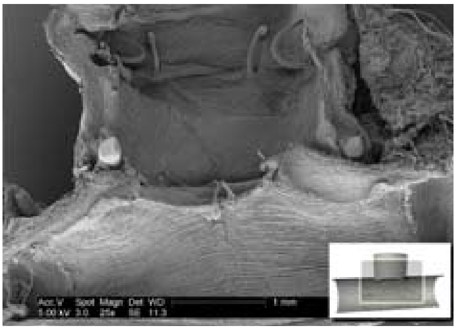


Figure 7.32.
SEM overview of the carotid artery in the pig directly after the laser procedure

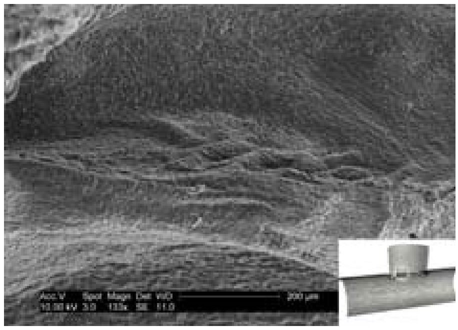


Figure 7.33.
SEM close-up of the laser edge of an ELANA anastomosis in a pig after 2 months.

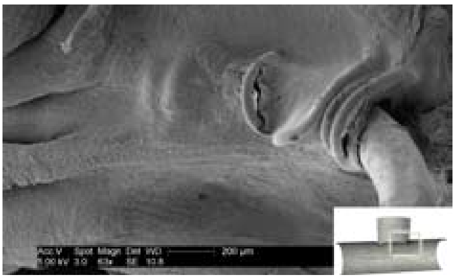


Figure 7.34.
SEM close-up of the laser edge of an ELANA anastomosis in a pig after 3 months.

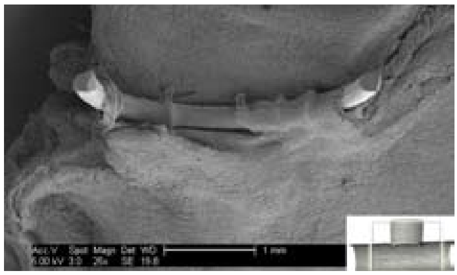


Figure 7.35.
SEM close-up of the laser edge of an ELANA anastomosis in a pig after 6 months.

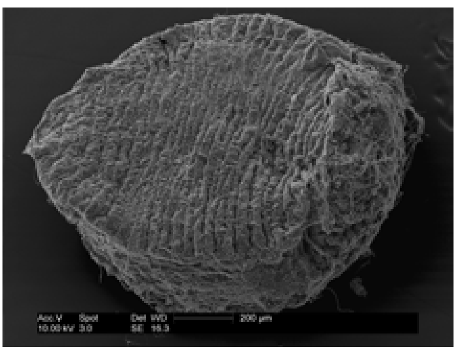


Figure 7.36.
SEM of the flap which has been retrieved from the ELANA anastomosis in the same pig as in Figure 7.32.

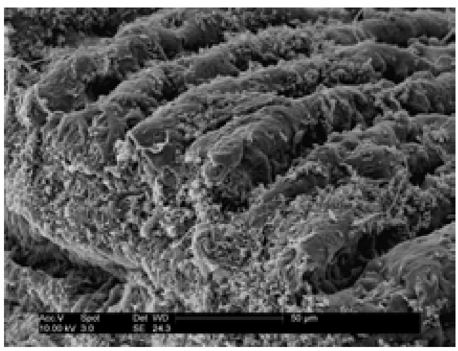


Figure 7.37.
Close-up of the laser edge of the flap in Figure 7.36. The adventitial and medial layers are clearly distinguishable.

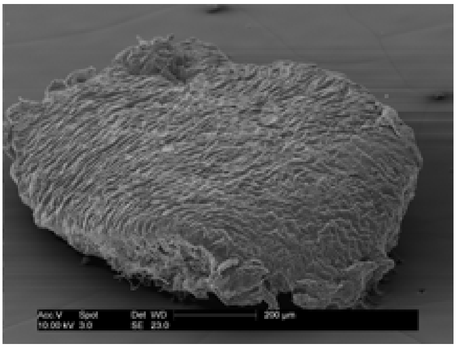


Figure 7.38.
SEM overview of a human flap which has been retrieved during an ELANA procedure (this patient was not part of the discussed case material).

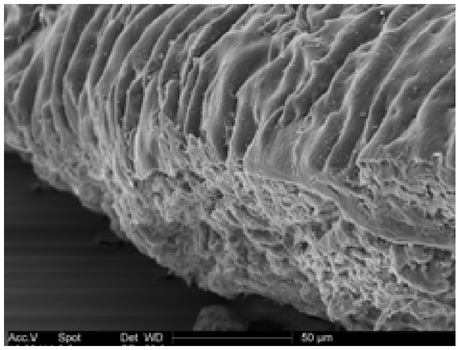


Figure 7.39.
Close-up of the laser edge of the flap in Figure 7.38. The adventitial and medial layers are clearly distinguishable.

changed during the last century. The recipient artery is temporarily occluded with two clamps. Between them, an opening is cut into the wall. The end of the donor vessel is connected to the recipient vessel with the endothelial layers of both vessels closely approximated. Still the backbone of modern vascular surgery, Carrel's technique has been highly successful. However, its inherent flaw is the temporary occlusion of the recipient vessel. A critically ischemic area may become infarcted during the procedure. As the brain is extremely dependent on a continuous blood supply, Carrel's techniques are almost impossible to use on cerebral arteries. It is therefore surprising that no attempts have been made to develop a non-occlusive anastomosis technique, apart from the abortive animal experiments by Eck (1878) and Yahr (1960). With the ELANA technique a laser catheter, which is introduced into the graft, is used to make a hole in the wall of the recipient artery, leaving part of the adventitial and medial layers of the recipient artery exposed to the blood stream. This is contrary to Carrel's adage that close approximation of the endothelial layers is an absolute prerequisite for a successful anastomosis, which may explain why so few surgeons followed this line of thinking. Exposure of the other layers of the blood vessel to the blood stream would lead to thrombus formation and occlusion.

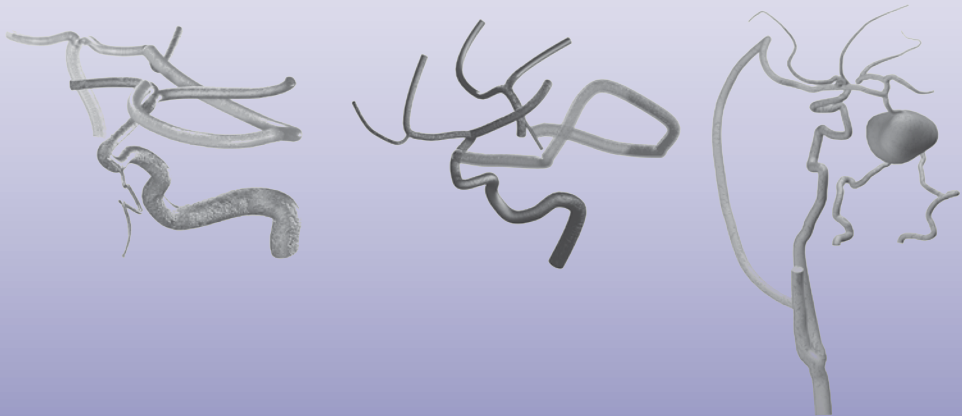
In order to investigate the results of this exposure, we have conducted a long-term pig survival experiment (see previous Chapter).[272] In pigs, directly after the laser procedure, the laser edge is very sharp, and no thrombi can be observed. Still, the medial and adventitial layers can be observed separately (see Figure 7.32). After 2 months, the laser edge is completely covered with endothelial cells, and no different layers can be distinguished (see Figure 7.33. to 7.35.). The different layers can also be observed clearly in the punched-out flap (see Figure 7.36. and 7.37.). As the laser is able to create an incision completely through the vessel wall, all layers can be seen. Especially the medial and intimal layers would be important. In Figure 7.37. both intimal and medial layer can be observed in the flap. The same can be observed in human flaps retrieved during successful ELANA procedures (see Figure 7.38. and 7.39.). The separate layers can be distinguished clearly. As the laser cuts alike on both sides (that is, at the flap side as well as at the remaining laser edge within the anastomosis) it is to be expected that a similar surface is left exposed to the blood stream. This exposure is in contrast to Carrel's adage. In the pig survival experiments this laser edge was observed to completely integrate with the rest of the inside of the anastomosis. Therefore, we are very glad that we can now present similar images with similar results as obtained from human anastomoses.

Conclusion

The SEM images show the start of re-endothelialization of the platinum ring at 4 days, and complete re-endothelialization of the anastomosis site somewhere between 31 days and 5 years post-operatively. At 5 years post-operatively, the ELANA anastomoses is seen to be wide open, fully round, and with a continuous layer of endothelium covering the inside of the anastomosis. We conclude that the re-endothelialization of ELANA anastomoses in human is likely to occur, thereby proving that Carrel's adagio of perfect intima-intima apposition does not necessarily needs to be obligatory for the creation of patent human anastomoses.

Part IV

Clinical Application

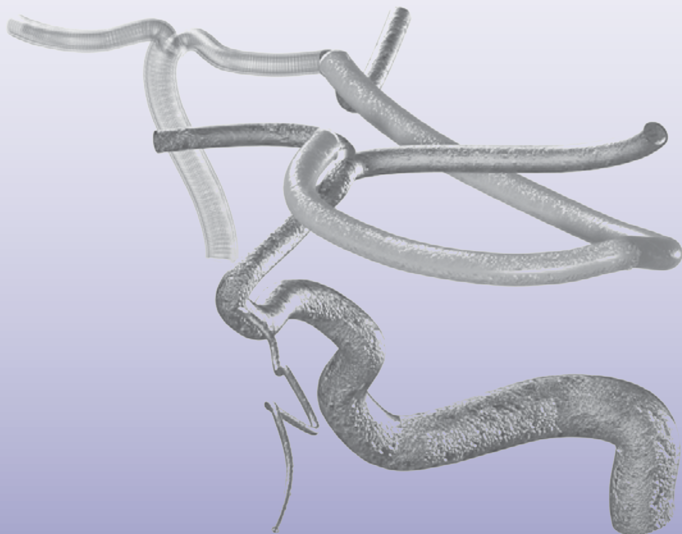


Previous page
3D reconstructions of the bypasses described in the next chapters.

Next page
3D reconstruction of a patient with an ICA-P2 bypass. The bypass originates from the intracranial ICA part (or the very first segment of the A1) and inserts into the P1-P2 segment of the posterior cerebral artery. Thus a connection between the anterior and postior has been created in the treatment of posterior fossa ischemia.

Chapter 8

Construction of an ICA-P2 Bypass



The ELANA technique: Construction of a New Posterior Communicating Artery in a Patient with Poor Posterior Fossa Circulation

C.A.F. Tulleken, H.J.N. Streefkerk, A. van der Zwan

Neurosurgery 50:451-420, 2002

Construction of a New Posterior Communicating Artery in a Patient with Poor Posterior Fossa Circulation

Abstract

Oobjective and importance:
The carotid and the vertebrobasilar circulation were connected, effectively creating a new posterior communicating artery (PComA). The excimer laser-assisted nonocclusive anastomosis technique is a new anastomosis technique whereby formerly untreatable patients may be treated with an intracranial artery-to-intracranial artery bypass procedure. This report is the first one in which an angiographically proved patent internal carotid artery-posterior cerebral artery segment P1 bypass is presented.

Clinical presentation:
Our patient presented with repeated episodes of vertebrobasilar ischemia because of vertebral artery occlusion and stenosis.

Intervention:
An internal carotid artery-posterior cerebral artery segment P1 bypass procedure was performed. Because the patient experienced transient ischemia in the left cerebral hemisphere at the end of postoperative angiography procedure, no radiological intervention was performed, and the patient refused to undergo a new radiological intervention at a later stage.

Techniques:
Both anastomoses were made using the excimer laser-assisted nonocclusive anastomosis technique.

Concusion:
Intraoperative flowmetry was performed using an ultrasound flowmeter, which disclosed blood flow of 35 ml/min through the bypass. We hope that this new PComA suffices to protect the patient from infarction in the territory of the vertebrobasilar circulation.

Introduction

This report describes a patient who presented with repeated episodes of vertebrobasilar ischemia caused by vertebral artery (VA) occlusion and stenosis. A connection between the carotid and vertebrobasilar circulation was made, effectively creating a new posterior communicating artery (PComA). Both anastomoses were performed using the excimer laser-assisted nonocclusive anastomosis (ELANA) technique. Intraoperative flowmetry using an ultrasound flowmeter showed a flow of 35 ml/min through the bypass. A complete circle of Willis, in which all of the constituent parts have a mini-mal diameter of 2 mm, provides good protection against brain infarction in pa-tients with severe stenosis or occlusion of one or more cerebripetal arteries. The component of the circle of Willis that is the most variable in diameter is the PcomA.[294, 295] If the PComA is lacking or has a small diameter on both sides the vertebrobasilar circulation cannot be used to rescue the carotid circulation when both internal carotid arteries (ICAs) are occluded, and vice versa (i.e., when both VAs or the basilar artery [BA] are occluded).[237]

Because the ELANA technique enables the neurosurgeon to create anastomoses with all of the major cerebripetal arteries at the base of the brain in a completely safe way,[53, 123, 140, 179-181, 271, 273, 274, 299, 300, 303-306, 313], for several years we entertained the idea of creating a new PComA in these patients. In this case report, we present the first angiographically proved, newly created PComA in a patient with poor posterior fossa circulation.

Case Report

A 50-year-old man experienced repeated episodes of vertebrobasilar ischemia. An angiogram showed that he had an occlusion of the left VA and severe stenosis of the right VA at its origin. On the right side, the posterior cerebral artery (PCA) was the continuation of the PComA (embryonic situation), and no P1 segment was present. He had a rudimentary PComA on the left side.

The causes of the ischemic episodes were most likely hemodynamic because they always occurred during physical exercise. The first episode occurred while the patient was weightlifting, and the episodes afterward happened during similar circumstances. Of course, an embolic event can never safely be excluded, although it is less likely, because the patient experienced ischemic episodes despite receiving anticoagulation treatment.

An earlier attempt to create an anastomosis between the external occipital artery (OA) and the right posteroinferior cerebellar artery (PICA) was not successful, because the branch of the PICA that was used as the recipient artery was small. Intraoperative flow measurements showed a flow of only 7 ml/ min. Therefore, we decided to make a connection between the carotid and the vertebral circulation by creating a new PComA on the left side.

Operation

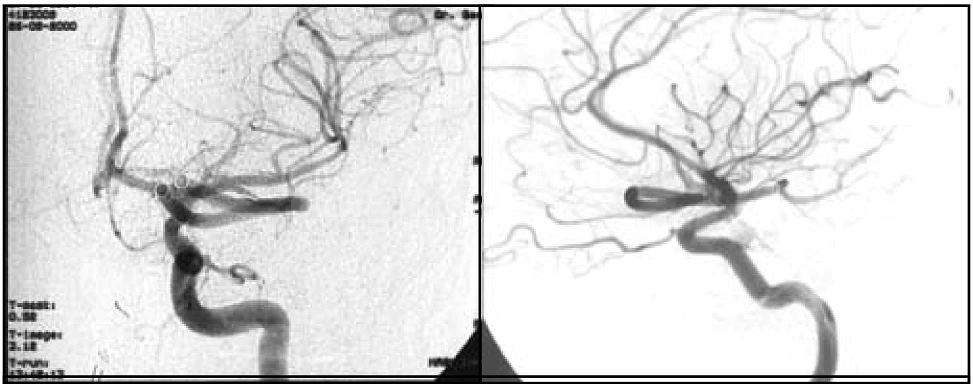
Using left-sided frontotemporal trephination, we opened the sylvian fissure extensively. The left PCA was approached via a lateral route of the ICA and the middle cerebral artery. After excision of the greater saphenous vein graft (SVG), a connection was made between the SVG and the wall of the recipient artery. A platinum ring with a diameter of 2.6 mm was attached to the wall of the PCA at the P1–P2 transition using four 9-0 Prolene sutures (this procedure has extensively been described elsewhere). A 10-cm section of the SVG was connected at its downstream end to the wall of the PCA with eight 9-0 Prolene polypropylene sutures (Ethicon, Inc., Norderstedt, Germany), which passed around the platinum ring and superficially penetrated the wall of the recipient artery and fully penetrated the wall of the SVG. A second platinum ring with a diameter of 2.8 mm was attached to the wall of the intracranial ICA at the level of the bifurcation by using four 8-0 Prolene sutures, which passed the wall only superficially through its adventitial and medial layers. Another part of the SVG with a length of 10 cm was connected at its upstream end to the wall of the ICA using eight 8-0 Prolene sutures, which passed around the platinum ring, superficially penetrating the wall of the ICA and fully penetrating the wall of the SVG.

Opening of the anastomosis sites

After the initial suturing was completed, the excimer laser catheter was introduced into the SVG, which was connected to the PCA, and pushed until the tip touched the wall of the PCA inside the anastomosis site. A vacuum was then produced in the laser catheter using a high-pressure suction device to establish firm contact between the catheter tip and the vessel wall. The excimer laser was activated for 5 seconds (10 mJ at 40 Hz), punching out a full-thickness disc of the arterial wall with a diameter similar to the diameter of the laser catheter tip (2.2 mm). The catheter was withdrawn, and because the high-pressure vacuum was continued, the disc of the arterial wall remained attached to the laser tip until it was removed. Profuse bleeding from the SVG was observed, so a temporary clip was applied to the SVG to stop the bleeding.

The same procedure was repeated to open the anastomosis between the SVG and the ICA. Both SVG parts were shortened to a length of approximately 3 cm, and the free ends were cut obliquely so that a sharp angle resulted after both parts were connected using a simple end-to-end anastomosis. When both temporary clips on the graft ends were removed, a flow of 35 ml/min was recorded through the bypass using an ultrasound flowmeter (Transonic Systems, Inc., Ithaca, NY).

We obtained a cerebral angiogram on the day after the operation that showed that the bypass was patent (Fig. 8.1.). A three-dimensional (3-D) reconstruction was made to clarify the location of the bypass. Our intention was to ask the interventional radiologist to insert a stent at the origin of the right VA to remove the stenosis. Before the creation of the new PComA, this procedure had been considered too risky. Because the patient experienced transient ischemia



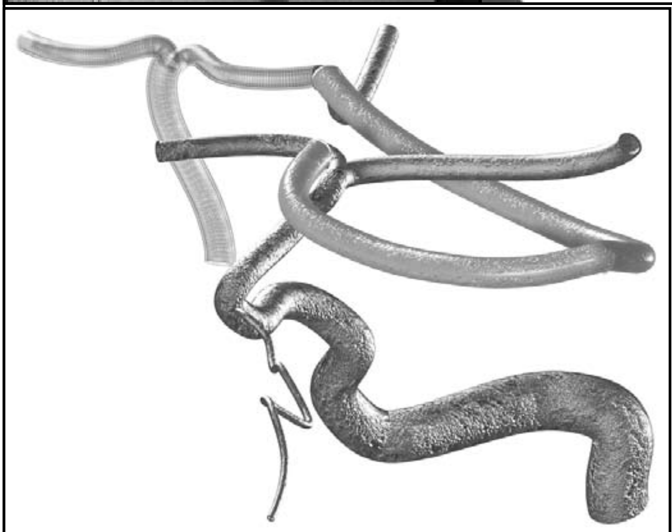


Figure 8.1.
AP (upper left) and lateral (upper right) angiograms of the patent, reconstructed PComA bypass. A computer generated 3D reconstruction of the bypass was made (left). The original two-dimensional angiograms were used as a template. We thought that an artist's 3D reconstruction of these vessels would be more useful than a 3D digital subtraction angiogram, a magnetic resonance angiogram, or a computed tomographic angiogram, because it would allow us to emphasize the PComA bypass and show the BA and the P1 segment of the PCA. In the anterior angiograms, the BA and the P1 segment did not fill, of course, so the images of these arteries were computer generated, using the posterior angiograms as guide. The 3D reconstruction should also bear some resemblance to the conventional drawings of the cerebripetal arteries. This image was created using a 3D modeling and animation software package: 3D Studio Max r3.1 (3D Max), which is manufactured by Discreet, a division of Autodesk, Inc.(San Rafael, CA, USA). The 3D reconstruction of the ICA, the OphthA, the M1, A1, P1, P2, BA, and the PComA bypass was created by following (tracing) the centers of the vessels in 3D Max, using the angiograms as background, and creating several paths of editable splines. After those splines where lofted using the diameters of the original vessels, as shown on the anigograms, the 3D images where created. Under careful auspices of the senior author (CAFT), the curves of the blood vessels were slightly adjusted, so that any artifacts of the spline modeling were discarded. Increasing the path steps of the lofting ensured nice curves. The image has a total of 27 objects with 113,000 faces. To obtain a realistic image of skin, the abdominal aorta of a rabbit was photographed. This textured image was used as the source for all of the blood vessels. The platinum rings were given a highly glossed texture. The anterior vessels and the P2 were given a dark, nonopaque red color with a slightly glossy effect. To show the bypass, the graft was given a lighter red colore with an opacity of 80%, so that the platinum rings would be visible. Because the BA and the P1 did not fill in the angiograms, they were given a higher opacity. After that, a point of view was chosen to render the final image.

in the left cerebral hemisphere at the end of the angiography procedure, no intervention was attempted, and the patient refused to undergo a new radiological intervention at a later stage. Postoperative magnetic resonance flowmetry measurements failed for technical reasons, because it was very difficult to obtain tangential images of this very curved bypass until now. The magnetic resonance angiogram, however, proved that the bypass was still patent. After several months, the patient was in very good condition, and no further ischemic episodes occurred.

Discussion

Overview of the literature

In their very extensive review in 1985, Ausman concluded that a small number of patients with vertebrobasilar insufficiency could be treated with an extracranial-to-intracranial (ECIC) bypass procedure to the PICA, the PCA, or the superior cerebellar artery (SCA).[16, 28] Indeed, as early as 1976, Ausman was the first to report,[24] at the same time as but independently of Khodadad,[173] that they had achieved posterior fossa revascularization in a patient by performing a VAPICA anastomosis with interposed radial artery graft procedure. Many EC-IC bypass procedure reports followed. Hopkins in 1987 and Regli in 1995 performed the following EC-IC bypass revascularization procedures: OA-PICA, VA-PICA, superior temporal artery (STA)-SCA, and subclavian artery-PCA branch.[151, 233]

Numerous reports of bypass procedures performed to treat vertebrobasilar insufficiency to the PICA have been published as well. Ausman reported his results with side-to-side OA-PICA revascularization procedures in 1988 and 1990.[21, 22, 27] In 1982, Roski described the experience in performing OA-PICA end-to-side revascularization.[237] Sundt and Piepgras, in 1978, published an early report of OAPICA bypass surgery.[281] Other reports have described neurosurgical results after EC-IC bypass procedures performed to treat vertebrobasilar insufficiency to the anteroinferior communicating artery (AICA). Ausman reported their experiences with an OA-hemispheric branch of AICA procedure in 1981 and with an OA-AICA end-to-side procedure in 1988 and 1990.[18, 22, 27] In 1979,[23] 1981,[17] 1982,[19] and 1990,[22] Ausman also described the results after performing STA-SCA end-to-side procedures that required less than 1 hour of occlusion time. In addition, Sundt reported two cases in which they performed PCA-SCA anastomoses in 1981,[279] and el-Fiki described the experience with STA-SCA bypass surgery in 1985.[101]

Several neurosurgical groups have reported using EC-IC procedures involving the PCA. Sundt reported using a side-to-side PCA-SCA procedure involving the P2 segment of the PCA in 1981 and an STA-SCA procedure in 1985.[279, 286] Hopkins in 1982 and 1983, described an STA-SCA anastomosis procedure.[148, 149] Eguchi performed an end-to-end STA-P2 segment procedure that they reported in 1983,[99] and an end-to-side external carotid artery-P3 segment procedure was described by Nagasawa in 1999.[215] A clinical trial of EC-IC bypass procedures in the posterior circulation has never been performed, however, so an exact definition of patients with symptoms of posterior ischemia who might benefit from this low-flow bypass procedure does not exist. Even if such a trial were performed, the patient group might not have been identified (see, e.g., EC-IC Bypass Study [11, 29, 289]), perhaps because the anastomoses described in the publications involved low-flow re-vascularization procedures and usually were created in a cortical branch of the cerebral or cerebellar recipient artery.

In aneurysm surgery, EC-IC bypass procedures to the PCA also have a publication history of almost 2 decades—for example, Spetzler since 1982[149, 151, 264, 322] and Sundt in 1982[283]. In 1984, Heros and Ameri encountered a ruptured giant aneurysm after performing an anastomosis procedure to the PCA.[142] A remarkable attempt to create a high-flow anastomosis to the more proximal branches of the posterior arteries was described by Sekhar, who even managed to make an ICA-BA connection.[246] Unfortunately, it is not possible to apply the conventional anastomosis techniques used in giant aneurysm surgery in patients with vertebrobasilar insufficiency, owing to the much higher intolerance of such patients for temporary vessel occlusion, which results in temporary ischemic problems.

The ELANA technique, however, is directly applicable in the posterior circulation. In 1998, we published an article on an anastomosis to the P1 segment of the PCA.[299]. In that patient, we used the SVG as an interposition graft, as we did in most of our patients. The SVG has a good long-term patency rate and is easier to apply than a radial artery graft, especially for stitching in a small, deep gap. We used the radial artery in some patients as an interposition graft without complications, but we think that using the SVG rather than the radial artery is safer because of the small (though not zero) risk of ischemic complications in the patient's arm.

Because of its nonocclusive character, the ELANA technique, which we described for the first time in 1992,[305] removes the restrictions on the choice of intracranial recipient and donor arteries when the construction of an EC-IC or IC-IC bypass is contemplated. As a consequence, a number of new EC-IC and IC-IC bypass procedures have been designed and applied successfully in patients. In this case report, we describe the latest addition to our armamentarium of bypasses: an IC-IC bypass between the intracranial ICA and the P1 segment of the PCA, creating a new PComA. Both anastomoses were created using the ELANA technique. Both the ICA and the PCA were approached via the sylvian fissure. To reach the P1 segment of the PCA, we laterally passed the ICA and the proximal portion of the middle cerebral artery. We are approaching what we regard to be the ultimate goal in reconstructive vascular neurosurgery: the reconstruction of an incomplete and therefore insufficient circle of Willis. The only way to create a nonocclusive anastomosis is with the aid of the excimer laser. Also, there are a considerable number of indications for high flow bypass procedures involving this technique. Therefore, it is desirable that an excimer laser apparatus be available in all those neurosurgical centers in which vascular neurosurgery is an important topic. After a period of intensive training in the experimental animal laboratory, every neurosurgeon with a special interest in vascular neurosurgery should be able to perform the ELANA procedure in the cerebripetal arteries at the base of the cranium.

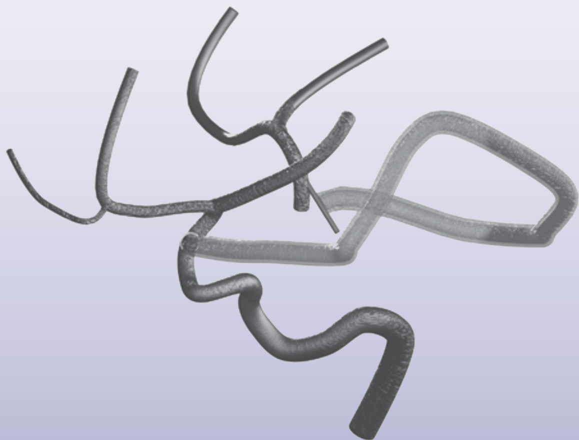
Acknowledgements

We thank Dr. Ir. R.M. Verdaasdonk and H.J. Mansvelt Beck for their continued support of the ELANA technique.

Next page
3D construction of a patient with an ICA-SCA bypass. The bypass originates from the intracranial ICA part and inserts into the superior cerebellar artery. Thus a connection between the anterior and postior has been created in the treatment of a giant BA aneurysm.

Chapter 9

Construction of an ICA-SCA Bypass



The ELANA technique: Constructing a High Flow Bypass using a Non-occlusive Anastomosis on the ICA and a Conventional Anastomosis on the SCA in the Treatment of a Fusiform Giant Basilar Trunk Aneurysm
H.J.N. Streefkerk, J.F.C. Wolfs, W. Sorteberg, A.G. Sorteberg, C.A.F. Tulleken
Acta Neurochir (Wien). 2004 Sep;146(9):1009-19; discussion 1019

Constructing a High Flow Bypass using a Non-Occlusive Anastomosis on the ICA and a Conventional Anastomosis on hte SCA in the Treatment of a Fusiform Giant Basilar Trunk Aneurysm

Abstract

Case material
A patient with a partially thrombosed fusiform giant basilar trunk aneurysm presented with devastating headache and symptoms of progressive brain stem compression. Having an aneurysm inaccessible for endovascular treatment, and after failing a vertebral artery balloon occlusion test, he was offered bypass surgery in order to exclude the aneurysm from the cerebral circulation and relieve his symptoms.

Intervention
A connection between the intracranial internal carotid artery and the superior cerebellar artery was created whereupon the basilar artery was ligated just distally to the aneurysm. The proximal anastomosis on the internal carotid artery was made using the excimer laser-assisted non-occlusive anastomosis (ELANA) technique, while a conventional end-to-side anastomosis was used for the distal anastomosis on the superior cerebellar artery.

Results
Intra-operative flowmetry showed a flow through the bypass of 40 ml/min after ligation of the basilar artery. An angiogram 24 hours later showed normal filling of the bypass and the vessels supplied by it, but also disclosed a subtotal occlusion of the proximal ipsilateral middle cerebral artery with delayed filling distally. The patient, who had a known thrombogenic coagulopathy, died the following day.

Conclusion
Autopsy showed no signs of ischemia in the territories supplied by the bypass, but a thrombus in the proximal middle cerebral artery and massive acute hemorrhagic infarction with swelling in its territory and uncal herniation. Multiple fresh thrombi were found in the lungs. The ELANA anastomosis showed re-endothelialisation without thrombus formation on the inside.

Introduction

Giant cerebral aneurysms endanger patients through subarachnoidal haemorrhage, cerebral ischemic events, or by their mass effect on the brain. As their anatomy is often quite complex, and they regularly contain considerable amounts of thrombotic material, treatment of these lesions remains a challenge. Successful management of giant aneurysms hence includes securing any point of aneurysm rupture, preserving or restoring adequate blood flow to the artery's perfusion territory, as well as relief of their mass effect on the brain. To achieve some or all of these goals, the use of a bypass may become imperative.[23]

The excimer laser-assisted non-occlusive anastomosis (ELANA) technique allows constructing bypasses to the major cerebral arteries without interrupting blood flow to the brain.[273, 299, 303, 313] This new technique thus becomes very attractive in situations of poor collateral function of the circle of Willis. Furthermore, it allows construction of intracranial-intracranial bypasses.[273, 297, 300, 313] In this paper we want to convey our management of a patient with a partially thrombosed fusiform giant basilar trunk aneurysm. Having an aneurysm deemed inaccessible to endovascular treatment, and after failing a vertebral artery balloon occlusion test, our patient underwent bypass surgery using the ELANA technique.

Pre-operative status

This 36 year old Norwegian male with a partially thrombosed fusiform giant basilar artery aneurysm presented with devastating headache and symptoms of progressive brain stem compression. He had considerable difficulties in walking and swallowing, and in the end he could sleep in a half-sitting position only. Fifteen years earlier he had suffered an ischemic stroke, leaving him with a right-sided hemiparesis. He also had a familial coagulopathy with a liability to develop thromboses and had earlier experienced multiple venous thromboses.

His angiogram of the anterior cerebral circulation revealed a slightly dilated left internal carotid artery (ICA) and normal configuration of both middle cerebral arteries (MCAs) and anterior cerebral arteries (ACAs) (see Figure 9.1.). No posterior communicating arteries could be visualized. In the posterior circulation we found a partially thrombosed fusiform giant aneurysm of the basilar artery (BA) that extended to just below the superior cerebellar arteries (SCAs) (see Figure 9.2.). Its circulated portion was long and torturous. The right vertebral artery (VA) was found to be occluded. The BA supplied both SCAs and both posterior cerebral arteries (PCAs). A transcranial Doppler (TCD) monitored angiographic balloon test occlusion (BTO) of the vertebrobasilar circulation was performed (see Figure 9.3.). Upon closing his remaining left VA at the C1 level our patient instantly complained of dizziness. Fifteen seconds later he started to yawn, after 30 seconds he felt extremely tired, and at 45 seconds he was unresponsive and his pupils started to dilate. When the balloon was deflated, he became responsive again, and could fully co-operate after 3 minutes. TCD recordings of the P1 segment of the

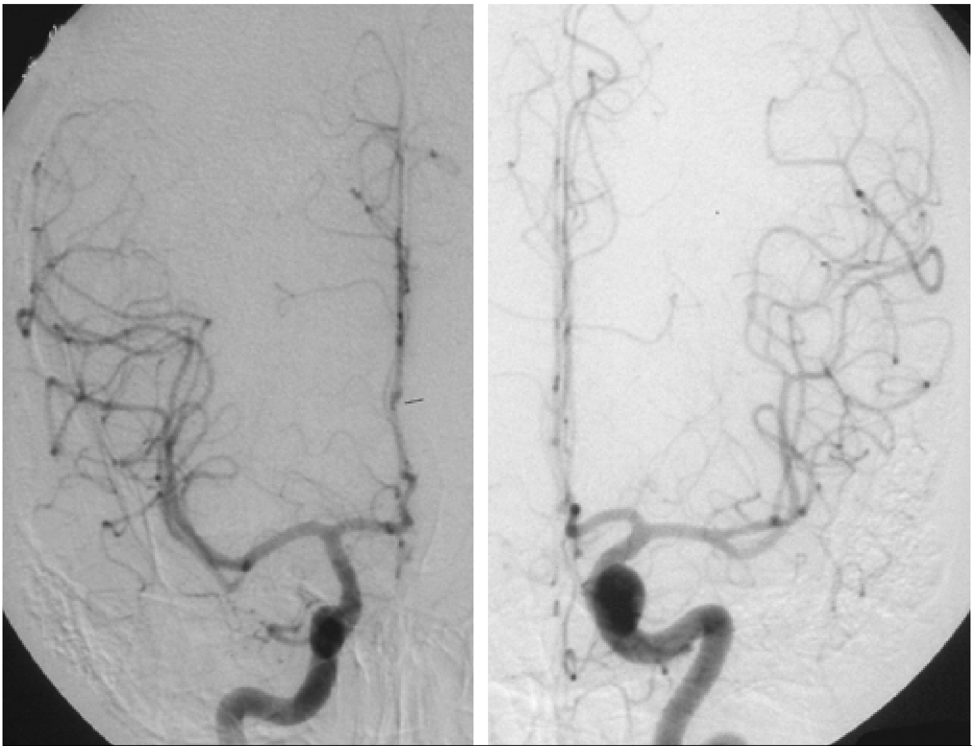


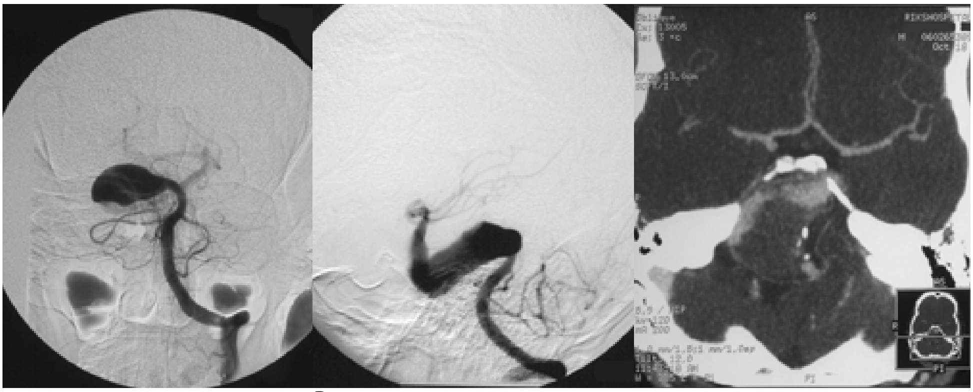
Figure 9.1.
Preoperative anterior angiograms showed no stenoses or occlusions of the middle cerebral arteries.

PCA showed almost cessation of flow upon balloon inflation (Fig 9.3.B). Immediately upon balloon deflation, there was a swift hyperaemic restoration of flow in his left PCA (Fig 9.3.C).

As the patient suffered from unbearable symptoms we felt we could not decline his request for treatment. The aneurysm was considered inaccessible to any endovascular treatment, and because of the lack of collateral function of his circle of Willis, he was offered surgery, including a bypass procedure. We initially planned to insert a bypass between the intracranial ICA and the distal BA using the ELANA technique on both anastomosis sites. Depending on his postoperative clinical condition and cerebral angiographic findings, the option for additional endovascular vessel closure remained open.

Surgical procedure

Using a left sided fronto-temporal trephination the Sylvian fissure was exposed. A left sided approach was chosen because the aneurysm was located mostly on the right side, while the top of the BA had become dislocated to the left. After opening of the dura, retractors were inserted and the optic nerve was exposed from under the frontal lobe. The ICA was dissected up to its bifurcation, and the Sylvian fissure was split so that the MCA was partially exposed.



A B C

Figure 9.2.
Pre-operative angiograms of the posterior circulation and a Computed Tomographic Angiogram of the circle of Willis. A) An early phase PA angiogram of the BA showing the aneurysm just distal of the AICA. B) A lateral angiogram in a slightly later phase shows the torticollous course of the aneurysm, with the origin of the SCA just distal of the aneurysm. C) The size of the aneurysm is much larger than suspected on angiography alone. Both thrombosed as well as non-thrombosed parts of the aneurysm are clearly visible.

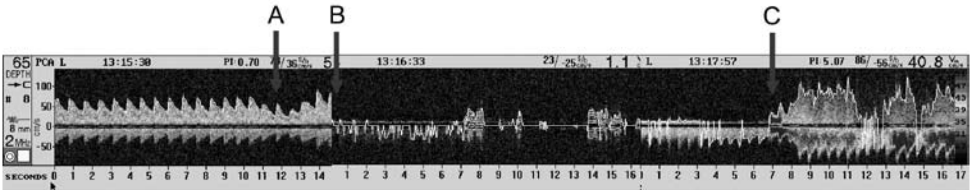


Figure 9.3.
Collage of the left PCA trace during BTO of the left VA. Initial short incomplete testocclusion at A. Upon complete occlusion of the VA (B) a complete cessation of flow in the PCA can be observed. Forty-five seconds later the patient was unresponsive and his pupils started to dilate. The arrow at C indicates balloon deflation and re-established flow in the PCA. Pay attention to the large overshoot in velocity and the patient's tachycardia.

In this manner the top of the BA could be accessed through the area between the optic nerve, the ICA and the ACA, and the area above the MCA and the ACA.[295] The SCA had its origin just distally to the aneurysm and could be reached only via the subtemporal and transtentorial approach. Upon opening of the dura the temporal lobe was found to be unexpectedly oedematous and therefore Mannitol was administered. Unfortunately, all the superficial veins of both legs showed signs of pre-existing thromboses, stenoses, and occlusions that might be linked to his coagulopathy. Only after a lengthy exploration could an experienced cardiac surgeon harvest a vein of sufficient length. However, even this vein showed signs of previous thrombosis and recanalisation.

A platinum ring with a diameter of 2.8 mm was attached to the wall of the ICA using four 9/0 Prolene sutures. A portion of the vein with a length of approximately 10 cm was connected at its upstream end to the wall of the ICA using 8 sutures 9/0 Prolene. These sutures passed around the platinum ring, superficially penetrating the wall of the recipient artery, and fully penetrating the wall of the vein. The excimer laser catheter was then introduced into the upstream portion of the vein which was connected to the ICA, and pushed up until the tip touched the wall of the ICA at the anastomosis site. A vacuum was then produced in the laser catheter using a high vacuum suction device, thereby establishing a firm contact between the catheter tip and the vessel wall. The excimer laser was activated for 5 seconds (output energy of 10 mJ with a pulse frequency of 40 Hz, a pulse length of 100 ns, and a light frequency of 308 nm), punching out a full-thickness disc of arterial wall ("flap") with a diameter similar to the diameter of the laser catheter tip (2.2 mm). The catheter was withdrawn, and, since the high vacuum suction was continued, the flap stayed attached to the laser catheter tip until it was manually removed. Profuse back bleeding from the vein was observed. The stump was then flushed with Heparin-saline solution, and a temporary clip was applied to stop the bleeding.

On inspection, the distal BA was found not suitable for an ELANA anastomosis. We therefore chose the SCA as the recipient vessel. However, as this artery had a diameter of only 1.5 – 1.6 mm, and a very thin wall, a conventional End-to-Side anastomosis was used to connect a downstream portion of the vein to the SCA. After extensive flushing of this anastomosis with Heparin-saline solution, the anastomosis was filled with Heparin-saline solution and a temporary clip was placed on the free end of the vein. Both portions of the vein were shortened to a length of about 3 cm, and the free ends were cut obliquely so that a sharp angle resulted after connecting both free ends using a simple End-to-End anastomosis made with 8/0 Prolene sutures. When both temporary clips on the vein were removed a flow of 8 to 13 ml/min could be observed, which was in the expected magnitude because the territory of the SCA is relatively small.

The distal portion of the aneurysm seemed to have a rather thin wall, without any thrombus. Because of the relatively low volume flow through the bypass, the BA was ligated distally to the aneurysm and just proximally to the SCAs using a long straight aneurysm clip. The flow through the bypass then increased to 35 – 44 ml/min, and remained stable at 40 – 41 ml/min throughout the remaining of the operation. After obtaining good haemostasis, the retractors were removed. The temporal lobe had remained quite oedematous; however, echo examination at this stage did not identify any sign of cerebral haematoma. A piece of Lyodura was inserted to achieve watertight closure of the dura. The bone was replaced using Craniofix, and the skin was closed in one layer, leaving a drain. After skin closure, Doppler measurements of the bypass showed adequate blood flow velocity with a normal pulsatile pattern. The surgical procedure took 15 hours.

Post-operative course

An angiogram 24 hours after the operation (Fig. 9.4b,c,d) showed normal filling of the bypass and the superior part of the posterior circulation via the SCA. Except for contrast filling of a small proximal portion, the aneurysm itself had thrombosed. However, a subtotal occlusion of

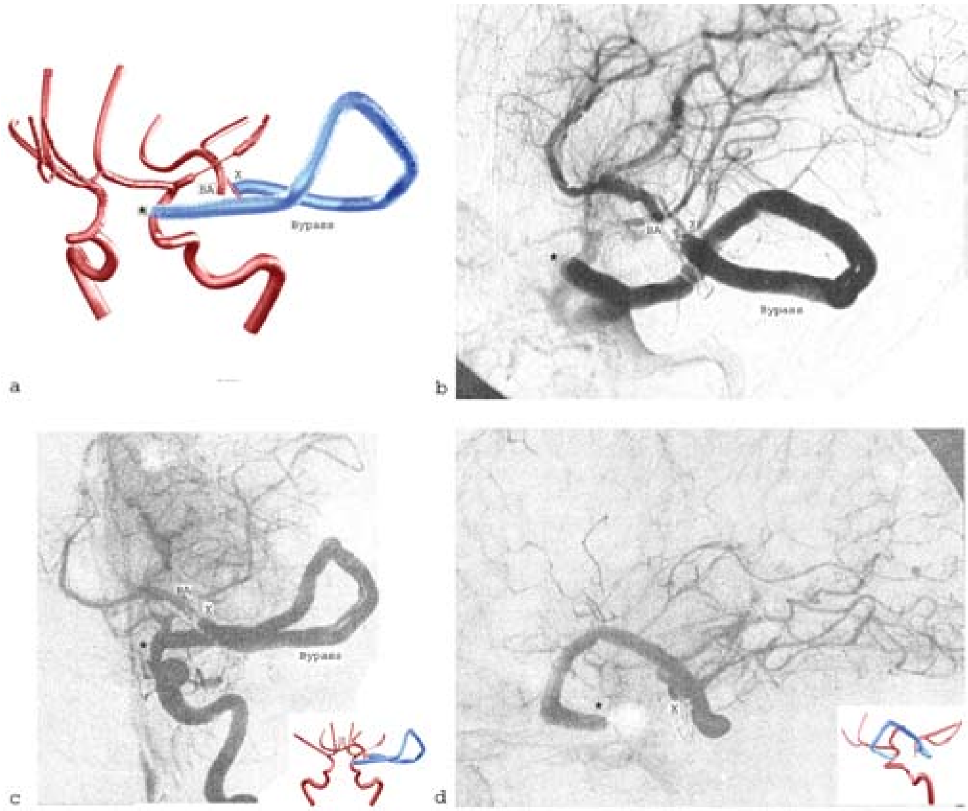
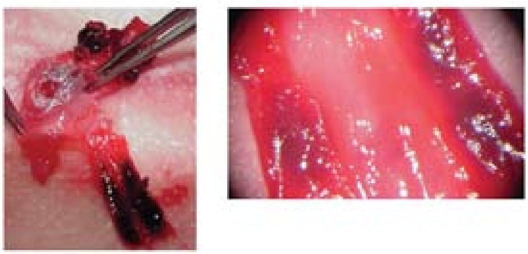


Figure 9.4.
Postoperative angiograms. For presentation purposes we created an artist's impression of the bypass (A), with almost the same angle as the oblique angiogram of the bypass (B). We have described the technique of making the artist's impression elsewhere.33 The ELANA anastomosis is clearly visible (*) as well as the distal conventional anastomosis with the SCA (X). Nice filling of both PCA territories was also observable on the a-p angiogram (C) and the lateral angiogram (D).



A B

Figure 9.5.
At autopsy the ICA was cut open and both the ELANA anastomosis as well as the MCA stenosis were observed (A). At high magnification the MCA stenosis turned out to be quite organized (B) with a remaining lumen of less than 40%. An embolus was found inside this lumen, which explained the complete occlusion of the MCA as observed on the angiograms.

the proximal left MCA was observed, with delayed filling of the distal MCA region. Clinically, the patient did not regain consciousness after anaesthesia, and passed away two days after the operation. At autopsy the ICA, ACA, and the bypass contained no thrombus. The proximal left MCA, however, contained a thrombus with a length of 5 mm that was firmly attached to the arterial wall on its lateral aspect, and that obstructed its lumen for about ¾ of the diameter (Fig. 9.5A,B). The internal wall of the arteries looked normal without any sign of atherosclerosis. The endothelial layer of the bypass was uninterrupted and with the microscope no thrombi could be found.

The ELANA anastomosis was also examined. Microscopically it was seen to be wide open and without any blood clots (Fig 9.6. A). It was cut open transversally to expose the endothelium of the vessel. Examination with a scanning electron microscope (SEM, Philips XL30LAB) was also performed (Fig. 9.6.D,E,G,H). The flap removal after the laser ablation procedure had, as usual, left a protruding rim, because the diameter of the laser catheter tip (2.2 mm) is smaller than the inner diameter of the platinum ring (2.8 mm). A small thrombus could be seen underneath this rim (Fig. 9.6.C). No thrombus had formed on the laser edge itself. Almost the entire platinum ring was covered with fibrin between the ICA and the vein (Fig 9.6.E and H).

The autopsy disclosed no acute infarction of the brainstem, the cerebellar hemispheres or within the PCA territories. The brainstem showed old small infarctions with gliosis. A massive acute infarction with a hemorrhagic component was seen in the left MCA territory with brain swelling and uncal herniation. Moreover, multiple lung emboli were detected. The heart did not contain any thrombus, and there was no septal defect between the right and the left side.

Discussion

Even today, after major developments in direct surgical and/or endovascular treatment of aneurysms, the outcome of giant fusiform basilar trunk aneurysms is still unfavourable. Although these aneurysms are considered among the most difficult lesions to treat, large studies reporting on the outcome of different treatments are sparse. This reflects the rarity of the lesion. Giant intracranial aneurysms are aneurysms greater than 25 mm, and comprise approximately 5% of all intracranial aneurysms.[213] Of these, only 8% occur in the posterior circulation.[97] In general, fusiform intracranial aneurysms are found at autopsy with a prevalence of < 0,1%.[155] Basilar trunk aneurysms of all sizes comprise only 1 - 2% of all intracranial aneurysms.[307] We could not find any prevalence numbers on giant fusiform basilar trunk aneurysm, as even Weir in his major contribution summarizes these aneurysms with all other vertebrobasilar aneurysms.[330] It is estimated that, if untreated, 80% of patients presenting with giant aneurysms and brain compression die within a few years.[148, 246] Complete angiographic and morphologic assessment using 4 vessel digital subtraction angiography, CT(A), MR(A) is essential in all aneurysm cases. Multiple angles should provide an accurate view of both the aneurysm and the morphology of the circle of Willis. For posterior circulation aneurysms especially the morphology and flow of

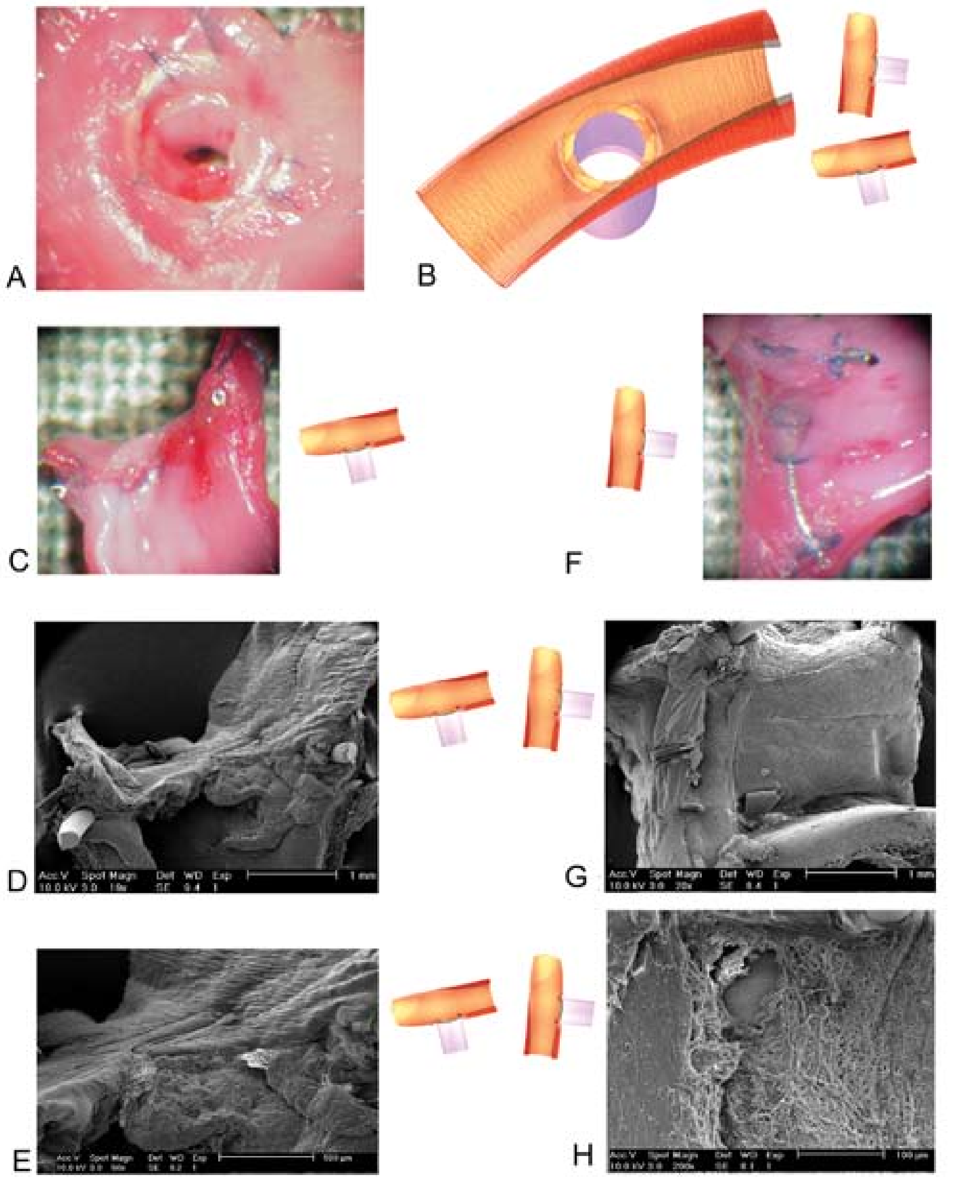


Figure 9.6.
At autopsy the inside of the ELANA anastomosis looked very smooth without any thrombi (A). We cut the internal carotid artery transversely (B) to look from the inside. We then cut the anastomosis in two parts (C and F). Both parts were then viewed at intermediate (D and G) and high (E and H) magnification using the scanning electron microscope (SEM). A small thrombus could be observed (C, D, and E). This thrombus was located on the outside of the anastomosis in the direction of the SCA, alongside the edge which had been formed after the laser ablation procedure. Any larger thrombi originating from this site whould have been flushed away during the completion of the bypass (see text). On the other side of the anastomosis the beginning of re-endothelialisation could be observed (F, G, H)

the PComAs should be assessed. The Allcock test (VA angiograms with ICA compression) has been described to observe patency of the PComAs.[167, 221] Treatment is also very demanding as, since perforators to the midbrain and pons emerge from the BA throughout its length, there is a constant danger of brain stem infarction.[95]

Clinical Series of Fusiform Giant Basilar Trunk Aneurysms

With the variety of treatments little is known about the clinical outcome of these aneurysms. Few series have been described in literature. In 1984 Pelz described 22 cases of giant basilar trunk aneurysms in a series of 71 cases of vertebrobasilar occlusion for giant aneurysms.[221] The proximal BA was clipped in 12 cases, in another 6 bilateral VA occlusion was performed. No specific outcome was given for the giant basilar trunk aneurysms; however, these patients were included in the large series published in 1996 by Drake.[95] In that year Drake, Peerless, and Hernesniemi reported on a lifetime experience of vertebrobasilar aneurysm surgery for 1767 cases.[95] In this famous book they published the results on 59 cases with giant basilar trunk aneurysms. Direct clipping of the aneurysm was performed in 7 cases, 3 with excellent outcome, and 4 with poor results. Another 7 aneurysms were trapped, 3 with excellent or good results, 1 with poor results and 3 deaths. Hunterian ligation was applied in 39 cases using basilar clips (19), basilar tourniquet (10), or vertebral ligation (10), 29 with excellent or good results, 3 with poor results and 7 deaths. Three patients were intolerant of complete BA occlusion, two of which died from rupture of the aneurysm. The third was treated with an ECA – P2 bypass, which occluded. An OA – P2 bypass also became occluded, however, he now tolerated BA occlusion due to excellent collateral flow to the SCAs and an enlarged PComA.

Seifert reported on a series of 24 patients with basilar trunk or vertebrobasilar junction aneurysms.[243] Among these were 3 small BA trunk aneurysms, 9 large, 1 giant, and 3 fusiform. Of the latter, one was treated with ventriculostomy alone, and died of subsequence SAHs. The others were all operated upon. Another patient with a fusiform BA trunk aneurysm died from progressive brain stem infarction after a clip had to be placed on the BA because of intraoperative rupture. Specific outcome of the other giant and fusiform BA trunk aneurysms was not given. However, of the 16 patients with BA trunk aneurysms, outcome was excellent in 7, good in 4, and poor in 3. The remaining two patients have been described above and died.

Anson, Lawton, and Spetzler operated on 8 patients with a dolichoectatic BA aneurysm.[13] Two patients were treated with anticoagulant therapy only, with fair to good results. Four patients were treated by thrombectomy using a special ultrasonic aspirator, endarterectomy, and aneurysmorrhaphy using clips to reconstruct the parent vessel. One of these patients had very good outcome (GOS 1), three had poor outcome (GOS 2-3), and one died. In two other patients a STA – SCA bypass was deemed necessary prior to parent vessel occlusion. One of these patients had a proximal balloon occlusion of the BA with excellent outcome; the other received a distal clip occlusion and died 9 months later of respiratory complications. In 1997 the same group published on the management of a series of 28 patients with a large or giant mid-BA aneurysm which included patients of the aforementioned study on dolichoectatic BA aneurysms.[187] Eleven patients had transient treatment-associated cranial nerve deficits. Neurologically, three patients were permanently worse as a result of treatment. All three aneurysms were clipped completely, but the patients awoke with new neurological deficits, one of them died 1.3 years after treatment. Overall, 12 patients had good outcomes, 9 had moderate disabilities, 3 had severe disabilities, and four died.

Pre-operative Evaluation of Treatment Options

The extent and progression of our patient's brain stem compression pushed us to carry out the treatment he requested, because, left untreated, his quality of life was unacceptable poor and his life-expectancy was deemed to be short.[148, 246] At first, we considered the possibility of endovascular treatment. Theoretically, the aneurysmal sac could be embolized with glue.[72] The use of this technique should only be applied in cases of very distally located aneurysms in small arteries, in which accidental occlusion of the parent artery would not be critical.[72] In 1989 Higashida reported successful treatment of a large ectatic mid-BA aneurysm.[144] Initially, a single balloon was placed into the dome of the aneurysm with preservation of the BA. Follow-up angiography 7 months later showed residual filling of the aneurysm. A second procedure was performed in which two more balloons were guided up the VA and BA and placed so as to occlude both aneurysm and BA. The post-embolization angiogram demonstrated complete obliteration of the aneurysm and the mid-BA. The patient tolerated this procedure well, and after 2 weeks was able to sit up and walk with assistance. Another patient with a large mid-BA aneurysm was treated with balloon embolization of the sac with excellent results. Two patients with similar aneurysms were treated with occlusion of the the mid-BA with good results. A fifth patient with a giant aneurysm of the mid-BA was treated in the same way. Transient ischemia complicated this case as important perforators were occluded during test occlusion. However, she died from rupture of a 2nd untreated aneurysm.

Hodes reported in 1991 on BA balloon occlusion in three patients with an unclippable BA aneurysm while the patients were awake.[146] In all three cases collateral blood supply was confirmed by injection of both ICAs which filled the superior portion of the BA through the PComAs. One patient developed paralysis 2 hours after balloon occlusion of the mid-BA, and died 5 days later. Another patient with a giant fusiform aneurysm of the BA underwent successful test occlusion of the VA with adequate collateral supply through the PComA. When traction was applied for balloon detachment, the balloon migrated proximally, and during deflation of the balloon for repositioning, the patient became comatose, and died 3 weeks later. Treatment of the third patient was successful, as he was young, with excellent collateral circulation. In 2000, Firat reported on a child with a partially thrombosed giant BA aneurysm of which the patent portion was successfully occluded with coils.[108] Gradual improvement was observed within a few days of the intervention, and all symptoms resolved within 6 months.

At 1 year MRI showed further shrinkage of the aneurysm, and only the coils and a rim of thrombus surrounding them remained in the sac. Uda reported in 2001 on the successful endovascular treatment with of 41 basilar trunk aneurysms, 5 of which were large, and 5 were giant.[307] Four of the large aneurysms had excellent outcome. One resulted in death. Also four of the giant aneurysms had fair to excellent outcome, the remaining case resulting in death. Another 2 giant and 1 large aneurysm were located at the vertebrobasilar junction and had excellent to good outcome. In 2002 Jones reported successful coil embolisation of a giant mid-BA aneurysm in a 19 months old child with tuberous sclerosis.[162] Result was excellent. We also found a report by Kato in 2001 of 132 cases which were found during "brain checkup".[168] Among these were 2 BA trunk aneurysms which were treated successfully, however without giving any specifics on the outcome. Another large series of 39 aneurysms which were treated with endovascular techniques was published by Wanke in 2002.[326] Among these there was one patient with a BA tip aneurysm and a large BA trunk aneurysm. Both aneurysms were successfully treated. No specifics were given on the outcome of this patient. Sluzewski reported in 2003 the results of coil embolization of 31 large or giant aneurysms.[259] His study included one patient with a giant basilar trunk aneurysm which had thrombosed only partially. After two repeated coilings complete occlusion was obtained 17 months after the first procedure, with excellent outcome. Wenderoth reported on 3 similar cases of BA occlusion in the treatment of giant fusiform BA aneurysms.[331] All three patients had nice PComAs which contributed to the decision of complete BA occlusion. The aneurysms were all completely occluded and the patients had excellent clinical outcome.

In our patient, the configuration of his fusiform giant aneurysm, along with the considerable mass of thrombo-embolic material within the sac, prohibited conventional coil embolisation or embolisation with liquid materials.[72] Next, the possibility of stenting was considered for our patient. However, we rejected this because the length and the complex curvature of the circulated portion of the aneurysm made us afraid of vessel rupture during stent placement. Moreover, in this specific aneurysm, we thought the option of flow stagnation and consecutive aneurysm shrinkage to be limited.

Recently though, stenting of intracranial vessels has been applied successfully in the treatment of giant aneurysms or aneurysms with extraordinary wide necks.[160, 200, 318] Islak reported in 2002 on the successful treatment of 2 patients with giant intracranial aneurysm using endovascular stents.[160] One of these cases involved a giant aneurysm extending from the vertebrobasilar junction to the mid BA almost up to the AICAs. A stent was inserted through the VA into the BA up to the mid-basilar level. Then the stent was deployed to cover the inflow zone without diminishing patency of the AICAs. The lumen of the aneurysm was almost completely thrombosed, although the aneurysm was not occluded by the stent. Four months later the neurological state of the patient had improved considerably and the aneurysm was found to have "decreased in mass effect". In 2003 Vanninen published on a similar stent technique in 12 patients with intracranial aneurysms.[318] Among these there was one patient with a large broad-based BA trunk aneurysm which presented with SAH and who was successfully treated with the placement of a stent. Two years later some visual impairment remained, but she could work again.

As a last endovascular option we considered therapeutic BA or VA sacrifice. The rationale for such a treatment is to reverse the flow of blood in the BA and thereby induce thrombosis and successively reduction of aneurysm size while adequate blood supply to the brain stem is maintained[108]. This treatment has been effective in giant aneurysms both in the anterior and posterior cerebral circulation.[89, 146, 260] However, our patient failed the VA balloon test occlusion. His collateral capacity between the anterior and posterior cerebral circulation was indeed so limited that he was unresponsive within 45 seconds of VA occlusion. The simultaneous TCD recordings also showed that, upon VA closure, the flow through the P1 segment, now the only supply to the infratentorial region had almost ceased. TCD measures blood velocities in real-time and continuously, has a superior time-resolution, and is therefore an excellent tool in conjunction with very short-lasting occlusion tests. In the anterior circulation TCD has previously been used in this context.[260] His poor collateral capacity excluded the surgical option of merely Hunterian ligation of the BA or the VA.[89, 95] We considered direct surgical reconstruction of this specific aneurysm, even under profound hypothermia and circulatory arrest, to be beyond reach. Our patient was hence offered a surgical solution involving the use of a bypass.

Bypass Surgery in the Treatment of Giant Basilar Trunk Aneurysms

Drake was the first to describe ligation of the BA or VA in the treatment of giant BA aneurysms.[89] Using a tourniquet which could be placed at surgery and tightened afterward with the patient awake the BA or VA could be occluded some time postoperatively.

In 1984 Heros and Ameri reported the rupture of a giant BA tip aneurysm after the construction of a ECA – PCA bypass just before intended occlusion of the BA.[142] The patient was admitted with symptoms of progressive brain stem compression. The Allcock test failed to show PComAs, so it was assumed that she would not tolerate primary BA occlusion. After the successful construction of the bypass using a saphenous vein graft a tourniquet was placed around the BA just proximal of the aneurysm. Tightening of the tourniquet was planned 36 hours after the operation. The patient died in a few hours, and at autopsy a massive SAH was found. The vein graft suture line was intact and there was no indication of ante mortem thrombosis of the graft. Heros and Ameri discussed that there was a significant risk of graft occlusion immediately after surgery, and that the decision to delay the BA occlusion would add a margin of safety. This was confirmed by a problematic awakening immediately after surgery. They concluded that the hemodynamic changes induced by the bypass were partially responsible for the rupture. Also the simple exploration and manipulation of the aneurysm could have attributed to that.

Cardiopulmonary bypass with profound hypothermia and circulatory arrest has been used in the treatment of vertebrobasilar and BA trunk aneurysms, as reported by Sullivan.[277] Six patients had a clippable, but broad neck. The seventh, published as a case report elsewhere,[246] had a fusiform vertebrobasilar aneurysm extending to midbasilar. She presented with tetraparesis and stupor. The aneurysm was approached by a suboccipital craniotomy and total petrosectomy approach with anterior mobilization of the petrous segment of the ICA and posterior mobilization of the facial nerve in order to facilitate the placement of a graft from the cervical ICA to the mid-BA. Circulatory arrest occurred when the core temperature had been below 18 degrees Celsius. During this period, the aneurysm was dissected from perforators and partially emptied of clot and blood. A vein graft from the ICA to the PCA was made, with the intention of subsequently occluding the proximal VA. Then a low flow through the bypass was observed, presumably because of the small calibre of the PCA. The bypass was replaced by an ICA – mid-BA bypass. One year later, she was back in school again, with mild facial paresis and no hearing on one side. Sullivan also mentioned two more patients with giant fusiform BA aneurysms with heavy thrombosis and without neck, which were considered inoperable.

Combining Bypass Surgery and Endovascular Procedures

The combination of bypass surgery and coil embolisation has been described by Ewald in 2000.[103] Eight cases of giant intracranial aneurysms were treated with revascularization and coil embolisation. Only one patient had a mid-basilar aneurysm and was treated with a STA – PCA bypass, after which the BA was occluded between the AICAs and the SCAs. The patient survived, however, with a tetraplegia and cranial nerve paresis. Badie reported in 2000 a similar case.[31] However, an initial STA – SCA bypass was constructed, after which the VA was meant to be occluded using coils. Patency of both bypasses was confirmed using color and pulsed Doppler information. The flow through the initial STA – SCA bypass was considered too low; therefore it was replaced by an ECA – SCA bypass using a saphenous graft. Follow-up MRA after 14 months revealed near-complete resolution of the aneurysm and a patent bypass. The patient returned to part-time employment at his previous occupation.

Surgical procedure

Fusiform giant BA aneurysms have previously been treated with a revascularization procedure, using an EC-IC bypass to the PCA or the SCA.[142, 148, 246, 277, 300] In our patient we created an IC-IC bypass between the ICA and the SCA, using the ELANA technique for the ICA anastomosis, and a conventional End-to-Side technique for the SCA anastomosis. We have previously made IC-IC bypasses using the intracranial ICA as donor (and a piece of the greater saphenous vein as graft) with satisfactory results in a number of patients where either M1, A1, or PComA aneurysms were bypassed.[297, 300] The advantage of the IC-IC bypass over an EC-IC bypass (with the ECA, STA, or OA as donor) is the calibre and therefore the flow volume of the donor vessel (usually the intracranial ICA bifurcation). Moreover, the creation of the ELANA anastomosis with the intracranial ICA is safe since no temporary occlusion of this vessel is required, and the technique is relatively easy.

The flow following ligation of the BA (40 ml/min) seemed sufficient to provide adequate flow to the superior part of the posterior circulation, a postulate supported by the postoperative angiogram and the findings at autopsy, showing no signs of ischemia or infarction in the brainstem, the cerebellar hemispheres, or the PCA territories. With this patient expiring before postoperative MRA flow measurements could be obtained, an anticipated further increase in blood flow could not be confirmed.[313] However, as an ELANA anastomosis on the ICA is capable of very high flows,[140, 140, 297, 299, 300, 313] we assume that the blood flow through the bypass in time would have approached the blood flow through the distal BA under normal circumstances as was shown in other patients. [297, 313]

From our experiments in the animal laboratory and from more than 165 ELANA anastomoses in patients, we have not experienced thrombus formation proximally or distally to the ELANA anastomoses.[297, 299, 300, 313] So, what was the cause of the subtotal occluded MCA in this patient? He was known to have a familial coagulopathy which we tried to counteract with pre-operative salicylic acid, and at autopsy multiple lung thrombi were found. However, no thrombus was found in the heart, or any septal defects, reducing the possibility that a cardiac embolus had migrated to the brain. Also, the vein used for the bypass showed signs of previous thrombosis and recanalisation. The possibility that a thrombus had formed in the short stagnated flow portion (stump) of the bypass proximal to the temporary clip (by the ELANA site) before the two parts of the bypass were connected, and somehow migrated into the ICA and further into the MCA cannot be excluded. However, one could also hypothesize that, despite the preoperative angiograms of the anterior cerebral circulation showing no M1 narrowing, the thrombus actually might have formed even before the ELANA anastomosis was created. If this assumption is correct, it would then explain the unforeseen left temporal lobe oedema noticed upon opening of the dura.

Fresh emboli in cerebral arteries can be liquefied using endovascular thrombolytic agents with successful clinical results. These agents should, however, be used only prior to the ischemic areas becoming infarcted, i.e. a maximum of 6 hours after the ictus and never when hypodense areas can be visualized on the CT scan. In our patient, having being comatose and showing delayed filling of the left MCA region 24 hours after completion of the 15 hour procedure, we assumed to have reached beyond the time frame recommended for thrombolytic treatment.

The accumulation of some thrombotic material in the angle formed by the small rim of the ICA wall, which is present at the anastomosis site (because the inner diameter of the platinum ring is 2.8 mm and the outer diameter of the laser tip is 2.2 mm) and the inside of the vein graft, is always seen in our experiments and is part of the process which leads in two weeks time to a full endothelialisation of the anastomosis site, and in two months time to a complete flattening-out of the rim, which results in an anastomosis with approximately the same diameter as the platinum ring (2.8 mm).[338] This case report shows that the same changes can be seen within 48 hours after the ELANA anastomosis in a patient as are seen in our chronic animal experiments, which in the end lead to a complete endothelialisation.

Conclusion

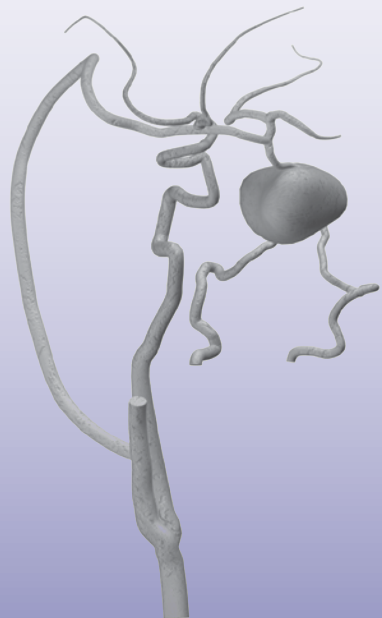
We think that for this patient it was justified to create an ICA-SCA bypass prior to BA occlusion. Although we applied a surgical clip in order to occlude the BA, we might as well have performed that action using endovascular means. The application of the ELANA technique went smoothly and the anastomosis showed nearly complete endothelialisation. It is very sad that despite our many efforts of countering the thrombopathy, next to the creation of a bypass, and the exclusion of the aneurysm from the circulation, our patient succumbed to the result of a MCA occlusion.

Acknowledgements

We want to thank H.J. Mansvelt Beck, A. van der Zwan, and R.M. Verdaasdonk for their continued support of the ELANA technique both in the experimental laboratory as well in the theatre.

Chapter 10

Construction of an ECA-BA Bypass



High Flow Revascularization of the Brain
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Acta Neurochir (2005)[Suppl] 94:143-148

High Flow Revascularization of the Basilar Artery in the Treatment of a Giant Vertebro-basilar Aneurysm

Abstract

High flow revascularization of the brain is hampered by the fact that temporary occusion of a major cerebral artery is necessary to create the distal anastomosis, which may result in brain ischemia. The excimer laser-assisted non-occlusive anastomosis (ELANA) technqiue circumvents this problem. In this paper we elucidate the development of a non-occlusive way to make anastomoses to the major cerebral arteries.

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3D reconstruction of an ECA-BA bypass (with cooperation of J.P. Bremmer). The bypass originates from the extracranial ECA and inserts into the basilar artery. Thus a connection between the extracranial and postior circulation has been created in the treatment of a giant BA aneurysm.

Introduction

The idea to increase the amount of blood flow to the ischemic brain, bypassing any stenoses or occlusions, seems so simple. However, it is still difficult to define which group of patients, who are at risk for a major stroke, will benefit from Extracranial-to-Intracranial (EC/IC) bypass surgery. EC/IC Bypass surgery was developed to improve the cerebral blood flow (CBF) in patients with complete carotid occlusion or ICA stenosis not amenable to extracranial endarterectomy. The International randomized EC/IC Bypass Study showed that the conventional EC/IC bypass, in which the superficial temporal artery (STA) is connected to a cortical branch of the middle cerebral artery (MCA), does not prevent the occurrence of stroke or transient ischemic attacks (TIAs) in patients with symptomatic atherosclerotic lesions of the MCA and/or internal carotid artery (ICA) compared to a non-surgical treated group.[11] The most important critique on the study concerned the evaluation of patients before exclusion or inclusion and randomization in the study.[15] Apart from the clinical criteria, the only additional examination consisted of bilateral carotid angiography. It is therefore not surprising that a new EC/IC bypass trial has been launched in which patients are examined with more advanced techniques to measure the CBF and the oxygen extraction of the brain.[6] Normaly, changes in cerebral perfusion pressure (CPP) have little effect on the CBF due to the autoregulation capacity of the brain. If the CPP decreases the cerebral blood volume (CBV) increases because of the autoregulated vasodilation, thus preserving adequate CBF. Autoregulation fails when the capacity for vasodilation has been exceeded and CBF begins to decline. At that stage, the brain still has the capacity to extract more oxygen (increased oxygen extraction fraction (OEF)) when oxygen supply has decreased due to diminished CBF. Sufficient augmentation of the blood supply should increase the CBF and decrease the OEF.

However, the conventional STA-MCA bypass only has a limited capacity to increase the blood flow to the brain due to the relatively small size of both donor an recipient bloodvessel. It is possible to create a bypass with a higher capacity by choosing a larger donor vessel, like the more proximal segments of the STA or the external carotid artery (ECA), and/or to interpose a large venous graft between donor and recipient vessel. One of the advantages to use a cortical branch of the MCA as recipient vessel, is that these branches usually have many collaterals. Therefore, it is quite safe to temporarily occlude such a branch in order to create the distal anastomosis of the bypass, using the conventional anastomosis technique originally described by Carrel,[59] and improved by Yasargil for use in EC/IC bypass procedures.[342, 344] Even if there are no collaterals, the occlusion of a cortical branch creates temporary ischemia in only a very small part of the brain which may not be clinically relevant. To make a very high capacity bypass to the brain, a larger (more proximal) recipient artery should be chosen.[145] However, these vessels do not have many collaterals, so occlusion will create temporary ischemia in a rather large portion of the brain. Patients at risk for cerebral ischemia usually use their collaterals already at maximum, diminishing even further the window of time during which the surgeon may create a conventional anastomosis. Also, the risk of hyperperfusion after the creation of the bypass increases when choosing a more proximal recipient vessel. So, in order to safely create high flow bypasses to the brain and thus increase the CBF, it is necessary to choose a large donor vessel (i.e. the ECA), to use an interposing vein graft, and to connect that graft to a proximal cerebral artery in a non-occlusive way. In this paper we want to elaborate on the techniques with which we have tried to create such a bypass.

In 1902, Carrel described the principles for creating vascular anastomoses, which have hardly changed during the last century.[59] The recipient artery is temporarily occluded with two clamps. Between them, an opening is cut into the wall. The end of the donor vessel is connected to the recipient vessel with the endothelial layers of both vessels closely approximated. Still the backbone of modern vascular surgery, Carrel's technique has been highly successful. However, its inherent flaw is the temporary occlusion of the recipient vessel. A critically ischemic area may become infarcted during the procedure. As the brain is extremely dependent on a continuous blood supply, Carrel's techniques are almost impossible to use on cerebral arteries. It is therefore surprising that no attempts have been made to develop a non-occlusive anastomosis technique, apart from the animal experiments by Eck and Yahr.[98, 341]

Materials and Methods

Twenty-five years ago we started animal experiments in order to make high-flow revascularization procedures of the brain a safe and effective procedure. First, the end of the donor vessel is connected to the recipient artery using sutures, which pass through the wall of the recipient artery superficially, and fully through the wall of the donor vessel. Subsequently, a cutting device, which is introduced into the donor vessel, is used to make a hole in the wall of the recipient artery, leaving part of the adventitial and medial layers of the recipient artery exposed to the blood stream. This is contrary to Carrel's adage that close approximation of the endothelial layers is an absolute prerequisite for a successful anastomosis, which may explain why so few surgeons followed this line of thinking. Exposure of the other layers of the blood vessel to the blood stream would lead to thrombus formation and occlusion.

In many animal experiments we showed that non-occlusive anastomoses will remain patent, thanks to 2 technical innovations.[296, 301, 303, 338] The first was the use of the Excimer laser (see Figure 10.2.E) to cut a full-thickness disc of recipient artery wall at the anastomosis site. The laser catheter consists of two concentric circles of 60 micron fibres arranged around the periphery of a thin-walled catheter with an internal diameter of 2.0 mm. A small metal grid is mounted 0.5 mm from the tip. The catheter is introduced into the donor vessel, so that the tip touches the wall of the recipient artery (see Figure 10.1.E). Vacuum is then induced within the lumen of the catheter, causing a firm fixation of the wall to the grid and the laser fibres. When the laser is activated a full-thickness disc of recipient artery wall is cut out, creating a functional anastomosis. The second innovation is the application of a platinum ring with a diameter of 2.8 mm, which is attached onto the end of the donor vessel (see Figure 10.1.A-C). The donor

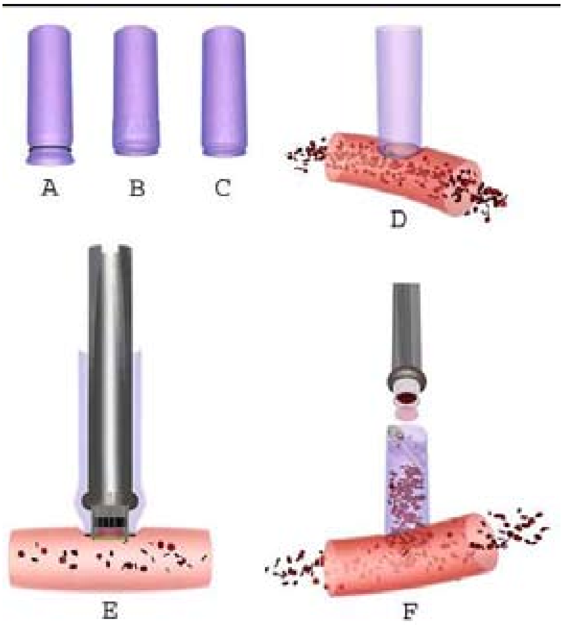


Figure 10.1.
The ELANA technique. A) A platinum ring is placed over the end of the donor vessel. B) The end of the donor vessel is then everted over the platinum ring. C) The donor vessel is fixated to the platinum ring with several sutures, after which the excessive end of the everted part is cut of. D) The donor vessel is then attached to the recipient vessel using sutures which pass the platinum ring, completely pass the wall of the donor vessel, and only superficially penetrate the wall of the recipient vessel. E) The ELANA catheter is introduced into the open end of the donor vessel, so that the tip touches the wall of the recipient vessel inside the platinum ring. Vacuum suction is aplied, ensuring a firm fixation of the laser fibers to the vessel wall. When the laser is activated, a full-thickness portion (flap) of the wall of the recipient artery is cut out. F) Due to the continued vacuum suction, the flap is recovered when the catheter is withdrawn from the now functional anastomosis.

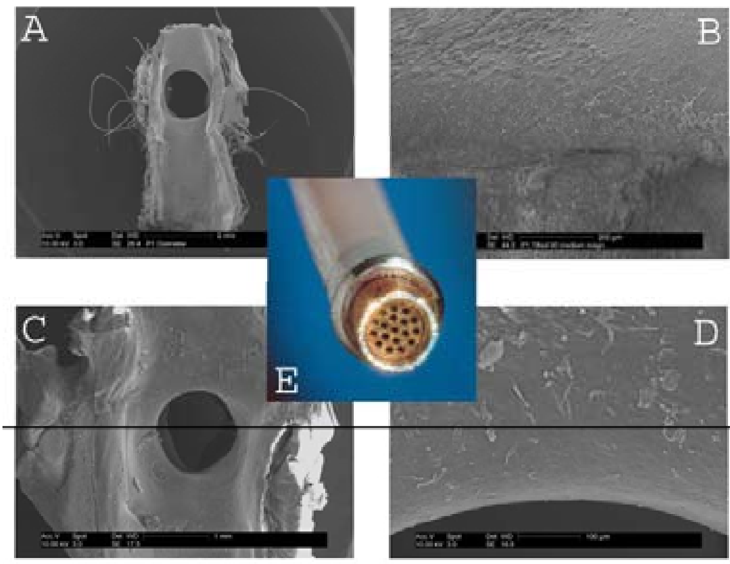


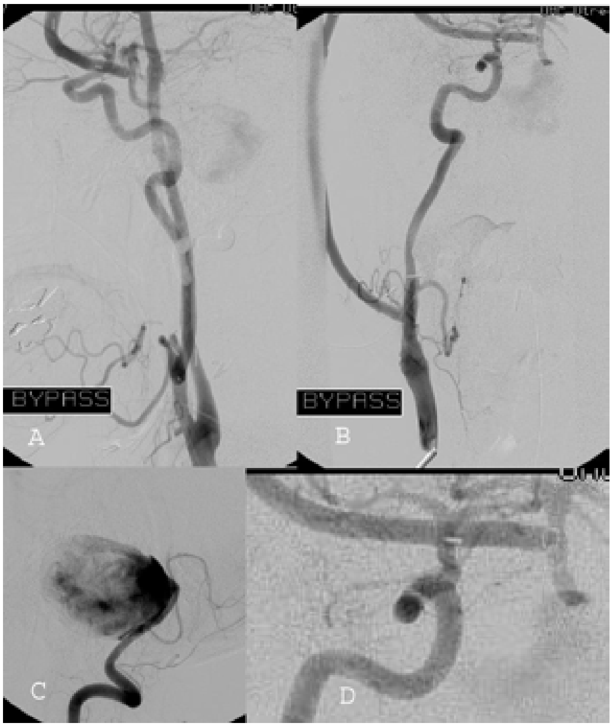
Figure 10.2.
Scanning electron microscopic (SEM) images of 2 anastomoses (A,B,C,D) and an image of the ELANA catheter tip (E). In (A), the inside of the posterior cerebral artery is shown at the site of the anastomosis with the bypass, three weeks after its construction (see text). The bypass is coming towards the camera, and its lumen is clearly visible. A high magnification image of the edge of the vessel wall (B), which has been ablated by the excimer laser (E) shows a smooth surface with re-endothelialization. Similar images of an anastomosis with the intracranial internal carotid artery (C and D) were taken more than 5 years after its construction (see text). The laser edge is very well re-endothelialized in the high magnification image(D).

vessel is then connected to the recipient vessel (see Figure 10.1D.), using sutures around the platinum ring, which fully pass through the wall of the donor and superficially pass the wall of the recipient artery. The effect of the platinum ring is fourfold: 1) It flattens the wall inside the ring, which facilitates the penetration of the laser tip over its full circumference; 2) The ring dictates the shape of the anastomosis, which is always round with a diameter of 2.8 mm; 3) It guides the tip to the correct position; 4) The ring prevents the tip from further entering the lumen after penetration of the wall, because it stops the catheter at a circular protuberance, 1.5 mm from the tip.

Results

During the last seven years the excimer laser-assisted non-occlusive anastomosis (ELANA) technique, has been applied in 170 patients with giant intracranial aneurysms, skull base tumours, or progressive brain ischemia.[273, 274, 297, 300, 313] The long term patency was 90% with an average flow in the bypass of 150 ml/min. In one patient with a giant aneurysm of the basilar artery we used the ELANA technique twice to create a connection between the internal carotid artery and the posterior cerebral artery. He died three weeks after the operation because of respiratory failure. Angiography showed that the bypass was patent and at autopsy both anastomoses appeared fully endothelialised, which was later confirmed by scanning electron microscopic evaluation (see Figure 2A, with a high magnification in 2B). Another patient, in whom we ligated the internal carotid artery after the construction of a bypass because of a skull base tumour, died 5 years later because of tumour recurrence. The ELANA anastomosis was removed at autopsy for scanning electron microscopy (see Figure 2C, with high magnification in 2D). The anastomosis site was well endothelialised and the rim of recipient artery wall with the adventitial and medial layers had disappeared.

Our group has published on the clinical results of the ELANA technique in a small series of 15 patients with a high risk of recurrent stroke with promising results.[179, 180] We offer an ELANA EC/IC bypass procedure only to those patients who have ongoing symptoms of cerebral ischemia, after unilateral or bilateral ICA occlusion has been observed, despite antitrombotic treatment and endarterectomy of a contralateral ICA stenosis or ipsilateral ECA, and in whom the symptoms are likely to be of haemodynamic origin. An exception has been made for a patient who presented with repeated episodes of vertebrobasilar ischemia because of vertebral artery occlusion and stenosis. An ICA-posterior cerebral artery segment P1 bypass procedure was performed, effectively creating a new posterior communicating artery.[297] All patients had a proven hypoperfusion of the brain. In this very carefully selected group of patients we have been able to create EC/IC and IC/IC bypasses to all proximal cerebral arteries of the brain, depending on the location and extend of the occlusive vascular lesions. Several times we could not proceed with the ELANA technique because of severe athereosclerosis of the ICA, the proximal MCA, or the proximal ACA. We then created a conventional EC/IC bypass to a non-sclerotic



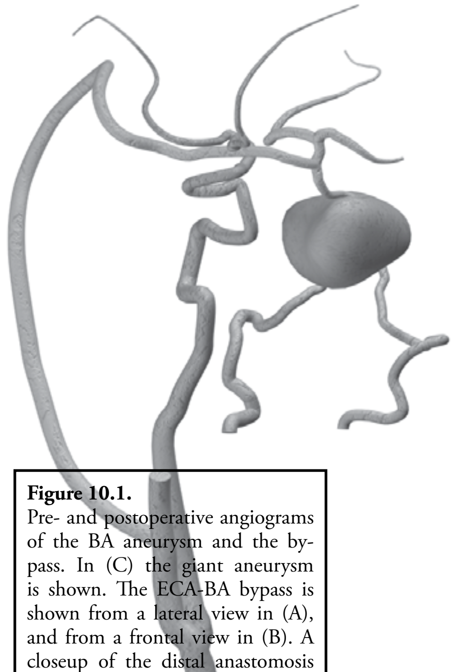


Figure 10.1.
Pre- and postoperative angiograms of the BA aneurysm and the bypass. In (C) the giant aneurysm is shown. The ECA-BA bypass is shown from a lateral view in (A), and from a frontal view in (B). A closeup of the distal anastomosis to the BA is shown in (D). Note the small platinum ring which has been attached to the distal BA. The image above is the 3D reconstruction.

cortical branch of the MCA, because using a sclerotic recipient vessel may lead to rupture of the anastomosis.

So, it is possible to consider every cerebral artery as a recipient artery for bypass surgery. Recently, we treated a patient with a giant VA-BA aneurysm (see figure 3c), which was increasing in size during the last months. The last two months our patient could not continue his work as a policeman, and suffered from progressive brainstem deficits with dysarthria, swallow problems, vertigo and ultimately a tetraparesis. He obviously had a bad prognosis, and we expected that his life-expectancy would be very short. Clinically, our patient did not tolerate bilateral VA occlusion, in order to reverse the flow in the BA and thus preventing the aneurysm from growing. Therefore, a "jump" bypass was considered between the intracranial ICA and the PCA, like the bypass made in the afore-mentioned patient. We also considered making an ECA-PCA bypass. Both bypasses should then supply sufficient bloodflow to the posterior circulation, while ligation of both VAs would reverse the flow in the aneurysm. We started by occluding the left VA using two endovascular balloons. Our patient tolerated this without problems. We then operated him. Using a pterional approach, we found that the BA-bifurcation was located quite high, and the BA, distally of the aneurysm, looked very healthy and accessible. Of course, creating a conventional anastomosis to the BA was out of the question. In the literature we could find only one case under deep hypothermic circulatory arrest during which a conventional anastomosis to the BA was made.[246] The ELANA technique allowed us to attach a venous graft to the BA through the small opening formed by the ICA, the A1 and the optic nerve, without occuding the BA. A nice flap of BA wall was retracted and this anastomosis was used to create an ECA-BA bypass, through which a flow of 55 ml/min was observed. This flow was observed with the right VA still open. We then ligated also this VA and the flow through the bypass increased to 95 ml/min. Due to the reversed flow in the aneurysm, there was now a high chance that a thrombus will create within the aneurysm, which hopefully would not occlude the BA itself. BA occlusion, however, was not likely to occur because of the continued flow to the PCAs, SCAs and AICAs. Angiography showed that the bypass supplied the posterior circulation (see figure 3A,B,D), and our patient was improving and started to talk and move his limbs. After the operation his condition stabilized. There were signs of improvement. Two weeks later, MRA and CTA scans showed progression of thrombus formation within the aneurysm. However, there was also some progression of the neurological deficits. Four weeks later, the patient suffered a fatal subarachnoidal haemorrhage, which probably originated from the remnant of the aneurysm.

Discussion

The ELANA technique is an additional tool in the neurosurgical armamentarium. It can be used to attach bloodvessels to otherwise inaccessible cerebral vessels, creating high flows. Whether to use this technique in patients endangered for stroke is still undefined. We have selected only those patients who have suffered multiple TIAs or minor stroke due to ICA occlusions inaccessible for endarterectomy, and who have a proven hypoperfusion of the brain. The results of the new EC/IC bypass trial might show that even more patients will improve when treated with revascularization techniques.

Various techniques to apply the platinum ring onto the recipient vessel are under investigation. The latest developments in our laboratory concentrate on the possibility of making a facilitated sutureless ELANA. The first results of animal experiments on rabbits using this method look very promising.

Acknowledgements

We want to thank all members of the ELANA Researchgroup Utrecht for their continued support both in the experimental animal laboratory as well as in the theatre. Next to the authors, the ELANA Researchgroup Utrecht consists of H.J. Mansvelt Beck, R.M. Verdaasdonk, A.van der Zwan, B. Verweij and M. Münker.

Chapter 11

Intracranial-to-Intracranial Bypass Surgery

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In Preparation

Intracranial-to-Intracranial Bypass Surgery in the Treatment of Giant Aneurysms

Abstract

Object

Giant cerebral artery aneurysms, which cannot be excluded directly by surgical clipping or endovascular coiling, can sometimes, be treated by several combinations of revascularization and vessel occlusion. Despite that, these aneurysms have a high complication rate. As opposed to conventional revascularization procedures, bypasses made using the ELANA technique do not require temporary occlusion of the major cerebral arteries, thus enabling us to use them for bypass surgery.

Methods

We present a retrospective study with 42 patients with giant intracranial aneurysms, who were treated with intracranial-to-intracranial bypass surgery using the excimer laser-assisted non-occlusive anastomosis (ELANA) technique and conventional anastomosis techniques, as a stand-alone option or in combination with aneurysm clipping, coiling, or vessel occlusion. The objective of this study was to assess the technical results of the ELANA technique and to evaluate the clinical results.

Results

Sixty-one ELANA procedures were performed to create 61 successful anastomoses (100% success rate). There were no ELANA related complications. Twenty-one patients (50%) suffered direct post-operative neurosurgical complications. Six patients (14%) suffered non-neurosurgical complications. Temporary post-operative neurological deficits were found in 12 patients (29%), permanent neurological deficits in 9 (21%). There was no intra-operative mortality. Two patients died from a rebleed. Three patients died because of fatal cerebral vessel thrombosis. One patient died of a myocardial infarction and one of unknown cause. Post-operatively, 26 patients (62%) had the same or better Rankin Grade as pre-operatively.

Conclusions

We conclude that the ELANA technique is a viable and safe technique. We found it a reliable tool in the treatment of giant cerebral aneurysms. However, despite the different surgical and endovascular tools available us, this group of patients remains very difficult to treat.

Introduction

Giant cerebral aneurysms

Giant cerebral aneurysms still form a therapeutic problem for neurosurgeons. By definition, these aneurysms have a diameter of 25 mm or more. Because of their mass-effect, they often cause clinical symptoms before subarachnoid hemorrhage occurs, due to rupture of the aneurysm. However, as the risk of rupture during life is between 20 and 70 percent,[333, 334, 346] treatment of an unruptured giant aneurysm is absolutely indicated. Similar action is warranted for a ruptured giant aneurysm, as the risk of a fatal rebleed is between 30 and 70 percent as well.[220, 335, 336]

Traditionally, aneurysm management involves direct surgical clipping. However, only about 50 percent of all giant aneurysms can successfully be treated by operative clipping alone.[92, 189, 190] The last years, endovascular neuroradiologic interventions have contributed considerably to the ways by which aneurysms can by taken out of the circulation.[147, 259] However, a group of giant aneurysms remains that cannot be clipped directly or occluded using coils, glue, or balloons. If a direct approach is considered impossible, occlusion of the parent vessel with or without revascularization procedure has frequently been reported as a viable alternative.[44, 78, 92, 143, 148, 240, 268, 282, 319] Usually, a balloon test occlusion (BTO) of the parent artery is performed in order to test whether the parent vessel can be occluded without performing a revascularization procedure or not.[197]

Bypass surgery prior to parent vessel occlusion has been described ever since Yasargil made the first STA-MCA anastomosis.[344] The occlusion of the parent vessel can then be performed intra-operatively using vascular hemo clips, or post-operatively by endovascular means. However, using conventional anastomosis techniques, it remains difficult to connect a graft to the major cerebral vessels, due to the temporary occlusion of the recipient vessel with the risk of ischemia.

The ELANA technique

The ELANA technique has extensively been described elsewhere.[140, 180, 274, 297, 305] We are able to make an anastomosis to the major cerebral arteries without (temporarily) occluding these vessels using this technique. The objective of this paper is to make a technical assessment of the ELANA technique in the treatment of patients with giant intracranial aneurysms, and to report our results with treating these patients.

Patients and Methods

We present a retrospective study with 42 patients with a giant aneurysm of the anterior and posterior circulation, who were treated with intracranial-to-intracranial bypass surgery using the excimer laser-assisted non-occlusive anastomosis (ELANA) technique and conventional anastomosis techniques, as a stand-alone option or in combination with aneurysm clipping, aneurysm coiling, or parent vessel occlusion. Before operation all patients were examined clinically. A magnetic resonance imaging and a cerebral computed tomography were also done in all patients, as well as a cerebral pan-angiography (including imaging of the external carotid artery). A balloon occlusion test was not routinely performed.

In all patients the primary aneurysm was classified according to the Yasargil modified Hunt & Hess Scale (see Appendix B, Table 1.).[343] The modified Rankin Scale (see Appendix B, Table 2.) was used to assess the patients pre-operatively, directly post-operatively and at late follow-up.[33, 317] Appendix B. Table 3. gives an overview of all patients. All patients harbored a giant aneurysm which was considered impossible to clip either on angiography or at intra-operative observation in an earlier operative procedure. Also, all aneurysms were considered non-coilable, with three previously coiled cases (case 5, 12, 40) in whom the coils had impacted with refilling of the aneurysm. All patients were treated with at least one bypass procedure. For each bypass procedure the volume blood flow (in ml/min) through the bypass was measured directly after connection of the bypass, during temporary parent vessel occlusion, and at the end of the operation, using an ultrasound flow meter (Transonic Systems, Inc, Ithaca, New York) with a 3 mm flow probe around the bypass.

All 42 cases were operated by the senior author (CAFT) between 1993 and 2004 with an IC-IC bypass. For every bypass the anatomical location of the proximal and distal anastomoses was noted, as well as the anastomosis technique (ELANA or conventional). We only considered an ELANA anastomosis to be successful if a forceful retrograde stream of blood would appear from within the bypass graft immediately after the laser procedure. Usually, a temporary hemo clip was then placed on the graft to prevent excessive back bleeding, leaving the recipient vessel completely untouched. In every ELANA anastomosis the successful connection with the recipient artery was evaluated (successful or not) together with the retrieval of the laser ablated flap (successful retrieval, not retrieved and anastomosis discontinued, not retrieved and anastomosis used for bypass).

Results

Patient presentation

Eighteen patients presented without any symptoms, 15 patients had no significant disability despite minor symptoms, and 9 patients presented with several grades of disability. Four aneurysms were located at the anterior communicating artery (AcomA). Four other aneurysms were located at the intracranial internal carotid artery (ICA), 3 of which were positioned at the bifurcation. Eighteen aneurysms were located at the M1 segment of the middle cerebral artery (MCA) and 9 at the M2 segment (usually at the bi- or trifurcation). There were 6 basilar artery (BA) aneurysms, two of which were located at the top, one at the superior cerebellar artery (SCA) segment, one at the BA trunk (anterior inferior cerebellar artery (AICA)-SCA segment)

Table 11.1. Aneurysm Location and Outcome

		Postoperative Rankin Grade						
Aneurysm site	Nr of patients	6 (Death)	5 (Severe disability)	4 (Moderate disability)	3 (Able to walk)	2 (Slight dis-ability)	1 (No disability despite symp-toms)	0 (No symp-toms)
AComA	4	1			1		1	1
BA SCA	1							1
BA top	2	1	1					
BA trunk (AICA-SCA)	1	1						
BA VA junction	2	2						
ICA top	3						1	2
ICA pcoma	1							1
MCA M1 left	9			1		2		6
MCA M1 right	9	1		1		1	2	4
MCA M2 left	3	1						2
MCA M2 right	6			1				5
VA	1							1
Total	42	7 (16.7%)	1 (2.4%)	3 (7.1%)	1 (2.4%)	3 (7.1%)	4 (9.5%)	23 (54.8%)

Table 11.2. Interventions

Surgical procedure	Nr of patients
Clipping of aneurysm with prophylactic bypass	12
Bypass surgery with parent vessel occlusion	18
Bypass surgery with late aneurysm clipping	1
Bypass surgery with aneurysm coiling	4
Bypass surgery without any clipping, coiling, or occlusion	9
Total	44 (Case 12 and 15 were entered twice)

and two at the vertebro-basilar (VA-BA) junction. One aneurysm was located at the intracranial vertebral artery. For an overview of the location of all aneurysms see Table 11.1.

Surgical results

Five different types of interventions were performed (see Table 11.2.). In 12 patients (except for case 28) the aneurysm was clipped in the same procedure after a bypass procedure was performed, to ensure the blood flow, while clipping the aneurysm. In each of those cases the aneurysm was clipped without permanent occlusion of the parent vessel. In 18 patients a bypass procedure was performed after which the parent vessel was occluded either by intra-operative clipping or post-operatively using endovascular means (usually first with a balloon test occlusion, followed by permanent balloon occlusion). Bypass surgery and post-operative aneurysm coiling was performed in 4 patients. In 9 patients only a bypass was created. In table 6 two cases have been entered twice: case 12 had his 1st bypass procedure without any clipping, coiling or occlusion. The 2nd bypass procedure was performed after 1 year and was followed by ICA occlusion. The 1st bypass procedure of case 15 consisted of an EC-IC bypass from the ECA to the M5 without any clipping, coiling or occlusion of his M1 aneurysm. The 2nd bypass procedure was performed after 1 month with an IC-IC bypass of the intracranial ICA to the M2 with occlusion of the ICA in the treatment of a similar M1 aneurysm.

Table 11.3. gives an overview of the different bypass procedures. In 34 patients a "simple" interposed bypass graft was used. A bypass with a proximal ELANA anastomosis and a distal conventionally sutured anastomosis was used in 27 of these 34 patients. However, in 9 patients the ELANA technique was used for both proximal and distal anastomoses. In 1 of these, the proximal ELANA anastomosis did not produce a flap, and the anastomosis was discontinued (case 14). Instead a conventional anastomosis on the external carotid artery (ECA) was used. In order to treat aneurysms located at a bifurcation, a "Y-bypass" (with one proximal anastomosis and two distal anastomoses) was used in 7 cases, all of which had a proximal ELANA anastomosis. In four of these, one of the distal anastomoses was also made with the ELANA technique. In one patient (case 12) two fully functional bypasses were made to the M2 and the M3 before the ICA was occluded.

The ELANA technique was used for 61 anastomoses (see Table 11.4.). Although a flap was retrieved using the ELANA catheter in only 51 anastomoses (84% flap retrieval), a successful connection was achieved in all anastomoses (100% successful connections). No ELANA related complications were observed.

During the years the ELANA suturing technique has changed a little, while using the same laser procedure. Three different techniques can be distinguished. In three cases (3,18,28) a side-branch assisted suturing technique was used, which has earlier been described elsewhere.[304] Essentially the platinum ring was sutured within the everted end of the bypass graft. Then that end was connected to the recipient artery. Through a side-branch, which had already been sutured side-to-end to the graft at a short distance of the ring, the catheter was inserted to create a hole in the wall of the recipient artery. In the afore-mentioned cases this technique was used to create 3 flaps out of 3 anastomoses (100% successful connections with 100% flap retrieval).

Although successful, we found it easier not to use the side-branch with the whole graft. Instead, we used the conventional suturing technique, in which the graft was cut in two parts with special care for the identification of the in-flow and out-flow ends.[299] Then the ring was sutured to the wall of the recipient vessel, after which the graft was sutured onto the recipient

Table 11.3. Different bypass procedures

Surgical procedure	Nr of patients
"Simple" interposed bypass graft	34
- ELANA – to – ELANA	8
- ELANA – to – Conventional	27
- conventional – to - ELANA	1
"Y-bypass"	7
- ELANA – to – ELANA & Conventional	4
- ELANA – to- Conventional & Conventional	3
"Double barrel bypass"	1
- ELANA – to - ELANA	1
- ELANA – to – Conventional	1
Total	42

Table 11.4. ELANA procedures and location

Artery	Nr of ELANA procedures	
ICA	38	
- successful connection		38
- flap		32
- no flap		6
M1	8	
- successful connection		8
- flap		5
- no flap		3
M2	6	
- successful connection		6
- flap		5
- no flap		1
A1	3	
- successful connection		3
- flap		3
A2	2	
- successful connection		2
- flap		2
P2	4	
- successful connection		4
- flap		2
- no flap		2
VA	1	
- successful connection		1
- flap		1
Total anastomoses	61	
- Total successful connections	61	(100%)
- Total catheter flap retrieval	51	(84%)

Table 11.5. Bypass Patency

Intervention	Nr of bypasses		Average follow-up (days)
Intraoperative aneurysm clipping with the protection of a prophylactic bypass	3		
- Patent		3	43
Late aneurysm coiling after bypass surgery	3		
- Patent		3	85
Vessel occlusion after bypass surgery	5		
- Patent		3	484
- Not patent		2	284
No clipping, coiling or occlusion after bypass surgery	10		
- Patent		4	100
- Not patent		6	40
Total bypasses	21		
- Patent		13	
- Not patent		8	

vessel using the ring as guide. The catheter was inserted into the open end of the graft and the laser procedure was completed in the same way as in the side-branch assisted technique. This conventional suturing technique was used 36 times. In all cases a successful connection with the recipient artery was made (100% successful connections). However, in 7 cases no flap was retrieved (case 6 both anastomoses without flap; case 14 proximal anastomosis without flap; case 15 the distal anastomosis in the 1st operation and the proximal anastomosis in the 2nd operation; case 19 the proximal anastomosis in the 2nd operation; case 36, and case 41 giving an 80% successful flap retrieval rate).

The advanced suturing technique involved the evertion of end of the cut graft around the platinum ring. That end was then connected to the recipient artery, and we then proceed with the laser procedure. This advanced suturing technique was used 22 times, also with a 100% successful connection result. However, in 8 anastomoses no flap was retrieved (case 10, 11, 15, 22, 23, giving a 73% successful flap retrieval rate).

In 21 patients the post-operative patency of the bypass was evaluated (see Table 11.5.). In 3 of these a prophylactic bypass procedure was performed, and the bypasses were found to be patent after approximately 1 month. In 3 patients, in whom the aneurysm was coiled after bypass surgery, the bypasses were also found to be patent after approximately 3 months. Three patients, who where treated with parent vessel occlusion after bypass surgery had a patent bypass after 1.2 years. However, 2 similar patients did not have patent bypass after 10 months. In 1 of these patients (case 33) the clip, with which the vessel was occluded, was insufficient, resulting in recanalization of the parent vessel. In 10 patients in whom only bypass surgery was performed without clipping, coiling, or parent vessel occlusion, only 4 were found to be patent after approximately 3 months.

Clinical results

In total, 19 patients (45%) suffered from direct post-operative neurosurgical complications (see Table 11.6.). Of these, 6 patients had an intracranial hematoma which was surgically relieved (3 patients with a subdural or epidural hematoma, 3 other patients with an intracerebral hematoma not caused by aneurysm rupture). Five patients had a post-operative hydrocephalus which was countered with an external ventricle drain (EVD), or with a ventriculo-peritoneal drain if the EVD was occluded or otherwise insufficient. Insertion of one EVD caused an intracerebral hemorrhage (case 9) which was surgically relieved (this case is included within the 45% neurosurgical complications). Aneurysm rebleed occurred in 5 patients (cases 2, 10, 28, 36, 41), 2 of which were fatal (case 10 and probably case 28). Post-operative epileptic seizures occurred in 3 patients and were successfully countered with anti-epileptic medication. In 1 patient a bone flap infection occurred, resulting in an epidural abscess (case 39). Six patients (14%) suffered from non-neurosurgical complications (see Table 11.7.). Of these, 4 had a pneumonia, which was successfully countered with antibiotics. The remaining 3 patients suffered from a lung embolus, a myocardial infarction (case 33, who died of unknown cause), and a phlebitis. Temporary neurological deficit (see Table 11.8.) was found in 12 patients (29%), varying from temporary hemiparesis to transient global amnesia. However, permanent deficit (see Table 11.9.) was found in 9 patients (21%), of which 6 patients suffered from hemiparesis, 3 from dysphasia, 2 from facial palsy, and 2 from cranial nerve III/IV/VI palsy.

Table 11.10. summarizes the post-operative deaths. Patient 2 died because of a fatal rebleed from the aneurysm in the time between the bypass operation and the planned occlusion of the A1. Patient 8 died from a thromboembolic occlusion of the ipsilateral media. This case was extensively described elsewhere in a case report.[274] Patient 9 suffered from severe brain stem compression because of a giant VBA. After an ICA-P2 bypass the dominant VA was oc-

Table 11.6. Neurosurgical complications

Surgical complications	Nr of Patients	
Bypass occlusion	4	
Postoperative cerebral artery occlusion	3	
Hydrocephalus	5	
Rebleed of aneurysm (before coiling, late clipping or late parent vessel occlusion)	5	
Intracranial haematoma	6	
- Intracerebral haematoma		3
- Subdural haematoma		1
- Epidural haematoma		2
Epileptic seizures	3	
Bone flap infection	1	
Meningitis	3	
Epidural abscess	1	

Table 11.7. Non-neurosurgical complications

Non-surgical complications	Nr of Patients
Pneumonia	4
Lung embolus	1
Myocardial infarction	1
Phlebitis	1

Table 11.8. Post-operative temporary deficit

Post-operative temporary deficit	Nr of Patients
Temporary hemiparesis	8
Temporary dysphasia	4
Temporary facial palsy	4
Temporary dysarthria	2
Transient global amnesia	1

Table 11.9. Post-operative permanent deficit

Post-operative permanent deficit	Nr of Patients
Hemiparesis	6
- arm and leg	4
- arm only	2
Dysphasia	3
CN III/IV/VI palsy	1
Central facial palsy	2
Psychological deterioration	1
Total nr of patients (% of all patients)	9 (21%)

Table 11.10. Post-operative deaths

Deaths	Nr of Patients	Case nrs
Rebleed of aneurysm before coiling or parent vessel occlusion	2	2, 28
Contralateral (to bypass anastomoses) cerebral vessel occlusion	1	8
Cerebral vessel occlusion due to continuing aneurysm thrombosis	1	9
endovascular stent thrombosis	1	10
Unknown. Autopsy not allowed	1	6
Myocardial infarction	1	33
Total nr of patients	7	

Table 11.11. Pre-operative Rankin score and Outcome

Pre-operative Rankin Grade	Nr of patients	Post-operative Rankin Difference		
		Worse	Same	Better
0 (No symptoms at all)	18	4	14	
1 (No significant disability despite symptoms)	15	7	2	6
2 (Slight disability, unable to carry out all previous activities)	2	1		1
3 (Moderate disability, able to walk without assistance)	1			1
4 (Moderately severe disability, unable to walk without assistance)	2	1		1
5 (Severe disability, bedridden, incontinent, requiring attention)	4	3		1
Total	42	16 (38.1%)	16 (38.1%)	10 (23.8%)

Table 11.12. Unruptured Aneurysms and Outcome

Unruptured aneurysms: N = 19		Post-operative Rankin Grade						
Yas H&H	Nr of Patients	6	5	4	3	2	1	0
0a	10	2		1		1	2	4
0bI	4	1				1	1	1
0bII	3	1						2
0bIII	2	2						
Total	19	6 (32%)	0	1 (5%)	0	2 (11%)	3 (16%)	7 (37%)

Table 11.13. Ruptured Aneurysms and Outcome

Ruptured aneurysms: N = 23		Post-operative Rankin Grade						
Yas H&H	Nr of Patients	6	5	4	3	2	1	0
Ia	10			1				9
Ib	1						1	
IIa	7		1					5
Iib	2				1			1
IIIa	1							1
U	2	1		1				
Total	23	1 (4.3%)	1 (4.3%)	2 (8.7%)	1 (4.3%)	0	1 (4.3%)	16 (70%

Table 11.14. Anterior Circulation Aneurysms and Outcome

		Pre- / Postop Rankin Difference		
Aneurysm site	Nr of patients	Worse (nr of which are dead)	Same	Better
AComA	4	2 (1)	1	1
ICA	4	1 (0)	1	2
MCA M1	18	6 (1)	8	4
MCA M2	9	2 (1)	4	3
Total	35	11 (3)	14 (40%)	10 (29%)

Table 11.15. Posterior Circulation Aneurysms and Outcome

		Pre- / Postop Rankin Difference		
Aneurysm site	Nr of patients	Worse (nr of which are dead)	Same	Better
BA	6	5 (4)	1	
VA	1		1	
Total	7	5 (4)	2	0

cluded and the flow in the BA was reversed. The aneurysm continued to thrombose, resulting in occlusion of the BA branches, which led to severe brain stem ischemia. Life support was discontinued. Patient 10 had a similar aneurysm and also presented with severe brain stem compression. During placement of endovascular stent complete thrombosis of stent occurred, despite administration of plavix and fragmin resulting in bi-occipital and cerebellar infarctions. Life-support was discontinued. In 2 patients autopsy was not allowed so the exact cause of death could not be determined.

Table 11.11. gives an overview of the outcome of all patients classified by pre-operative Rankin Grade. Of the 33 patients without pre-operative disability, 22 achieved a similar or better post-operative Rankin Grade. In 26 patients (62%) overall outcome was the same as or better than pre-operatively. Nineteen patients were operated upon because of an unruptured aneurysm (see Table 11.12.). In this group 10 patients (53%) were without disability (Rankin Scales 0 and 1) after surgery. However, six patients (32%) died (cases 2, 6, 8, 9, and 28). Twenty-three patients had had a subarachnoid hemorrhage before surgery (see Table 11.13.). Seventeen of these (74%) were without disability (Rankin Scales 0&1) after surgery. One patient died (case 10; see paragraph on post-operative deaths). Of the 35 patients, who had a giant anterior circulation aneurysm (see Table 11.14.), 24 patients (69%) had the same or better post-operative Rankin Grade, 11 got worse (31%), of which 3 died (8.6% of 35 patients). Seven patients had a giant posterior circulation aneurysm (see Table 11.15.). Of these 5 had a worse post-operative Rankin Grade (71%), 4 of which died.

Discussion

Ideally, the best treatment for these aneurysms would be a complete exclusion of the aneurysm from the circulation, in order to prevent a subarachnoid hemorrhage, or rebleeding, combined with a decrease in mass-effect. If direct clipping or endovascular coiling of the aneurysm is considered impossible, occlusion of the parent vessel would be the best way to achieve that goal. However, there is a group of patients who will not tolerate parent vessel occlusion, depending on the location of the aneurysm, the size of the aneurysm, and the (leptomeningeal or other) collaterals.

Aside from the obvious pan-vessel angiography, MRI-, and CT-scans, which are performed in order to obtain the necessary 3D anatomical information, when parent vessel occlusion is considered, there should also be an assessment of the patient's tolerance of vessel occlusion. In our opinion, an endovascular balloon occlusion test (BTO) prior to bypass surgery is a valid solution.[93, 94] Apart from the angiographic and clinical observations during the BTO,[316] transcranial Doppler (TCD) flow velocity measurement can be helpful, especially in the management of posterior circulation aneurysms.[274]

Table 11.16. Intra-operative Flow measurements by Indication

Surgical procedure by indication		Nr of patients	Mean intra-operative flow ml/min ± 1SD (range)	
Bypass procedure	Cases		During temporary occlusion of parent vessel	At the end of the operation
ICA – A2 for AComA aneurysm				
- Without A1 occlusion	Case 1,2	2	32.5 (25-40)	19.5 (14-25)
- With A1 occlusion	Case 3	1	40	55
ICA – M1/M2 for ICA top aneurysm				
- Without M1 occlusion	Cases 11-14	4	61.3 ± 13.2 (50-80)	9.3 ± 14.1 (0-30)
ICA/M1 – M1/M2/M3 for M1/2 aneurysm				
- Without M1 occlusion	Cases 16,18,19(2x),24,26,32,36,37,39,40(2x)	10	41.7 ± 13.8 (20-60)	22.0 ± 11.6 (8-44)
- With M1 occlusion	Cases 15,17,21,22,23,25,27,30,33,35,38	11	46.2 ± 21.8 (22-100)	44.9 ± 14.0 (18-65)
Posterior Circulation				
ICA – P2 for BA-top aneurysm	Case 6 (temporary VA occlusion) Case 7 (temporary BA top occlusion)	2	25 (20-30)	2 (0-4)
ICA – SCA for BA-SCA aneurysm	Case 5 (temporary BA trunk occlusion)	1	65	12
ICA – SCA for BA-trunk aneurysm	Case 8 (occlusion of BA trunk)	1	35	41
ICA – P2 for VA-BA junction aneurysm	Cases 9 (occlusion of VA)	1	70	70

Intra-operative decision to make a bypass

Sometimes, even with all the information gathered with the above mentioned techniques, it will be hard to determine what will be the best therapeutic course. In such cases we would prefer to see intra-operatively if it is feasible to directly clip the aneurysm with preservation of the parent vessel. The decision to make a bypass is then made upon the intra-operative observation that the aneurysm cannot be clipped safely without (temporarily) occluding the parent vessel. Those patients, in whom a bypass was not deemed necessary, were not included in this study. In 12 cases it was possible to directly clip the aneurysm only under the protection of the before created IC-IC bypass (see Table 11.2.).

Table 11.17. Intraoperative Flowmeasurements by occluded artery

Bypass procedure	Occluded vessel	Nr of patients	Mean intra-operative flow during occlusion ml/min ± 1SD (range)
ICA – A2	A1	3	35 ± 8.7 (25-40)
ICA/M1 – M1/M2/M3	M1	27	47.4 ± 17.8 (20-100)
ICA – P2/SCA	VA/BA	5	44 ± 22.2 (20-70)

Intra-operative Flow through the bypass during temporary vessel occlusion

Depending on the location of the aneurysm and the proximal and distal anastomoses of the bypass, a certain flow can be expected through the bypass. We have summarized the intra-operative bypass flows in Table 11.16. Of course, the flow through the bypass at the end of the operation was also very much depending on whether the parent vessel had been occluded or not. However, in those cases where the M1/2 was temporarily occluded and a bypass was created from the intracranial ICA or the very proximal M1, the average flow through the bypass was observed to be 47.4 ± 17.8 ml/min (see Table 11.17.). These values are slightly lower than mentioned in the literature (expected flow through the M1 between 50-80 ml/min),[104] which may partly be explained by the increased resistance of the bypass due to its several curves. We did not directly measure the flow through the parent vessel, as this would expose that vessel to additional manipulation and would be for scientific purposes only. Also, that information would not have changed our management. Instead, we used only the direct flow measurements through the bypass, which was easy to achieve by placing the probe around the part of the bypass which was located most superficially. If the flow during temporary parent vessel occlusion was much lower than expected, in these cases below 25 ml/min, all anastomoses were evaluated. In all cases the ELANA anastomoses were found to be perfectly in order and the conventionally sutured anastomoses was found to be narrowed by misplaced sutures. Those anastomoses were remade. For the 3 cases in which the A1 was temporarily occluded a similar management was used. Average flow through the bypass was 35 ± 8.7 ml/min which is also slightly lower than expected (expected A1 flow between 40-60 ml/min).[104]

Posterior Circulation Aneurysm Management

A different type of management was used for the 7 cases with a VBA or basilar aneurysm. As complete extraction of the aneurysm out of the circulation was considered impossible (to avoid brain stem ischemia),[89-92] bypass surgery with flow reversal by occlusion of the BA or VA was the treatment of choice, in order to induce thrombosis of the aneurysm. In 5 cases (cases 5, 6, 8, 9, 10) the PComAs were either very small or absent and the bypass was made to ensure sufficient blood flow in the complete upper basilar region after BA or VA occlusion. Upon temporary occlusion the flow to the upper BA region was observed to be 20 to 70 ml/min (average 44 ± 22.2 ml/min). Despite this flow, permanent occlusion was not performed in 3 cases (cases 5, 6, 10). In these cases, unfortunately, cases 6 and 10 died before permanent occlusion could take place. In case 5 the bypass was found to be occluded post-operatively, so permanent occlusion was considered too dangerous. Permanent occlusion was performed in cases 8, 9, and 42.

Case 8 died because of a thromboembolic complication which has been extensively described elsewhere.[274] In case 9 the aneurysm was indeed induced to thrombose. However, this process also extended to the numerous brain stem branches resulting in ischemia. As case 42 suffered a VA aneurysm at the PICA segment, her case was quite a different matter. After bypass surgery to the PICA, the PICA was occluded distally of the aneurysm. Several days after surgery, the aneurysm was coiled completely; with excellent result.

Timing of parent vessel occlusion

We found it quite difficult to decide at what moment to occlude the parent vessel. It is rather unsatisfactory to find the bypass to be occluded after several days, even though the patient does not have any symptoms. It is, of course, a tragedy if the bypass occludes and causes a stroke. In many cases, we therefore chose not to permanently occlude the parent vessel intra-operatively, but we waited and observed whether the bypass would remain patent. If the bypass occluded, the brain would still have its normal blood supply through the parent artery. However, that leaves the risk; in 4 cases the bypass was found to be occluded and had to be remade (cases 13, 15, 18, 23). After that the aneurysm was clipped, coiled, or the parent vessel occluded; with excellent result.

In total, 9 bypasses were made after which no coiling, clipping or parent vessel occlusion was performed (cases 2, 5, 6, 7, 10, 12, 29, 31, 40). Cases 5, 6, and 10 have been mentioned above. In case 7 no further interventions were performed after multiple complications (Rankin 5). Case 2 died after a rebleed. Case 12, who had an ICA bifurcation aneurysm, received another bypass 1 year after the first bypass procedure. The first bypass (ICA-M3) was observed to have a nice flow (28 ml/min). After the second bypass (A1-M2 with 38 ml/min) the ICA was occluded with excellent result. Case 31 was lost to follow-up. Case 29 had a spontaneous thrombosis of the aneurysm with excellent result. Case 40 had an aneurysm that could not be coiled or otherwise excluded after his bypass because of multiple small MCA sidebranches originating from aneurysm. However, she also had an excellent outcome. Considering the clinical outcome of these patients we think that our relatively conservative management concerning occlusion in these cases may be justified. However, in case 2 it would certainly have been better if we would have taken the aneurysm out of the circulation earlier.

Overall flap retrieval rate

As mentioned before, the ELANA technique was 100% successful in making anastomoses. Also, no ELANA related complications were observed. However, we did not succeed in retrieving every flap of arterial wall out of the anastomosis (overall flap retrieval rate of 84%, see table 8). From our laboratory experiments (unpublished) we know that the flap, if not retrieved using the ELANA catheter, will be pushed against the inside of the wall of the graft in case of an inflow anastomosis, or against the inside of the wall of the recipient artery in case of an outflow anastomosis. In either case, the flap will become continuous with the wall, and a new

Table 11.18. Retrieval of Flaps and Outcome

Flap category	Nr of anastomoses (% of total ELANA anastomoses)	Postoperative modified Rankin Grade		
		Worse (% of category)	Same (% of category)	Better (% of category)
Successful connection, catheter flap retrieval, anastomosis used for bypass.	50 (82%)	9 (18%)	22 (44%)	19 (38%)
Successful connection, no catheter flap retrieval, no manual flap retrieval, anastomosis discontinued.	2 (3%)		1 **	1 ***
Successful connection, no catheter flap retrieval, no manual flap retrieval, anastomosis used for bypass.	9 (15%)	2 (22 %)*	3 (33%)	4 (45%)
Unsuccessful connection, No retrograde blood flow	0			
Total ELANA anastomoses	61			

* (case 6; pt died cause unknown, case 36 hemiparesis due to postoperative cerebral edema)
** (Case 19; continued with a conventional anastomosis to the STA)
*** (Case 15; continued with a conventional anastomosis to a cortical media branch)

endothelial lining will cover both the flap and the inside of the anastomosis. The groups are too small and the procedures too varied to find any significant differences in flow between the anastmoses with complete flap retrieval and those without. However, the average maximum measured flow (maximum of during temporary occlusion and at end of operation) through bypasses which contained one or more ELANA anastomoses without complete flap retrieval was 40.9 ml/min (cases 6, 11, 15, 22, 23, 35, 36), so we know that such anastomoses do not necessarily form a large flow obstacle (no flow measurements in cases 10, 14, 15, 41).

Lastly, we looked at the clinical consequences of non-successful flap retrieval in all 9 patients (see Table 11.18.). Two patients died (case 6; cause unknown, autopsy not allowed, and case 10; endovascular stent complication with fatal infarctions). Seven patients achieved the same or better post-operative Rankin score. Of these, case 41 had a rebleed and came out moderately severe disabled (Rankin score 4). The other eight had an excellent outcome. Of course we cannot exclude the possibility of the unsuccessful flap retrieval being the cause of death in case 6. However, pre-operatively this patient was severely disabled (Rankin Score 5) with a quadriparesis, dysarthria, and a left NIII palsy due to the mass-effect of a giant BA top aneurysm. Directly post-operative clinical status was similar to pre-operative and she lived for 75 days before dying. If the unsuccessful flap retrieval would have caused any problems we would have expected them directly after surgery. So it is much more likely that she just succumbed to her severe clinical state.

Variation in ELANA suturing technique

As mentioned in the patients and methods we used three different suturing techniques for attaching the graft onto the wall of the recipient vessel. The main difference between the side-branch assisted technique with the current advanced ELANA technique is, obviously, the artificial side-branch. Theorethically, this side-branch can cause two different problems; 1. During the laser procedure the location and the direction of the side-branch could cause a mis-positioning of the laser catheter, causing a non-successful retrieval of the flap. As all three anastomoses were completely successful, including successful flap retrieval, this problem did not occur. Secondly, after the connection of the bypass the side-branch was occluded, causing a part which might have facilitated the development of thrombi. This would then be reflected in ischemic complications in the regions supplied by the bypass. All three cases (3, 18, 28) were without neurological deficits directly post-operatively. Case 28 died after a rebleed two weeks after surgery. The other two had excellent outcome, so we did not observe any ischemic complications.

The main reason to change the suturing technique to the conventional ELANA technique was the ease of use of the parts of the bypass graft and the very clear overview of the location of the platinum ring while attaching it onto the wall of the recipient artery. Insertion of the catheter was also easier as the open end of the bypass graft can be moved freely to accommodate the laser catheter without extensive manipulation of the end of the graft which was attached to the recipient artery. Theorethically, the conventional ELANA technique also has some problems. As the end of the graft is not everted from inside out around the platinum ring but attached directly to the outside of the platinum ring, the inside of the anastomosis is slightly wider than when the other techniques are used. This would give the tip of the laser catheter slightly more space to move to a non-centrated position. We considered this a minor problem, as our experiments in the laboratory showed excellent results with this technique. However, the possibility of off-positioning the laser catheter may account for the 80% flap retrieval rate (no flap in cases 6, 14, 15, 19, 36, 41).

Secondly, the way of attaching the graft onto the ring and the wall of the recipient artery is more prone to leakages. Indeed, quite often an extra stitch had to be placed after the laser procedure was completed to successfully counter some small leaks. In these cases, we found the ultrasound flow meter to be extra helpful in avoiding narrowing the anastomosis site. In total the conventional ELANA technique was used for 36 anastomoses with a 100% successful connection rate. One patient (case 6) died; probably not from the unsuccessful retrieval of the flap (see the paragraph on overall flap retrieval). In cases 15 and 19 the ELANA anastomosis was discontinued because of the unsuccessful flap retrieval. At that time we were still unsure about the consequences of unsuccessful flap retrieval. Both patients had an excellent outcome. In cases 14 and 41 the anastomoses were used for a prophylactic bypass. The bypass made in case

14 was occluded on purpose with hemoclips after the aneurysm had successfully been clipped, with excellent outcome. Case 41 also had an excellent outcome.

We switched to the advanced ELANA technique, which is the synthesis of both the side-branch assisted and the conventional ELANA technique. For this technique the bypass graft was cut in two parts. Special care was taken for the identification of the inflow and the outflow ends of the graft. The anastomosis end of the graft was then everted over the platinum ring, in a similar way as in the side-branch assisted technique. This end was then connected to the recipient artery, leaving the open end free to be manipulated (within certain limits, of course) during the laser procedure. The advantages are now obvious, as there should be less leakages, and more guidance of the laser catheter to a centered position within the platinum ring from the everted graft. With this advanced ELANA technique 22 anastomoses have been made with a 100% successful connection rate. In 8 anastamoses (5 patients) no flap was retrieved. All patients except case 10 had an excellent outcome. Case 10 died because of severe endovascular stent thrombosis.

Patency of the ELANA anastomoses

In 7 cases the bypass was found to be occluded and a new bypass was made (cases 13, 15, 18, 19, 23, 28, 40). If the first bypass was completely occluded (cases 15, 19, 40), a new bypass was made with excellent outcome in all three cases. However, it is very interesting to note that if the bypass was only partially occluded, this occlusion was found either at the distal conventional anastomosis (cases 18, 23, 28) or in the middle of the bypass (case 13). In all 4 cases the ELANA anastomoses seemed to be the only remaining non-occluded part, which could then be used for the creation of the new bypass. All cases had excellent outcome, except case 28 who died of a rebleed.

Clinical Outcome

Despite the various techniques which were available to us, we found this group of patients very difficult to treat. The high complication rate (see tables 11.6. to 11.9.) and mortality (see table 11.10.) urges us to stay modest. In a recent meta-analysis, Raaymakers et al found 7.4% mortality and 26,9 morbidity for giant anterior circulation aneurysms and 9.6% mortality and 37,9 morbidity for giant posterior circulation aneurysms, stating that the actual mortality and morbidity rates may even be higher than that.[230] We found it encouraging that in 26 of our patients (61.9%, see table 11.11.) we “did not do worse”. However, that still leaves 16 patients (38.1%) who had a severe outcome, 7 of whom died from various causes.

Conclusions

We conclude that the ELANA technique is a viable and safe technique. We found it to be a reliable tool in the treatment of these giant or giant fusiform cerebral aneurysms. Despite the different surgical and endovascular tools available us, this group of patients remains very difficult to treat.

Acknowledgements

We would like to thank H.J. Mansvelt Beck, A. van der Zwan, and R.M. Verdaasdonk, together with his group, for their support in the experimental animal laboratory and in the clinical settings.

Part V

Discussion and Conclusions

Chapter 12

Discussion

Discussion

As described in the preface, the ELANA technique is an arterial anastomosis technique, which allows for a complete end-to-side anastomosis to a cerebral artery without occluding that recipient artery. First a graft with a platinum ring in its distal end is stitched onto the wall of the recipient. Then a laser catheter is inserted inside the graft so that the tip touches the wall of the recipient artery within the platinum ring. Vacuum suction is activated within the laser catheter, ensuring a firm fixation of the laser fibres to the wall of the recipient artery. When the laser is activated, a circular cut is ablated in the wall, effectively creating the anastomosis. Upon retraction of the laser catheter, the punched-out portion of arterial wall is also withdrawn with the catheter because of the continued vacuum suction. Attaching the free end of the graft with another graft will complete the bypass procedure.

In this thesis we have addressed the applicability of the ELANA technique in experimental and clinical settings. In this chapter we will discuss the various aspects of this applicability in more detail. The first part concerns the technical aspects of the technique. We will then discuss the applicability of the vacuum suction in a controlled experimental setup. A part is devoted to discussion of the application of the ELANA technique in experimental animals and its re-endothelialization. At last we will discuss the application of the technique in patients.

End-to-Side aspects

As mentioned before, the ELANA technique allows for the creation of an end-to-side intracranial anastomosis. There are quite some situations where a surgeon would prefer an end-to-end anastomosis over an end-to-side anastomosis. These situations usually include the excision of a diseased part of the original blood vessel, and then reconstructing the excised part using an interposed graft. The ends of the graft are then connected to the stumps of the original artery using two end-to-end anastomoses. This will then recreate the "normal" situation. However, the main disadvantage is the necessecity of temporary occlusion of the artery. Also, assessment of the major arteries of the brain usually means working in a very deep and narrow operation space. This can make it very difficult to make end-to-end anastomoses, as the surgeon needs to access all sides of the original artery which may be difficult to assess. Also, it can be hard to allow for any discrepancies in size between the interposed graft and the stumps of the original artery.

However, such end-to-end anastomoses can not be created using the ELANA technique. The main advantage of the end-to-side ELANA anastomoses is that the original artery remains in situ and is only minimally manipulated. Even though this makes it impossible to exactly recreate the "normal" situation, the latter might actually be a disadvantage when working in a deep and narrow operation area and where the excised diseased artery had a very close relationship with vital structures like the optic nerve, or the brainstem. Indeed, the ELANA technique then

Table 12.1. Various EC-IC bypass procedures

Bypass procedure	Low Flow	Intermediate Flow	High Flow
Flow (ml/min)	15 - 35	35 - 80	80 - 250
Donor Artery	STA OA	STA OA	ECA CCA
Graft	None	RA	SVG RA EpigA
Recipient Artery	MCA M3 cx ACA A3 cx PCA P3 cx SCA AICA PICA	MCA M2-3 ACA A2-3 PCA P2-3	MCA M1 ACA A1 PCA P1-2 ICA bifurc

allows for an anastomosis to a safer part of the artery in the target area which is large enough to receive the graft and the platinum ring. Only eight deep sutures on the lateral sides of the recipient artery are needed to attach the ring (with the graft) onto the recipient artery. These stitches are easier to place than the stitches at the posterior side of an end-to-end anastomosis. Also, small discrepancies in size between the graft and the recipient are smoothed out because of the platinum ring in the end of the graft. It may even be so that if the graft is well connected to the ring, and the ring is well attached to the wall of the recipient, there might be less risk of occlusion of the anastomosis as compared to the anastomosis of a large graft which is connected in an end-to-end way to a smaller recipient.

Non-occlusive and High Flow Aspects

High Flow capacity of a bypass and a non-occlusive anastomosis technique are closely related to each other. Whether a bypass has high flow capacity is dependent on the choice of donor artery, graft, recipient artery, and the demand of the flow region supplied by the bypass (see Table 12.1.). Therefore, the choice of bypass is also depending on the indication. We will discuss the different indications later on, especially as the indications for cerebral ischemia have not yet been well identified. However, for aneurysm surgery, the bypass should carry approximately the same amount of flow as the original vessel which is to be bypassed.[140] Therefore, depending on the site of the aneurysm, a bypass should be chosen according to the amount of flow through the parent vessel of the aneurysm. Unfortunately, this is not always possible. However, for example, in case of a giant partially thrombosed ICA bifurcation aneurysm, an ECA-M1 bypass with a SVG would be a logical choice. The parent vessel, the ICA, usually carries a very high flow (200 ml/min). The supplied area of the brain also has a high demand of flow. Therefore, choosing a large donor artery (ECA or CCA), a suitable graft (SVG, or RA), and a large recipient artery (M1 or A1), would allow for a really high flow bypass (200 ml/min).[140]

An alternative would be to excise the aneurysm, and to interpose a graft between the stumps of the parent vessel.[248] This would mean that the parent vessel would have to be occluded for a certain amount of time, during which the supplied brain tissue would be derived of blood flow with the risk of ischemia. Upon reconnection, that same tissue would immediately be exposed to a high blood flow, possibly causing local hyperperfusion as sometimes seen after EC-IC by-pass surgery in Moya-Moya disease and in carotid endarterectomy procedures.[112, 184, 270, 308, 350]

Using the ELANA technique, the temporary vessel occlusion during the anastomosis procedure has been removed. This allows the surgeon to create bypasses to arteries otherwise inaccessible. Of course, the major arteries of the brain pose the biggest risk for ischemia during temporary vessel occlusion.[288] The ELANA technique was developed especially to be able to create anastomoses to the major arteries in a non-occlusive way. A similar non-occlusive technique has earlier (1964) been described in its experimental stage by Yahr and Strully.[341] A donor vessel is glued in a side-to-side fashion to a stained recipient artery using 2-methyl-cyanacrylate (glue). The common wall thus created is exposed by opening the end of the donor vessel on a bias. Copper is applied carefully to the inner surface of the donor vessel to facilitate laser ablation by a neodymium laser. However, we could not find any clinical studies using this technique, so we presume that it has never been applied on patients.

Laser-Assisted aspects

Wavelength ("Color")

Laser light has one specific color (monochromatic) and can therefore be used to selectively damage tissue (particles) of a specified color. The wavelength or color of the laser light is related to the depth of the penetration of the light into the tissue. At first, the light will be scattered. Consequently, the light will be absorbed by pigments like melanin and hemoglobine in case of visual and near-infrared light. Mid- and far-infrared light will predominantly be absorbed by tissue-water, while UV light is absorbed by tissue-proteins. The Excimer laser produces an ultraviolet laser beam at a wavelength of 308 nanometer. The light is absorbed in a 50 micrometer layer of tissue, turning it instantly to explosive water vapor, with related mechanical effects. This provides a clean cutting of tissue, with minimal thermal effects. After the laser beam has ablated the wall of the recipient artery, the ultraviolet laser light is mostly absorbed by the bloodstream. Therefore, the Excimer laser beam is ideal for the ablation of a vessel wall, without immediate danger to the opposite wall.

Concentrated light beam and delivery system

Laser light remains concentrated in a small beam over a long distance so using small optical instruments, it is possible to focus light to a spot smaller than 100 micrometer without making contact with the target. The laser light can also be coupled into small silica fibres (optical fibres) so every site in the human body is accessible. The ELANA laser catheter was constructed to be able to deliver the laser light to an anastomosis site more than 3 meters distance from the apparatus (see Figure 12.1. and 12.2.). The main disadvantage of using a bundle of 180 optical

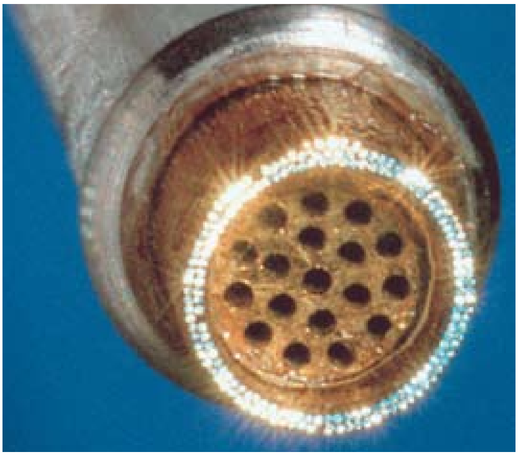

Figure 12.1.
The ELANA catheter. A bundle of 180 small fibers enabled the configuration of a circle with two rows of laser fibers. To prevent damage to the fibers, the laser beam is not fully focussed to the bundle, resulting in a high coupling energy loss of 80 - 90%.

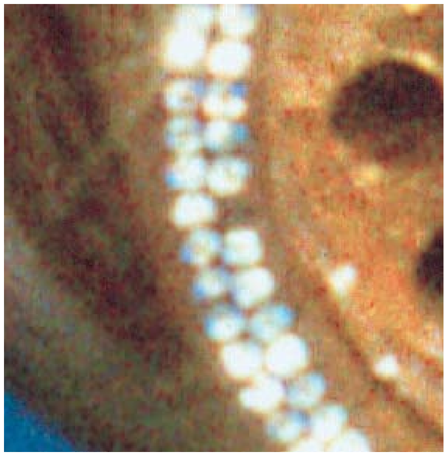

Figure 12.2.
Close-up of Figure 12.1. The laser fibers can clearly be distinguished. Even if one fiber is damaged, the second rows of fibers will insure complete punching of the to-be-ablated portion of arterial wall.

fibres in the ELANA catheter is the large amount of energy loss. Usually, only 10 to 20% of the input energy is available at the catheter tip. However, as this is more than enough for the laser procedure, a simple energy feedback system in the laser apparatus will ensure that there is sufficient input energy with a consistent output energy level before proceeding with the laser procedure.

Puls length and puls frequency

There is a clear distinction between laser systems which generate light continuously, “continuous laser devices”, and laser devices which generate short pulses of laser light, “pulsed laser devices”. Using continuous laser devices will gradually heat the tissue by exposing the tissue to laser light for a period of seconds. Pulsed laser devices, however, generate laser light which is so intense that within microseconds ablative temperatures are being obtained in the tissue. The pulse length is in the range of microseconds down to nanoseconds. The laser pulses can be generated shortly after each other with frequencies of tens up to thousands pulses per second (pulse frequency). The Excimer laser that we use delivers pulses of around100 ns at a frequency of 40 Hz with energies up to 100 mJ. This ensures very focal ablation of the vessel wall. The Excimer Laser was introduced our hospital in 1992 when Tulleken also reported on the results of the Nd:YAG laser. The main advantage of the Excimer laser compared with the Nd:YAG laser is that no noticable heat is produced, minimizing damage to the surrounding tissue. This was first confirmed in experimental settings by the clinical physics department in our hospital.

Table 12.2. Various ELANA suturing techniques

No. 1. Sidebranch-assisted	No. 2. Conventional suturing	No.3. Advanced suturing
• Ring attached into the end of the complete graft. • Graft with ring attached to recipient. • Side-branch created on the side of the graft. • Laser catheter inserted into side-branch.	• Graft cut in half. • Ring attached to the wall of the recipient. • Graft attached to the recipient using the ring as guide. • Laser catheter inserted into open end of cut graft.	• Graft cut in half. • Ring attached into the end of the cut graft. • Graft with ring attached to recipient. • Laser catheter inserted into open end of cut graft.
• Vacuum suction • Laser procedure	• Vacuum suction • Laser procedure	• Vacuum suction • Laser procedure

Platinum Ring

The ELANA technique involves a platinum ring. This ring was introduced in 1996 when Tulleken published on the "modified Excimer laser-assisted high-flow bypass operation.[304] During the initial experiments without the ring, it was not always possible to remove the portion of arterial wall from within the anastomosis. Many times, this piece stayed attached to the rest of the artery, held in place by two tissue bridges at the lateral sides of the recipient. The most probable cause seemed to be the misalignment of the laser fibres, so that there was less contact of the laser fibres with the lateral parts of the recipient artery. The platinum ring resolved that problem. When attaching this ring, the portion of arterial wall becomes flat, and the laser fibres can all be placed in full contact with the wall of the recipient. Another advantage of the platinum ring is that the diameter of the anastomosis is predefined by the ring. Also, the ring facilitates the correct placement of the laser catheter onto the wall of the recipient artery, within the circumference of the platinum ring. Another advantage is that the ring prevents the laser catheter to damage the opposite wall as the outer diameter of the catheter is larger than the inner diameter of the ring.

Suturing Aspects

At the moment of writing, there are several ways to attach the necessary pieces of the ELANA technique. When Tulleken started his research on minimally-occlusive anastomosis techniques, he published on an end-to-side anastomosis in which ¾ of the graft was sutured onto the wall of the recipient artery.[293] Then the recipient was temporarily occluded, a hole was cut in the wall of the recipient on the anastomosis site, and the remainder of the sutures was completed. Temporary occlusion was less than 5 minutes. For the ELANA technique, the principle of first attaching the graft onto the recipient before creating a hole remains the same. We can now distinguish three forms of ELANA suturing techniques (see Table 12.2.):

The main differences between the Sidebranch-assisted (No. 1) technique and the Conventional suturing technique (No. 2) are that in the latter the graft has been cut in two parts and the laser catheter is inserted into the open end of the cut graft instead into an artificial side-branch.

Also, using a graft which has been cut in two, leaves more room for error in placing the graft in the correct flow direction. Cutting the graft in two needs attention to the direction of flow as incorrect positioning of the venous valves may result in a non-patent bypass. As all surgeons are been aware of this possible problem, this has never occurred in our hospital. After the completion of the two end-to-side anastomoses, the two parts need to be anastomosed using a conventinal end-to-end anastomosis. An extra anastomosis carries its own technical risks. However, for us it also created more flexibility in the construction of the bypass, as it allowes us to exactly cut the bypass at the correct length. It also helps us to prevent bypass kinking as we can cut both ends obliquely and thus create a "cornered" end-to-end anastomosis.[180] This artificial "open kink" is positioned exactly at the entrance of the skull at the trephination site which is the most probable site for kinking, and since the introduction of this procedure we have not encountered any kinking problems.

Using the conventional suturing technique, the platinum ring is attached to the recipient first, instead of fixating it in the end of the graft. The main advantage of this technique is that the surgeon has a clear overview over the recipient artery during the attachment of the platinum ring. When the recipient can be reached only using a deep and narrow space, for instance when accessing the posterior cerebral artery using a frontotemporal approach, attaching the platinum ring first, and after that, attaching the graft to the platinum ring and onto the wall of the recipient is easier controlled than using the sidebranch-assisted technique with a complete graft to the same recipient. This conventional suturing technique has been used for all pig experiments described in chapter 7.

However, attaching the ring and then the graft to the recipient takes more surgical time intracranially. Also, in more experienced hands, the clearer overview of the conventional suturing is not really necessary. Therefore, the advanced suturing technique combines the advantages of the first two suturing techniques. Taking advantage of the cut graft, and fixating the ring in the end of the graft prior to intracranial attachment to the recipient, the advanced technique allows for an easy and relatively fast ELANA suturing technique.

Vacuum Suction aspects

The vacuum suction device within the laser catheter was introduced in 1996 at the same time as the platinum ring. A high-vacuum suction pump is attached to the end of the internal tubing of the laser catheter. After the tip of the catheter has been placed on the wall of the recipient artery within the platinum ring, the vacuum suction is activated, and the laser fibres become firmly attached to the wall. Also, the part of the wall which is located within the circle of laser fibres becomes firmly attached to the small metal grid within the lumen of the catheter, 0,4-0,5 mm from the tip. This small metal grid also helps retrieving the punched-out portion of arterial wall after laser activation. Upon withdrawing of the catheter, this flap stays attached to the metal grid due to the continous vacuum suction. We have elaborated on the different

Table 12.3. ELANA Application in Experimental Animals

Author	Suturing technique	Animals	Grafs	Nr of ELANA	Application rate	Flap rate	Patency rate
Tulleken 1995, 1996[303, 304]	Sidebranch-assisted	Rabbits	Human vein	10	100%	100%	90% (9/10)
Tulleken 1997[306]	Sidebranch-assisted	Rabbits	Human vein	30 (including first 10)	93% (28/30)	?	93% (28/30)
Wolfs 2000[337]	Conventional	Rabbits	Internal jugular vein	14	100%	79% (11/14)	92% (13/14)
Streefkerk	Conventional	Pigs	CCA	28	100%	100%	86% (24/28)

configurations of holes within the small metal grid (see Appendix A). The current configuration is a compromise between best vacuum suction force and ease of production.

Application in Experimental Settings

The first part of this thesis focussed on a good experimental environment to measure the vacuum suction forces. Fortunately, our EPM model proved applicable not only for simple measurements, but also for learning and practicing skills. Several residents and young neurosurgeons have practiced vascular anastomosis techniques on the EPM, managing several anastomoses in one real artery with real intraluminal pressure. However, the increase in learning curve can best be observed in learning the ELANA Technique. We performed a small pilot study with several experienced neurosurgeons and several young neurosurgeons who first learned the technique in the EPM and then switched to living rabbits. Their results in the rabbits were much better than we hoped for. Therefore, in our clinic, ELANA trainees first perform the complete procedure several times on the EPM. Only when sufficient familiarity with the procedure has been obtained, then the ELANA technique is practiced in a living rabbit model. In this way we have tried to compile a training course for the duration of one week. Indeed, it is possible to get acquainted with the ELANA technique during this time. However, to really learn it probably takes 2-4 weeks. We consider this an acceptable learning curve for a novel technique for experienced vascular neurosurgeons, with which it is possible to safely access arteries which are otherwise inaccessible.

Extrapolation of experimental results

To state the obvious, experimental settings should be reproducable, they should deliver consistent results under controlled circumstances. We have defined the variables in the chapter on the EPM v3. If an experimental setup complies with these criteria then the results should be reproducable. These criteria are only possible within an experimental in-vitro setup. Therefore, we performed the vacuum suction studies within a limited in-vitro setup. The main advantage of using this limited in-vitro setup is, of course, the reproducability. It may be difficult to extrapolate the vacuum suction results to regular bloodvessels in an ex-vivo setup (EPM v3), still

Table 12.4. Causes for Unsuccessful Application

Problem Description	Results	Solutions
1. With a graft too large, the inner diameter of the lumen may be too small to allow the laser catheter to pass.	No laser ablation of the recipient wall resulting in unsuccessful anastomosis.	Do not use grafts with an inner diameter of >4.0 mm or atherosclerotic grafts.
2. With a stitch too far within the anastomosis site, extensive wall tension within the platinum ring will disrupt the anastomosis site before completion of the laser activation.	Partial laser ablation of the recipient wall resulting in successful anastomosis, but no flap retrieval.	Carefull placement of the stitches, i.e. partially outside the platinum ring in order to "assemble" more vessel wall without extensive wall tension within the anastomosis site.
3. Without a perpendicular positioning of the catheter onto the vessel wall, not every laser fibre is in contact with the wall.	Partial laser ablation of the recipient wall resulting in successful anastomosis, but no flap retrieval.	Correct placement of the ring onto the wall of the recipient, and correct insertion of the catheter into the graft within the platinum ring, perpendicularly to the recipient.
4. Too long laser activation combined with too much pressure of the catheter tip on the vessel wall will flatten the recipient vessel with danger of burning the posterior wall.	Posterior vessel wall disruption resulting in bleeding.	Laser activation duration should be fixed at 200 pulses. Pressure of the catheter tip onto the recipient should be light so that the vessel retains its morphology.
5. Without an intact vacuum system, the laser fibres are not continously in contact with the vessel wall.	Partial laser ablation of the recipient wall resulting in successful anastomosis, but no flap retrieval.	Preoperative and peroperative function check of the vacuum suction tube and the catheter tip is obligatory.
6. Without an intact laser activation and conducting system, laser ablation of the recipient will not occur.	No laser ablation of the recipient wall resulting in unsuccessful anastomosis.	Preoperative and peroperative function check of the laser activation and conducting system is obligatory.

in a living rabbit, or in a patient. The latex has a much more consistent surface than an ex-vivo bloodvessel. However, in our opinion, the differences between the various small metal grids within the vacuum tubes should also be noticable on living bloodvessels.

Application in rabbits

Successful application of the ELANA technique in rabbits has been amply proven (see Table 12.3.).[303, 304, 306, 337] The first rabbit experiments of the "real" ELANA technique, that is, the technique including the Excimer laser and the platinum ring, were published in 1995. Twenty-five rabbits underwent abdominal aorta bypass surgery with a human vein graft anastomosed to the aorta using two ELANA anastomoses. The first 15 rabbit experiments were used as pilot to develop the "modified" laser-assisted technique (using the Sidebranch-assisted suturing technique, see Table 2.). In the last 10 rabbits, 20 complete ELANA anastomoses were created in which the lumen of the anastomosis had exactly the same diameter as the tip of the laser catheter (100% anastomosis application rate). In all cases the punched-out portion of arterial wall was successfully retrieved from the anastomosis. Due to unknown reasons the bypass occluded in 1 rabbit.

In 1997 Tulleken published again on the appliation in rabbits,[306] however in a larger study, including the above mentioned study. In 2 of the 30 rabbits the anastomosis was unsuccessful. Whether or not a flap was retrieved was not mentioned. Short-term patency rate was 93%. In 2000, a rabbit study was published in which the conventional suturing technique was used. Even though a successful anastomosis was created (100% successful anastomosis rate), in 3 cases (21%) there were no flaps retrieved from the anastomosis. Patency rate, however, was 92%, proving that a remaining flap does not necessarily lead to an obstructed anastomosis. Overall successful anastomosis rate is 95% (42/44) with an unknown flap retrieval rate and a patency rate of 93% (41/44).

To find the reason for the less-than-100%-rates, several factors should be considered (see Table 12.4.). First of all (no 1.), the platinum ring and the graft should correctly be attached onto the wall of the recipient artery. If the graft is attached to the platinum ring first (sidebranch-assisted and advanced suturing techniques), then the graft should not have a diameter larger than 4.0 mm. If the graft is larger, the vessel wall will fold excessively over the platinum ring, effectively decreasing the lumen inside the ring. The same applies for using atherosclerotic grafts. A decreased lumen will cause the catheter to get stuck in the graft without the laser fibres touching the wall of the recipient artery. This way, no successful anastomosis can be obtained. However, if the ring is first attached to the wall of the recipient, and then a very large graft is attached onto the wall using the ring as guide, leakage will occur through the excessive graft folds after the laser procedure. A successful anastomosis can be obtained, and the leakage may be countered with an extra stitch.

One or more stitches which have been placed too far inside the platinum ring will cause a very high tension of the wall of the recipient at the anastomosis site (see Table 12.4. Nr 2.). The recipient wall is never consistently of the same thickness. Therefore, during laser activation, some parts of the vessel wall will have been ablated earlier than other parts. If the anastomosis surface tension forces surpass the vacuum suction forces, the vacuum suction will be lost, and the laser ablation will only partially succeed. Even though the anastomosis may be successful, there will be a high risk of flap retrieval failure.

Another problem may arise if the laser catheter has not been positioned perpendicularly to the wall of the recipient artery (see Table 12.4. Nr 3.). Upon activation of the laser system, only those fibres which are in contact with the vessel wall will ablate a part of the recipient. Even

Table 12.5. Anastomosis Studies with Medial- / Adventitial Exposition to the Blood Stream

Author	Anastomosis technique	Subjects	Anastomosed vessels	Patency rate	Complete re-endothelialization
Eck 1877[98]	Eck's fistula	8 dogs	S2S hepatic vein to inferior caval vein anastomosis	12.5% (7 dogs died, one dog ran away after two months)	No re-endothelialization studied
Yahr & Strully 1964[341]	Laser assisted non-occlusive	Rats or dogs	unknown	unknown	unknown
Tulleken1979, 1988 [293, 296]	Minimally occlusive	20 rats	Left CCA transposed on right CCA	100%	3 weeks
Imer 1996[158]	Minimally occlusive	30 rats	Left CCA transposed on right CCA	93% (28/30)	Within 2 months
Tulleken 1992[301]	Nd:YAG laser assisted	65 rabbits	Left CCA transposed on right CCA (adventitial and partial medial layers removed in 30 rabbits)	65% 95% (with layers removed)	Unknown
Tulleken 1993[305]	Excimer laser assisted with closed tip	6 rabbits	Left CCA transposed on right CCA	100%	Within 6 weeks
Heijmen 1998[139]	Conventional suturing	18 pigs	Left CCA transposed on right CCA (intima-adventitia apposition compared with intima-intima apposition under high flow conditions)	100%	Unknown
Buijsrogge 2002[55]	Conventional suturing	32 pigs	Internal thoracic artery to left anterior descending artery anastomosis (intima-adventitia apposition compared with intima-intima apposition under low flow conditions)	88% (28/32)	Histology only
Wolfs 2000[337]	ELANA	14 rabbits	Jugular vein transposed on abdominal aorta (application under intermediate flow conditions)	92% (13/14)	More or less after 9 days
Streefkerk	ELANA	28 pigs	Left CCA transposed on right CCA (ELANA versus conventional anastomosis under high flow conditions)	86% (24/28)	Within 2 months
Streefkerk	ELANA	4 humans postmortem	4 ELANA anastomoses on the intracranial ICA and 1 ELANA anastomosis on the P1/2	100%	Within 1 month

though this results in a successful connection between the graft and the recipient, there will be a high risk of flap retrieval failure.

Too much pressure on the catheter tip will flatten the wall of the recipient artery (see Table 12.4. Nr 4.). Theorethically, a dangerous situation can occur if the laser is activated and both the anterior and posterior walls of the recipient are ablated. This is only possible of the wall is indeed flattened during the last part of the laser activation, and a high amount of laser pulses is given. Total number of laser pulses should not exceed 200. More important is the correct positioning of the catheter. The flattening of the wall due to excessive catheter pressure can easily be observed in in-vitro practice on the EPM v3. It is therefore very important to practice the ELANA technique in a model first. After a little training, flattening of the wall is easily avoided. In Table 12.4., the last two items (intact vacuum suction system and intact laser activation system) are both technical problems which should be practiced together with a laser physicist. Knowlegde of the vacuum suction system and the laser activation system is easily obtained during a laboratory session. Usually, if there is a problem with either, it should be solved by the laser physicist.

Application in pigs

In this thesis we studied the application and re-endothelialization of the ELANA technique in 28 pigs, and we compared the results with the results of a conventional E2S anastomosis technique. The successful anastomosis rate was 100%, as was the flap rate. However, due to various reasons, two pigs died, and two pigs had symptoms of ischemia, so the bypass patency turned out to be 83%. Comparing these results with conventional anastomoses is difficult, as the bypasses consisted of an ELANA anastomosis, a conventional E2E anastomosis, and a conventional E2S anastomosis. Of course, the bypass patency rate is dependent on the function of all three anastomoses., if one of them fails, the bypass will occlude. We can, however, compare the speed with which the anastomoses are made. Although total anastomosis time for ELANA anastomosis is slightly longer than for conventional anastomosis, the time of surgery which is spend within the operation area is less. Much time is spend on the laser system. However, temporary vessel occlusion time is much more important. The ELANA technique eliminates this period, which is its main advantage.

Re-endothelialization

An overview of anastomosis studies where medial and adventitial layers were exposed to the blood stream is given in Table 12.5. The re-endothelialization studies described in this thesis complement the studies which have been performed before. Apart from the abortive experiments performed by Eck, who described the first non-occlusive anastomosis procedures, all studies show patency rates above 86%. And even this figure, as described in this thesis, is skewed as the non-patent bypasses may have been occluded due to problems with the conventional anastomosis. That is, bypasses, made using only the ELANA technique, may have led to a much better patency. However, such a study would have required more animals. Besides, the main goal was to compare the re-endothelialization of ELANA anastomoses versus conventional anastomoses. This goal has been achieved. The extrapolation of the results obtained from experimental animal studies to the clinical patients situation can be very difficult. Therefore, we were very grateful for the permission of 4 patients' families to study the intracranial ELANA anastomoses in a postmortem situation. The SEM results in these 4 patients indicate that re-endothelialization in humans is not much different from the experimental animal situation. Even though the studied group is very small (4 patients with 5 ELANA anastomoses), it may be safe to state that in the clinical situation the ELANA anastomosis will have been completely re-endothelialized within 1 month. This is in contrast with Carrel's adage that exposition of the adventitial layer is always thrombogenic.

Application in Clinical Settings

The application of the ELANA technique in clinical settings has been shown in several case reports and 6 patients series (see Table 7). Successful application is depending on the correct indication, the local (pathological) anatomy, the correct choice of donor, recipient and graft, and the correct execution of the ELANA technique. The previously discussed chapters mainly focussed on the last part, that is, the correct execution of the ELANA technique. In this part we want to discuss the other factors important for successful clinical application.

Bypass Surgery for Giant Aneurysms and Skull Base Tumors

In general, there are 2 different indications for cerebral bypass surgery. First, a section of blood-vessel has changed pathologically, and needs to be bypassed in order to be able to remove or exclude the pathologic part. The rest of the brain usually has no signs of pathology and can be considered normal. This is the case in intracranial aneurysms, highly vascularized skull base tumors, or tumors encasing a major artery. The technical advancements in the treatment of intracranial aneurysms are proceeding rapidly. Now the neurosurgeon has to "compete" with the endovascular neuroradiologist in the treatment of clippable and coilable aneurysms. In general, the choice of treatment of such aneurysms depends on its parent vessel, neck size, morphology, general size and mass effect, intraluminal partial thrombosis, side-branches, and whether it has ruptured or not. Aneurysms with a large neck size will be more difficult to clip surgically, which is still the gold standard.[169] Coiling of that same aneurysm will also be difficult, however, the use of intraluminal stent placing before coiling has made it possible to also coil or glue large-neck aneurysms.[14, 45, 202] An aneurysm which points in a certain direction, for instance, towards the brain stem, might be very difficult to approach, making surgical clip placement hard. Coiling, or filling the aneurysm with glue might then be more appropriate. However, even with the current high-resolution Computed Tomographic Angiography and Digital Substraction Angiography, the morphology of the aneurysm is still best evaluated intraoperatively.[120] A giant aneurysm may cause neurological deficit due to its size (mass effect). If such a giant aneurysm is partially thrombosed, it will be difficult to place a clip so that the aneurysm is completely excluded from the circulation. Coiling a partially thrombosed aneurysm may initially be successful, however, there is danger of impaction of both the thrombus and the coils, leaving a part of the aneurysm exposed to the blood stream. [159, 166, 193, 198, 239] If a patient has a good clinical grade after a subarachnoidal hemorrhage, most centers have a policy of early surgery. However, for patients in poor grades delayed surgery may be advisable. It is yet unclear whether this counts for endovascular coiling as well. If any vital side-branches arise from the dome of the aneurysm, clipping or coiling may prove fatal as the side-branches will be occluded.[95]

Table 12.6. ELANA Application in Clinical Settings

Author	Nr of patients	Indications	Bypass procedures	Application and flow
Tulleken 1996[304]	25	6 giant ICA aneurysms 2 skull base meningeoma 12 hemodynamic cerebral ischemia	20 STA-intra-cranial ICA 5 ECA-intra-cranial ICA	5 unsuccessful ELANA => conversion to conventional STA-MCA cx
Tulleken 1997[306]	40	15 giant aneurysms 10 skull base tumors 15 hemodynamic cerebral ischemia	Various STA – intra-cranial ICA ECA – intra-cranial ICA	1 spontanous recipient artery dissection due to atherosclerosis. 3 patients without flap retrieval => ELANA not used for permanent bypass. In 2 of these the catheter was faulty. Patency of 92%. Intraop flow of 120 – 190 ml/min
Tulleken1998[299]	1	Giant BA trunk aneurysm	ECA-P1/2	Intraop flow 70 ml/min Postop flow 110 ml/min
Graamans 1998[123]	1	Skull base angiofibroma	ECA –intra-cranial ICA	Intraop flow 150 ml/min Postop flow 170 ml/min
Klijn 1998[179]	15	Hemodynamic cerebral ischemia	OA – intracranial ICA/M1/A1 STA – intracranial ICA/M1/A1	Perioperatively 3 patients with ipsilateral stroke due to non-patent bypass 1 died of myocardial infarction Improvement of CO2 reactivity postoperatively
Tulleken 1999[300]	33	giant aneurysms skull base tumors hemodynamic cerebral ischemia	Various (flow recordings in 33 patients)	ECA-ICA/M1 intraop flow postocclusion 111 ml/min Postop flow 137 ml/min STA/OA – ICA/M1 intraop flow 119 ml/min Postop flow 138 ml/min ECA – P1/2 postop flow 120 ml/min ICA – M2/3 postop flow 45 ml/min ICA – A2 intraop flow 60 ml/min Postop flow 90 ml/min ICA – P1/2 intraop flow 130 ml/min Flap retrieval rate 92% (83/90)
Van der Zwan 2001[313]	34	26 giant aneuryms 8 hemodynamic cerebral ischemia	Various (flow recordings in 34 patients)	See Tulleken[300] 1999
Hendrikse 2003[140]	7	Giant ICA aneurysms	ECA/STA – intra-cranial ICA/A1	Postop bypass flow 199 +/- 72 ml/min
Tulleken[297]	1	Posterior fossa ischemia	Intracranial ICA – P1/2	Intraop flow 35 ml/min
Streefkerk[274]	1	Giant fusiform BA trunk aneurysm	Intracranial ICA – SCA	Intraop flow 40 ml/min
Streefkerk[271]	1	Giant vertebrobasilar aneurysm	ECA – BA	Intraop flow 95 ml/min
Streefkerk	42	Giant intracranial aneurysms (AcomA, BA, ICA, MCA)	Various	82% successful anastomoses Various intraoperative flows (partially Tulleken 1999)

Therefore, there are many reasons why a giant aneurysm may be uncoilable, unclippable. An alternative treatment is to occlude the parent artery with or without a bypass. Creating an EC-IC bypass has been part of the neurosurgical armamentarium since Yasargil made the first extracranial-intracranial bypass in the dog.[342] Usually, an occlusion test of the parent artery is performed prior to surgery in order to test the necessity of the bypass. If a bypass is necessary, unfortunately, it is not possible to treat every patient – who has a giant uncoilable or unclippable aneurysm – with a bypass, as the conventional anastomosis techniques involve the temporary occlusion of the parent vessel. Especially in those patients in whom the results of the test occlusion pointed to a bypass, the temporary occlusion of the parent vessel may cause brain ischemia. Also, as the conventional bypasses usually are connected to second or third generation of branches (M2-3 or A2-3), the amount of flow may not be enough to compensate for the bypassed parent artery.

The ELANA technique addresses these last two points, i.e. it is possible to create a bypass to the major cerebral arteries (ICA, A1, M1, P1) without temporary occlusion of these vessels. This gives the surgeon several options: 1. bypass of the parent artery, occlusion of the parent artery; 2. bypass of the parent artery, temporary occlusion of the parent artery, clipping or excision of the aneurysm, restoration of flow through the parent artery; 3. bypass of the parent artery, coiling of the aneurysm or filling it with glue in a later stage, either with or without occlusion of the parent vessel. A first prospective series of 7 patients with ICA aneurysms and ICA occlusion was published by Hendrikse (see Table 8) with very positive results.[140]

All three options with the ELANA technique have extensively been studied and this thesis discusses 42 patients in chapter 15. Of course, this study could not be performed in a randomized trial as there are no alternatives to the ELANA technique, and it would therefore not be ethical to withhold this treatment to an otherwise untreatable patient. Also, many times, the decision which treatment is best can only be made intraoperatively. For instance, during several operations, where preoperatively we expected to have to use a bypass, the aneurysm could be clipped quite well, and we did not need the ELANA technique. In other cases, the patient was referred to our center for high flow revascularization only after the referring surgeon peroperatively had found the aneurysm to be unclippable.

For giant unclippable and uncoilable aneurysms we found the ELANA technique to be an elegant and safe technique with which we were able to offer otherwise untreatable patients a viable alternative in the form of non-occlusive cerebral revascularization.

Revascularization for Cerebral Ischemia

Secondly, the brain may lack sufficient blood supply, i.e. there is cerebral ischemia. The well-known EC-IC Bypass Study was initiated to perform a prospective randomized trial to compare medical management (aspirin treatment) with combined surgical (STA-MCA bypass) and medical treatment of intracranial vascular occlusions and stenoses. The study failed to confirm the hypothesis that STA-MCA anastomosis in combination with medical treatment was more effective than medical treatment alone in the prevention of stroke or stroke-related deaths. Therefore, the use of STA-MCA anastomosis for this indication declined worldwide.

However, during the last years, the advances in diagnostic methods have made it possible to distinguish a group of patients with “hemodynamic cerebral ischemia”, which may be the group of patients most in need of cerebral revascularization. This group has a proven ICA or MCA occlusion or stenosis and suffers from multiple TIAs or progressive stroke despite optimal medical treatment. On PET scan these patients lack vacular reactivity as the blood vessels are maximally dilated to supply the blood-craving brain with blood. Also the amount of oxygen extracted from the blood by the cerebral tissue is increased (increased OEF). It is this group of patients that should benefit from bypass surgery. Whether this should be low/intermediate flow bypass surgery (using conventional anastomosis techniques to the secondary MCA branches) or high flow (using the ELANA technique) remains to be studied. Using a mathematical flow model, Hillen hypothesized that the small caliber of a third generation branch of the MCA may limit the increase in blood flow that can be derived from conventional STA-MCA bypas.[145] A first prospective case series of 15 patients, selected on approximately the above mentioned criteria, showed improvement of cerebrovascular reactivity after high flow ELANA bypass surgery, however, no control group was available (see Table 12.6.).[180] Application of the ELANA technique in posterior fossa ischemia has been discussed in chapter 9. Revascularization procedures carry a known surgical risk. When considering surgery for cerebral ischemia, this risk should be calculated with the high risk of stroke in a selection of patients with frequent recurrent episodes of cerebral ischemia despite medical treatment.

Currently, a new study on surgery for carotid artery occlusion (COSS) is underway using PET scan and other sophisticated methods as described above.[126] We will have to await the results. Even so, we are positive that, if the results of the COSS are negative, high flow cerebral revascularization using the ELANA technique might have a positive result on cerebral ischemia.

Chapter 13

Conclusions

Conclusions

The aim of this thesis was to investigate the technical and clinical applicability of the ELANA technique in order to analyse the creation of successful non-occlusive intracranial anastomoses. Therefore, we formulated three criteria with which the ELANA technique should comply

1. Anastomoses made with the ELANA technique should be easy to create in experimental settings as well as in clinical settings.

2. Anastomoses made with the ELANA technique should re-endothelialize as well as conventionally sutured anastomoses in experimental settings as well as in clinical settings.

3. The ELANA technique should enable surgeons to create a bypass to otherwise inaccessible cerebral arteries in a safe way.

In chapter 5 we described the development of a suitable in-vivo model in which the ELANA technique can be studied. This model does not only allow for easy study of the ELANA characteristics, but it has now been incorporated as a main training tool in the training courses for ELANA trainees. Although it is not an answer to the first question, it does give a perfect experimental setting to learn the ELANA technique, easying the way for successful clinical application of the ELANA technique.

As the pig study described in chapter 6 allowed for a successful anastomosis rate of 100%, and the IC-IC bypass surgical study described in chapter 11 achieved the same successful anastomosis rate, we think that the first question should be answered positively; Anastomoses made with the ELANA technique are indeed easy to create in experimental as well as in clinical settings. A careful sidenote concerns the retrieval of the flaps. In our clinical series of chapter 11 the total flap retrieval rate was 84%. Despite the theorethical danger of thrombosis, there was no relation between the flap retrieval and clinical outcome.

Concerning the re-endothelialization, both the results of the pig experiments of chapter 6, as well as images obtained from the 4 postmortem cases described in chapter 7 allow for a positive statement; Anastomoses made with the ELANA technique indeed re-endothelialize as well as conventionally sutured anastomoses in experimental settings as well as in clinical settings. The final prove of the re-endothelialization in clinical settings may be very hard to obtain as only postmortem studies will give the final answer. Fortunately, most patients treated with the ELANA technique are still alive.

The possibility of creating a bypass to the major cerebral arteries has been proven in numerous publications.[68, 80, 191, 224, 248, 267] However, in order to safely access the intracranial ICA, M1, A1, and P1, the ELANA technique is quite an instrument, as described in the three case reports (chapters 8-10) and the IC-IC bypass case series (chapter 11). In our opinion, the creation of an intracranial anastomosis to the above mentioned arteries is best performed using the ELANA technique because of its ease of use and its non-occlusive characteristics.

Chapter 14

Future Aspects

Future Aspects

The future of the ELANA technique is very exciting. We think that we are at the start of a new era of bypass surgery, as the methods of revascularization are easier and more safe. At this moment, cerebral revascularization is still the area of high-skilled vascular neurosurgeons. And even these outstanding men and women have to practice for several weeks in in vitro models and in the animal laboratory before being able to start treating patients. Several factors play a role in the general acceptance of cerebral bypass surgery.

Technical Advancements

The standards in the surgical technique are continuously in progress. In the decades after the negative results of the EC-IC Bypass Study, two major techniques have been a breakthrough: the use of the platinum ring, and the use of the excimer laser. Although we have extensively investigated both factors, so that we can treat patients safely, we can expect further refinement and better applicability in these areas.

Suturing Techniques

At this moment, even the Advanced Suturing Technique (see chapter 11) takes some microvascular skills to perform. Also, it is still necessary to manipulate the recipient artery intracranially, as the graft with the platinum ring needs to be attached to it. A minimum of eight sutures are deemed necessary to firmly attach the graft onto the recipient, all within a deep operation space (see chapters 8-11). Currently, a new technique is under development with which it is possible to eliminate these sutures, and, instead, use a fluent solitary movement to attach the graft onto the recipient. Anastomosis time would be shortened to a mere 2 minutes! Initial experiments on rabbits are very promising...

Wall Excision Techniques

The necessity to remove a part of the wall of the recipient artery in non-occlusive anastomosis techniques is obvious. To use an excimer laser for this procedure has been proven to be a good technique, with nice re-endothelialization (see chapters 6 and 7). However, an excimer laser is a very expensive piece of equipment, which needs special maintenance by highly trained people. It will be exciting to see whether a more simple approach can give similar results.

Technical and Clinical Database

We have collected our patient information from the paper patient files. Unfortunately, the contents of these files have only recently been collected in an electronic database. As the information technology progresses, so will our means of collecting data. A standardized form is now under development to collect all technical and clinical data from the bypass procedures in our patients. It is good to know that the other neurosurgical centres in the world, where the ELANA technique is applied (Mannheim - Germany, Helsinki - Finnland, Bern - Zwitserland) or will be applied (New York - United States of America) are very enthousiastic in sharing information on patients and revascularization techniques. For example, our colleagues in Mannheim have used an endoscope, intraoperatively, to search and retrieve flaps, which have not been retrieved during the withdrawal of the laser catheter. An international cooperation on the development of the technique, with the information collected in an international database, will be of benefit to both surgeons and patients.

General Agreement on Indications

Cerebral revascularization has been an acceptable treatment in aneurysm surgery almost since the first EC-IC bypass patient. However, since the negative results of the EC-IC bypass study, the search for a subgroup of patients with symptoms of cerebral ischemia is still continuing (see chapter 2). It will be very interesting to see what the results of the new Carotid Occlusion Surgery (COS) trial will be on “low-flow” bypass surgery for cerebral ischemia.[125, 126] We are convinced that, even if the COS trial will carry a negative result on low-flow bypass surgery, there will still be a place for non-occlusive high-flow revascularization in patients with cerebral ischemia. Further research will be very necessary in this area.

Appendix A

The ELANA Vacuum System

The ELANA vacuum suction system

Abstract

Objective
In order to investigate which configuration of holes in the small metal grid in the tip of the catheter allow for a maximum vacuum suction force, we used a tensile and compression machine to apply forces to a fixated vacuum suction tube with various metal grid configurations.

Materials and Methods
The different vacuum tubes were each in turn placed in the moving part of the tensile and compression machine. The tip was positioned on the latex glove within the hole of the fixation plate. The tensile and compression machine was then calibrated at zero Newton (N). The vacuum suction was then activated (t=0sec). At t=10sec the moving part of the tensile and compression machine displaced the vacuum tube upwards with a speed of 1 mm / min. We then measured the maximum force (N) applied by the vacuum suction at the moment that vacuum suction was lost.

Results
Larger holes in the grid allow for higher vacuum suction force. Less holes along the outside of the grid also significantly enhance the vacuum suction force.

Conclusion
In the process of creating a suitable grid for production, a grid with many holes crowded around the center will give the best results in vacuum suction force.

Introduction

The ELANA technique is a novel technique with which the neurosurgeon is able to create intracranial anastomoses without occluding the recipient artery. This technique has extensively been described elsewhere.[273, 274, 299, 300, 304] In summary, a platinum ring is attached to the wall of the recipient artery. The graft is then stitched to the wall of the recipient artery using the platinum ring as guide. Then the excimer laser catheter is introduced into the graft with the tip touching the wall of the recipient artery inside the platinum ring. The catheter tip consists of two circular layers of laser fibres surrounding a hollow tube with a small metal grid in the tip through which vacuum suction can be applied. When the tip touches the wall of the recipient artery, the vacuum suction is applied and the laser fibres become firmly fixated to the recipient artery. The excimer laser is then activated, and a hole is created in the wall of the recipient artery. Upon retractraction of the catheter, the punched-out flap of arterial wall is also withdrawn from the anastomosis.

In order to investigate which configuration of holes in the small metal grid in the tip of the catheter allow for a maximum vacuum suction force, we used a tensile and compression machine to apply forces to a fixated vacuum suction tube with various metal grid configurations.

Materials and Methods

We sought to standardize as many parts as possible. Therefore we used 8 similar vacuum tubes (see Figure A.1.) with a length of 10 cm and an inner diameter of 2.0 mm with various metal

Grid A
Surface. =-.480 mm^2.

Grid B
Surface.= 0.565 mm^2.

Grid C
Surface.= 0.708 mm^2.

Grid D
Surface. = 0.565 mm^2.

Grid E
Surface. = 0.478 mm^2.

Grid F
Surface. = -0.708 mm^2.

Grid G
Surface. = 0.762 mm^2.

Grid H (similar to grid B, however, twice as thin)
Surface. = 0.565 mm^2.

grids in the tip, at 0.5 mm distance of the end of the tube. For each metal grid (A to H) we calculated the surface of the holes. The configuration of the holes in the metal grid was based on the following assumptions. In order to compare the different surface sizes, grids C,F, and G, having a significantly larger surface, were compared with grid B. Grid B is the grid which is used in our clinically applied catheters. In order to compare a small amount of large holes with more small holes, grids A,E, and G were compared with grids B,C,D,F, and H. Also, a large hole in the center may allow for a larger vacuum suction force, therefore, grids E, and G were compared with grid B. Similarly, many holes along the outside of the grid (grids D, and G) was compared with grid B. Lastly, we compared grid H with grid B, as grid H had a similar configuration as grid B, however the grid was twice as thin.

The vacuum tubes were tested on a standardized piece of latex glove with a size of 10x10 mm. This piece of latex was fixated in a specialized hollow fixation metal. A small metal fixation plate with a hole of 2.6 mm or a hole of 10.0 mm was tightly screwed onto the latex onto the fixation metal using 4 screws. This plate mimicks the platinum ring (inner diameter of 2.6 mm) in the clinical settings. We chose to also use the 10.0 mm fixation plate in order to observe whether the diameter of the "ring" would make a difference. The inside of the hollow fixation metal was filled with water with a pressure of 100 mmHg. This pressure was chosen as an easily reproducable pressure and mimicking the clinical settings. The fixation metal, with the piece of latex, was then fixated within the non-moving part of the tensile and compression machine (Tensile and Compression Testing Machine DY 30/31 MTS Sintech 200 M).

The different vacuum tubes were each in turn placed in the moving part of the tensile and compression machine. The tip was positioned on the latex glove within the hole of the fixation plate. The tensile and compression machine was then calibrated at zero Newton (N). The vacuum suction was then activated (t=0sec). At t=10sec the moving part of the tensile and compression machine displaced the vacuum tube upwards with a speed of 1 mm / min. We then measured the maximum force (N) applied by the vacuum suction at the moment that vacuum suction was lost. That is, at the moment that the maximum distance of displacement was reached with continous contact between the latex and the vacuum tube tip. For every grid 10 measurements were performed on 3 different pieces of latex (4 measurements on pieces 1 and 2, two measurements on piece 3.).

Results

The results of the vacuum suction forces using grids C,F, and G, compared with grid B, are given in Table 1. Using a paired T-test the differences in forces are significant. Grids C,F, and G allow for a significant higher vacuum suction force than grid B.

Table 1. 10 mm fixation plate. Waterpressure between 100 and 102 mmHg.

	Grid			
	C	F	G	B
Newton	0,180	0,188	0,179	0,140
	0,166	0,170	0,158	0,137
	0,233	0,205	0,163	0,166
	0,221	0,213	0,176	0,166
	0,231	0,222	0,179	0,167
	0,228	0,215	0,173	0,156
	0,193	0,181	0,176	0,146
	0,191	0,186	0,179	0,160
	0,190	0,186	0,177	0,157
	0,203	0,194	0,181	0,159
Mean	0,204	0,196	0,174	0,155
SD	0,023	0,017	0,008	0,011

The results of the vacuum suction forces using grids A,E, and G, compared with grid C,D,F, and H, are given in Table 2. Using a paired T-test the differences in forces are significant. Grids A,E, and G allow for a significantly higher vacuum suction force than grid B. However, no significant differences could be found between groups AEG and CDFH. Still, some big holes allow for a higher vacuum suction force than grid B does.

Table 2. 10 mm fixation plate. Waterpressure between 100 and 102 mmHg.

	Grid							
	A	E	G	B	C	D	F	H
Newton	0,193	0,220	0,179	0,140	0,180	0,194	0,188	0,184
	0,164	0,213	0,158	0,137	0,166	0,199	0,170	0,182
	0,211	0,242	0,163	0,166	0,233	0,204	0,205	0,182
	0,200	0,229	0,176	0,166	0,221	0,217	0,213	0,165
	0,206	0,254	0,179	0,167	0,231	0,203	0,222	0,177
	0,195	0,240	0,173	0,156	0,228	0,208	0,215	0,191
	0,184	0,217	0,176	0,146	0,193	0,195	0,181	0,179
	0,173	0,213	0,179	0,160	0,191	0,212	0,186	0,176
	0,186	0,222	0,177	0,157	0,190	0,201	0,186	0,174
	0,181	0,223	0,181	0,159	0,203	0,200	0,194	0,178
Mean	0,189	0,227	0,174	0,155	0,204	0,203	0,196	0,179
SD	0,015	0,014	0,008	0,011	0,023	0,007	0,017	0,007

Comparing a big hole in the center, as in grids E and G, with grid B, also a significantly higher vacuum force can be observed (table 3.)

Table 3. 10 mm fixation plate. Waterpressure between 100 and 102 mmHg.

	Grid		
	E	G	B
Newton	0,220	0,179	0,140
	0,213	0,158	0,137
	0,242	0,163	0,166
	0,229	0,176	0,166
	0,254	0,179	0,167
	0,240	0,173	0,156
	0,217	0,176	0,146
	0,213	0,179	0,160
	0,222	0,177	0,157
	0,223	0,181	0,159
Mean	0,227	0,174	0,155
SD	0,014	0,008	0,011

Comparing the grids without several holes along the outside of the grid, as in grids D and G, with grid B, which has the holes evenly distributed over the grid, a significantly higher vacuum force can be observed (table 4.)

Table 4. 10 mm fixation plate. Waterpressure between 100 en 102 mmHg.

	Grid		
	D	G	B
Newton	0,194	0,179	0,140
	0,199	0,158	0,137
	0,204	0,163	0,166
	0,217	0,176	0,166
	0,203	0,179	0,167
	0,208	0,173	0,156
	0,195	0,176	0,146
	0,212	0,179	0,160
	0,201	0,177	0,157
	0,200	0,181	0,159
Mean	0,203	0,174	0,155
SD	0,007	0,008	0,011

Conclusion

As described in the results, the ideal grid would have a large hole in the center and several small holes crowded around the center without many holes along the outside of the grid. Unfortunately, such a grid would be expensive and difficult to make. Therefore, we now use a grid similar to grid D. The holes in the center are close to each other, however, they are of the same size (0.1 mm in diameter).

Adendum

At the moment of writing the manufacturing procedure of the small metal grids has changed, leaving these investigations outdated.

Appendix B

Patient Information Tables

Tables

Table 1. The Yasargil modified Hunt & Hess Classification[343]

Grade	Clinical findings
0a	Unruptured aneurysm, no neurological deficit
0bI	Unruptured large or giant aneurysm associated with neurological and mental deficits; I: Normal consciousness, minor neurological deficit
0bII	Unruptured large or giant aneurysm associated with neurological and mental deficits; II: Normal consciousness, moderate neurological deficit
0bIII	Unruptured large or giant aneurysm associated with neurological and mental deficits; III: Somnolent, severe neurological deficits
0bIV	Unruptured large or giant aneurysm associated with neurological and mental deficits; IV: Drowsy, severe neurological deficits
0bV	Unruptured large or giant aneurysm associated with neurological and mental deficits; V: Comatose, severe neurological deficits
Ia	Asymptomatic after subarachnoid hemorrhage
Ib	Alert and oriented, no meningismus, but with focal pronounced neurological deficit after subarachnoid hemorrhage (excluding singular Cranial Nerve III-IV palsies)
IIa	Alert but with headache and meningismus after subarachnoid hemorrhage; No focal neurological deficit
IIb	Alert but with headache and meningismus after subarachnoid hemorrhage; With focal neurological deficit
IIIa	Lethargic, confused, disoriented, combative after subarachnoid hemorrhage; No focal neurological deficit
IIIb	Lethargic, confused, disoriented, combative after subarachnoid hemorrhage; With focal neurological deficit
IV	Semi comatose, responding to pain but not to voice after subarachnoid hemorrhage. Pupils are reactive to light, but patient may show extensor posturing. Although it may be possible in most cases to lateralize neurological deficits, there is no prognostic benefit to assigning "a" and "b" categories to these patients
V	Comatose, maximal dilated nonreactive pupils to light, extensor posturing, no or poor respiratory function, no reaction to pain
U (= Unknown)	Sedated or intubated patients

Table 2. Modified Rankin Scale[33, 317]

Grade	Clinical findings
0	No symptoms at all
1	No significant disability; able to carry out all usual daily routines
2	Slight disability; unable to carry out some previous activities but able to look after affairs without assistance
3	Moderate disability; requiring some help but able to walk without assistance
4	Moderate severe disability; Unable to walk without assistance.
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

Table 3. Patient Information

Case 1.
This 54 year old female suffered from pain in both arms, a balance disturbance to the right side, and dysphasia, which mostly (except for the dysphasia) disappeared within 4 days. Angiography showed an unruptured giant anterior communicating artery aneurysm (Yasargil modified H&H grade 0bI, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal ELANA anastomosis with successful flap retrieval on the A2 segment of the anterior cerebral artery (ICA-A2 bypass). Intraoperative bypass flow was 14 ml/min, which increased to 40 ml/min when the A1 was temporarily occluded. As the aneurysm could successfully be clipped intraoperatively, the bypass was prophylactic. No postoperative complications occurred. Postoperative follow-up was 501 days with a postoperative mRankin grade 1. Postoperative flow measurements were not performed.

Case 2.
This 62 year old female suffered from homonym hemianopsia on the right side. Angiography showed an unruptured giant anterior communicating artery aneurysm (Yasargil modified H&H grade 0bI, preoperative mRankin grade 1). An Y-bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, a first successful distal ELANA anastomosis with successful flap retrieval on the A2 segment of the anterior cerebral artery, and a second distal conventional anastomosis on a cortical branch of the anterior cerebral artery (ICA-Y-A2/Acx). Intraoperative bypass flow was 25 ml/min, no temporary or permanent vessel occlusion was performed. The aneurysm could not successfully be clipped intraoperatively, therefore, the flow through the bypass was competitive with the aneurysm parent vessel. Endovascular aneurysm occlusion was planned postoperatively. Postoperative follow-up was 8 days , after which she succumbed to a subarachnoid hemorrhage (postoperative mRankin grade 6) before endovascular intervention could take place. Postoperative flow measurements were not performed, however, postoperative angiography showed the bypass to be patent.

Case 3.
This 70 year old female suffered from severe headache and vomiting. Angiography showed a ruptured giant anterior communicating artery aneurysm (Yasargil modified H&H grade IIa, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on the A2 segment of the anterior cerebral artery (ICA-A2 bypass). Intraoperative bypass flow was 50 ml/mi, measured after permanent A1 occlusion. No postoperative complications occurred. Postoperative follow-up was 1872 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 4.
This 52 year old male suffered from meningismus and was desoriented. Angiography showed a ruptured giant anterior communicating artery aneurysm (Yasargil modified H&H grade IIb, preoperative mRankin grade 2). An Y-bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a first successful distal conventional anastomosis on the left A2 segment of the anterior cerebral artery, and a second successful distal conventional anastomosis on the right A2 (ICA-Y-A2/A2 bypass). Intraoperative bypass flow was 55 ml/min after one A1 had been permanently occluded. Postoperative meningitis occurred and was successfully countered. Postoperative follow-up was 47 days with a postoperative mRankin grade 3. Postoperative flow measurements were not performed.

Case 5.
This 67 year old male was without symptoms. Angiography showed an unruptured giant basilar artery - superior cerebellar artery aneurysm (Yasargil modified H&H grade 0a, preoperative mRankin grade 0) which had been partially coiled. A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on the superior cerebellar artery (ICA-SCA bypass). Intraoperative bypass flow was 12 ml/min, which increased to 65 ml/min when the basilar artery was temporarily occluded just proximally of the aneurysm, and he superior cerebellar artery. No permanent clipping or occlusion was performed. Temporary postoperative hemiparesis

occurred, and a pneumonia. Postoperative follow-up was 1709 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed as the bypass turned out to be not patent on angiography.

Case 6.
This 47 year old female suffered from dysarthria, left oculomotor palsy, and quadriparesis. Angiography showed an unruptured giant basilar top aneurysm (Yasargil modified H&H grade 0bIII, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis without successful flap retrieval on the intracranial internal carotid artery, and a successful distal ELANA anastomosis, also without successful flap retrieval on the P2 segment of the posterior cerebral artery (ICA-P2 bypass). Intraoperative bypass flow was 4 ml/min, which increased to 30 ml/min when the basilar artery was temporarily occluded just proximally of the aneurysm. No permanent clipping or occlusion was performed, therefore the flow through the bypass was competitive with the flow through the basilar artery. Postoperative follow-up was 75 days, after which the patient died of unknown reasons (postoperative mRankin grade 0). Postoperative flow measurements were not performed.

Case 7.
This 57 year old female suffered from a decreased consciousness with dysarthria. Angiography showed a ruptured giant basilar top aneurysm (Yasargil modified H&H grade IIa, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal ELANA anastomosis with successful flap retrieval on the P2 segment of the posterior cerebral artery (ICA-P2 bypass). No clipping or occlusion was performed, therefore, the flow through the bypass was competitive with the flow through the basilar artery. Intraoperative bypass flow was not measured. Postoperative complications included a hydrocephalus. Postoperative follow-up was 152 days with a postoperative mRankin grade 5. Postoperative flow measurements were not performed.

Case 8. (case report of Chapter 9: Constructing an ICA-SCA bypass)
This 36 year old male suffered a right sided hemiparesis with a central right facial paresis. Also, he had a dysarthria, and eye-movement disorders resulting in diplopia. Angiography showed an unruptured giant basilar trunk aneurysm (Yasargil modified H&H grade 0bII, preoperative mRankin grade 4). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on the superior cerebellar artery (ICA-SCA bypass). Intraoperative bypass flow was 41 ml/min. The basilar artery was permanently clipped just distally from the aneurysm and proximally of the superior cerebellar artery. Postoperative occlusion of the ipsilateral middle cerebral artery occurred 4 days postoperatively (mRankin grade 6). Postoperative flow measurements were not performed, however, postoperative angiography showed the bypass to be patent.

Case 9.
This 57 year old male suffered from quadriplegia, severe dysarthria, and bilateral facial palsy. Angiography showed an unruptured giant vertebrobasilar junction aneurysm (Yasargil modified H&H grade 0bIII, preoperative mRankin grade 5). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal ELANA anastomosis with successful flap retrieval on the P2 segment of the posterior cerebral artery (ICA-P2 bypass). Intraoperative bypass flow was 70 ml/min, after which the dominant vertebral artery was occluded. To counter postoperative hydrocephalus, an external ventricular drain was inserted. Continued thrombosis of the aneurysm caused fatal occlusion of the branches of the basilar artery after 31 days (mRankin grade 6). Postoperative flow measurements were not performed.

Case 10.
This 66 year old male was unconscious due to severe brain stem compression. Angiography showed a ruptured giant vertebrobasilar junction aneurysm (Yasargil modified H&H grade U, preoperative mRankin grade 5). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the M1 segment of the middle cerebral artery, and a successful distal ELANA anastomosis without successful flap retrieval on the P2 segment of the posterior cerebral artery (M1-P2 bypass). Intraoperative bypass flow was 4 ml/min. No permantent clipping or occlusion was performed as endovascular treatment was planned postoperatively. The patient died 16 days later due to an intracerebral hematoma, possibly caused by a rebleed

of the aneurysm. During endovascular treatment a stent was inserted, which completely thrombosed and caused multiple (probably fatal) infarctions. Postoperative flow measurements were not performed.

Case 11.
This 61 year old female suffered from temporary hemiparalysis left with dysarthria. Angiography showed an unruptured giant intracranial internal carotid artery bifurcation aneurysm (Yasargil modified H&H grade 0a, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal ELANA anastomosis without successful flap retrieval on the M2 segment of the middle cerebral artery (ICA-M2 bypass). Intraoperative bypass flow was 6 ml/min, which increased to 55 ml/min when the M1 was temporarily occluded. As the aneurysm could successfully be clipped intraoperatively, the bypass was prophylactic. Postoperative pneumonia occurred. Postoperative follow-up was 580 days with a postoperative mRankin grade 1. Postoperative flow measurements were not performed.

Case 12.
This 45 year old male was without any symptoms. Angiography showed a ruptured giant intracranial internal carotid artery bifurcation aneurysm (Yasargil modified H&H grade Ia, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the A1 segment of the anterior cerebral artery, and a successful distal conventional anastomosis on the M1 segment of the middle cerebral artery (A1-M1 bypass). Intraoperative bypass flow was 30 ml/min, which increased to 80 ml/min when the A1 was temporarily occluded. However, no permanent clipping or occlusion was performed, therefore, there remained a competitive flow through the bypass. No postoperative complications occurred after this operation. A second bypass operation was performed 1 year later, using a successful proximal ELANA anastomosis with successful flap retrieval on the A1 segment of the anterior cerebral artery, and a successful distal ELANA anastomosis with successful flap retrieval on the M2 segment of the middle cerebral artery, resulting in a double barrel bypass (as the first bypass was still patent, however, the aneurysm was still filling with blood) (A1-M1 bypass and A1-M2 bypass). Intraoperative flow through the second byapss was 38 ml/min, after which the internal cartoid artery was occluded in the neck. Postoperatively, the patient suffered a lung embolus, a hemiparesis with facial palsy and dysarthria (all temporary). Postoperative follow-up (after the first bypass) was 1530 days with a postoperative mRankin grade 0. Postoperative flow measurements showed a flow in the first bypass of 28 ml/min.

Case 13.
This 52 year old female suffered from a severe headache with vomitting, meningismus, and several episodes of generalized epileptic seizures. Angiography showed a ruptured giant intracranial internal carotid artery aneurysm (Yasargil modified H&H grade IIa, preoperative mRankin grade 2). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery proximally of the aneurysm, and a successful distal ELANA anastomosis with successful flap retrieval on the M1 segment of the middle cerebral artery (ICA-M1 bypass). Intraoperative bypass flow was 78 ml/min. No permanent clipping or occlusion was performed, therefore, the flow through the bypass was competitive with the flow throught the internal carotid artery. One month after the operation, the bypass was found to be occluded in the middle of the graft. As both ELANA anastomosis sites were still patent, the occluded bypass segment was excised, and a new bypass was created by interposing a graft between both bypass stumps using conventional end-to-end anastomoses. No postoperative complications occurred. As the aneurysm could then be clipped, the bypass was prophylactic. Postoperative follow-up was 78 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 14.
This 36 year old female suffered from a discrete central facial paresis and decreased movement of the right hand. Angiography showed an unruptured giant internal carotid artery - posterior communicating artery aneurysm (Yasargil modified H&H grade 0b1, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis without successful flap retrieval on the intracranial internal carotid artery, and a successful distal ELANA anastomosis with successful flap retrieval on the M1 segment of the middle cerebral artery. The proximal ELANA anastomosis was discontinued and a new conventional anastomosis was made on the external carotid artery in the neck (ECA-M1 bypass). Intraoperative bypass flow was 0 ml/min, which increased to 50 ml/min when the internal carotid artery was temporarily occluded. As the aneurysm could successfully be

clipped intraoperatively, the bypass was prophylactic. Postoperatively, temporary hemiparesis, facial palsy, and dysarthria were observed. No permanent postoperative neurologic deficits were found. Postoperative follow-up was 256 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 15.
This 44 year old male suffered from severe persistent headaches. Angiography showed an unruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade 0b1, preoperative mRankin grade 1). A bypass was created using a successful proximal conventional anastomosis on the external carotid artery in the neck, and a successful distal ELANA anastomosis without successful flap retrieval on the M1 segment of the middle cerebral artery, just distally from the aneurysm. The distal anastomosis was discontinued, and a conventional anastomosis was made with a cortical branch of the middle cerebral artery (M1-Mcx bypass). Intraoperative bypass flow was 10 ml/min. No permanent clipping or occlusion was performed, therefore, the flow through the bypass was competitive with the flow through the internal carotid artery. As angiography still showed filling of the aneurysm, the patient was re-operated after one month. A bypass was created using a successful proximal ELANA anastomosis without successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on the M2 segment of the middle cerebral artery (ICA-M2 bypass). Intraoperative flow through the bypass was 30 ml/min. Postoperatively, the aneurysm was coiled and the internal carotid artery was occluded. Postoperative follow-up was 845 days. Temporary hdysphasia and psychologic deterioration was observed, without permanent deficit (mRankin grade 0). Postoperative flow measurements were not performed, however, the bypass was found to be patent on angiography.

Case 16.
This 47 year old female suffered from slight dysphasia with disorientation in time. Angiography showed an unruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade 0b1, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on the M2 segment of the middle cerebral artery (ICA-M2 bypass). Intraoperative bypass flow was 24 ml/min, which increased to 50 ml/min when the M1 was temporarily occluded proximally from the aneurysm. As the aneurysm could successfully be clipped intraoperatively, the bypass was prophylactic. Postoperatively, temporary hemiparesis, facial palsy, and dysphasia was observed. No permanent neurologic deficits were observed. Postoperative follow-up was 1520 days with a postoperative mRankin grade 2. Postoperative flow measurements were not performed.

Case 17.
This 21 year old male suffered from complex partial epileptic seizures. Angiography showed a ruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade IIIa, preoperative mRankin grade 3). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on the M2 segment of the middle cerebral artery (ICA-M2 bypass). Intraoperative bypass flow was 60 ml/min, after permanent occlusion of the M1 segment, just proximally of the aneurysm. No postoperative complications occurred. Postoperative follow-up was 589 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 18.
This 48 year old female presented with an episode of severe headache. Angiography showed a ruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade Ia, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on cortical branch of the middle cerebral artery (ICA-Mcx bypass). Intraoperative bypass flow was 15 ml/min, which increased to 40 ml/min when the M1 was temporarily occluded. As the bypass occluded at the distal anastomosis before endovascular coiling of the aneurysm could be performed, a new bypass was created after 1 week. The proximal ELANA anastomosis was still open, and the occluded segment of the bypass was removed. A new bypass was created using an interposed graft between the stump of the proximal anastomosis and a new conventional anastomosis on an M3 segment of the middle cerebral artery (ICA-M3 bypass). Intraoperative bypass flow was 44 ml/min. Postoperatively, the aneurysm was

coiled. No postoperative complications occurred. Postoperative follow-up was 956 days (after the first bypass procedure) with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 19.
This 51 year old female presented with an episode of severe headache. Angiography showed a ruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade Ia, preoperative mRankin grade 0). An Y-bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, a first successful distal conventional anastomosis on an M2 segment of the middle cerebral artery, and a second successful distal conventional anastomosis on the other M2 (ICA-Y-M2/M2 bypass). Intraoperative bypass flow was 8 ml/min, which increased to 56 ml/min when the M1 was temporarily occluded. No permanent clipping or occlusion was performed, and the bypass occluded. She was again operated (after 1 year), and a bypass was created using a successful proximal ELANA anastomosis without successful flap retrieval on the intracranial internal carotid artery, and a successful distal ELANA anastomosis with successful flap retrieval on an M2 segment of the middle cerebral artery (ICA-M2 bypass). The proximal ELANA anastomosis was discontinued, and a conventional anastomosis was made with the superficial temporal artery (STA-M1 bypass). As the aneurysm could be clipped only partially intraoperatively, postoperative endovascular coiling was performed. No postoperative complications occurred. Postoperative follow-up was 377 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed, however, angiography showed the second bypass to be patent.

Case 20.
This 10 year old girl was sedated and ventilated. Angiography showed a giant anterior communicating artery aneurysm (Yasargil modified H&H grade U, preoperative mRankin grade 5). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery (ICA-M3 bypass). Intraoperative bypass flow was 4 ml/min, which increased when the M1 was temporarily occluded. As the aneurysm could successfully be extracted, and a successful interposition of a vein graft between the proximal and distal M1 stumps was performed, the bypass was prophylactic. Postoperatively, she suffered from progressive hydrocephalus, which was countered using an external ventricle drain. This was complicated by meningitis. Partial complicated epileptic seizures were successfully countered with carbamazepine treatment. The patient remained with permanent dysphasia and hemiparesis. Postoperative follow-up was 704 days with a postoperative mRankin grade 4. Postoperative flow measurements were not performed.

Case 21.
This 43 year old male presented with an episode of severe headache and meningismus. Angiography showed a ruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade IIa, preoperative mRankin grade 1). An Y-bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, a first successful distal ELANA anastomosis with successful flap retrieval on a M2 segment of the middle cerebral artery, and a second successful distal conventional anastomosis on a M3 segment (ICA-Y-M2/M3 bypass). Intraoperative bypass flow was 65 ml/min, which increased to 100 ml/min after the M1 had been permanently occluded. Postoperatively, a grand mal epileptic seizure occurred once. The patient remained with a permanent hemiparesis, which diminished during later follow-up. Postoperative follow-up was 608 days with a postoperative mRankin grade 2. Postoperative flow measurements were not performed.

Case 22.
This 46 year old female suffered from an episode of severe headache and meningismus. Angiography showed a ruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade IIa, preoperative mRankin grade 0). An Y-bypass was created using a successful proximal ELANA anastomosis without successful flap retrieval on the intracranial internal carotid artery, a first successful distal conventional anastomosis on a M3 segment of the middle cerebral artery, and a second successful distal conventional anastomosis on another M3 (ICA-Y-M3/M3 bypass). Intraoperative bypass flow was 40 ml/min. The aneurysm was partially clipped, as one M3 branch was dependent on retrograde flow through the aneurysm. No postoperative complications occurred. Postoperative follow-up was 12 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 23.
This 55 year old male suffered from an episode of severe headache. Angiography showed a ruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade Ia, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery (ICA-M3 bypass). Intraoperative bypass flow was not measured. However, at the end of the operation the bypass occluded at the distal anastomosis, and the bypass procedure was discontinued. Two-and-a-half weeks later, a new Y-bypass was created using a successful proximal ELANA anastomois without successful flap retrieval on the M1 segment just proximally of the aneurysm, a first successful distal ELANA anastomosis, also without successful flap retrieval on the M2 segment, and a second successful distal conventional anastomosis on a M3 segment of the middle cerebral artery (M1-Y-M2/M3 bypass). The M1 was occluded and the aneurysm was extirpated. Flow through the bypass was 38 ml/min. No postoperative complications occurred. Postoperative follow-up was 20 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 24.
This 57 year old male presented without any symptoms. Angiography showed an unruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade 0a, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery (ICA-M3 bypass). Intraoperative bypass flow was 15 ml/min, which increased to 60 ml/min when the M1 was temporarily occluded. As the aneurysm could successfully be clipped intraoperatively, the bypass was prophylactic. No postoperative complications occurred. Postoperative follow-up was 117 days with a postoperative mRankin grade 0. Postoperative flow through the bypass was 40 ml/min.

Case 25.
This 59 year old female suffered from discrete psychologic deterioration. Angiography showed an unruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade 0a, preoperative mRankin grade 1). An Y-bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, a first successful distal ELANA anastomosis with successful flap retrieval on a M2 segment of the middle cerebral artery, and a second successful distal conventional anastomosis on another M2 segment (ICA-Y-M2/M2 bypass). Intraoperative bypass flow was 60 ml/min (with 35 ml/min through the distal ELANA anastomosed M2, and 25 ml/min through the distal conventionally anastomosed M2). The aneurysm was taken out of the circulation by permanently occluding the M1. Temporary hemiparesis and facial palsy was probably due to the temporary occlusion of the conventionally anastomosed M2 branch. Postoperative meningitis was observed, together with a subdural hematoma. Postoperative follow-up was 328 days with a postoperative mRankin grade 2. Postoperative flow measurements were not performed.

Case 26.
This 35 year old female presented without any symptoms. Angiography showed an unruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade 0a, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery. Intraoperative bypass flow was 15 ml/min, which increased to 35 ml/min when the M1 was temporarily occluded. As the aneurysm could successfully be clipped intraoperatively, the bypass was prophylactic. No postoperative complications occurred. Postoperative follow-up was 10 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed, however, angiography showed the bypass to be patent.

Case 27.
This 70 year old male suffered from headache, vertigo, and tinnitus. Angiography showed an unruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade 0a, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the first segment of the middle cerebral artery (M1) just proximally of the aneurysm, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery. Intraoperative bypass flow was 44 ml/min. The aneurysm was taken out of

the circulation by permanently occluding the M1. Postoperative intracerebral hematoma was observed. Postoperative follow-up was 776 days with a postoperative mRankin grade 1. Postoperative flow measurements were not performed.

Case 28.
This 46 year old male presented without symptoms. Angiography showed an unruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade 0a, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the M1 segment of the middle cerebral artery just proximally of the aneurysm, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery (M1-M3 bypass). Intraoperative bypass flow was 44 ml/min. No permanent clipping or occlusion was performed. Several days postoperatively, the bypass occluded at the distal conventional anastomosis. Three weeks after the first operation a new bypass was constructed using a conventional anastomosis with the proximal ELANA bypass stump, and a new distal conventional anastomosis on a cortical branch of the middle cerebral artery (M1-cx bypass), and the aneurysm was successfully clipped. No intraoperative flow measurements were performed. Initially, the patient had a temporary hemiparesis. However, he recovered without any neurologic deficits. Two weeks postoperatively, he suffered a fatal intracerebral hemorrhage (mRankin grade 6). Postoperative flow measurements were not performed. Autopsy was not allowed.

Case 29.
This 60 year old female presented without symptoms. Angiography showed an unruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade 0a, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M2 segment of the middle cerebral artery. Intraoperative bypass flow was 30 ml/min. Postoperatively, the aneurysm spontaneously thrombosed. The patient suffered a pneumonia, cardial decompensation, resulting in respiratory insufficiency, which was countered effectively. During recovery, she also suffered an episode of transient global amnesia. Postoperative follow-up was 417 days with a postoperative mRankin grade 0. Postoperative flow through the bypass was 32 ml/min.

Case 30.
This 61 year old female presented with an episode of severe headache and meningismus. Angiography showed a ruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade Ia, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M2 segment of the anterior cerebral artery (ICA-M2 bypass). Intraoperative bypass flow was 50 ml/min, which increased to 60 ml/min when the M1 was temporarily occluded, after which the M1 was permanently occluded. Postoperatively, she suffered an epidural hematoma, and a hemiparesis, possibly due to the temporary occlusion during the distal anastomosis procedure. Postoperative follow-up was 30 days with a postoperative mRankin grade 4. Postoperative flow through the bypass was 60 ml/min.

Case 31.
This 45 year old male suffered from a subtle left facial paralysis, and hemiparesis. He also had a discrete dysphasia. Angiography showed a ruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade Ib, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery (ICA-M3 bypass). Intraoperative bypass flow was 18 ml/min. No permanent clipping or occlusion was performed. No postoperative complications occurred. Postoperative follow-up was 19 days with a postoperative mRankin grade 1. Postoperative flow measurements were not performed, however, on angiography, the bypass was observed to be patent.

Case 32.
This 41 year old female presented with severe headache, meningismus, and desorientation. Angiography showed a ruptured giant middle cerebral artery (M1) aneurysm (Yasargil modified H&H grade IIa, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery (ICA-M3 bypass). Intraoperative bypass flow

was 20 ml/min, which increased to 28 ml/min when the M1 was temporarily occluded. As the aneurysm could successfully be clipped intraoperatively, the bypass was prophylactic. Postoperative hydrocephalus was successfully countered. She also suffered a temporary hemiparesis. Postoperative follow-up was 233 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 33.
This 72 year old male presented without symptoms. Angiography showed an unruptured giant middle cerebral artery (M2) aneurysm (Yasargil modified H&H grade 0a, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery (ICA-M3 bypass). Intraoperative bypass flow was 50 ml/min, after which the M2 was occluded just proximally of the aneurysm. Initial temporary hemiparesis improved with resolving of the symptoms. However, the clip on the M2 was insufficient, as it was a temporary hemoclip, allowing for recanalization of the middle cerebral artery, and thus of the aneurysm. The aneurysm was then coiled, resulting in thrombosis of the middle cerebral artery, and later of the complete ipsilateral internal carotid circulation. One week later, he suffered an acute myocardial infarction with possible rupture of a known abdominal aorta aneurysm. No autopsy was allowed. Postoperative follow-up was 22 days with a postoperative mRankin grade 6. Postoperative flow measurements were not performed.

Case 34.
This 44 year old male suffered from an episode of aphasia. Angiography showed a ruptured giant middle cerebral artery (M2) aneurysm (Yasargil modified H&H grade Ia, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery. Intraoperative bypass flow was not measured. The aneurysm was taken out of the circulation by permanently occluding the M2. No postoperative complications occurred, apart from a temporary dysphasia. Postoperative follow-up was 50 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 35.
This 42 year old male presented without any symptoms. Angiography showed a ruptured giant middle cerebral artery (M2) aneurysm (Yasargil modified H&H grade IA, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis without successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on A M3 segment of the middle cerebral artery. Intraoperative bypass flow was 42 ml/min, after which the M2 was permanently occluded. Postoperatively, temporary hemiparesis and dysphasia was observed, together with a single focal epileptic seizure. Postoperative follow-up was 344 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed, however, on angiography, the bypass turned out to be patent.

Case 36.
This 55 year old female suffered from several episodes of generalized epileptic seizures and persistent headache. Angiography showed an unruptured giant middle cerebral artery (M2) aneurysm (Yasargil modified H&H grade 0a, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the M1 segment of the middle cerebral artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery (M1-M3 bypass). Intraoperative bypass flow was 8 ml/min, which increased to 50 ml/min when the M2 was temporarily occluded. As the aneurysm could successfully be clipped intraoperatively, the bypass was prophylactic. Postoperatively, the patient suffered a hydrocephalus and a hemiparesis, possibly due to edema. Also, pneumonia and phlebitis was observed. Shortly after the operation she suffered from a rebleed from the aneurysm. The aneurysm was trapped and the M1 was permanently occluded. Postoperative follow-up was 64 days with a postoperative mRankin grade 4. Postoperative flow through the bypass was 48 ml/min.

Case 37.
This 58 year old female suffered from numbness and incoordination of her left hand. Angiography showed an unruptured giant middle cerebral artery (M2) aneurysm (Yasargil modified H&H grade 0bII, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional

anastomosis on a M3 segment of the middle cerebral artery (ICA-M3 bypass). Intraoperative bypass flow was 35 ml/min, which increased to 45 ml/min when the M2 was temporarily occluded. The aneurysm was successfully coiled postoperatively. No postoperative complications occurred. Postoperative follow-up was 15 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 38.
This 55 year old female presented with an episode of severe headache. Angiography showed a ruptured giant middle cerebral artery (M2) aneurysm (Yasargil modified H&H grade Ia, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M2 segment of the middle cerebral artery (ICA-M2 bypass). Intraoperative bypass flow was 40 ml/min, after which the M2 was occluded. Postoperatively, temporary hemiparesis occurred. Postoperative follow-up was 957 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed, however, angiography showed that the bypass was patent.

Case 39.
This 48 year old female suffered from superior quadrant anopsia on the left side. Angiography showed a ruptured giant middle cererbral artery (M2) aneurysm (Yasargil modified H&H grade Ia, preoperative mRankin grade 1). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M2 segment of the middle cerebral artery (ICA-M2 bypass). Intraoperative bypass flow was 20 ml/min, which increased to 55 ml/min when the M1 was temporarily occluded. As the aneurysm could successfully be clipped intraoperatively, the bypass was prophylactic. Postoperatively, she suffered a bone flap infection with epidural abscess, and epidural hematoma. These were successfully countered. Postoperative follow-up was 1462 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 40.
This 44 year old female presented with an episode of generalized epileptic seizure. Angiography showed a ruptured giant middle cerebral artery (M2) aneurysm (Yasargil modified H&H grade Ia, preoperative mRankin grade 0), which had partially been coiled. A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery. Intraoperative bypass flow was 40 ml/min, No permanent clipping or occlusion was performed because of three M2-3 branches originating from the aneurysm. The bypass occluded, probably due to the competetive flow with the M1. Three months later, a new bypass was made using a successful proximal ELANA anastomosis with successful flap retrieval on the M1 segment of the middle cerebral artery, and a successful distal conventional anastomosis on the M2. Again, no permanent clipping or occlusion was performed. No postoperative complications occurred. Postoperative follow-up was 1545 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 41.
This 47 year old female presented with an episode of severe headache, however, she suffered a rebleed of the aneurysm on admission. Angiography showed a ruptured giant middle cerebral artery (M2) aneurysm (Yasargil modified H&H grade IIb, preoperative mRankin grade 4). A bypass was created using a successful proximal ELANA anastomosis without successful flap retrieval on the intracranial internal carotid artery, and a successful distal conventional anastomosis on a M3 segment of the middle cerebral artery (ICA-M3 bypass). Intraoperative bypass flow was not measured. As the aneurysm could successfully be clipped intraoperatively, the bypass was prophylactic. No postoperative complications occurred. Postoperative follow-up was 1249 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Case 42.
This 48 year old female presented with severe headache and meningismus. Angiography showed a ruptured giant vertebral artery aneurysm (Yasargil modified H&H grade IIa, preoperative mRankin grade 0). A bypass was created using a successful proximal ELANA anastomosis with successful flap retrieval on the vertebral artery, and a successful distal conventional anastomosis on the posterior inferior cerebellar artery. Intraoperative bypass flow was 15 ml/min. The posterior inferior cerebellar artery was permanently occluded, and postoperatively,

the aneurysm was successfully coiled. No postoperative complications occurred. Postoperative follow-up was 50 days with a postoperative mRankin grade 0. Postoperative flow measurements were not performed.

Appendix C

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Appendix D

Summary, Samenvatting in het Nederlands

Summary

Summary

The Excimer Laser-Assisted Non-occlusive Anastomosis (ELANA) technique is a technique with which the neurosurgeon is able to make a vascular connection to the major cerebral blood vessels, without (temporarily) occluding the recipient artery. The ELANA technique was first described by Tulleken et al in 1993, and has been in continuous development ever since. After the first series of successful experiments in the animal laboratory, Tulleken proceeded to use this technique in patients who are in need of cerebral bypass surgery. During the last decade, more than 300 rabbit experiments have been performed, and over 250 patients have been treated. However, at the beginning of the studies described in this thesis, several questions still stood.

Are ELANA anastomoses easy to create in experimental settings as well as in clinical settings? Do they re-endothelialize as well as conventionally sutured anastomoses? And is the ELANA technique well applicable to otherwise inaccessible cerebral arteries?

High flow revascularization of the brain is hampered by the fact that temporary occlusion of a major cerebral artery is necessary to create the distal anastomosis, which may result in brain ischemia. The ELANA technique allows for end-to-side anastomosis to a cerebral artery without occluding that recipient artery. First a graft with a platinum ring in its distal end is stitched onto the wall of the recipient. Then a laser catheter is inserted inside the graft, so that the tip touches the wall of the recipient artery within the platinum ring. Vacuum suction is activated within the laser catheter, ensuring a firm fixation of the laser fibres to the wall of the recipient artery. When the excimer laser is activated, a hole is ablated in the wall, effectively creating the anastomosis. Upon retraction of the laser catheter, the punched-out portion of arterial wall is also withdrawn with the catheter because of the continued vacuum suction. A temporary hemoclip is then applied over the free end of the graft to prevent excessive backbleeding. Attaching the free end of the graft with another graft will complete the bypass procedure.

In order to learn such microvascular skills, several experimental models are available which diminish the need for experimental animals. We defined criteria with which such models should comply, and we tested whether the models described in the literature, as well as our own practice model, comply with these criteria. All practice models can be categorized in three stages; beginner, moderate, and advanced. Our ELANA Practice Model (EPM) complies with almost all criteria as defined in the beginner- and moderate stages, and has much in common with the models which are categorized in the advanced stage. Therefore, we conclude that the EPM can be used to learn microvascular skills for a very long time, before the need for living animals arises. This last aspect remains an inescapable condition for practicing microvascular skills. However, using the EPM, or another practice model, the amount of experimental animals can be drastically reduced.

We assessed the re-endothelialization of the ELANA anastomoses versus conventional anastomoses on the carotid arteries in pigs using scanning electron microscopy. In 28 pigs, a bypass with one ELANA and one conventional anastomosis was made on the left common carotid artery (CCA) using the right CCA as graft. All patent end-to-side anastmoses were evaluated intraoperatively with the ultrasound flow meter and postoperatively using scanning electron microscopy at 2 weeks, 2 months, 3 months, and at 6 months. All patent anastomoses (48) showed complete re-endothelialization, including all 24 ELANA anastomoses in which the endothelium covered the rim and the laser edge completely. No endothelial differences were observed between conventional and ELANA anastomoses. We therefore conclude that, in long-term experiments, ELANA anastomoses will re-endothelialize comparably with conventional anastomoses.

In order to estimate the extrapolation of the results obtained in the pig studies, we evaluated scanning electron microscopic images of the ELANA anastomoses in 4 patients with a cerebral bypass, who died of causes not directly related to the bypass procedure. In all ELANA anastomoses older than 4 days, the laser edge was very smooth. Endothelial cells on the laser edge were observed only in case 4 (5 years postoperatively). The platinum ring could only be observed to be partially without covering in case 1 (4 days postoperatively). In all other anastomoses, a different suturing technique had been used, so that the ring was not exposed to the blood stream, and thus could not be evaluated. We conclude that, in human, the re-endothelialization of the platinum ring starts after 4 days, and the re-endothelialization of the laser edge completes between 31 days and 5 years, after which the anastomoses are wide open, almost fully round, and with a continuous layer of endothelium covering the inside of the anastomosis.

The clinical application of the ELANA technique is described in three case reports (a patient with poor posterior fossa circulation, and two patients with a giant basilar artery aneurysm) and a short series of patients (n=42) who recieved an intracranial-to-intracranial bypass surgery in order to treat a giant, unclippable or uncoilable aneurysm.

In the first case, the carotid and the vertebrobasilar circulation were connected, effectively creating a new posterior communicating artery (PComA). Our patient presented with repeated episodes of vertebrobasilar ischemia because of vertebral artery occlusion and stenosis. An intracranial internal carotid artery-to-posterior cerebral artery P1 segment bypass procedure was performed. Because the patient experienced transient ischemia in the left cerebral hemisphere at the end of postoperative angiography procedure, no radiological intervention was performed, and the patient refused to undergo a new radiological intervention at a later stage. Both anastomoses were successfully made using the excimer laser-assisted nonocclusive anastomosis technique. Intraoperative flowmetry was performed using an ultrasound flowmeter, which disclosed blood flow of 35 ml/min through the bypass. We hope that this new PComA suffices to protect the patient from infarction in the territory of the vertebrobasilar circulation.

The second patient presented with a partially thrombosed fusiform giant basilar trunk aneurysm and suffered from a devastating headache and symptoms of progressive brain stem compression. Having an aneurysm inaccessible for endovascular treatment, and after failing a vertebral artery balloon occlusion test, he was offered bypass surgery in order to exclude the aneurysm from the cerebral circulation and relieve his symptoms. A connection between the intracranial internal carotid artery and the superior cerebellar artery was created whereupon the basilar artery was ligated just distally to the aneurysm. The proximal anastomosis on the internal carotid artery was made using the excimer laser-assisted non-occlusive anastomosis (ELANA) technique, while a conventional end-to-side anastomosis was used for the distal anastomosis on the superior cerebellar artery. Intra-operative flowmetry showed a flow through the bypass of 40 ml/min after ligation of the basilar artery. An angiogram 24 hours later showed normal filling of the bypass and the vessels supplied by it, but also disclosed a subtotal occlusion of the proximal ipsilateral middle cerebral artery with delayed filling distally. The patient, who had a known thrombogenic coagulopathy, died the following day. Autopsy showed no signs of ischemia in the territories supplied by the bypass, but a thrombus in the proximal middle cerebral artery and massive acute hemorrhagic infarction with swelling in its territory and uncal herniation.

Our third patient suffered from progressive brainstem deficits with dysarthria, swallow problems, vertigo and ultimately a tetraparesis, due to a giant vertebrobasilar aneurysm. He obviously had a bad prognosis, and we expected that his life-expectancy would be very short. The ELANA technique allowed us to attach a venous graft to the BA through the small opening formed by the ICA, the A1 and the optic nerve, without occuding the BA. A nice flap of BA wall was retracted and this anastomosis was used to create an ECA-BA bypass, through which a flow of 55 ml/min was observed. This flow was observed with the right VA still open. We then ligated also this VA and the flow through the bypass increased to 95 ml/min. Due to the reversed flow in the aneurysm, there was now a high chance that a thrombus will create within the aneurysm, which hopefully would not occlude the BA itself. BA occlusion, was not likely to occur because of the continued flow to the PCAs, SCAs and AICAs. Angiography showed that the bypass supplied the posterior circulation, and our patient was improving and started to talk and move his limbs. After the operation his condition stabilized. There were signs of improvement. Two weeks later, MRA and CTA scans showed progression of thrombus formation within the aneurysm. However, there was also some progression of the neurological deficits. Four weeks later, the patient suffered a fatal subarachnoidal haemorrhage, which probably originated from the remnant of the aneurysm.

We also present a retrospective study with 42 patients with giant intracranial aneurysms, who were treated with intracranial-to-intracranial bypass surgery using the excimer laser-assisted non-occlusive anastomosis (ELANA) technique and conventional anastomosis techniques, as a stand-alone option or in combination with aneurysm clipping, coiling, or vessel occlusion. The objective of this study was to assess the technical results of the ELANA technique and to evaluate the clinical results. Sixty-one ELANA procedures were performed to create 61 successful anastomoses (100% success rate). There were no ELANA related complications. Twenty-one patients (50%) suffered direct post-operative neurosurgical complications. Six patients (14%) suffered non-neurosurgical complications. Temporary post-operative neurological deficits were found in 12 patients (29%), permanent neurological deficits in 9 (21%). There was no intra-operative mortality. Two patients died from a rebleed. Three patients died because of fatal cerebral vessel thrombosis. One patient died of a myocardial infarction and one of unknown cause. Post-operatively, 26 patients (62%) had the same or better Rankin Grade as pre-operatively. We conclude that the ELANA technique is a viable and safe technique. We found it a reliable tool in the treatment of giant cerebral aneurysms. However, despite the different surgical and endovascular tools available us, this group of patients remains very difficult to treat, with a high morbidity. This is also reflected in the three afore mentioned case reports and in the literature.

Considering all studies described in this thesis, we think that anastomoses made with the ELANA technique are indeed relatively easy to create in experimental as well as in clinical settings. A 100% successrate in all pigs, all case reports and in the short clinical series should be ample proof. A careful sidenote concerns the retrieval of the flaps. In our clinical series of chapter 11, the total flap retrieval rate was 84%. Although there is the theorethical danger of thrombosis, there was no relation between the flap retrieval and clinical outcome. These results may be biased due to the fact that in a very few cases the anastomosis was discontinued, despite the successful creation of the anastomosis.

Concerning the re-endothelialization, anastomoses made with the ELANA technique indeed re-endothelialize as well as conventionally sutured anastomoses in experimental settings as well as in clinical settings. The final prove of the re-endothelialization in clinical settings may be very hard to obtain as only postmortem studies will give the final answer. Fortunately, most patients treated with the ELANA technique are still alive.

The possibility of creating a bypass to the major cerebral arteries has been proven in numerous publications.[68, 80, 191, 224, 248, 267] However, in order to safely access the intracranial ICA, M1, A1, and P1, the ELANA technique is quite an instrument, as described in the three case reports (chapters 8-10) and the IC-IC bypass case series (chapter 11). In our opinion, the creation of an intracranial anastomosis to the above mentioned arteries is best performed using the ELANA technique because of its ease of use and especially its non-occlusive characteristics.

Samenvatting

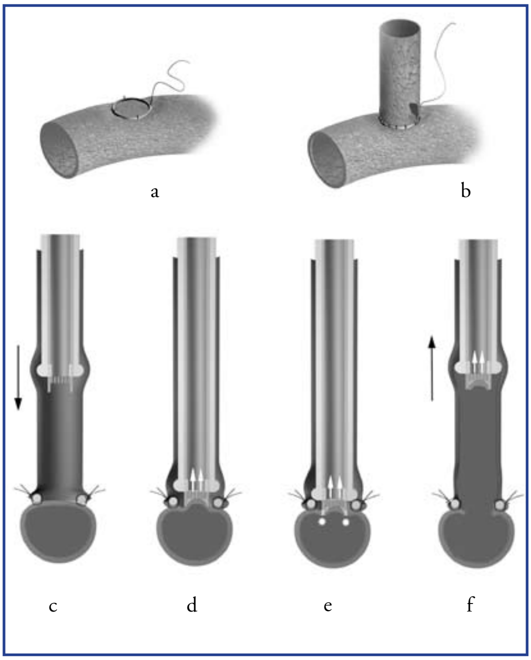
Samenvatting

De Excimer-laser-geAssisteerde Niet-afsluitende Anastomosis (ELANA) techniek is een techniek waarmee de neurochirurg een vaatverbinding (anastomosis) kan maken naar de grote bloedvaten aan de basis van het brein, zonder dit bloedvat (tijdelijk) af te sluiten. De ELANA techniek is voor het eerst beschreven door Tulleken in 1993, en is sindsdien voortdurend in ontwikkeling. Na de eerste series succesvolle experimenten in het dieren laboratorium is Tulleken deze techniek ook in patiënten gaan toepassen bij wie bypasschirurgie noodzakelijk was. Gedurende de laatste tien jaar zijn er meer dan 300 konijnenexperimenten uitgevoerd, en meer dan 250 patiënten behandeld. Echter, aan het begin van de hier beschreven studies was er nog een aantal vragen.

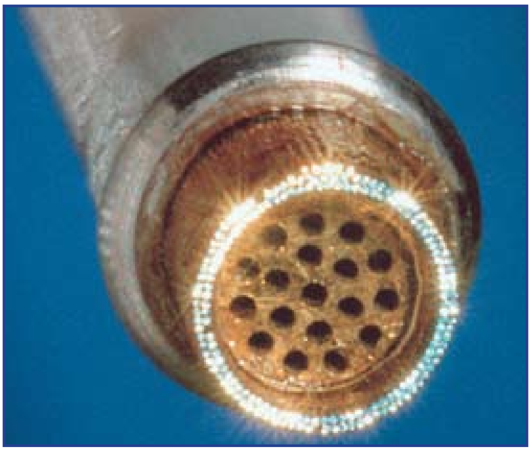
Zijn ELANA vaatverbindingen gemakkelijk te maken, zowel in experimentele situaties, als in klinische situaties? Vindt er een even goede re-endothelialisatie plaats als bij de conventioneel gemaakte vaatverbinding? En is de ELANA techniek goed te gebruiken op bloedvaten die anders erg moeilijk zijn te bereiken?

Hernieuwde bloedvoorziening van het brein met een grote bloedstroom is moeilijk vanwege het feit dat, normaliter, de tijdelijke afsluiting van het bloedvat, welke noodzakelijk is om de vaatverbinding te maken, kan resulteren in een tekort aan bloed in dat deel van het brein. Met de ELANA techniek is het mogelijk om een vaatverbinding te maken naar een hersenarterie, zonder dit ontvangende bloedvat te hoeven af te sluiten (zie Figuur S.1.). Hierbij wordt eerst het extra bloedvat, met daarin een platinum ring, op de wand van het ontvangende bloedvat genaaid. Vervolgens wordt een lasercatheter (zie Figuur S.2.) ingevoerd in het open uiteinde van het extra bloedvat, zodat de tip van de catheter komt te rusten op de wand van het ontvangende bloedvat, binnen de platinum ring. Er wordt vacuüm gecreëerd binnenin de lasercatheter, waardoor de laser fibers een goed contact hebben met de wand van het ontvangende bloedvat. Wanneer de excimer-laser wordt geactiveerd, wordt er een gat gevormd in de wand, waardoor de vaatverbinding een feit is. Als de lasercatheter wordt teruggetrokken, komt het, door de laser gevormde flapje van de wand mee, vanwege het continue vacuum. Een tijdelijke clip wordt gebruikt om het vrije eind van het extra bloedvat af te sluiten, om onnodig bloedverlies te voorkomen. Door het vrije uiteinde aan een ander bloedvat aan te sluiten wordt de bypassprocedure gecompleteerd.

Dit soort microvasculaire chirurgie vergt veel oefening. Hiervoor is reeds een aantal experimentele modellen beschikbaar, waardoor het gebruik van proefdieren kan worden verminderd. Wij hebben de criteria beschreven waaraan dit soort modellen dient te voldoen, en wij hebben getest of de modellen die in de literatuur zijn beschreven, zowel als ons eigen oefenmodel (zie Figuur S.3.) voldoen aan deze criteria.



Figuur S.1.
Theorie van de ELANA techniek. Een platinum ring met een diameter van 2.6, 2.8, of 3.0 mm wordt vastgehecht op de wand van het ontvangende bloedvat(a). De beide mediane hechtingen worden alleen heel oppervlakkig vastgezet, slechts gedeeltelijk door de wand van het ontvangende vat heen. De twee laterale hechtingen gaan wel geheel door de wand heen. Daarna wordt het extra bloedvat vastgehecht op de wand, waarbij de ring als gids wordt gebruikt (b). Alle 8 hechtingen worden slechts zeer oppervlakkig gezet, waarbij alleen door de media en adventitia heen wordt gestoken. De excimer laser wordt vervolgens ingebracht in het open einde van het extra vat (c). Nadat de tip van de catheter in aanraking komt met de wand van het ontvangende vat binnenin de platinum ring, wordt er vacuüm gezogen via de catheter, waardoor er een stevig contact ontstaat tussen de laserfibers en de wand van het ontvangende bloedvat (d). Na 2 minuten vacuüm wordt de excimer-laser geactiveerd, en wordt er een gat in de wand gecreëerd (e). Als dan de catheter wordt teruggetrokken, komt het gelaserde flapje mee vanwege het continue vacuüm (f). Om verdere bloeding to voorkomen wordt er een tijdelijke clip gezet op het extra vat. Dit laatste wordt dan met een ander bloedvat verbonden, waarna de bypass compleet is.



Figuur S.2.
De ELANA lasercatheter. Deze catheter bestaat uit 180 laserfibers, gearrangeerd in een dubbele circel, rondom een vacuum buis met in het uiteinde een zeefje. Rondom de laser fibers bevindt zich een ring met een buitendiameter van > 3 mm. De dubbele rij laserfibers (maximale diameter 2.2 mm) vergroot de kans op een sucesvolle creatie van een flapje. Het zeefje bestaat uit 18 gaatjes met een diameter van 0,1 mm. Middels het vacuüm kan hierdoor een trekkracht worden gerealiseerd van ongeveer 0,2Newton (zie Appendix A.). Hierdoor wordt het flapje dan ook meegenomen bij het terugtrekken van de catheter na de laserprocedure. De buitenring is bedoeld om te voorkomen dat de laser de tegenoverliggende wand van het bloedvat beschadigt, aangezien de catheter nu niet verder door de platinum ring heen kan zakken.

Figuur S.3.
Het ELANA Practice Model (EPM) versie 3. Dit model bestaat uit een grijs bakje waarin twee holle buisjes zijn geplaatst. Tussen de buizen kan een bloedvaatje worden opgespannen. Hierbinnen kan met vloeistof druk worden opgebouwd. Voor oefendoeleinden kan er een doorzichtige tafel boven worden gezet, met een variabel gat om de moeilijkheidsgraad te vergroten.

Alle oefenmodellen kunnen worden ingedeeld in drie stadia; beginner, middelmatig en gevorderd. Ons ELANA oefenmodel (ELANA Practice Model of EPM) voldoet aan bijna alle criteria zoals gedefinieerd in de stadia beginner en middelmatig, en heeft veel gemeen met de modellen die in het gevorderde stadium vallen. Daarom kunnen wij concluderen dat de EPM heel lang kan worden gebruikt om microvasculaire technieken aan te leren, voordat het nodig is om te oefenen op proefdieren. Dit laatste zal altijd nodig blijven om op een goede manier microvasculaire ervaring op te doen. Echter, indien men gebruikt maakt van het EPM, of een ander oefenmodel, dan kan het aantal proefdieren drastisch worden verminderd.

Re-endothelialisatie is het proces waarbij de binnenbekleding (endotheel) van de vaatverbinding, welke is onderbroken vanwege het chirurgisch ingrijpen, weer aangroeit, zodat het één geheel vormt binnen de twee gedeelten van de vaatverbinding. Wij hebben de re-endothelialisatie onderzocht van de ELANA vaatverbindingen ten opzichte van conventioneel gemaakte vaatverbindingen op de halsslagaderen van varkens, en deze geëvalueerd middels de scanning electronen microscoop. In 28 varkens werd een bypass gemaakt op de linker halsslagader met één ELANA en één conventionle vaatverbinding, en met de rechter halsslagader als extra bloedvat. Alle functionele vaatverbindingen (48) werden tijdens de operatie geëvalueerd middels de ultrasound flowmeter, en middels de scanning electronen microscoop op 2 weken, 2 maanden, 3 maanden en 6 maanden na de operatie. Alle vaatverbindingen vertoonden complete re-endothelialisatie, inclusief alle 24 ELANA vaatverbindingen waar het endotheel het blootgestelde gedeelte van mediale en buitenste vaatlaag bedekte, evenals de scherpe rand die is gemaakt door de laser, en ook de platinum ring (zie Figuur S.4.). Wij concluderen daarom dat, in lange-termijn experimenten, ELANA vaatverbindingen even goed zullen re-endothelialiseren als conventionele vaatverbindingen.

Om de resultaten van de varkensstudie te kunnen extrapoleren naar de mens, hebben wij scanning electronen microscopische fotos van ELANA vaatverbindingen in 4 patiënten geëvalueerd. Deze patiënten waren overleden aan complicaties die niet direct gerelateerd waren aan bypasschirurgie. In alle ELANA vaatverbindingen die ouder waren dan 4 dagen was de gelaserde rand heel glad. Endotheelcellen op deze rand konden alleen worden gezien bij patiënt 4 (5 jaar na bypass operatie, zie ook Figuur S.5.). De platinum ring was bij patiënt 1 (4 dagen na operatie) slechts gedeeltelijk bedekt met endotheel. In alle andere vaatverbindingen was een andere hecht-techniek gebruikt waarbij de ring niet was blootgesteld aan de bloedstroom, en dus ook niet kon worden geëvalueerd. Wij concluderen dan ook dat, bij mensen, de re-endothelialisatie van de platinum ring kan starten vanaf 4 dagen, en dat de re-endothelialisatie van de gelaserde rand voltooid is ergens tussen de 31 dagen en 5 jaar na operatie. Hierna

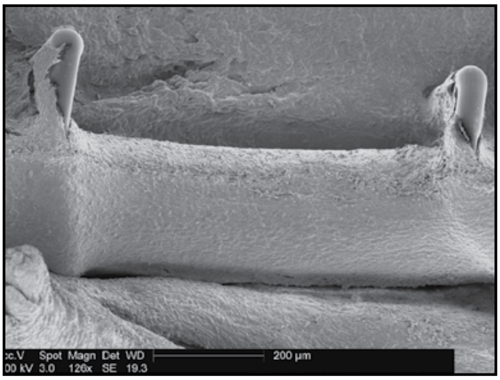


Figure S.4. (ELANA in een varken, 6 mnd na operatie)
De SEM foto op hoge vergroting van de ELANA vaatverbinding laat zien dat de platinum ring volledig bedekt is met endotheelcellen. De 9/0 Prolene hechtingen waren eerst strak aangetrokken rondom de platinum ring, het weefsel van het ontvangende bloedvat en het weefsel van het extra bloedvat, maar zijn nu zichtbaar losser vanwege de fixatietechniek voor de SEM.

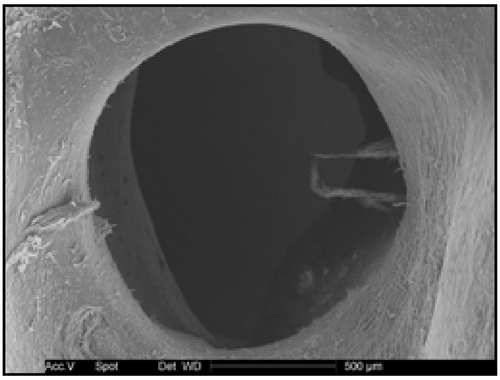


Figure S.5. (ELANA in een patient, 5 jaar na operatie)
De SEM foto op iets lagere vergroting (dan Figuur S.4.) van de ELANA vaatverbinding laat zien dat de contouren van de platinum ring nog net herkenbaar zijn. Verdere vergrotingen laten zien dat de randen volkomen glad zijn, waarbij er regelmatig endotheelcellen zichtbaar zijn.

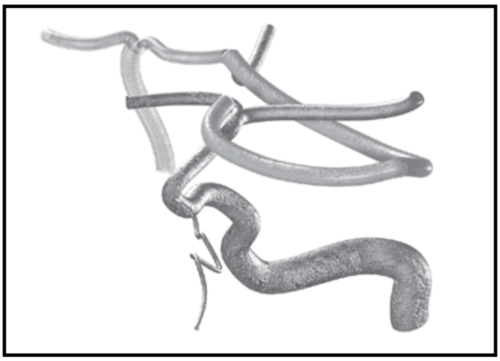


Figure S.6. (3D reconstructie van een nieuwe PComA)
Een verbinding tussen de voorste circulatie van de arteria carotis interna naar de achterste circulatie (P1/2 segment van de achterste hersenarterie: arteria cerebri posterior). Normaal loop hier een achterste communicerend bloedvat (PComA), die bij deze patient afwezig was. De patient had hier veel klachten aan. Een bypass zorgde ervoor dat er weer voldoende bloed naar het achterste gedeelte van het brein kon stromen.

zijn de vaatverbindingen wijd open, bijna volledig rond, en is de binnenkant van de vaatverbinding volledig bedekt met een continue laag van endotheel.

De klinische applicatie van de ELANA techniek is beschreven in drie patiënt verslagen (één patiënt met te weinig bloed in de achterste schedelgroeve en twee patiënten met een gigantisch aneurysma van de arteria basilaris) en in een studie met een klein aantal patiënten (42) die een intracraniële-naar-intracaniële bypass heeft gekregen om een gigantisch, niet-clippable, niet-coilable aneurysma uit de circulatie te halen.

In de eerste patiënt werd de bloedvoorziening vanuit de halsslagaders en die vanuit de arteriae vertebrales met elkaar verbonden, waardoor er een nieuwe arteria communicans posterior (PComA) ontstond (zie Figuur S.6.). Onze patiënt presenteerde zich met herhaaldelijke episodes van bloedtekort in de hersenstam en het achterste gedeelte van het brein in verband met een afsluiting van één arteria vertebralis en een gedeeltelijke afsluiting van de andere arteria vertebralis. Een bypass werd gemaakt vanuit het intracraniële gedeelte van de halsslagader (arteria carotis interna of ICA) naar het eerste segment van de achterste hersenarterie (arteria cerebri posterior of PCA), met de bedoeling om later het aneurysma dicht te maken middels een neuroradiologische interventie met coils. Beide vaatverbindingen werden met succes gemaakt middels de ELANA techniek. Aangezien de patiënt tijdens de angiografie procedure ná de bypass operatie een tijdelijk bloedtekort in de hersenen kreeg, kon deze coil procedure niet doorgaan. De patiënt weigerde daarna een volgende poging. Tijdens de operatie werd er door de bypass een flow gemeten van 35 ml/min. Wij hebben goede hoop dat deze nieuwe PComA goed genoeg zal zijn om de achterste schedelgroeve van voldoende bloed te voorzien, zodat de patiënt geen klachten meer zal hebben.

De tweede patiënt presenteerde zich met een gedeeltelijk getromboseerd gigantisch aneurysma van de stam van de arteria basilaris (juist voor de hersenstam). Hij had daarbij ook veel last van een verschrikkelijke hoofdpijn en klachten passend bij een verdrukking van de hersenstam. Aangezien het aneurysma niet benaderbaar was middels een endovasculaire behandeling, en aangezien hij het simpelweg afsluiten van de beide arteriae vertebrales niet kon verdragen zonder uitvalsverschijnselen, werd hem bypasschirurgie aangeboden. Er werd een bypass gemaakt tussen het intracraniële gedeelte van de ICA en de bovenste arterie van de kleine hersenen (arteria cerebelli superior of SCA, zie Figuur S.7.). De proximale vaatverbinding op de ICA werd met succes gemaakt met de ELANA techniek, terwijl een conventionele techniek werd gebruikt voor de distale vaatverbinding met de SCA. Flowmetingen lieten een flow door de bypass zien van 40 ml/min nadat de arteria basilaris was afgesloten. Een angiogram 24 uur na de operatie vertoonde een normale vulling van de bypass, maar ook een subtotale afsluiting van de middelste hersenarterie (arteria cerebri media of MCA). De patiënt, die overigens bekend was met een stollingsstoornis, overleed de volgende dag. Autopsie werd toegestaan en vertoonde geen bloedtekort in het gebied wat verzorgd werd door de bypass, maar wel een stolsel in de MCA met daarachter een beeld van hemorrhagisch infarct, oedeem en inklemming.

Onze derde patiënt had veel klachten van de hersenstam met spraakproblemen, slikproblemen, draaiduizeligheid en uiteindelijk verlamming, vanwege een giant vertebrobasilair aneurysma. Hij had duidelijk een slechte prognose, met een zeer korte levensverwachting. De ELANA techniek maakte het mogelijk om een extra bloedvat aan te sluiten op de arteria basilaris zelf, zonder deze af te sluiten. Uiteindelijk werd

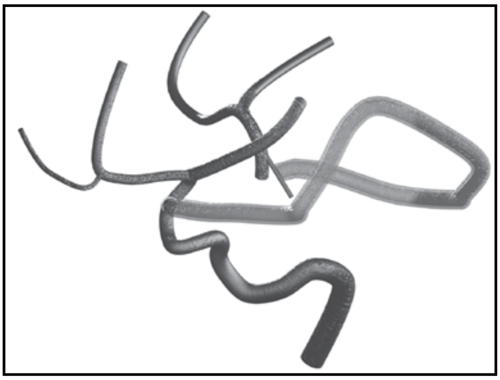


Figure S.7. (3D reconstructie van een ICA-SCA Bypass)
Een verbinding tussen de voorste circulatie van de arteria carotis interna naar de achterste circulatie; arteria cerebelli superior was gemaakt. De patient had veel klachten aan een gigantisch aneurysma net caudaal van de distale vaatverbinding van de arteria basilaris. Een bypass zorgde ervoor dat er weer voldoende bloed naar het achterste gedeelte van het brein kon stromen, zodat we de arteria basilaris konden afsluiten.

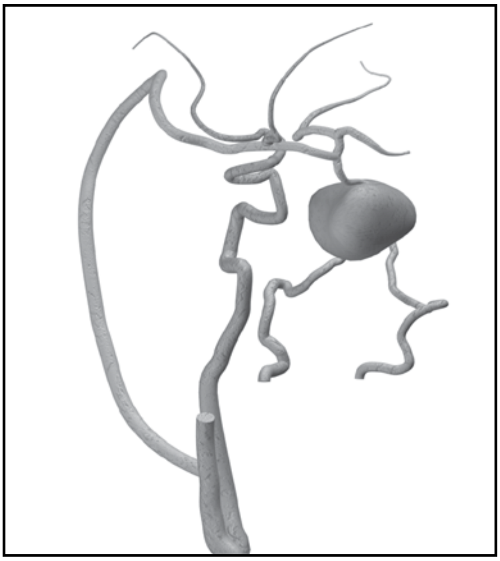


Figure S.8. (3D reconstructie van een ECA-BA Bypass)
Ook de derde patient had veel klachten van een gigantisch aneurysma van de arteria basilaris. Eén arteria vertebralis werd pre-operatief afgesloten. Vervolgens werd de bypass gemaakt naar de arteria basilaris ruim boven het aneurysma. Daarna werd de andere arteria vertebralis afgesloten. De bedoeling was dat de omgekeerde flow in het aneurysma ervoor zou zorgen dat het bloed in het aneurysma zou stollen. Helaas is het aneurysma voor die tijd geruptureerd met fatale gevolgen.

deze vaatverbinding gebruikt voor het maken van een bypass vanuit buiten de schedel, aldaar aangesloten op de buitenste halsslagader (arteria carotis externa of ECA), en van daaruit middels de ELANA techniek aangesloten op de arteria basilaris (zie Figuur S.8.). Vervolgens werd de arteria vertebralis gesloten. Angiografie bevestigde dat de bypass zorgde voor voldoende bloed in de achterste schedelgroeve, en de patiënt verbeterde, en begon weer te bewegen. Helaas was het niet mogelijk om het aneurysma volledig af te sluiten omdat dan de arteria basilaris ook af zou sluiten, en de hersenstam geen bloed meer zou krijgen. De bedoeling was dan ook dat de omkering van de bloedstroom ervoor zou zorgen dat het aneurysma kleiner zou worden, zonder helemaal af te sluiten. Twee weken later werd middels magnetische resonantie angiografie en computed tomografische angiografie vastgesteld dat het stolsel binnen het aneurysma zich uitbreidde. Vier weken later overleed de patiënt aan een hersenbloeding, waarschijnlijk afkomstig van de nog open resten van het aneurysma.

Wij beschrijven ook nog een terugkijkende studie met 42 patiënten met gigantische aneurysmata, die zijn behandeld met intracraniële-naar-intracraniële bypasschirurgie, middels de ELANA techniek, al dan niet in combinatie met het clippen van het aneurysma, coilen, of het volledig afsluiten van het verziekte bloedvat zelf. Het doel van de studie was om de technische resultaten van de ELANA techniek te onderzoeken en de klinische resultaten te evalueren. Eén-en-zestig ELANA vaatverbindingen werden uitgevoerd, waarvan ook 61 met succes (100% succes percentage). Er ontstonden geen complicaties vanuit de ELANA techniek. Eén-en-twintig patiënten (50%) kregen een directe postoperatieve neurochirurgische complicatie. Zes patiënten (14%) kregen een niet-neurochirurgische complicatie. Tijdelijke neurologische uitval werd bij 12 patiënten (29%) gezien, permanente uitval bij 9 (21%). Er was geen intra-operatieve mortaliteit. Twee patiënten overleden na de operatie vanwege een nieuwe bloeding vanuit het aneurysma. Drie patiënten overleden aan een fatale hersenbloedvat afsluiting. Eén patiënt kreeg een fatale hartaanval, en één patiënt overleed zonder dat de oorzaak bekend is. Na de operatie hadden 26 patiënten (62%) dezelfde of een betere mRankin graad vergeleken met pre-operatief. Wij concluderen dat de ELANA techniek een goede en veilige techniek is om vaatverbindingen te maken. Het is een betrouwbaar instrument in de behandeling van gigantische intracraniële aneurysmata. Echter, ondanks de verschillende chirurgische en endovasculaire mogelijkheden die tot onze beschikking staan, blijft deze groep patiënten zeer moeilijk te behandelen, met een hoge morbiditeit. Dit blijkt ook uit de drie voorafgaande patiënt verslagen en uit de literatuur.

Wanneer we alle studies in overweging nemen die zijn beschreven in deze dissertatie, dan menen we dat vaatverbindingen middels de ELANA techniek inderdaad relatief gemakkelijk te maken zijn in een experimentele of klinische omgeving. Een 100% succesvolle vaatverbinding rate in alle varkens, alle patiënt verslagen en in de studie met 42 patiënten zou voldoende moeten zijn om dit te bewijzen. Een waarschuwing is echter op zijn plaats met betrekking tot het verkrijgen van de flap. In onze klinische serie van hoofdstuk 11 is de totale flap rate 84%. Hoewel er een theoretische mogelijkheid is dat het niet verkrijgen van een flap het ontstaan van een bloedprop zal bevorderen, konden wij geen relatie vinden tussen het verkrijgen van een flap en de klinische uitkomst. Het is mogelijk dat deze resultaten minder nauwkeurig zijn omdat in enkele gevallen de vaatverbinding niet is gebruikt, ondanks het feit dat er een succesvolle vaatverbinding was gemaakt.

Met betrekking tot de re-endothelialisatie denken wij dat de vaatverbindingen, gemaakt met de ELANA techniek, inderdaad even goed re-endothelialiseren als conventionele vaatverbindingen, zowel in een experimentele omgeving, als bij patiënten. Het uiteindelijke bewijs dat men dit zo mag stellen bij patiënten is waarschijnlijk erg moeilijk te verkrijgen omdat dit alleen middels post-mortem studies kan. Gelukkig leven de meeste patiënten nog die behandeld zijn met de ELANA techniek.

De mogelijkheid om een bypass te maken naar de grote bloedvaten aan de basis van het brein is reeds veelvuldig beschreven in de literatuur. [68, 80, 191, 224, 248, 267] Echter, de ELANA techniek is een uitstekend instrument om veilig een vaatverbinding te maken naar de intracraniële ICA of naar de eerste segmenten van de hersenarteriën, zoals is beschreven in de drie patiënt verslagen en in de studie. Naar onze mening is de ELANA techniek de beste manier om een vaatverbinding te maken vanwege de relatieve eenvoud en met name de niet-afsluitende eigenschappen.

Appendix E

Dankwoord, Curriculum Vitae, Publications

Dankwoord

Dankwoord

Wetenschappelijk onderzoek doe je nooit alleen. Ik ben op mijn onderzoekerspad ontzettend veel mensen tegengekomen die ik het liefst allemaal zou willen bedanken. In 1997 kwam ik in contact met professor Tulleken (destijds hoofd van de afdeling Neurochirurgie, UMC-Utrecht). Hij liet mij eerst twee weken meelopen in de neurochirurgische kliniek, alvorens hij mij introduceerde bij Dr A. van der Zwan (neurochirurg, UMC-Utrecht). Het gesprek met beiden, nadat ik eind 1998 mijn wetenschappelijke stage met succes had afgerond, resulteerde in de aanbieding om het voorliggend promotie onderzoek te gaan doen, wat ik toen natuurlijk met beide handen heb aangenomen (2000).

Geachte professor dr. C.A.F. Tulleken, beste professor. Uw inspirerende ideeën en oneindig optimistische houding ten aanzien van het ELANA onderzoek hebben de basis gevormd van de inhoud van dit boekje. Als promotor bent u niet alleen mijn wetenschappelijke vader geweest, maar daarbij heeft u het mogelijk gemaakt dat ik op fantastische wijze en op een constructieve manier mijn computerverslaving heb kunnen benutten. Uw manier van begeleiden betekende dat ik mij volledig vrij kon ontwikkelen binnen het onderzoek. Voor de wetenschappelijke begeleiding was het voor mij fantastisch dat u een van de meest bereikbare mensen bent, en ik denk dan ook met veel plezier terug aan de wekelijkse vroege gesprekken en aan de ritjes naar Naarden. Ik zal uw begeleiding zeker missen.

Geachte Dr. A. van der Zwan, beste Bart. Als co-promotor leerde jij mij de prioriteiten binnen het onderzoek in het oog te houden en de stof te blijven structureren. Ik dank je voor je constructieve feedback.

Bij het aanvangen van het promotie-onderzoek werd ik geïntroduceerd bij twee andere mensen die minstens even belangrijk zijn geweest. Dit zijn Dr. ir R.M. Verdaasdonk en dhr. H.J. Mansvelt Beck (afdeling Medische Technologie en Multimedia, UMC Utrecht).

Geachte Dr. ir. R.M. Verdaasdonk, beste Ruud. Het toepassen van de Excimer laser was natuurlijk een gouden vondst. Als co-promotor heb jij structuur aangebracht in mijn wilde ideeën voor telkens nieuwe experimenten. Altijd rustig en doortastend wist je mij er met solide argumenten van te overtuigen dat sommige vaten toch echt aanbranden als je ze te lang blootstelt aan laserlicht. Ik dank je voor je begeleiding en hulp bij het uitvoeren van de laser procedures. Het warme en spontane contact tussen onze families koester ik.

Geachte H.J. Mansvelt Beck, beste Rik. Waar zou ik zijn geweest zonder jou? In ieder geval ergens zonder resultaten. De resultaten van dit proefschrift waren voor een belangrijk deel afhankelijk van jouw technische inzet bij de laserprocedures. Dit geldt voor zowel de klinische operaties, de dier-experimentele operaties alswel de technische experimenten. Zo ontzettend heb je mij verwend, dat ik maar hoefde te kikken en binnen een week had je *het betreffende apparaat gemaakt. Natuurlijk wel met zulke aanpassingen dat ik het veel handiger kon gebruiken dan ik zelf had bedacht. Ik dank je voor je koffie, jouw gesprekken, en al die andere kleine en grote dingen.*

Bart van der Zwan introduceerde mij vervolgens bij professor Berend Hillen (destijds hoofd van de afdeling Anatomie, UMC-Utrecht). Na een zeer ingewikkeld gemeenschappelijk congres in Toulouse, bleek de relatie tussen bypass en wiskundig flow model van de bloedvaten aan de basis van de hersenen zeer groot te zijn.

Geachte Prof. dr. B. Hillen, beste Berend. Jij hebt mij laten zien dat levensgenieten en goed werk leveren prima kunnen samengaan. Ik heb gemerkt dat het uitstekend mogelijk is om een vergelijking met 16 onbekenden op te lossen onder het genot van een sociaal geaccepteerde bloedverdunner. Jammer dat ik het onderzoek niet heb kunnen afmaken. Ik kijk vooruit naar onze samenwerking in Nijmegen.

De validatie van het flowmodel bracht een aantal verschillende meetmethoden met zich mee die wij op vrijwilligers wilden gaan toepassen. Prof.Dr. A van Huffelen (hoofd van de afdeling Klinische Neurofysiologie, UMC-Utrecht) toonde zich meer dan bereid om mee te werken met de TCD/Doppler metingen. Daarnaast waren Dr.Ir. C. Bakker, Dr. J.H. Seppenwolde, en Dr. J.Hendrikse (afdeling Radiologie en Beeldvorming, UMC-Utrecht) zeer geïnteresseerd in flowmetingen met behulp van de MRA.

Geachte Prof. dr. A. Van Huffelen, beste professor. Hartelijk dank voor de enthousiaste medewerking. De resultaten lieten zich te laat aandienen om mee te kunnen met dit boekje, maar dat ligt niet aan uw afdeling. Integendeel! Natuurlijk wil ik ook graag de twee perfecte laboranten bedanken voor al het werk wat zij hebben verzet.

Geachte Dr. Ir. C. Bakker, beste Chris. Onze eerste echte ontmoeting in Toulouse genereerde al meteen zoveel ideen voor onderzoek, dat wel tien promovendi daarop hadden kunnen promoveren. Dank je wel voor jouw hulp.

Ik wil daarnaast ook alle patiënten bedanken die hebben meegewerkt aan het onderzoek.

Het werd al snel duidelijk dat het onderzoek naar de ELANA techniek zich voor een belangrijk deel zou gaan afspelen in het dierexperimenteel laboratorium. Prof. Tulleken was hier uiteraard een goede bekende en in eerste instantie mocht ik hem dan ook assisteren in het lab. Zodoende maakte ik kennis met de biotechnici en dierverzorgers aldaar.

Beste Hans, Nico, Herman, Jannie, en Elly. Ik wil jullie danken voor de voortreffelijke ondersteuning voor, tijdens, en na al mijn pogingen tot het maken van anastomoses. Er zijn twee dingen die ik graag naar voren wil brengen. Ten eerste heb ik gezien dat jullie ontzettend veel hart voor de dieren hebben, wat natuurlijk ook het onderzoek ten goede is *gekomen. Daarnaast heb ik ook een groot deel van mijn microchrirurgische vaardigheden van jullie geleerd. Ook hiervoor mijn dank.*

Beste Cindy, Adrie, en Cees. Hartelijk dank voor jullie liefdevolle zorg voor onze konijntjes en varkentjes. Zij waren (en zijn) bij jullie in de allerbeste handen! Paulien, bedankt voor al dat regelwerk!

De experimenten in het laboratorium vergden niet alleen de inspanningen van de biotechnici en dierverzorgers. Rik Mansvelt Beck was vrijwel altijd aanwezig tijdens de experimenten, zeker wanneer het ging om een nieuw techniek of een ander soort aanpassing. Maar ook de Medische Laser Afdeling was goed vertegenwoordigd. Indien Ruud Verdaasdonk onverhoopt niet beschikbaar was, sprongen de andere fysici voor hem in. Zeker in de beginperiode van het onderzoek werd er nogal met lasers gesjouwd tussen ziekenhuis en laboratorium. Daar kon ik altijd wel hulp bij gebruiken. Maar natuurlijk ook met de daadwerkelijke laserprocedure!

Beste Matthijs, Christiaan, Herke-Jan, en Arjan. Bedankt voor jullie technische en mentale ondersteuning tijdens alle experimenten. Op de een of andere manier wisten jullie altijd een bepaald soort rust en zekerheid te geven waardoor wij het rotsvaste vertrouwen hadden (terecht of niet) dat we deze keer echt wel weer een flap zouden trekken, en indien niet, dat dat dan zeker niet aan de laser lag (gelukkig was dat ook echt niet zo, toch?).

Naarmate het onderzoek vorderde werd het duidelijk dat het verkrijgen en uitwerken van de resultaten ontzettend veel tijd zou vergen. Gelukkig werd ik daarin bijgestaan door een groot aantal medisch studenten. Een aantal van hen is nu al lang en breed arts en ergens in opleiding.

Beste Sanne, Jasper, Jochem, Ester, Marcel, Joris, Jeroen, Flip, Marije, Ladbon, en Maaike. Hartelijk dank voor jullie inzet bij het maken van de scanning electronen microscopische en licht microscopische plaatjes, het onderzoeken en uitproberen van de 2e en 3e versies van het EPM, en het uitzoeken van "enkele" patiëntgegevens! Jochem, je bent een fantastische opvolger in het lab!

Al geruime tijd werd professor Tulleken bezocht door buitenlandse neurochirurgen. Mij werd vervolgens de kans gegeven om samen met hen in het dierenlaboratorium te werken aan het leren van de ELANA techniek.

Dear Dr. David Langer, Mr. Kare Fugleholm, Mr. Buhpal Chitnavish, Dr. Lena Kivipelto, Professor Juha Hernesniemi, Professor Gerardo Conesa, Dr. Alfredo Puca, Mrs. Joan Grieve, Mr. Nick Philips, Mr. Scott Ross, Dr. David Sinclair, Dr. Peter Vajkoczy, Dr. Sturiale, Dr. Bortolotti, Dr. A. Mendelowitsch. Thank you so much for your patience with the "medical student in the lab". Seeing so many skillfull, talented and even legendary neurosurgeons at work in our laboratory made my Ph.D. study a treasure and a real treat. You absolutely have made your visits memorable, and I am very proud to say that I have had the chance *to work with neurosurgeons who were the first to apply the ELANA technique in their own country! From you I also learned that the way of life of a (more than) full-time neurosurgeon does not mean forgetting to live! Thank you very much!*

Voor de beeldvormng van de ELANA techniek heb ik veelvuldig gebruik mogen maken van de kunde en kunst van onze afdeling Medische Technologie en Multimedia.

Beste Wim, beste Chris, hartelijk dank voor die prachtige foto's van onze modellen, de konijntjes, de varkentjes en natuurlijk van onze patiënten!

De staf van de afdeling Keel-, Neus-, Oorheelkunde van het UMC St Radboud, met name professor K. Graamans en professor C. Cremers, wil ik bedanken voor het feit dat zij mij hebben willen aannemen in de opleiding tot Keel-, Neus-, Oorarts. Ik heb er zin in!

Mijn "nieuwe" collega-assistenten wil ik bedanken voor het feit dat ik nu al ontzettend veel van jullie geleerd heb, en natuurlijk dat de samenwerking zo plezierig verloopt!

Lieve vrienden, dank voor jullie vriendschap en steun en de culinaire hoogstandjes.

Mijn ouders wil ik bedanken voor het feit dat zij mij in de gelegenheid hebben gesteld om geneeskunde te gaan studeren.

Beste René, beste Tim, ons verbindt veel meer dan de geneeskunde en wetenschap samen. Dat jullie als paranimf naast mij staan betekent heel veel voor mij!

Lieve Margriet en Anton, jullie betrokkenheid en steun bij het mogelijk maken van dit proefschrift is moeilijk voldoende op waarde te schatten! Ik ben daar ontzettend blij mee.

Liefste Jaike, ik kan mij geen fijnere levenspartner dromen. Dit boekje is óók jouw verdienste omdat jij zóveel voor mij hebt opgevangen! Ik dank je voor wie je bent en dat jij bij me bent. Met rozen zijn wij begonnen, met rozen gaan we nu genieten. Vanaf nu is voor ons beiden.

Lieve God, U wil ik danken voor al dat moois op aarde. Het is fijn om hier te zijn.

Henk Johan N. Streefkerk

Malden, september 2005

Curriculum Vitae and Publications

Curriculum Vitae

Henk Johan N. Streefkerk was born on Octobre 27, 1974 as Nanang Abdi Arifianto in Malang in Indonesia. Five months later he was adopted by his Dutch parents and came to The Netherlands. In 1992 obtained the V.W.O. diploma (Gymnasium β) at the Christelijk Lyceum Zeist in Zeist. Medical school was commenced at the Utrecht University. During his studies, he worked as a student-assistent at the departments of anatomy and celbiology (courses Anatomy, Neuro-anatomy, Endocrinology, and Celbiology). In the fourth year, a research project was started at the department of Neurosurgery at the University Medical Center in Utrecht (UMC Utrecht)("The High Flow Cerebral Bypass; A Study On Flowmetry", supervision by Prof. dr. C.A.F. Tulleken en dr. A. van der Zwan). Immediately after obtaining his M.Sc., he started with the research described in this thesis, made possible by the Catharijne Stichting and the Hersenstichting Nederland. In order to support the widespread use of the ELANA technique among Dutch and International neurosurgeons, the ELANA course was developed, a handbook (Companion) to the ELANA technique was made, and he worked as a trainer for the ELANA course at the common animal experimental laboratory in Utrecht. A website for the ELANA technique was developed and taken over by the ELANA company. For presentation purposes, a 3D animation of the ELANA technique was made, which has now frequently been used for scientific presentations, medical programs, and commercials in The Netherlands, Finland, Zwitserland, and the United States (NBC). After finishing the scientific research he also finished medical school in 2004 (M.D.). He also found his mother in Indonesia, and met her for the first time. Later, he worked as a medical advisor for the ELANA company. At the moment of writing, he is a resident at the department of Otorhinolaryngology at the Radboud University Medical Center in Nijmegen, The Netherlands (supervisor: Prof. dr. K. Graamans). He is married (2000) to Jaike Wolfkamp, and has two children (Aimee and Anton, both born 2003).

Curriculum Vitae

Henk Johan Nanang Streefkerk werd op 27 oktober 1974 geboren als Nanang Abdi Arifianto te Malang in Indonesië. Vijf maanden later werd hij door zijn Nederlandse ouders geadopteerd en kwam vervolgens naar Nederland. In 1992 behaalde hij het V.W.O. diploma (Gymnasium β) aan het Christelijk Lyceum Zeist te Zeist. De studie geneeskunde werd aansluitend begonnen aan de Rijksuniversiteit Utrecht. Tijdens de studie geneeskunde werkte hij als student-assistent bij de vakgroepen anatomie en celbiologie (Anatomie, Neuro-anatomie, Endocrinologie, en Celbiologie). Vanaf het vierde studiejaar werd een wetenschappelijke stage verricht op de afdeling neurochirurgie van het Universitair Medisch Centrum Utrecht (UMC Utrecht)("The High Flow Cerebral Bypass; A Study On Flowmetry" o.l.v. Prof. dr. C.A.F. Tulleken en dr. A. van der Zwan). Direct na zijn doctoraal examen in 1999 werd aangevangen met het onderzoek dat tot dit proefschrift heeft geleid, waarbij de Catharijne Stichting de aanstelling als onderzoeker mogelijk heeft gemaakt, gesteund door de Hersenstichting Nederland. In het kader van het onderzoek en de verspreiding van de ELANA techniek onder nederlandse en buitenlandse neurochirurgen werd de ELANA course ontworpen, een handboek (Companion) gemaakt voor de techniek, en was hij ook werkzaam als trainer van de ELANA course in het gemeenschappelijk dierenlaboratorium in Utrecht. Daarbij is er een website ontworpen die thans door de ELANA B.V. is overgenomen. Ten behoeve van de presentatie van de ELANA techniek is er een 3D animatie van de techniek gemaakt, welke nu veelvuldig is gebruikt; onder andere voor wetenschappelijke presentaties, medische programmas en commercials in Nederland, Finland, Zwitserland, en de Verenigde Staten. Na het beëindigen van het onderzoek heeft hij in 2004 zijn studie geneeskunde afgerond. Overigens heeft hij toen ook zijn moeder in Indonesie weer ontmoet. Hierna is hij in dienst geweest bij de ELANA B.V. als medisch adviseur. Op dit moment is hij in opleiding tot Keel-, Neus-, Oorarts in het Radboud Universitair Medisch Centrum in Nijmegen (opleider: Prof. dr. K. Graamans). Hij is getrouwd (2000) met Jaike Wolfkamp, en heeft twee kinderen (Aimée en Anton, beide in geboren in 2003).

List of publications

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3. Companion to the ELANA Technique 2005. H.J.N. Streefkerk, C.A.F. Tulleken (editors). Annemarie Tulleken Foundation Utrecht 2005. In press.
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11. Companion to the ELANA Technique. H.J.N. Streefkerk, A. van der Zwan, R.M. Verdaasdonk, C.A.F. Tulleken. Annemarie Tulleken Foundation Utrecht 2001.
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