

ASSESSMENT OF CAROTID ENDARTERECTOMY

By

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From

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Michael Ellis Gaunt
June 1995

Dedicated to Ann and Elizabeth

"You may think you know something about something, but unless you can measure it your knowledge is of a very meagre kind"

Lord Kelvin of Largs (1824-1907)

Yet had Fleming not possessed immense knowledge and an unremitting gift of observation he might not have observed the effect of the hyssop mould. 'Fortune', remarked Pasteur, 'favours the prepared mind.'

Andre Maurois (Emile Herzog; 1185-1967)

Abstract : Assessment of Carotid Endarterectomy

Michael Ellis Gaunt. BSc. MB. ChB. FRCS (Eng). FRCS (Ed).

A major cause of perioperative strokes during carotid endarterectomy is intraoperative embolisation. Previous studies have identified that intraoperative embolisation can be detected by monitoring with transcranial Doppler sonography (TCD). However, these studies were unable to demonstrate a convincing link between embolisation and the development of neurological deficits and therefore, the clinical relevance of these TCD detected emboli remained uncertain. This study aimed to accurately determine the incidence and clinical relevance of TCD detected intraoperative embolisation during carotid endarterectomy. To do this 100 consecutive patients undergoing carotid endarterectomy were monitored with TCD. To assess the clinical impact of intraoperative embolisation all patients underwent the following pre- and postoperative assessments: neurological and cognitive function; retinal fundoscopy and automated visual fields; CT and MRI brain scans. During analysis of the intraoperative TCD recordings the operation was divided into its constituent stages and for each stage the number and character of emboli were determined. It was found that the majority of intraoperative emboli were characteristic of air and not associated with an adverse clinical outcome. However, emboli occurring during the dissection and recovery stages of the operation were characteristic of particulate emboli and associated with the development of neurological and cognitive deficits. In particular, gross, persistent particulate embolisation during the recovery phase of the operation heralded early carotid artery thrombosis and was associated with the development of major neurological deficits. The TCD detection of particulate emboli occurred before the development of neurological signs and with early operative intervention to correct the defect, neurological deficit could be avoided. This finding represents an important new clinical application of TCD monitoring and provides direct clinical evidence for the role of platelet emboli in the aetiology of stroke.

The second part of the study was concerned with comparing methods of quality control to detect technical defects which may lead to embolisation. The techniques compared were Angioscopy, B-mode ultrasound, continuous wave Doppler and TCD. Angioscopy detected major technical errors in 12 patients (4 intimal flaps, thrombus in 8). TCD detected shunt malfunction in 13 patients (2 potentially serious) in addition to particulate embolisation detected during dissection and recovery. Continuous wave Doppler and B-mode ultrasound images were technically inadequate in 9 and 24 patients respectively and neither technique altered clinical management.

Therefore it was concluded, that a combination of TCD monitoring and completion angioscopy provided the maximum yield in terms of diagnosing technical error and establishing the cause of perioperative morbidity and mortality.

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ABBREVIATIONS

↑ or ↓	increase or decrease
+/-	with or without
7/0, 6/0 etc.	gauge of suture thickness
ACA	anterior cerebral artery
AF	amaurosis fugax
BA	basilar artery
BMU	B-mode ultrasound
CABG	coronary artery by-pass graft
CBF	cerebral blood flow
CCA	common carotid artery
CEA	carotid endarterectomy
CI	confidence intervals
CIA	confidence interval analysis
CO ₂	carbon dioxide
CRAO	central retinal artery occlusion
CT	computerised tomogram
CWD	continuous wave Doppler
DAT	digital audio tape
dB	decibel
Dis	Dissection
DNA	deoxyribonucleic acid
DP	distal patch
DUR SH	during shunting
EC - IC bypass	extracranial artery to intracranial artery bypass
ECA	external carotid artery
ECA FL	restoration of flow through the external carotid artery
ECST	European carotid surgery trial
EEG	electroencephalogram
FFT	fast Fourier transforms
i.u.	international units
ICA	internal carotid artery
ICA FL	restoration of flow through the internal carotid artery

IOND	intraoperative neurological deficits
IR	inversion recovery
LMN	lower motor neurone
LSV	long saphenous vein
MANIP	manipulation of the artery phase
Mb	megabyte
MCA	middle cerebral artery
MCAV	middle cerebral artery velocity
MHz	megahertz
MI	myocardial infarct
MP	mid-patch
MRI	magnetic resonance imaging
NASCET	North American symptomatic carotid endarterectomy trial
NIH	National Institute of Health (USA)
NMR	nuclear magnetic resonance
O ₂	oxygen
op	operation
P1	first part of posterior cerebral artery
P2	second part of posterior cerebral artery
PC	personal computer
PCA	posterior cerebral artery
PDGF	platelet derived growth factor
PP	proximal patch
PTFE	polytetrafluoroethylene
RAM	random access memory
RDS	Rankin disability scale
REC	recovery phase
RF	radiofrequency
SE	spin echo
secs	seconds
SH OP	shunt opening
SR	saturation recovery
SSEP	somatosensory evoked potentials

T	tesla
T1	Time 1 (MRI)
T2	Time 2 (MRI)
TCD	transcranial Doppler
TCO	transcerebral oximetry
TGF - B	transforming growth factor B
UMN	upper motor neurone
VA	vertebral artery
WC	Wechsler concentration
WOA	Wechsler orientation A
WOB	Wechsler orientation B
WLM	Wechsler logical memory
WDS	Wechsler digit span
WPA	Wechsler paired associate

PUBLICATIONS ARISING FROM THIS THESIS

PUBLISHED PAPERS

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**PART THREE: A Comparison of Quality Control Methods
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PART ONE : CHAPTER 1

STROKE AND CAROTID ARTERY SURGERY

CHAPTER 1

STROKE

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1.1 Introduction

In this first chapter the terms used to describe the different forms of stroke will be defined. The importance of stroke as a major cause of morbidity and mortality will be emphasised by reference to epidemiological data provided by studies from the UK and around the world. The aetiology and pathogenesis of stroke will be outlined, starting with a description of the anatomy of the extracranial and intracranial circulation and proceeding through the mechanisms leading to stroke to a brief description of the theories pertaining to the development of atheromatous plaque at the carotid bifurcation. Data will be presented describing the evolution of theories related to the mechanism of stroke which eventually formed the rationale for surgical treatment of carotid artery disease. Finally, a description will be given of the role of stroke in shaping world events by its effect on prominent figures throughout history.

1.2 Definitions [Bannister, 1985; Whisnant *et al*, 1990]

Stroke is a focal neurological deficit due to a vascular lesion. It is usually of rapid onset and, by definition, lasts longer than 24 hours if the patient survives.

A stroke is said to be 'completed' when the deficit has reached its maximum, usually within 6 hours of onset. It is 'in-evolution' when it is becoming worse, usually within 24 hours of onset.

The signs are those of an acute upper motor neurone lesion of one side, including the face. Aphasia is usual when the dominant hemisphere is affected. The limbs are at first flaccid and areflexic. Headache is unusual and consciousness is not lost. After a variable period the reflexes recover and become exaggerated, and an extensor plantar response appears.

Transient Ischaemic Attack (TIA). This is a focal neurological deficit lasting less than 24 hours. There is complete recovery. The attack is usually of sudden onset and is caused when blood flow through the internal carotid artery or one of its branches is temporarily interrupted. A hemispheric TIA results, with symptoms referable to the corresponding neural tissues affected. Patients usually have sudden weakness and numbness of the arm, face or leg contralateral to the area of vascular compromise. Dysphasia and hemineglect may also occur.

Amaurosis fugax consists of monocular visual symptoms, usually a 'shutter-like' loss of vision and results from transient compromise of the ophthalmic artery, the first branch of the internal carotid artery.

Vertebrobasilar TIA occurs with episodic interruption of flow through the basilar or vertebral arteries or their branches. Symptoms, including dizziness, diplopia and ataxia, are less stereotypical, making diagnosis difficult.

1.3 Epidemiology of Stroke

Incidence and prevalence of stroke

Each year 130,000 people in the UK suffer a stroke. Stroke is the single most common cause of physical disability and the third biggest cause of death in this country. In the UK, stroke accounted for 12% of all deaths in 1990 [Health of the Nation, 1993]. In the under 65 age group the death rate stroke was 12.5/100,000 population but in the over 65s the death rate rises to 265/100,000. The incidence of stroke in the UK is 195/100,000 population [Oxfordshire Community Project, 1983] and the prevalence of stroke patients in the community is 486/100,000 [Marquardsen, 1980].

The reported incidence of stroke in the USA is 200/100,000 population, with a death rate of approximately 50%. The disease is more common in men and the incidence increases with age from 300/100,000 men aged 55 to 64 years to 1440/100,000 men aged 75 to 84 years [Moore *et al.* 1992]. Approximately two thirds of those individuals who survive stroke for 1 month are permanently disabled to some degree. Stroke prevalence rates have identified two million surviving stroke victims in the USA. Nearly one half of the strokes appeared in the distribution of the carotid artery and most were associated with an atherosclerotic plaque occurring within 3 cm of the bifurcation of the common carotid artery [Moore *et al.* 1992].

Data pooled from number of large community based sources including the Harvard Stroke Registry [Mohr *et al.* 1978], the Lausanne Stroke Registry [Bogousslansky *et al.* 1988], and the Oxfordshire Community Project [Henrich *et al.* ; Sandercock *et al.* 1989] indicates that one third of strokes have an embolic source due to major atheromatous disease and about an equal number have a cardiac source. Of the final third, one stroke in four is attributable to

Stroke

lacunar infarction due to obstruction of lenticulostriate arteries and arterioles and the remainder are due to less common causes, dissections, fibromuscular dysplasias, atheroembolic embolism from the aorta [Karalis *et al.* 1991], or immune-mediated coagulation abnormalities: antiphospholipid antibodies [Barnett, 1993].

Risk Factors For Stroke

Risk factors were first identified by the Framingham study and confirmed by more recent studies [Wolf *et al.* 1986; Sandercock *et al.*, 1989]. The commonest risk factor is age with more than doubling of incidence rates (for all strokes) for each successive decade [Wolf *et al.*, 1989]. Hypertension is the second most common risk factor and this risk operates irrespective of age or sex and throughout the range of blood pressure. Definite hypertension (systolic BP>160 and diastolic >95) triples the rate of atherosclerotic brain infarction [Wolf *et al.*, 1989]. However control of hypertension reduces stroke occurrence as well as stroke mortality [Wolf *et al.*, 1989].

Cardiac impairment ranks as a third risk factor [Wolf, 1990; Wolf *et al.*, 1989]. The Framingham study showed that at any level of blood pressure subjects with cardiac disease have more than twice the risk of stroke [Wolf *et al.*, 1989]. Diabetes mellitus and cigarette smoking are independent risk factors with a relative 3-fold and 1.5-fold increased risk respectively [Wolf *et al.*, 1986; Shinton *et al.*, 1989].

Transient ischaemic attacks (TIAs) precede about 10% of strokes [Wolf *et al.*, 1986; Sandercock *et al.*, 1989; Dennis *et al.*, 1989]. Preceding TIAs occur in about 50% of patients with atherothrombotic infarction, in 20% with lacunar infarction and in approximately 10% of all cerebral emboli [Toole, 1990].

Economics of Stroke

In the USA the economic burden of stroke is enormous and rapidly escalating costing an estimated 15.9 to 20.6 billion dollars annually. In a recent Massachusetts study the cost for a male stroke victim of age 35 to 54 years was more than \$188,000 per patient [Wolf *et al.* 1989].

In the UK, a study of the cost of stroke to the NHS performed in three District Health Authorities in the South East Thames region identified that in-patient care was responsible for 93% of overall cost for stroke [Bryan *et al.* 1993]. This

Stroke

consisted of £100-£150/day for each patient who stayed in hospital for a median time of 30 days. Out-patient care, physiotherapy, speech therapy and occupational therapy, CT scan and GP care accounted for 5% of total cost. While only a small minority of strokes are referred by the GP to hospital, inpatient costs for stroke is an estimated £5 billion pounds per year [Bryan *et al*, 1993].

For the population as a whole the incidence of stroke is gradually decreasing however the elderly population as a proportion of the whole population is increasing. Therefore it is likely that the numbers of strokes will increase and stroke costs will continue to rise [Rose FC. 1993].

Incidence of Strokes/TIAs suitable for CEA

The incidence of TIA in the UK is 20,000 per annum while the number of minor strokes is 30,000 per annum [Dennis, Warlow. 1991]. These 50,000 patients may be considered suitable for further investigation with a view to surgery. 68% of these are under 75 years of age and 80% of those have carotid atherosclerosis. However only 20% have severe carotid stenosis in the range 70-99% and this leaves approximately 6000 patients suitable for carotid endarterectomy. If one considers the results of recent multicentre trials on the mortality and morbidity avoided by carotid endarterectomy one can estimate that operating on 6000 patients will avoid approximately 600 strokes a year [Warlow, 1993].

In addition to the economic benefits of preventing strokes there are considerable social and personal benefits to the individual patients and their families. These benefits are difficult to quantify but cannot be ignored when assessing the relative risks of differing treatment modalities.

The evidence described above establishes the position of stroke as a major health problem in medical, sociological and economic terms. The occurrence of a stroke has major implications on all those fronts for the patient, his family and society.

In order to understand the aetiology of strokes and the surgical basis for treatment a thorough knowledge of the vascular anatomy of the head and neck is required. This will now be described in detail.

1.4 Anatomy of the Extracranial and Intracranial Circulation (Gray's Anatomy)

The blood supply of the brain comes from four main arteries, the two anterior carotid arteries and two posterior vertebral arteries. The common carotid arteries differ in length and in their mode of origin. The right artery begins at the bifurcation of the brachiocephalic artery behind the right sternoclavicular joint and is confined to the neck. The left artery springs from the highest part of the arch of the aorta immediately behind and to the left of the brachiocephalic artery and therefore consists of a thoracic and a cervical portion. The cervical parts of both the common carotid arteries have similar courses from the sternoclavicular joint to the level of the upper border of the thyroid cartilage where they bifurcate into the internal and external carotid arteries. The external carotid artery branches supply blood to the structures of the face and neck. The internal carotid artery (ICA) supplies the greater part of the cerebral hemisphere, the eye and its accessory organs and sends branches to the forehead and nose. The ICA has no branches in the neck but it ascends to the base of the skull, and enters the cranial cavity through the carotid canal in the petrous temporal bone. It then runs forward through the cavernous sinus, lying in the carotid groove on the side of the body of the sphenoid bone, and ends below the anterior perforated substance of the brain by dividing into the anterior and middle cerebral arteries. In the petrous bone the ICA has two small branches, the caroticotympanic and the pterygoid. In the cavernous sinus cavernous branches supply the trigeminal ganglion and the walls of the cavernous and inferior petrosal sinuses. Anastomoses occur with branches of the middle meningeal artery. The hypophyseal branches supply the pituitary gland and the meningeal branch supply the dura of the anterior fossa. Anastomoses occur with the posterior ethmoidal artery. From the cerebral part of the ICA, as it emerges from the cavernous sinus, the ophthalmic artery branches off to supply the eye. The ophthalmic artery itself has 18 branches which supply not only the retina and eye but also the eyelids, lacrimal gland, sinuses and the nose. Numerous anastomoses occur with branches of the external carotid artery which can act as a source of collateral blood supply in cases of internal carotid artery occlusion.

The terminal branches of the ICA are the anterior cerebral artery (ACA) and the middle cerebral artery (MCA). The anterior cerebral artery is the smaller of the two branches and passes forward, above the optic nerve to the commencement

of the longitudinal fissure. Here it comes into close relationship with the opposite artery and is joined by a short transverse trunk called the anterior communicating artery. From this point the two ACAs run side by side in the longitudinal fissure, curving around the genu of the corpus callosum, and running backwards along the upper surface of the structure to its posterior extremity, where they end by anastomosing with the posterior cerebral arteries. The ACAs give off both central and cortical branches. In particular the frontal branches supply the 'leg area' of the motor cortex.

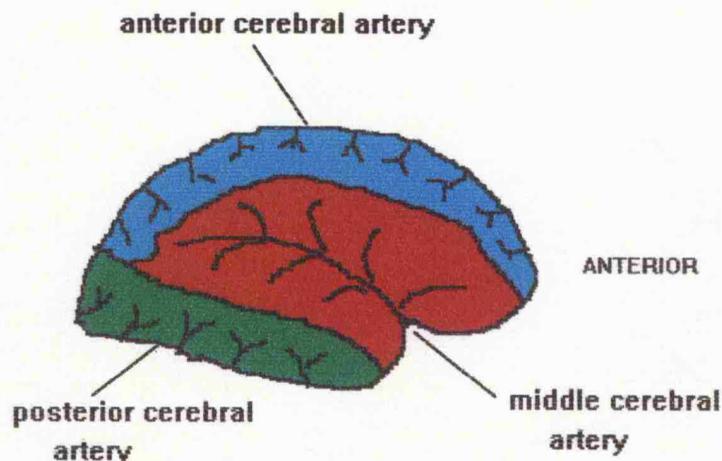


Figure 1.1 Illustration showing the lateral surface of the cerebral hemisphere and the areas supplied by the cerebral arteries.

The MCA runs first laterally in the lateral cerebral sulcus and then backwards and upwards on the surface of the insula, where it divides into branches which are distributed to the insula and to the lateral surface of the cerebral hemisphere. The central branches are small arteries from the commencement of the MCA which enter the substance of the brain through the anterior perforated substance. They are arranged in two sets: the medial striate arteries ascend through the lentiform nucleus, and supply it, the caudate nucleus, and the internal capsule; the lateral striate arteries, ascend over the lower part of the lateral aspect of the lentiform nucleus (in the external capsule) and then, bending medially, traverse this nucleus and the internal capsule to supply the caudate nucleus. One of this group is larger than the rest and is liable to rupture. The cortical arteries supply the orbital area of the frontal lobe. The

Stroke

The frontal branches supply the precentral and the middle and inferior frontal gyri. The parietal branches supply the postcentral gyrus, the lower part of the superior parietal lobule and the whole of the inferior lobule. The temporal branches supply the lateral surface of the temporal lobe. Therefore the cortical branches of the MCA supply the motor area (excluding the 'leg area') of the cerebral cortex, its corresponding somesthetic area and the auditory area.

The posterior communicating artery runs backward from the internal carotid above the oculomotor nerve, and anastomoses with the posterior cerebral, a branch of the basilar artery. It is frequently larger on one side than on the other. A few small central branches pierce the brain to supply the thalamus. The anterior choroidal artery is a small but constant branch which leaves the ICA near the posterior communicating artery to supply the crus cerebri.

The Circulus Arteriosus (circle of Willis)

The circle of Willis is an anastomosis between the two vertebral arteries and the two internal carotid arteries. This circle is situated in the cisterna interpeduncularis at the base of the brain and encloses the optic chiasma and the contents of the interpeduncular fossa. It is formed as follows: the two anterior cerebral arteries are joined to each other by the anterior communicating artery.; behind the basilar artery divides into the two posterior cerebral arteries, each of which is joined to the internal carotid artery of the same side by the posterior communicating artery. However there are numerous variations and some arteries are frequently absent or hypoplastic and the circle incomplete. The anomalies were summarised in a review of published studies which identified that in approximately 90% of circles there is a complete 'circular' channel but in a large majority of cases one or other of the formative vessels is sufficiently narrowed in calibre to cast doubt on its functional value as a collateral route [Fields *et al*, 1965]. The proximal segment of the posterior cerebral artery is particularly labile being often much reduced or even absent. Similarly the proximal segment of the anterior cerebral artery is similarly affected.

Stroke

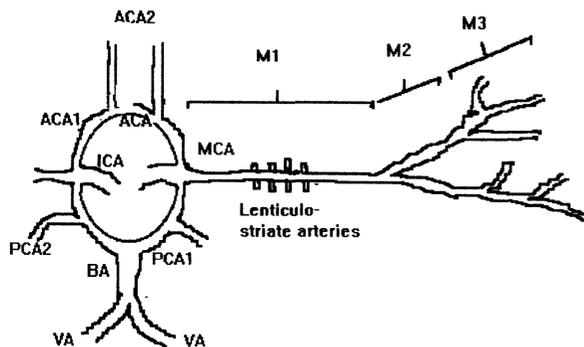


Figure 1.2 : Diagrammatic representation of circle of Willis and middle cerebral artery. ICA = internal carotid artery; MCA = middle cerebral artery; M1,M2,M3, = major divisions of MCA; ACA1 = 1st part of anterior cerebral artery; ACA2 = 2nd part anterior cerebral artery; PCA1 = 1st part of posterior cerebral artery; PCA2 = 2nd part posterior cerebral artery. ACA = anterior communicating artery. VA = vertebral artery; BA = Basilar artery.

The anterior and posterior communicating arteries are also, commonly hypoplastic or absent. Angiographic evidence suggests that defective or absent collateral circulation of this kind may be encountered in one third of individuals [Sedzmir, 1959].

1.5 Pathology and Pathogenesis

The underlying pathology predisposing patients to stroke is atherosclerosis and in particular the formation of the atheromatous plaque at the carotid bifurcation.

There are three principal lesions of atherosclerosis; the fatty streak, the gelatinous plaque and the fibrous plaque [Solberg, Eggen, 1971] Formation of atherosclerotic plaque is thought to be underway by the teenage years. Fatty streaks become visible within the intima of large- and medium-sized vessels consisting of subintimal deposits of lipid within macrophages and smooth muscle cells [Stary, 1983]. Both gelatinous plaque and fatty streak are considered to be the precursors of atherosclerotic plaques as they develop at the same anatomical sites [Leary, 1941; Robertson *et al.* 1963].

The fatty streak appears as a minimally raised yellow lesion and tends to affect vessels such as the carotid, superficial femoral, infrarenal aorta and coronary arteries more frequently than the subclavian, profunda femoris or brachial arteries. Vessels of conduction, points of origin of side branches or bifurcations

bifurcations appear to develop atherosclerosis more commonly than vessels of supply. At present it is generally believed that only a minority of fatty streaks progress to form fibrous plaques, the remainder either do not progress or do not change with time [McMillan, Lusby, 1993].

The gelatinous plaque is characteristically composed of extra-cellular matrix and fluid; the gelatinous plaque has a relatively low lipid content [Smith, Staples, 1988; Smith, 1988] and is more commonly found in the infra renal aorta.

Fibrous plaque consists of a varying number of smooth muscle cells, macrophages, connective tissue including collagen, and extracellular lipid deposits. Both cell types within the plaque become swollen with lipid globules forming foam cells. The lipids within the fibrous plaque occur mainly as cholesterol esters and oxysterols. The lipids are also found lying in an extracellular location close to the internal elastic lamina [Hata *et al*, 1974]. Some fibrous plaques undergo degeneration, with formation of a complex plaque consisting of areas of necrosis and calcium precipitates. A fibrous cap often forms over collections of cholesterol and free lipid deposits, creating an inherently unstable plaque which may eventually rupture [Friedmen, van Den Bovenkamp, 1966; Davies, Thomas, 1984; Bock, Lusby, 1992].

Pathogenesis of Carotid Plaque Formation

Three basic mechanisms have been proposed to explain the development of atherosclerosis. They are: (1) the thrombotic; (2) the endothelial damage/platelet and; (3) the insudation of plasma theory.

Rokitansky proposed that atherosclerosis resulted from the repeated deposition of blood components on the arterial intima which then became incorporated into the vessel wall leading to fibrous tissue formation - the thrombogenic theory [Rokitansky, 1852]. The observation that adhesion of microthrombi to coronary vessel wall is a very common event lent support to this theory [Duguid, 1946]. The majority of such thrombi are removed by fibrinolysis however there is evidence that thrombi may persist in areas of disturbed endothelial function in the absence of ulceration of the intimal layer [Lusby *et al*, 1982]. Areas of disturbed blood flow, as exhibited at the site of vessel bifurcation are associated with increased endothelial cell turnover and disturbed function allowing microthrombi to accumulate. Thrombus is a rich

Stroke

source of platelets which can release a number of growth factors or mitogens including platelet derived growth factor (PDGF) which stimulates smooth muscle cell recruitment and proliferation. Platelets also secrete transforming growth factor-B (TGF-B) which also has a role in connective tissue synthesis. Endothelial cells can also secrete a variety of mitogens including PDGF on exposure to activated coagulant factors such as activated factor X or thrombin [McMillan, Lusby 1993].

Therefore the deposition of thrombus on the luminal surface can initiate some of the known mechanisms critical to atherogenesis and is compatible with the presence of observed blood products within fibrous plaque. However, the amount of lipid present in such lesions is in general greater than could be derived from thrombi and therefore it is generally concluded that thrombi play little part in the basic atheromatous process [Born, 1992].

Endothelial injury has been proposed as an important factor in the development of the atherosclerotic plaque [Ross, 1981; Ross, 1986]. Endothelial damage allows lipoprotein influx and the adherence of circulating platelets and monocytes -The Response to Injury Theory [Ross, 1981]. Platelets release several smooth muscle cell mitogens [Ross *et al.* 1974; Oka, Orth, 1983] and it is known that proliferation of smooth muscle cells, vital to the development of atherosclerosis, is reduced if platelets are absent from the circulation [Moore *et al.* 1976; Friedman *et al.* 1977].

However, evidence exists that atheroma can develop in the absence of endothelial denudation [Ross, Wright, 1984; Ross, 1986; Ross *et al.* 1986]. In animal studies, leucocytes (monocytes and lymphocytes) have been observed to adhere to the endothelial surface and subsequently migrate between endothelial cells to a subendothelial location. Monocytes have the capacity to internalise lipoproteins as a result of trans-endothelial transport, eventually forming foam cells [Brown, Goldstein, 1983]. Monocytes are an important component of the inflammatory reaction within plaques with the ability to damage neighbouring cells by secreting toxic substances and to stimulate connective tissues growth by secretion of fibroblast growth factors [Leslie *et al.* 1984; Dohlman *et al.* 1984]. At a later stage, smooth muscle cells migrate from the media and accumulate in the intima where they also acquire lipid deposits forming foam cells. However, at present, there is no clinical or pathological evidence of this experimental lesion occurring in humans.

The insudation of plasma theory proposes that lipid accumulates in plaque by the normal physiological insudation of plasma lipoproteins, however the lipid is biochemically altered by endothelial cells and macrophages creating acetylated and oxidised derivatives [Steinberg *et al*, 1985]. The modified lipids, mainly derived from low density lipoproteins [Stenders, Siversmit, 1981], accumulate in macrophages and smooth muscle cells forming foam cells. A humoral response and the presence of T-lymphocytes may contribute to the inflammatory reaction within plaque. Many of these T-cells seen within fibrous plaque are in an activated form and therefore are able to secrete a number of cytokines, e.g. interferon (IFN) or IL-1. These factors can induce further cellular recruitment and proliferation contributing to progression of the atherosclerotic lesion. In particular, IL-1 can induce endothelial cells to secrete and express the gene for PDGF, the mitogen which stimulates smooth muscle cell infiltration and proliferation. The antigen responsible for this cellular immune response is unclear. However modified lipid is a potential candidate [McMillan, Lusby 1993].

In addition to cellular mechanisms it is likely that haemodynamic forces play an important role in the site of atherogenesis, in the natural history of plaque and the production of symptoms. Endothelial ulceration of the intima can result from altered haemodynamics of flow or from degenerative breakdown within an increasingly heterogeneous plaque. Localised thrombosis may occur over the complex plaque, possibly due to exposure to thrombogenic subintimal collagen or as a result accumulation of damaged blood elements in areas adjacent to turbulent flow [Imparato *et al*, 1979]. Thrombi are frequently found in association with carotid plaque ulceration or fracture [Lusby *et al*, 1982] but this is usually a secondary event. Arterial thrombosis follows platelet aggregation at the site of endothelial breakdown, forming cellular masses, which may give rise to distal emboli or arterial occlusion.

Atherosclerotic lesions especially complex plaque, have a predilection for formation at bifurcations. Autopsy and angiographic studies of the carotid bifurcation have shown that carotid plaque commonly forms on the outer wall of the carotid sinus opposite the external carotid artery [Bauer *et al*.1962; Solbert *et al*.1971]. In a series of experiments [Zarins *et al*.1983,1992; Ku *et al*. 1983, 1985] it was demonstrated that areas of flow separation, low shear stress, slow clearance and flow oscillation occurred at the outer wall of the carotid bulb and

these findings correlated with the development of the early atherosclerotic plaque. Zarins suggested that oscillating shear stress increases endothelial permeability producing an increased ingress of plasma constituents into the subintima [Zarins *et al.* 1983].

Smooth muscle cells are the principal cellular element of the carotid plaque and the abnormal proliferation of smooth muscle cells is a key event in the formation of the atherosclerotic plaque. An important mitogen for cultured smooth cells is platelet derived growth factor (PDGF). In a series of in vitro experiments correlating haemodynamic forces and the growth and release of PDGF by smooth muscle cell, it was demonstrated that very low shear stress can facilitate abnormal proliferation of smooth muscle cells, and that high flow shear stress favours the release of PDGF-like mitogens [Sterpetti *et al.* 1993]. Therefore at arterial sites where both these forms of shear stress are present, e.g. carotid bifurcation, a paracrine form of interaction may occur which favours the formation of plaque.

Haemodynamic factors may also be important in the breakdown of the carotid plaque after it has formed leading to embolic symptoms. The pressure and velocity relationships of Bernoulli's principle are important, especially after stenosis reaches a point where flow is altered. In this situation, pressure in the stenotic segment falls while velocity increases in a proportional fashion. The resulting differential in pressure across the lesion can cause an 'unroofing' force on the plaque surface which is transmitted across the fibrous cap into the complex, unstable elements underneath. The combined effect of the high proximal pressure and the unroofing force generated just downstream can cause acute fracture of a plaque, with embolisation of its contents or progression to thrombotic occlusion [Bock, Lusby, 1992].

1.6 Mechanism of Stroke

Excluding uncommon causes (such as venous thrombosis, arteritis and arterial dissection), most strokes are caused by thrombosis of a vessel supplying neuronal tissues, embolus from a proximal vessel or the heart, haemorrhage or lacunar infarction resulting from thrombo-obliteration of small cerebral arteries secondary to hypertension [Mohr *et al.*, 1978. Bogousslavsky *et al.*, 1988. Timsit *et al.*, 1990. Henrich *et al.*, 1986. Sandercock *et al.*, 1989].

Thrombosis

Progressive narrowing of a vessel to the point of occlusion can result in a stroke if the brain tissue supplied by that vessel has insufficient collateral blood supply. Larger intracranial vessels may thrombose, leading to infarction in the absence of adequate collateral supply [Bock, Lusby, 1992]. Occlusion of the MCA gives rise to different patterns of infarction depending on the section of MCA affected, (Figure 1.1). Occlusion of M3 branches causes superficial cortical infarcts. Occlusion of M2 branches causes both subcortical and cortical infarcts. Occlusion of the M1 section causes infarction of the whole MCA territory. When occlusion occurs in a penetrating lenticulostriate artery which have an end-vessel pattern of blood supply a small wedge-shaped lacunar infarct in the basal ganglia or internal capsule often results. Thrombosis of the extracranial vessels may also occur, resulting in an abrupt reduction in cerebral flow and causing infarction in those areas without alternate blood supply. If flow is insufficient only to borderline areas between adjoining regions of vascular supply, a watershed infarct may result [Russell, Barucha, 1978; Whisnant et al, 1990].

Embolism

A variety of materials may abruptly embolise, occluding any of the cerebral vessels and causing a sudden reduction in flow identical to that seen in thrombosis. If the embolus remains long enough to cause neuronal cell death, stroke results. If the embolus disaggregates before this point, TIA occurs instead. Emboli may be composed of red cell or platelet aggregates, cholesterol crystals, fibrous material, atheromatous plaque calcium or the breakdown products of plaque rupture [Bock, Lusby, 1992].

Embolism may even result from a thrombotic cause when the internal carotid artery occludes the resulting thrombus propagates distally to the point of origin of the first branch, the ophthalmic artery, or to the circle of Willis. The tip of this propagated thrombus may break off, resulting in a vessel-to-vessel embolus to more distal cerebral vessels [Riles *et al*, 1994]. This thromboembolic mechanism may be responsible for strokes in patients with occlusion of the internal carotid artery. An occluded internal carotid artery can also embolise up a patent external carotid artery giving rise to the 'carotid stump syndrome'[Cassidy *et al*. 1992].

Vessel Occluded	Pattern of Infarction
ICA (no collateral flow)	Infarction of MCA and ACA territory.
ICA (collateral flow)	Watershed infarction: infarction of watershed areas with PCA and contralateral vessels.
MCA1	Infarction of MCA territory and lenticulostriate territory
MCA2	Subcortical and cortical infarcts within MCA territory
MCA3	Cortical infarcts in MCA territory.
Lenticulostriate arteries	Lacunar infarction in internal capsule

Table 1.1: Pattern of infarction caused by different levels of occlusion within the cerebral vasculature. ICA = internal carotid artery. MCA = middle cerebral artery (1,2,3 = major divisions proximal to distal). PCA = Posterior cerebral artery [Whisnant et al, 1990].

Intracranial Haemorrhage

Acute intracranial haemorrhage arising from subarachnoid or intracerebral vessels is the remaining major cause of stroke. Neuronal death results from increased intracranial pressure due to the space occupying properties of the haemorrhage and subsequent oedema; vasospasm is also implicated [Bock, Lusby, 1992].

1.7 Effects of Cerebrovascular Atherosclerosis: The Flow Vs Embolism Theories

In 1909, William Osler writing in Principles and Practice of Medicine attributed apoplectic stroke largely to cerebral haemorrhage, cases of cerebral infarction were attributed to intracranial occlusive disease and the role of extracranial occlusive disease was largely ignored [Osler, 1909]. This view dominated medical thinking for many years despite earlier reports by Gull [1855], Savory

Stroke

[1856], Broadbent [1871], Penzolt [1881] and indeed Chiari [1905] all of whom associated extracranial occlusive disease with cerebral ischaemia. This view was supported by an article by J. Ramsey Hunt writing in the American Journal of Medical Science in 1914 who reported that both partial and complete occlusions of the innominate or carotid arteries could be responsible for the symptoms of 'cerebral intermittent claudication' [Ramsey Hunt, 1914].

The development of the technique of cerebral arteriography marked a significant advance in the investigation of carotid artery disease. The technique was first described by Moniz in 1927 and in 1936 the first case of carotid artery thrombosis was diagnosed by arteriography by Sjoqvist [Moniz, 1927; Sjoqvist, 1936]. A further four cases were reported in 1937 and by 1951 101 cases diagnosed by this technique had been described in the literature [Moniz, 1927; Johnson, Walker, 1951]. The new technology of angiography provided visualisation of the neck vessels and since a high percentage of stroke patients were seen to have stenoses near the carotid bifurcation, the flow-reduction theory of cerebral ischaemia was proposed [Denny-Brown, 1951]. According to this theory, symptoms of cerebral insufficiency were caused by a combination of spasm of the cerebral vessels and distal flow reduction caused by a critical stenosis at the carotid bifurcation [Denny-Brown, 1951]. This provided an explanation of multiple transient episodes as well as focal cerebral infarction. Sympathetic ganglionectomy and vasodilators were used to combat spasm but achieved little if any success [Risteen, Volpitto, 1946; Millikan, 1965]. Despite this failure of medical treatment, further credibility was given to the theory by the success of a new surgical procedure, carotid endarterectomy, in preventing cerebral ischaemia by removing the stenotic lesion at the carotid bifurcation.

However, critical analysis of the theory revealed several paradoxes. Firstly it was noted that patients with TIAs almost invariably ceased experiencing episodic symptoms when the diseased vessel became occluded or when ligation was performed which should have increased symptoms by reducing blood flow even further. Transient drops in blood pressure, the most plausible mechanism by which such symptoms could be caused by a fixed stenotic lesion, were not found in patients experiencing TIA while under observation in hospital [Kendall, Marshall, 1963]. Also, cerebral blood flow was shown not to increase significantly after carotid endarterectomy, nor decrease significantly after occlusion or ligation [Adams *et al*, 1963]. Finally the international

randomised trial of a flow-enhancing surgical procedure, extracranial-intracranial bypass, was shown to be of no benefit in preventing strokes [EC-IC Bypass Study Group, 1985].

Embolisation to the brain of fragments of atherosclerotic plaque or thrombotic material arising in association with carotid lesions seemed to best explain the episodic and sudden nature of cerebral ischaemia. Embolisation could account for the relief of symptoms afforded by carotid endarterectomy, and for the resolution of transient ischaemic episodes seen with ligation or occlusion.

Direct evidence for the embolic theory was provided by the observation of emboli traversing the retinal vessels during attacks of amaurosis fugax [Fisher, 1959; Russell, 1961]. Also, patients describing the symptoms of amaurosis fugax were often found to have cholesterol deposits within the retina on fundoscopic examination [Hollenhorst, 1961. Russell, 1961]. Several clinical studies demonstrated that patients with complex or ulcerated carotid plaques were more likely to experience neurological symptoms than patients with smooth, uncomplicated lesions [Imparato *et al*, 1983. Lusby *et al*, 1982].

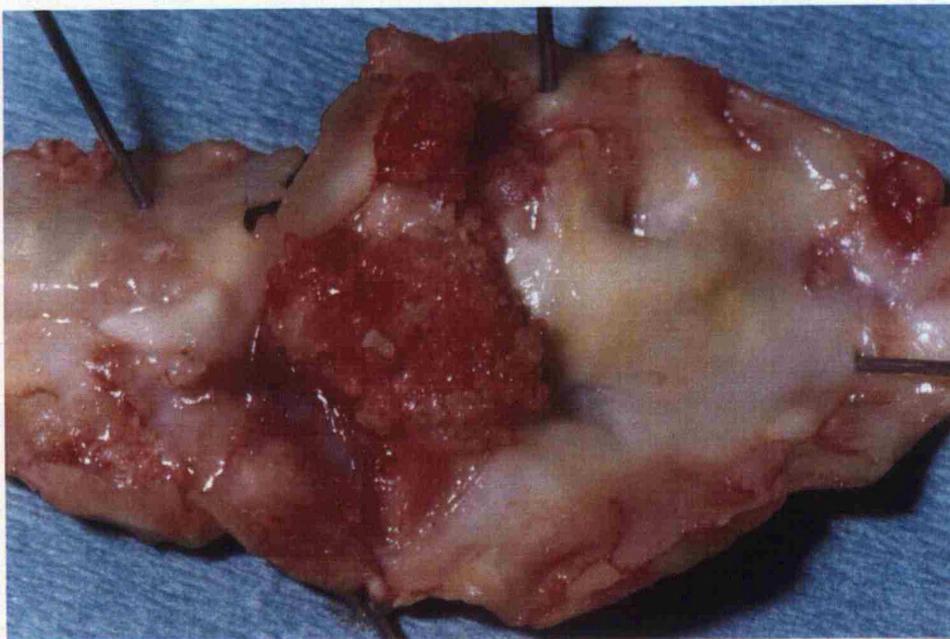


Figure 1.3: Picture of a typical, friable carotid plaque removed at carotid endarterectomy.

Therefore, the embolic theory has been accepted as the main mechanism of stroke associated with carotid artery stenosis. The operation of carotid

Stroke

endarterectomy prevents strokes by removing the source of emboli from the carotid bifurcation.

1.8 History of Stroke

The origin of the word "stroke" relates to the Ancient Greek view that the sudden loss of speech or the use of limbs was a punishment from the Gods. People were "struck down", "struck dumb" or struck blind as a punishment for their human sins. The term "apoplexy" was also used to describe these symptoms. People apoplectic with rage or grief are unable to co-ordinate an appropriate response to a situation, one of the most frustrating symptoms for any stroke patient.

Many important historical figures have suffered strokes and it is interesting to speculate on the effect of these occurrences on historical events.

Edward III, succeeded the throne of England at the age of 14 from his father Edward II in 1327. Edward III is most remembered for founding the Order of the Garter and also starting the Hundred Years War against France. Late in his life, after the death of his Queen, Phillipa in 1369, Edward resorted to a succession of mistresses, the most notable being Alice Perrers. In a summertime at Sheen in 1377, deserted by his family and irritated by priapism and shingles in addition to serious arterial disease, Edward had a terminal stroke. Alice Perrers quickly stripped the rings off his fingers and deserted him. Presumably the stroke was not of the dominant hemisphere as a priest found him some hours later and heard the King say "Miserere Jesu" before he died.

Charles II succeeded as King of England, Scotland and Ireland at the age of 19, after the execution of his father on January 30, 1649. Within a few days the Rump Parliament abolished the monarchy and Charles fled to France and England became a republic. However Parliament restored the monarchy in 1660 and Charles returned to England and was proclaimed King. Charles is said to have dabbled in experimental science but with little success. He died after a stroke on February 6, 1685 at Whitehall Palace and is buried in Westminster Abbey.

James II was the last Catholic monarch of England but he could not find enough Catholic followers to support him on the throne. When several Anglican Bishops were put on trial for sedition six English magnates asked

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William of Orange to contest the crown. William landed in Torbay and James rode to meet him. However, James was deserted by his generals, including Churchill, not yet Duke of Marlborough. James, unable to fight, left for Ireland where, eventually, he was defeated, but carefully not killed by the new King William at the battle of the Boyne on July 1, 1690. James died in exile 6 months after a paralytic stroke at St Germain, 1701.

George I ruled for 13 years until he died from a paralytic stroke in 1727, said to have been caused by indigestion from melons consumed when he was not fully recovered from sea-sickness. The exact mechanism remains obscure [Smith, 1974].

Louis Pasteur had a series of transient ischaemic attacks involving largely his speech, before he finally died in 1895 [Fields, Lemak, 1989].

In more modern times, Marshall Paul von Hindenburg's decision to authorise Hitler to form a cabinet in 1933 certainly altered the course of history. Theoretically von Hindenburg had the means to frustrate Hitler's rise to power in Germany but weakened by a stroke, from which he later died, von Hindenburg was either unable or unwilling to involve himself in controversy [Freidlander, 1972]. However, some historians argue that the seeds of the second world war were sown even earlier than this when American president Woodrow Wilson was incapacitated by a stroke. This led to America failing to sign the Treaty of Versailles and support the League of Nations. Wilson later died of a further stroke on 3 February 1924 [Freidlander, 1972].

Meanwhile, in Russia, Lenin had been responsible for installing Joseph Stalin into important political positions, but reports of Stalin's excessively violent methods were seen as a threat to Lenin's own leadership. Lenin wanted Leon Trotsky to assume a more prominent role and eventually become his successor. However before this could be achieved, Lenin suffered several transient ischaemic attacks eventually leading to a complete right hemiplegia and his death at the early age of 54. Stalin assumed power and Trotsky was forced into exile in South America where he was later assassinated by Stalin's agents [Fields, 1989].

Towards the end of the second world war Stalin met with Winston Churchill and Franklin Delano Roosevelt at Yalta to decided the shape of post-war Europe.

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Roosevelt had suffered from severe symptoms of cerebrovascular insufficiency for over two years and whether this affected the agreements and was the origin of the subsequent cold war is open to debate [Freidlander, 1972].

More recently President Dwight Eisenhower was said to have suffered from "little strokes" although he ultimately succumbed to the complications of ischaemic heart disease [Thomson, 1993]. Carlos Menem, President of Argentina, suffered a TIA in the departure lounge of an Argentinian airport. Clinical investigation showed that a severe carotid stenosis was the cause and a carotid endarterectomy cured him of symptoms.

In Britain, William Whitelaw, then deputy Prime Minister suffered a stroke in December, 1987. Whitelaw was said to be the only man Margaret Thatcher would listen to and was regarded by many as a restraining influence on her. The stroke forced his retirement and the remainder of the Thatcher administration was characterised by a succession of unpopular policies and acrimonious resignations of senior figures until her own resignation on Thursday 22nd November 1990 [Thatcher, 1993].

Finally, I recently met Professor Charles Robb at a Vascular Surgical Research meeting. Professor Robb and his colleague HHG Eastcott performed the first reported operation to remove a symptomatic carotid stenosis at St Mary's hospital, London in 1954. This landmark operation is acknowledged as the origin of modern carotid artery surgery for embolic disease. At this meeting Professor Robb still displayed a keen interest in carotid artery surgery, despite having undergone a carotid endarterectomy himself only six months before, performed by one of his former trainees with an obviously excellent result.

1.9 Summary

In this first chapter I have described the different forms of stroke and how they occur. A detailed description has been given of the anatomy of the extra/intracranial circulation which is important for the understanding of both the aetiology and surgical treatment of carotid artery disease. The importance of stroke as a major health problem has been emphasised by reference to epidemiological data which shows stroke to be the third commonest cause of death in this country, but perhaps more importantly, the biggest cause of major disability. The huge financial cost of stroke to both the individual and society

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has been described. This data has been used to provide justification both for surgical prevention and the need for the reduction of iatrogenic neurological deficits as a result of surgery to the absolute minimum.

In the following chapter I will describe the technique of carotid endarterectomy and the indications and the criteria for selection of patients suitable for surgery. The complications associated with this surgery will be described and then the monitoring and quality control methods available to try and reduce them.

CHAPTER 2

CAROTID ARTERY SURGERY

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2.1 Introduction

In chapter one I outlined the pathological basis for thromboembolic strokes arising from carotid bifurcation atherosclerosis. It was the understanding of the embolic nature of these strokes which led to the introduction of carotid endarterectomy to remove the atheromatous source of the emboli at the carotid bifurcation. However, the indications for performing the operation have remained controversial and it was not until the results of two large multicentre, randomised trials were published demonstrating a large benefit of CEA over the alternative medical therapy, that clear guidelines have emerged. The results of these two studies have had an enormous impact on the performance of carotid artery surgery and will be described and discussed in detail in this chapter.

The development of carotid surgery will be described from the early operations for trauma performed in the eighteenth century up to the modern day. I will then describe in detail the method of carotid endarterectomy used on all the patients in this study as a basis for a discussion of the alternative methods currently in use.

Finally, I will describe the complications that can arise from surgery and explore the various strategies for reducing the incidence of complications by the use of quality control and monitoring methods. The use of these methods to identify the causes of perioperative morbidity/mortality is central to the theme of this thesis.

2.2 History of Carotid Artery Surgery

The first recorded operations on the carotid arteries were ligation of the vessel as a result of trauma. John Abernathy is credited with the first deliberate ligation to control haemorrhage from a torn carotid artery following goring by the horn of a cow in 1798. The patient died 30 hours later of infection and Abernathy abandoned the procedure [Abernathy, 1804]. David Fleming, ships surgeon aboard HMS Tonnant performed the first successful ligation of the carotid artery on 17th October 1803. The patient had attempted suicide by cutting his throat [Keevil, 1949].

Carotid Artery Surgery

In 1805 Sir Astley Cooper ligated the carotid as treatment for an aneurysm and although the patient died, he repeated the operation in 1808, this time successfully [Cooper, 1836].

In 1809, Benjamin Travers ligated the common carotid artery for a carotid-cavernous fistula and by 1868 over 600 hundred cases of carotid ligation had been reported with a mortality of 43%, mostly attributable to post-operative infection and haemorrhage [Hamby, 1952].

Date	Surgeon	Procedure	Outcome
1798	Abernathy	carotid ligation-trauma	Died-stroke 30 hours
1803	Fleming	carotid ligation-trauma	Survived
1805	Cooper	carotid ligation-aneurysm	Died-sepsis
1808	Cooper	carotid ligation-aneurysm	Survived
1809	Travers	carotid ligation-carotid-cavernous fistula	Survived
1951	Carrea	resection of stenosed ICA-anast ECA to ICA	Survived
1953	Strully	carotid endarterectomy	Procedure abandoned-no retrograde flow
1953	DeBakey	carotid endarterectomy	Survived (not reported until 1975)
1954	Eastcott	resection and CCA to ICA anastomosis	Survived - provided impetus for modern carotid surgery

Table 2.1 Table describing the historical development of carotid artery surgery. CCA = common carotid artery, ICA = internal carotid artery, ECA = external carotid artery.

Carotid Artery Surgery

Ligation of the carotid artery as treatment for trauma or aneurysm remained the only operation on the carotid arteries until the 1950's. Carrea performed the first successful reconstruction of the carotid artery on 20th October 1951 on a male stroke patient with a stenosis of the left internal carotid artery. The stenosed area was resected and the external carotid artery anastomosed to the internal carotid [Carrea, 1955]. The first thromboendarterectomy of the internal carotid artery was attempted on 28 January 1953 by Strully and colleagues but they were unable to attain retrograde flow. The first successful carotid endarterectomy was performed by Dr Michael DeBakey on the 7th August 1953 (but not reported until 1975) on a 53 year old man with a frank stroke and a complete occlusion of the left carotid artery. Good retrograde flow was obtained and a completion arteriogram showed a successful result and the patient lived for many years [DeBakey, 1975].

However the operation which gave the greatest impetus to carotid surgery was performed by Eastcott on the 19th May 1954 at St Mary's Hospital, London. A woman with a stenosis of the left carotid bifurcation and a history of 33 TIAs underwent resection of the carotid bifurcation and end-to-end anastomosis between common and internal carotid arteries to restore blood-flow. Eastcott describes in his account of the operation how the patient was first referred to a consultant neurologist, Dr Denis Brinton. Brinton had previously worked in Boston and was aware of the work of Fisher on carotid embolic symptoms and correctly identified the carotid source for this patient's symptoms with the aid of arteriography. The Professor of surgery, Charles Robb, was consulted and agreed that surgery appeared to offer the best hope of cure. However the operation was actually performed by Eastcott as the day for which it was arranged was one during which a distinguished group of American surgeons were to visit St Mary's. Among them were Drs M. DeBakey and E.J. Wylie. E.J. Wylie had first introduced the technique of thrombo-endarterectomy for aortoiliac disease and both he and DeBakey suggested that an endarterectomy would be appropriate in this situation. However, Eastcott had considerable experimental and some clinical experience of carotid arterial resection and grafting and therefore, preferred this approach. Eastcott describes how the patient lay anaesthetised in an ice water bath until her body temperature fell to 28°C which was performed as an attempt at cerebral protection. Clamps were applied, the external carotid was ligated a little above its origin, the stenosed segment was resected and the common carotid was anastomosed end to end with the internal carotid stump. Clamp time was 28 minutes. No heparin was

Carotid Artery Surgery

used. The patient was completely relieved of her symptoms and lived for many years eventually dying at the age of 86 of congestive cardiac failure. However, not long after this providential success, three early postoperative deaths at St Mary's confirmed Eastcott's original reservations concerning the clamping of the carotid artery and highlighted the importance of assessing the adequacy of collateral blood flow during this critical stage [Eastcott, 1993].

In the following years several operations were tried including resection with homograft, resection with vein graft and subclavian-carotid nylon bypass graft. As experience increased various procedures were abandoned and endarterectomy became the standard operation for treatment of carotid atherosclerosis [Thomson, 1992]. However many controversies remain regarding the indications for performing the operation among them, the operative method, the use of shunts, and the application of methods for monitoring and quality control.

2.3 Indications for Carotid Endarterectomy

The success of early operations to relieve symptoms and prevent strokes led to carotid endarterectomy to become one of the most commonly performed vascular operations in the USA [Rothwell, Warlow, 1993]. However as more operations were performed the morbidity and mortality associated with the operation became more apparent and this prompted some authors to question the appropriateness of the procedure. An influential editorial appeared in the journal 'Stroke', which raised serious doubts regarding operative indications, morbidity and deaths in community hospitals and the role of medical treatment and risk-factor control [Barnett *et al.* 1984]. This view was strengthened by the development of effective drug therapy for known risk factors associated with stroke such as hypertension and hyperlipidaemia. In addition, evidence was accumulating that aspirin therapy was also effective at preventing both cerebrovascular and cardiovascular events [Antiplatelet Trialists' Collaboration, 1988; Barnett, 1990]. Therefore an alternative medical therapy for carotid disease was proposed consisting of controlling hypertension, reducing hyperlipidaemia and daily, low dose aspirin therapy. Confidence in the operation was dented, especially among physicians, which caused widespread variations in referrals from neurologists and ophthalmologists [Rothwell, Warlow, 1993]. The result was that, in effect, carotid endarterectomy was reserved for those patients whose symptoms were not controlled by medical

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therapy and the number of operations performed sharply reduced towards the end of the 1980's [Rothwell, Warlow, 1993].

However, the controversy remained and eventually two large international, multicentre trials were initiated to investigate which was the more appropriate therapy, medical therapy alone or medical therapy and surgery. These trials, which both produced definitive answers, were The European Carotid Surgery Trial (ECST) and The North American Symptomatic Carotid Endarterectomy Trial (NASCET). The results of these studies had profound effects on the treatment of carotid stenosis and therefore both will be discussed in more detail

The European Carotid Surgery Trial (1991)

The ECST had its origins in the success of the UK-TIA Aspirin Trial which was launched in the late 1970's by a group of British Neurologists. It became apparent that the same machinery could be used for a randomised trial of carotid endarterectomy in a similar cohort of patients and in 1980 a group of neurologists and vascular surgeons met to draw up a protocol. Randomisation began in 1981 initially only in the UK but later included French centres (1982), Dutch centres (1983) and by 1987, 63 collaborating centres in 12 countries [Rothwell, Warlow, 1993].

Aims:

The trial aimed to answer the following questions in three main categories of stenosis - mild (0-29%), moderate (30-69%) and severe (70-99%):

1. What is the risk of death or stroke in the 30 days following carotid endarterectomy?
2. In patients who survive surgery for 30 days without a stroke, what is the long-term risk of disabling or fatal stroke?
3. What is the risk of stroke in patients not treated with surgery?

Inclusion Criteria

The criteria for inclusion were ' Any patient irrespective of age, sex, or race, who, within the 6 months prior to randomisation, had experienced any combination of TIA, amaurosis fugax, retinal infarction, minor ischaemic stroke or non-disabling major ischaemic stroke within the distribution of one or both internal carotid arteries, and who had a stenosing and/or ulcerating lesion of the symptomatic artery at its origin in the neck, was eligible for the trial'.

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However an important aspect of the inclusion criteria was an 'uncertainty principle'. A patient who satisfied the entry criteria was only entered in the trial if the neurologist or surgeon were 'substantially uncertain' whether to recommend surgery. This was designed to overcome ethical difficulties but did mean that not all patients who satisfied the entry criteria were entered in the trial.

Exclusion Criteria

Patients were excluded on the following grounds: a) patient preference; b) poor general health; c) little if any carotid stenosis; d) ICA occlusion, or distal stenosis more severe than at the bifurcation; e) a lesion thought to be technically inoperable; f) other more likely sources of embolism (e.g. recent myocardial infarction, mitral stenosis, atrial fibrillation, etc.) whose TIAs are thought not to be due to atherothromboembolism; g) vertebrobasilar events only; h) previous carotid endarterectomy of the symptomatic artery.

Investigations

Baseline blood tests were performed and all patients underwent a carotid angiogram prior to randomisation. Computerised tomographic brain scans were recommended for all patients and copies of all angiograms were sent to the trial office for the purpose of determining the exact degree of stenosis. This was determined by measuring the lumen at the site of the greatest stenosis and comparing this to the estimated diameter of the carotid bulb. This was a different method to the one used in the NASCET study.

Treatment

Patients were randomised by telephone and all patients received 'best medical treatment' which included advice to stop smoking, aspirin, treatment of hypertension, hyperlipidaemia etc. All operations were performed by the designated collaborators themselves.

Follow-up

Patients were seen by a collaborating neurologist at 4 months and 1 year after randomisation, and annually thereafter.

Results

Interim results were published in the Lancet in 1991 showing that endarterectomy was beneficial in recently symptomatic patients with a severe

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carotid stenosis, but was of no value in patients with mild stenosis.

Recruitment of patients with moderate stenosis continues. The data leading to these conclusions were derived from the results of 2200 patients, of which 1152 were patients with either mild or severe disease. Of these patients 60% had been randomised to surgery and 40% to 'no-surgery'.

There were seven deaths within 30 days of operation compared with no deaths in 'no surgery' patients over an identical period of time. Death or disabling stroke occurred in 22 'surgery' patients (3.3%), and if all strokes producing symptoms for more than 7 days are included, the figure rises to 44 (7.5%) patients.

The number of deaths during follow-up due to other causes were similar in 'surgery' and 'no surgery' groups (8.3% Vs 8.6%) and similar in the mild and severe stenosis groups (8.0% Vs 9.8%).

During the 3 year follow-up period there was an eight fold reduction in the number of ipsilateral disabling or fatal strokes in severely stenotic patients allocated to surgery compared with no surgery (5/455 Vs 27/323, $2p < 0.0001$). In patients with mild stenosis there was no difference in the number of ipsilateral ischaemic strokes between the 'surgery' and 'no surgery' groups (1/219 Vs 0/155).

In the severe stenosis group there was a six fold reduction in strokes lasting more than seven days in the surgery group (9/455 Vs 44/323, $2p < 0.0001$). In the mild stenosis group there was no statistically significant difference (6/219 Vs 2/155).

Risk Factors

In the 'no surgery' group there were three interrelated adverse prognostic factors, other than the degree of carotid stenosis - a history of stroke, residual neurological signs and infarction on the pre-randomisation CT scan. In the surgery group factors predicting an adverse 30-day outcome were systolic blood pressure above 160mmHg, and performance of surgery in under 1 hour.

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	Surgery	No Surgery
Severe stenosis-deaths/disabling stroke in 30 days	3.3%	0
Severe stenosis-all strokes in 30 days	7.5%	0
Severe stenosis-deaths-other causes in 3 years	8.3%	8.6%
Severe stenosis-disabling stroke/death in 3 years	5/455	27/323
Mild stenosis-disabling stroke/death in 3 years	1/219	0/155
Severe stenosis-strokes longer than 7 days in 3 years	9/455	44/323
Mild stenosis-strokes longer than 7 days in 3 years	6/219	2/155

Table 2.2 Table comparing the main outcomes in the ECST of surgery Vs no surgery for mild and severe carotid stenosis

Conclusions

Endarterectomy is beneficial in recently symptomatic patients with a severe carotid stenosis (>70%), but of no value in patients with mild stenosis (<30%). Assessment of the moderate group continues.

The North American Symptomatic Carotid Endarterectomy Trial (NASCET: 1991)

The study was conducted at 50 centres in the United States and Canada. Each centre had a rate of less than 6% for stroke and death occurring within 30 days of operation for at least 50 consecutive carotid endarterectomies performed within the previous 24 months. The NASCET study followed the setting-up of the European trial but had essentially the same aims and used the same three

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categories of stenoses of mild (0-29%), moderate (30-69%) and severe (70-99%) however the methodology of determining the degree of arterial stenosis was significantly different. The effect of this will be discussed later.

Inclusion Criteria

All patients with definite focal retinal and hemispheric events within 120 days of entry, and related to atherosclerotic stenosis of 30% or greater were eligible for randomisation. The lesion had to be technically suitable for endarterectomy.

Exclusion Criteria

Patients were excluded on the following grounds: a) mentally incompetent or unwilling to give informed consent; b) no angiographic visualisation of both carotid arteries and their intracranial branches; c) an intracranial stenosis more severe than the surgically accessible lesion; d) organ failure of kidney, liver or lung or had cancer likely to cause death within five years; e) a cerebral infarction on either side that deprived the patient of all useful function in the affected territory; f) had symptoms that could be attributable to non-atherosclerotic disease; g) a cardiac valvular or rhythm disorder likely to be associated with cardioembolic symptoms; or h) had previously undergone an ipsilateral carotid endarterectomy.

Investigations

Baseline investigations to identify inclusion and exclusion criteria and identify risk factors were performed. All patients underwent bilateral selective carotid arteriography, CT brain scan and Duplex ultrasonography of the carotid arteries. All angiograms were measured and recorded in the Central Office by the Principal Neuroradiographer using a jewellers eyepiece marked in tenths of a millimetre. The percent stenosis was determined by calculating the ratio of the luminal diameter at the point of greatest stenosis and the luminal diameter of the first normal part of the artery beyond the bulb.

Treatment

Patients were randomised according to a computer-generated randomisation schedule in the Data Management Center to either medical care alone or medical care plus surgery. All patients received antiplatelet therapy (1300 mg of aspirin per day or a lower dose if necessitated by side effects) and, as indicated control of hypertension, hyperlipidaemia and diabetes mellitus.

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Follow-up

Patients were assessed at 30 days postoperatively by the surgeon. Study neurologists performed medical, neurologic and functional status assessments of all patients one month after entry, then every three months for the first year, and every four months thereafter.

Results

Interim results were published in the New England Journal of Medicine in August 1991 and showed that carotid endarterectomy was beneficial for patients with severe, symptomatic carotid stenoses. Recruitment of patients with moderate stenoses continues.

These conclusions were based on the results of 672 patients recruited with severe stenoses who were randomised to medical and surgical treatment.

In the 30 day postoperative period 18 surgical patients (18/328, 5.5%) had cerebrovascular events; 12 events were minor, 5 were major (i.e. causing a functional deficit persisting >90 days), and 1 was fatal. One patient died suddenly after surgery, for a rate of 5.8% for all perioperative stroke and death. However the rate for major stroke and death was 2.1% and the fatality rate was 0.6%.

In the comparable period the 'no surgery' group, 11 patients suffered (11/331, 3.3%) cerebrovascular events, 8 were minor 2 were major and 1 was fatal giving a 3.3% rate for all strokes and death in the 32 day post-randomisation period.

The benefits of carotid endarterectomy were expressed according to life table analysis and showed that the cumulative risk of any ipsilateral stroke at 2 years were 26% in the 'no surgery' group and 9% in the surgery group. Therefore carotid endarterectomy afforded an absolute risk reduction of 17+/-3.5%. For a major or fatal ipsilateral stroke, the corresponding estimates were 13.1% and 2.5% - an absolute rate reduction of 10.6+/-2.6%. Carotid endarterectomy also reduced the risk of more minor events such as non-disabling and transient strokes. The NASCET study also identified certain subgroups who seemed to benefit from carotid endarterectomy. There were 20 patients with contralateral carotid occlusions in both 'surgery' and 'no surgery' groups (20/328 & 20/331). The 32-day stroke and death rate was no different in the 'no surgery' and

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'surgery' groups. Surgery reduced the 2-year risk of stroke or death from 56.4% in the 'no surgery' group to 20.4% in the 'surgery' group.

	Surgery	No Surgery
Deaths/disabling stroke in 30 days	2.1%	0.9%
All strokes in 30 days	5.8%	3.3%
Deaths-other causes in 3 years	15/328	21/331
Disabling stroke/death in 2 years	8/328	29/331
Stroke longer than 7 days in 2 years	26/328	61/331

Table 2.3 Table comparing the main outcomes in the NASCET of surgery vs no surgery

The numbers were too small to be accorded statistical significance but seemed to support the conclusion that contralateral occlusion was not a contraindication to surgery [Barnett, 1993b].

The study also identified that age was not a barrier to successful and beneficial carotid surgery, patients with retinal symptoms alone were at a lower risk of experiencing stroke without surgery than patients with hemispheric symptoms alone (17% Vs 44%) although surgery was still beneficial. Patients with angiographic evidence of carotid ulceration and silent CT infarcts were at increased risk of stroke if treated medically.

2.4 Discussion of the ECST and NASCET Studies

Carotid endarterectomy is the first surgical operation to be subjected to this rigorous scientific investigation of its efficacy. The unequivocal benefit of carotid endarterectomy over medical treatment alone was surprising, not because of previous underestimation of the success of surgical treatment but because of the previous gross underestimation of the failure of medical treatment alone for patients with severe stenosis.

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In addition to demonstrating the benefits of endarterectomy the studies provided valuable information on the operative mortality and morbidity that needed to be achieved in order to obtain that benefit. These studies set important standards of investigation and reporting for the conduct of future studies into this subject.

However there were important differences in the conduct between the two trials which require careful consideration.

Both trials used the same classification of carotid stenosis into mild, moderate and severe based on measurements of preoperative angiograms, However their methods of determining the degree of stenosis were significantly different. The NASCET study compared the luminal diameter of the stenosis with the luminal diameter of the first section of normal artery distal to the stenosis while the ECST compared the luminal diameter of the stenosis with the diameter of the carotid bulb. Since the diameter of the carotid bulb is invariably greater than the more distal ICA the ECST patients were estimated to have a greater degree of stenosis than the NASCET patients. A recent study measuring 700 ECST angiograms by both methods showed that only 48% of patients classified as severe by ECST would have been included in the NASCET severe stenosis group. The 70% NASCET stenosis measures over 80% by the ECST method. Similarly the 70% ECST stenosis measures around 50% by the NASCET method [Rothwell, personal communication]. Since the risk of stroke increases with degree of stenosis this is likely to explain why the absolute benefit of surgery appears greater in the NASCET severe stenosis patients.

However, with regard to the degree of stenosis there are two important factors to consider. First, the degree of stenosis is not thought to be directly responsible for the symptoms, rather it is embolism which is thought to be responsible for the pathology. Increasing stenosis merely increases the likelihood that embolisation will occur. Therefore, the division of patients into the three bands based on the degree of stenosis is artificial and arbitrary and is unlikely, therefore, to have hard edges. The moderate stenosis band contains patients who have a stenosis of 31% who have, one could assume, a risk of stroke not significantly different from a patient with a 29% stenosis i.e. very small. Similarly, a patient in the moderate band with a stenosis of 69% could be expected to have a risk of stroke similar to patient with a 71% stenosis in the severe band. Therefore, it must be hoped that when the results from the two

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studies are available for patients with moderate stenosis, they will include a subgroup analysis which will take account of the anomalies in measuring the degree of stenosis.

The method used to determine the degree of stenosis in both trials was by means of biplanar angiography, which in 1981, was the most accurate and reliable method commonly available. Since that time colour Duplex ultrasound scanning has become more popular and widely available. The main disadvantage of angiography is that it is associated with a definite morbidity and mortality [Hankey *et al.* 1990]. This was not included in the analysis of the trials because angiography occurred before randomisation, however in clinical practice it is an important consideration. In TIA patients the neurological morbidity is 3.4% and the disabling stroke rate is 1.3% [Hankey *et al.* 1990]. Duplex scanning is a non-invasive technique for estimating the carotid stenosis and is not associated with any significant morbidity. In addition the B-mode pictures give a great deal of information regarding the character of the plaque. Evidence is now accumulating that certain plaque characteristics are associated with an increased risk of neurological symptoms and it is hoped that further research in this area may identify high risk patients irrespective of the degree of stenosis [Bock, Lusby, 1992].

Finally, an important caveat was attached to both trials concerning the morbidity and mortality associated with surgery. The advantage of surgery over medical treatment alone can only be achieved if the morbidity and mortality of an operating surgeon is similar to that in the trials. Indeed the authors of the NASCET study estimated that if a surgeons major mortality and morbidity was greater than 10% then there was no benefit from surgery. This emphasises the importance of attempting to minimise perioperative complications. This may be particularly relevant for patients in the moderate stenosis group if surgery is to be beneficial.

In order to minimise complications it is necessary to identify what is going wrong and then develop strategies to detect these complications before any adverse consequences have occurred. In this way, it may be possible to reduce the morbidity and mortality associated with the operation, therefore allowing more people to benefit.

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	NASCET	ECST
Study Population	USA & Canada -50 centres	14 European countries -80 centres
Imaging technique	biplanar angiography	biplanar angiography
Definition of carotid stenosis	luminal diameter of stenosis Vs diameter of normal distal ICA	Luminal diameter of stenosis Vs diameter of carotid bulb
Definition of severe carotid stenosis	>70%	>70%
No of patients in severe group	328	455
Perioperative death/ disabling stroke rate	2.1%	3.3%
All perioperative strokes	5.8%	7.5%
Follow-up period	2 years	3 years
Follow-up strokes	8/328	9/455
Risk reduction over no surgery	8 fold reduction in risk	10 fold reduction in risk

Table 2.4 Table comparing the methods and results for the severe carotid stenosis groups undergoing surgery in the NASCET and ECST studies.

2.5 The Operative Technique of Carotid Endarterectomy

I will now describe the method of carotid endarterectomy used by the surgeons in this study. This description will be used as a basis for a discussion of alternative methods which are currently in use and in particular areas of controversy such as the use of an intraluminal shunt and patch angioplasty.

Anaesthesia

A light general anaesthesia is given utilising an isoflurane inhalational agent which reduces the oxygen requirement of the brain and acts as a cerebroprotectant against ischaemia [Messick *et al*, 1987; Meyer, 1992]. Continuous intra-arterial blood-pressure monitoring is performed throughout

the operation. Blood pressure is maintained at the patient's normal preoperative level.

Operative Technique

The patient is positioned on the table supine with the head turned away from the side to be operated-on. A sandbag is placed under the shoulder blades and the head placed on a rubber head-ring to slightly elevate the head and neck without undue extension. An oblique incision is made along the anterior border of the sternocleidomastoid muscle and centred over the carotid bifurcation. Dissection is continued deep to the anterior border of sternocleidomastoid until the carotid sheath is entered. The carotid artery is identified and adequate exposure of the common, internal and external carotid arteries is obtained.

The mandibular branch of the facial nerve, the vagus nerve, the hypoglossal nerve and superior laryngeal nerve are sought and preserved. The carotid sinus area is infiltrated with 1% lignocaine and 0.5% bupivacaine solution to prevent hypotension and bradycardia. Arterial slings are placed around the common, internal and external carotid arteries and the superior thyroid artery.

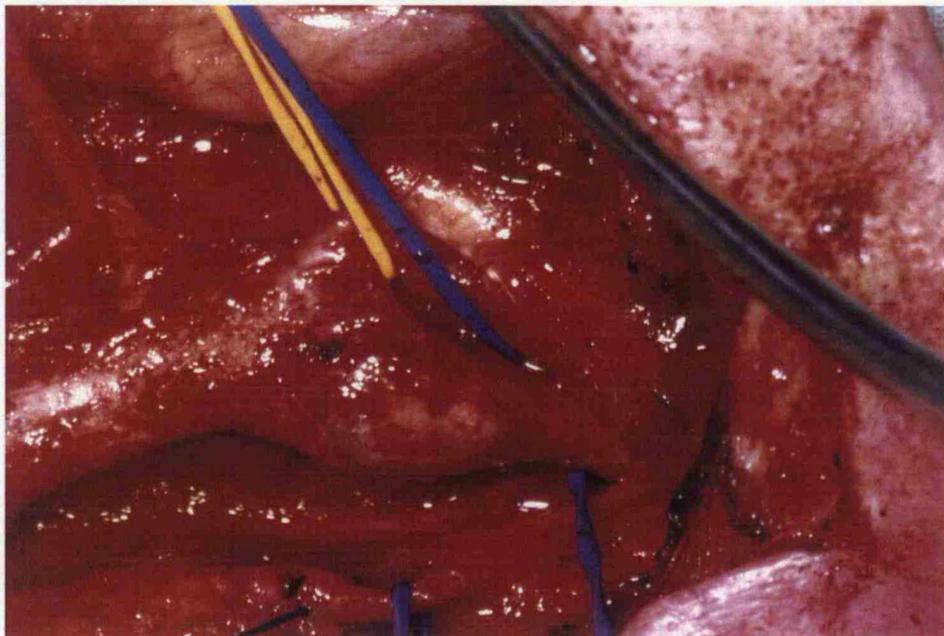


Figure2.1: Picture illustrating the dissection of the carotid bifurcation. ECA=yellow sling, ICA = open blue sling, superior thyroid artery=red sling.

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Systemic heparinisation is then performed by the intravenous injection of 5000 i.u. of heparin. A Pruitt-Inahara Shunt is then prepared for insertion by testing the inflation and deflation of the retaining balloons and excluding any air bubbles. The external carotid artery is then occluded using an arterial clamp, then the common carotid and finally the internal carotid. A linear arteriotomy is made from the common carotid into the internal carotid beyond the extent of the plaque. The larger end of the shunt is then inserted into the common carotid artery and the retaining balloon inflated. The blood-flow from the common carotid is then vented through the shunt to ensure patency. The smaller end of the shunt is then inserted into the internal carotid artery and the retaining balloon inflated. Blood-flow is then restored through the shunt. The operation may now be performed without undue haste. The appropriate plane between atheroma and media is entered with a flat-bladed dissector and the plaque dissected from the common carotid, the bifurcation, first portion of the external carotid and that portion of the internal carotid containing plaque. proximal and distal endpoints are then secured with several, interrupted 7/0 Prolene sutures to prevent dissection when blood flow resumes. The endarterectomy surface is examined carefully under loupe magnification (2.5X) to ensure a smooth surface free of debris, roughened areas, ulcerations or other irregularities. The arteriotomy is then closed using a patch angioplasty of long saphenous vein using a running suture of 6/0 polypropylene. When the closure is within 1cm of completion the shunt is clamped, the internal carotid balloon is deflated and the distal limb of the shunt removed. The internal carotid artery is clamped quickly behind it. The procedure is then repeated for the common carotid artery. The vessels are then flushed with 0.9% Normal saline. Just prior to the final few sutures the internal carotid artery is back vented to clear any debris and then reclamped. With the angioplasty complete the clamp is removed from the external carotid artery and then the common carotid artery allowing any remaining debris to be swept into the external carotid distribution. The clamp is then removed from the internal carotid artery and flow restored to the brain. The heparin is then reversed with protamine if necessary.

Post-operative care

The patient is awoken in theatre and then transferred to a high dependency area in the theatre recovery department. Intra-arterial blood pressure monitoring continues and neurological examinations are performed every 10 minutes. When the patient is conscious, pain-free and has been

haemodynamically stable for several hours the patient is returned to high dependency area of the surgical ward.

2.6 Alternative techniques of Carotid Endarterectomy

Anaesthesia

General anaesthesia is the most popular method in the USA and UK, however, the use of local anaesthetic techniques is also widespread. The advocates of local anaesthesia claim that it is easier to detect the development of neurological deficits and therefore correct them, because the patient is conscious. Assessment of the neurological status can be performed by asking the patients questions or even performing intraoperative psychometric testing [Evans *et al*, 1988]. Motor strength is tested intermittently by assessing hand-grip or compression of 'squeaker toys' [Imparato, 1993]. Disadvantages of this technique include: not all patients are psychologically suitable; general anaesthesia may need to be introduced in unfavourable circumstances if the operation takes longer than expected or the patient becomes anxious; patient anxiety with the technique is associated with difficulty in controlling intraoperative blood pressure and a higher incidence of intra- and post-operative myocardial infarctions [Davis *et al*, 1990; Gewertz, McCaffrey, 1987].

General anaesthesia removes patient anxiety and is generally more convenient for the surgeon however monitoring of the patients neurological state is, by necessity, indirect and at present there is no one method that is superior [Gewertz, McCaffrey, 1987].

Surgery: Insertion of a Temporary Shunt

Although in this centre it is routine practice to insert a temporary shunt this is not the case in many centres around the world. Some centres do not utilise a shunt at all while others selectively shunt based on the results of certain tests performed at the time of clamping [Imparato, 1993]. Theoretically, in a patient with a good collateral blood supply around the circle of Willis there should be no need to insert a shunt. However, as I have already described, there is evidence to suggest that up to a third of people do not have a complete circle and it is reasonable to assume that a proportion of those people may be put at risk [Fields *et al*, 1965; Sedzmir, 1959]. Sundt and colleagues demonstrated a high correlation between postocclusion cerebral blood flow values and intraoperative EEG findings [Sundt *et al*, 1983]. Cerebral blood flow(CBF) was

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measured using the Xe133 washout technique in 1,352 consecutive carotid endarterectomies. CBF values less than 10ml/min/100g always produced ischaemic changes in the EEG. Sundt considered that 15ml/min/100g was the lower limit of tolerable hypoperfusion but he inserted a shunt in all patients with lower than 18ml/min/100g to allow for some error in measurement. Blood flow through shunts varies between different types of shunt and shunts of different lumen size. In a series of experiments investigating blood flow through different shunts, Beard, estimated that a shunt blood flow should be at least 75ml/min to exclude the possibility of ischaemia [Beard, 1993]. This estimate was based on the CBF figure of 15ml/min/100g of brain tissue and assuming an ipsilateral cerebral hemisphere weight of 500g and no collateral circulation due to an inadequate circle of Willis. Beard found a wide variation in shunt blood flow from 32ml/min up to 250 ml/min (median 92ml/min) indicating that some shunts may not totally remove the risk of ischaemia. Further, the figure of 15ml/min/100g was an indicator of global cerebral ischaemia, however, areas of previous infarction are already compromised and there is evidence that these areas are more susceptible to ischaemic damage and may require high rates of blood flow to avoid extension of infarction [Naylor *et al*, 1992]. The exact requirements of the brain at the time of operation are difficult to assess accurately therefore a policy of shunting every patient minimises the risk of ischaemic damage .

Opponents to shunting point out several disadvantages: shunts that are indwelling may obstruct the performance of the operation; insertion of a shunt may be difficult and cause trauma to artery, this may lead to embolisation of dislodged debris or postoperative thrombosis on an area of damaged endothelium; external slings used to hold certain shunts in place may also damage the artery; shunts may malfunction which is difficult to recognise intraoperatively and may be falsely reassuring; shunts may be malpositioned or become occluded or kinked [Imparato, 1993].

For the opponents of shunting the strategy for avoiding ischaemic damage depends on the swift performance of the operation to minimise the time cerebral blood-flow is reduced by carotid clamping. Several large series published by individual surgeons ascribing to this philosophy quoted morbidity and mortality rates (9-13%) which were similar at the time to those obtained by surgeons who did use shunts [Baker *et al*, 1984; Littoy, *et al*, 1984]. However the recent European Carotid Surgery Trial identified carotid surgery being

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completed in under one hour as being associated with a significantly higher surgical morbidity and mortality [Rothwell, Warlow, 1993].

Selective shunting is practised by many centres. This method depends on employing some assessment method to assess the effect of carotid clamping and only inserting a shunt if that method indicates a problem.

One method is to measure the internal carotid stump pressure above the internal carotid artery clamp as an indicator of collateral blood supply. In the original description of the technique a stump pressure above 25mmHg was considered adequate [Moore, Hall, 1982], however with greater experience 50mmHg, or even 75mmHg has been suggested [Imparato, 1993]. This method has the disadvantages that it is invasive, involving penetrating the ICA with a needle and also, unless repeated readings are taken throughout the operation, the stump pressure is only an indicator of the adequacy of cerebral collateral flow at the time of the measurement [Imparato, 1993]. In addition several studies have described cases where ischaemia occurred despite an adequate stump pressure [Hobson *et al*, 1974; Kelly *et al*, 1979; Kwan *et al*, 1980].

Another method is to perform electroencephalogram monitoring of brain function throughout the operation. The effect of carotid clamping on neuronal function is directly measured and a deterioration in function can be detected at any time during the clamped period, and corrected by shunt insertion. However disadvantages of EEG is that it is cumbersome to set-up and requires expert interpretation. EEG only detects changes in the surface layers and therefore cannot detect damage occurring deep within the brain [Gewertz, McCaffrey, 1987].

Once again, various studies have shown good results with this approach using either of the assessments.

Surgery: Patch Angioplasty

Whether to close the arteriotomy with a patch of vein, prosthetic material or not, is another area of controversy. Once again surgeons fall into three groups: those who always patch [Riles *et al*, 1990]; those who patch selected cases [Greenhalgh, 1993]; and those who never patch. A recent survey of the members of an American vascular society revealed that out a total of 23,873

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carotid endarterectomies only 7.4% of cases were patched [Tawes, Treiman, 1991].

Proponents of patching maintain that inserting the patch prevents artificial narrowing of the artery by direct closure. If one takes a 1mm depth of bite with the suture on one side of the arteriotomy and a similar bite on the other side of the arteriotomy, when the suture is tied, one can estimate that the artery has been narrowed by approximately 2mm [Greenhalgh, 1993]. Proponents of patching ascertain that this predisposes to an higher incidence of early carotid thrombosis and later recurrent stenosis [Eikelboom et al, 1988]. Recurrent stenosis is a relatively benign condition but early thrombosis can cause a stroke or even death in patients with poor collateral flow and is to be avoided. Insertion of a 3-4mm width of patch prevents this narrowing and is said to lower the incidence of carotid thrombosis [Ranaboldo *et al.* 1993].

However a major complication of patch angioplasty is patch rupture. This was originally thought to be a very rare complication but a confidential survey carried among American vascular surgeons showed that vein patch rupture had occurred in 0.7% of 1,760 cases [Tawes, Treiman, 1991]. The evidence suggested that vein patch rupture was (with the exception of one case) confined to vein harvested from the ankle. Further studies into the tensile strength of vein from various sites in the body found that upper thigh vein had the greatest resistance to rupture and therefore it was recommended that upper thigh vein was used for carotid angioplasty in future [Archie, Judd Green, 1990].

Alternatives to vein include expanded Polytetrafluoroethylene (PTFE) and woven Dacron with have both advantages and disadvantages. PTFE patches have been associated with prolonged bleeding through stitch holes and there is a reported case of suture line disruption [McCready *et al.*, 1992]. There is less experience with using Dacron but there does not appear to be the same bleeding problem although being made of artificial material it shares with PTFE the risk of infection [Eikelboom *et al.*, 1988].

A recent multicentre randomised trial of patch versus no-patch showed a significant reduction in perioperative morbidity and mortality by using carotid patch angioplasty [Ranaboldo *et al.* 1993].

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	Advantage	Disadvantage
Local anaesthesia	Enables direct assessment of neurocognitive state	↑ patient anxiety ↑ incidence of MI ↑ brain O ₂ requirement Patient movement
General anaesthesia	No patient anxiety Cardiovascular control No time limit on operation	Indirect assessment of neurocognitive state Complications of general anaesthesia
Intraluminal shunt	Blood supply independent of collaterals No time limit on operation	False sense of security Emboli on insertion May occlude during operation
No intraluminal shunt	Avoids insertion and risk of emboli	Blood supply dependent on collaterals Requires quick surgery
Primary closure	Simple, secure closure Takes less time Minimal risk of rupture	Narrows artery Increased risk of thrombosis
Patch angioplasty	Avoids narrowing artery Lower risk of thrombosis	Vein patch rupture Prosthetic patch infection.

Table 2.5 Table illustrating the main advantages and disadvantages of different techniques of carotid endarterectomy. ↑ = increased, MI = myocardial infarct, O₂ = oxygen.

2.7 Complications of Carotid Endarterectomy

Preoperative complications

The most serious preoperative complication is death or stroke prior to surgery. Both the ECST and NASCET stressed a time period during which it is optimal in which to perform the operation. NASCET specified that operations should be performed within 120 days of the onset of symptoms for the maximum benefit to be obtained.

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Operative Complications (Table 2.6)

The risk of death and/or major stroke after carotid endarterectomy is 2-4% although this rises to 5.5-7.5% if all minor strokes are included [ECST & NASCET, 1991]. In addition CT scan evidence suggests that up to 12% of patients suffer silent cerebral infarction during the operation [Berguer *et al*, 1986]. Certain patients appear to be at higher risk of operative stroke, including those with a history of crescendo transient ischaemic attacks or recent stroke, CT evidence of infarction, a residual preoperative neurological deficit, complex ulcerated plaque on preoperative angiogram or Duplex scan and a contralateral carotid occlusion [ECST & NASCET, 1991]. Operating predominantly on patients who are high risk may result in a higher rate of complications than those quoted from the trials.

Two thirds of strokes are thought to occur during surgery of which 80% are thought to be embolic in origin and 20% haemodynamic [Krul *et al*. 1989].

Haemodynamic strokes may occur as a consequence of inadequate collateral cerebral blood supply during carotid clamping, a critical reduction in boundary zone perfusion pressure secondary to intracranial occlusive disease, or as a consequence of shunt complications (occlusion, kinking, malposition, spasm), [Naylor *et al*. 1992].

Embolic strokes may occur due to embolisation of atheromatous debris from the carotid plaque during carotid dissection or mobilisation. Shunt insertion may dislodge plaque distally which embolises to the brain once flow is restored through the shunt. Embolisation may arise from technical defects such as intimal flaps which may be clamp induced, shunt induced or dissection from the distal end-point of the carotid endarterectomy. Embolisation may also arise from other defects such as stenoses caused by arteriotomy closure or suturing of the distal toe-end of a patch angioplasty [Hertzer, 1989; Naylor *et al*. 1992; Riles *et al*, 1994]. The development of transcranial Doppler monitoring has revealed that air embolisation also occurs at restoration of flow through the shunt and on completion of the endarterectomy [Padayachee *et al*. 1986; Spencer *et al*, 1990; Naylor *et al*. 1991]. The clinical effect of this air embolisation is unknown and was one of the areas of investigation for this study.

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Perioperative and Early Postoperative Complications

Thrombotic strokes may be caused by a combination of embolisation from the initial thrombotic mass and haemodynamic factors when the thrombus eventually occludes the artery. Various causes of vessel thrombosis have been published including, perioperative hypotension, uncorrected internal carotid artery kink or loop or a hypoplastic internal carotid artery, perishunt thrombosis. Causes of platelet-fibrin thrombus include the rare idiopathic predisposition or heparin induced platelet antibody or more commonly endarterectomy surface irregularity or an intimal flap [Hertzer, 1989; Naylor *et al*, 1992; Riles *et al*, 1994].

Intracerebral haemorrhage is another cause of perioperative stroke and is usually related to uncontrolled hypertension during, or more usually, after carotid endarterectomy. The presence of intracerebral aneurysms is thought to increase this risk and is one of the arguments for performing preoperative cerebral angiography [Gelabert, Moore, 1990]. The benefits of detecting intracerebral aneurysms must be balanced against the accepted morbidity and mortality of angiography itself. Avoiding this complication depends on the maintaining a stable blood-pressure during and after the operation [Gelabert, Moore, 1990].

Haemorrhage from the operated artery can occur. Bleeding from the suture line can occur leading to the formation of a substantial haematoma which may cause a degree of tracheal obstruction, even in the presence of a functioning wound drain. More spectacular haemorrhage can occur several days after the operation caused by rupture of a vein patch or disruption of a suture line [McCready *et al*. 1992].

Late Postoperative Complications

The use of artificial patch material as a patch angioplasty may be associated with infection, as is the case with the use of such material in any body site [McCready *et al*. 1992].

Restenosis occurs within the first year but is a relatively benign condition and is not usually associated with a return of symptoms. Restenosis represents myointimal hyperplasia and therefore is not prone to embolisation [Moore, 1993].

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COMPLICATION	COMMENTS
EMBOLISM	
Emboli during carotid dissection	Friable carotid plaque dislodged by handling of bifurcation
Emboli during insertion of shunt	Plaque dislodged by insertion of shunt.
Emboli on opening of shunt	Air and plaque/thrombus in CCA and ICA embolises on restoration of blood flow
Emboli during shunting	Thrombus forming during shunting or air due to shunt malfunction
Emboli during restoration of blood flow through ECA	Air and plaque/thrombus in CCA and ECA embolises on restoration of blood flow; may enter MCA territory
Emboli during restoration of blood flow through ICA	Air and plaque/thrombus in CCA and ICA embolises on restoration of blood flow
Delayed postoperative embolism	Non-occluding thrombus forming at endarterectomy site embolises
Atheroemboli from aortic arch	Plaque/thrombus from disease in aortic arch embolises
Cardiac embolus	Embolus from heart
Cerebral angiography	Air emboli within solution and plaque/thrombus dislodged by performance of technique
Cardiac Surgery	Emboli generated by simultaneous cardiac surgery
THROMBOSIS	
Perioperative hypotension	Hypotension results in thrombosis of the carotid artery
Perishunt thrombosis	Thrombus forms either proximal or distal to shunt due to obstruction of flow or turbulence
Immediate postoperative carotid artery thrombosis	Thrombosis of the artery in the hours following operation

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Hypoplastic internal carotid artery	Develops distal to very severe carotid stenosis
Delayed postoperative thrombosis	Thrombosis occurring after the initial postoperative period; days 1-4.
HAEMODYNAMIC	
Hypotension	Results in inadequate cerebral blood flow
Bradycardia	As hypotension
Carotid clamping	Inadequate collateral cerebral blood flow if no shunt employed
Shunt malfunction	Inadequate cerebral blood flow, may not be detected by surgeon
Shunt induced spasm	Insertion of shunt induces spasm of internal carotid artery
Intracranial disease or thrombosis	Inadequate blood flow distal to intracranial stenotic disease
Occlusion of contralateral internal carotid artery	Reduces collateral cerebral blood flow.
Intracranial haemorrhage	May be caused by hyperperfusion in immediate postoperative period or/and intracranial aneurysms
Incomplete circle of Willis	Inadequate cerebral collateral blood flow
MISCELLANEOUS CAUSES	
Strokes in other vascular territories	Secondary to ischaemia or embolism
Carotid cavernous sinus fistula	Rare abnormality
Patch angioplasty rupture	More common with ankle vein patches
Suture disruption with cervical haemorrhage	Possibly secondary to suture damage
Wound infection with cervical haemorrhage	Necrosis of patch or artery, increased risk with prosthetic patch
Global anoxia, premature extubation	Anaesthetic complication
Myocardial infarction	More common with local anaesthetic

Table 2.6 Causes of stroke in the perioperative period of carotid endarterectomy [Hertzler, 1989; Naylor *et al*, 1992; Riles *et al*, 1994]

Finally, the general complications of undergoing a general anaesthetic in this atherosclerotic group of patients are particularly pertinent. In some reported series perioperative cardiac complications have been the major source of mortality and morbidity [Riles *et al.* 1979; Hertzler, 1989].

The causes of stroke in the perioperative period of carotid endarterectomy are many and various (Table 2.6) but detecting and preventing these complications appears the key to reducing perioperative morbidity and mortality. Two main strategies have developed to achieve this, the application of intraoperative monitoring methods to detect ischaemia and the use of completion quality control methods to detect technical errors which can cause perioperative thrombosis and embolism.

2.8 Quality Control and Monitoring Methods

Carotid endarterectomy depends on the highest standards of surgical and perioperative care if a successful outcome is to be guaranteed. However, I described in the section on the history of carotid surgery that at the time when the only operation performed on the carotid artery was ligation, this had a mortality of 43%, and much of that was due to sepsis [Thompson, 1993]. The use of modern surgical techniques would reduce the mortality of ligation even further, therefore, it reasonable to assume that for the majority of patients, the occlusion of one carotid artery is not automatically associated with a major stroke and/or death. Indeed, occlusion removes the threat of further embolisation and patients who have a severe carotid stenosis that progresses to occlusion and survive are often relieved of their symptoms [Bock, Lusby, 1992]. Similarly, there are many cases of asymptomatic postoperative carotid artery occlusion which are only discovered if the opposite artery becomes symptomatic and undergoes investigation [Cuming *et al.*, 1993]. These patients have an intact circle of Willis and good collateral cerebral blood supply that means occlusion of one carotid artery does not result in a stroke or any neurological deficit. In such patients ligation of the symptomatic carotid artery would cure them of their symptoms because ligation would remove the source of emboli and would not reduce the blood flow to the brain sufficiently to result in a neurological deficit. However, there are several major reasons why carotid artery occlusion is undesirable. The main reason is that, at present, there is no reliable method to predict the effects of long term occlusion of one carotid

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artery and, therefore, one cannot predict with absolute certainty that any individual patient would be suitable for this treatment. Secondly, if the opposite carotid artery should later become symptomatic itself, the prognosis is much worse if the contralateral artery is occluded [Barnett, 1993].

Therefore, the surgical aim of carotid endarterectomy is to produce a patent artery, without stenosis and free from the risk of embolisation.

The use of modern surgical techniques has meant that the risk of major stroke/death from carotid endarterectomy has been reduced to 2-4% [NASCET, ECST]. However there is evidence that the use of monitoring and quality control methods could reduce the complication rate even further and this is important if CEA is to benefit patients with lesser degrees of carotid artery stenosis [Naylor *et al.* 1992].

2.9 Quality Control Methods

It has been estimated that 65% of perioperative strokes may be related to technical error resulting from defects in surgical technique [Riles *et al.* 1994]. The major morbidity/mortality rates from surgery can vary widely, ranging from 1.5% at major centres performing many operations to 20% reported from occasional operators [Thompson, 1983; Barnett, 1984]. Therefore, it is perhaps surprising that given the potential importance of technical error there is no commonly accepted method of quality control. One problem is the many different types of technical defects which can result in neurological deficits. No one method of quality control can detect all potential defects and, so far, and no one method of quality control has been demonstrated as superior to the others. The different types of technical errors which have been identified as resulting in perioperative morbidity/mortality are illustrated in Table 2.7.

The ideal quality control method would detect all technical errors, be safe and simple to apply and interpret, and be easily absorbed into the operative routine. No such ideal method exists, however, a number of different quality control measures have been applied to CEA and the advantages and disadvantages associated with these methods will now be described.

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TECHNICAL ERROR	COMMENTS
Embolism during operation	
-air embolism	shunt malfunction or restoration of blood flow
-particulate embolism	dissection of bifurcation, insertion and/or opening of shunt, postoperative period
Intimal flaps	
-clamp induced	clamp applied across plaque
-residual	shelf of atheroma at end of operation not secured
-shunt induced	difficult shunt insertion raises flap of intima
Incomplete endarterectomy	roughened surface is site for thrombus/embolus formation
Suture stenosis	
-distal arteriotomy closure	
-toe of patch angioplasty	
Uncorrected ICA kink	after endarterectomy artery often elongates and kinks
Thrombus formation	
-Idiopathic	no identifiable cause
-Heparin dependent	heparin induced antibody predisposes to thrombosis
-wall irregularity	predisposes to thrombus formation
-intimal flap	thrombus forms behind flap
-perishunt thrombosis	proximal/distal to shunt
Haemodynamic errors	
-carotid clamping	inadequate cerebral collateral blood supply
-shunt occlusion or kinking	often unrecognised by surgeon
-shunt malfunction	inadequate blood supply through shunt
-shunt-induced arterial spasm	spasm of ICA caused by insertion of shunt
-intracranial stenosis/thrombosis	inadequate blood supply distal to intracranial stenosis
Intracranial haemorrhage	
-hyperperfusion	disturbed baroreceptor function results in hypertension and cerebral hyperperfusion
-intracranial aneurysms	may rupture secondary to hypertension

Table 2.7 Table illustrating technical errors identified as resulting in perioperative morbidity/mortality [Hertzer, 1989; Naylor *et al*, 1992; Riles *et al*, 1994]

Angiography

In 1967 Blaisdell applied intraoperative angiography following CEA in 100 patients and detected unacceptable defects in 26 cases [Blaisdell *et al*, 1967]. Further studies have confirmed the usefulness of this technique and there is evidence of a reduction of perioperative morbidity and mortality as a result [Courbier *et al*, 1986]. However, difficulties in obtaining reliable intraoperative images of the carotid bifurcation and an associated morbidity/mortality with the technique has prevented angiography from being widely applied as a completion method [Hankey *et al*, 1990].

Continuous Wave Doppler

Continuous wave Doppler (CWD) consists of an hand-held pencil-type probe applied to the surface of the artery after restoration of blood flow and enables an assessment of blood flow velocity across the endarterectomy site [Seifert, Blackshear, 1985]. The advantage of this method is that it is simple to apply and interpret and can be applied by the surgeon independent of technicians. However, unless the angle of insonation is standardised and specific velocity readings taken, interpretation consists of subjective assessment of the auditory signal. An increase in audible tone is taken to indicate a stenosis while the absence of signal indicates occlusion [Seifert, Blackshear, 1987]. However, this method provides no information regarding the structure of the abnormality.

B-mode Ultrasound/Duplex

B-mode ultrasound (BMU) consists of an hand-held probe applied to the surface of the artery, but the probe is much larger than the CWD probe. BMU provides a real-time grey-scale image of the artery and endarterectomy site enabling abnormalities such as arterial kinks and intimal flaps to be identified. The technique is more complex and may need a second operator to adjust the controls to obtain satisfactory images and experience is needed to correctly interpret the images [Dilley, Bernstein, 1986].

Duplex ultrasound combines the B-mode images and velocity measurements to provide a combined assessment of the structural components of a defect and its effect on blood flow [Schwartz *et al*, 1988]. Colour Duplex, provides a colour coded image of the blood flow velocity in combination with the grey-scale image [Harris, Horrocks, 1995]. Both methods provide a comprehensive assessment of the operated artery but consist of very expensive equipment and

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require considerable expertise both to obtain accurate images and to interpret them correctly.

Angioscopy

Angioscopy consists of a flexible fibreoptic telescope that can be inserted into the artery after completion of the endarterectomy but before final restoration of flow. Pressurised saline irrigation through an integral irrigation port simulates blood flow and serves to illustrate abnormalities such as thrombus or intimal flaps. These abnormalities may then be corrected prior to restoration of flow. However, angioscopy provides no information regarding blood flow through the endarterectomised artery [Mehigan, Alcott, 1986].

Therefore each quality control method has advantages and disadvantages and in the absence of a comparative study it is difficult to determine which method is superior (table 2.8).

Technique	Advantages	Disadvantages
Angiography	Established technique Direct anatomical images of blood flow	Inadequate images/ radiation No haemodynamic data requires technicians Morbidity/mortality
Continuous wave Doppler	Simple technique No technicians	Subjective analysis gross defects only
B-mode Ultrasound	Non-invasive Structural defects identified	Technical help, large probe Image interpretation No haemodynamic data
Duplex Ultrasound	Haemodynamic & structural data	Technical help needed Image interpretation, probe size Expensive equipment
Colour Duplex	as above	as above more expensive
Angioscopy	Direct images easy to interpret Correct defects prior to restoring flow	Applied before restoration of flow No haemodynamic data

Table 2.8: Table describing the advantages and disadvantages of alternative methods of quality control

One aim of this thesis was to undertake a comparative study in the same cohort of patients of these alternative methods and assess how close each method came to the ideal. A comparison was performed of completion angiography, CWD and B-mode ultrasound and a full account will be described later in this thesis.

2.10 Intraoperative Monitoring Methods

Another common strategy employed to reduce perioperative mortality/morbidity is the application of intraoperative monitoring of cerebral function and blood supply. The ideal method would detect all conditions known to be associated with adverse clinical consequences, be safe and simple to apply, simple to interpret and absorbed easily into the operative routine. However, in common with quality control techniques a number of methods have been advocated but once again no one method has proved to be superior.

Direct Observation

The simplest and least expensive means of monitoring cerebral function is direct assessment of the conscious patient. The technique requires a complete and detailed review of the procedure to reduce patient anxiety in addition to constant reassurance throughout the operation. Premedication requires a parasympatholytic agent to reduce salivation and the need for repeated swallowing during the operation. Sedation is usually necessary but the dose must not be high enough to affect the assessment of the level of consciousness. During draping, the face and airway must be protected to avoid inducing claustrophobia [Gewertz, McCaffrey, 1987].

A combination of deep and superficial cervical plexus blockade is performed with a long acting local anaesthetic such as bupivacaine. Even so further injections of local anaesthetic into structures such as the carotid sheath may be required [Peitzman *et al.* 1982].

Intravenous heparin is administered and a "trial clamping" of the internal carotid artery is performed. Most patients with clamp intolerance demonstrate the effects of ischaemia within 1-3 minutes by a decreasing level of consciousness, motor weakness or inability to perform mental tasks. However neurological signs can develop later in the procedure so the patients status

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needs to be reviewed every 3 to 5 minutes. If signs of ischaemia occur a shunt is inserted [Gewertz, McCaffrey, 1987].

The disadvantages of this method include continuing concern regarding patient compliance, movement during delicate stages of the operation. In the elderly or those with a preoperative neurological deficit the maintenance of an airway without excessive movement may prove difficult. A major theoretical disadvantage is that cerebral metabolism is at its greatest during the awake state and therefore greater cerebral blood flow is required which may be particularly important in patients with a pre-existing ischaemic focus. These marginally supplied areas may be at risk of extending under such circumstances [Gewertz, McCaffrey, 1987].

Internal Carotid Artery Stump Pressure

This technique was first described by Michel and colleagues in 1966 and involves the direct puncture of the common carotid artery with a 19- 20 gauge needle with the more proximal common carotid and external carotid arteries occluded by clamps. The mean pressure in the artery should reflect collateral perfusion from the both the vertebrobasilar and contralateral carotid arteries [Michel *et al.* 1966]. The early studies related a greater number of neurological deficits to those patients whose stump pressure was less than 25mmHg and were not shunted [Moore, Hall, 1982]. Initial recommendations were that shunts should be inserted in patients with stump pressures below the threshold. Further experience saw the threshold rise to 50mmHg and some authors recommended 70mmHg [Ricotta *et al.*, 1983].

However the ability of stump pressures to predict ischaemia has been questioned when compared with other methods. Kelly and colleagues noted that 6% of patients demonstrated ischaemic EEG changes despite stump pressure in excess of 50mmHg. In 125 patients undergoing carotid endarterectomy under local anaesthesia 24 lost consciousness within 1 minute of carotid artery occlusion even though a third of these had stump pressures over 50mmHg [Kelly *et al.*, 1979]. And in another study comparing stump pressure to cerebral blood flow measurement McKay and colleagues found that 24% of patients had stump pressures greater than 50mmHg but cerebral blood flow less than 18ml/min/100g which is considered the lowest level of hypoperfusion tolerable [McKay *et al.*, 1976].

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The reliability of stump pressure measurements are affected by anaesthetic agents and the systemic blood pressure [McKay *et al.* 1976]. Furthermore the method does not account for the presence of a MCA stenosis distal to the circle of Willis which would cause a lower perfusion pressure in that territory than indicated by the carotid stump pressure [Martin *et al.*, 1994].

Intraoperative Measurement of Cerebral Blood Flow

The most commonly applied method of measuring cerebral blood flow involves the intra-arterial injection of an inert radioactive gas, xenon 133. The time taken for the beta emissions to washout of the brain is measured by an extracranial collimated sodium iodide scintillation counter focused on the head and face area of the motor cortex. The calculation of flow is based on the Kety-Schmidt analysis of distribution volume and characteristics of the inert gas. The initial slope or "fast component" of the washout curve relates directly to regional blood flow. Injections are made before clamping to calculate a baseline and again immediately before internal carotid clamping to obtain the washout [Gewertz, McCaffrey, 1987].

Sundt and colleagues found a high correlation between postocclusion CBF values and EEG findings. CBF values less than 10ml/min/100g were invariably associated with ischaemic changes on the EEG. Ischaemic changes were usually associated with CBF below 15ml/min/100g and to allow a margin for safety all patients were shunted with CBF of 18ml/min/100g or less [Sundt *et al.*, 1983]. However, further studies by Morawetz and colleagues failed to demonstrate a correlation between CBF of less than 10ml/min/100g and the development of postoperative neurological complications. In their study of 129 carotid endarterectomies, 22 patients had CBF less than 13ml/min/100g and 8 had CBF less than 9ml/min/100g and none developed any neurological complications. Five neurological complications developed in patients with CBF greater the 20ml/min/100g. The average time of carotid clamping in this study was 20 to 30 minutes which correlates with primate studies that indicate that 20-30 mins of CBF less than 10ml/min/100g can be tolerated with full neurological recovery [Morawetz *et al.*, 1984; Symon, 1980].

Xenon 133 measurements by intra-arterial injection depend on complete delivery of the indicator into the region of interest and freedom from "scatter" and other artefacts affecting the counting [Marcus *et al.* 1981]. The technique of single-photon emission computed tomography reliably excludes these

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artefacts but, in common with Xenon, both techniques remain useful research tools that have not gained wide routine use because of the equipment and expertise necessary to produce accurate results [Gewertz, McCaffrey, 1987].

Electroencephalogram (EEG)

The scalp-recorded EEG is an indicator of the summated postsynaptic potentials arising from cortical neurons in the vicinity of the recording electrodes. Action potentials, which have rapid time courses and small currents, are thought to contribute relatively little to the EEG recordings.

Multiple cup electrodes are filled with conductive jelly and attached to the scalp with collodion. Electrodes are placed at spaced intervals over the scalp and in particular over the vulnerable "watershed" areas of the cerebral arteries. There are usually two electrodes connected to one input of a differential amplifier. The output is the difference in voltage between the two electrodes. The amplitude of EEG outputs is an index of the amount of EEG activity present and the frequency of the output indicates the type of activity. The EEG can be composed of predominantly slower frequencies (delta, theta), or faster frequencies (alpha, beta). In general, cortical ischaemia will produce smaller amplitude and slower frequencies.

The raw data from EEG requires expert interpretation however signal processing using Fourier analysis available on many commercially available machines provides an easy to understand visual display which is more suitable for clinical use [Naylor *et al.* 1992].

Intraoperatively normal EEG readings can be affected by various anaesthetic agents. Barbiturates produce slowing, reduction in amplitude and with higher doses, burst suppression patterns and/or isoelectric EEG. This dose-dependent depression of cerebral activity can mimic the effects of cerebral ischaemia. The volatile halogenated agents produce alterations of frequency content at lower concentrations and reductions in amplitude at higher concentrations which, again, can mimic cerebral ischaemia. Narcotic agents can have a similar effect [Pilchlmayr *et al.*, 1984].

Physiologic changes such as severe hypotension, hypothermia, hypo- and hypercarbia can all affect the EEG and must be excluded when changes occur [Gewertz, McCaffrey, 1987].

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The EEG is most useful for detecting ischaemia as a result of carotid cross-clamping. In a series of 105 consecutive procedures Ivanovic and colleagues described three patterns of EEG response to clamping of the internal carotid:

1. Mild or no power reduction.
2. Marked power reduction, characterised by reduction of EEG spectral power by more than 50% in one or two frequency bands.
3. Global power reduction, reflecting a 50% reduction of EEG power in all frequency bands [Ivanovic *et al*, 1986].

Insertion of a shunt caused a gradual reversal of power reduction which was complete within 5 minutes. More patients had a reduction of high frequencies but without power reduction and the authors concluded that loss of fast activity alone was not associated with residual neurological deficits. No neurological deficits were detected in those patients that were shunted and it was recommended that all patients with global power reduction should be shunted [Ivanovic *et al*, 1986].

There are several drawbacks to using EEG as a monitoring device. EEG cannot predict embolic events, which are thought to cause the majority of intraoperative strokes. Caution is also advised when using EEG to monitor patients with prior strokes or reversible ischaemic neurological deficits. These patients may have cortical tissue in the "ischaemic penumbra", electrically silent but viable, which may be pushed into infarction by cross-clamping. Since the tissue may be electrically silent at the time of operation it is not possible to use EEG to monitor this tissue. A further drawback is that EEG may not detect ischaemia affecting the internal capsule [Gewertz, McCaffrey, 1987].

Evoked Potentials

The potential value of somatosensory evoked potentials (SSEPs) in carotid surgery was first evaluated by Markand and colleagues in 1984. Somatosensory evoked potential recording involves the electrical stimulation of a peripheral nerve e.g. median nerve and recording the resultant afferent volley at different points along its path and ultimately on the scalp overlying the relevant somatosensory receiving area. Since this neuronal activity is dependent on cerebral blood flow it has been proposed that somatosensory evoked potentials may be a simple and sensitive monitor of cerebral ischaemia.

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dependent on cerebral blood flow it has been proposed that somatosensory evoked potentials may be a simple and sensitive monitor of cerebral ischaemia.

The critical parameters are the absolute latencies, which represent the time that the ascending volley takes to traverse various portions of the pathway to the cortex. In general, cerebral ischaemia produces longer latency, smaller amplitude cortical responses [Gewertz, McCaffrey, 1987]. The criteria for shunting include a 50% reduction in amplitude of the primary cortical wave and prolongation of the central conduction time by 1ms [Naylor *et al.* 1992].

The rate at which these stimuli can be delivered is limited by the properties of the cortex, therefore the information obtained is intermittent every 20 to 200 seconds. The cortical components of the somatosensory evoked potentials are preferentially attenuated by anaesthetics and especially the volatile halogenated agents used in carotid endarterectomies [Gewertz, McCaffrey, 1987].

However SSEPs do provide information regarding the functioning of the internal capsule. However the most devastating effects of ischaemia is motor paralysis and SSEPs are only an indirect monitor of the motor pathways and subject to the assumption that insults to motor pathways will be reflected in changes in conduction along sensory pathways [Gewertz, McCaffrey, 1987].

Motor evoked potentials are elicited by stimulation of the motor tracts through the scalp and skull and the resulting efferent activity is measured in the spinal cord, peripheral nerves and muscles. Experience with this method is still limited [Levy *et al.* 1984].

Reflected Near-infrared Light Spectroscopy (Transcerebral oximetry)

One of the most recent developments in cerebral perfusion monitoring is the use of reflected near-infrared light spectroscopy or transcerebral oximetry (TCO) [McCormick *et al.* 1991]. The TCO comprises a near-infrared light source and two photodetectors. The probe is placed on the scalp and near-infrared light at wavelengths of between 650 and 1100nm is reflected by the underlying tissues in a parabolic curve. The detector 10mm from the source receives light reflected and attenuated predominantly through scalp, skull and a superficial area of brain. The detector 27mm from the source receives light attenuated by scalp, skull and a larger and deeper section of brain tissue.

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Infrared light of wavelength 600-1300nm penetrates human tissue to a depth of several centimetres. Within the brain this light is attenuated by chromophores - oxyhaemoglobin, deoxyhaemoglobin and oxidised cytochrome a3. The ratio of deoxyhaemoglobin to oxyhaemoglobin is calculated to provide a reading for intracerebral blood oxygenation and the signal from the superficial structures is subtracted from the that of the deeper structures to calculate the oxygen saturation of the blood in the brain [McCormick *et al*, 1991]. The technique was originally described for use over the frontal lobes [McCormick *et al*, 1991], but the technique has recently been adapted to provide more meaningful results over the parietal lobe and the territory of the middle cerebral artery [Williams *et al*, 1994]. This has involved increasing the source-detector distances to 30 and 40mm respectively; the authors inserted a shunt if cerebral oxygenation fell by more than 10% on clamping [Williams *et al*, 1994].

The advantages of this technique are that it enables continuous monitoring of cerebral oxygenation. However, although this is a new technique which has not yet been fully evaluated there are several theoretical drawbacks. This technique provides only an indirect measure of both neuronal function and cerebral blood supply. Oxygenation is sampled over one superficial segment of brain tissue which may not be representative of other superficial areas brain or more important deep areas e.g. internal capsule. TCO does not have a role in detecting cerebral emboli [Williams *et al*, 1994b].

Transcranial Doppler Sonography

Transcranial Doppler Sonography uses a low frequency ultrasound beam to penetrate the skull at its thinnest points and insonate the basal cerebral arteries. For monitoring of carotid endarterectomy the temporal "window" is used to insonate the middle cerebral artery which supplies blood to the motor and sensory cortex, and can be regarded as the intracranial continuation of the internal carotid artery above the circle of Willis. Transcranial Doppler utilises the Doppler principle to measure the velocity of blood flow within the MCA and with the use of fast Fourier spectral analysis produces a visual display on a video monitor which is easy to interpret. The MCA velocity is a reliable indicator of blood flow although it should be stressed it is not actually a measure of blood flow because the diameter of the MCA being insonated is unknown. This information has been used to assess the adequacy of cerebral collateral blood supply at clamping, the adequacy of shunted blood flow and the blood flow once flow is restored through the endarterectomised artery

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[Naylor *et al.* 1991; Halsey, 1993]. Most importantly, TCD can also detect intraoperative embolisation and since this is thought to be the major cause of IOND, TCD has a major advantage over the other monitoring methods [Krul *et al.*, 1989; Riles *et al.*, 1994].

	Advantages	Disadvantages
Direct observation	Simple, direct inexpensive	Patient compliance Sedation necessary Increased cerebral blood flow requirement
ICA Stump pressure	Well established technique Direct measurement	Intermittent measure ? reliability Affected by anaesthetic and blood pressure Neuronal function ignored
Cerebral blood flow measurement	Accurate	Difficult techniques Requires expertise and expensive equipment No measure of neuronal function Cannot detect emboli
Electro-encephalogram (EEG)	Measures neuronal function	Only superficial areas of brain assessed Infarcts are silent areas Cannot detect embolisation only neuronal effects
Somatosensory evoked potentials (SSEP)	Assesses internal capsule function	Indirect measure of motor neurones Intermittent assessment Cannot detect emboli
Transcerebral oximeter (TCO)	Measures cerebral oxygenation	Superficial brain layer one area of brain Cannot detect emboli
Transcranial Doppler (TCD)	Assesses cerebral blood supply and detects emboli continuously	10% of patients no signal. No assessment of neuronal function

Table 2.9 Table describing the advantages and disadvantages of alternative methods of intraoperative monitoring

Early experience of monitoring with TCD identified certain stages of the operation that were particularly associated with embolisation, in particular the

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restoration of blood flow when the shunt was opened and at the end of the operation [Padayachee *et al.*, 1986, Spencer *et al.*, 1990, Naylor *et al.* 1991; Jansen *et al.*, 1993]. The amount of embolisation detected was surprisingly high and led some people to question whether the signals said to represent emboli did in fact do so. This prompted a considerable number of both flow-rig, animal and clinical studies to confirm the validity of the original assumptions [Russell *et al.* 1991; Berger *et al.* 1990; Albin *et al.* 1989]. This has been successfully achieved however continued clinical experience revealed only a tenuous link between the amount of embolisation detected and an adverse clinical outcome which appeared contradictory to the accepted theory that embolisation was the cause of most IOND. The exact clinical relevance of intraoperative embolisation, detected by TCD monitoring needed to be established and it was this end that this current study was designed to achieve.

2.11 Summary

In this chapter the indications and various techniques of performing carotid endarterectomy and the known causes of perioperative morbidity and mortality have been described. The different quality control measures and monitoring methods that have been applied to try and reduce the incidence of perioperative complications have been outlined.

This forms the basis for the selection of methods that were used in this study to investigate whether the causes of perioperative complications could be identified and prevented. The aims and scope of this thesis will be described in more detail in the next chapter.

CHAPTER 3

SCOPE AND DESIGN OF THIS STUDY

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3.1 Introduction

In the previous chapter I described how intraoperative embolisation and uncorrected technical errors have been identified as the main cause of perioperative morbidity/mortality during carotid endarterectomy. The main strategies employed to try and reduce perioperative morbidity and mortality have been intraoperative monitoring and quality control methods. A number of methods have been successfully applied but all have disadvantages and no one method has proved to be superior.

Among monitoring methods Transcranial Doppler (TCD) is a relatively new technique capable of detecting intraoperative embolisation which has been identified as a major cause of perioperative morbidity/mortality. Several studies have demonstrated that TCD detected embolisation is very common during CEA but the relationship between this and the development of neurological deficits remains unclear [Padayachee *et al*, 1986; Spencer *et al*, 1990; Naylor *et al*, 1991; Jansen *et al*, 1994]. Therefore, the second part of this thesis describes a study to investigate incidence and clinical relevance of TCD detected intraoperative embolisation.

The third part of the thesis describes a study to compare the ability of four different quality control methods to detect technical error during CEA. Difficulties with applying angiography at this site have prompted a search for alternative quality control methods. Three such alternatives are angioscopy, B-Mode ultrasound (BMU) and continuous wave Doppler (CWD). Individual studies have demonstrated their potential application during CEA but no study has been performed to compare these techniques in the same cohort of patients.

The fourth quality control method compared was TCD. TCD has been proposed as a monitoring method detecting intraoperative ischaemia and embolisation. But in previous studies it has been noted that TCD was able to detect errors of surgical technique [Naylor *et al*, 1991]. However, there exists no quantitative or qualitative data defining the role of TCD as a continuous quality control method, detecting errors of surgical technique as they occur during the operation. Therefore, besides investigating TCD as a monitoring method the ability of TCD to detect technical error was also investigated.

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It was hoped that data from the intraoperative TCD monitoring study combined with the data from the completion quality control study would provide a better understanding of factors associated with the development of perioperative morbidity and mortality.

Finally each major complication that occurred during this study was thoroughly investigated to elucidate the cause and identify any avoidable factors. These cases are discussed in more detail in the final part of the thesis.

An outline of the aims and study design of the main parts of the thesis is given below.

3.2 Intraoperative Embolisation - Study Design and Rationale

In the previous chapter I described how embolisation was established as the largest single cause of IOND during carotid endarterectomy [Krul *et al.* 1989; Riles *et al.* 1994]. However, much of the importance of intraoperative embolisation had been inferred indirectly as there was no direct method of detecting embolisation. Embolisation was assumed if all other known causes e.g. haemodynamic insufficiency had been excluded. The arrival of TCD monitoring enabled this embolisation to be detected as it occurred during the operation. However earlier studies failed to demonstrate a strong link between intraoperative embolisation and the development of neurological deficits [Padayachee *et al.* 1986; Spencer, 1990; Naylor *et al.* 1991; Jansen *et al.* 1994]. The majority of patients in these studies experienced embolisation but very few resulted in perioperative neurological deficits.

It became clear that intraoperative embolisation was much more common than previously thought and the idea that one embolus caused one neurological deficit was not representative in the majority of cases. Also the term "embolisation" was imprecise. It did not differentiate between emboli of different composition (i.e. air or particulate), different size and the rate and number of emboli [Spencer, 1992].

Another possibility why earlier studies failed to demonstrate a clear relationship between embolisation and neurological deficits was that the majority of neurological deficits were subtle and even silent and therefore were not discovered by routine post-operative examination.

Scope and Design of the Thesis

Berguer, using pre and post operative CT brain scans, demonstrated that 12% of patients undergoing carotid endarterectomy experienced silent cerebral infarction [Berguer *et al*, 1986]. Similarly, Shaw, using pre- and postoperative psychometric testing showed that up to 79% of patients experienced a decrease in mental ability after coronary artery bypass surgery [Shaw *et al*, 1986]. Ten percent of these patients were overtly intellectually disabled and a major part of this was ascribed to intraoperative embolisation. Pugsley demonstrated that cognitive deterioration following CABG could be reduced by reducing the amount of intraoperative embolisation [Pugsley *et al*, 1990].

Blauth used intraoperative retinal angiography in 10 patients undergoing CABG to demonstrate that all had evidence of intraoperative retinal embolisation after 40-160 minutes of extracorporeal circulation. In addition 3 patients had focal leakage's of dye and 6 had foci of abnormal drainage, although all abnormal features had resolved by the time of the postoperative examination (5-14 days) [Blauth *et al*, 1986].

The phenomenon of intraoperative embolisation has been greatly investigated in cardiac surgery due to the significant number of patients displaying overt neurological and cognitive deterioration in the postoperative period [Shaw *et al*, 1986]. The cardiac by-pass procedure and the artificial oxygenation of blood inevitably generate emboli that have been attributed to air and which can be reduced by the use of membrane oxygenators instead of bubble oxygenators [Padyachee *et al*, 1987]. However, the assessment of cognitive function in cardiac surgery patients is complicated by the considerable physiological and electrobiochemical changes that occur in a patient after a period of extracorporeal circulation. Therefore, changes in cognitive function may reflect the effect of these physiological insults and it is difficult to isolate the effect of embolisation alone.

In CEA the situation is much simpler. The homeostatic mechanisms of the patient are not disturbed and theoretically, under conditions of normotensive, normocarbic anaesthesia any deterioration in brain function should be an effect of either haemodynamic factors caused by carotid clamping or embolisation. Eliminating haemodynamic effects by insertion of an intraluminal shunt into every patient and continuously monitoring its function by TCD monitoring, allows the possibility of studying the effect of intraoperative embolisation much

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more accurately. Therefore the aim of this study was to apply similar methods to those used to investigate the effects of embolisation in cardiac surgery with the addition of brain scanning and accurate quantification and characterisation of emboli to provide a comprehensive assessment of the clinical effect of intraoperative embolisation.

Therefore, a study was performed to investigate the clinical significance of microembolisation detected by TCD in 100 consecutive patients undergoing CEA.

The aims of the study were:

1. To quantify and characterise the emboli occurring during carotid endarterectomy and in the immediate postoperative period by continuous TCD monitoring.
2. To detect any clinical consequences of intraoperative embolisation by the following investigations:
 - a) Pre- and post-operative CT and MRI brain scans
 - b) Pre- and post-operative automated 120 point Humphrey visual fields and retinal fundoscopy.
 - c) Pre- and post-operative neurological examination.
 - d) Pre- and post-operative psychometric testing.

All of these investigations were performed by independent specialists in the relevant field and the data was analysed to identify any association between the embolic and clinical data. A more detailed account will be described in the relevant sections.

3.3 Quality Control - Study Design and Rationale

Another major cause of intraoperative morbidity/mortality identified during carotid endarterectomy is technical error [Hertzer, 1989; Naylor *et al*, 1992; Riles *et al*, 1994].

Blaisdell used intraoperative angiography to demonstrate that up to 26% of patients have technical abnormalities following carotid endarterectomy including a 5% on-table occlusion rate [Blaisdell *et al*, 1967]. However, angiography has many practical disadvantages as well as a recognised mortality and morbidity that adds to that of the operation. In a review of the angiographic risk in mild cerebrovascular disease, obtained by combining the results of eight prospective and seven retrospective studies the estimated risk of stroke or TIA was 4% and the risk of disabling neurological deficit was 1% with a mortality rate of <0.6% [Hankey *et al*, 1990].

However, similar results to angiography have been achieved using alternative, less invasive methods such as, B-mode ultrasound [Dilley, Bernstein, 1986], continuous wave Doppler ultrasound [Seifert, Blackshear, 1985], and angioscopy [Towne, Berhard, 1977]. Individual studies of these techniques have confirmed their potential application in the assessment of CEA. In addition, experience with TCD monitoring has highlighted its role in detecting intraoperative episodes of ischaemia and embolisation. However, the application of this technique as a quality control measure, detecting abnormalities associated with operative technique had not been investigated. Therefore the second part of this study used TCD, angioscopy, B-mode ultrasound and continuous wave Doppler to assess prospectively 100 consecutive patients undergoing CEA. The aims were threefold:

1. To compare the ability of the techniques to detect technical error.
2. To assess the feasibility of applying each of the techniques for routine use.
- 3) To assess whether applying these methods provided useful information as to the cause of perioperative neurological complications.

The methods used to achieve these aims will be described in more detail in the relevant chapters.

3.4 Patient Recruitment and Investigation

Both parts of this study were performed simultaneously on the same cohort of patients, therefore the admission procedures and characteristics of these patients will be described here. The aim was to gather data prospectively on 100 consecutive patients undergoing carotid endarterectomy. This figure was chosen because it was estimated that there would be sufficient end-points to allow analysis and that from our department's workload, this number of operations could be achieved within the time available to complete the study.

Inclusion Criteria

The criteria for inclusion were all patients admitted to Leicester Royal Infirmary for carotid endarterectomy between June 1992 and February 1994 and who consented to the study (100% compliance). All patients had severe symptomatic carotid stenoses affecting the ipsilateral artery.

Exclusion Criteria

There was no exclusion criteria providing the patient satisfied the inclusion criteria and gave consent to the study.

Investigations

A full medical history and examination were obtained from each patient. In addition routine chest x-ray, electrocardiogram, haematological and biochemical profiles were obtained preoperatively. To standardise data collection a printed history proforma was completed for each patient (Appendix 2) which consisted of preoperative, operative and postoperative sections.

In the preoperative section of the proforma space was provided for a routine medical history but specific information was sought for symptoms of amaurosis fugax, central retinal artery occlusion, TIA, stroke with full recovery and stroke with residual deficit. The duration of each symptom was recorded along with the number of episodes and the date of the most recent episode. Specific data was also collected on the risk factors for stroke - diabetes mellitus, hypertension (+/- treatment), claudication, cardiac disease and smoking.

A full physical examination was carried out and recorded. In particular the blood pressure and peripheral pulses (+/-bruits) were noted.

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Included in the proforma was a section for completion at the time of the preoperative colour Duplex ultrasonic investigation of the carotid arteries which was performed 1-4 days before operation. The degree of stenosis and plaque morphology was recorded in the proximal CCA, distal CCA, ICA and ECA of both carotid arteries and a colour Duplex photograph was obtained and attached to the proforma.

At operation the operating surgeon was required to complete the operative section which recorded which surgeon performed the operation, the side of the operation, the total shunt time, clamp times, type of patch angioplasty used, length of arteriotomy, time from clamp release to haemostasis, level of bifurcation, positioning of intimal tacking sutures and the surgeon's impression of the plaque morphology. A diagram of both the plaque and the suturing of the patch angioplasty, indicating the position of the knots was required.

Sections were also completed for the results of the intraoperative monitoring and quality control measures.

The patient's postoperative progress and out-patient follow-up were also recorded on the proforma.

There were two copies of the proforma for each patient. One copy was incorporated in the patients' notes and replaced the conventional history and continuation sheets. Data was transferred from this copy to the other copy that was used to store the data on each patient until this could be transferred to a computerised data base. A separate proforma was used to record pre- and postoperative ophthalmological findings (appendix 3)

Computerised Data Collection

Data from the proforma on each patient was entered into a database loaded onto an Elonex personal computer (PC-425X, 486 Mhz, 340 Mb hard disc, 80 Mb RAM). The database used was DataEase(DataEase International Inc. USA, 1989). Dataease is a database that enables data to be entered in form mode but can transform the data in a spreadsheet, enabling statistical analysis of any variable selected by the operator. Data can be obtained in the form of printed paper reports or transferred to other computer applications through an ASCII file on floppy disc.

3.5 Patient Data

The characteristics of the patients used in this study are summarised in Table 3.1. The majority of patients were men (68:32) and the median age of the patients was 67, the youngest being 45 and the oldest 82. The most common presenting symptom was TIA, closely followed by amaurosis fugax. Thirty one patients had experienced a stroke and 17 of these had resulted in residual deficit.

The median time since the most recent episode was 24 weeks with a range from 1 day to 4 years. This last patient, who had experienced a stroke with a residual deficit insisted on having the operation performed despite the lack of recent symptoms. The median number of ischaemic episodes was 9 with a range of 1 to 82. A significant proportion of patients had the presence of risk factors for stroke, the most common being smoking with 76 patients either smokers or ex-smokers. Hypertension was the next commonest factor with 60 patients-all treated, known to have high blood pressure. Fourteen patients were diabetic, 6 of whom were insulin dependent diabetics. Nineteen patients had suffered a myocardial infarct and 28 patients complained of angina (controlled). Thirty-six patients gave a history of intermittent claudication in addition to cerebral ischaemia. Only 68 patients had a carotid bruit audible to auscultation despite all patients having a patent, severely stenosed carotid artery. This reinforces the impression that the presence of a bruit is a common, but not essential finding in the diagnosis of carotid artery stenosis.

Preoperative colour Duplex scanning revealed that all patients had >70% stenosis on the symptomatic side with a mean stenosis of 82%(80-84, 95% CI). In addition to this 16 patients had severe contralateral carotid stenosis and 21 patients had a contralateral carotid artery occlusion.

Operatively, 59 operations were performed by two consultant surgeons and 41 performed by senior registrars (7 surgeons in total). A shunt was inserted in 97 patients and was not inserted in three patients due to technical difficulties. The mean time for shunting was 65 mins (SE =3.4) and the mean clamp times before and after shunting were 3.9 mins and 7.6 mins respectively. A patch angioplasty was used in all but one case and the material used was thigh vein- 56 cases, PTFE - 8 cases and Dacron 36 cases.

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Variable	Number
No of Men	68
No of Women	32
Median Age (range)	67 (45-82)
No of Diabetic	14
Treated Hypertensives	60
Hx of Myocardial infarction	19
Hx of Angina	28
Hx of Claudication	36
Presence of carotid bruit	68
Hx of Amaurosis Fugax	42
Hx of TIA	47
Hx of stroke + full recovery	14
Hx of stroke + residual deficit	17
Most recent episode (weeks-median + range)	24 (0.1-208)
Number of episodes (median +range)	9 (1- 82)
No with severe contralateral carotid stenosis	16
No with contralateral carotid occlusion	21

Table 3.1 Characteristics of 100 patients undergoing carotid endarterectomy: Preoperative Details

Variable	Value
No of shunts inserted	97
mean time of shunting	65 mins
clamp time : pre-shunt insertion	245 secs
clamp time : post-shunt insertion	495 secs
patch angioplasty used	99
thigh LSV vein	56
PTFE	8
Woven Dacron	36
Time to haemostasis	8.8 mins
Total blood loss	539 mls

Table 3.2 Characteristics of 100 patients undergoing carotid endarterectomy: Intraoperative Details. PTFE = polytetra-fluoroethylene. LSV = long saphenous vein.

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The mean length of the arteriotomy was 7.9cm. The mean time from clamp release to haemostasis was 8.8 mins with a mean total blood loss for the operation of 539 millilitres. All patients received intraoperative heparinisation consisting of 5000 i.u. intravenous given one minute before initial clamping of the carotid artery.

3.6 Comparison of Data with ECST and NASCET

A comparison of the base-line characteristics with the patients in the ECST and NASCET studies shows them to be comparable (Table 3.3). Overall the Leicester patients were older and had a greater incidence of severe contralateral carotid stenosis and occlusion. ECST used the mean age (62.2) while NASCET used the median (65). In the Leicester patients the mean (66.5) and median (67) ages were similar and demonstrated a slightly older cohort. The NASCET study identified that surgery was equally beneficial to older patients and concluded there was no evidence to support an upper age limit for carotid endarterectomy [Barnett, 1993].

However, the NASCET study did identify that patients with contralateral carotid artery occlusion were at increased risk of stroke from both medical and surgical treatments. The 32 day stroke/death rate for these patients was 10% for both medical and surgical treatments however surgery reduced the 2 year risk of stroke from 56.4% in the medical group to 20.4% in the surgical group. The conclusion was that although these patients are at increased risk of surgery, this risk is justified because the long term benefits are so significant and therefore should not be considered a contraindication for surgery.

The Leicester cohort included a high percentage of patients with contralateral carotid occlusion (21%) therefore one would expect the incidence of perioperative stroke/death to be higher in the cohort as a whole and in this subgroup in particular. Interestingly the NASCET study found that contralateral severe stenosis (70-99%) was not associated with an increased risk of surgery [Barnett, 1993]. Similarly, the degree of ipsilateral stenosis, within the severe band, was not associated with additional surgical risks.

However, secondary analysis did reveal that the degree of high grade stenosis did correlate with degrees of risk reduction after surgery. The absolute risk reduction for all ipsilateral stroke at two years was 26 percent (90-99%

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stenosis), 18 percent (80-89% stenosis) and 12 percent (70-79% stenosis) [NASCET, 1991]. In the Leicester cohort 32% of patients were in the 90-99% stenosis group compared to 22% of patients in the NASCET group. Furthermore 74% of Leicester patients were in the 80-99% stenosis group compared to 60% of the NASCET group. Therefore, one can conclude that from the standpoint of both ipsilateral stenosis and contralateral occlusion the Leicester patients were at higher risk of perioperative strokes/death but were poised to gain greater stroke-free benefit in the long term as a result of surgery.

	Leicester	ECST	NASCET
Age	67(median) 66(mean)	62.2 (mean)	65 (median)
Sex ratio (M : F)	68:32	70:30	68:32
TIA's (+ Am F) %	47(65)	(78)	68
Stroke (including silent CT infarct) %	31(52)	(50)	33
Previous MI %	19	27	18
Angina %	19	-	22
Periph vasc disease %	36	19	15
Diabetic %	14	9	17
Hypertension %	60	-	60
Current Smokers (ex) %	18(58)	56	37
Contralateral carotid occlusion %	21	-	6
Contralateral carotid stenosis 70 - 99%	16	-	8
Ipsilateral stenosis			
70 - 79%	26	-	40
80 - 89%	42	-	38
90 - 99%	32	-	22

Table 3.3 Comparison of baseline characteristics of Leicester patients with patients in the NASCET and ECST. Am F = amaurosis fugax, CT = computerised tomogram, MI = myocardial infarct.

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The ECST did not specifically examine the effect of ipsilateral/contralateral carotid stenosis on clinical outcome.

With regard to other variables and risk factors the three cohorts appear very similar. In the ECST study the incidence of TIAs and amaurosis fugax were expressed as a combined figure (78%). In the Leicester cohort the incidence of TIAs was 47% and amaurosis fugax alone was 18% giving a combined figure of 65%. The incidence of TIAs in the NASCET study was higher at 68%. However when one examines the incidence of stroke patients entering the trials the Leicester and NASCET figures are similar 31% and 33% respectively. In the ECST stroke patients were combined with those patients with evidence of silent infarction on preoperative CT scan giving a combined figure of 50%. In the Leicester cohort 21 patients had evidence of silent cerebral infarction giving a combined figure of 65% which is significantly higher than the ECST figure. Subsequent analysis of 352 NASCET patients with symptoms of TIA only identified that the incidence of asymptomatic CT infarcts was 34.4% [Streifler *et al*, 1992]. Both studies identified patients with pre-existing neurological deficits or silent CT infarction at greater risk of stroke than other TIA patients given medical therapy only. Therefore, once again surgery in these patients would produce a greater than expected long stroke free interval [Barnett, 1993].

One reason for the excess of high risk patients within the cohort may be related to the position of Leicester as a tertiary referral centre for carotid surgery. Eighteen percent of patients in the cohort originated from other health authorities and some had been advised against surgery in their own area.

A review of the operative details reveals a practice comparable with other surgeons in Great Britain and Ireland. In this study an intraluminal shunt was inserted in all but three cases, where technical difficulties prevented safe insertion. In a survey of surgical practice performed in 1989 38% of vascular surgeons always inserted a shunt, 59% sometimes or rarely used a shunt and only 3% never used one [Murie, Morris, 1991]. Insertion of a shunt minimises the risk of haemodynamic strokes during the operation, enabling the operation to be performed in an unhurried manner. The ECST identified surgery being performed in under one hour as being associated with higher perioperative morbidity. This situation provides adequate time for training of surgeons, indeed in this study 41% of operations were performed by higher surgical trainees.

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In this study a patch angioplasty was used in all but one case, that being a particularly large diameter artery. The use of patch angioplasty is less widespread with only 2% of surgeons always using patch angioplasty, sometimes using in 18% and rarely by 22% [Murie, Morris, 1991]. In the course of the study there was a move away from upper thigh vein to specially manufactured Dacron carotid patches. These were found to be more convenient and avoided the morbidity and discomfort of the longitudinal scar in the groin necessary to harvest suitable thigh vein which was sometimes of disappointing quality. Expanded Polytetrafluoroethylene (PTFE) patches were associated with very prolonged time to haemostasis after clamp release, in one case up to one hour ten minutes and their use was short lived.

3.7 Summary

In this chapter I have outlined the aims and design of the two main studies that are the basis of this thesis. Both are prospective studies of the same 100 consecutive patients undergoing carotid endarterectomy at our institution. The selection and investigation of these patients have been outlined and their baseline characteristics have been described. The baseline characteristics of these patients have been compared to those patients in the ECST and NASCET studies. The Leicester cohort of patients were found to be older, have a greater degree of ipsilateral carotid stenosis and a much greater incidence of contralateral carotid occlusion therefore identifying these patients as a high risk cohort. One reason for the excess of high risk patients may be the position of Leicester as a tertiary referral centre for carotid surgery.

The thesis will now divide into three different sections. Section two will describe the study into the incidence and clinical relevance of TCD detected intraoperative embolisation; section three will describe the study comparing different methods of quality control; section four will describe the case histories and subsequent investigations of some complications that occurred in the course of the study and finally the thesis will end with a discussion of the main findings arising from this thesis and the direction of future research.

PART TWO : CHAPTER 4

**THE CLINICAL RELEVANCE OF INTRAOPERATIVE EMBOLISATION
DETECTED BY TRANSCRANIAL DOPPLER MONITORING DURING
CAROTID ENDARTERECTOMY.**

Transcranial Doppler Sonography

CHAPTER 4

TRANSCRANIAL DOPPLER SONOGRAPHY

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4.1 Introduction

Part two of the thesis describes the study to determine the incidence and clinical relevance of intraoperative embolisation detected by TCD monitoring. Chapter 4 contains a summary of the history and development of TCD and then proceeds to outline the theoretical basis of TCD monitoring and the detection of emboli.

Chapter 5 describes the method and materials of intraoperative TCD monitoring and then presents the results of intraoperative embolus detection. The operation was divided into different stages and the number and character of emboli detected in each stage were determined. The chapter ends with a discussion of the significance of the different number and character of emboli detected at each stage.

The next three chapters (6,7,8) associate the findings of chapter five to clinical outcome. Chapter 6 describes the neurological and cognitive findings, chapter 7 the ophthalmologic findings and chapter 8 the CT and MRI scans.

Part two ends with a discussion of the section as a whole, describing the clinical relevance of the TCD detected emboli in this study.

4.2 History and Development of TCD

The first transcranial Doppler recordings were performed by Rune Aaslid in the department of neurosurgery in Bern in the summer of 1981 and the results published in 1982 [Aaslid *et al*, 1982]. The idea of investigating the intracranial circulation with ultrasound was first proposed in 1960 by Kaneko working in Osaka while developing the clinical uses of ultrasound [Satomura, Kaneko, 1960; Kaneko, 1986]. However this concept was rejected by his colleague Satomura in favour of using the technique to investigate the extracranial circulation and this may have delayed the development of TCD for more than 20 years. The skull was considered a significant barrier to the penetration of ultrasound waves however the problem can be minimised by using a lower frequency of ultrasound. The first TCD machine was a 2MHz pulsed Doppler machine originally designed for cardiac use. Advances in microprocessor technology have established the technique as a useful method for studying cerebral haemodynamics and detecting cerebral embolisation enabling the

technique to be increasingly applied in a wide variety of clinical situations [Aaslid, 1992].

4.3 The Doppler Principle as Applied to TCD

This theory was first described by the Austrian physicist Christian Doppler in 1842 and describes the relationship between the velocity of objects and the frequencies of transmitted and reflected sound waves [Doppler, 1842].

In brief, if sound waves of a given frequency are transmitted towards a moving object the frequency of the reflected waves depends to certain extent on the direction of the object. If the object is moving towards the source the reflected waves will have a higher frequency, whereas if the object is moving away the reflected waves will have a lower frequency. The degree of frequency shift depends on the velocity of the object and therefore the velocity can be estimated if the frequency shift is known. Mathematically this relationship is described by the following formulae:

$$f_1 = f_0 \left(\frac{V+c}{c} \right) = f_0 \left(\frac{1+V}{c} \right)$$

f_1 is the frequency of ultrasound received by a red blood cell moving towards the source with a velocity, V .

f_0 = frequency of transmitted wave.

c = propagation velocity of ultrasound.

In this example the red blood cell is assumed to be moving towards the source. f_1 is transmitted from the moving blood cell; however this cell moves a distance of V/f_1 while transmitting one entire wave. Therefore the actual wavelength (λ_2) will be shorter and therefore the frequency is higher = f_2 .

$$\lambda_2 = \left(\frac{c-V}{f_1} \right)$$

$$f_2 = \frac{c}{\lambda_2} = \left(\frac{f_1}{1-\frac{V}{c}} \right) = f_0 \left(\frac{1+\frac{V}{c}}{1-\frac{V}{c}} \right)$$

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The Doppler shift (f) is the difference in frequency between the transmitted frequency and the received frequency:

$$f = f_2 - f_0 = 2 \cdot f_0 \cdot \frac{V}{c}$$

An object travelling with a velocity of 1m/sec will give a shift of about 2.5kHz at an f_0 of 2 MHz and 5kHz if the Doppler ultrasound frequency is 4 MHz. Therefore to avoid confusion on most units the velocity is expressed as cm/sec. However this calculation of the velocity only applies if the object is travelling parallel to the line of insonation. Usually an angle ϕ exists between the direction of movement of the object and the line of insonation and this causes the measured velocity to be lower than the actual velocity. However if the angle of insonation is known, this effect can be corrected for using this formula:

$$V = \frac{c}{2 \cdot \cos \phi} \cdot \frac{f}{f_0}$$

Unfortunately, it is not possible to measure the angle of insonation when using TCD however the most often insonated, the middle cerebral artery (MCA) runs perpendicular to the surface of the skull for a considerable distance from its origin [Aaslid *et al*, 1982]. Insonating the artery from the posterior temporal window the angle of insonation is seldom greater than 30° which means that the measured velocity is at least 87% of the true velocity. Therefore absolute values for velocities measured by TCD have an inbuilt error which must be taken into account when analysing MCA velocity data [Aaslid *et al*, 1992].

Sample Volume

The sample volume is the spatial region from which the TCD detects the Doppler shifts. Most TCDs have a beam width of 3-4mm that coincides with the diameters of the basal cerebral arteries. The TCD samples Doppler shifts from within that width however the sensitivity is greater at the centre of the beam and signals become weaker laterally [Arnolds *et al*, 1989].

The axial component of the sample volume is determined by the technique of range gating. Pulses of ultrasonic waves are sent out from the transmitter at a preset pulse repetition frequency (PRF). The transmitter then stops and a time elapses before the receiver switches on and receives returning Doppler shifts

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for fixed duration. Only signals received during this time are used to determine the Doppler shift and these signals correspond to those signals reflected from anatomical structures at a certain depth. The depth can be altered by altering the time interval before the receiver receives signals. The length of the sample volume can be altered both by increasing the duration of transmission or receipt of signals. Most TCDs use long sample volumes (5-12mm) in order to improve the signal to noise ratio and therefore ease the detection of the basal cerebral arteries [Aaslid, 1992].

The sensitivity of the sample volume is greatest at the centre and weakest at the edges in all directions. Therefore objects which reflect a high proportion of incident ultrasound waves passing through the sample volume will be detected over a greater distance than other objects which reflect less ultrasound [Smith *et al*, 1994].

Velocity Profiles and Doppler Spectra

The Doppler equation derived above, was for a single blood cell reflecting an ultrasonic wave. In practice the situation is much more complicated. When insonating an artery each moving component contributes to a mixture of Doppler shifts consisting of many frequencies. Spectral analysis enables the signal power of each velocity component to be determined and colour coded to give a visual computer display. The average velocity profile of blood flowing in an artery is typically parabolic with the velocities of the different blood cells displayed throughout the spectrum. The outline of this spectral display corresponds to the maximal Doppler shift and, therefore, the maximal velocity component of the velocity profile = V_{max} . This, in turn, corresponds with the velocity of blood flow in the centre of the arterial lumen and is the more accurate measure for most monitoring purposes.

Volume Flow

It should be stressed that TCD measures the velocity of blood flow and not the volume of blood flow [Naylor, 1991]. This is because the diameter of the artery cannot be determined accurately enough to enable calculation of absolute volume flow in millilitres. Although some authors have found a good correlation between measures of cerebral blood flow such as ^{133}Xe SPECT and regional mean cerebral transit time and TCD velocity values an individual value can only be considered an indicator of the amount of blood flow and not an absolute measure [Sorteberg *et al*, 1990; Naylor *et al*, 1991]. In the clinical

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situation this 'indication' of blood flow can be used to detect large falls in cerebral blood flow known to be associated with neurological damage. A MCA velocity of less than 10-15cm/sec during carotid clamping has been associated with a flattening of the EEG in some cases and therefore, has led to recommendations that the MCA velocity should be maintained above this level [Spencer, 1992; Steiger, 1992]. However, due to the reasons explained above, the absolute values for MCA velocity can be inaccurate and Halsey suggested that the percentage fall in MCAV on carotid clamping as a more reliable indicator of ischaemia. It was found that if the MCAV fell to less than 40% of its preclamp value this was associated with mild cerebral ischaemia and less than 15% was severe ischaemia [Halsey, 1993].

4.4 TCD Examination Techniques

Transcranial Doppler sonography exploits three areas of the skull where the bone is relatively thin and therefore provides less of a barrier to the penetration of ultrasonic waves. These areas are known as acoustic windows and are located as follows; the transtemporal window [Aaslid *et al.* 1982], the transorbital window [Spencer, Whisler 1986] and the transoccipital window [Arnolds, von Reutern 1986]. The transtemporal window is the most commonly used and is located over the temporal bone just superior to the zygomatic arch. The transtemporal window is used to insonate the middle cerebral artery and therefore was the site used for our monitoring of carotid endarterectomy.

Although radiological studies have shown that the transtemporal area is the most consistently radiolucent area of the skull [Taveras, Wood, 1976], insonation is still impossible in approximately 10% of subjects due to hyperostosis [Feinber *et al.* 1990]. This predominantly occurs in post-menopausal women and is due to a localised increase in the density of the inner table of the skull [Taveras, Wood, 1976].

The transorbital window utilises the thin orbital plate of the frontal bone, the optic canal and/or the superior orbital fissure to insonate the intracranial portion of the internal carotid artery and the ophthalmic artery. Although attenuation is much less through this window and the carotid sinus may be insonated, the acoustic intensity needs to be carefully controlled to reduce exposure to the eye [Spencer, Whisler, 1986]. Also the effects of prolonged

insonation (2-4 hours) is unknown and therefore the application of this technique for intraoperative monitoring is restricted.

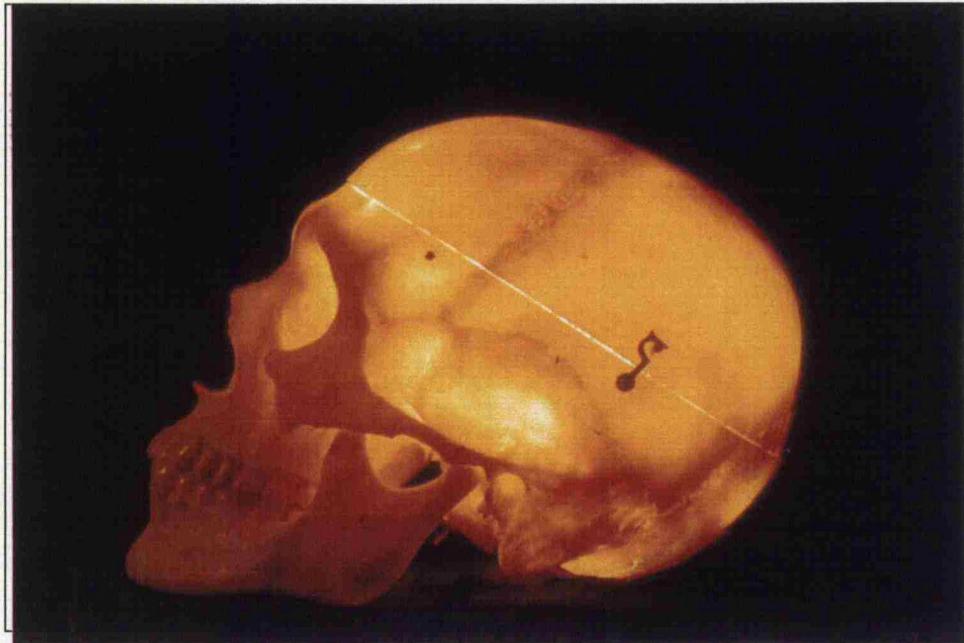


Figure 4.1 Photograph illustrating a skull illuminated from the inside to demonstrate the thin areas of bone

The transoccipital window provides access to the intracranial portions of the vertebral and basilar arteries by exploiting the gap between the cranium and the atlas. However adequate access requires considerable neck flexion on the part of the patient which is uncomfortable for many patients and may be impossible in the older age group. This position of the neck is unsuitable for the performance of carotid endarterectomy and the insonation of these arteries would not be expected to detect any emboli which had their origin in the carotid artery. Therefore this window was not used for monitoring.

Examination of the Middle Cerebral Artery.

The transtemporal window is divided into three regions, posterior, middle and anterior moving from the area just in front of the ear and above the zygomatic arch, forwards [Fujioka, Douville, 1992]. The posterior transtemporal window is the most commonly used but if no window is found the other regions should be investigated. The probe is placed on the posterior temporal area with some aqueous ultrasound coupling gel between the probe and the skin. The acoustic intensity is set to 100% of its maximum, the sample volume placed at a depth of

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55mm and the probe angled slightly forwards and upwards. From this position small alterations in depth and angle are made until a Doppler signal is obtained. The angle and position is further adjusted to obtain the maximum MCA velocity possible thereby ensuring that the angle between the line of insonation and the direction of blood flow is as low as possible (see explanation above). For a positive identification of the MCA the following criteria should be satisfied [Fujioka, Douville, 1992]:

1. With the probe positioned on the posterior temporal window the probe should be angled slightly anterior and superior.
2. The Doppler spectral signal obtained should have a positive deflection (indicating blood-flow towards the probe) , the systolic upstroke should be steep (except in cases of severe flow limiting proximal stenoses) and the time averaged mean velocity should be in the region of 55 ± 12 cm/sec.
3. On increasing the depth (55-64mm), the signal should bifurcate, with a negative deflecting signal becoming visible in addition to the positive deflection. This indicates that the point of bifurcation of the internal carotid artery into the anterior (negative deflection-flow away from the probe) cerebral artery (ACA) and middle (positive deflection-flow towards the probe) cerebral artery (MCA). Increasing the depth further and angling the probe more anteriorly should yield a predominantly negative deflection indicating insonation of the anterior cerebral artery alone(65-70mm).
4. On decreasing the depth, the MCA signal should be detectable to at least 45mm although the angle of the probe may need to be adjusted to take account of bends in the artery. Only the middle cerebral artery is detectable at these shallow depths because it runs outwards towards the skull for 16-20mm of its course before bifurcating.
5. Having identified the MCA and ACA, the probe should now be angled posteriorly and the depth increased to 60-70mm and the posterior cerebral arteries identified. The P₁ segment has a positive deflection but usually has a less steep systolic upstroke and a velocity in the region of 39 ± 10 cm/sec. The P₂ has a negative deflection and a velocity of 40 ± 10 cm/sec.

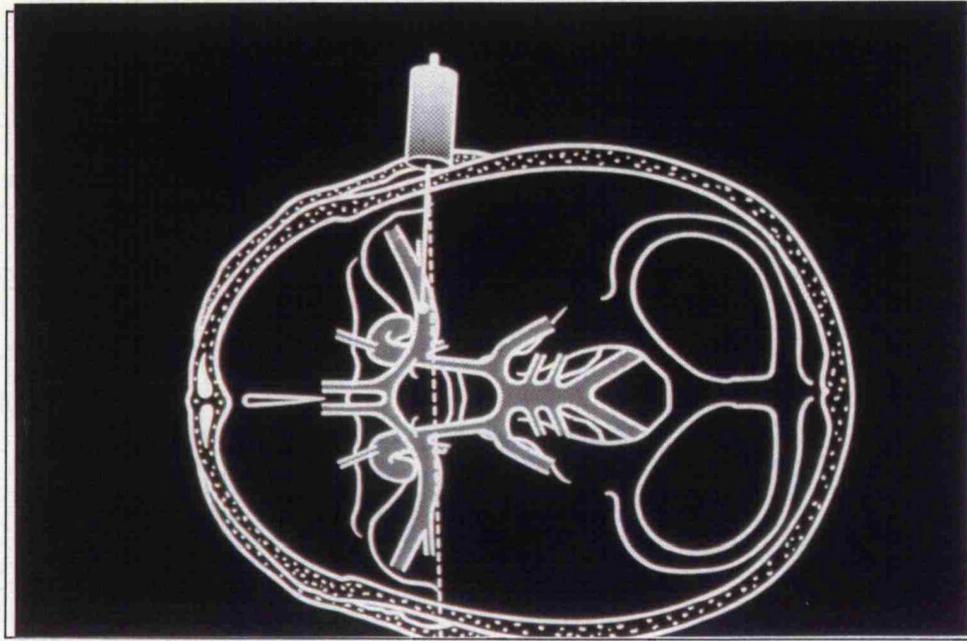


Figure 4.2 Diagram illustrating the TCD insonation of the circle of Willis.

Exceptions to the Criteria.

It is probably safe to say that the only criterion which does not vary is the fact that blood flow in the MCA should always be towards the probe. However anatomical variations and altered directions and velocities of flow due to disease can make positive vessel identification very difficult.

A very severe ipsilateral carotid stenosis or occlusion can reduce flow to such an extent that the direction of blood flow in the anterior cerebral artery is reversed providing a collateral blood supply. In such a case the bi-directional signal at the bifurcation is never obtained because the blood is still flowing towards the probe. This gives the impression that the middle cerebral artery can be traced to a much greater depth than would be normally expected.

Alternatively, in cases of reduced ipsilateral carotid blood flow the amount of blood flowing through the posterior cerebral artery increases considerably. In such a patient the MCA signal is detectable but the systolic upstroke may be damped and the velocity reduced so that it does not resemble a typical MCA waveform. The P₁ segment of the posterior cerebral is the strongest signal with a steep systolic upstroke and a higher blood flow velocity and therefore closely mimic the MCA and can lead to monitoring of the wrong artery.

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However the probe will be noted to be angled slightly posteriorly and if angled further posteriorly no other signals will be detected [Fujioka, Douville, 1992].

Operative Changes

If the MCA has been correctly identified and is being continuously monitored during carotid endarterectomy the velocity should fall when the ipsilateral carotid artery is clamped. The degree of fall will be determined by the adequacy of the collateral vessels to increase their blood supply to compensate for the loss of carotid supply. However the velocity should never fall to zero as there is usually some collateral blood flow even if it is inadequate to avoid ischaemia. If the velocity does fall to zero it is likely that the internal carotid artery has been insonated by mistake. This is because the ICA is below the circle of Willis and therefore below the collateral blood supply. If the velocity increases it is highly probable that the posterior cerebral artery has been insonated. Blood flow in the PCA increases on carotid clamping to compensate for the reduced supply from the carotid. The blood flow in the ACA also increases but is usually a weaker signal than the posterior [Otis, Ringelstein, 1992].

Carotid Artery Compression Tests

Compression of the ipsilateral carotid artery is a useful technique that helps to identify the insonated artery in the way described during carotid clamping. However it is not a suitable technique for use in patients with stenotic carotid disease because of the risk of dislodging plaque and causing a stroke [Saver, Feldmann, 1993].

4.5 Detection of Intraoperative Ischaemia using TCD monitoring

The ability of ultrasound to detect emboli of different materials had been well established for some time [Spencer *et al.* 1969]. However, early investigators using TCD to monitor carotid endarterectomy concentrated on the ability of TCD to predict cerebral ischaemia at the time of carotid clamping [Padayachee *et al.* 1986]. The fall in MCA velocity at the time of clamping was correlated with a number of other methods of detecting cerebral ischaemia such as awake testing, EEG, SSEP, measures of cerebral perfusion and more recently mean cerebral transit time [Naylor *et al.* 1992]. Although it has already been described that MCA velocity is not a measure of blood flow several investigators found a good correlation between these methods and low MCA

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values indicating ischaemia. Several investigators found that an MCA velocity between 10-15cm/sec correlated with a decrease in frequency and amplitude of waveforms during EEG monitoring indicating cerebral ischaemia [Spencer, 1992; Steiger, 1992]. However, Halsey found the relative decline in MCAV more reliable at correlating with ischaemia detected with EEG. A decline in MCAV to less than 40% of original MCAV carried a mild risk of ischaemia, less than 15% correlated with a severe risk of ischaemia [Halsey, 1993].

However, a disadvantage of substituting TCD, a purely haemodynamic method, for direct measures of cerebral ischaemia is that some patients with recent infarction or other foci of cerebral ischaemia may have no tolerance to any reduction in MCA blood flow. These patients would be detected by the direct measures of cerebral ischaemia but missed by TCD which merely indicate an MCAV adequate in the majority of subjects.

The rationale for employing many of these methods was to provide a basis for the selective insertion of intraluminal shunts which are considered by many surgeons to be an hindrance to the performance of carotid endarterectomy and associated with intraoperative morbidity [Halsey, 1992].

In our study all patients (except three) were shunted, therefore TCD had only a minor role in the detection of cerebral ischaemia. However, as will be described later, TCD did prove particularly valuable in detecting shunt malfunction which was not otherwise apparent.

4.6 Doppler Ultrasound Detection of Cerebral Emboli [Russell, 1992]

The theory of how Doppler ultrasound can measure blood flow velocity towards or away from the probe using the change in Doppler shift has already been explained. In addition to measuring the frequency of ultrasound waves returning to the Doppler receiver the amount of ultrasound is also measured and expressed as the amplitude or signal power. The amount of ultrasound reflected depends on both the size and the acoustic impedance of the substance being insonated.

Acoustic impedance (Z) is a measure of the resistance to sound passing through a medium and is a product of density (ρ) and velocity (c), i.e., $Z = \rho \cdot c$ and is expressed in units of $\text{kg/m}^2/\text{sec}$. High density materials have an high

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acoustic impedance while low density materials have a low acoustic impedance. The amount of sound that is reflected at an interface depends on the acoustic impedance change from one substance to another. A large difference in the acoustic impedance at the interface between two materials will result in a large amount of ultrasound being reflected. The reflection coefficient (α_R) =

$$\left(\frac{Z_2 - Z_1}{Z_2 + Z_1} \right)^2$$

α_R = reflection coefficient.

Z_1 = acoustic impedance of medium 1.

Z_2 = acoustic impedance of medium 2.

Multiplying this relation by 100 gives the percentage reflection of ultrasound waves at the interface. The same percentage is reflected whether going from a substance of high acoustic impedance to one of low impedance or vice versa. In the case of the blood/air interface the % reflection is 99.9% and therefore air emboli in blood produce very high intensity signals. With particulate emboli consisting of platelet aggregates the acoustic impedance coefficients are similar therefore the % reflection is lower and particulate emboli produce lower intensity signals.

When ultrasound is directed at an object or interface which is larger than one wavelength in size the percentage reflection accurately predicts the amount of ultrasound reflected. This is known as specular reflection. If the incident ultrasound travels perpendicular to the object then the reflected ultrasound travels back along the same line. If the incident ultrasound strikes the object at an angle then the angle of reflection is equal to the angle of incidence. However if the object is smaller than one wavelength then the reflected ultrasound is scattered in all directions, non-specular reflection, and the intensity of the ultrasound signal returning to the receiver will be reduced. However, decreasing the ultrasound frequency can improve the detection of emboli by improving the embolus blood ratio (EBR) of the signal. In the TCD situation a relatively low frequency of 2MHz is also needed in order to penetrate the skull.

Detection of Different Embolic Materials Using Doppler Ultrasound

Because gas causes a large reflection of ultrasound and is, therefore, relatively easy to detect, the earliest reports of emboli detection were primarily of gas emboli particularly in relation to the study of decompression sickness in divers. Spencer detected gaseous emboli in the vena cava and aorta of sheep and swine during decompression experiments using hyperbaric air. Later the presence of gaseous emboli were identified in the peripheral veins and pulmonary arteries during decompression experiments using human volunteers [Spencer *et al*, 1968, 1969]. Air emboli have been detected during open heart surgery [Padayachee *et al*. 1987], hip arthroplasty [Svartling, 1988], neurosurgery and carotid endarterectomy [Padayachee *et al*. 1986; Spencer *et al*, 1990; Naylor *et al*, 1991]. Other authors have described the detection of emboli consisting of solid element or particulate emboli. Kelly and colleagues detected emboli signals in the femoral veins of patients following fracture of the tibia or femur which they proposed were probably fat emboli [Kelly *et al*, 1972]. Herndon and colleagues described similar findings during hip replacement [Herndon *et al*, 1975]. Spencer detected emboli in the middle cerebral artery using TCD, during the initial dissection of the carotid artery during carotid endarterectomy. These emboli were considered to be particulate because the arterial system had not been entered and, therefore, air should not have been present [Spencer *et al*, 1990]. Spencer, who performed much of the early work identifying air emboli has recently described the criteria used during his research for the identification of emboli within the cardiovascular system:

1. They are short transients, less than 0.1 sec ranging 3 to 60 dB above the background Doppler blood velocity spectrum.
2. They are unidirectional within either the advancing or receding velocity spectrum.
3. Their duration in the spectrum is inversely proportional to their velocity.
4. They are random in occurrence in the cardiac cycle.
5. They usually change frequency/velocity as they pass through the sample volume.
6. They sound to the ear like harmonic chirps, whistles, or clicks, depending on their velocity [Spencer, 1992].

The amplitude or power of the embolic signal is best measured by comparison to the adjacent spectrum of red cells. The fast Fourier transform spectral display used in most TCDs uses colour coding to differentiate signals of

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different amplitude. Therefore, emboli produce high intensity signals which stand out from the surrounding lower intensity signals of the blood. The intensity of the signal is measured in decibels and the intensity of a particular embolus can be measured by raising the noise threshold level until the emboli signal disappears. In general, air emboli produce signals of a higher intensity than particulate emboli. However in the clinical situation it is difficult to differentiate between the two [Spencer, 1992].

Russell attempted to clarify this question using a rabbit model [Russell *et al*, 1991]. The artery used was the aorta since this has a diameter similar to the MCA in humans. Emboli, suspended in saline were injected in to the left renal artery and detected by an ultrasound probe positioned over the distal aorta. Emboli were used which were thought to be involved in cerebral emboli; whole blood clot, platelet rich thrombi, human atheromatous material from a carotid plaque and subcutaneous rabbit fat. Volumes of air from 0.1-6.0 μ l were also injected. All of the emboli that were introduced into the aorta were readily detected using the criteria outlined above. All the emboli caused Doppler signals that were at least 15dB greater than that of the surrounding blood. Emboli composed of air or fat produced stronger signals compared to those due to clotted whole blood, platelets, or atheromatous material. For the clotted blood samples there was a correlation between signal intensity and embolus size. However, with the methodology described it is unlikely that pure samples were injected without contamination with air microemboli. Similar results have been obtained by injecting air or aggregates of particulate material into rhesus monkeys, [Albin *et al*. 1989]. Kessler and colleagues detected endogenously generated, ¹¹¹In labelled platelet aggregates embolising to the brain [Kessler *et al*, 1992]. The emboli were generated by the insertion of thrombogenic segments of vascular grafts into the carotid artery. Transcranial Doppler was used to detect the particulate embolisation which coincided with the accumulation of the radiolabelled platelets in the relevant hemisphere detected by scintillography.

Further, evidence for the embolic nature of these signals comes from experiments using two probes situated at different sites on the same artery detecting embolic signals sequentially. Spencer used one probe situated over the cervical internal carotid and a second probe situated over the ipsilateral MCA. For every MCA embolic signal detected there was an ICA signal which occurred 0.3-0.7 sec earlier. The time difference represented the variation in

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the velocity of blood flow and the time taken for an embolus to travel from the ICA to the MCA [Spencer, 1992].

Intraoperative TCD monitoring

Padayachee was the first to describe the use of TCD to monitor patients during carotid endarterectomy in a study of 19 patients [Padayachee *et al*, 1986]. This study concentrated on the variation of MCAV at different stages of the operation and in particular on the decline in velocity on carotid clamping. Uniquely, the authors described an increase in MCAV associated with diathermy, however this was in all probability an artefact caused by electrical interference, which is commonly seen during monitoring and has not been described subsequently. However, the authors commented that high intensity signals, attributed to air micro-embolisation were detected in all patients at the commencement of shunting without the development of neurological deficits. Emboli were not detected at other stages of the operation. Later, Padayachee described the use of intra-operative TCD monitoring to detect air micro-embolisation in 27 patients during coronary artery by-pass surgery [Padayachee *et al*, 1987]. Air emboli were frequent when bubble oxygenators were used to oxygenate the blood compared to no emboli with membrane oxygenators. In addition, the number of air emboli increased as the gas flow rates in the bubble oxygenators increased providing strong evidence for the intraoperative detection of this phenomena.

Spencer described the detection of embolic signals, similar to those of air emboli, during the initial dissection phase of carotid endarterectomy prior to arteriotomy [Spencer *et al*, 1990]. However these signals were unlikely to be air emboli because the arterial system had not been breached and, therefore, these signals were attributed to 'formed element' or 'particulate' emboli. Spencer also described the TCD detection of particulate emboli in the immediate postoperative period in two patients who had developed neurological deficits. In one of these patients the artery was re-explored and thrombus was found to have accumulated on the endarterectomy site. Particulate emboli have also been detected by TCD in patients with implanted prosthetic valves and atrial fibrillation [Berger *et al*, 1990; Tegeler *et al*, 1990]. Both of these conditions are known to be associated with microemboli.

Naylor prospectively monitored 30 consecutive patients undergoing CEA and detected intraoperative embolisation in 15 [Naylor *et al*, 1991]. Embolisation

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was observed in one patient during carotid mobilisation, in one patient during carotid clamping, in 12 immediately after shunt insertion and restoration of flow and in eight following final clamp release and restoration of flow. However, once again, there was no evidence that these episodes of embolisation were the cause of intraoperative neurological deficits.

Jansen prospectively monitored 130 operations and detected 75 episodes of embolisation in 55 patients [Jansen *et al*, 1993]. In 54 patients embolisation was not associated with postoperative neurological deficits or intraoperative EEG abnormalities. One patient experienced massive embolisation after clamp release and suffered an intraoperative stroke which resolved postoperatively. Embolisation during manipulation of the artery before cross clamping was observed in ten cases and after final clamp release in 39 cases. In eight cases embolisation was detected on release of the external carotid artery clamp and three cases during insertion of a temporary intraluminal shunt. In only two cases, both with several hundreds of emboli, did the EEG show transient but diffuse slow wave activity with a maximum of delta activity in the ipsilateral hemisphere. The other episodes of cerebral embolisation were not detected by the EEG expert system. None of the patients with evidence of intraoperative embolisation had evidence of ischaemia on the postoperative CT brain scan.

However none of these studies was designed to specifically investigate clinical outcome and therefore, the clinical relevance of TCD detected embolisation remains uncertain.

4.7 Summary

This chapter has described the theoretical basis for the determination of blood flow velocity and the detection of embolisation by TCD. Evidence has been presented for the ability of ultrasound to detect emboli within the cardiovascular system and for the ability of TCD to detect emboli of different materials within the middle cerebral artery. The aim of the study was to apply this knowledge to the clinical situation and determine, accurately the incidence and clinical significance of intraoperative embolisation by measuring all previously described methods of determining clinical outcome in the same cohort of patients. In the subsequent chapters I will describe the methodology used to achieve these aims and present the results.

CHAPTER 5

INTRAOPERATIVE TCD MONITORING

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5.1 Introduction

The criteria for differentiating emboli from artefact, and air and particulate emboli have already been described in chapter 4. This chapter describes how those criteria were used to quantify and characterise the emboli occurring at different stages during carotid endarterectomy. In subsequent chapters the number and character of emboli will be correlated with a number of clinical outcomes : neurological and cognitive deficits (chapter 6); fundoscopic and visual fields deficits (chapter 7) and CT and MRI brain scan abnormalities (chapter 8).

Previous investigators have demonstrated the ability of TCD to detect intraoperative embolisation and a common finding was that the incidence of intraoperative embolisation far exceeded the incidence of neurological deficits [Padayachee *et al*, 1986; Spencer *et al*, 1990; Naylor *et al*, 1991; Jansen *et al*, 1994]. However, none of these studies was designed to specifically examine clinical outcome and therefore the exact clinical relevance of this TCD detected embolisation remained uncertain.

In order to investigate the clinical relevance of TCD detected embolisation further it was necessary to examine the intraoperative embolic events in more detail than previous studies. Therefore, for each stage of the operation emboli were differentiated from artefact and characterised into air and particulate emboli using the criteria previously described. Haemodynamic ischaemia was minimised by the routine shunting of every patient and confirmed by comparison with the TCD criteria for haemodynamic ischaemia [Halsey, 1992].

5.2 Materials and Methods

Equipment

Patients were monitored intraoperatively using a SciMed (Bristol, UK) PCDop 842 2 MHz TCD with the probe placed on the transtemporal window to insonate the middle cerebral artery. The PCDop 842 transcranial Doppler flow meter and real-time Fast Fourier spectrum analyser incorporates a 286 personal computer with hard disk storage of blood flow signals, however, the system was modified in the Department of Medical Physics at Leicester University to enable

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much greater storage onto digital audio tape [Bush, Evans, 1993]. The transcranial Doppler mode utilised 2MHz pulsed Doppler with a PRF of 5.2-20.8 kHz. Depth range was 0.5-12cm with a receive width of 15 μ secs (equivalent to 1.16cm), and transmission width of 11.6 μ secs. Ultrasound intensity for the 2MHz pulsed was 200 mW/cm² maximum. Doppler waveforms consisted of directional mean and maximum Doppler shift frequencies and power. The Doppler spectrum consisted of 10 colour/grey scale (variable spectral intensity using threshold control) and Doppler processing consisted of a 256 point Fast Fourier Transform (6.9msec including real time trace extraction). Frequency ranges consisted of 2, 2.5, 4, 5, 8, 10, 13.3 and 20 kHz and the time scale was 6.25, 12.5 and 25 seconds per sweep. RF gain was 0 - 50dB [Manufacturer's data sheet, SciMed UK].

The computer consisted of a ComputerAdd 325S PC computer with 40 Mb hard disk, 1.44Mb 3.5" diskette drive, 2 Mb memory and enhanced keyboard with data displayed on a 14" VGA colour monitor (IBM Model 8512).

Software functionality included automatic and manual selection and accumulation of waveforms, cursor readout of traces and averaged waveforms, calculation of average maximum and mean frequencies, peak systolic frequencies, pulsatility and resistance indices, systolic/diastolic ratio and spectral broadening index. Manual entry of angle of probe to flow enabled calculation of average maximum, mean velocities and peak systolic velocities.

The audio output of the PC Dop 842 which delivered signals to the PC for FFT analysis via a two-way lead was modified to incorporate a three way output with one output connected to a Sony Digital Audio Tape recorder (model TCD-D10). Therefore this enable simultaneous display and recording of the PC Dop signal output onto DAT tape for postoperative playback and analysis. The DAT tapes used were DAT tape 122TD(HHb Communications, 73-75 Scrub Lane, London NW10 6QU). The dynamic range of the DAT recorder was 90 dB.

The dynamic range of the PcDop had also been modified in the Department of Medical Physics to increase the effective dynamic range to enable Wigner analysis of emboli signals. In operating mode the PC Dop 842 had an effective decibel range of 20dB and therefore air emboli signals regularly overloaded the

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system. An additional circuit board was introduced into the PCDop to provide an attenuated channel with a dynamic range of additional 40dB. This increased the effective dynamic range of the PCDop to 60dB enabling greater analysis of embolic signals without overloading. Two channels were utilised within the TCD for the display of forward and reverse flow. However, for monitoring purposes the flow in the MCA is always forward therefore one of the channels was incorporated to display the signals via the attenuated channel. The threshold of this attenuated channel was too high to allow the normal blood spectral envelope to be visualised therefore the only signals to appear were the higher intensity signals associated with embolisation [Smith *et al*, 1994].

Preoperative Interrogation of circle of Willis

A complete examination of the circle of Willis was performed on all patients 1-4 days preoperatively to provide a guide for the intraoperative placement of the probe. The methods used to identify the relevant arteries has already been described (chapter 4). In difficult cases the site of successful insonation of the MCA was marked on the skin with an indelible ink marker.

Intraoperative Monitoring

The TCD probe was positioned over the relevant MCA after the patient had been anaesthetised and positioned correctly on the operating table. Once the correct segment of MCA was found the probe was fixed in this position using the elasticated head band and probe holder illustrated. The detachable handle on the probe was then removed and the probe protected during the operating by attaching the metal head guard to the operating table (Figure 5.1). All TCD signals were continuously recorded onto digital audio tape (DAT) via the DAT recorder connected to the TCD for postoperative playback and analysis.

A written record was kept during every operation of the tape counter readings when the different stages of the operation occurred and when emboli were detected. At the time of each event the blood pressure (intra-arterial line) and end-tidal CO₂ readings from the anaesthetic line were also recorded along with the MCAV (appendix 3). Each DAT tape used was labelled with the tape number, patients name and the date of the operation. Monitoring was performed continuously throughout the operation and continued for a variable time after the reversal of anaesthesia.

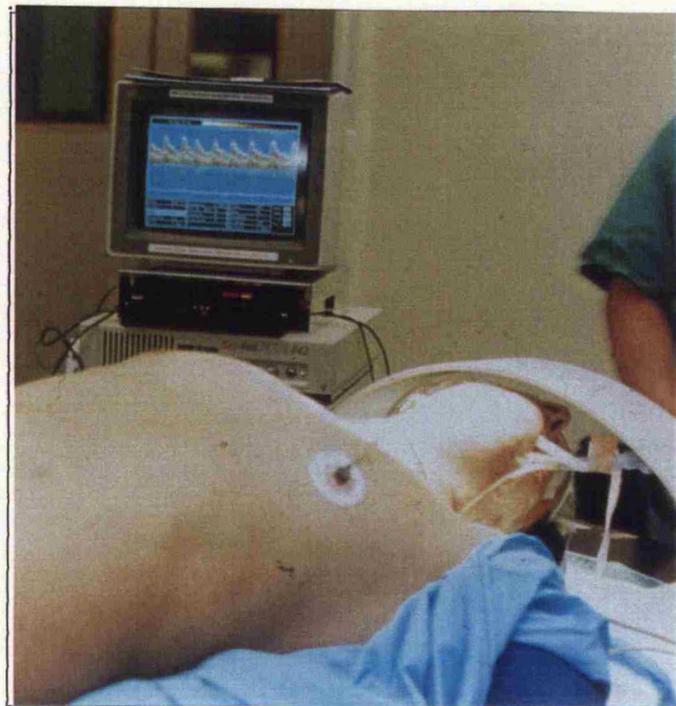


Figure 5.1: Picture illustrating the Intraoperative TCD monitoring set-up. The patient is on the operating table with the TCD probe attached to the right temporal region using the elasticated head-band. The TCD waveform is displayed on the colour monitor.

Post-operative Analysis

All tapes were replayed and reanalysed postoperatively in a quiet room away from the noise and activity of the operating theatre. Possible embolic signals were scrutinised to check they met the criteria necessary for positive identification and classified into predominantly air or particulate using the criteria already described (Chapter 4).

For the purposes of analysis, the operation was divided into different stages and the number and predominant character of emboli for each staged were determined. The operative stages were:

- 1. Dissection (Dis).** Preparation of the skin to clamping of the common carotid artery.
- 2. Shunt opening (Sh Op).** Carotid clamping to 30 seconds after re-establishment of blood flow through the shunt.

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- 3. Shunting Phase (SH).** 30 seconds after shunt opening to immediately before restoration of blood flow through the external carotid artery.
- 4. External carotid artery blood flow (ECA FL).** The restoration ECA flow to immediately before restoration of internal carotid artery flow.
- 5. Internal carotid artery blood flow (ICA FL).** The first 30 seconds of internal carotid blood flow.
- 6. Post CEA manipulation (Manip).** 30 seconds after restoration of flow to cessation of manipulation of the artery.
- 7. Recovery (Rec).** Cessation of manipulation to the end of the recording, approximately 30 minutes.

The number of emboli was calculated for each stage and for the operation as a whole. The number of particulate and air emboli for each stage was determined.

Duration of Embolisation

The duration of each embolus was determined by freezing the image on the TCD screen which has a time base of 6.25 seconds. The start of an embolus was marked by placing the cursor over the first increase in signal amplitude. The cursor was then moved to the end of the increased signal amplitude and the time between these two points was automatically calculated by the computer. The duration of the emboli was calculated for each stage and for the operation as a whole. The duration of air and particulate embolisation was also determined.

Statistical Analysis

Statistical analysis was performed using the CIA computer programme [Gardner *et al*, 1991]. Non-parametric data compared using medians obtained by the Wilcoxon method and expressed with 95% confidence intervals. Parametric data was compared using means and 95% confidence intervals where appropriate.

5.3 Results

Successful intraoperative TCD monitoring was achieved in 91% of operations. Reasons for unsuccessful monitoring were hyperostosis (6%) and equipment

Intraoperative TCD Monitoring

failure (3%). Embolisation was detected in 92% of successfully monitored operations and the median number of emboli per operation was 39 (95% CI 29 to 48.5, K=1598). The median duration of embolisation for each operation was 3.28 seconds (95% CI 2.5 to 4.3, K= 1598). The number, duration and predominant character of emboli for each stage were as follows:

Dissection (Dis)

Embolisation was detected in 23 (25%) out of 91 patients during the dissection phase of the operation. The predominant character of the emboli during this phase were particulate. Emboli characteristic of air occurred in only two instances due inadvertent penetration of the artery while injecting local anaesthetic around the carotid sinus. These were not counted in the analysis.

The median number of emboli was 8 (95% CI 4 to 14, K =66) and the median duration of embolisation for this phase was 0.5 secs (95% CI 0.225 to 0.8 secs, K=66).

Shunt Opening (Sh Op)

Embolisation was detected in 71 (78%) patients during this phase. The character of the emboli was predominantly air and quickly cleared. The median number of emboli was 5.5 (95% CI 4 to 7, K=936) and the median duration of embolisation for this phase was 0.325 secs(95% CI 0.225 to 0.5 secs, K=936).

Shunting (SH)

Embolisation was detected in 48 (53%) patients during this phase. The predominant character of emboli was air and precipitated by handling of the shunt or malfunction of the shunt allowing air to enter the arterial system. The median number of emboli during this phase was 6 (95% CI 4 to 9.5, K=397) and the median duration of embolisation for this phase was 0.3 seconds (95% CI 0.2 to 0.6 secs, K=397).

However, two patients experienced gross air embolisation during this phase associated with puncture of the distal retaining balloon of the Pruitt-Inahara shunt. Patient 22 experienced intermittent signals characteristic of air, 7 minutes 21 seconds after flow had been established through a Pruitt-Inahara shunt. After 26 of these emboli had been detected the distal limb of the shunt

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became dislodged from the ICA because the distal retaining balloon had deflated. The shunt was replaced in the ICA but attempted reinflation of the distal retaining balloon resulted in a shower of emboli. Four attempts to reinflate the balloon produced 64 discrete embolic episodes and 11 seconds of embolisation detected in prolonged showers all typical of air embolisation. A diagnosis of a ruptured distal shunt balloon was made and therefore substituted for a new shunt. Once flow was re-established through the new shunt no further emboli were detected. The clamp time had been 3 minutes 40 seconds. Examination of the original shunt confirmed that the distal balloon had been punctured probably by inadvertent needle-stick injury.

Patient 7 experienced 254 emboli secondary to a similar shunt malfunction with a total duration of embolisation of 14.2 seconds, 3.2 seconds longer than patient 22.

External Carotid Artery Opening (ECA FL)

Embolisation was detected in 48 (53%) patients during this phase of the operation which was predominantly characteristic of air embolisation. The median number of emboli was 9 (95% CI 6 to 13, K=397). The median duration of embolisation for the phase was 0.65 secs (95% CI 0.4 to 1.0 secs, K=397).

Internal Carotid Artery Opening (ICA FL)

Embolisation was detected in 83 (91%) patients on final clamp release and restoration of flow through the ICA and once again the predominant character of the emboli was air. The median number of emboli was 10.5 (95% CI 8 to 13, K=1312) and the median duration of embolisation for this phase was 0.925 (95% CI 0.6 to 1.325 secs, K=1312).

Manipulation (Manip)

Embolisation was detected in 45 (49%) patients during this phase of the operation. The predominant character of the emboli was characteristic of air precipitated by the insertion of extra sutures to bleeding points or the application of ultrasound probes. The median number of emboli was 14.5 (95% CI 9.5 to 23.5, K=328) and the median duration was 1.05 secs (95% CI 0.625 to 1.5, K=328).

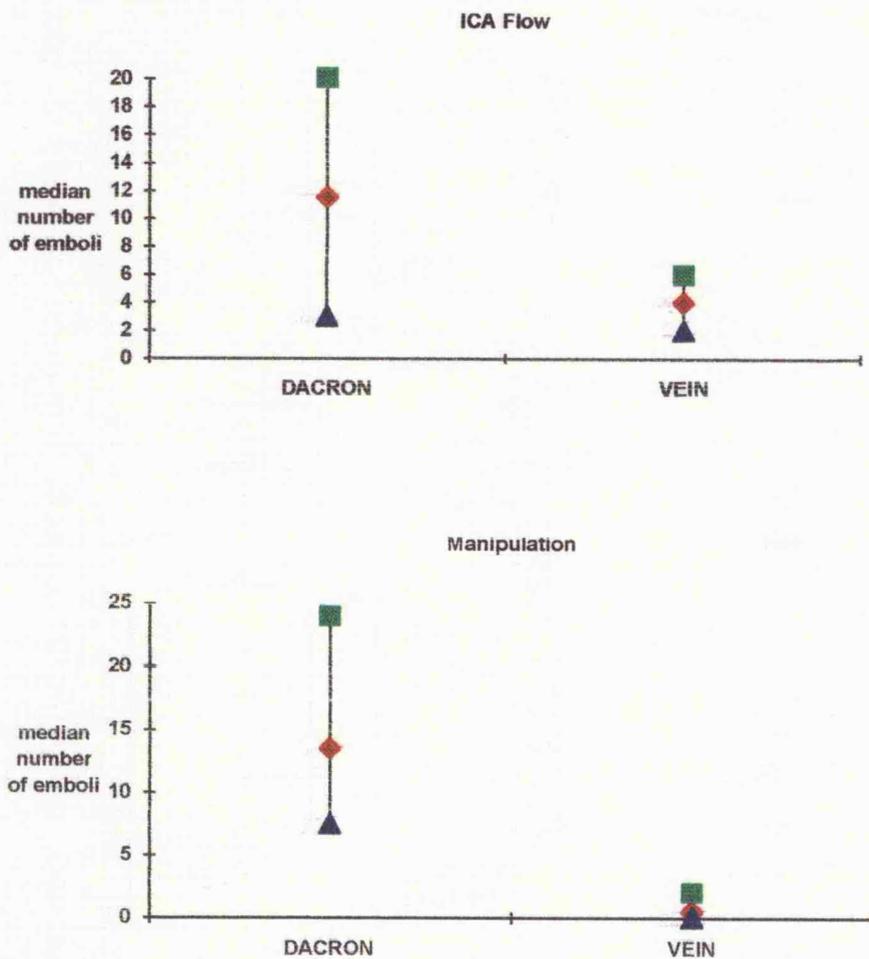


Figure 5.2: Graph illustrating the higher median number of emboli occurring during restoration of ICA flow and manipulation phase associated with the use of Dacron patches compared to Vein.

During the two stages, restoration of ICA flow and manipulation there was a significantly lower number of emboli associated with the use of vein patch angioplasty compared to the use of woven Dacron. The median number of emboli occurring with the use of vein was 7 (95% CI 5 to 10, K=397) and with the use of Dacron the median number was 28 (95% CI 19 to 42.5, K=160). The difference between the medians was -18 (95% CI -27 to -6; 99% CI -30 to -4, K=536) indicating there was significant lower number of emboli associated with the use of vein patches compared with woven Dacron during these stages of the operation. This excess embolisation was characteristic of air and was

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presumably due to dislodgement of air microbubbles trapped within the interstices of the Dacron patch. However, the excess embolisation was not associated with adverse neurological or cognitive outcome (see chapter 6).

Recovery (Rec)

Embolisation was detected in 6 (6.5%) patients during this phase which was predominantly characteristic of particulate. The median number of emboli was 176 (95% CI 5 to 672, K=1) and the mean duration was 8.82 secs (95% CI 0.25 to 33.6, K=1). Two patients had only 5 and 7 emboli respectively which indicated isolated emboli which ceased spontaneously. Patient 33 (Patient A-Figures 5.4-5.5) experienced 44 particulate episodes over a 40 minute period after clamp release but once again these stopped spontaneously and therefore, re-exploration of the artery was not performed). However the final three patients in this group experienced severe, persistent particulate embolisation which in each case was associated with incipient carotid thrombosis and terminated, only, by reoperation and removal of the thrombus. The ability of TCD to detect incipient carotid thrombosis has not previously been appreciated, therefore, these cases will now be described in more detail.

Patient 53

Patient 53 (Patient B-Figures 5.6-5.8), a 72 year old man underwent CEA as treatment for a symptomatic 90% stenosis of the left ICA. The right ICA was occluded. TCD monitoring revealed a MCA velocity of 42 cm/sec at the start of the operation and this was maintained throughout the dissection phase. On clamping of the carotid artery the MCA velocity fell to 23cm/sec but improved to 45cm/sec when flow was re-established through the shunt. At the end of the operation flow was restored through the endarterectomised ICA and the MCAV improved to 64cm/sec. Six minutes after restoring flow, signals consistent with particulate emboli began to be detected every 15-20 seconds and the MCA velocity started to fall. After 40 minutes the MCA velocity had fallen to 26cm/sec, only slightly higher than the MCA velocity when the carotid artery was clamped. The neck was reopened and on gentle palpation of the artery a shower of particulate emboli were detected and the MCA velocity improved to 42cm/sec. On opening the artery a mass of platelet thrombus was found adherent to the endarterectomy site which almost totally occluded the ICA. The thrombus was removed but no underlying technical error was discovered. An heparin infusion was commenced and blood flow was re-established through

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the artery and this time MCA velocity was maintained and only occasional emboli were detected. The patient had experienced 672 particulate embolic episodes.

Patient 98

Patient 98 (Patient C-Figure 5.9-5.11), a 48 year old man underwent operation for a symptomatic 95% stenosis of the left carotid artery causing a 2 month history of frequent TIAs. The contralateral artery was 40% stenosed. Initial MCA velocity was 28.3cm/sec which fell to 17cm/sec on carotid clamping. MCA velocity improved to 39cm/sec on establishment of blood flow through the endarterectomised artery and the MCA velocity improved to 62cm/sec. As the patient was waking from the anaesthetic in theatre, three signals consistent with particulate emboli were detected over a nine minute period. In the recovery room more particulate emboli were detected but neurological examinations performed every 10 minutes were normal and the MCA velocity did not decrease. However, 1 hour 54 minutes later, and after 157 embolic episodes the patient developed a right arm monoparesis. The patient was returned to theatre and on opening the artery a non-occluding mass of platelet thrombus was found adherent to the endarterectomy surface causing a 50% stenosis. No underlying technical defect was found. An intravenous heparin infusion was commenced and flow was re-established through the artery. Middle cerebral artery velocity was maintained and only occasional particulate emboli detected. The patient had experienced 157 particulate embolic episodes prior to reoperation. However an interesting feature of this case was that 17 of these emboli appeared large enough to temporarily obstruct blood flow through the MCA.

Patient 99

Patient 99 (Patient D-Figure 5.12-5.13), a 64 year old man underwent CEA for treatment of 70% stenosis of the left carotid artery causing multiple TIAs. The right carotid artery was occluded. Initial MCA velocity was 77cm/sec which fell to 7 cm/sec on carotid clamping. The MCA velocity improved to 44cm/sec after flow was restored through a Pruitt-Inahara shunt. At the end of the operation flow was restored through the endarterectomised artery and MCA velocity improved to 94cm/sec. Nine minutes after flow was restored TCD signals consistent with particulate emboli began to occur every 1-2 minutes. The emboli became more frequent and within 24 minutes the MCA velocity fell to

22cm/sec. A spontaneous shower of particulate emboli was detected and MCA velocity improved immediately to 58cm/sec. The neck was reopened, on the basis of the TCD findings alone, and a mass of platelet thrombus, causing a 30-40% stenosis was found adherent to the endarterectomy surface overlying a tacking suture. The thrombus was removed and an intravenous heparin infusion commenced. Flow was restored once again and the MCA velocity improved to 90cm/sec and was maintained postoperatively with no further emboli. The patient had experienced 348 particulate emboli.

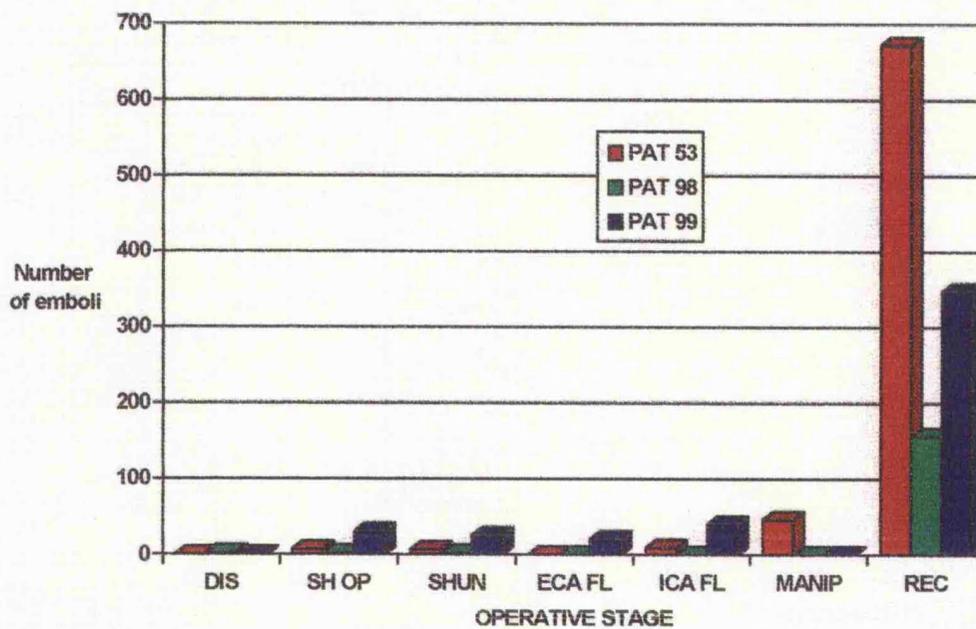


Figure 5.3: Graph showing the number of emboli experienced at each operative stage by those patients with early postoperative carotid thrombosis.

These cases illustrate the ability of TCD monitoring to detect early carotid artery thrombosis following carotid endarterectomy. Diagnosis was based on the detection of persistent particulate embolisation during the recovery phase. In two cases persistent embolisation was associated with a corresponding fall in MCA velocity as the ICA gradually occluded. However in one case (Patient 98) the MCA velocity remained constant and diagnosis was based on the detection of persistent embolisation alone. This represents an important new clinical application of TCD monitoring and the implications of this will be discussed in greater detail later.

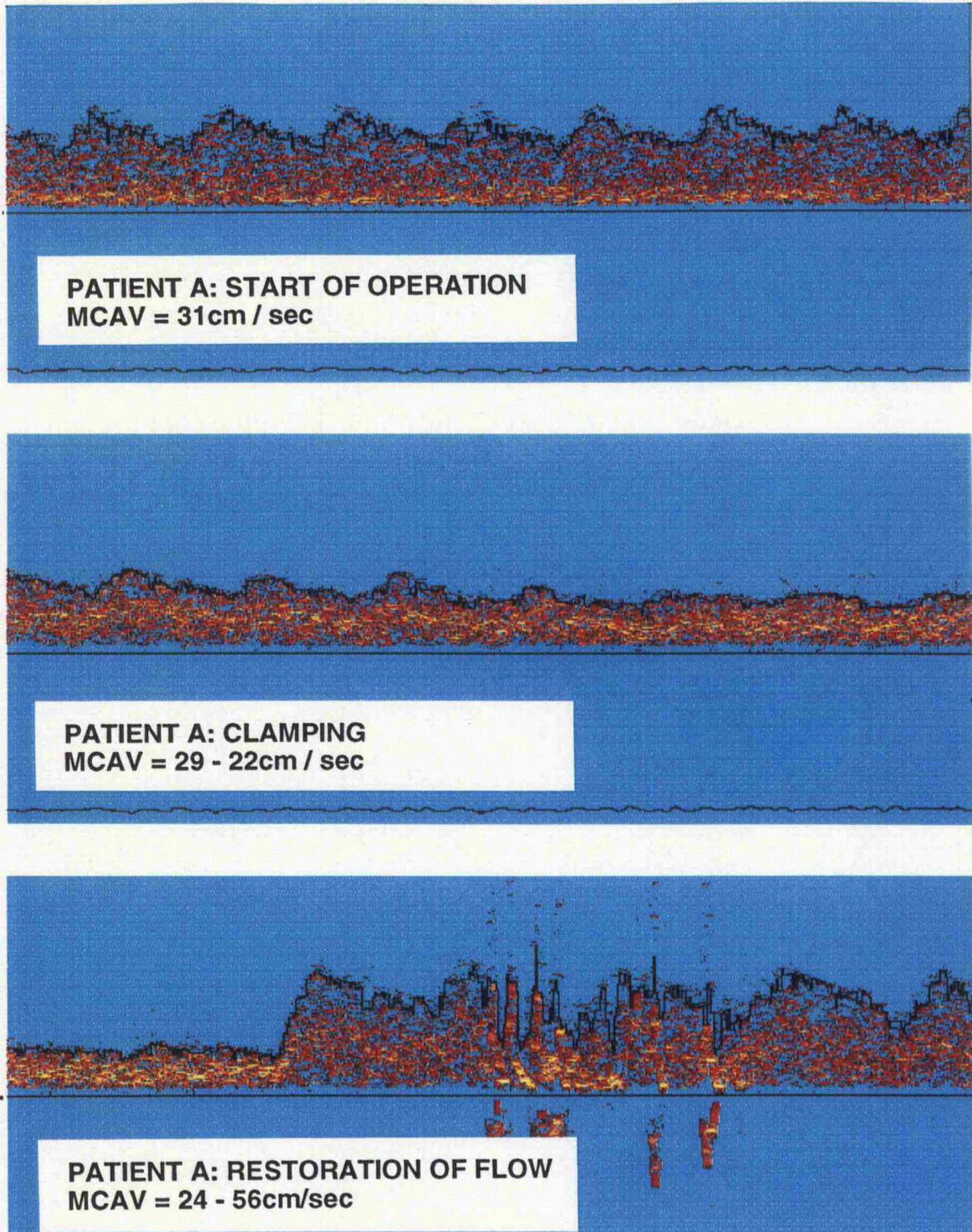


Figure 5.4: Patient A (33) ; TCD printouts illustrating MCAV changes at different stages of the operation. The typical overloading signals of air emboli are shown at restoration of flow (bottom).

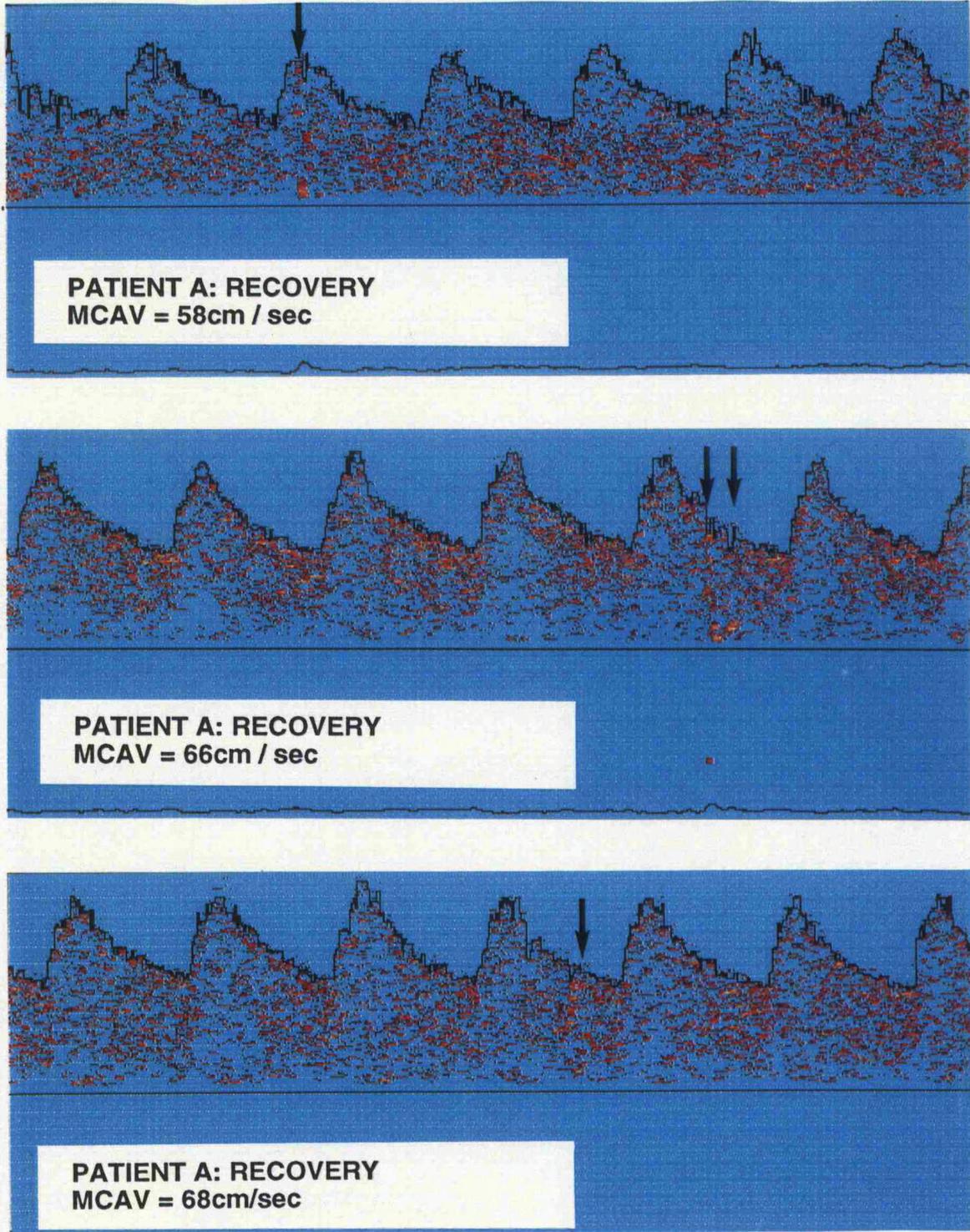


Figure 5.5: TCD printouts from the recovery phase illustrating the detection of the more subtle particulate emboli signals (arrows). The emboli stopped spontaneously without causing any neurological deficit.

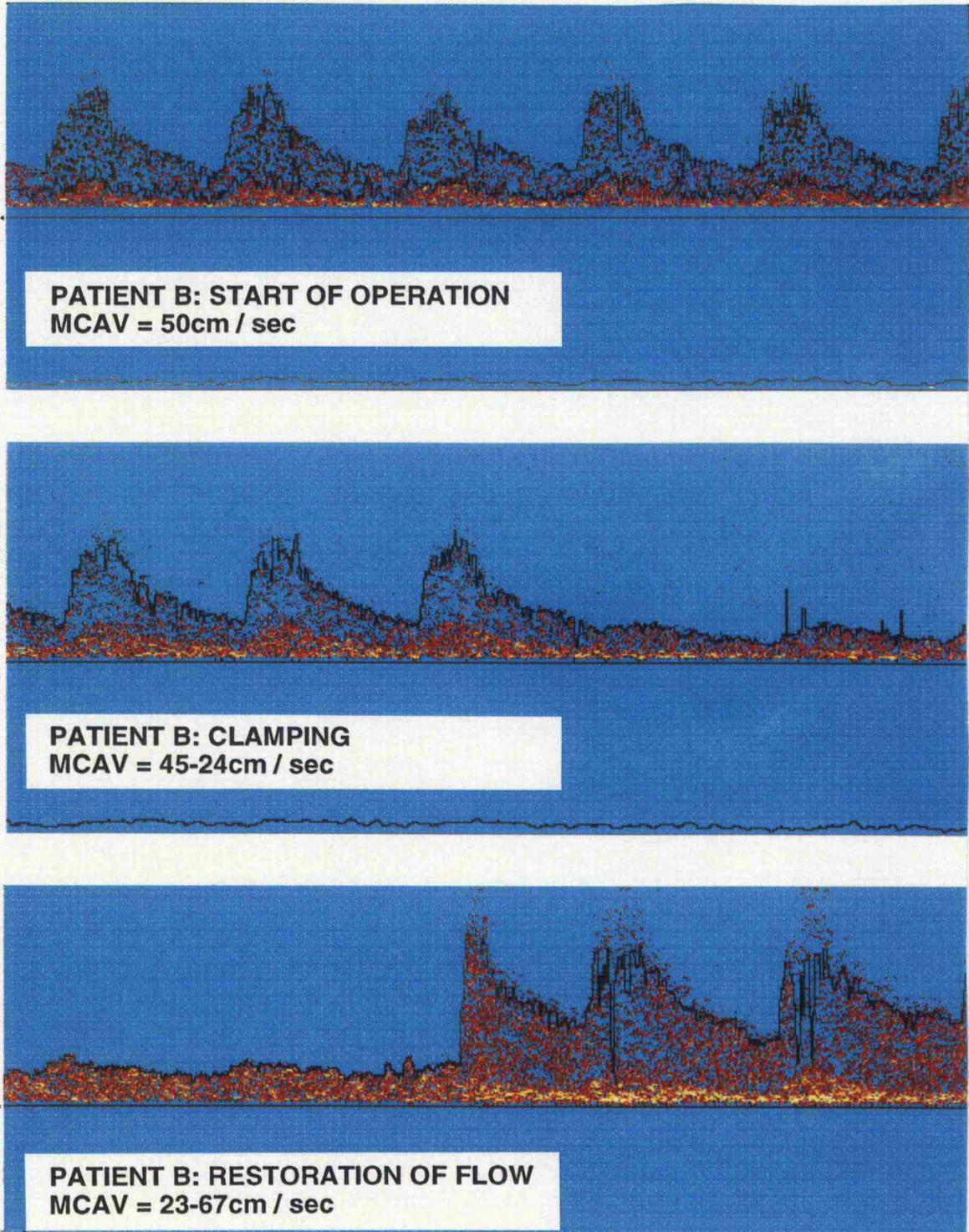


Figure 5.6: Patient B (53); TCD printouts illustrating the MCAV changes at different stages of the operation. MCAV falls to 24cm/sec on clamping of the ICA.

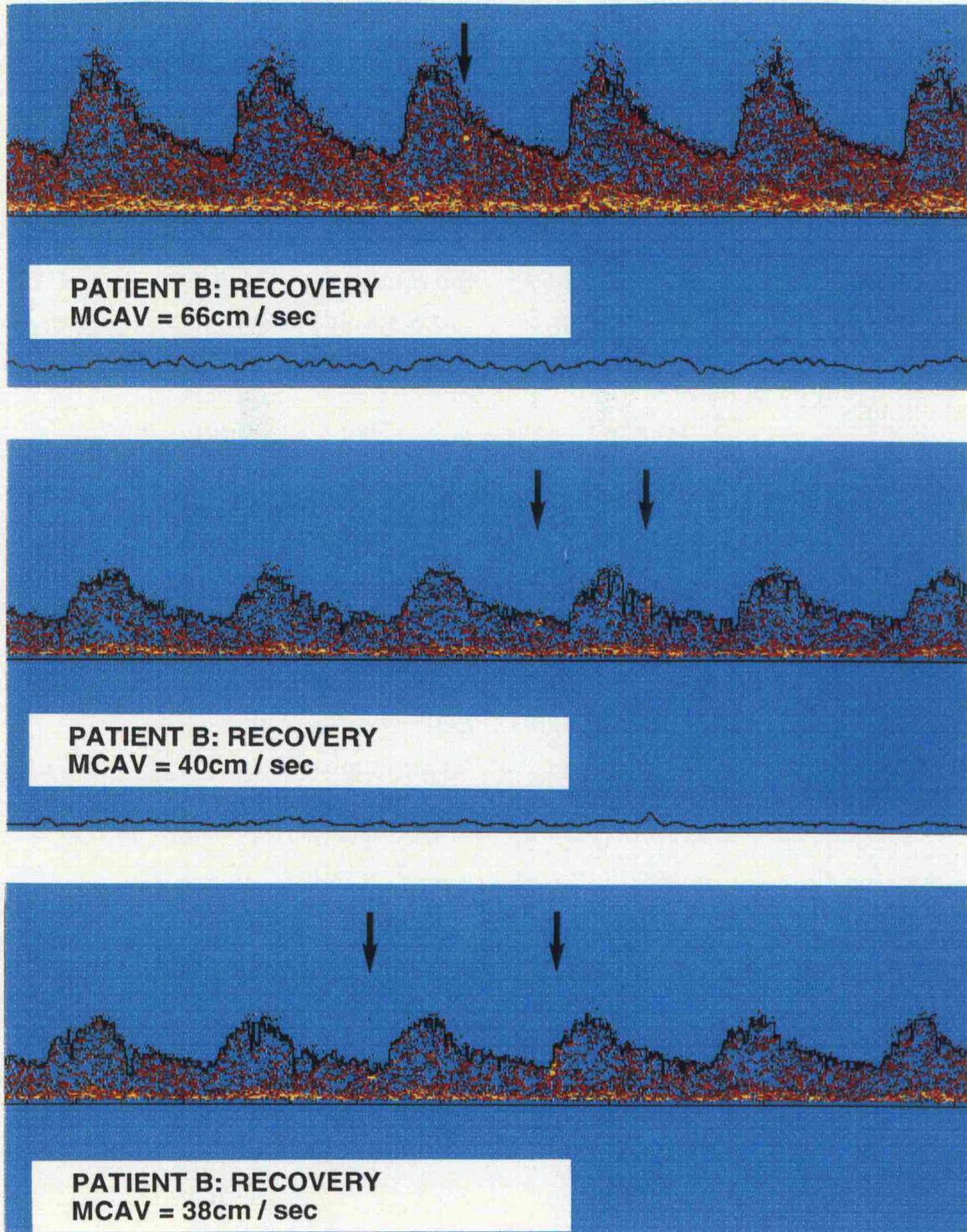


Figure 5.7: Subtle particulate embolic signals start to be detected (arrows) within 6 minutes of restoration of flow. Continued embolisation is associated with a gradual fall in MCAV.

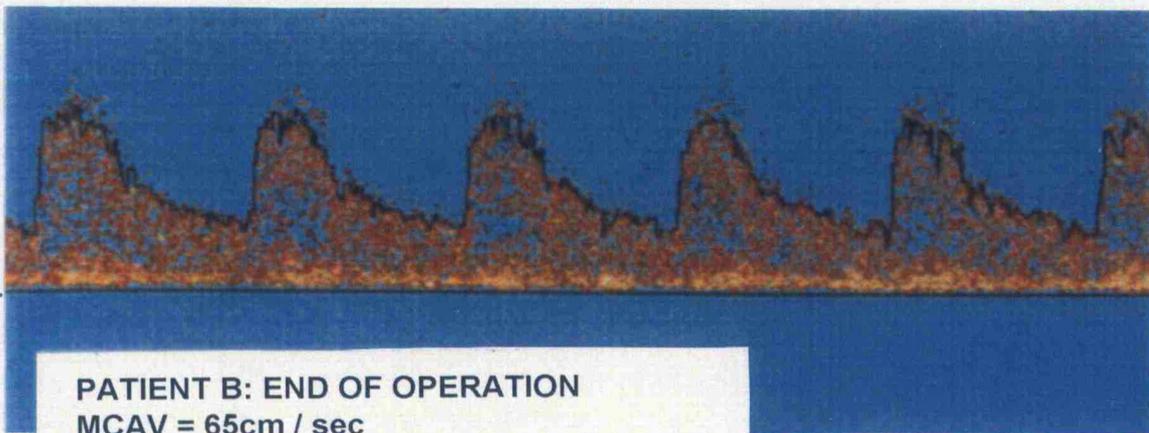
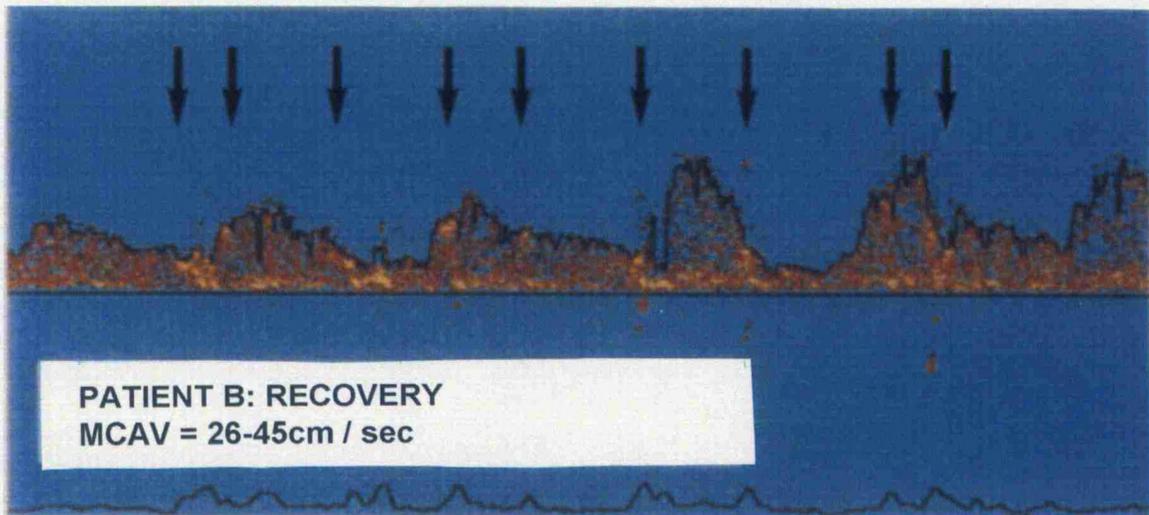
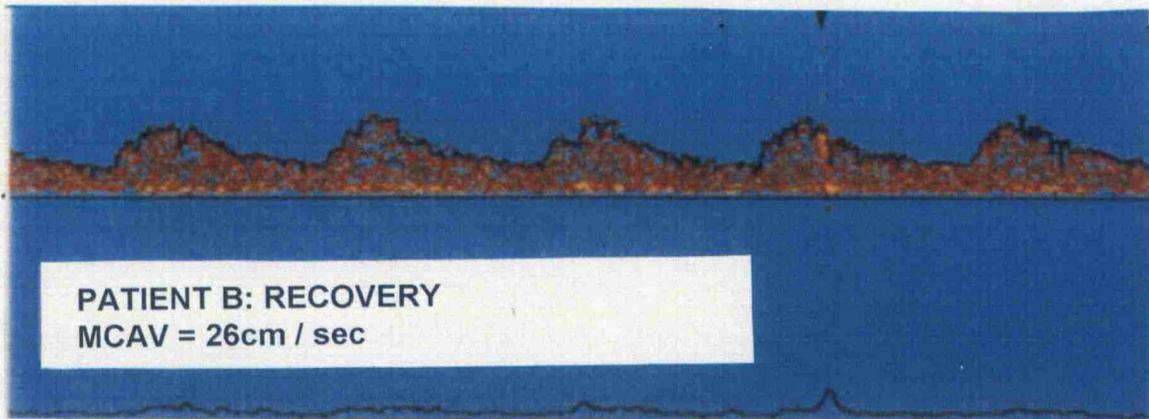


Figure 5.8: MCAV falls to a level just above that recorded when the ICA was clamped; emboli are still occurring (top). Handling of the carotid bifurcation provokes a shower of particulate emboli and is associated with a sudden increase in MCAV from 26-45 cm/sec (middle).

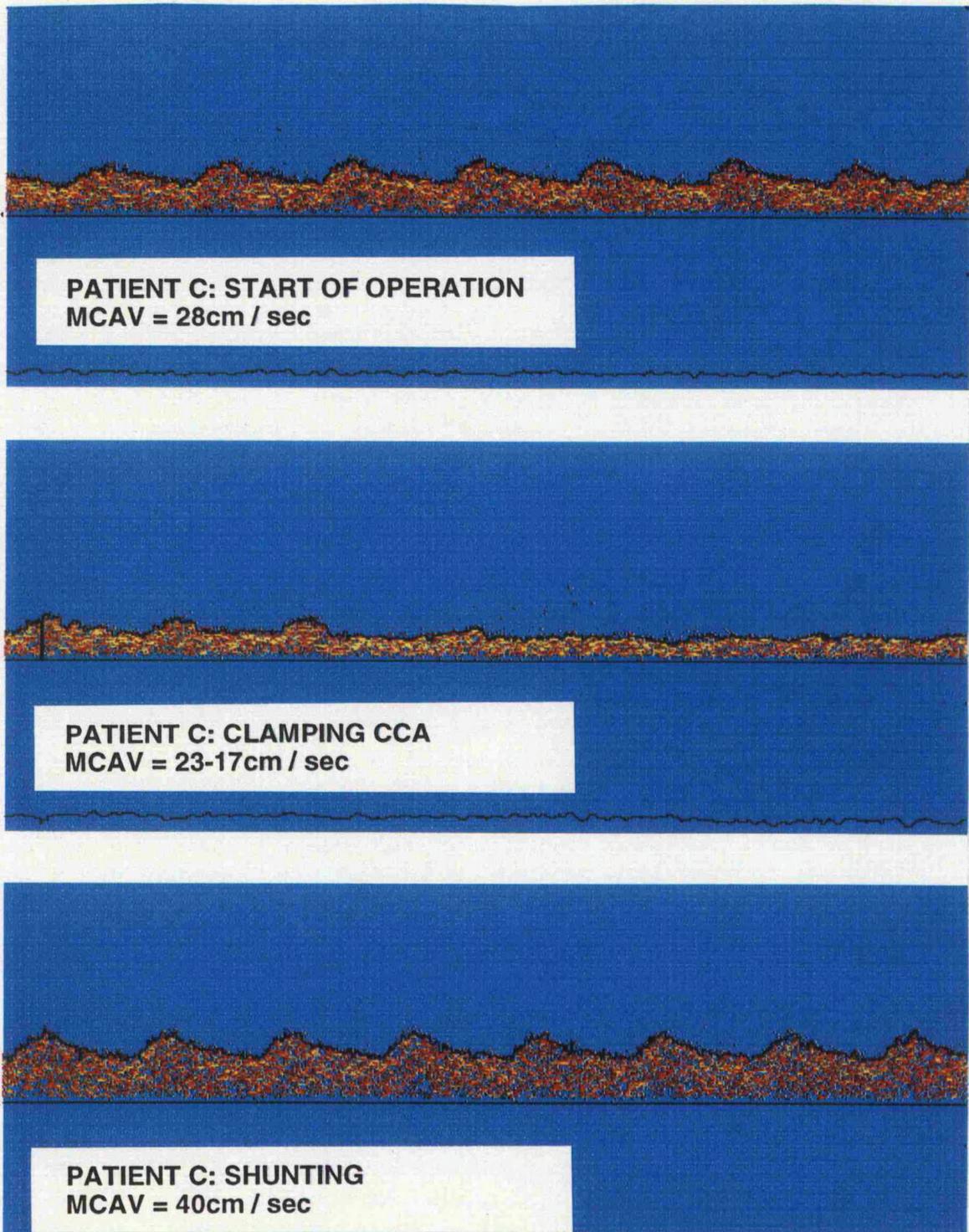


Figure 5.9: Patient C (98); TCD printouts illustrating the change in MCAV at different stages of the operation. MCAV is low initially and falls even further on clamping indicating poor intracerebral collateral blood flow (middle). MCAV improves considerably when an intraluminal shunt is opened (bottom).

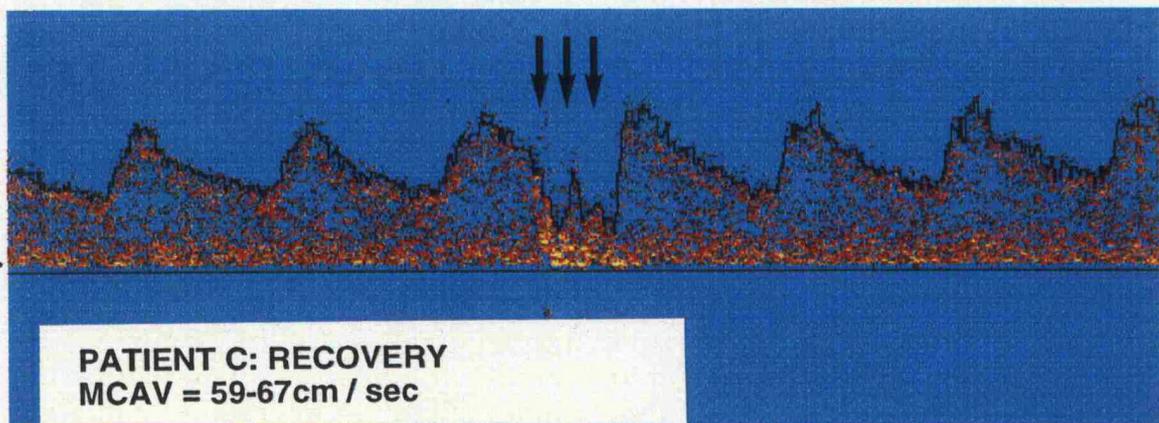
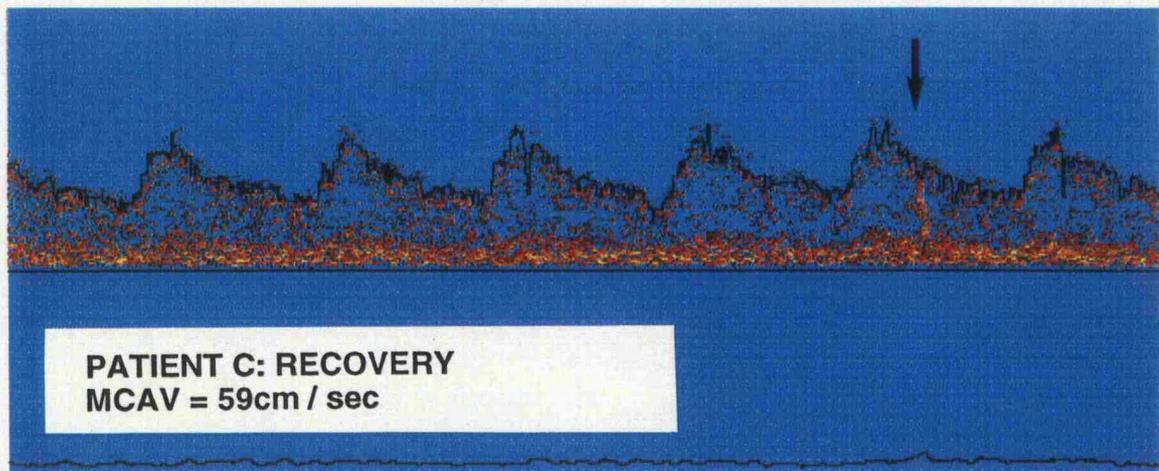
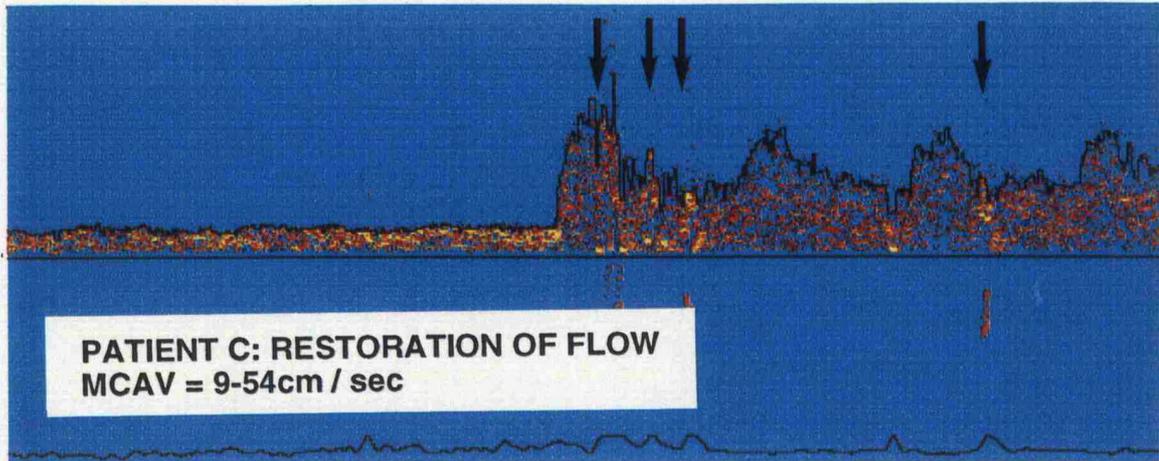


Figure 5.10: Typical air emboli are seen at restoration of flow (top) MCAV improves to 54cm/sec. Patient awake in the recovery area - first particulate embolus is detected (middle). Emboli continue to occur, some are big enough to distort the MCA waveform (bottom). However MCAV does not fall - neurological examination is normal.

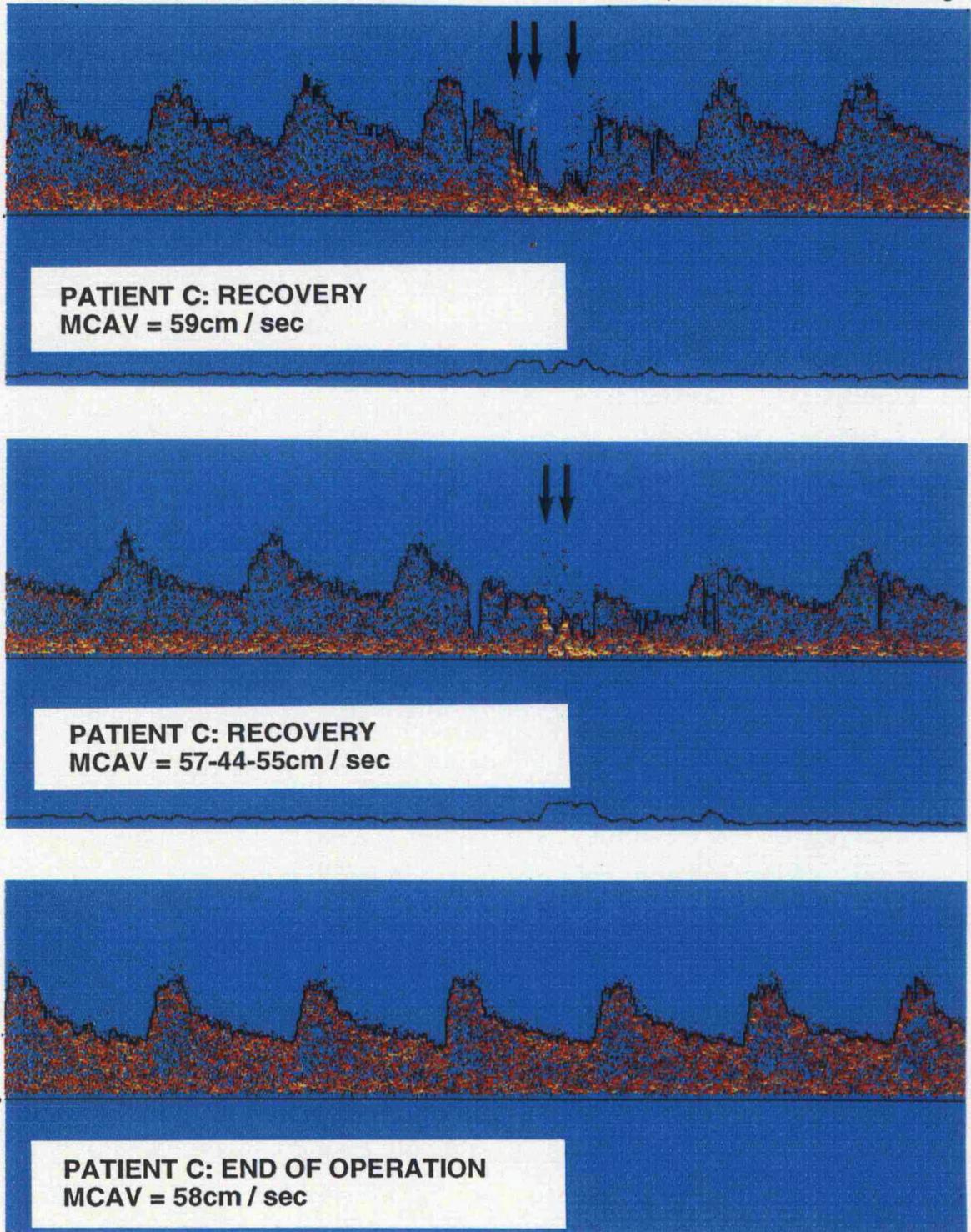


Figure 5.11: More emboli cause distortion of the MCA waveform (top), in one case MCA waveform takes 2-3 cardiac cycles to recover (middle). After 1 hour 54 minutes and 157 emboli patient develops a neurological deficit. At re-exploration non-occluding thrombus is removed from the ICA.

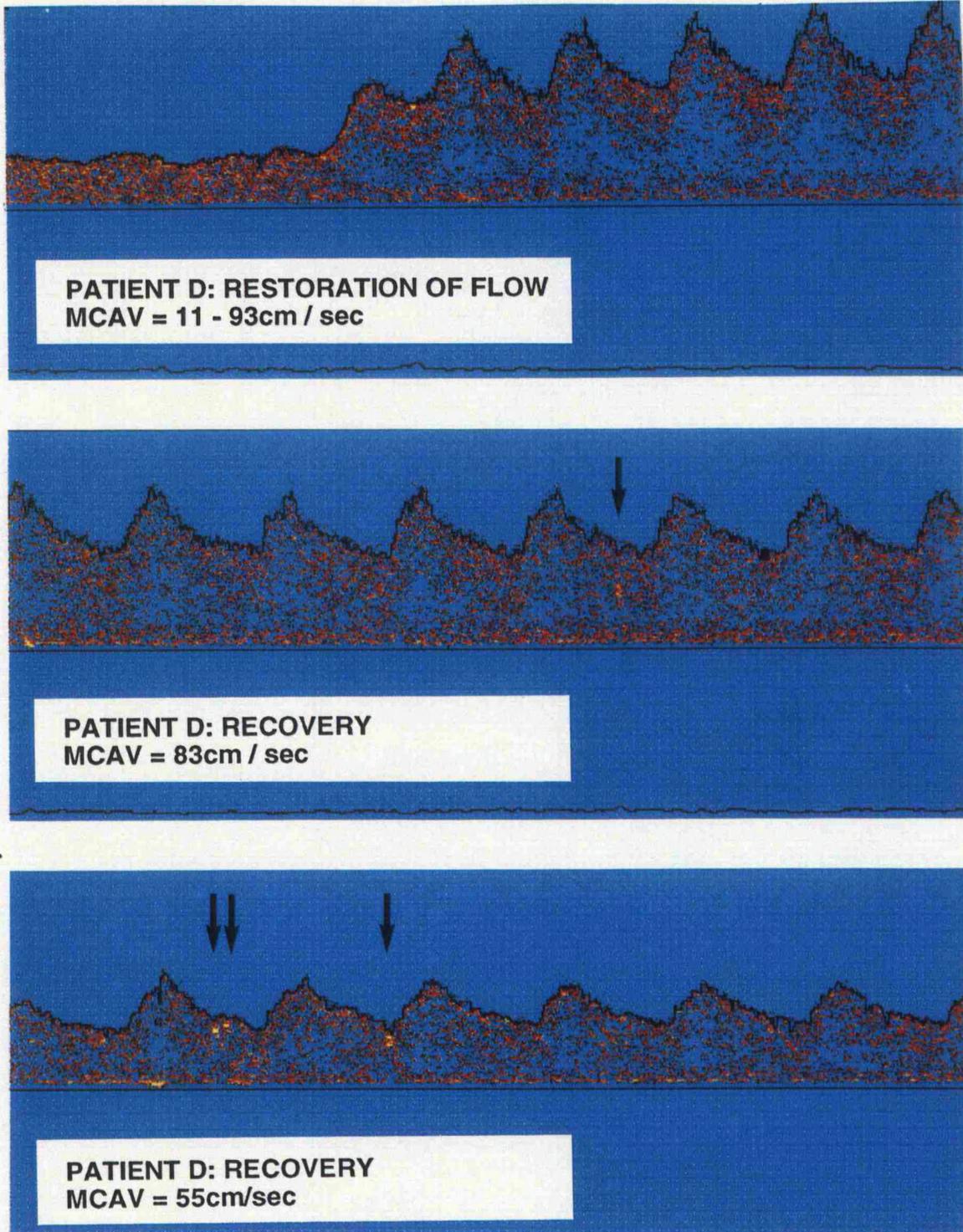


Figure 5.12: Patient D (99); TCD prinouts at restoration of flow, MCAV increases from 11-93 cm/sec. Particulate emboli are detected associated with a gradual fall in MCAV.

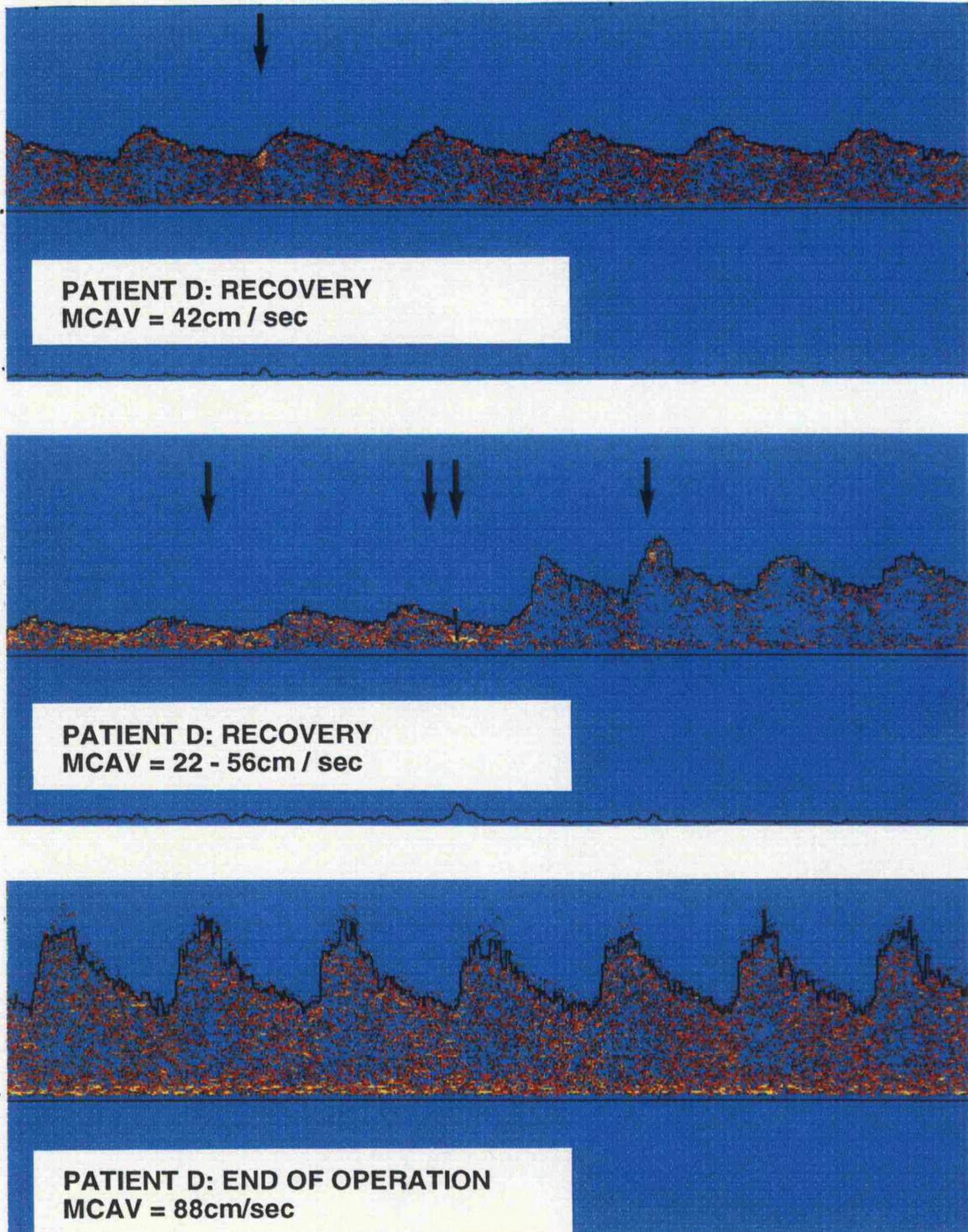


Figure 5.13: Emboli continue to occur and MCAV to fall (top). Handling of bifurcation dislodges emboli and is associated with an increase in MCAV (middle). Thrombus is removed from ICA and flow restored and maintained (bottom).

Although, only a small number of patients experienced emboli during the recovery phase, the amount of embolisation was considerable. The majority of patients (91%) experienced embolisation at the time of restoration of blood flow through the ICA. The frequency and amount of embolisation for all operative stages are illustrated in Table 5.1 and figures 5.3 and 5.14-5.16.

Operative Stage	Number patients (%)	median number of emboli (95% CI)	median duration of emboli (95% CI)	character of emboli
Operation	91	30 (25-40)	2.65(2.1-3.4)	
Dissection	23 (25%)	8 (4-14)	0.5(.225-.8)	Part.
Shunt open	71 (78%)	5.5 (4-7)	0.325(.225-.5)	Air
Shunting	48 (53%)	6 (4-9.5)	0.3(.2-.6)	Air
ECA flow	48 (53%)	9 (6-13)	0.65(.4-1.0)	Air
ICA flow	83 (91%)	10.5 (8-13)	.925(.6-1.325)	Air
Manipulation	45 (49%)	14.5 (9.5-23.5)	1.05(.625-1.5)	Air
Recovery	6 (6.5%)	176 (5-672)	8.82(.25-33.6)	Part.

Table 5.1: Results of TCD detected emboli related to operative stage.

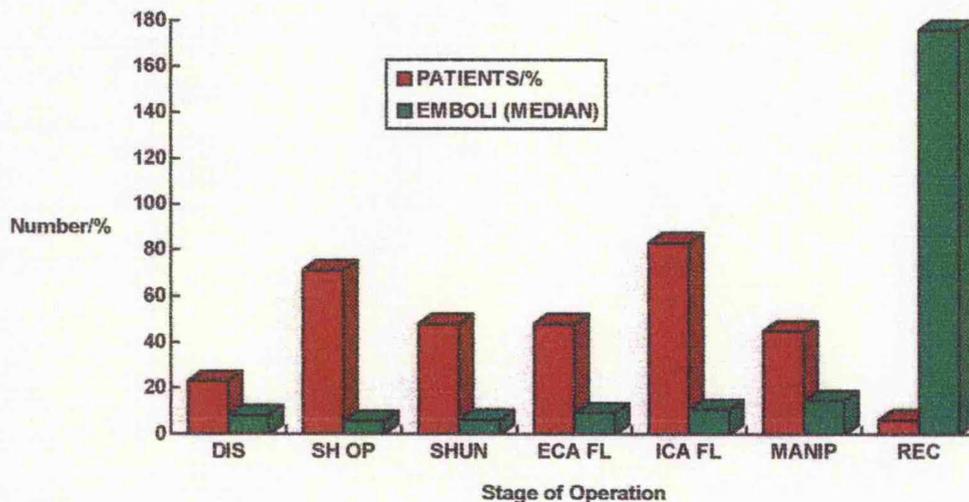


Figure 5.14: Graph showing the number of patients experiencing emboli at each operative stage and the median number of emboli for those patients experiencing emboli.

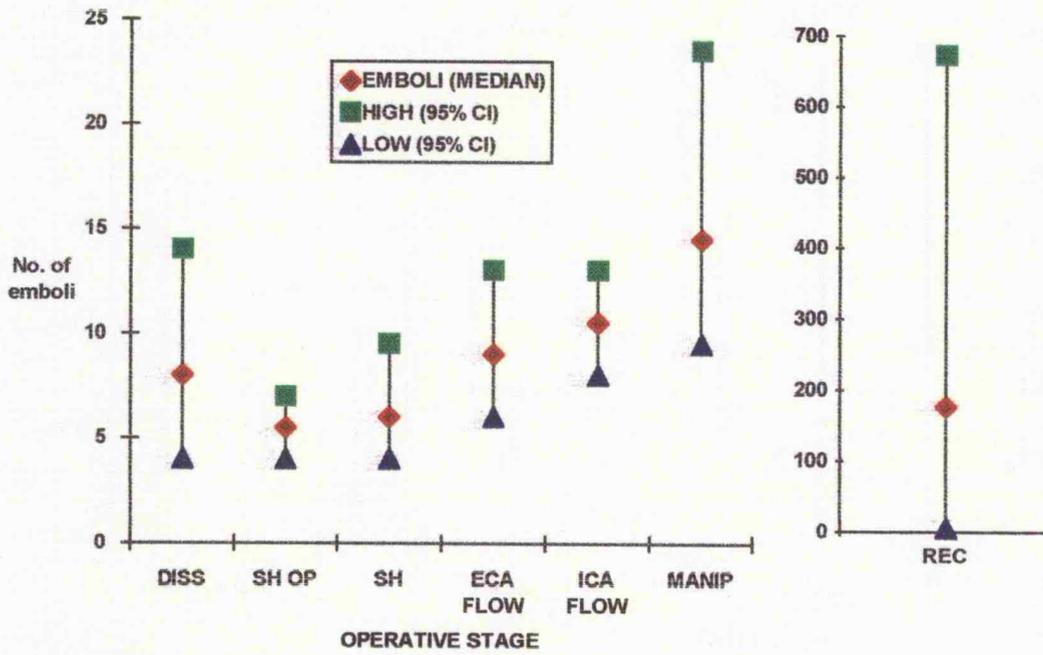


Figure 5.15: Graph showing the median number of emboli for each operative stage (95% CI)

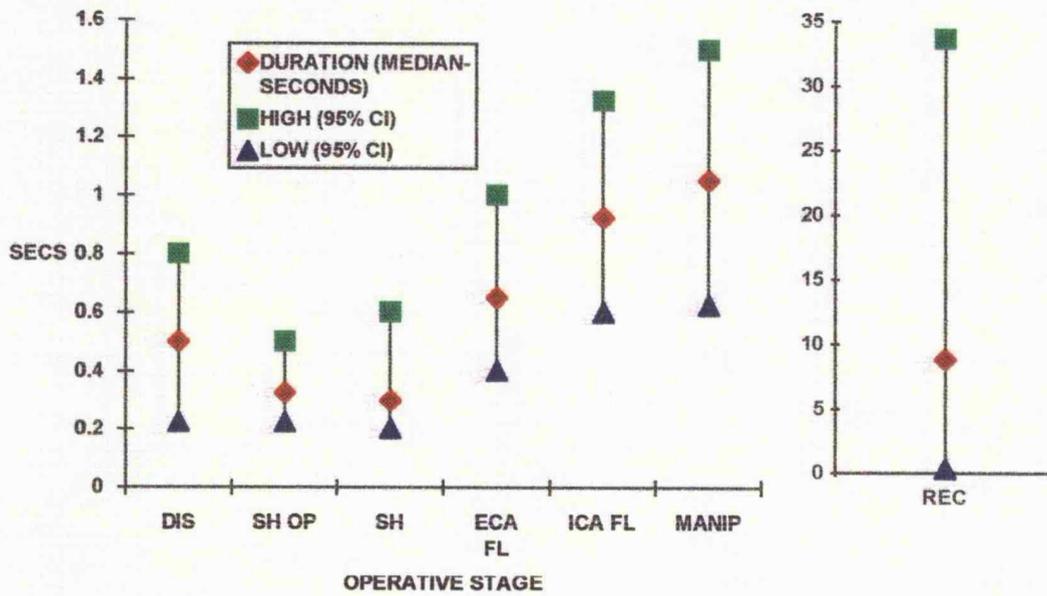


Figure 5.16: Graph showing the median (95% CI) duration of embolisation for each operative stage

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Haemodynamic Data

In order to minimise the effect of haemodynamic factors an intraluminal shunt was inserted in all but three patients. Technical difficulties prevented insertion in these three patients. However, in order to confirm that haemodynamic factors had been minimised the MCAV was recorded at each significant operative stage.

	mean MCAV	standard deviation	standard error	95% Confidence intervals
Dissection	46.6	15.4	1.69	43.3 to 50
Clamping A	26.8	12.6	1.38	24 to 29.5
Shunting	39.9	11.8	1.3	37.4 to 42.5
Clamping B	25.8	11.5	1.26	23.3 to 28.3
Recovery	55.6	18.3	2.01	51.6 to 59.6

Table 5.2: The sample mean MCAV with 95% confidence intervals recorded at different stages of the operation.

	mean %	standard deviation	standard error	95% confidence intervals
Clamping A	59.8	20.8	2.29	54.7 to 65
Shunting	88.2	23.7	2.6	83.6 to 92.7
Clamping B	57.6	23	2.52	52.6 to 62.6
ICA Flow	124	35.2	3.87	116 to 132

Table 5.3: The sample mean MCAV at different stages of the operation expressed as a percentage of MCAV during dissection.

The MCAV of thirteen patients fell below 40% of the preclamp value indicating a mild risk of ischaemia but only three patients had MCAV below 15% indicating a severe risk of ischaemia [Halsey, 1992]. However, because of routine shunting, the mean time of ischaemia was only 2.2 minutes. Once

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shunting had commenced no patient had a MCAV in the risk of ischaemia category.

5.4 Discussion

The division of the operation into its constituent stages enabled a more detailed analysis of the number and character of intraoperative emboli. In the absence of an established method of differentiating air from particulate emboli based purely on TCD signal criteria alone, this strategy has enabled a clinically useful differentiation to be applied to CEA surgery. However the limitations of this strategy are that outside the two stages, dissection and recovery, which can reasonably be assumed to consist of particulate emboli, a degree of caution must be exercised in the interpretation of the remaining embolic data. Embolisation during other stages was found to be predominantly characteristic of air. However, the use of the word 'predominantly' was chosen to indicate the possibility that particulate emboli may have occurred simultaneously with air emboli during some of the stages, but the more subtle particulate emboli signals were masked by the overloading air emboli signals.

Restoration of flow through the ICA was identified as the phase of CEA most commonly associated with embolisation predominantly characteristic of air, occurring in 91% of monitored operations. Alternatively, embolisation during the recovery phase was uncommon being detected in only 6 patients. However, embolisation during this phase was identified as being highly significant as the emboli were characteristic of particulate emboli and if persistent indicated the incipient thrombosis of the recently operated artery. The previously reported incidence of TCD detected embolisation during CEA has varied from 45% [Jansen *et al* 1993], 50% [Naylor *et al* 1991] and 61% [Spencer *et al*, 1990] to 89% [Padyachee *et al*, 1986]. The high incidence of embolisation in our study probably reflects recent advances in emboli identification and TCD equipment.

Twenty-three patients (25%) experienced particulate embolisation during the initial dissection of the carotid artery bifurcation. The emboli occurred singly and were predominantly precipitated by direct handling of the artery, ceased on clamping of the carotid artery and did not recur during shunting. These emboli

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probably represented the dislodging of unstable plaque contents or adherent thrombus from the surface of the carotid plaque. Embolism during this phase of the operation has been cited as a cause of intraoperative stroke [Hertzer, 1989; Naylor *et al*, 1992; Riles *et al*, 1994]. The first study of TCD monitoring during CEA described by Padyachee and colleagues described 'fluctuation' in MCA velocity caused by manipulation of the carotid bifurcation in 79% of patients [Padyachee *et al*, 1986]. In this first experience of TCD monitoring of CEA the possibility of these fluctuations being due to emboli was not considered, however, although fluctuations in MCA velocity can occur, the illustration published as an example of one of these fluctuations had features suggestive of an embolus. Therefore, one might reasonably conclude that some of these fluctuations were in fact due to emboli. Naylor identified emboli during this phase in only 1 of 30 monitored operations, Jansen identified embolisation in 10 (8%) cases and Spencer identified emboli in 12% of cases, two of which were precipitated by handling of the carotid artery [Naylor *et al*, 1991; Jansen *et al*, 1994; Spencer *et al*, 1990]. However, our finding of embolism occurring in 25% of patients indicates that this is a much more common event than was previously thought. Jansen described embolization during this phase as occurring singly with a total duration of less than 10 seconds. While the finding of emboli occurring singly coincides with our findings the description of the duration of embolisation being less than 10 seconds far exceeds our own findings of a median duration of embolisation of 0.5 seconds (95% CI 0.225 to 0.8 secs). Jansen calculated the duration of embolisation from videotape recordings which is unlikely to be accurate. The method used in this study consisted of freezing the fast Fourier image of the embolus on the time calibrated monitor screen and the measurement of the duration by the manual placement of the cursor at the start and finish of the embolic signal. Such a method is unlikely to be precise but produced durations of embolisation comparable to those described by Spencer and colleagues [Spencer *et al*, 1990]. An estimation of duration of embolisation was performed to enable comparison with studies which had described duration, as compared to the number of emboli, as the method for estimating the amount of embolisation [Spencer *et al*, 1990; Jansen *et al*, 1994].

The increased incidence of emboli detected during the dissection stage compared with other studies probably reflects the increased sensitivity of our

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methods and equipment to detect this phenomenon. The numbers of emboli are relatively low compared to other stages but this figure probably represents an underestimate of the number of emboli possible. The operating surgeon often reacted to our warning of continued embolisation by clamping the carotid artery earlier than normal to prevent further, potentially harmful emboli. Nevertheless this finding indicates another potentially useful role of TCD, that of, alerting the surgeon to the occurrence of potentially harmful embolisation and enabling measures to be taken to prevent this.

Seventy-one patients (78%) experienced emboli on opening the shunt and this was predominantly characteristic of air. This air probably represented air microemboli attached to the inside of the shunt and dislodged once blood flow was restored. Generally this embolisation occurred in showers, quickly cleared and only persisted if there was a malfunction of the shunt. However, it should be emphasised that small amounts of particulate emboli occurring simultaneously with air emboli would not have been detected due to masking of the subtle particulate signals by the overloading air emboli signals. Particulate embolisation has been detected at this stage using different methods. Beezley inserted a Javid shunt in to the CCA of 15 patients undergoing CEA. Blood was flushed out of the shunt in the routine manner to remove any particulate debris. After completion of this manoeuvre blood was then flushed through a macropore filter to trap any further atheromatous debris. Evidence of atheromatous debris were detected in 13% of patients indicating that particulate embolisation can still occur despite careful flushing of the shunt [Beezley, 1985].

Padyachee described embolisation in 89% of patients on shunt opening [Padyachee *et al*, 1986]. Padyachee attributed these to air and commented that the apparently large amount of embolisation was not associated with an adverse neurological outcome in any of the patients. Jansen described embolisation associated with the use of a shunt in 19% of cases, primarily during the introduction of the shunt while Naylor described emboli in 80% of shunted patients after shunt insertion [Jansen *et al*, 1993; Naylor *et al*, 1991]. In the patients monitored by Spencer a shunt was not utilised by the surgeon [Spencer *et al*, 1990].

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Forty-eight patients (53%) experienced emboli during shunting. However this figure may represent an overestimate because it includes the removal of the shunt prior to clamping of the ICA when the majority of emboli occurred. However emboli did occur during shunting and were usually provoked by manipulation of the shunt and probably represented a slight dislodgement of the distal retaining balloon allowing a small amount of air to enter the circulation. In two cases persistent embolisation occurring during shunting provided an early warning of shunt malfunction relating to puncture and deflation of the distal retaining balloon of the Pruitt-Inahara shunt. Shunt malfunction detected by TCD monitoring has also been described by Naylor and colleagues. In one patient, two episodes of defective flow caused by inadvertent kinking of a Javid shunt were immediately detected and rectified. In a second patient, the MCA signal after insertion of a Pruitt-Inahara shunt was lower than expected. Partial deflation of the distal balloon and repositioning of the shunt led to rapid signal improvement [Naylor *et al*, 1991]. These cases serve to indicate another useful role of TCD, that of continuously monitoring for shunt malfunction.

Forty-eight patients (53%) experienced emboli at restoration of blood flow through the external carotid artery. Once again these emboli were predominantly air and represented small bubbles not cleared by routine flushing procedures although small amounts of particulate emboli could not be excluded. Emboli reached the MCA via the collateral anastomosis between the facial and ophthalmic arteries. Prior to TCD monitoring of CEA, this manoeuvre was thought to prevent embolisation to the MCA by dispersing any thrombus harmlessly throughout the territory of the external carotid artery. TCD monitoring highlighted the presence of these patent collateral pathways between the external and internal carotid arteries and indicated that potentially harmful embolisation via this pathway was still possible [Naylor *et al*, 1991; Beard *et al*, 1993;]. Spencer described a patient experienced multiple episodes of amaurosis fugax and MCA particulate emboli despite an occluded ICA [Spencer *et al*, 1990]. This indicates that symptomatic emboli can still reach the MCA territory of the brain despite an occluded ICA. Episodes of embolic retinal infarction have been described via a patent ECA in the presence of an occluded ICA and this mechanism has been proposed as an indication for performing an ECA endarterectomy [Walker *et al*, 1994].

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Neither Padyachee nor Naylor included restoration of ECA flow as a separate stage in their analysis however Jansen did report embolisation in 6.5% of cases [Jansen *et al*, 1993]. Spencer reported that 7 patients (7.6%) of patients experienced air emboli during restoration of ECA flow. In one patient 14 cumulative seconds of embolisation occurred through the ECA before the ICA crossclamp was removed and this patient suffered a temporary postoperative neurological deficit as a result [Spencer *et al*, 1990].

The majority of patients (91%) experienced embolisation at restoration of blood flow through the ICA although once again this was predominantly air. This occurred immediately on clamp release and quickly cleared although a few cases were prolonged beyond the first 30 seconds of flow and usually indicated a significant suturing defect of the patch angioplasty. A greater amount of embolisation was experienced with prosthetic patch material as opposed to vein and probably represented the dislodgement of air trapped between the interstices of the Dacron graft material. Patients experienced air embolisation during this stage despite extensive and careful flushing and backventing procedures and is probably unavoidable. TCD is very sensitive to the presence of air and in vitro experiments have demonstrated that volumes as small as 1 uL can be detected [Russell, 1992]. Therefore it is unlikely that routine flushing and backventing procedures would succeed in removing these residual small volumes of air.

Naylor and colleagues reported embolisation during restoration of ICA blood flow in 27% of patients and Jansen in 48% [Naylor *et al*, 1991; Jansen *et al*, 1994]. Spencer reported embolisation in 61% of patients at restoration of ICA blood flow [Spencer *et al*, 1990]. The amount of embolisation was expressed as cumulative seconds of embolisation and 15% of patients experienced 0.1-0.5 seconds, 12% experienced 0.5-1.0 seconds, 20% experienced 1-5 seconds and 14% experienced 5-25 seconds [Spencer *et al*, 1990]. No neurological deficits were associated with embolisation during this stage. In general embolisation at this stage is reported as being without clinical consequences. However in one study, using simultaneous EEG and TCD monitoring, one patient experienced a large number of emboli at the time of restoration of flow

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and this was associated with a paroxysmal deterioration of the EEG and transient hemiparesis on waking from anaesthesia [Steiger, 1992].

Manipulation of the artery (insertion of sutures to bleeding points, pressing with ultrasound probes etc.) resulted in episodes of embolisation in 45 patients but once again this was predominantly air. Air embolisation during this phase was more common and of greater amount when Dacron patches were manipulated. But this probably represented dislodgement of tiny air bubbles trapped within the interstices of the material.

No previous study has included this stage in their analysis however Jansen does describe the occurrence of emboli in one case caused by the nurse applying an adhesive plaster to the wound and two cases as the patient was moved off the operating table.

Only 6 patients (6.5%) experienced emboli during the recovery period. However persistent particulate embolisation in this postoperative period was found to represent incipient thrombosis of the endarterectomy site and ceased only on reoperation. Spencer describes two cases where particulate emboli were detected in the postoperative period. In the first case emboli were detected soon after closure of the arteriotomy and at each TCD examination for two subsequent days. The patient did not undergo re-exploration of the operated artery and sustained a severe bilateral stroke. In the second case particulate emboli were detected 12 minutes after closure of the arteriotomy and continued for several hours. Eventually the patient developed a right hemiparesis and as a result of this, was returned to theatre and the artery re-explored. A dissecting intimal flap with associated thrombus was found at the clamp site of the CCA. Spencer postulated that the repeated particulate emboli were responsible for the development of the neurological deficit [Spencer *et al*, 1990]. Naylor describes the use of TCD to assess two patients found to have minor neurological deficits on recovery from anaesthesia but this was used to confirm good MCA velocity and avoid unnecessary re-exploration [Naylor *et al*, 1991].

Thrombosis of a recently endarterectomised carotid artery is a cause of perioperative stroke in 1-2% of all CEA [Naylor *et al*, 1992; Riles *et al*, 1994],

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and is associated with high morbidity and mortality. Current methods to detect this serious complication depend on regular neurological observations in the recovery room, however, by the time neurological signs appear it is likely that permanent neurological damage has already occurred [Naylor *et al*, 1992].

	Padayachee et al, 1986	Spencer et al,1990	Naylor et al, 1991	Jansen et al, 1994	Gaunt 1995
Number of Patients	19	91	30	98	91
Total Operation (%)	89	61	50	45	92
Diss (%)	-	12	3	8	25
Sh Op (%)	89	-	80	19	78
SH (%)	-	-	-	-	53
ECA flow (%)	-	7.6	-	6.5	53
ICA flow (%)	-	61	27	48	91
Manip (%)	-	-	-	-	49
Recovery (%)	-	2.2	-	-	6.5

Table 5.4 Table comparing the percentage of patients experiencing embolisation at different stages of CEA detected by TCD monitoring in four published series with the findings in this thesis.

Postoperative analysis of the TCD recordings from the three cases of early carotid thrombosis reveal that the first particulate emboli were detected 6-9 minutes after final restoration of flow, but before a regular pattern of emboli was established. The detection of this complication by TCD monitoring had not previously been well described, therefore in the first two cases the clinical significance of the emboli was not immediately appreciated. However in the final case, immediate intervention to remove the thrombus was performed, based on the TCD evidence of persistent particulate embolisation and our experience of the previous two cases. The three cases described in this thesis illustrate that TCD monitoring provides an early warning of carotid thrombosis, before the development of neurological signs. Therefore, immediate operative intervention based on this TCD evidence has the potential to prevent or

Intraoperative TCD Monitoring

minimise neurological sequelae and represents a major clinical application for TCD monitoring.

Subsequent to our experience of diagnosing ICA thrombosis using TCD an American group have described a case report of the same phenomenon [Doblar *et al*, 1994]. That case describes the thrombosis of the ICA within 16 minutes of restoration of blood flow through the endarterectomised artery. No intraluminal shunt was used in this case and the endarterectomy was completed with a cross-clamp time of 29 mins. At clamping MCAV fell from 36cm/sec to 13cm/sec gradually rising during the clamp time to 19cm/sec. At final restoration of flow MCAV increased to 39cm/sec. Two minutes after restoration of flow a 9 minute period of profound hypotension occurred, thought to be caused by an anaphylactic reaction to protamine sulphate. During this period MCAV fell to 13cm/sec but failed to increase from this level after restoration of normal blood-pressure. The artery was re-explored and a 1cm length of thrombus was removed from the proximal ICA. No technical defect was found and therefore thrombosis was presumed to be secondary to the period of hypotension. Low molecular weight dextran was given for antithrombotic effect and when blood flow was re-established MCAV increased to 46cm/sec and was maintained.

This case report provides further evidence for the ability of TCD monitoring to detect early carotid artery thrombosis. However, in this case no reference is made to the detection of emboli and the diagnosis was made purely on the fall in MCAV. In two of our cases carotid artery thrombosis was associated with a fall in MCAV but in the second case the MCAV was well maintained and diagnosis was based purely on the detection of persistent particulate embolisation. The detection of this embolisation is crucial because a diagnosis based on a fall of MCAV to low levels would fail to diagnose those patients with good collateral cerebral blood supply indicated by a minimal fall in MCAV on carotid occlusion. Spencer provides further evidence to support this conclusion in his description of the development of a neurological deficit in the postoperative period. Multiple particulate emboli were detected originating from thrombus associated with an intimal flap in the CCA, but this was not associated with a fall in MCAV [Spencer *et al*, 1990].

Intraoperative TCD Monitoring

Based on these results, the criteria for re-exploration would consist of persistent particulate embolisation in the recovery period with or without a fall in MCAV towards the level measured at the time of carotid clamping. However, in the absence of embolic signals, a significant decline in MCAV in the postoperative period should also be considered for re-exploration.

Finally, the data on the MCAV during different stages of the operation confirms that the policy of inserting intraluminal shunts minimised the risk of haemodynamic stroke. Using the Halsey criteria, thirteen patients were in the mild risk of ischaemia because their MCAV fell to below 40% of the preclamp value [Halsey, 1992]. In three patients the MCAV fell to below 15% of the preclamp value indicating a severe risk of ischaemia. However the time of exposure to this level of ischaemia was very short and consisted of the time taken to insert an intraluminal shunt. On average shunts provided 88.2% of the preclamp blood flow and therefore reduced the risk of haemodynamic stroke to a very low level. This provides further evidence that the recorded neurological deficits were caused by TCD detected intraoperative embolisation.

5.5 Summary

The materials and methods used to monitor the operations with TCD have been described. The amount and character of embolisation occurring during each stage of the operation has been recorded. Two phases of the operation have been identified as being associated with particulate emboli: dissection and recovery. The remaining phases of the operation were predominantly associated with air emboli.

Persistent particulate embolisation detected by TCD monitoring in the recovery phase has been identified as indicating incipient carotid artery thrombosis. TCD evidence of embolisation occurs before the development of neurological deficits and immediate operative intervention to correct this defect, based on this TCD evidence has the potential to avoid major neurological deficits.

In the next chapter the neurological and cognitive deficits associated with intraoperative embolisation will be described in more detail.

CHAPTER 6

NEUROLOGY AND PSYCHOMETRIC TESTING

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6.1 Introduction

The main outcomes measured after carotid endarterectomy have traditionally been major neurological deficit, stroke and death. However, in order to provide a thorough assessment of the clinical importance of intraoperative embolisation, more subtle but important abnormalities of brain function not readily detected by routine clinical examination needed to be considered. Therefore, a more detailed and precise neurological examination, performed by an independent specialist in Neurology, was used to determine the incidence of all neurological deficits after carotid endarterectomy and relate these to episodes of intraoperative embolisation.

An assessment of perioperative cognitive function was also performed by the same independent neurologists. Postoperative deterioration in cognitive function may have important consequences with regard to daily living and employment. For example, a patient employed in a sedentary job but requiring sophisticated reasoning and problem-solving ability may not be significantly handicapped by a neurological deficit of the non-dominant hand. However, the loss of the ability to calculate, problem-solve or a deficiency of short term memory may result in the loss of employment or have a significantly adverse effect on other important social interactions.

Therefore, cognitive function was investigated using a battery of psychometric tests to cover a broad range of cerebral function. Once again any abnormalities were related to episodes of intraoperative embolisation.

6.2 Materials and Methods.

The pre- and postoperative assessments were performed by an independent neurologist blind to the embolic status of the patient. A detailed neurological and cognitive assessment was performed 1-2 days before the operation and repeated 5-7 days after the operation when the patient was fully alert, mobile, eating and drinking and requiring only paracetamol analgesia. The assessments were performed in a quiet room off the ward. In addition a detailed neurological examination was performed immediately after surgery in the recovery room in order to detect any transient deficits.

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Neurological examination.

Neurological examination of the following parameters was performed :

Gait, Speech, Cranial nerves 1-12, Primitive reflexes (palmomental, grasp, pout). Upper limb power, tone, co-ordination, sensation (including cortical), reflexes (brachioradialis, biceps, triceps, Hoffman). Lower limb power, tone, co-ordination, sensation (including cortical), reflexes (knee, ankle, plantars). Muscle power was assessed using the MRC grading from 0, no contraction, to 5, full power [Clarke, 1987].

In addition each patient was assessed according to the National Institute of Health (NIH) Stroke Scale (appendix 1) and the Rankin Disability Scale (RDS-appendix 1).

Cognitive Function

Cognitive function was assessed by the same independent neurologists using a 30 point assessment including tests of orientation, recognition, instant recall, delayed recall, long term recall, calculation, sentence construction and visuospatial skills. In addition a further assessment was performed using a selection of Wechsler cognitive function tests consisting of Wechsler orientation A and B (WOA & WOB), Wechsler concentration (WC), logical memory (WLM), paired association (WPA), and digit span (WDS). Details of the questions in each test are described in appendix 1.

Data Analysis

All neurological deficits were recorded but for the purpose of relating these to intraoperative embolisation, only upper motor neurone deficits were considered significant.

Cognitive function tests were scored according to the recognised standards [Wechsler, Stone, 1945; Wechsler D, 1955]. For the 30 point assessment, Wechsler orientation A and B and the Wechsler concentration test the same questions were used before and after the operation. However, for the Wechsler logical memory, paired association and digit span, Form 1 was used preoperatively and Form 2 postoperatively to minimise practise effects [appendix 1].

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Intrasubject change between test scores before and after operation has been found to provide the best measure of the effects of operation on cognitive function [Grustad, Hane, 1975]. The means and standard deviations for each test carried out before operation were obtained by use of the scores of the entire sample for that test. A patient was considered to show significant deterioration on a particular test if his score deteriorated more than one standard deviation below his score before the operation [Shaw *et al*, 1986]. Clinical experience with the Wechsler tests suggests they have high test-retest reliability coefficients [Matarazzo *et al*, 1980] and that general surgical operations and general anaesthesia produce very few changes in psychometric function [Gruvsted *et al*, 1962].

Statistical Analysis

Groups were compared using medians, calculated by the Wilcoxon method, and 95% confidence intervals for the number and character of emboli. Values were calculated using the CIA statistics programme [Gardner *et al*, 1991].

6.3 Results : Neurological Function

Minor Neurological Deficits

Thirteen patients experienced a temporary LMN facial palsy ipsilateral to the operated side. This was caused by local traction on the nerve during the course of the operation and was not an effect of embolisation. Similarly, 4 patients experienced a LMN XII nerve palsy due to operative traction on the hypoglossal nerve. In all cases the effect was temporary and had resolved by six months after the operation. One patient experienced a temporary glossopharyngeal nerve palsy following a particularly high neck dissection.

Neurological Deficit	Number of Patients	Outcome
ipsilateral LMN facial palsy	13	Resolved
ipsilateral LMN hypoglossal palsy	4	Resolved
ipsilateral LMN glossopharyngeal palsy	1	Resolved

Table 6.1. Table illustrating the type number and outcome of minor postoperative neurological deficits. LMN = lower motor neurone

Major Intraoperative Neurological Deficits

Complete pre- and postoperative examinations were obtained on all patients in the study. The incidence of permanent intraoperative neurological deficits was 2% with a further 2 patients experiencing temporary deficits. The two permanent deficits consisted of a right hand monoplegia, right leg monoparesis and expressive dysphasia in one patient (NIH = 11, RDS=4) and a right hand monoparesis in another (NIH=1, RDS=2). The temporary deficits consisted of right hand monoparesis which resolved completely within 24 hours and a worsening of a pre-existing hemiparesis which resolved within three days. The findings of the pre- and postoperative neurological examinations of these four patients are described in more detail in Table 6.2.

Key to Table 6.2: Abbreviations

↑	up-going
↓	down-going
+	present but weaker
++	normal force
+++	stronger than normal
-ve	negative
<	less
<<	much less
<<<	very much less
0-5	MRC grading of muscle power (appendix 1)
L	left
LMN	lower motor neurone
N	normal
NIH	National Institute of Health Stroke Score (appendix 1)
RDS	Rankin Disability Scale Score (appendix 1)
R	right
temp	temporary deficit
UMN	upper motor neurone

TABLE 6.2: NEUROLOGICAL EXAMINATION

		PATIENT NUMBER						
		22	53	98	99			
Neurological Test	PRE-OP	POST-OP	PRE-OP	POST-OP	PRE-OP	POST-OP	PRE-OP	POST-OP
Gait	normal	ataxic	normal	ataxic	normal	normal	normal	normal
Speech	normal	normal	normal	expressive dysphasia	normal	mild exp dysphasia	normal	normal
Cranial Nerves	normal	normal	normal	R UMN 7th L LMN 12th	normal	mild UMN 7th	normal	normal
Primitive Reflexes								
Palmomental	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Grasp	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Pout	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
RDS	2	3 (temp)	0	4	0	2	0	1 (temp)

Upper Limbs	22 pre	22 post	53 pre	53 post	98 pre	98 post	99 pre	99 post
Power	R4, L5	R3-4, L5	R5, L5	R1, L5	R5, L5	R4, L5	R5, L5	R4, L5
Tone	R<, LN	R<<, LN	RN, LN	R<<<, LN	RN, LN	R<, LN	RN, LN	RN, LN
Co-ordination	R<, LN	R<<, LN	RN, LN	R<<<, LN	RN, LN	R<, LN	RN, LN	RN, LN
Sensation	RN, LN	RN, LN	RN, LN	R<<, LN	RN, LN	RN, LN	RN, LN	RN, LN
Reflexes								
BJ	R++, L++	R++, L++	R+, L+	R+++, L+	R++, L++	R++, L++	R+, L+	R+, L+
SJ	R++, L++	R++, L++	R+, L+	R+++, L+	R++, L++	R++, L++	R+, L+	R+, L+
TJ	R++, L++	R++, L++	R+, L+	R+++, L+	R++, L++	R++, L++	R+, L+	R+, L+
Hoffman	R-ve, L-ve							
Lower Limbs								
Power	R4, L5	R4, L5	R5, L5	R3, L5	R5, L5	R5, L5	R5, L5	R5, L5
Tone	RN, LN	RN, LN	RN, LN	R<, LN	RN, LN	RN, LN	RN, LN	RN, LN
Co-ordination	R<, LN	R<, LN	RN, LN	R<, LN	RN, LN	RN, LN	RN, LN	RN, LN
Sensation	RN, LN	RN, LN	RN, LN	R<, LN	RN, LN	RN, LN	RN, LN	RN, LN
Reflexes								
RJ	R++, L++	R++, L++	R+, L+	R+, L+	R++, L++	R++, L++	R++, L++	R++, L++
AJ	R++, L++	R++, L++	R+, L+	R+, L+	R++, L++	R++, L++	R++, L++	R++, L++
Plantars	R↓, L↓							
NIH Score	1	2 (temp)	0	11	0	1	0	1 (temp)

6.4 Major Neurological Deficits: Association with intraoperative embolisation

The four patients described above were the only patients with identifiable neurological deficits in the immediate postoperative period and all four patients experienced significant episodes of intraoperative embolisation identified by TCD monitoring. Two permanent deficits and one temporary deficit were associated with gross particulate embolisation detected during the recovery phase. The remaining temporary deficit was associated with an episode of gross air embolisation due to shunt malfunction occurring in a susceptible patient with a pre-existing hemiparesis. A detailed description of these episodes of intraoperative embolisation has already been provided in chapter 5. However in summary:

Patient 53 experienced 672 particulate emboli and 33.6 seconds of particulate embolisation during the recovery phase, but before reversal of anaesthesia, associated with thrombosis of the endarterectomised artery and the development of a permanent right arm monoplegia, right leg monoparesis and expressive dysphasia (NIH = 11; RDS = 4).

Patient 98 experienced 157 particulate emboli and 7.85 seconds duration of particulate embolisation during one hour and fifty minutes of the recovery phase monitored by TCD. Neurological examinations performed every ten minutes after the end of the operation were normal until the one hour fifty minute stage when the patient started to develop a right arm monoparesis. The patient was returned to theatre and a large but non-occluding mass of thrombus was removed from the carotid bifurcation. The patient recovered well but a monoparesis confined to the right hand persisted (NIH = 1, RDS = 2).

Patient 99 experienced 348 particulate emboli and 17.4 seconds duration of particulate embolisation during the recovery phase. This time the patient was returned immediately to theatre and a non-occluding mass of thrombus was removed from the carotid bifurcation. Post-operatively a slight weakness of the right hand was demonstrated, however this had completely resolved by 24 hours with no residual deficit (NIH = 1, RDS = 1).

Patient 22 experienced 215 air emboli and 22 seconds duration of air embolisation when the distal retaining balloon of the intraluminal shunt was

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accidentally punctured by a misplaced suture needle. Three attempts to reinflate the balloon before the problem was diagnosed contributed to the overall amount of embolisation. This patient, who had a pre-existing hemiparesis from a previous stroke prior to the operation experienced a slight worsening of his hemiparesis which had resolved by the third postoperative day (NIH 1 to 2; RDS 2 to 3) .

In each of these patients an excess amount of embolisation was associated with the episodes described above, compared with the rest of the operation (Figure 6.1). This is particularly the case for patients experiencing embolisation during the recovery phase.

There is a marked discrepancy between the percentage of patients experiencing emboli at each operative stage compared with the percentage of neurological deficits associated with embolisation at that stage (Figure 6.2). The majority of patients experience embolisation at the time of restoration of flow through an intraluminal shunt and at final restoration of flow through the ICA, however, there was no neurological deficit associated with embolisation at these stages. Conversely, embolisation in the recovery phase is uncommon but is associated with the development of neurological deficits. In particular, persistent embolisation in the recovery phase resulting in greater than 100 emboli, was always associated with the development of major neurological deficits (Table 6.3).

Patient number	Number of Emboli	Outcome
64	5	No neurological deficit
65	7	No neurological deficit
33	44	No neurological deficit
98	157	Permanent right hand monoparesis
99	348	Temporary right hand monoparesis
53	672	Permanent right hemiplegia

Table 6.3. Table listing the patients experiencing embolisation during the recovery phase, the number of emboli and the neurological outcome.

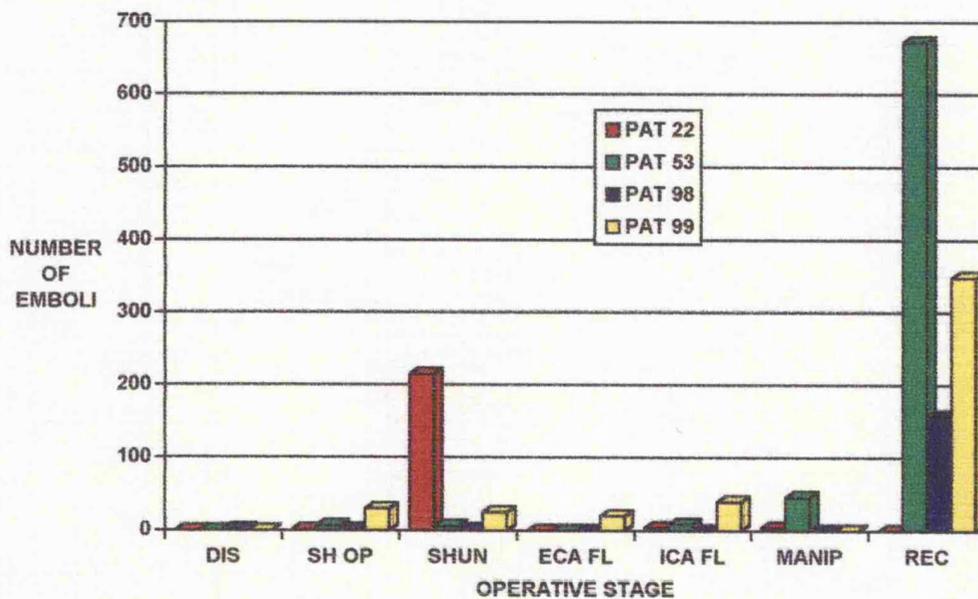


Figure 6.1. Graph illustrating the amount of embolisation at each operative stage for each of the four patients with postoperative neurological deficits.

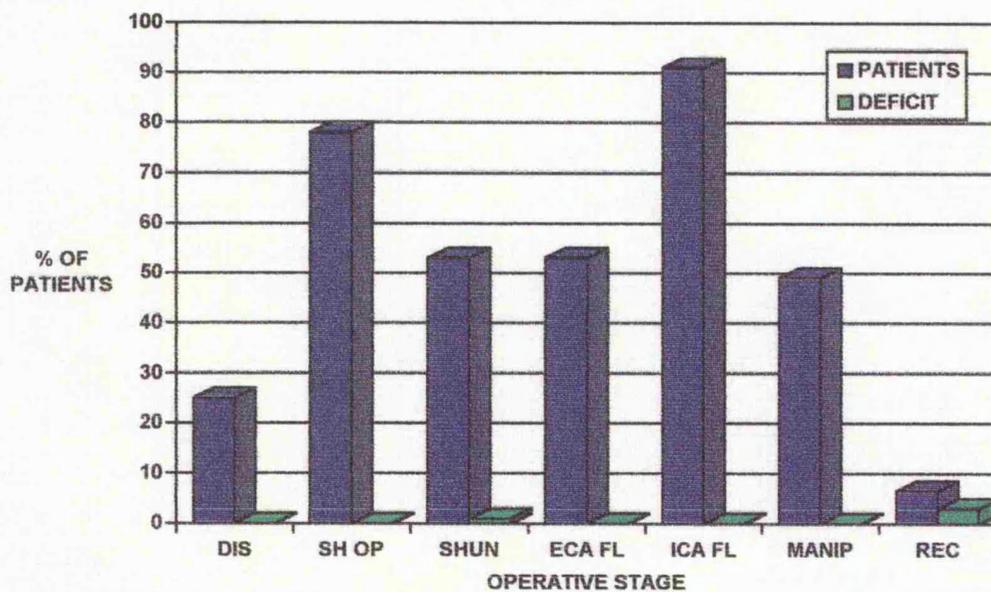


Figure 6.2. Graph illustrating the percentage of patients experiencing emboli at each operative stage compared with the percentage experiencing neurological deficits.

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While all patients developing neurological deficits experienced a significant number of emboli (> 100 embolic episodes) not all patients experiencing this number of emboli developed neurological deficits.

Twelve patients experienced more than more than 100 intraoperative embolic episodes (112 -672). Two of these patients developed permanent neurological deficits (157 and 672 emboli) and two patients developed temporary monopareses (348 and 215 emboli). The remaining eight patients (112, 125, 127, 127, 191, 215, 242 and 283 emboli) did not develop major or minor neurological deficits. The mean number of emboli experienced by those patients developing a neurological deficit was 298 (95% CI 109 to 816, df 3, $t=3.18$) and the mean number of emboli for those patients who did not develop a neurological deficit was 168 (95% CI 125 to 226, df 7, $t=2.36$). However, the number of patients is small and although there was a trend for more emboli to experienced by those developing neurological deficits this was not statistically significant. The ratio of the means was 1.77 (95% CI 0.95 to 3.31).

Similarly, the same twelve patients experienced more than 6 seconds duration of embolisation. All patients with neurological deficits experienced a significant duration of embolisation (7.85, 12.2, 17.4 and 33.6 seconds). However, the remaining 8 patients also experienced a significant duration of embolisation (6.35, 6.4, 6.5, 7.6, 9.5, 11, 14.2, 20 seconds) without developing any neurological deficit. There was no statistically significant difference between the duration of embolisation experienced by those patients developing a neurological deficit (mean=15.4 secs, 95% CI 5.79 to 40.9, df 3, $t=3.18$) and those not developing a neurological deficit (mean=9.46 secs, 95% CI 6.59 to 13.3, df 7, $t=2.36$). The ratio of the means was 1.63 (95% CI 0.842 to 3.14)

Comparison of Air Embolisation and Particulate Embolisation

Separate analysis of the association of neurological deficits with air or particulate embolisation provides a more conclusive indication of the clinical significance of intraoperative embolisation.

Nine patients experienced greater than 100 episodes of air embolisation but only one patient developed a temporary neurological deficit and this resolved completely within 2 days. Therefore there is a poor correlation between gross air embolisation during CEA and the development of neurological deficits. The

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temporary neurological deficit consisted of a slight worsening of pre-existing hemiparesis. In contrast, three patients experienced greater than 100 particulate emboli during the recovery period associated with carotid artery thrombosis and all developed neurological deficits (two permanent, one temporary).

Although the numbers of patients are small, these results provide evidence for a strong association between gross particulate embolisation during the recovery phase and the development of neurological deficits. Gross air embolisation during CEA would appear to be less clinically significant.

6.5 Results : Cognitive Function

Complete sets of data were obtained for 94/100 patients. Preoperative testing was missed in four cases and postoperative testing in two. Out of 94 patients tested, 37 patients had a significant decrease in psychometric scores in one or more psychometric tests. A significant decrease was considered to be a postoperative deterioration by more than one standard deviation (Table 6.4).

Cognitive Test	Mean Score	Maximum Score
30 point assessment (30 Pt Ass)	28.5 (SD 2.5)	30
Wechsler orientation A (WOA)	3.7 (SD 0.74)	4
Wechsler orientation B (WOB)	4.9 (SD 0.64)	5
Wechsler concentration (WC)	6.0 (SD 2.0)	10
Wechsler logical memory (WLM)	4.9 (SD 2.8)	8
Wechsler digit span (WDS)	11 (SD 2.6)	15
Wechsler paired associate (WPA)	9.1 (SD 3.25)	15

Table 6.4: Mean scores and Standard Deviations for all preoperative cognitive tests

Of the 37 patients who experienced a postoperative deterioration in postoperative cognitive function, 26 deteriorated in one test, 6 patients deteriorated in two, one patient deteriorated in three and four patients deteriorated in four or more.

Cognitive Function Test	Number
30 Pt Ass	8
WO A	2
WO B	8
WC	9
WLM	6
WDS	5
WPA	21

Table 6.5: Number of patients deteriorating for each cognitive test

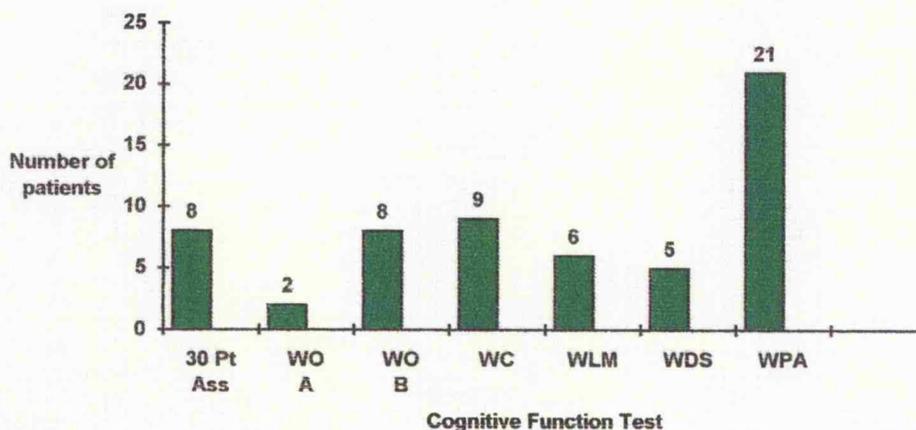


Figure 6.3: Graph showing Number of patients deteriorating postoperatively for each psychometric test

The Wechsler paired association test was the most sensitive at detecting postoperative deterioration in cognitive function. The Wechsler concentration test, Wechsler orientation B and the 30 point cognitive assessment the next most sensitive. The Wechsler orientation A was the least sensitive (Table 6.5, Fig 6.3).

Postoperative Deterioration of Cognitive Function: Association with intraoperative embolisation.

There was a trend, but no statistically significant association between the number of intraoperative emboli and deterioration in cognitive function. The

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median number of embolic episodes experienced by patients demonstrating a fall in postoperative cognitive function scores was 52 (95% CI 35.5 to 100, K = 171). The median number of emboli for those patients with no deterioration was 32.5 (95% CI 24 to 44, K = 537). The difference between the medians was 12 (95% CI -2.0 to 34, K = 681).

Similarly, there was no statistically significant association between the duration of intraoperative embolisation and deterioration in cognitive function. The median duration of embolisation experienced by patients demonstrating a fall in postoperative cognitive function scores was 3.76 seconds (95% CI 2.175 to 8.599, K = 171). The median duration of embolisation for patients with no deterioration was 3.22 seconds (95% CI 2.35 to 4.315, K = 537). The difference between the medians was 0.2 seconds (95% CI -0.850 to 1.85, K = 681).

Within the group of patients who deteriorated in cognitive function post operatively there was a trend for patients who deteriorated in 2 or more tests to have experienced a greater number of emboli although this was not statistically significant. The median number of emboli for those patients deteriorating in only one test was 43 (95% CI 24.5 to 70, K=74) and for those patients deteriorating in more than two tests the median was 104 (95% 31.5 to 338.5, K=11). The difference between the medians was 29 (95% CI -12 to 131, K=74).

Similarly, the median duration of embolisation for patients deteriorating in one test was 3.2 seconds (95% CI 1.81 to 8.35, K=74) and that for patients deteriorating in 2 or more tests was 7.19 (95% CI 1.875 to 27.6, K=11). The difference between the medians was 1.5 (95% CI -1.25 to 8.95, K=74).

Comparison of Air and Particulate Emboli Associated with Cognitive Deficit

There was no statistically significant difference in the number of air emboli experienced between those patients with a deterioration of cognitive function (median=40, 95% CI 28 to 60, K=171) and those without (median=31, 95% CI 22.5 to 40.5, K=537). Difference between the medians was 4 (95% CI -7.0 to 21, K=681).

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Similarly, there was no difference in the duration of air embolisation between the two groups. The median duration of air embolisation in patients with a cognitive deficit was 2.92 (95% CI 1.9 to 4.7, K=171) and the median duration of embolisation without cognitive deficit was 3.08 (95% CI 2.25 to 4.1, K=603). The difference between the medians was -0.2 (95% CI -1.2 to 0.9, K=681).

However there was a statistically significant difference between the number of particulate emboli experienced by those suffering a postoperative deterioration in cognitive function and those who did not. The median number of particulate emboli experienced by those patients with no deterioration in cognitive function was 4 (95% CI 2.5 to 5.5, K=11). The median number of particulate emboli in patients experiencing a deterioration in cognitive function was 14.8 (95% CI 7.5 to 23, K=11). The difference between the medians was statistically significant (median = 11, 95% CI 1 to 20, K=31).

Similarly, there was a statistically significant difference between the duration of particulate embolisation. The median duration of particulate embolisation in patients with a postop deficit was 1.55 seconds (95% CI .675 to 26.575, K=11). The median duration in patients without a deficit was 0.3 (95% CI 0.15 to 0.45, K = 26). The difference between the medians is 0.8 (95% CI 0.25 to 15.2, K = 45. 99% CI 0.05 to 17.2, K = 34).

Within those patients with cognitive deficit there is a strong trend for greater cognitive deficit to be associated with greater number and duration of particulate embolisation. The median number of particulate emboli in patients deteriorating in one test was 0 (95% CI 0 to 3, K=74) while the median number of particulate emboli in patients deteriorating in 2 or more tests was 24.5 (95% 0 to 337.5, K=11).

The difference between the medians was 14 (95% CI 0 to 42 K=75, 99% CI 0 to 157, K=58). Similarly for duration of particulate embolisation those deteriorating in one test the median duration was 0 (0 to .375, K=74) while for those deteriorating in two or more tests the median duration was 1 second (95% CI 0 to 26.5, K=58). The difference between the medians was 0.55 (95% CI 0 to 2.15, K=74, 99% CI 0 to 7.85, K=58).

Analysis of Emboli by Stage and Deterioration in Cognitive Function

In the dissection stage 23 patients experienced emboli and of those 11 experienced a deterioration in postoperative cognitive function and 12 did not.

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The patients who did not deteriorate had a median number of emboli of 4 (95% CI 2.5 to 5.5, K=14) while those who did have a postoperative cognitive deficit had a median number of 14.8 (95% CI 7.5 to 23, K=11). The difference between the medians was 11 (95% CI 1 to 20, K=34; 99% CI 1.0 to 22, K=25). In effect all patients experiencing more than 10 emboli during this stage experienced a deterioration in postoperative cognitive function.

Operative Stage	Dissection	Shunt Opening	Shunting	ECA Flow	ICA Flow	Manip
Cognitive Deficit	14.8 (7.5- 23)	7.0 (3.5 - 14)	5.0 (2.5 - 8.5)	11.5 (5 -18)	10 (6.5 -18)	12.5 (8 -28)
No Cognitive Deficit	4 (2.5-5.5)	5.5 (3.5-8.5)	6.5 (4 -19)	8 (5.5-17.5)	12 (8.5-16.5)	20 (12-32)
Difference between Medians	11 (1-20)	0 (-1.03.0)	-1.0 (-4-1.0)	-1.0 (-5.0-3.0)	-1.0 (-5.0-3.0)	3.0 (-3 -4.0)

Table 6.6: Median number of emboli (95% CI) for each operative stage experienced by patients with and without postoperative cognitive deficit.

With exception of the recovery stage there was no statistically significant association between an increase in number and duration of embolisation and cognitive deterioration during the other operative stages (Figure 6.6).

Although, one must be cautious when analysing each operative stage in isolation as emboli occurring in other stages may also affect postoperative outcome, the strong association between embolisation in the dissection stage and the deterioration of postoperative cognitive function, provides further evidence for the deleterious effect of particulate embolisation on cognitive function.

6.6 Discussion

The results of this chapter show a clear association between particulate embolisation and the development of neurological and cognitive deficits. In particular, this study has identified that gross persistent particulate embolisation in the recovery phase is associated with thrombosis of the operated artery and the development of major neurological deficits. TCD

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evidence of embolisation in this stage occurs before the development of neurological signs and provides an early warning. Prompt operative action to correct the defect based on the TCD evidence has the potential to prevent or minimise the neurological deficit.

In addition, this study has demonstrated that an increasing amount of particulate embolisation, both in the dissection and recovery phase is associated with the development of postoperative cognitive deficits.

In contrast, there is a poor association between air embolisation and the development of neurological and cognitive deficits. This study could only identify one temporary neurological deficit with an episode of intraoperative air embolisation. This consisted of a temporary worsening of a pre-existing hemiparesis in a patient who experienced an episode of gross air embolisation as a result of a ruptured distal retaining balloon on an intraluminal shunt and attempts at reinflation. The significance of this temporary deficit resulting from a rare intraoperative complication affecting a particularly susceptible patient to routine practice is open to debate. In general the poor association of air embolisation with neurological deficits is consistent with other studies of TCD monitoring during carotid endarterectomy [Padyachee *et al*, 1986; Spencer *et al*, 1990; Naylor *et al*, 1991; Jansen *et al*, 1994].

However, evidence does exist that air embolisation should not be disregarded completely. Fritz and Hossman produced cerebral ischaemia and prolonged EEG changes by injecting 0.6 ml of air/blood foam into the innominate artery of cats [Fritz, Hossman, 1979]. Moody described histological evidence of the damage caused to brain microvasculature by air emboli [Moody *et al*, 1990]. Menkin and Schwartzman described five cases of neurological deficits associated with cerebral air embolism and Spencer related a post-operative hemiparesis following carotid endarterectomy to a significant episode of intra-operative air embolisation [Menkin and Schwartzman, 1977; Spencer *et al*, 1990]. Pugsley and colleagues demonstrated that post-operative neuropsychological abnormalities could be reduced by decreasing the number of air emboli during cardiac by-pass [Pugsley *et al*, 1990] and recently, Markus described the possible relation of air embolism to neurological deficits following carotid angiography, especially in susceptible patients with recent cerebral infarcts, such as our patient, and recommended procedures to reduce this [Markus *et al*, 1993].

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Therefore, it may be safer to conclude that air embolisation is of little clinical consequence when it occurs in the volumes normally associated with CEA. However, every effort should be made to limit its occurrence whenever possible.

Therefore, this study has identified that the differentiation of air and particulate emboli is crucial to the assessment of the clinical significance of intraoperative embolisation detected by TCD. As yet absolute differentiation of the two types of emboli based on TCD criteria alone is not possible. However, a clinically useful differentiation is possible if the TCD criteria are combined with the stage of operation. Using these combined criteria it was possible to identify that emboli occurring during the dissection and recovery phases of CEA were particulate. Particulate embolisation may occur at other stages but identification is difficult due to coexisting air embolisation.

However, major neurological deficits were only associated with gross particulate embolisation in the recovery phase and these three cases will now be discussed in more detail.

The emboli detected in these three cases were predominantly characteristic of particulate emboli and occurred in the recovery phase of the operation. Each case was associated with incipient thrombosis of the recently endarterectomised carotid artery and the development of major neurological deficits.

Thrombosis of a recently endarterectomised artery occurs in 1-2% of cases and a large proportion suffer a stroke or die despite early intervention [Naylor, 1992, Riles *et al*, 1994]. Current methods to detect this serious complication depend on regular neurological observations in the recovery room, however by the time neurological signs appear it is likely that a degree of neurological damage has already occurred. Postoperative analysis from these three cases reveal that the first particulate emboli were detected 6-9 minutes after final restoration of flow, but before a regular pattern of emboli were established. Earlier operative intervention based on this TCD evidence may have prevented the permanent neurological deficits but at the time, the significance of what was being observed was not appreciated because similar cases had not previously been reported. However, a further case has recently been reported which supports our finding that early postoperative carotid artery thrombosis can be

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detected by TCD monitoring but in this case the diagnosis was based solely on a low MCAV [Doblar et al, 1994]. In two of our cases MCAV did fall but in neither case did MCAV fall to levels known to put the patient at risk of haemodynamic stroke [Halsey, 1993].

In the remaining case MCAV did not fall and diagnosis was based on the detection of persistent particulate embolisation and the development of a right arm monoparesis in the recovery room. In this case the neurological examinations were performed every 10 minutes by myself. The patient was conscious and communicative and able to obey commands without hesitation. The weakness of his right hand developed one hour and 53 minutes after restoration of flow and after 157 particulate emboli. My neurological examination of the right hand performed ten minutes earlier had been completely normal. Throughout this time the MCAV had varied around 57-63cm/sec and had not fallen to the clamp level of 23cm/sec. Therefore one may conclude that the neurological deficit occurred solely as a result of the particulate emboli. This case represents the first direct clinical evidence that platelet emboli can cause a neurological deficit and supports the assumption that the detection of emboli is crucial to the diagnosis of early carotid artery thrombosis. It is likely that if surgical re-exploration had been performed and the thrombus in ICA removed earlier, that neurological deficit could have been avoided.

Therefore persistent particulate embolisation, with or without an accompanying fall in MCAV is associated with the development of neurological deficits. However, there appears to be no exact relationship between the amount of particulate embolisation and the severity of neurological deficit. Patient 98 experienced 157 particulate emboli and (7.85 seconds duration) and developed a permanent deficit, patient 99 experienced 348 particulate emboli (17.4 seconds duration) and developed only a temporary deficit. However, patient 53 experience 672 particulate emboli (33.6 seconds duration) and developed an hemiparesis. Current evidence suggests that the clinical effect of TCD-detected embolization is multifactorial and depends on the number, size and character of the emboli, as well as on patient susceptibility related to inadequate collateral cerebral circulation and the presence of pre-existing infarcts [Spencer, 1992].

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However another factor is that our assessment of the amount of embolisation is incomplete. While we can accurately count the number of emboli and characterise them into air and particulate, the assessment of duration is an approximation and is dependent on multiple factors. At present there is no reliable and commonly accepted method of determining the size of an embolus and this would be needed to provide a comprehensive assessment of the amount of embolisation. Interestingly, in the case of patient 98, although only 157 embolic episodes occurred 17 of these episodes appeared large enough to distort the middle cerebral artery waveform. In some instances the MCA waveform took several cardiac cycles to return to its previous velocity possibly indicating an embolus large enough to partially occlude the MCA or one of its branches (Figure 5.9).

Therefore, the conclusion from this part of the study is that persistent particulate embolisation in the recovery phase, with or without an accompanying fall in MCAV, is associated with carotid artery thrombosis and the development of major neurological deficits. Detection of particulate emboli during this phase provides an early warning and surgical intervention to remove the thrombus has the potential to prevent the development of neurological deficits.

There was no overall correlation between the total number of intraoperative emboli and psychometric deterioration. However when the number of emboli from each operative stage were correlated with psychometric deterioration an association with particulate embolisation during the dissection stage was apparent.

The emboli occurring during the dissection stage were assumed to be particulate because the arterial system had not been entered, the TCD embolic signals were characteristically particulate, emboli were often precipitated by direct handling of the carotid bifurcation and ceased on carotid clamping. TCD monitoring provided a warning that embolisation was occurring enabling the surgeon to modify the surgical approach to minimise further, potentially harmful, embolisation.

There was no correlation between the number of emboli occurring during other stages of the operation and a deterioration in cognitive function. In particular, there was no association between the amount of air embolisation detected and

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a decrease in cognitive scores. However, the cause of cognitive deterioration in some of the remaining patients is unclear. A possibility exists that potentially significant particulate embolisation occurred during other stages of the operation but was not detected because the subtle particulate emboli signals were masked by the extraspectral aliasing associated with air emboli occurring at the same time. Our group is currently investigating the use of different forms of spectral analysis to differentiate between air and particulate emboli more accurately, especially during restoration of flow and other stages of the operation where the two forms of emboli may occur simultaneously [Smith *et al*, 1994].

Previous studies have found that cognitive function can improve after carotid endarterectomy although it is difficult to eliminate practise effects from the analysis [Haynes *et al*, 1976]. Preoperative symptoms can influence postoperative performance as patients with a history of TIAs tend to perform better postoperatively, than patients with known infarcts [Mononen *et al*, 1990]. One study has related postoperative deterioration to intraoperative episodes of ischaemia, as indicated by somatosensory evoked potentials, however I am unaware of any study to relate postoperative cognitive function to intraoperative embolisation [Cushman *et al*, 1984].

6.7 Summary

The results of this chapter show a clear association between particulate embolisation and the development of neurological and cognitive deficits. In particular, this study has identified that gross persistent particulate embolisation in the recovery phase is associated with thrombosis of the operated artery and the development of major neurological deficits. TCD evidence of embolisation in this stage occurs before the development of neurological signs and provides an early warning. Prompt operative action to correct the defect based on the TCD evidence has the potential to prevent or minimise the neurological deficit.

In addition, this study has demonstrated that an increasing amount of particulate embolisation, both in the dissection and recovery phase is associated with the development of postoperative cognitive deficits.

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With the exception of one case in a particularly susceptible patient, intraoperative air embolisation was not associated with the development of either neurological or cognitive deficits in the postoperative period.

In the next two chapters the association between intraoperative embolisation and cerebral and retinal infarction will be explored.

CHAPTER 7

FUNDOSCOPY AND VISUAL FIELDS

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7.1 Introduction

Amaurosis fugax is one of the commonest embolic symptoms described by patients presenting for carotid endarterectomy. The term translates as 'fleeting blindness' and is often described as a black curtain descending over the field of vision in one eye. The loss of vision, from a part or whole of the visual field, is complete but temporary and lasts from a few seconds to hours. It is caused by the temporary occlusion of a small retinal vessel by an embolus which quickly disaggregates and passes on. If a larger embolus lodges in the central retinal artery, ischaemia of a large proportion of the retina can occur and if prolonged can lead to infarction and permanent blindness in that eye. Evidence of embolisation can be detected on fundoscopy where emboli can be seen lodged in the branches of the retinal artery [Whisnant *et al*, 1990].

It was Fisher who first drew attention to the association between transient unocular visual loss and a contralateral hemiplegia in patients with stenosis or occlusion of the internal carotid artery [Fisher, 1952]. However, evidence of retinal embolisation had been described many years before. In 1859 Von Graffe first described the characteristic early fundoscopic findings of central retinal artery occlusion (CRAO) in a man with aortic valvular disease [Von Graffe, 1859]. In 1894 Benson made three observations on a man during transient attacks of blindness and saw the inferior temporal artery become bloodless for a distance of four disc diameters. The bloodless segment moved distally sometimes in a jerky fashion synchronous with the heart-beat, and on reaching a vessel bifurcation it suddenly disappeared, leaving a normal fundus [Benson, 1894]. Similar white segments of artery were visible in photographs of the fundus presented by Mylius taken during a prolonged attack in a patient complaining of fleeting blindness [Mylius K, 1928]. Foerster and Guttman witnessed an attack of visual loss in the lower field of the right eye in a man of 34 who also had a left hemiplegia [Foerster, Guttman . 1933].

Fisher, himself gave a lucid description of the passage of a white embolus through the retinal arteries during an attack of monocular blindness in a patient with carotid stenosis [Fisher, 1959]. Later, Russell presented a description of the passage of an embolus through the retinal vessel whose progress was monitored by repeated fundoscopic examinations over the course of 45 minutes. The passage of this retinal embolus coincided with the development of a contralateral hemiplegia. An emergency carotid endarterectomy was

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performed where the ICA was found to be occluded by thrombus which extended into the ophthalmic artery. The patient never recovered and subsequent post-mortem findings showed a thrombotic occlusion of the MCA at a branch point in the neighbourhood of an area of cerebral infarction and other evidence to support the atheromatous/ thrombosed internal carotid artery as the source of both these emboli [Russell, 1961]. Later studies identified that patients presenting with amaurosis fugax were at increased risk of stroke and survival could be improved by carotid endarterectomy [Wylie, Ehrenfeld, 1970]. Further studies identified that patients with visible emboli on retinal fundoscopy had a marked decrease in survival [Savino *et al*, 1977].

The aim of this part of the study was to use retinal fundoscopy and visual field testing to detect evidence of intraoperative embolisation to the eye and correlate this to episodes of intraoperative embolisation detected by TCD monitoring.

7.2 Materials and Methods

All patients underwent the following pre- and post operative assessment.

Automated Visual Field Testing

The visual fields of both eyes were tested independently on the Humphrey Field Analyser (Allergan Humphrey, 2992 Alvarado St, San Leandro, CA 94577) using a Full-Field 120 point screening test, stimulus size three, white light. A three-zone screening strategy was used which first located defects using a threshold related strategy. The field analyser measured the patient's central and peripheral threshold at four primary points at the centre and periphery of the field during the first phase of the test to provide reference values (expressed in decibels-dB) to construct the patients expected visual field.

Defects were classified as relative or absolute. Defects classified as relative were deeper than 6dB but are not present when the brightest possible stimulus was presented (10,000 apostilbs or 0dB).

Patients were seated comfortably facing the chin cup and headrest of the field analyser. The patient held a response button which produced an audible click and tone to indicate when it had been activated.

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The patient was informed to look straight ahead at a steady yellow light. Other lights would flash, one at a time off to the side of the yellow light. Some of these lights would be bright, others dim and the patient was instructed to press the response button whenever they saw a light.

The non-tested eye was then occluded with an eye patch and the patient positioned against the chin cup and head rest looking into the field analyser. The patient was then aligned correctly and maintained in this position with use of a video eye monitor.

A demonstration test was then performed. During the demonstration test the field analyser presented stimuli but the patient's responses were not recorded. When the operator was satisfied that the patient understood what to do the test was started.

The test was repeated for each eye. At the completion of the test a printout of the visual field for each eye was obtained. On the diagrammatic representation of the visual field points seen were represented as 'o', relative defects as 'x' and absolute defects as '•'.

The type of test and test parameters were printed at the top of the printout along with the patient data, date, and time. Also recorded were the number of points seen and the number of relative defects. The printout also included a number of indices of test reliability:

1. Fixation Losses. If a patient responded to a stimulus that was presented to the blind spot, a fixation loss was recorded. A high fixation loss score indicates that the patient did not fixate well during the test. If the rate of fixation losses exceeded 20% the test was unreliable.

2. False Positive errors. During the examination approximately one of forty test points was a false positive trial. The projector moved as if to present a stimulus, but no stimulus was shown. A high false positive score indicates that the patient was pressing the button when no stimulus had been presented. If the false positive rate exceeded 33% the test was unreliable.

3. False Negative Errors. During an examination the field analyser occasionally presented a very bright stimulus in an area of previously established sensitivity. If the patient did not respond, a false negative error was recorded. A high number of false negative errors indicated an inattentive patient, poor fixation or a physical condition that made it difficult for the patient to respond. If the false negative rate exceeded 33% the whole test was unreliable.

Each patient was given a score for points seen out of 120 for each eye. Absolute defects were awarded no score and relative defects scored a half a point.

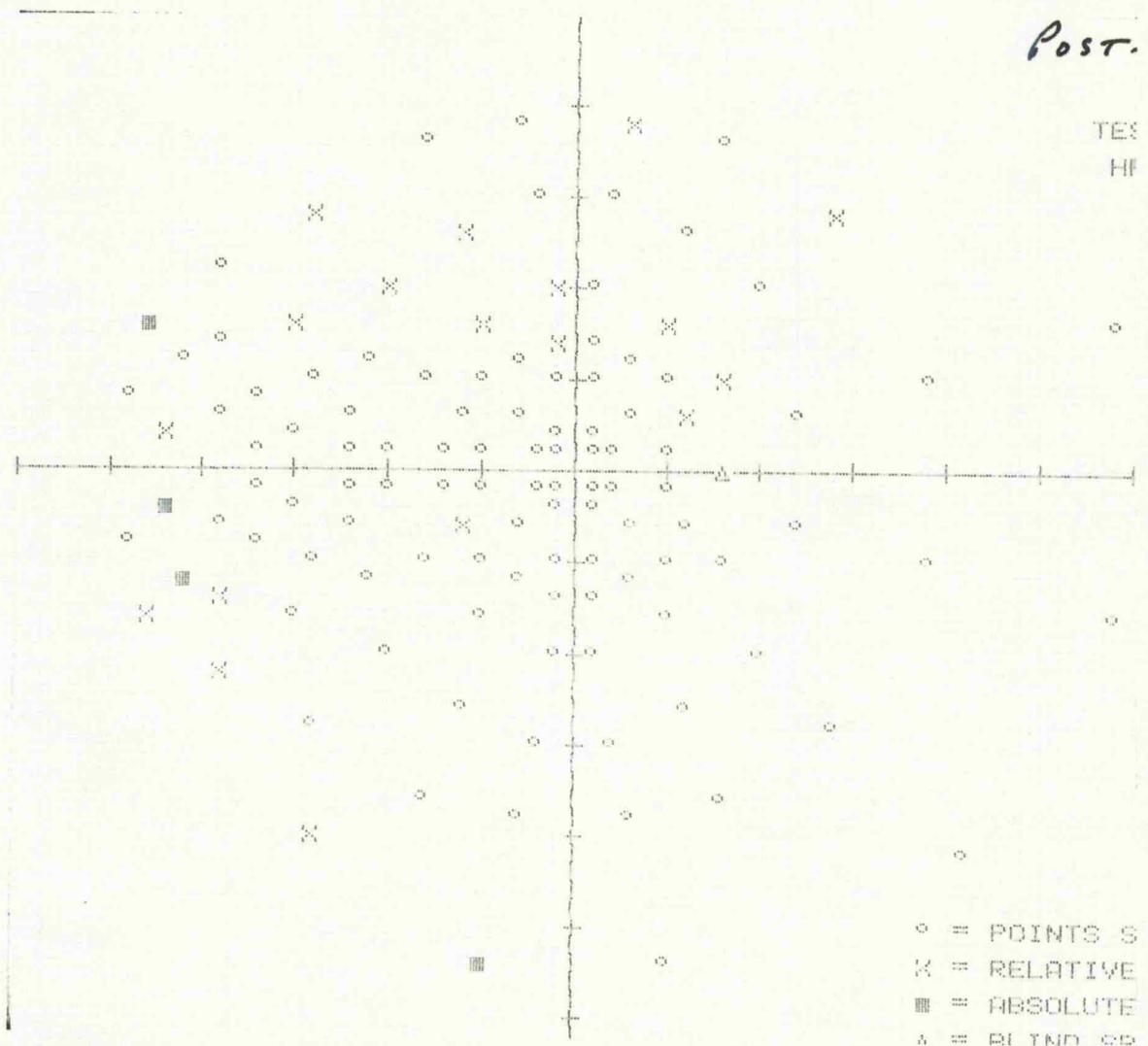


Figure 7.1: Example of the Allergan Humphrey visual field printout for the right eye of a patient in the postoperative period.

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Fundoscopy

After completing the visual field test the patients fundi were examined under induced pupillary dilatation (Timoptol and Pilocarpine). Assessments were performed by an independent ophthalmologist who was unaware of the embolic status of the patient. Abnormal findings were recorded on a specially printed results sheet dedicated to the study (appendix 3). This results sheet recorded: the visual acuity in each eye including the visual acuity with pin-hole correction; the ophthalmologists assessment of the history of amaurosis fugax; the presence of corneal opacities (graded from absent (0) to dense (3)); the intraoperative pressure measured in each eye.

Abnormalities of the fundi were also recorded including the site of the abnormality recorded on a diagrammatic representation of the fundus and annotated with relevant comments. The postoperative appearance was compared with the preoperative findings.

Data Analysis: Fundoscopy

The preoperative and postoperative findings were compared for both the ipsilateral and contralateral eye. Evidence of new embolisation was correlated with intraoperative episodes of embolisation detected by TCD monitoring.

In addition, the initial preoperative findings were recorded and correlated to symptoms attributed to amaurosis fugax for the eye ipsilateral and contralateral to the symptomatic carotid artery.

Also the preoperative fundoscopic findings for the ipsilateral and contralateral eye were correlated with their respective visual field scores to indicate the type of embolic defect which would significantly reduce visual field scores.

Data Analysis: Visual Fields

Visual field scores from different groups of patients were compared by calculating medians and 95% confidence intervals. Medians of visual field scores were calculated separately for the eye ipsilateral and contralateral to the operated side. Pre- and post-operative medians and 95% CIs were compared for the eyes ipsilateral and contralateral to the operated side [Gardner *et al*, 1991].

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Preoperatively, the significance of a history of retinal embolisation was assessed by comparison of the ipsilateral visual field scores of patients presenting with amaurosis fugax with the ipsilateral scores of patients without a history of amaurosis fugax. Also within the AF group, scores were compared for the ipsilateral and contralateral eyes.

The significance of embolisation detected by retinal funduscopy on visual field scores was assessed by comparing the median visual field scores for the affected and unaffected eyes. Also, the ipsilateral median visual field scores of those patients with fundoscopic evidence of retinal embolisation was compared with those patients without evidence of retinal embolisation.

Postoperatively, visual field scores were compared with preoperative scores for both the ipsilateral and contralateral eyes. A decrease in the ipsilateral eye score associated with no deterioration or improvement in the contralateral eye score was recorded as significant.

Deterioration in ipsilateral eye scores, independent of contralateral deterioration, were correlated to episodes of intraoperative embolisation.

Finally, the ipsilateral visual field scores of groups of patients with embolisation profiles known to be associated with postoperative cognitive and neurological deficits were compared. These groups of patients were: those with greater than 100 intraoperative embolic episodes; those with TCD evidence of particulate embolisation; those with greater than 10 intraoperative particulate emboli.

Statistical Analysis

Statistical analysis was performed using the CIA computer programme [Gardner *et al*, 1991] to obtain medians and 95% confidence intervals for the visual field scores.

7.3 Results: Fundoscopy

Preoperative Findings

Complete pre and postoperative examinations were obtained in 91 patients. A convincing history of amaurosis fugax was obtained from 42 patients and of these, five had evidence of embolisation on funduscopy. A further six patients

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had fundoscopic evidence of embolisation but no symptoms attributable to amaurosis fugax.

Other significant eye conditions were also detected. One patient had chronic simple glaucoma, two had optic atrophy, one had retinosis, one had myopic degeneration and six had evidence of hypertensive retinopathy.

Fundoscopy-Postoperative Findings

Postoperatively, only one patient had evidence of new embolisation. This consisted of two small emboli affecting the periphery of the retina and this was not associated with a deterioration in visual field scores.

One further patient had evidence of an intraoperative embolus but this was in the contralateral eye and therefore was not considered in the analysis. Interestingly, this patient did have significant carotid disease in the contralateral artery (>90% stenosis).

The retinal funduscopy study did not yield sufficient end-points to merit correlation with episodes of intraoperative embolisation.

7.4 Results: Visual Fields

Complete sets of data were obtained for 91/100 patients. Reasons for incomplete sets of data were mechanical failure of automatic visual field tester, missed examinations, two patients died prior to postoperative testing and two patients were unable to co-ordinate reliable responses, recording an unacceptably high percentage of fixation losses and false negatives.

There was no statistically significant difference in the median scores for the ipsilateral eye preoperatively (median = 110 95% CI 107 to 112.5, Wilcoxon K=1598) or postoperatively (median = 109 CI 105 to 111.5, Wilcoxon K=1598) for the sample as a whole. The difference between the medians = 0.25 (95% CI -0.75 to 1.75, K=1561). Similarly, there no difference in the contralateral eye between preoperative scores (median=112 95% CI 108.5 to 114, K=1598) and postoperative scores (median=112 95% CI 108.75 to 114, K=1598). The difference between the medians = 0.25 (95% CI -1 to 0.5, K=1561).

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Interestingly there was no difference between the medians of the ipsilateral and contralateral eyes preoperatively -1.0 (95% CI -2.25 to 0.25, K=1598) but postoperatively the small deterioration in the ipsilateral eye was sufficient to result in a significant difference between ipsilateral and contralateral eyes score at the 95% CI level (median = -1.5, 95% CI -3 to -0.5, K=1598). The cause for this is not immediately apparent.

	Ipsilateral Eye Median (95% CI)	Contralateral Eye Median (95% CI)	Difference between medians (95% CI)
Preoperative	110 (107-112.5)	112 (108.5-114)	-1.0 (-2.25 to 0.25)
Postoperative	109 (105-111.5)	112 (108.75-114)	-1.5 (-3 to -0.5)
Difference between medians	0.25 (-0.75-1.75)	0.25 (-1 to 0.5)	

Table 7.1: Table illustrating the pre- and postoperative median visual field scores for both the ipsilateral and contralateral eye.

Visual Fields : Amaurosis Fugax (AF)

To assess the effect on visual field scores of a history of retinal embolisation the visual field scores of those patients with a positive history of AF were analysed further. Comparison of the medians of the affected eye (median=111, 95% CI 107.75 to 115, K=328) and the unaffected eye (median=114, 95% CI 108.75 to 115.75) suggested a trend towards lower scores being recorded in the affected eye although this did not reach statistical significance. The difference between the medians was -1.75 (95% CI -4.25 to 0.5, K=328).

However, further analysis revealed that the ipsilateral eye score of those patients with a negative history for AF (median=108) was lower than the ipsilateral eye scores of those patients with a positive history of AF (median =111).

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Visual Fields : Fundoscopic Evidence of Retinal Embolisation

Eleven patients had preoperative evidence on fundoscopy of retinal embolisation. The median score for the affected eye was 108 (95% CI 69.75 to 113.75, K=11) while the median score for the unaffected eye was 112 (95% CI 99.25 to 117.5, K=11). Once again there was a trend for embolisation to be associated with lower visual field scores, although this was not a statistically significant difference. The difference between the medians was -2.62 (95% CI -26.5 to 0.5, K=11).

Two of these patients had significant differences in their ipsilateral and contralateral visual field scores. One patient had fundoscopic evidence of an infarcted vessel (ipsi=102.5, contra=119) and one patient had 3 major emboli (ipsi=22.5, contra=79.5). But apart from these two there no strong evidence that lesser degrees of embolisation significantly affected the visual fields.

	History of AF (median-95% CI)	Fundoscopy evidence of embolisation (median-95% CI)
Ipsilateral eye	111 (107.75 to 115)	108 (69.75 to 113.75)
Contralateral eye	114 (108.75 to 115.75)	112 (99.25 to 117.25)
Difference between medians	-1.75 (-4.25 to 0.5)	-2.62 (-26.5 to 0.5)

Table 7.2: Table illustrating the visual field scores for the ipsilateral and contralateral eyes of those patients with a history of amaurosis fugax and/or fundoscopic evidence of retinal embolisation.

Postoperative Changes in Visual Field Scores

A postoperative deterioration in visual field score in the eye ipsilateral to the operated artery but not in the contralateral eye was considered to be significant.

Thirty-four patients had a postoperative deterioration in their ipsilateral eye score, 40 improved their ipsilateral score and 17 remained the same. Of the 34

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who deteriorated, 23 had a corresponding deterioration in the contralateral eye. The median ipsilateral deterioration was 5.5 (95% CI 4 to 7.5, K=183). Eleven patients had a deterioration in ipsilateral eye scores but with no deterioration in the contralateral eye, the median deterioration was 2.75 (95% CI 1 to 4.75, K=11).

Thirty-two patients had a postoperative deterioration of their contralateral eye, the median deterioration was 3.75 (95% CI 2 to 6, K=160). Eleven of these patients had a postoperative deterioration in the contralateral eye without deterioration in the ipsilateral eye. The median deterioration was 1.38 (95% CI 0.75 to 3.75, K=11).

There was no statistically significant difference between the magnitude of deterioration in the ipsi- and contralateral eyes (median difference =0.5, 95% CI -0.5 to 3, K=31). In addition, none of these cases had fundoscopic evidence of embolisation and none had experienced episodes of gross intraoperative embolisation.

	ipsilateral deterioration	contralateral deterioration	ipsilateral deterioration only	contralateral deterioration only
No of patients	34	32	11	11
Median (CI) deterioration	5.5 (4 to 7.5)	3.75 (2 to 6)	2.75 (1 to 4.75)	1.38 (0.75 to 3.75)
Difference between medians (CI)			0.5 (-0.5 to 3)	

Table 7.3: Table comparing the number of patients and the median (95% CI) postoperative deterioration in visual field scores for the ipsilateral and contralateral eyes

Visual Field Scores of Patients Experiencing Significant Episodes of Intraoperative Embolisation

Twelve patients who had experienced greater than 100 intraoperative embolic episodes did not have emboli on retinal funduscopy or statistically significantly

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lower postoperative ipsilateral visual field scores. The difference between the medians of the pre- and postoperative ipsilateral eye scores was 2.0 (95% CI - 0.75 to 4.75, K=11).

Patients who had TCD evidence of intraoperative particulate emboli did not have emboli on funduscopy or a statistically significant difference between ipsilateral pre- and postoperative visual field scores. The median difference was 0.5 (95% CI -2.25 to 3, K=74).

Patients who experienced more than 10 intraoperative particulate emboli did not have emboli on funduscopy or a statistically significant difference between ipsilateral pre- and postoperative visual field scores. The median difference was 2 (95% CI -4 to 6.75, K=6).

7.5 Discussion

The purpose of this study was to investigate whether perioperative evidence of retinal embolisation, identified by retinal emboli on funduscopy or a significant deterioration in post-operative visual field scores, correlated with episodes of intraoperative embolisation detected by TCD monitoring.

Evidence of intraoperative retinal embolisation has been demonstrated in patients undergoing coronary artery by-pass surgery [Blauth *et al*, 1986]. Blauth and colleagues used intraoperative retinal angiography to demonstrate the temporary occlusion of retinal vessels by emboli in 10 patients undergoing coronary artery bypass surgery [Blauth *et al*, 1986]. The diagnostic criterion for an occlusion was absence of filling of a vessel throughout the angiographic phase. All 10 patients had microvascular occlusions demonstrated intraoperatively, however these changes had resolved when funduscopy, visual field analysis and fluorescein angiography were repeated postoperatively indicating a transient effect of these emboli.

The purpose of this study was to detect clinically significant embolisation and, therefore, intraoperative angiography was unnecessary as significant emboli should have produced effects detectable by funduscopy and visual field testing 2-3 days postoperatively.

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However, retinal funduscopy yielded insufficient end-points to enable any correlation with TCD detected embolisation. This suggested that either intraoperative retinal embolisation during CEA is a very rare phenomena or that in common with CABG operations, intraoperative retinal emboli during CEA are transient and produce few clinical consequences.

The evidence produced by Blauth and colleagues suggests that the second explanation is the more likely and this is consistent with experimental work performed by Patterson and colleagues which demonstrated that platelet microaggregate occlusion of retinal vessels can resolve within 20 minutes of embolisation [Patterson *et al*, 1967]. However, there is considerable evidence that not all retinal emboli resolve. Hollenhorst first described the embolic origin of cholesterol crystals visible in the retina on fundoscopic examination and in a later study of 205 patients with visible retinal emboli demonstrated that the presence of these emboli was associated with a decreased survival rate [Hollenhorst 1961; Pfaffenbach, Hollenhorst 1973]. In a study of CRAO Savino identified visible retinal emboli in 72 out of 117 patients presenting with this condition, once again visible emboli was associated with a marked decrease in survivorship [Savino *et al*, 1977].

Retinal emboli have been examined histopathologically and have been found to consist of cholesterol crystals [David *et al*, 1963], platelet aggregates [McBrien *et al*, 1963], fibrin and blood cells [Zimmerman 1965] as well as neutral fat [Cogan *et al*, 1964].

However in this study the independent ophthalmologist assessed that 42 patients described a convincing history for AF, however only 5 (12%) had positive fundoscopic evidence of retinal embolisation. This suggests that for this cohort, the majority of retinal emboli large enough to cause symptoms are transient phenomena and do not result in any permanent pathological changes to the retina. As a group, patients with a history of amaurosis fugax did not have significantly lower visual field scores when the affected eye was compared with the unaffected eye or when compared with ipsilateral eye of patients with a negative history. Indeed, AF positive patients scored better than AF negative patients for the eye ipsilateral to the symptomatic artery.

Interestingly, a further 6 patients had positive fundoscopic evidence of embolisation but no history of amaurosis fugax. This would suggest that a

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small number of patients experience silent retinal infarction possibly occurring during sleep. However, given the poor prognosis of patients with visible emboli it would be interesting to investigate whether patients with silent retinal infarction form a separate high risk group who would benefit from CEA. Certainly the fact that they presented with other embolic symptoms would support their high risk status.

Patients with retinal emboli on fundoscopy did not have significantly worse visual field scores compared to the unaffected eye or compared with the ipsilateral eye scores for patients without visual symptoms or signs. Only two patients had significantly worse visual field scores for the affected eye compared to the unaffected eye. One had an infarcted vessel while the other had three large emboli affecting major branches. Lesser degrees of embolisation did not appear to adversely affect visual field scores.

Therefore, these results would suggest that while amaurosis fugax is a common symptom among patients presenting for CEA only a small percentage have fundoscopic evidence of embolisation. And within these patients only major retinal emboli or vessel infarction results in a clinically significant reduction in visual fields.

Overall, there was no significant deterioration in visual field scores postoperatively for either the ipsilateral or contralateral eye. Thirty-four patients did have a postoperative deterioration in their ipsilateral eye scores but in 23 of them this occurred in conjunction with a deterioration in contralateral eye scores and therefore probably reflected a cerebral effect rather than a retinal event. Eleven patients had an isolated ipsilateral deterioration independent of contralateral deterioration but the magnitude of deterioration was not significantly greater than the deterioration of the eleven patients who had an isolated contralateral deterioration.

Forty patients improved their ipsilateral scores and 17 remained the same. Therefore there is no evidence that the deterioration in ipsilateral eye scores occurred other than by chance. Only two patients had fundoscopic evidence of postoperative retinal embolisation, one to the ipsilateral eye the other to the contralateral eye. Neither eyes had significantly worse visual field scores postoperatively.

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Finally the visual field scores were analysed for three cohorts of patients with significant episodes of intraoperative embolisation detected by TCD. Some of these patients had experienced neurological and cognitive deficits as a result of this gross particulate embolisation. However, none of these patients had fundoscopic evidence of retinal embolisation and none had a significant deterioration in visual field scores postoperatively.

7.6 Summary

In conclusion, this study did not detect any clinically significant retinal embolisation occurring as a result of carotid endarterectomy. Preoperative evidence would suggest that for emboli to significantly reduce the visual field score in an eye the emboli need to be large and to occlude a major retinal arterial branch. This did not occur in this series.

CHAPTER 8

CT AND MRI BRAIN SCANS

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8.1 Introduction

Previous studies have identified that silent cerebral infarction is not uncommon in patients with carotid artery disease in the absence of neurological deficit [Norris, Zhu, 1992]. In the ECST study patients undergoing CEA with evidence of silent cerebral infarction on preoperative CT scan were assigned to the same prognostic group as those patient with a residual neurological deficit [ECST, 1992]. However, there is evidence to support the idea that silent cerebral infarction may also occur during CEA. In a study of 100 consecutive carotid endarterectomies Berguer and colleagues described a silent postoperative cerebral infarction rate of 12%, however the cause of these infarcts was not identified [Burger *et al*, 1986].

In this part of the study we aimed to investigate whether intraoperative emboli were associated with the development of silent cerebral infarcts. We used CT brain scanning for all patients and MRI brain scans for the last 50 consecutive patients when the MRI scanner became available for use in our hospital.

8.2 History of The Computed Tomography of X-rays [Sutton, 1987]

A new method of forming images from x-rays was developed and introduced into clinical use by the British physicist Godfrey Hounsfield in 1972, and is referred to as computed tomography (CT) or computerised axial tomography (CAT).

Hounsfield's work was based on research into data retrieval and transformation and his basic and revolutionary assumption was that measurements taken of X-rays transmitted through the body contained information on all the constituents of the body in the path of the beam. By using multidirectional scanning of the object multiple data were collected. Their interpretation required a mathematical solution using a computer to perform the calculations. This information could then be presented in a conventional raster form and from these results a two dimensional picture could be produced.

8.3 Theory of CT scanning.

In computed tomography the X-ray output is collimated to a very narrow beam. While passing through the patient it is partially absorbed, and the remaining

CT and MRI Brain Scans

photons of the X-ray beam fall on radiation detectors instead of X-ray film. The detector response is directly related to the number of photons impinging on it and so to tissue density, since a greater proportion of X-ray photons passing through dense tissue are absorbed than are absorbed by less dense tissues. When they strike the detector the X-ray photons are converted to scintillations which can be quantified and recorded digitally.

The information is fed to a computer which produces different readings as the X-ray beam is traversed around the subject. This information, which represents the absorption in each tiny segment of the section traversed is presented in analogue form as a two-dimensional display of the matrix on a screen where each numerical value is represented by a single picture element (pixel). Presentation is usually in the form of a grey scale in which whiteness is proportional to the X-ray attenuation coefficient of tissue at each point of the scan. Thus radio-opaque materials appear white and radiolucent tissues appear black according to a scale known as the Hounsfield scale.

CT Scan Infarcts

The cardinal sign of infarction is an area of decreased attenuation within the cerebral substance. Typical locations are within the known territory of a major vessel or in the region of the basal ganglia and internal capsule. So-called 'watershed infarcts' may be seen at the margins of a major vascular territory, e.g. the posterior frontal and parieto-occipital zones. Infarcts are often triangular in shape though they can appear rounded in axial cross-section and involve both the white and peripheral grey matter.

The area of diminished density, accompanied by mild mass effect may be seen as early as 6 hours after the onset of symptoms, but in many cases is not clearly visible during the first 24 hours depending on the quality of the CT images. At first the margins of the infarcted area are poorly defined, although a few infarcts are clearly marginated from the outset. The density of the lesion becomes progressively lower over the succeeding weeks, until it approaches that of cerebrospinal fluid in a mature infarct. Some infarcts may appear isodense at about three weeks.

A type of infarct whose appearance differ markedly from those described above is the uncommon haemorrhagic infarct. This is commonest with a major embolus. There is patchy increased density throughout the affected region,

CT and MRI Brain Scans

often with some mass effect, or there may be haemorrhage at the cortical margins of the infarct. The CT appearances may resemble those of an haemorrhage or haemorrhagic contusion rather than a simple infarct.

8.4 History and Theory of Magnetic Resonance Imaging (MRI): [Sutton 1987]

The first successful nuclear magnetic resonance (NMR) experiments were described by Bloch and Purcell independently in 1946 however it was Damadian(1972) and Lauterbur (1973) who indicated the potential of NMR to obtain images of the human body [Sutton, 1987].

The nuclear part of NMR refers to the fact that certain atomic nuclei (those with unpaired protons or neutrons) possess an intrinsic spin. Since the nucleus is positively charged, it generates a small magnetic field when it spins. The most abundant spinning nucleus in the human body is the hydrogen nucleus or proton found in water and lipids.

Nuclei placed within a magnetic field tend to align with the force of the field. The spinning protons wobble or precess about the axis of the main magnetic field. The precessional motion is slow relative to the faster spinning motion. Some of the protons line up parallel to the magnetic field (lower energy level) and some line up antiparallel (higher energy level). The small excess of protons lining up in parallel produces the net magnetisation upon which the NMR signal is dependant.

Resonance refers to a change in the basic energy levels of the nuclei which have already been placed within a magnetic field. A radiofrequency (RF) field applied at the same frequency as the precessing nuclei and at right angles to the main magnetic field can be used to excite or flip the small excess of protons in the lower energy level into a higher energy state. Energy is absorbed from this transition and subsequently released to the environment as the protons relax back to their lower energy state and equilibrium. This release of energy can be recorded as an electrical signal and indicates that resonance has occurred.

The way in which a specific nucleus is selected for study is related to the resonant frequency of the RF field being unique for that nucleus at a specified

CT and MRI Brain Scans

magnetic field strength. In the case of protons the resonant frequency is 42.6 megahertz (MHz) at 1.0 tesla field strength.

The MR Signal

When an RF pulse is applied to magnetised tissue at the appropriate resonant frequency for protons, resonance is induced. When this RF pulse is turned off the excited protons return to equilibrium releasing their absorbed energy to the environment at the same resonant frequency producing the MR signal. The strength (amplitude) of the signal will depend on the number of measurable protons (proton density). The relaxation of the protons back to equilibrium and the lower energy state is termed the spin-lattice relaxation. It is exponential and referred to by the time constant ' T_1 '.

During relaxation the aligned protons quickly get out of phase due to small variations in local magnetic fields. This loss of phase is termed spin-spin relaxation which is also exponential and referred to by the time constant ' T_2 '.

The principle factors determining contrast in MRI are the heterogeneous distribution of T_1 and T_2 relaxation times within different tissues.

The main RF pulse sequences used in MRI are saturation recovery (SR), inversion recovery (IR) and spin echo (SE). Inversion recovery images are strongly T_1 dependent while spin echo sequences are T_2 dependent.

There are four main tissue MR parameters which contribute to the signal intensity of an image - proton density, T_1 and T_2 relaxation times and blood flow. The appearance of a structure varies according to which MR parameter is being measured. Protons giving rise to an MR signal are mainly those in cell water and lipids. Protons in DNA, proteins and compact bone do not usually contribute to the signal.

MRI Scan - Infarcts

Infarcts have a long T_1 and a long T_2 . Lesions are seen earlier from onset, appear more extensive and are detectable for a longer period when compared to CT. More lesions are detected on MRI, especially in the brainstem and subcortical sites, which are difficult areas for CT because of adjacent bony artefacts.

CT and MRI Brain Scans

	T ₁ (ms)	T ₂ (ms)	Water content (%)
Grey matter	757 +/-24	73 +/-1	74
White matter	520 +/-17	69 +/-1	84
CSF	>2000	>300	97
Liver	424 +/-29	54 +/-1	71
Spleen	662 +/-18	76 +/-2	79
Pancreas	576 +/-44	55 +/-3	88
Muscle	564 +/-15	41 +/-1	79

Table 8.1 Typical MR tissue values at 0.26T [Sutton, 1987].

8.5 Materials and Methods

CT Brain Scans

Brain scans were performed on a Siemens (series 2) computerised tomogram x-ray scanner (Siemens, Germany) obtaining 12 transcranial slices. Patients were scanned 1-4 days preoperatively and between the fifth and seventh day postoperatively.

MRI Brain Scans

MRI brains scans were obtained using T₁, T₂ weighted images on a Siemens Magnetom (1 Tesla) magnetic resonance imaging scanner (Siemens, Germany). Patients were examined 1-4 days preoperatively and between the fifth and seventh day postoperatively.

Data analysis

All scans were reviewed by one independent radiologist unaware of the embolic status of the patient. Patient identification and the date of the scan were obscured and replaced with a study number and the letter 'A' and 'B' which were randomly assigned to pre-operative and post-operative scans. All preoperative and postoperative pathological changes were recorded and new lesions correlated to embolic events during the operation.

8.6 Results : CT Brain Scans

Complete sets of pre- and post-operative scans were obtained in 93/100 patients. Reasons for incomplete sets of data were due to mechanical failure of the scanner and administrative difficulties.

Preoperative Results

Evidence of preoperative infarction in the hemisphere ipsilateral to the operated side was present in 39 patients and evidence of contralateral infarction was present in 22. Six patients had evidence of infarction in the contralateral hemisphere only and eleven patients had evidence of watershed infarction (Figure 8.1).

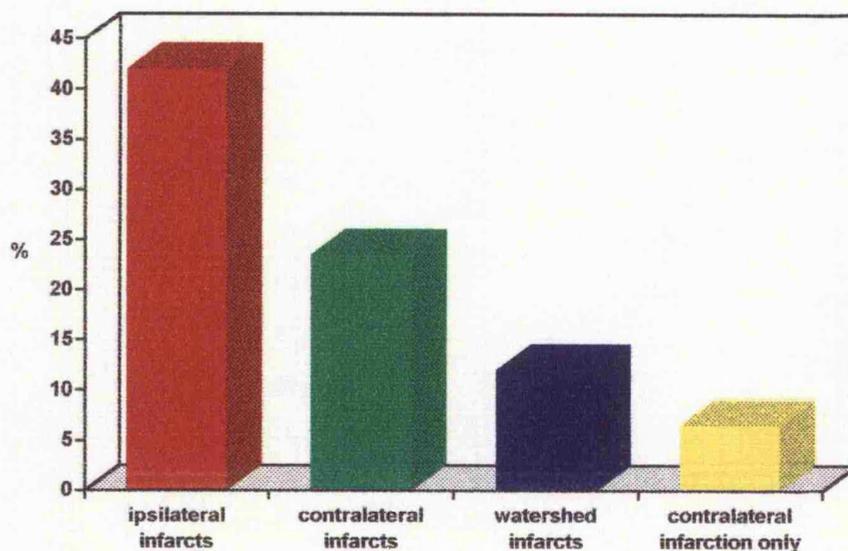


Figure 8.1: Bar chart illustrating the distribution of patients with evidence of brain infarction on preoperative CT brain scanning.

Twenty patients had evidence of silent cerebral infarction. Ten patients presented with a history of TIA's, 6 presented with a history of amaurosis fugax and 3 presented with a history of both (Fig 8.2). One patient was asymptomatic.

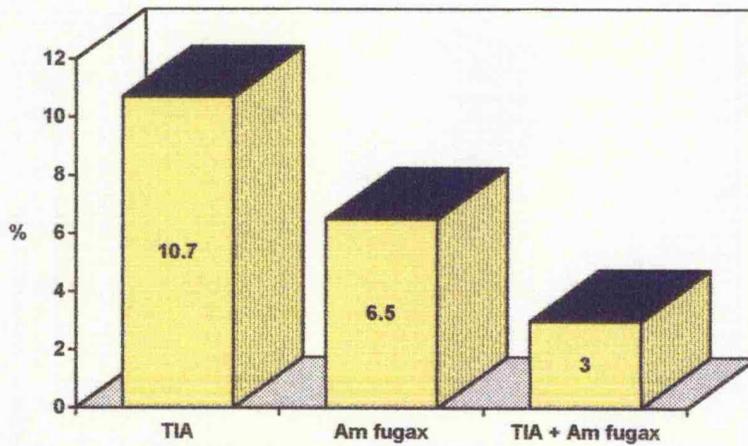


Figure 8.2: 3-D bar chart illustrating the distribution of presenting symptoms of patients with evidence of preoperative silent cerebral infarction

Association of Infarction with Carotid Artery Stenosis

For all patients with preoperative CT infarcts the mean stenosis of the ipsilateral carotid artery was 82.1% (SD 8.94) compared with 81.3% (SD 9.38) for patients with no CT infarcts. There was no significant difference between the means = 0.718 (SE of difference=1.89, df 91, t=1.98, 95% CI -3.04 to 4.48).

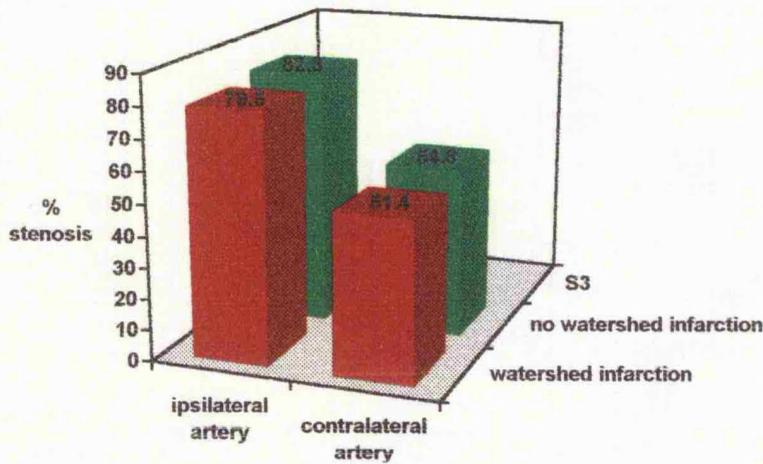


Figure 8.3 3-D bar chart comparing the degree of carotid artery stenosis associated with watershed infarction and no watershed infarction

CT and MRI Brain Scans

The results of the eleven patients with watershed infarction were analysed further to assess the association with ipsilateral and contralateral carotid artery stenosis (Fig 8.3). The mean ipsilateral carotid artery stenosis for patients with evidence of watershed ischaemia was 79.5 (SD 8.5) while that for patients without was 82.3 (SD 9.2). There was no significant difference between the means (difference = -2.78, SE of difference = 2.93, df 91, $t=1.98$, 95% CI = -8.59 to 3.02).

Similarly, the mean contralateral artery stenosis in patients with evidence of watershed infarcts was 51.4% (SD 38.5) while the mean stenosis for patients without infarction was 54.8 (SD 33.8). The difference between the means was not significant (-3.41 SE of difference = 11, df 91 $t=1.98$, 95% CI -25.2 to 18.4).

Postoperative Results

New post-operative infarcts were detected in only three patients. These patients were patients 53, 98 and 99 who had all experienced gross particulate embolisation in the recovery phase associated with incipient carotid artery thrombosis. All new infarcts were in the parietal region within the territory of the MCA and their appearance was consistent with embolisation.

8.7 Results : MRI Brain Scans

Complete sets of pre and postoperative scans were obtained in 46/50 patients. There were no new infarcts identified by MRI scanning compared to CT scanning both preoperatively or postoperatively.

8.8 Discussion

New postoperative brain infarction was only associated with episodes of gross particulate embolisation in the recovery phase. Air embolisation and particulate embolisation occurring at other stages of the operation were not associated with the development of new CT brain infarcts. This included one patient with gross air embolisation during the shunting phase associated with distal retaining balloon rupture of the Pruitt-Inahara shunt and repeated attempts at reinflation. The patient experienced a temporary worsening of a pre-existing hemiparesis which resolved after three days but the CT brain scan performed at five days did not show any extension of the original infarct or any new infarction.

CT and MRI Brain Scans

Patients experiencing particulate embolisation during the dissection phase which were found to be associated with the development of postoperative cognitive deficits were not associated with CT brain infarction or MRI infarction. This finding is in contrast to the findings of Jansen and colleagues who found an association between greater than 10 emboli during dissection and an increased incidence of silent MRI infarction [Jansen *et al*, 1994], however, this only consisted of two cases and the association was weak.

The findings of this study are also in contrast to those of Buerger and colleagues who described a 12% silent perioperative infarction rate in patients undergoing carotid endarterectomy [Buerger *et al*, 1986], but are consistent with those of Sise and colleagues who found no evidence of silent infarction following CEA [Sise *et al*, 1988]. This absence of silent cerebral infarction is important confirmation that the monitoring methods used in this study did not miss clinically significant intraoperative events. Further supporting evidence is provided by the MRI study which also failed to detect silent cerebral infarction and correlated well with the CT findings.

Preoperatively, 20% of patients had evidence of silent cerebral infarction with the most common symptoms described by this group being TIAs. The finding of silent cerebral infarction in patients presenting with TIAs is well described with an incidence of between 12-70% [Grigg *et al*, 1988]. Upto 11% of patients with clinical signs of stroke but no history of stroke were found to have CT lesions unrelated to the presenting stroke [Chodosh *et al*, 1988]. Also, approximately 20% of patients with asymptomatic carotid stenosis have infarcts confirmed on CT scan [Ricotta *et al*, 1985]. In surgical series describing preoperative CT scanning, silent infarcts have been described in 12-48% of patients with TIAs [Graber *et al*, 1984; Sise *et al*, 1988; Street *et al*, 1988]. In the NASCET study 34.4% of patients presenting with TIAs and high grade carotid stenosis had CT evidence of silent cerebral infarction [Streifler *et al*, 1992]. In the ECST patients with silent CT infarction were grouped with patients exhibiting residual neurological deficits so no specific data is available.

There may be several reasons for silent infarction. Patients may experience cerebral embolisation during sleep and may be unaware of transient symptoms or alternatively, fleeting or minor symptoms may be dismissed by both the patient and attending physician [Norris, Zhu 1992].

CT and MRI Brain Scans

The significance of silent infarction for this study is that first it can occur and secondly the presumed mechanism is embolisation occurring either preoperatively or intraoperatively [Norris, Zhu 1992]. However, in this study peroperative cerebral infarction was only associated with gross particulate embolisation in the recovery phase and gross air embolisation and lesser degrees of particulate embolisation occurring at other stages of the operation were not associated with infarction.

The incidence of cerebral infarction as a whole was not associated with a significantly greater degree of ipsilateral carotid stenosis and the presence of watershed infarction was not associated with a significantly greater degree of ipsilateral or contralateral carotid stenosis. It is possible that the integrity of the circle of Willis is of greater importance in the aetiology of watershed infarction than the stenosis of the carotid arteries alone.

No new infarcts were detected by MRI scanning compared to CT scanning. Generally, MRI is considered to be more sensitive in detecting new infarcts and therefore this was important confirmatory evidence that significant infarcts were not being missed by CT.

8.9 Summary

Silent peroperative infarction was not detected on CT or MRI scanning. The only infarcts detected occurred in three patients associated with gross particulate embolisation in the recovery phase and clinically apparent neurological deficits.

Gross intraoperative air embolisation and lesser degrees of particulate embolisation occurring during other phases of the operation were not associated with silent cerebral infarction.

CHAPTER 9

**DISCUSSION OF THE CLINICAL RELEVANCE OF TCD DETECTED
EMBOLISATION DURING CAROTID ENDARTERECTOMY**

The Clinical Relevance of Embolisation

The Clinical Relevance of TCD Detected Embolisation During Carotid endarterectomy

This study has confirmed that intraoperative embolisation is very common during CEA and was detected in 92% of successfully monitored operations. However the majority were of no clinical significance. In particular, intraoperative emboli were not associated with silent CT infarction or visual field deficits. Apart from one patient with gross air embolisation following shunt complications, there is no evidence that air emboli were associated with any clinical sequelae.

However, this study has identified two stages during CEA when clinically significant embolisation occurs. More than 10 particulate emboli occurring during initial dissection is associated with a deterioration in postoperative cognitive function while persistent particulate embolisation during the recovery phase is an indicator of incipient carotid thrombosis and the development of major neurological deficits. Early intervention based on the TCD evidence of embolisation has the potential to avoid adverse clinical consequences related to these events.

Thrombosis of a recently endarterectomised artery occurs in 1-2% of cases and a large proportion suffer a stroke or die despite early intervention [Naylor *et al*, 1991]. Current methods to detect this serious complication depend on regular neurological observations in the recovery room, however by the time neurological signs appear it is likely that a degree of neurological damage has already occurred. Postoperative analysis of the TCD recordings from the three cases of early carotid thrombosis reveal that the first particulate emboli were detected 6-9 minutes after final restoration of flow, but before a regular pattern of emboli was established. This phenomena has not been widely described, therefore in the first two cases the clinical significance of the emboli was not immediately appreciated and operative intervention was slightly delayed, resulting in two minor strokes. However, in the final case immediate intervention to remove the thrombus, based on the TCD evidence of persistent particulate embolisation and our experience of the previous two cases, probably prevented a permanent neurological deficit. These cases provide important evidence for the direct role of platelet emboli in the development of neurological deficits, since, in none of the cases did MCA velocities fall to levels known to be associated with the risk of haemodynamic strokes [Halsey, 1993].

The Clinical Relevance of Embolisation

However the cause of thrombus formation remains unclear. Completion angiography excluded the presence of thrombus prior to restoration of flow and at re-operation no technical error was associated with the site of thrombus formation or the proximal and distal arteries. Correction of the defect consisted of removal of the thrombus, commencement of an heparin infusion and restoration of blood flow. Haematological studies performed in the last two patients to detect possible hypercoagulable states and abnormal platelet function were negative. However, continuing TCD monitoring into the postoperative phase offers the potential for early detection and correction of this complication before permanent neurological deficits occur, whatever the cause.

Significant, particulate embolisation occurring during initial carotid dissection was associated with a decrease in postoperative cognitive function. The emboli occurring during this stage were assumed to be particulate because the arterial system had not been entered, the TCD embolic signals were characteristically particulate, emboli were often precipitated by direct handling of the carotid bifurcation and ceased on carotid clamping. TCD monitoring provided a warning that embolisation was occurring enabling the surgeon to modify the surgical approach to minimise further, potentially harmful, embolisation.

There was no correlation between the number of emboli occurring during other stages of the operation and a deterioration in cognitive function. In particular, there was no association between the amount of air embolisation detected and a decrease in cognitive scores. However, the cause of cognitive deterioration in some of the remaining patients is unclear. A possibility exists that potentially significant particulate embolisation occurred during other stages of the operation but was not detected because the subtle particulate emboli signals were masked by the extraspectral aliasing associated with air emboli occurring at the same time. We are currently investigating the use of different forms of spectral analysis to differentiate between air and particulate emboli more accurately, especially during restoration of flow and other stages of the operation where the two forms of emboli may occur simultaneously [Smith *et al*, 1994].

Previous studies have found that cognitive function can improve after carotid endarterectomy although it is difficult to eliminate practise effects from the analysis [Haynes *et al*, 1976]. Preoperative symptoms can influence postoperative performance as patients with a history of TIAs tend to perform better postoperatively, than patients with known infarcts [Mononen *et al*, 1990]. One study has related postoperative deterioration to intraoperative episodes of

The Clinical Relevance of Embolisation

ischaemia, as indicated by somatosensory evoked potentials, however we are unaware of any study to relate postoperative cognitive function to intraoperative embolisation [Cushman *et al*, 1984].

Current evidence suggests that the clinical effect of TCD detected embolisation is multifactorial and depends on the number, size and character of the emboli as well as patient susceptibility related to an inadequate collateral cerebral circulation and the presence of pre-existing cerebral infarcts [Spencer, 1992]. Investigators have used TCD to detect particulate emboli occurring in patients with artificial heart valves. Some of these patients have several hundred particulate emboli passing through the MCA every day without developing any neurological deficits [Spencer, 1992]. It may be the case that a large number of emboli occurring in a short period of time is more significant because there is less time for an embolus to disaggregate before the next embolus occurs. Alternatively it may be the size of the embolus which is important but at present, there is no reliable method of estimating the size of an embolus using TCD signal criteria.

In conclusion, this study has provided evidence of the clinical significance of TCD detected embolisation during carotid endarterectomy. The majority of emboli are air and not associated with adverse clinical outcome. However persistent particulate embolisation is associated with the development of neurological and psychometric deficits. In particular, this study has highlighted the role of TCD monitoring in providing an early warning of incipient carotid thrombosis in the immediate postoperative phase. Early intervention, based on TCD evidence, may reduce the morbidity and mortality associated with this serious complication.

In addition, TCD also provides a warning that potentially harmful embolisation is occurring during the dissection of the carotid artery, providing the surgeon with the opportunity to modify his surgical approach in order to minimise their occurrence.

PART THREE : CHAPTER 10

**A COMPARISON OF QUALITY CONTROL METHODS APPLIED TO CAROTID
ENDARTERECTOMY**

Comparison of Quality Control

CHAPTER 10

QUALITY CONTROL

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Comparison of Quality Control

10.1 Introduction

In the section dealing with the history of carotid surgery I described how HHG Eastcott successfully performed the first operation to remove a severe carotid stenosis which was causing multiple TIAs. The patient survived and lived for many years, symptom free, until eventually dying of heart failure. However, following this fortuitous start the next three patients at St Mary's, on whom the operation was performed, all died in the early postoperative period [Eastcott 1993]. In these cases the cause was attributed to ischaemia at the time of carotid clamping and various strategies were devised to minimise this, including the use of intraluminal shunts. However despite the increased use of shunts, the success and failure of operations were often unpredictable [Eastcott, 1993]. Results have varied from large almost unblemished series such as those achieved by Thompson of Dallas, whose immense experience, with careful case selection and routine shunting yielded a total morbidity/mortality of 1.5% [Thompson, 1983] to figures from occasional operators yielding 20% [Barnett *et al*, 1984].

The success of individual operators to obtain low morbidity/mortality rates is to be applauded however the reason for their success is often difficult to define. The results of the recent ECST/NASCET trials mean that large numbers of patients now require CEA, the performance of which cannot be confined to that small number of surgeons publishing excellent results [Warlow, 1993]. Therefore attention has focused on methods independent of experience and individual ability to reduce perioperative complications. One of these methods is 'Quality Control'.

Quality control can be described as the application of methods to detect errors of surgical technique. A recent retrospective study of 3062 CEAs implicated errors in surgical technique as a major cause of perioperative morbidity/mortality, in particular Riles and colleagues estimated that 65% of perioperative strokes were related to deficiencies of surgical technique leading to thromboembolism in the early postoperative period [Riles *et al*, 1994]. Therefore the detection and correction of technical error may significantly reduce the perioperative morbidity and mortality associated with the operation. However, it is perhaps surprising that given the importance of technical error there is no commonly applied method of quality control [Naylor *et al*, 1992].

Comparison of Quality Control

The ideal quality control technique would detect all technical errors known to be associated with adverse clinical consequences, be simple to apply and interpret and be absorbed easily into the operative routine. The technique should also be safe and not contribute to intraoperative morbidity/mortality and have a low number of false positives resulting in unnecessary and possibly hazardous re-explorations of the artery.

A review of quality control methods has already been described (Chapter 2). In that review I described how disadvantages with using intraoperative angiography, in particular the difficulty in obtaining adequate views at this site and the morbidity/mortality associated with the technique, prompted a search for safer and more reliable methods of quality control. Individual studies of angioscopy [Mehigan, Alcott, 1986], B-mode ultrasound [Dilley, Bernstein, 1986] and continuous wave Doppler [Seifert, Blackshear, 1985] had demonstrated their potential application. However, in the absence of a comparative study using these techniques in the same cohort of patients, assessment as to the most appropriate technique to apply to carotid endarterectomy remains unresolved.

Experience with TCD monitoring has highlighted its role in detecting intraoperative episodes of ischaemia and embolisation but the application of this technique as a quality control technique has not previously been investigated [Aaslid 1992]. Although TCD has primarily been regarded as a monitoring method the instantaneous nature of the information on cerebral blood supply and embolisation provides the surgeon with information which may lead to a modification of surgical technique during the course of the operation. For example, handling of the carotid bifurcation may precipitate a shower of potentially harmful emboli which is detected by TCD and warns the surgeon to stop and consider an alternative operative approach [Naylor et al, 1991]. Alternatively, manipulation, by the surgeon, of an intraluminal shunt may result in occlusion of blood flow through the shunt resulting in a reduction in cerebral blood supply. The detection of this by TCD provides a warning to the surgeon that this has occurred and an opportunity to correct the abnormality before any adverse clinical effect [Naylor et al, 1991]. Although previous studies have noted the ability of TCD to detect these phenomena, no study has been performed to quantify the percentage of cases where TCD provides clinically useful information. Therefore, in addition to the completion methods described above, this study aimed to investigate the role of TCD as a continuous quality control

Comparison of Quality Control

measure detecting errors of operative technique as they occur during the operation.

In summary, the purpose of this part of the study was to compare the application of angioscopy, BMU, CWD and TCD as quality control methods during carotid endarterectomy. It was hoped that in addition to comparing the techniques, the information obtained from all the techniques would provide clues as to the aetiology of complications occurring in the postoperative period. The study was performed on the same cohort of patients as the TCD monitoring study whose baseline characteristics have already been described (Chapter 3). The remainder of this chapter consists of a description of the overall method used in the study. Subsequent chapters will describe the individual techniques and their results in more detail. This will be followed by an overall discussion in chapter 15.

10.2 Comparison of Quality Control Methods Applied to Carotid Endarterectomy: Scope and Design of the Study

A prospective, comparative study of the benefits and limitations of angioscopy, BMU, CWD, and TCD was undertaken in a consecutive series of 100 patients undergoing carotid endarterectomy. The aims were threefold:

- 1) to compare the ability of the techniques to detect technical error;
- 2) to assess the feasibility of applying each of the techniques for routine use;
- 3) to assess whether applying these methods provided useful information as to the cause of perioperative neurological complications.

10.3 Materials and Methods

Carotid endarterectomy with continuous intraoperative TCD monitoring was performed as previously described (chapter 5). The ipsilateral MCA was insonated through the transtemporal window and the probe held in position using a plastic probe holder and elasticated head band protected by a detachable metal head guard. Monitoring was continuous from commencement of

Comparison of Quality Control

anaesthesia to 30 minutes after restoration of flow and all signals were recorded onto digital audio tape for postoperative playback and analysis.

At completion of the endarterectomy and just prior to final patch closure, back-bleeding and flushing of all carotid vessels was performed with heparinised saline to remove any adherent thrombus prior to restoration of blood flow. A 2.8mm flexible angioscope (Olympus AF type 28C, Keymed, Southend-on-sea, UK) was inserted through the remaining, unsutured, gap between patch and arterial wall into the artery. The distal endarterectomy site was visualised first, followed by the midpoint and finally the proximal endarterectomy site and common carotid artery.

Following angioscopic examination, suturing of the patch was completed and blood flow restored through the endarterectomised artery. Assessment of the blood flow through the artery was then performed using BMU images and CWD velocity profiles. Both probes were covered in sterile, disposable plastic sheaths filled with water soluble acoustic gel and further sterile gel was used to provide acoustic coupling between the artery and the probes.

BMU images were obtained using a 10MHz nearfield probe (dimensions, 40mm x 10mm) connected to a B-mode ultrasound scanner (DRF 400, Diasonics Sonotron). Longitudinal images were obtained from common to internal carotid artery and the examination was considered adequate if both proximal and distal end-points were visualised. The examination was then repeated to obtain transverse images.

Spectral analysis of blood-flow along the endarterectomised artery was obtained using an 8MHz CWD probe and the SciMed PcDop 842 ultrasound processing unit. An angle of 60° to the artery was maintained as the probe was moved from CCA to ICA to include both end-points. Peak velocity readings were obtained from the whole length of the artery and, in addition, were recorded at the following fixed sites to enable comparison with post-operative Duplex scan velocities: CCA proximal to endarterectomy; proximal end of patch; mid-patch (opposite origin of ECA); distal end of patch and ICA distal to endarterectomy. A peak velocity in excess of 125cm/sec was considered to indicate a stenosis greater than 50%. All signals were recorded onto digital audio tape for post-operative playback and analysis.

Comparison of Quality Control

The nature and number of technical errors were determined for each method. Defects detected by angioscopy were corrected immediately prior to restoration of flow, therefore defects detected by BMU and CWD were considered as additional defects. The decision whether or not to correct a defect was taken by the operating surgeon.

Post-operative Surveillance

All patients underwent colour Duplex ultrasound scanning of the operated artery at 6 weeks and 6 months after CEA and all abnormal scans were compared with the intraoperative images. Minor defects, detected intraoperatively but not corrected, were examined to determine their significance and monitor progression. Peak velocity readings were obtained from the predetermined fixed points along the artery and compared with the intraoperative values obtained with CWD.

Data Analysis

True and false, positive and negative values were obtained for each technique based on the findings at re-exploration of the artery or findings at postoperative Duplex scan if re-exploration was not performed. A direct comparison of the accuracy of each technique was not possible because defects detected by angioscopy were corrected immediately and, therefore not subjected to examination by BMU and CWD. The ability of angioscopy to detect technical error prior to restoration of flow was considered an inherent advantage of the technique but this would have been negated if significant additional errors had then been detected by BMU or CWD.

10.4 Summary

The importance of technical error as a major cause of perioperative mortality/morbidity has been outlined and a brief description of various quality control methods has been given to supplement the more detailed comparisons described earlier in the thesis. The overall design and method of the study has been described as a basis for more detailed descriptions of the individual methods in subsequent chapters: Angioscopy (chapter 11); BMU (chapter 12); CWD (chapter 13) and TCD as a quality control method (chapter 14). An overall discussion of the study will then follow (chapter 15).

CHAPTER 11

ANGIOSCOPY

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11.1 Introduction

In this first chapter the results of the technical errors detected by angioscopy will be described and the results for BMU, CWD and TCD will be covered in later chapters. Unlike BMU and CWD, Angioscopy is applied prior to clamp release and final restoration of blood flow and this enables technical errors to be corrected immediately without the need to interrupt blood flow and reopen the artery. This was considered an inherent advantage of the technique although it prevented a direct comparison with BMU and CWD of detecting the same defects. However, this advantage would have been negated if additional defects had then been detected by BMU and CWD.

History of Angioscopy (Table 11.1)

Angioscopy or vascular endoscopy is the endoscopic examination of the luminal surface of blood vessels and vascular grafts [Stonebridge, Murie, 1992]. Angioscopy started with attempts to evaluate cardiac disorders and in 1913 Rhea and Walker used a rigid metal tube with a distal lens during thoracotomy to visualise the interior of the heart [Cutler *et al*, 1924]. This first attempt at 'cardioscopy' failed because a slightly inset lens allowed blood to obscure the field of view. In 1923 this design was modified to correct the fault but the first clinical use of the new scope resulted in the death of the patient [Allen, 1924]. A major problem with these early attempts was that blood obscured the view of anatomical structures and the absence of an effect method to prevent this, hampered the development of angioscopy for many years. In 1942 a distensible thin transparent plastic balloon was developed which was applied over the distal lens to displace the blood and improve the view, but in use this was found to obstruct intracardiac blood flow and therefore was not developed further [Harken, Glidden, 1942]. Animal experimenters in the 1950s developed clear plastic cardioscopes but these never progressed to use in humans [Butterworth, 1951; Bolton *et al*, 1951].

An advance occurred in 1964 when Silander described the use of a 90° side viewing rigid scope which was introduced via the internal jugular vein and avoided the need for thoracotomy [Silander, 1964]. The scope had a 4mm outer diameter and used a small transparent balloon over the lens to displace blood and was successfully used to view the right side of the heart in dogs. Later a slightly larger scope was used to inspect atrial defects in patients [Silander, 1964]. Later, the same principle was applied to examine the heart in

Angioscopy

a retrograde manner using a peripheral artery with an inflatable balloon to displace the blood [Gamble, Innis, 1967].

Blood displacement by pressured fluid irrigation was first attempted by Pinet and colleagues in 1966, but this was reported as being difficult and traumatic [Pinet *et al*, 1966]. Further experimental studies did achieve clearance with fluid irrigation but a requirement of the technique was the inducement of a unfeasibly low cardiac output and therefore this technique did not progress to use in patients [Dee, Crosby, 1967].

In 1966 Greenstone attempted to visualise the peripheral arterial system using a 7mm outer diameter flexible irrigating choledochoscope to examine the aorta of dogs and human cadavers. Using this technique it was possible to detect evidence of pathological disease such as atheromatous change and thrombus within the arteries [Greenstone *et al*, 1966].

The first angioscopic visualisation of human arterial reconstructions was performed using a combination of flexible and rigid scopes and pressure irrigation to inspect endarterectomy and thrombectomy sites in 45 patients [Vollmar, Junghans, 1969]. However the procedure was accompanied by serious complications including septicaemia from contaminated irrigation fluid and rupture at 4 femoral endarterectomy sites [Vollmar, Junghans, 1969; Vollmar, Storz, 1974]. However, the relative success of these studies prompted further interest in the technique and in 1973 a 5mm outer diameter flexible bronchoscope was used during femoral thrombo-endarterectomy and was described as a useful technique for detecting technical defects [Crispin, van Baarle, 1973]. In a post-mortem study Ollinger described the post-mortem endoscopic appearance of carotid artery atheroma and associated this with clinical syndromes before death [Ollinger, 1977].

Towne and Bernhard used a rigid 3.5mm outer diameter choledochoscope and right angled viewing arthroscope to inspect the technical result of 35 carotid endarterectomies. The scope was too large to insert in 5 cases and considered cumbersome in a further three. A considerable number of technical defects were detected particularly in the external carotid artery but the equipment was still considered too unwieldy to be applied routinely [Towne, Bernhard, 1977]. The application of angioscopy was revolutionised by advances in fibreoptic and computer microchip technology resulting in the development of smaller, flexible

Angioscopy

and steerable angioscopes with improved optical performance. The potential of this new technology was explored in a study by Mehigan and Alcott who used a variety of angioscopes varying in outer diameter from 2.8mm-3.6mm to examine carotid and femoropopliteal or tibial reconstructions [Mehigan, Alcott, 1986]. Magnified images were viewed on high resolution colour video monitors. Abnormalities were identified at both carotid and lower limb reconstructions and the authors reported no discernible trauma to the artery and examinations were complete within 5 minutes. The authors proposed that angioscopy was a feasible alternative to angiography as a quality control technique [Mehigan, Alcott, 1986].

The possibility of angioscopy as an alternative to arteriography was investigated further by White and colleagues who showed a significant disparity between the findings of angioscopy and arteriography in 21% of patients; the angioscopic findings caused an alteration in the operative procedure in 13% [White *et al*, 1987].

Miller and colleagues demonstrated the feasibility of applying angioscopy routinely in a large series of 136 lower limb assessments. Clinical decisions were made in 78 cases on the basis of angioscopic information. Once again there were no reported injuries to the artery or anastomosis due to angioscopy [Miller A *et al*, 1989].

Baxter and colleagues undertook a prospective comparison of angioscopy and arteriography in 49 cases of femorodistal bypass grafting. Arteriography was 95% specific but only 67% sensitive. Angioscopy altered management in 5 (10%) cases. Angioscopy detected additional intimal flaps in 2 cases, significant thrombus in a further case and excluded abnormality in two cases of filling defects seen on arteriography [Baxter *et al*, 1990].

Grundfest and colleagues found that 47% of in situ femoro-distal vein grafts had inadequately cut valves using an angioscope for post-valvulotomy inspection and 13% required further valvulotomy [Grundfest *et al*, 1985].

Recently Miller and colleagues completed the first prospective randomised trial of angioscopy and arteriography. A total of 293 patients undergoing primary saphenous vein infrainguinal bypass grafting were prospectively randomised and assessed with either completion angioscopy or angiography.

Angioscopy

Year	Investigators	Event
1913	Rhea and Walker	First attempt at cardioscopy: blood obscured view
1924	DS Allen	Modified cardioscope: death of patient
1942	Harken and Glidden	Transparent plastic balloon used to displace blood: obstructed cardiac blood flow
1964	Silander	Side view scope inserted via internal jugular vein to inspect right side of heart.
1966	Pinet	Fluid irrigation used: difficult and traumatic
1967	Gamble and Innis	Scope inserted via peripheral artery to inspect heart
1969	Vollmar and Junghans	Flexible scope used to inspect arterial reconstructions: septicaemia and vessel rupture
1977	Towne and Bernhard	Inspection of CEA sites: Defects detected but scopes too unwieldy
1980's		Advances in fibreoptic and microchip technology
1986	Mehigan and Alcott	CEA and lower limb sites inspected: suggested angiography as alternative to completion arteriography
1987	White <i>et al.</i>	Angioscopy more specific and sensitive than angiography for technical error
1989	Miller <i>et al</i>	Routine use of angioscopy in 136 lower limb reconstructions
1990	Baxter <i>et al</i>	Prospective comparison of intra-operative angioscopy and arteriography: angioscopy superior
1993	Miller <i>et al</i>	Prospective randomised trial angioscopy Vs arteriography in lower limb reconstructions: no statistical difference in graft survival

Table 11.1 Historical development of Angioscopy

Angioscopy

Although there was no statistical difference in the early graft failures between the two groups there was a trend favouring less failures in the angioscopy assessed group [Miller *et al*, 1993].

Although the potential of angioscopy to assess the technical result of CEA was recognised by investigators such as Towne and Bernard [Towne, Benhard, 1977] and Baxter [Baxter *et al*, 1990], recent studies have focused on the use of angioscopy in the lower limb. In this study we aimed to re-evaluate the role of angioscopy in CEA as a quality control method in comparison with other ultrasonic based quality control techniques.

11.2 Materials and Methods

A prospective study was undertaken of 100 consecutive patients undergoing carotid endarterectomy. Angioscopy was performed after completion of the endarterectomy and just prior to the insertion of the final few stitches in the patch angioplasty. Back-bleeding and flushing of all carotid vessels was performed in the usual way using heparinised saline to remove any adherent thrombus. The angioscope was then inserted as a final check immediately before restoration of flow (Figure 11.1).

The angioscope used was an Olympus AF type 28C (Keymed, Southend-on-sea, UK), 2.8mm outer diameter flexible angioscope with integral irrigation channel. Illumination was provided by a xenon light source (model CLV-A) image clarity improved and magnified by the Olympus image control unit (model OTV-A). Magnified images were viewed on an Olympus colour monitor. Constant irrigation with 0.9% Normal saline was provided via the integral irrigation channel using the Olympus Europe angiopump (type AP-E1). The irrigation was controlled by the operator via a foot switch providing low and high flow options. All procedures were recorded onto high resolution colour video tape for postoperative playback and analysis.

The distal endarterectomy site was visualised first, followed by the midpoint and finally the proximal endarterectomy site and common carotid artery. An examination was considered adequate if both endpoints were clearly visualised. Detected defects were classified as shown in table 11.1 and corrected immediately [Blaisdell *et al*, 1967]. Minor thrombus was removed by

further saline flushing while major defects required a partial reopening of the patch and removal of thrombus with forceps or suture repair of intimal flaps.

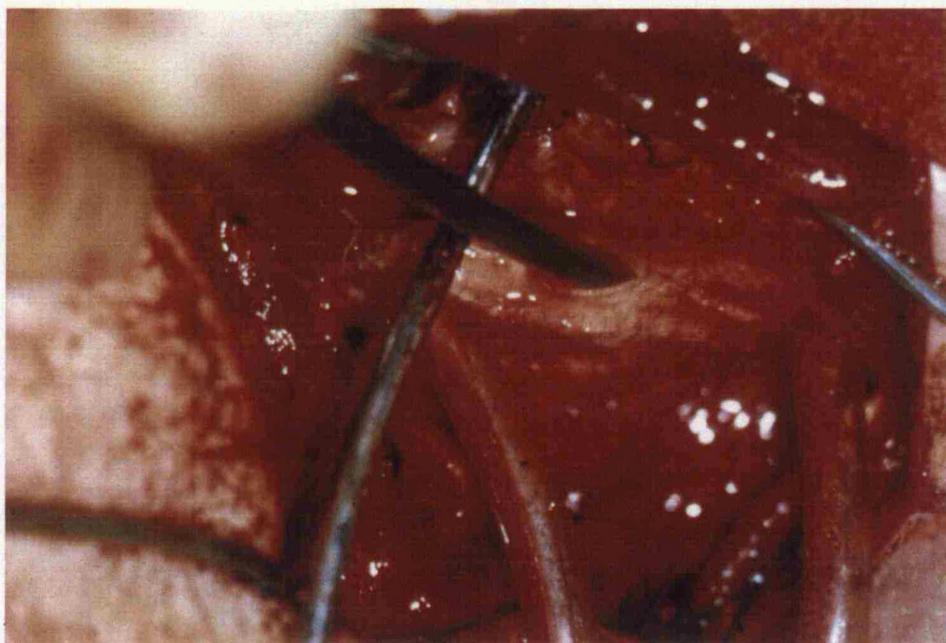


Figure 11.1: Picture illustrating the insertion of the angioscope.

Defect	Major	Minor	Insignificant
Intimal Flap (mm)	≥ 3	< 3	Fixed fronds of intima
Thrombus (mm)	≥ 3	< 3	< 1
Stenosis (%)	≥ 30	< 30	< 10

Table 11.1 Classification of technical defects [Blaidell *et al*, 1967]

Backbleeding was repeated after angioscopy and prior to insertion of the final sutures to close the angioplasty and restore blood flow.

Data Analysis

The number, type and site of detected defects were recorded. True and false, negative and positive values were determined on the basis of findings at re-exploration or in the case of negative angioscopy postoperative colour Duplex scanning performed at 6 weeks and 6 months after CEA.

Angioscopy

The adequacy of examination was determined as the ability to clearly visualise both proximal and distal end-points. The time taken to perform each procedure was also recorded. The duration of time to perform angioscopy was an estimate based on the clinical observation that without angioscopy, the clamp times before(A) and after(B) completion of the endarterectomy are usually the same. However, in this study, the second clamp time(B) included the time to perform the angioscopy and time to correct defects if detected. By subtracting time A from time B the approximate time to perform angioscopy was obtained. Means and 95% CI were calculated to enable comparison [Gardner *et al*, 1991].

11.3 Results

Adequate examinations were obtained in 98 patients.

Technical abnormalities were detected in 27 patients in the ICA and CCA. The defects detected in the ICA consisted of 4 intimal flaps (>3mm), 11 minor thrombi (<3mm) and 6 major thrombi (>3mm). The defects detected in the CCA consisted of 4 minor thrombi and 2 major thrombi. Small fixed fronds of intima were common and not considered abnormal. Angioscopy did not identify any arterial stenoses.

	CCA	ICA
Intimal Flap	0	4
Major Thrombus	2	6
Minor Thrombus	4	11
Stenosis	0	0

Table 11.2 Defects detected by Angioscopy

Duration of Angioscopy

The angioscopy examination was performed during the second clamp time. The first clamp time consisted of the formation of the arteriotomy and insertion of the intraluminal shunt. The second clamp time consisted of removal of the intraluminal shunt, backventing of the ECA, ICA and CCA, flushing with Normal saline, insertion of the angioscope, final suturing of the patch angioplasty and restoration of blood flow through the ECA and then the ICA. Angioscopy, therefore contributed to an extension of the second clamp time.

The mean duration of the first clamp time (A) was 245 seconds (95% CI 115.5 to 374.5 secs) while the mean duration of the second clamp time was 495 seconds (95% CI 426.5 to 563.7 secs). The mean duration of the second clamp time (B) with a normal angioscopic examination was 486 seconds (95% CI 416 to 557). The mean duration of the second clamp time when an intimal flap was detected and corrected was 765 seconds (95% CI 372 to 1158), a minor thrombus was 424 seconds (95% CI 310 to 538), a major thrombus was 601 seconds (95% CI 429 to 774).

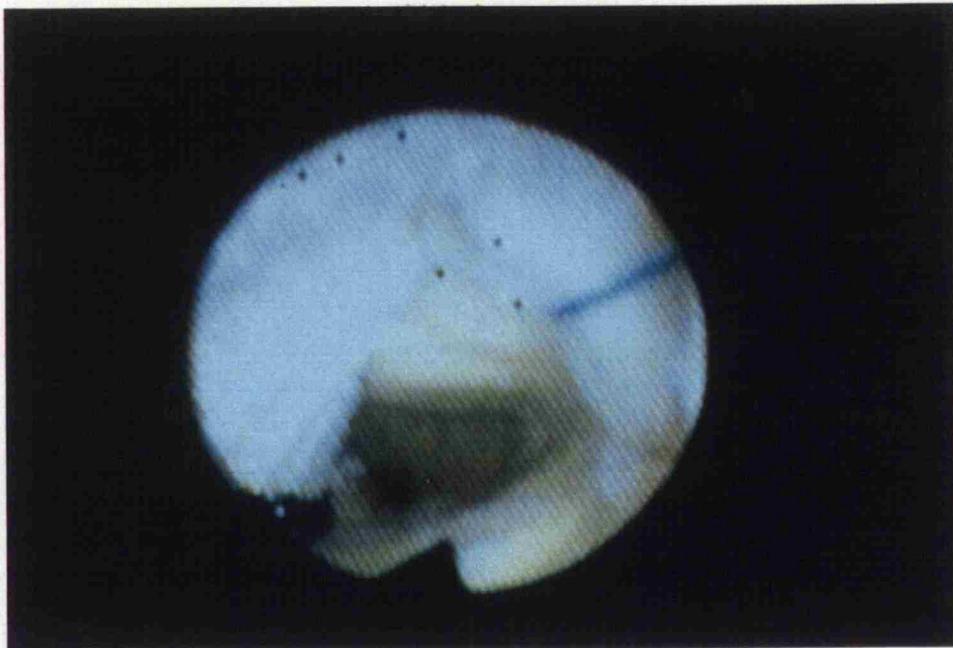


Figure 13.2: Picture illustrating the view inside a normal carotid endarterectomy.



Figure 11.3: Picture illustrating the angioscopic view of a major intimal flap at the distal end-point.



Figure 11.4: Picture illustrating the angioscopic view of a major piece of residual thrombus caught in the re-application of the distal ICA clamp after routine flushing and backbleeding.

	Duration secs (95% CI)
Clamp Time A	245 (115.5 - 374)
Clamp Time B	
Normal Angioscopy	486 (416 - 557)
Intimal Flap	765 (372 - 1158)
Minor Thrombus	424 (310 - 538)
Major Thrombus	601 (429 - 774)

Table 11.3 Illustrating the effect on clamp time of angioscopy and the correction of defects.

The second clamp time was of significantly longer duration than the first clamp time. The mean difference was 250 seconds (95% CI 106 to 395, se of diff 73.3, df 198, $t=1.97$) which the time taken to perform the angioscopy contributed. The duration of the second clamp time varied according to whether an abnormality was detected. Correction of an intimal flap took longer because it required the partial taking down of the patch angioplasty and resuturing. Similarly, removal of thrombus required a similar procedure in order to grasp the thrombus with forceps. Minor thrombus could often be removed with further saline flushing.

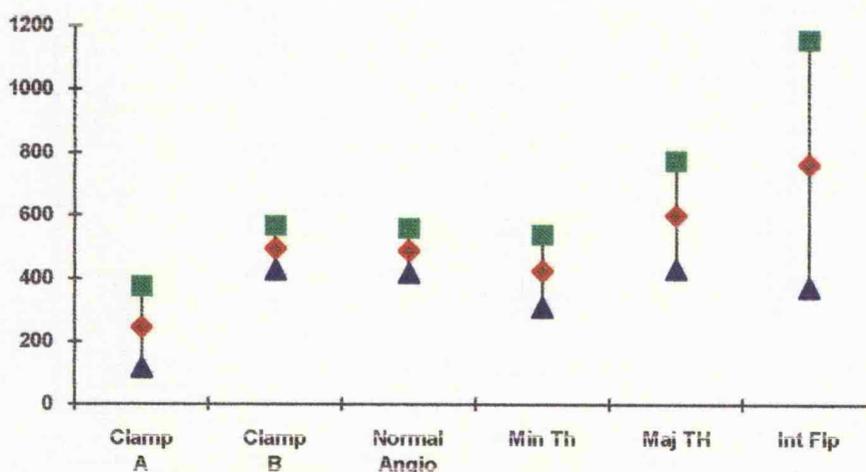


Figure 11.1: Graph illustrating the effect of angioscopy and correction of defects on the duration of clamp times

False Negatives and False Positives.

There were no false positives with angioscopy. All defects detected by angioscopy were confirmed on exploration of the artery. Angioscopy missed one 30% stenosis which was detected by B-mode and CWD but not corrected and confirmed at the 6 week follow-up Duplex scan. However this stenosis has had no clinical consequences and had not progressed at the time of the 6 month scan. The 6 week postoperative Duplex scan also identified two asymptomatic carotid occlusions, for which no cause could be identified, and one case of 75% restenosis at the distal end-point due to intimal hyperplasia. Two further patients had developed arterial kinks at the distal end-point and the mid-patch which review of the intraoperative video recordings confirmed were not present intraoperatively and probably developed in the postoperative period.

11.4 Discussion

Angioscopy proved to be a simple technique to perform enabling the surgeon to operate independently of technicians. The magnified images of the arterial lumen viewed on colour monitors required little specialised knowledge for interpretation and angioscopy enabled a full technical assessment in 98% of patients and was easily absorbed into the intraoperative routine.

Angioscopy proved a sensitive technique for the detection of intimal flaps and fragments of intraluminal thrombus. The flexible angioscope used in this study was easy to use and manipulate over the relatively short segment of carotid artery and the magnified colour images viewed head-up on the monitor were easy to interpret. The pressurised saline irrigation served to simulate blood flow and elevate defects such as intimal flaps into the field of view.

A major advantage of angioscopy was that defects were detected and corrected prior to restoration of flow, therefore avoiding the need to reopen the artery. This was particularly important with regard to fragments of intraluminal thrombus which may have been embolised distally as soon as flow was restored and therefore never detected by methods applied after this stage.

Angioscopy detected defects in 27% of patients and this proportion is consistent with other studies applying methods of quality control to CEA. Blaisdell found unacceptable technical defects in 26% of patients using

Angioscopy

intraoperative angiography [Blaisdell *et al*, 1967]. Using B-mode ultrasound to assess 155 CEA defects were detected in 27.7% [Flannigan *et al*, 1986] and using continuous wave Doppler to assess 229 CEAs abnormal results were obtained in 13% [Seifert, Blackshear, 1985].

The type and number of defects is also consistent with the findings of previous studies applying angioscopy to CEA. Towne and Bernhard used a rigid 3.5mm outer diameter choledochoscope and right angled viewing arthroscope to inspect the technical result of 35 carotid endarterectomies. Technical defects were detected particularly in the external carotid artery consisting of 13 intimal flaps and atheromatous debris in 25 cases. The internal carotid artery was inspected in 13 patients and significant atheromatous debris considered capable of embolisation was discovered in two cases [Towne, Bernhard, 1977]. Mehigan and Alcott used a variety of angioscopes varying in outer diameter from 2.8mm-3.6mm to examine 21 carotid reconstructions. Magnified images were viewed on high resolution colour video monitors. Abnormalities were identified at the ICA end-point in 4 cases, in the ECA in 18 cases and at the CCA endpoint in 6 cases [Mehigan, Alcott 1986]. The authors proposed that angioscopy was a feasible alternative to angiography citing the following advantages of angioscopy:

1. 3-dimensional, magnified, colour image of clarity ample for clinical decision making
2. Multiple examinations of various areas possible in a short period of time or after repeated manoeuvres.
3. Information is obtained with the vessel open, thus defects can be promptly corrected and immediately reassessed by reinsertion of the angioscope.
4. Endoscope can be manipulated without fear of injury to the vessel interior.
5. No potentially toxic or allergic substances are used.
6. Does not need technicians or other professionals for operation or interpretation.
7. Pressurised irrigation serves to simulate blood flow, highlighting any luminal defects and allowing their significance to be reliably assessed [Mehigan, Alcott, 1986].

Comparisons of angioscopy and arteriography have demonstrated that angioscopy is more sensitive and specific technique for the detection of technical error. White and colleagues showed a significant disparity between

Angioscopy

the findings of angioscopy and arteriography in 21% of patients; the angioscopic findings caused an alteration in the operative procedure in 13% [White *et al*, 1987]. Baxter and colleagues undertook a prospective comparison of angioscopy and arteriography in 49 cases of femorodistal bypass grafting. Arteriography was 95% specific but only 67% sensitive. Angioscopy altered management in 5 (10%) cases. Angioscopy detected additional intimal flaps in 2 cases, significant thrombus in a further cases and excluded abnormality in two cases of filling defects seen on arteriography [Baxter *et al*, 1990]. Grundfest and colleagues found that 47% of in situ femoro-distal vein grafts had inadequately cut valves using an angioscope for post-valvulotomy inspection and 13% required further valvulotomy [Grundfest *et al*, 1985].

However, a recent large prospective trial of the two techniques in lower limb reconstructions failed to demonstrate a statistically significant difference in graft survival between the two groups despite angioscopy detecting more technical errors. A total of 293 patients undergoing primary saphenous vein infrainguinal bypass grafting were prospectively randomised and monitored with either completion angioscopy or completion angiography. Forty-three bypasses were excluded from the study after randomisation, including 12 veins randomised to angiogram, deemed inferior and prepared with angioscopy. In the 250 bypass grafts (angioscopy 128, angiography 122) there were 39 interventions (conduit 29, anastomosis 8, and distal artery 2) with angioscopy and 7 with angiography. Twelve (4.8%) of the 250 grafts failed in less than 30 days, four (3.1%) of 128 in the angioscopy group and eight (6.6%) of 122 in the angiography group. Although there was no statistical difference in the early graft failures between the two groups there was a trend favouring angioscopy [Miller *et al*, 1993].

Therefore, it is interesting to speculate whether applying angioscopy to detect technical errors during CEA would significantly reduce perioperative mortality/morbidity. It may be reasonable to assume that given that the currently accepted stroke rate for CEA is 2-4%[ECST, NASCET] it is unlikely that all these patients with technical errors would have suffered a perioperative stroke if the defect had not been corrected. A recent large retrospective study established that uncorrected technical defects are a cause of perioperative stroke [Riles *et al*, 1994]. However, a disadvantage of retrospective studies is that while they may identify that some perioperative strokes are related to the

Angioscopy

presence of technical error, they give no indication as to whether technical errors are rare events and associated with strokes in all cases or common events associated with strokes in only a certain proportion. The evidence from the various quality control studies would suggest the latter. However, there are no criteria to predict in which patients technical defects will be significant, therefore the safest course of action is to correct all defects. This is a relatively straightforward procedure with angioscopy because the artery is still open.

A potential disadvantage of the application of angioscopy is that performance of the technique prolongs the ischaemic time during clamping [Mehigan, Alcott, 1986]. On average the performance of a normal angioscopic examination in this study prolonged the clamp time by 4 minutes. This is consistent with other studies who found that angioscopic examination of CEA took between 5-10 minutes [Towne, Bernhard, 1977; Mehigan, Alcott, 1986]. However, if an intimal flap was discovered and corrected this prolonged the clamp time by an average of eight minutes. Although primate studies have shown that over 20 minutes of ischaemia are necessary to precipitate permanent brain damage it must be considered that any unnecessary prolongation of the ischaemic time is unwelcome [Symon, 1980]. However, ischaemia would only occur at clamping in the presence of inadequate collateral flow around the circle of Willis. In this study the cerebral blood supply was continuously monitored using TCD and inadequate blood flow identified using the velocity criteria established by Halsey [Halsey, 1992]. In no case where the clamp time was prolonged to correct an abnormality did the patient's MCAV fall to a level during clamping indicating a risk of ischaemia. Also no patient who had a defect corrected experienced a postoperative neurological deficit. Therefore, it may be concluded that in the context of this study no patient was put at risk by prolonging the clamp time. If angioscopy was applied in the absence of TCD monitoring or TCD monitoring indicated a risk of ischaemia it may be necessary to reinsert the intraluminal shunt before correcting a major defect. However, it should also be considered that postoperative occlusion of the operated carotid in a patient with poor collateral cerebral blood supply would put the patient at considerable risk of stroke both from an haemodynamic reduction in blood supply and cerebral embolisation from thrombus. It is likely that the time required to diagnose the condition, return the patient to theatre, reopen the neck and correct the defect would be considerably longer than the time for intraoperative correction of the defect detected at angioscopy.

Angioscopy

Another potential disadvantage of angioscopy is the risk of damage to the interior of the vessel by insertion of the scope. There is evidence that angioscopy can cause damage to the intima although this can be minimised by the use of a suitably sized scope [Hsiang *et al*, 1992]. In previous clinical studies no major trauma has been related to the insertion of scopes to assess the carotid bifurcation [Towne, Bernhard, 1977; Mehigan, Alcott 1986]. In the context of CEA, the intimal damage caused by angioscopy is insignificant compared to the stripping of the intima to expose the underlying media which is the main part of the operation itself. However, it would be wise to exercise the greatest care during the insertion, manipulation and withdrawal of the scope to avoid any potential injury to the vessel.

A potential advantage of assessment techniques applied after restoration of blood flow is that all components of the reconstruction are functional whereas angioscopy is limited and cannot detect possible distortions of the vessel caused by pulsatile blood flow at arterial pressure [Mehigan, Alcott, 1986]. The results of comparative studies of angioscopy and arteriography would suggest that this factor is not significant. However, this study provided a further opportunity to explore this factor by comparing angioscopy with two other post-clamp release techniques, BMU and CWD.

11.5 Summary

The history of the development of angioscopy has been outlined followed by a detailed description of the materials, methods and results of angioscopy used in this study. In this study angioscopy proved to be a simple technique to perform enabling the surgeon to operate independently of technicians. The magnified images of the arterial lumen viewed on colour monitors required little specialised knowledge for interpretation. Angioscopy enabled a full technical assessment in 98% of patients and proved a sensitive technique for the detection of intimal flaps and fragments of intraluminal thrombus. A major advantage of angioscopy was that defects were detected and corrected prior to restoration of flow, avoiding the need to reopen the artery. Therefore angioscopy was found to satisfy many of the criteria associated with an ideal quality control method.

The ability of BMU and CWD to detect technical error in the same cohort of patients will be described in the next two chapters.

CHAPTER 12

B-MODE ULTRASOUND

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12.1 Introduction

The results of the technical errors detected by angioscopy have been described in the preceding chapter. The findings of BMU in the same patients will now be described and compared with those of angioscopy. The comparison is not a direct one because defects detected by angioscopy were corrected immediately and, therefore, not subjected to examination by BMU and CWD. The ability of angioscopy to detect technical error prior to restoration of flow was considered an inherent advantage of the technique but this would have been negated if significant errors had then been detected by BMU or CWD.

History of B-mode Imaging

The Titanic tragedy in 1912 was one of several incidents that led scientists to search for methods of detecting obstacles at sea. An Englishman, E.G. Richardson, had the idea of transmitting a "beam" of underwater sound and receiving echoes from submerged obstructions. This possibility was pursued with vigour during world war I, and in 1917, Paul Langevin succeeded in applying the pulse-echo method for the detection of submarines. His work was the foundation of sonar (sound navigation and ranging).

The first attempts to use ultrasound for medical diagnosis were based on the assumption that it would be possible to demonstrate tissue masses by their differential attenuations. Thus, the method would have been analogous to the transmission of x-rays in conventional radiology. However, while in vitro studies provided potentially useful images, this potential was not realised in vivo due to refraction, diffraction and attenuation effects and it is the reflection methods which have been applied successfully in medical ultrasound.

Theory of Continuous Real-time B-mode Imaging

Sound travels with a different velocity through mediums of different composition. When a wave meets the boundary between two media at normal incidence, if it propagates into the medium beyond the boundary, it does so without deviation. At an oblique incidence, the transmitted wave is deviated by refraction from the direction of the incident wave if the velocities of transmission in the media are not equal on each side of the boundary. Whether reflection occurs depends on the properties of the media on each side of the boundary, i.e. the characteristic impedances. Soft tissues have similar characteristic

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impedances, close to that of water. Consequently the fraction of energy reflected at the boundary between soft tissues is rather small. If, however the impedances between two tissues are very different as at the boundaries between soft tissues and gas or bone almost complete reflection occurs. The characteristic impedances of various human tissues are illustrated in table 12.1 [Kaye, Laby 1968].

Material	density (kg m^{-3})	Characteristic impedance ($10^6 \text{ kg m}^{-2} \text{ sec}^{-1}$)
Air	1.2	0.0004
Brain	1030	1.55-1.66
Blood	1060	1.62
Bone	1380-1810	3.75-7.38
Muscle	1070	1.65-1.74
Liver	1060	1.64-1.68

Table 12.1. Densities and Characteristic Impedances of Various Materials.
[Kaye, Laby, 1968]

Grey-Scale Echography

Grey scale echography is the term given to the B-mode imaging technique in which the position and the amplitude of an echo are both displayed on the echogram. The amplitude of echoes is determined by the impedance mismatch of different tissues as described above. The largest echo is obtained from a soft tissue-air interface, such as that encountered from an air-containing bowel. The next largest echo is obtained from a soft tissue-bone interface and soft tissue interfaces give rise to the smallest amplitude echoes.

In the analysis of echoes it is helpful to separate the reflecting interfaces into two classes according to their geometry. The first class encompasses interfaces that are larger than the ultrasound beam such as the boundaries of organs. When a large interface is normal to the ultrasonic beam, all of the energy is reflected back to the transducer, and a large echo is obtained.

The second class encompasses interfaces that are much smaller than the ultrasonic beam such as the structural and glandular organisation of tissues, commonly referred to as internal echoes. Small interfaces intercept only a

B-Mode Ultrasound

small portion of the incident beam and thus give rise to small echoes. The internal echoes provide the bulk of information used in the classification of soft tissues by grey-scale echography.

Because liquids are acoustically homogenous, they do not give rise to internal echoes. The echo-free content of liquid-filled structures is readily distinguishable from the grey level obtained from soft tissues, and a reliable identification of liquid-filled structures as small as 1mm in diameter directly from the B-mode echogram forms a major feature of grey scale echography.

Under the optimum viewing conditions, the human eye can distinguish about 30 shades of grey, whereas under normal viewing conditions, it can only distinguish 10 levels of grey. It is therefore not possible to display the vast range of echoes obtained, hence a selection process is employed to display the range of magnitude which is considered to be of maximum interest. It is by this mechanism that different biological structures can be identified non-invasively using B-mode ultrasound.

B-mode ultrasound: A Quality Control Technique

The experimental basis for the use of B-mode ultrasound as a quality control technique was developed by Coelho and colleagues who demonstrated that ultrasonography was more accurate than arteriography in detecting intimal flaps and intraluminal thrombi surgically created in canine aortas [Coelho *et al*, 1982].

The same group of investigators progressed to clinical studies using B-mode ultrasound to assess the technical result of carotid endarterectomies [Flannigan *et al*, 1986]. The detection rate of abnormalities in 27.7% of carotid endarterectomies was similar to the 26% incidence of technical abnormalities detected by Blaisdell using intraoperative arteriography [Blaisdell *et al*, 1967]. Therefore the authors concluded that B-mode ultrasound was a sensitive technique for the detection of technical errors following CEA and was a feasible alternative assessment technique to angiography.

Dilley and Bernstein compared intraoperative B-mode imaging with arteriography in 158 patients following carotid endarterectomy [Dilley, Bernstein, 1986]. The B-mode imager detected three patients with significant abnormalities missed on the arteriogram but failed to detect five other problems

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documented by arteriography. The authors concluded that neither technique was superior to the other but that the imaging technique had greater potential because of its ability to examine the vessel in several planes

Lane and colleagues compared two groups of patients undergoing carotid endarterectomy, one of which was assessed by intraoperative B-mode scanning and the other without intraoperative assessment [Lane *et al*, 1987]. The study showed that although intraoperative B-mode scanning identified a number of defects thought to be significant and enabled their correction there was no difference in postoperative morbidity or mortality between the scanned and unscanned groups.

Therefore, in previous studies B-mode scanning has been proven to be a sensitive method for detecting technical defects with significant logistical advantages over on-table angiography. However, in the absence of a comparative study with alternative methods of quality control to angiography, an assessment of the clinical application of B-mode ultrasound remains uncertain. This study aimed to address this question.

12.2 Materials and Methods.

A prospective study of intraoperative B-mode detection of technical error was performed in 100 consecutive patients undergoing carotid endarterectomy.

Carotid endarterectomy was performed in the standard method already described (Chapter 2). B-mode images (BMU) were obtained following angioscopic examination, final suturing of the patch angioplasty and restoration of blood flow.

BMU images were obtained using a 10MHz nearfield probe (dimensions 40mm x 10mm) connected to a B-mode ultrasound scanner (DRF 400, Diationics Sonotron). The probe was covered in a sterile, disposable plastic sheath filled with water soluble acoustic gel and further sterile gel was used to provide acoustic coupling between the artery and the probe. Longitudinal images were obtained from common to internal carotid artery and the examination was considered adequate if both proximal and distal endpoints were visualised. The examination was then repeated to obtain transverse images and defects classified according to the criteria outlined in table 11.1. Clinical decisions to

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reopen were based on the intraoperative images, but in addition all images were recorded onto high resolution videotape for postoperative analysis.

Post-operative Duplex Surveillance

All patients underwent colour Duplex ultrasound scanning of the operated artery at 6 weeks and 6 months after CEA and all abnormal scans were compared with the intraoperative images. Minor defects, detected intraoperatively but not corrected were examined to determine their significance and monitor progression.

Data Analysis

True and false positive and negative values were obtained based on either findings at re-exploration of the artery or findings at postoperative Duplex scan if re-exploration was not performed. The ability of angiography to detect technical error prior to restoration of flow was considered an inherent advantage of this technique but this would have been negated if significant additional errors had then been detected by BMU.

12.3 Results

Complete examinations were obtained in 76% of patients. Reasons for inadequate examinations consisted of difficulties in probe access in 16 cases, inability to obtain adequate images through artificial patch material in 6 cases and instrument failure in 2 cases. The main problem of probe access consisted of visualising the ICA end-point when the endarterectomy had been continued distally to obtain a satisfactory disease free artery or the in the cases of a high carotid bifurcation.

No additional thrombi or intimal flaps were detected by this method. B-mode apparently identified 2 minor stenoses (<30%) and 3 major stenoses (>30%) intraoperatively at the junction of the distal patch and ICA. Two of the major stenoses were re-explored but no correctable defects were found and postoperative Duplex scans were normal. Also, the two minor stenoses were not re-explored and postoperative Duplex scanning failed to confirm the presence of the minor stenoses. Only one >30% stenosis (not re-explored) was confirmed on postoperative scan. The reason for not exploring this case was that the surgeon had lost confidence in the technique after two previously unnecessary re-explorations.

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Number of Patients	Problem
16	Unable to insonate distal end-point
6	Unable to insonate through Dacron patch material
2	Instrument failure

Table 12.1 Reasons for unsuccessful examinations with B-mode ultrasound.

B-mode identified defect	Findings at Re-exploration	Findings at Post-Operative Duplex scan	Conclusion
minor stenosis	not performed	no stenosis	false positive
minor stenosis	not performed	no stenosis	false positive
major stenosis	no stenosis	no stenosis	false positive
major stenosis	no stenosis	no stenosis	false positive
major stenosis	not performed	30% stenosis	true positive: not corrected

Table 12.2 Outcome of investigation of technical defects apparently identified by B-mode ultrasound

Postoperative Duplex Carotid Scans

Successful follow-up examinations were obtained in 93% of patients.

Five patients with normal intraoperative findings had abnormalities on postoperative colour Duplex scanning at six weeks. Two patients had developed arterial kinks, one at the distal end-point and one at the midpatch which were not flow limiting. One patient had developed significant intimal hyperplasia at the distal endpoint causing a 75% stenosis but repeat scan at 6 months did not reveal any progression of the lesion. Review of the intraoperative video recordings of the B-mode examinations confirmed that these abnormalities were not present intraoperatively and probably developed in the postoperative period.

B-Mode Ultrasound

Two patients with normal intraoperative findings had undergone asymptomatic carotid artery thrombosis at the time of the 6 week postoperative scans. Both patients had normal intraoperative examinations. All patients were symptom free despite these abnormalities and had not suffered any adverse clinical consequences.

Post-operative Duplex Scan: 6 weeks	Post-operative Duplex Scan: 6 months
Arterial kink - distal end-point: vessel patent, symptom free	Arterial kink - distal end-point: vessel patent , symptom free
Arterial kink - mid-patch: vessel patent, symptom free	Arterial kink - mid-patch: vessel patent, symptom free
Intimal hyperplasia- 75% stenosis, vessel patent, symptom free	Intimal hyperplasia - 75% stenosis, vessel patent, symptom free
Carotid artery thrombosis - vessel occluded, symptom free	Carotid artery thrombosis - vessel occluded, symptom free
Carotid artery thrombosis - vessel occluded, symptom free	Carotid artery thrombosis - vessel occluded, symptom free

Table 12.3 Abnormal findings on postoperative Duplex scans at 6 weeks and 6 months: and clinical consequences.



Figure 12.1: Picture illustrating the larger BMU probe compared to the smaller CWD probe. Both probes are in their sterile plastic coverings.

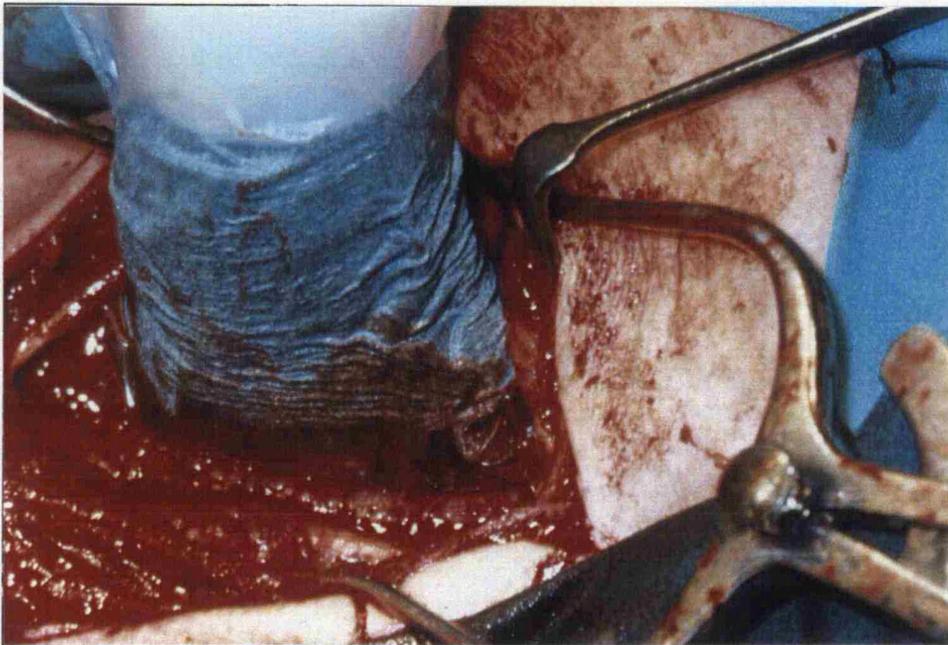


Figure 12.2: Picture illustrating the intraoperative use of the BMU probe.

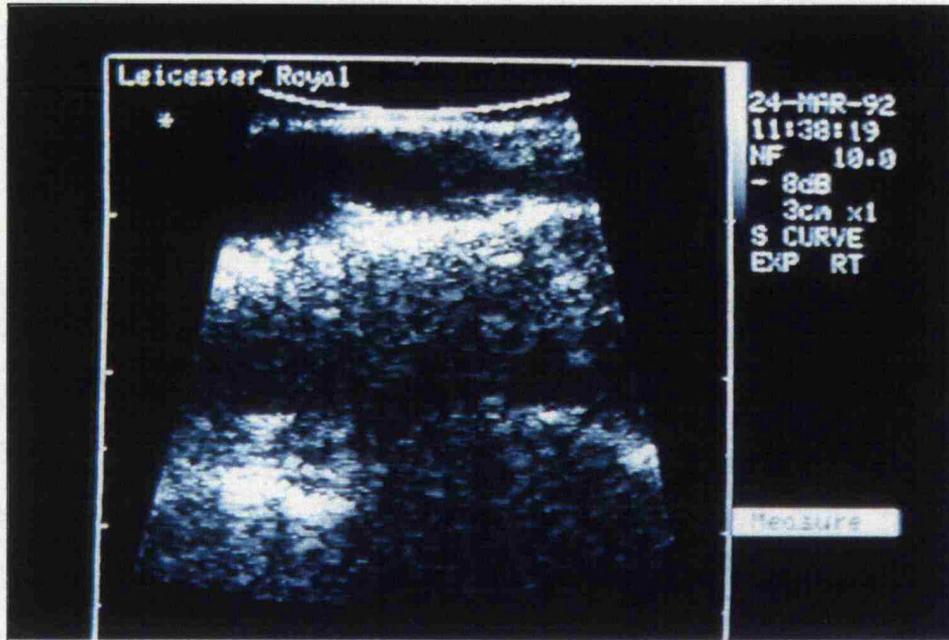


Figure 12.3: BMU image of a distal endarterectomy end-point. The appearance suggested a stenosis but at re-exploration this was not confirmed.

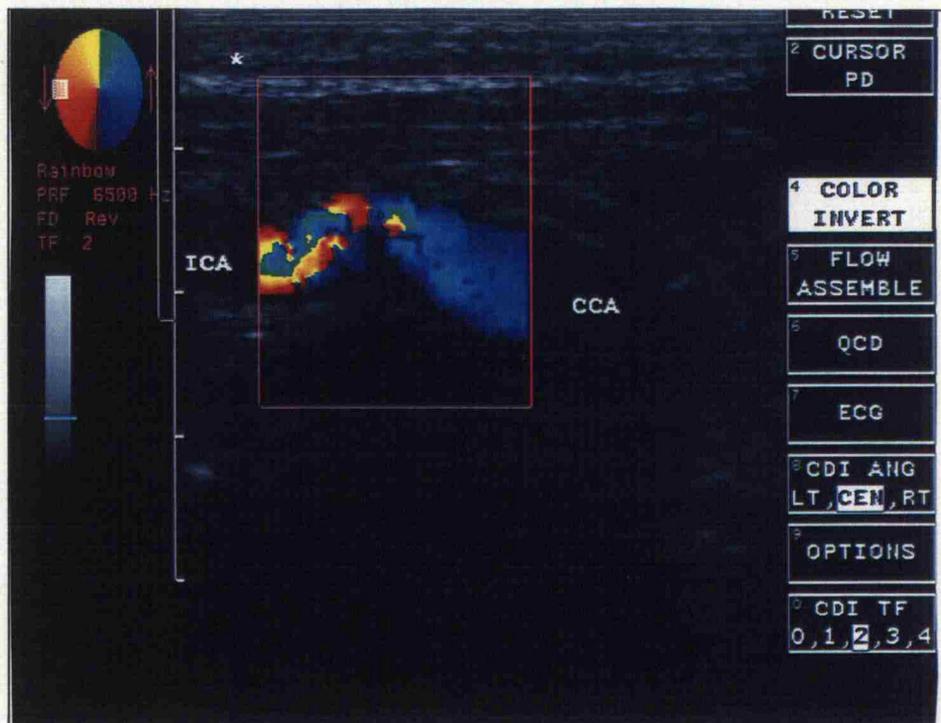


Figure 12.4: Colour Duplex picture of an arterial kink at the distal junction of patch and ICA which developed in the 6 weeks after CEA.

12.4 Discussion

Although previous studies have demonstrated that BMU is a sensitive technique for the detection of technical error when it is applied the low rate of adequate examinations achieved in this study casts serious doubts on the ability to apply this technique for routine assessment. Importantly, the main difficulty was associated with obtaining adequate images of the distal ICA end-point which is the most important area for any quality control technique.

Further disadvantages included the need for a qualified technician to be in attendance in order to assist with obtaining adequate images, the need for expertise to interpret the images and difficulty insonating through artificial patch material. This difficulty interpreting images contributed to the false positive identification of technical errors in two cases leading to unnecessary re-exploration. A further true positive stenosis was not re-explored because this occurred after the two false positive findings and the operating surgeon had lost confidence in the technique.

The low incidence of intimal flaps, stenoses and intraluminal thrombus contrasts with the findings of other studies. In previous studies, BMU has demonstrated intimal flaps down to 1mm in size both in-vitro and in-vivo, but in this study no additional intimal flaps were detected by BMU indicating a low incidence of false negatives with angiography. Experimental studies by Coelho and colleagues demonstrated that real time scanning could correctly identify defects such as strictures, intraluminal thrombi and subintimal haematomas created in a series of canine aortas and femoral arteries [Coelho *et al*, 1981]. Intimal flaps measuring 1mm were correctly identified 68% of the time, whereas flaps 2mm or greater were all identified. In 89.7% of cases measurement of flap size was within 1mm of the actual size for a correlation coefficient of 0.84 [Coelho *et al*, 1981]. In a second series of experiments intraoperative ultrasonography was compared with both portable and serial biplane arteriography in detecting intraluminal defects that were surgically created in canine aortas [Coelho *et al*, 1982]. All three techniques were equally accurate in detecting strictures but ultrasonography was more accurate and sensitive than both types of arteriography in detecting 2 and 5 mm intimal flaps and intraluminal thrombi.

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The same group of investigators progressed to use B-mode ultrasound to assess the technical result of 155 carotid endarterectomies in 143 patients [Flannigan *et al*, 1986]. Intraluminal defects were detected in 43 of the 155 arteries (27.7%). Intimal flaps were the most common defect found representing 73% of the total defects. Strictures of the arterial lumen were the next most common (18%). Arterial kinks, residual plaque, and intraluminal thrombus accounted for the remaining defects. Eleven of the 43 arteries were reopened to correct the more major defects consisting of intimal flaps greater than 3mm and stenoses greater than 30%. The detection rate of abnormalities in 28% of carotid endarterectomies was similar to the 26% incidence of technical abnormalities detected by Blaisdell using intraoperative arteriography [Blaisdell *et al*, 1967]. Therefore the authors concluded that B-mode ultrasound was a sensitive technique for the detection of technical errors [Flannigan *et al*, 1986].

Therefore, it may be expected that defects such as intimal flaps and intraluminal thrombi would have been detected by BMU if present. However, in this study BMU was applied after correction of defects detected by angioscopy which was applied prior to clamp release and restoration of flow. The absence of additional intimal flaps and intraluminal thrombi is further supporting evidence for the accuracy of angioscopy for detecting these defects.

The difficulty encountered in this study of insonating the distal end-point has been noted by other investigators. In a study comparing intraoperative B-mode imaging with arteriography in 158 patients following carotid endarterectomy, 13 of the 158 patients had technically unsatisfactory examinations, mainly because a high carotid bifurcation limited access to the upper carotid artery [Dilley, Bernstein 1986]. Further difficulties were that, although BMU detected three patients with significant abnormalities missed on the arteriogram BMU failed to detect five other problems documented by arteriography [Dilley, Bernstein 1986].

Another problem of applying BMU for the routine assessment of intraoperative procedures is the availability of the BMU scanner. Lane and colleagues compared two groups of patients undergoing carotid endarterectomy one of which was assessed by intraoperative B-mode scanning and the other without intraoperative assessment [Lane *et al*, 1987]. A total of 380 carotid endarterectomies were performed of which 175 were scanned and 205 were

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not. Although the number of patients scanned is large, patients were allocated to the two groups on the basis of the availability of the scanner and, therefore, one must assume that the scanner was unavailable on over 50% of occasions. This exposes logistical problems in using this technique for routine use. In the majority of hospitals these BMU and Duplex ultrasound scanners are fully utilised performing diagnostic procedures and only available occasionally for intraoperative use. The machines themselves are expensive and delicate and although the majority are mobile, moving the scanner through the hospital corridors and lifts on a regular basis exposes them to the risk of damage.

The purchasing of a BMU scanner dedicated for intraoperative would be justified if evidence existed of a clear benefit to patients of reduced postoperative morbidity/mortality. However, in the study by Lane, of the 175 carotid bifurcations out of 380 scanned 136 were normal and 39 showed some abnormality in any vessel (22%) [Lane *et al*, 1987]. The external carotid artery was the site of 21 abnormal postendarterectomy scans, the internal carotid artery in two and the common carotid artery in a further two. Defects consisted of residual atheroma, intimal flaps, intraluminal thrombus and stenosis. Defects were considered either major or minor and of the major abnormalities a total of twelve were corrected. The study showed that although intraoperative B-mode scanning identified a number of defects thought to be significant there was no difference in postoperative morbidity or mortality between the scanned and unscanned groups [Lane *et al*, 1987].

Therefore, although in previous studies B-mode scanning has been proven to be a sensitive method for detecting technical defects, with advantages over on-table angiography, this study has identified serious problems with applying the technique in the routine situation.

12.5 Summary

The theory and historical development of the technique of real-time B-mode ultrasound has been outlined. The materials, methods and results of this study have been described. No intimal flaps or thrombi were identified by this technique in addition to those already identified by angioscopy.

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Three major stenoses and two minor stenoses were apparently identified but only one of these stenoses was confirmed by either operative reexploration or postoperative scan.

BMU required technical support, both to obtain adequate images and to help with interpretation. Despite this adequate images including both upper and lower endpoints were only achieved in 76% of patients. Therefore, as a quality control method suitable for routine use this technique was considered inferior to angiography.

In the next chapter the results obtained with CWD will be described.

CHAPTER 13

CONTINUOUS WAVE DOPPLER

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13.1 Introduction

In the previous two chapters the results of the technical errors detected by angiography and BMU have been described. In this chapter the results of the CWD assessment on the same cohort of patients will be presented and compared with the other two methods. In common with BMU, the comparison with angiography is not a direct one because defects detected by angiography were corrected immediately and, therefore, not subjected to examination by BMU and CWD. The ability of angiography to detect technical error prior to restoration of flow was considered an inherent advantage of the technique but this would have been negated if significant additional errors had been detected by BMU or CWD. However, a direct comparison was possible between BMU and CWD.

History of CWD

The first report of the use of ultrasonic Doppler equipment for the detection of blood flow was by Satomura in 1959 [Satomura, 1959]. This report was followed the same year by a study of the different flow velocity patterns found in various peripheral arteries [Suzuki, Satomura, 1959] and a summary of this early work produced in English in 1960 [Satomura, Kaneko, 1960]. Satomura believed that the Doppler-shifted reflection was due to turbulence within the bloodstream however Kato and colleagues later proved that red blood cells were the source of the echoes [Kato *et al*, 1962]. Many investigations have shown that the Doppler frequency shift is proportional to the blood flow velocity and the device was first applied clinically in studies of the peripheral vascular system [Sumner *et al*, 1968]. Earlier systems did not indicate the direction of blood flow until a direction system was developed by McLeod [McLeod FD, 1967].

Theory of CWD (Reneman and Spencer, 1979)

In Doppler flow meters a beam of ultrasonic waves (at the MHz level) is transmitted from a vibrating crystal diagonally through the vessel wall into the bloodstream. Ultrasound backscattered from the particles in the flowing blood, mainly the red cells, is shifted in frequency by an amount proportional to the velocity of these particles. This frequency shift, which is obtained by mixing the transmitted and received signals, is in the audio range and is called the Doppler signal. The Doppler signal does not contain one single frequency, but

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a spectrum of frequencies (the Doppler spectrum). The variations in frequency distribution depend on such factors as unequal distribution of the red blood cell velocity over the cross-sectional area of the vessel, variations in the blood cell interspaces and divergence and non uniformity of the sound beams. In continuous wave Doppler (CWD) flow meters the Doppler signal contains power backscattered from red blood cells as well as from the vessel wall. The signals induced by lateral wall motion are low in frequency, but high in amplitude and attenuation is usually achieved by the use of high-pass filters.

Originally, determination of the mean frequency of the Doppler spectrum and conversion of the signal into an analog signal was performed using a zero-crossing meter. A disadvantage of analog tracings is that all the information present in the Doppler signal is reduced to one single line. More information can be obtained from Doppler signals when audio spectrum analysis is used. In this technique sonograms are produced in which frequencies are given as an instantaneous function of time and the intensity of the pattern represents the amplitude of the frequencies, indicating the number of red blood cells moving at a given velocity. From sonograms information can be obtained about the maximum blood flow velocity, the velocity distribution of the red blood cells-giving insight into the flow pattern-and the degree of lateral wall motion. In laminar flow, the outline of the sonogram defined as the line following the maximum frequencies during the cardiac cycle, is regular. In turbulent flow this outline becomes irregular due to the random changes in flow velocities occurring at any time during the cardiac cycle [Reneman, Spencer, 1979].

Doppler Ultrasound Transducers

The basic component of an ultrasonic transducer is the piezoelectric element, and the ultrasonic energy is produced by applying a voltage to the material. The surfaces of the element move in and out in synchronism with the applied voltage. This movement sets the particles of the medium that make contact with the surfaces into motion and propagates an ultrasonic wave.

In continuous wave Doppler (CWD), ultrasound waves are continuously transmitted and received using separate transmitter and receiver mounted on the same probe. Focusing of the ultrasound beam is dependent of both the distance between the receiver and transmitter and also their relative angles.

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In pulse-echo Doppler the operation of the instrument is initiated by a timer which causes the transmitter to generate a pulse of 50-500V that lasts about 1 usec, and this pulse causes the transducer to generate a short acoustic wave. The transducer also acts as a receiver during the time when it is not transmitting and converts the acoustic energy of the reflected echoes back into electrical signals. The timing of the pulses enables reflected echoes to be sampled from different depths within the tissues.

Continuous Wave Doppler: Examination Techniques

It rapidly became apparent that the Doppler ultrasonic velocity detector was a potentially valuable diagnostic tool and the earliest and most widespread surgical application was for the measurement of systolic blood pressure in arteries distal to obstructions even in the absence of palpable pulsation. However, with the usual 5-10MHz Doppler frequency range, signals can be obtained from most of the major arteries of the limbs, head and neck. For each examination the probe is coupled to the skin with a water-soluble gel to ensure efficient sound transmission. After locating the desired arterial signal, the examiner moves the probe medially or laterally to improve its volume. At the same time, the angle of the probe to the skin is adjusted to obtain the clearest signal. In most cases with the probe pointed either upstream or downstream along the axis of the vessel, the best signal will be obtained at an angle of 45-60 degrees to the skin [Reneman, Spencer, 1979].

Continuous Wave Doppler and Carotid Disease

Although pulsed Doppler techniques in combination with real-time B-mode imaging (Duplex) is now the method of choice for interrogation of the carotid bifurcation much early work was performed using CWD. Spencer and Reid used 5Mhz CWD to correlate Doppler frequency shift in 95 patients with internal carotid stenosis using carotid angiograms as a gold standard [Spencer, Reid, 1979]. Three Doppler criteria were compared: the maximum Doppler frequency at the stenosis; the ratio of the frequency at the stenosis (f_1) and a point 5cm distal to the stenosis (f_2) = f_2/f_1 ; and the square root of the product $f_2 \cdot f_1$. Their findings indicated that the frequency ratio correlated best with x-ray diameter stenosis [Spencer, Reid, 1979]. However, Zweibel and colleagues undertook a similar study correlating peak Doppler frequency with angiographic stenosis in 75 carotid arteries [Zweibel *et al*, 1982]. A precise estimation of severity of stenosis was not achieved through measurement of peak frequency however dividing stenoses into four main groups: <30%

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stenosis, 30-50% stenosis; 50-75% stenosis; >75% stenosis significantly improved the correlation indicated by an overall kappa value of 0.69. Spencer and Reid's method of comparing the frequency at the stenosis with a frequency obtained from a normal section of ICA 5cm distally was criticised as the atheroma often extended beyond this. Factors associated with inaccuracy were thought to be: 1) resistance to blood flow increases in direct proportion to the length of the stenosis, hence a longer stenosis can be expected to have a lower flow velocity and peak frequency than a short stenosis of the same degree of luminal narrowing. 2) Short stenoses may be difficult to insonate. 3) angle of insonation may vary with the course of the vessel. 4) Turbulence may cause spurious velocity readings. 5) Inadvertent compression of the artery by the probe. 6) Hypertension, decreased arterial compliance, and tachycardia may increase flow in the stenotic zone and cause spurious elevation of peak frequency. 7) bradycardia may reduce peak frequency [Zweibel *et al*, 1982].

Therefore, because of these factors CWD could not determine stenosis with absolute accuracy, however it was accurate enough to identify severe stenoses. In this context several investigators determined that the degree of stenosis became critical when it caused a drop in distal mean pressure. Studies on the carotid arteries indicated that a stenosis of the ICA became critical when the reduction in cross-sectional area was greater than 70%, which corresponded to a reduction in lumen diameter of 45% or more [Crawford *et al*, 1960; May *et al*, 1963].

Brown and colleagues undertook an in vitro and in vivo study of CWD determination of cross-sectional area stenosis [Brown *et al*, 1982]. In the in vitro study, where all variables could be controlled peak frequency shift correlated well with stenosis as did spectral broadening indices. In the clinical study, the method was less accurate but 162 cases were examined using 4MHz Doppler and peak frequencies of greater than 3.8KHz were diagnostic of severe internal carotid stenoses with a sensitivity of 92% and a specificity of 94%. This was better than ratios of frequencies obtained from different parts of the artery.

The development of Duplex and colour Duplex imaging enabled the accurate sampling of peak frequencies from known sites along the artery, including the area of maximum stenosis. In addition, Duplex enabled a more precise determination of the angle of insonation, leading to more accurate

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measurement of frequency shifts and calculation of arterial stenosis. Therefore Duplex ultrasound has succeeded CWD as the preferred non-invasive, diagnostic method of investigation of extracranial arterial disease.

However, CWD has been proposed as a quality control method during carotid endarterectomy because of its technical simplicity in use and relatively inexpensive equipment [Seifert, Blackshear, 1985].

The aims of the study with regard to CWD were to assess whether CWD could be applied routinely as a quality control technique. To assist in this we standardised the angle of insonation of the artery at 60 degrees to enable more accurate peak velocity values to be determined. A peak velocity in excess of 125 cm/sec was chosen to indicate a stenosis to be considered for re-exploration. The figure of 125cm/sec was based on data from Spencer and Reid which indicated that 120cm/sec approximated to a 50% stenosis [Spencer, Reid, 1979].

13.2 Materials and Methods

A prospective study was undertaken of 100 consecutive patients undergoing carotid endarterectomy.

At completion of the endarterectomy and restoration of blood flow through the endarterectomy assessment of the blood flow was performed using CWD. Spectral analysis of blood flow along the endarterectomised artery was obtained using an 8Mhz CWD probe and the SciMed PcDop 842 ultrasound processing unit. The probe was covered in a sterile, disposable plastic sheath filled with water soluble acoustic gel and further gel was used to provide acoustic coupling between the artery and the probe. An angle of 60 degrees to the artery was maintained as the probe was moved from CCA to ICA to include both end-points. Peak velocity readings were obtained from the whole length of the artery and, in addition, were recorded at the following fixed sites to enable comparison with postoperative Duplex scan velocities: CCA proximal to endarterectomy; proximal end of patch; mid-patch (opposite origin of ECA); distal end of patch and ICA distal to endarterectomy. A peak velocity in excess of 125cm/sec was considered to indicate a significant stenosis. All signals were recorded onto digital audio tape for post-operative playback and analysis.

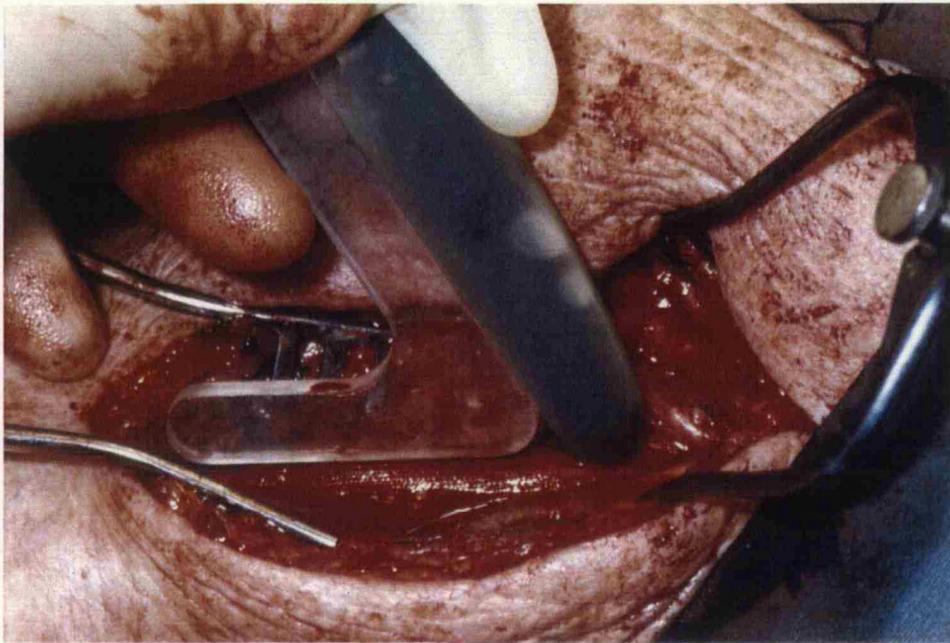


Figure 13.1: Picture illustrating the application of the CWD probe onto the artery using the plastic template to ensure the correct angle of insonation.

Postoperative surveillance

All patients underwent colour Duplex ultrasound scanning of the operated artery at 6 weeks and 6 months after CEA and all abnormal scans were compared with the intraoperative images. Minor defects, detected intraoperatively but not corrected were examined to determine their significance and monitor progression. Peak velocity readings were obtained from the predetermined fixed points along the artery and compared with the intraoperative values obtained with CWD.

Data Analysis

True and false, positive and negative values were obtained for each technique based on the findings at re-exploration of the artery or findings at postoperative Duplex scan if re-exploration was not performed.

Peak velocity readings taken at the five fixed points along the artery intraoperatively were compared with peak velocity readings taken at the same five sites 6 weeks and 6 months postoperatively. The sample mean and 95% confidence intervals (CI) were calculated for each fixed point at each scanning interval. Means and 95% CI were compared using repeated measure ANOVA with Bonferroni correction of p values to determine statistical significance

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(GraphPad InStat 1990, version 1.14). The sample mean peak velocities for each site were also compared at each scanning interval using the same analysis.

13.3 Results

Adequate examinations were obtained in 91% of patients. Reasons for inadequate examinations consisted of difficulty in obtaining accurate velocity readings from the distal ICA where a high endarterectomy had been performed and acute angulation of the probe to reach the endpoint made velocity comparisons with the rest of the artery unreliable.

Velocity readings in excess of 125cm/sec were detected in four patients. In 3 cases the velocity increases did not exceed 128cm/sec and did not coincide with a B-mode image suggesting a stenosis and therefore the artery was not re-explored. Postoperative Duplex scan did not confirm the presence of abnormality in these cases. In one case a velocity of 132cm/sec coincided with a B-mode image suggesting an arterial kink at the junction of the distal toe of the patch and ICA, however in the context of the operation, the operating surgeon considered that this was not significant and the artery was not re-explored. Postoperative Duplex scanning confirmed the presence of an arterial kink causing a 30% stenosis at the junction of the distal patch, this was not a significant flow limiting lesion. Duplex scan at six months did not show any progression of the stenosis.

Post-operative Duplex Scans

Successful, colour Duplex scans at both 6 weeks and 6 months were obtained in 93% of patients. Peak velocity measurements obtained at the five fixed points along the endarterectomised artery were recorded and compared with readings obtained intraoperatively at the same sites. The sample means and 95% confidence intervals of peak velocity readings are illustrated in table 13.1.

Comparison of Intraoperative and Postoperative Velocity Measurements

Peak velocity readings obtained from the five fixed points along the artery intraoperatively using CWD tended to be lower than velocity readings obtained from the same points postoperatively using colour Duplex scanning and pulsed wave Doppler(Table 13.2). There was no statistically significant difference between peak velocity measurements between the 6 week scans and 6 month

scans at any of the five points (ANOVA $p=0.5167$, Bonferroni p value, $p>0.05$). There was no statistically significant difference between the sample mean peak

	CCA	PP	MP	DP	ICA
CWD	44.04 (39.5-48.5)	40.22 (35.8-44.6)	36.18 (32.4-39.9)	41.37 (35.4-47.4)	63.4 (56.4-70.4)
Duplex 6 week	71.98 (65.7-78.3)	58.15 (52.2-64.1)	51.44 (45-57.9)	48.64 (41.1-56.1)	74.49 (60.5-88.5)
Duplex 6 month	74.84 (67.5-82.2)	65.13 (57.9-72.3)	55.51 (49.2-61.8)	52.4 (45.4-59.4)	70.56 (64.2-76.9)

Table 13.1 Comparing the sample mean peak velocity measurements (95% CI) at five fixed points along the artery intraoperatively, at 6 weeks and 6 months postoperatively.

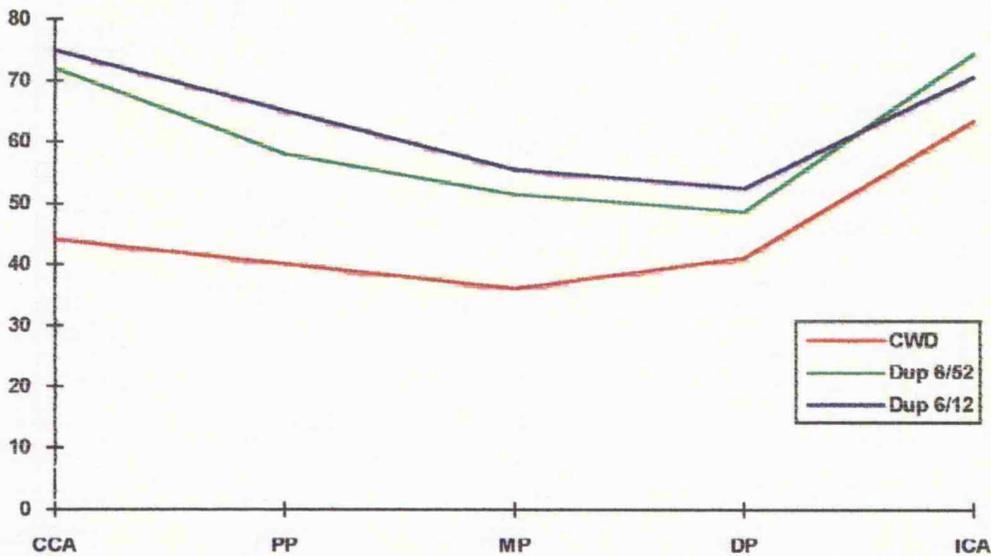


Figure 13.1 Graph illustrating the mean velocity measurements at five fixed points along the artery intraoperatively (CWD) and at 6 weeks and 6 months postoperatively.

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velocity obtained at the distal patch intraoperatively compared with the sample mean peak velocity at 6 weeks postoperatively (ANOVA $p=0.1395$, Bonferroni p value, $p>0.05$) and 6 months postoperatively (ANOVA $p=0.0255$, Bonferroni p value, $p>0.05$). Similarly, there was no statistically significant difference between the sample mean peak velocity obtained in the ICA intraoperatively compared with the sample mean peak velocity at 6 weeks postoperatively (ANOVA $p=0.1152$, Bonferroni p value, $p>0.05$) and 6 months postoperatively (ANOVA $p=0.3081$, Bonferroni p value, $p>0.05$).

However, for the remaining sites CCA, proximal patch and mid-patch the sample mean velocities obtained intraoperatively were significantly lower than those obtained at 6 weeks and 6 months postoperatively.

Arterial Site	Time Period	mean difference	p value	Bonferroni p
CCA	Intraop vs 6 week	-30.8	<0.0001	<0.001
	Intraop vs 6 month	-27.94	<0.0001	<0.001
	6 week vs 6 month	-2.86	0.5167	>0.05 ns
PP	Intraop vs 6 week	-17.93	<0.0001	<0.001
	Intraop vs 6 month	-24.91	<0.0001	<0.001
	6 week vs 6 month	-6.9799	0.1023	>0.05 ns
MP	Intraop vs 6 week	-15.26	0.0002	<0.001
	Intraop vs 6 month	-19.33	<0.0001	<0.001
	6 week vs 6 month	-4.07	0.3152	>0.05 ns
DP	Intraop vs 6 week	-7.27	0.1395	>0.05 ns
	Intraop vs 6 month	-11.03	0.0255	>0.05 ns
	6 week vs 6 month	-3.76	0.4412	>0.05 ns
ICA	Intraop vs 6 week	-11.09	0.1152	>0.05 ns
	Intraop vs 6 month	-7.16	0.3081	>0.05 ns
	6 week vs 6 month	3.93	0.5734	>0.05 ns

Table 13.2 Results of the repeated measurements ANOVA analysis for velocity readings taken at the five fixed points intraoperatively, 6 weeks and 6 months postoperatively (significance = <0.05).

A consistent finding at each scan was the statistically significant lower sample mean peak velocity readings at the mid- and distal patch compared with the

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sample mean peak velocity in the ICA (ANOVA, Bonferroni $p < 0.001$). However, intraoperatively, the sample mean peak velocity in the CCA and proximal patch points were also significantly lower than the ICA (ANOVA, Bonferroni $p = 0.001$).

13.4 Discussion

In this study CWD was the least satisfactory of the quality control techniques compared. Difficulty examining the distal end-point was experienced in 9% of cases and difficulty with signal interpretation also occurred. Although greater success in insonating the distal end-point was achieved with CWD (91%) compared with BMU (76%) the limited amount of information provided by CWD indicates that this technique has a limited role as a quality control technique in carotid endarterectomy.

Continuous wave Doppler has been proposed as quality control method during carotid endarterectomy because of its technical simplicity in use and relatively inexpensive equipment. However, advocates of the technique have used abnormal findings with CWD as a basis for further assessment with angiography rather than re-exploration of the artery based on the CWD evidence alone [Seifert, Blackshear, 1985].

Seifert and Blackshear used CWD to assess the technical result of 229 carotid endarterectomies [Seifert, Blackshear, 1985]. Auditory assessment of the signal pitch were used to identify abnormalities for further investigation using on-table angiography. Abnormal signals (absent signals and high pitched signals) were detected in 13% of cases. In 10 cases (4.3%) the abnormal signal was in the ICA. Intraoperative angiography was performed in eight of these and in two the arteries were reopened immediately. Of the eight angiograms, two were essentially normal and these arteries were not reopened. One demonstrated a very slight stenosis and the ICA was not reopened. The five other angiograms indicated areas of stenosis. In two of these a distal intimal flap was identified and repaired. In two others platelet aggregates were found. In one the distal closure was thought to compromise the lumen and the artery was closed with a Dacron patch. In the two cases reopened without angiography, distal intimal flaps were found. In 7 of 10 ICAs the intraoperative Doppler correctly identified a technical problem, however because angiograms

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were not performed in the patients who had a normal examination with CWD the number of abnormalities missed was not known.

In previous studies subjective changes in acoustic frequency were used to indicate the presence of technical abnormalities [Seifert, Blackshear, 1985]. We attempted to improve the reliability of the technique by standardising the angle of insonation and obtaining objective velocity readings.

Auditory assessment of Doppler sonograms has been demonstrated to be accurate with adequate training [Spencer *et al*, 1974] but is limited because of subjectivity [Zweibel *et al*, 1982]. In particular Zweibel and colleagues noted that an increase in loudness of a signal may be confused with an increase in pitch. Also they found that it was particularly difficult to differentiate mild and moderate stenoses with auditory evaluation. The greatest disadvantage of auditory interpretation was the extended learning period required during which errors of over and underestimation were common [Zweibel *et al*, 1982]. Less subjective and more precise Doppler methods such as the measurement of peak Doppler frequencies with on-line spectral analysis have been advocated [Zweibel *et al*, 1982].

In this study we attempted to improve the accuracy of CWD by providing more objective velocity readings. In the absence of any intraoperative study using this approach we chose a figure of 125cm/sec based on velocity data obtained by Spencer to indicate an approximate 50% stenosis. The 50% stenosis mark was chosen as a compromise between the limited ability of the technique to detect mild stenosis and Blaisdell's original findings of a 30% residual stenosis on completion angiography indicating a risk of postoperative thrombosis [Zweibel *et al*, 1982; Blaisdell *et al*, 1967]. However, due to the routine use of patch angioplasty there was a low incidence of anastomotic stenosis in this study and as a result the velocity reading of 125cm/sec was only exceeded in four cases. A stenosis was only confirmed in one of these cases and postoperative colour Duplex scanning classified this as a 30% stenosis. Therefore, although the three cases where a stenosis was not confirmed were considered to be false positives for the technique the other possibility exists that the figure of 125cm/sec does not truly indicate a 50% stenosis in this intraoperative situation and should be revised upwards. Possibly, further intraoperative studies would yield the answer but even accurate CWD velocity

Continuous Wave Doppler

readings would still provide less detailed information, compared with the other techniques, on which to base clinical decisions.

Alternative approaches to identifying technical error which were not investigated in this study, include the analysis of spectral broadening and the use of velocity ratios obtained from different parts of the artery to indicate abnormalities. Spectral broadening is caused by blood flow turbulence and may indicate underlying structural abnormalities [Gosling, King, 1974]. Hoff and colleagues used intraoperative Duplex scanning and spectral analysis to identify technical abnormalities during 44 carotid endarterectomies [Hoff *et al*, 1993]. Although no cases were reopened on the basis of intraoperative scanning the authors found a positive correlation between spectral broadening in the ICA and the development of postoperative complications. However the small numbers involved in this study and the retrospective nature of the diagnoses provide little information on which to identify those cases requiring re-exploration. In addition, the assessment of spectral broadening may also be subjective requiring experience in interpretation and may be unreliable in situations where factors other than technical error may introduce turbulence e.g. patch angioplasty.

Another alternative approach is to use the peak frequency ratio between the maximum frequency over the stenosis compared to the normal ICA frequency distal to the stenosis [Spencer, Reid 1979]. The use of ratios lessens the effects of fluctuating blood pressure levels which can affect peak velocity readings. However, a disadvantage of this method is that it may be difficult to find a normal distal ICA frequency with which to compare [Brown *et al*, 1982].

There is no evidence that CWD can detect small amounts of thrombus not large enough to distort carotid blood flow but potentially large enough to embolise to the brain resulting in neurological deficit [Lane, 1980]. However, in common with BMU, CWD is applied after final restoration of flow and therefore may not detect small amounts of intraluminal thrombus demonstrated by angiography, because this embolises distally at the time of clamp release.

The measurement of peak velocity at the five fixed points along the artery and comparison with postoperative Duplex scans velocities at the same points was useful to indicate if CWD could reliably detect variations in velocity along the length of the artery. There was little variation between the sample mean peak

Continuous Wave Doppler

velocity readings at all five points at the 6 week and 6 month postoperative scans indicating that consistent identification of the fixed points could be achieved. Similarly, for the distal patch and ICA points on the artery, intraoperative CWD velocities matched the postoperative Duplex velocities fairly well. However, there were significant differences in velocity at the midpatch, proximal patch and common carotid artery between intra-operative and postoperative methods. Absolute correlation was not expected because the velocity was measured on different ultrasonic equipment, slight variation in the position of sampling was to be expected and the postoperative scans used pulsed wave Doppler compared to CWD. Other factors such as relative intraoperative hypotension, increased compliance of the freshly reconstructed vessel and turbulence caused by the patch angioplasty may also have contributed to the relatively lower intraoperative velocities compared to postoperative measurements. However, although intraoperative velocities were lower than those measured postoperatively, the velocities at the different points were similar in relation to each other (Fig 13.1) indicating that CWD was able to identify velocities differences along the artery and would have identified a sudden velocity increase if one existed. Along the artery, peak velocities tended to be lower within the area of the patch, especially the mid- and distal patch areas. A possible explanation of this is an effect on blood flow velocity caused by the use of a patch angioplasty which widens the diameter of the lumen of the artery at these points. The clinical significance of this finding, if any, remains uncertain and may be a subject for further research.

CWD was originally proposed as a quality control technique because of the simplicity of application and interpretation of the technique. The equipment is inexpensive and easy to use but compared with angiography and BMU, provides less detailed information. The results of previous studies have suggested that CWD is useful in identifying severe stenoses and vessel occlusions however the lack of such abnormalities in this study prevented any further investigation of this ability. However, lesser degrees of abnormality are associated with adverse clinical outcomes and in detecting these CWD had no advantage over BMU or angiography.

13.5 Summary

The history and theory of CWD has been outlined followed by a detailed description of the materials, methods and results of CWD. No additional intimal

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flaps or thrombi were identified by this technique in addition to those already detected by angiography.

Significant stenoses were indicated in four patients but in three cases this proved to be a false positive finding and although in one patient a 30% stenosis was correctly identified, this was not corrected intraoperatively and was not associated with adverse clinical consequences.

Complete examinations were not obtained in 9% of patients due to an inability to obtain accurate velocity readings from the distal ICA where a high endarterectomy had been performed.

Due to the lower number of complete examinations, the lack of additional defects and the high percentage of false positives CWD was considered inferior to angiography as a quality control technique.

CHAPTER 14

TRANSCRANIAL DOPPLER AS A QUALITY CONTROL TECHNIQUE

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14.1 Introduction

The results for the completion quality control methods angioscopy, BMU and CWD have been described in preceding chapters. This chapter will describe the application of TCD monitoring as a continuous method of quality control, detecting errors of surgical technique while the operation is in progress.

Although individual instances of the ability of TCD to detect errors of surgical technique have been noted in previous studies [Naylor *et al*, 1991], no study has been performed to specifically investigate the role of TCD as a quality control method. In this study the aim was to quantify the number of cases where TCD monitoring provided useful information which led to a modification of surgical technique.

Experience with TCD monitoring has highlighted its role in detecting intraoperative episodes of ischaemia and embolisation. However, the application of this technique as a quality control measure, detecting abnormalities associated with intraoperative technique has not previously been investigated.

The theory and history of TCD has already been described in chapter 4 and therefore will not be repeated here.

14.2 Materials and Methods

This study was performed simultaneously on the same cohort of patients as the other quality control methods and the TCD monitoring study. The materials and methods for the TCD monitoring are the same as those described in chapter 5.

Data Analysis

The number, type and nature of each defect was recorded. True and false, positive and negative values were determined on the basis of either re-exploration of the artery, or detection and correction of the defect. The risk of ischaemia during shunt occlusion was determined using the TCD haemodynamic parameters described by Halsey [Halsey, 1993].

14.3 Results

Successful examinations were obtained in 91% of patients. Reasons for inadequate examinations were skull hyperostosis (6%) and equipment failure (3%).

TCD monitoring detected potentially significant technical errors in 41 patients.

TCD detected particulate embolisation during the dissection of the carotid artery in 23 patients. Early warning of this phenomena enabled modification of surgical technique in persistent cases (early distal ICA clamping) to avoid further embolisation.

TCD also identified shunt kinking/malfunction in 13 patients. In two, MCA velocities fell below 15% of preclamp value indicating a high risk of developing an haemodynamic stroke [Halsey, 1993].

TCD identified rupture of the distal retaining balloon of the Pruitt-Inahara shunt caused by a needle stick injury in 2 patients. The details of these two cases are described in chapter 5.

In 6 patients TCD detected unexpected particulate embolisation in the early postoperative phase. In 3 cases the embolisation was minor (<44 emboli) asymptomatic and self-limiting, however in three cases (157-672 emboli) embolisation was persistent and preceded carotid artery thrombosis and the development of serious neurological deficits. In two patients persistent embolisation coincided with a gradual decline of MCA velocity but in one patient MCA velocity remained constant and the TCD detection of embolic signals alone provided the diagnosis. In all three cases re-exploration of the artery revealed a mass of platelet thrombus adherent to a normal endarterectomy surface in the internal carotid artery 1-2cm from the bifurcation. No technical error was associated with the site of thrombus formation and all patients had normal intraoperative angioscopic, BMU and CWD examinations. Correction of the defect consisted of removal of the thrombus and commencement of a heparin infusion.

Technical Error	Number of Patients
Particulate embolisation during Dissection.	23
Shunt blood flow occlusion	13
Shunt balloon deflation	2
Early carotid artery thrombosis	3

Table 14.1 Technical errors detected by intraoperative TCD monitoring

14.4 Discussion

The results of this study provide evidence that TCD monitoring has a role as a quality control method during CEA. TCD was able to detect abnormalities of blood flow and embolisation instantaneously providing the surgeon with an early warning and therefore enabling corrective action to be taken to minimise any adverse clinical outcomes.

Embolisation during the dissection of the carotid bifurcation consists of particulate debris from unstable carotid plaque and is well recognised as a cause of intraoperative neurological deficits [Hertzer *et al*, 1978; Naylor *et al*, 1992; Riles *et al*, 1994]. In this study TCD has identified that embolisation may occur from unstable plaques in 25% of patients, even when employing the most careful operative technique. This incidence of embolisation is higher than described in previous studies of TCD monitoring of CEA [Padayachee *et al*, 1986; Spencer *et al*, 1990; Naylor *et al*, 1991; Jansen *et al*, 1993] and much higher than suggested from clinical studies [Riles *et al*, 1994]. However, none of these previous TCD studies were designed to specifically detect and investigate embolisation and therefore, may not have detected the subtle particulate embolic signals which occur during dissection. Similarly the results from the monitoring study would suggest that embolisation during dissection, in the numbers detected, is more commonly associated with cognitive function deficits detected by specific psychometric tests and were not apparent to routine clinical examination. Evidence from the monitoring study suggests that the adverse clinical effect of this embolisation is related to the number of emboli and TCD is the only monitoring method that can detect individual emboli and provide quantitative data on the number of emboli occurring. This gives

TCD: Quality Control

the surgeon the opportunity to modify his surgical technique to avoid further potentially harmful particulate emboli. During this study, in cases where embolisation was persistent, one solution was to clamp the carotid artery early and complete dissection of the bifurcation after insertion of an intraluminal shunt. Riles and colleagues advocate the early clamping of the ICA in all cases in order to avoid embolism during this stage [Riles *et al*, 1994]. However, this approach may prolong the clamp time and put the patient at risk of an haemodynamic deficit. The use of TCD enables the surgeon to limit this manoeuvre to those patients with evidence of embolisation in addition to indicating the adequacy of cerebral blood flow during clamping [Spencer *et al*, 1990; Halsey, 1993].

The blood-supply through an intraluminal shunt may be inadvertently occluded by handling during the course of the operation and the operating surgeon may be unaware of this. TCD was able to detect this kinking of the shunt immediately in 13 patients and warn the surgeon to correct the defect. This information may have been particularly important in preventing neurological deficit in two patients whose MCA velocity fell to below 15% of the preclamp velocity, indicating severe ischaemia [Halsey, 1993]. This finding highlights the importance of employing a monitoring method to ensure an intraluminal shunt continues to function efficiently after insertion. Considerable controversy exists concerning the advantages and disadvantages of shunting. While some studies have shown that shunting is of benefit in patients with poor collateral cerebral blood supply other studies have demonstrated no benefit and even an increase in perioperative complications associated with the use of a shunt [Jausseran *et al*, 1987; Halsey *et al*, 1992]. A major difficulty with demonstrating a clinical benefit from shunting is that the number of patients at risk of cerebral ischaemia during clamping is relatively small and there are numerous other causes of neurological deficit after CEA [Naylor *et al*, 1992; Riles *et al*, 1994]. However, the finding of this study of shunt malfunction in 13% of cases indicates that it would be advantageous in future studies investigating the role of shunting to employ a monitoring method to ensure the correct functioning of the shunt.

The finding of kinking occurring in 13% of cases is specific to the properties of Pruitt-Inahara shunts which were used predominantly in this study. However, kinking and occlusion may also occur with other types of shunts e.g. Javid, but no quantitative data exists with which to compare the two types.

TCD: Quality Control

Another property of the Pruitt-Inahara shunt is the employment of two inflatable balloons at each end to prevent displacement from the artery. The balloons are inflated with saline but this usually contains air bubbles which produce the characteristic TCD embolic signal [Markus *et al*, 1994]. TCD monitoring identified that these balloons may be accidentally punctured by a needle stick leading to cerebral embolisation of the saline/air contents of the balloon. If the puncture is not recognised and a hurried attempt at reinflation is attempted with an air filled syringe, then gross air embolisation to the brain can occur which, in one case, may have caused a temporary neurological deficit. Although only two cases occurred during the course of the study, both exhibited common TCD characteristics which may help for diagnosing this problem in the future and therefore, prevent further potentially harmful attempts at reinflation. The common TCD characteristics are:

- 1) a needle stick is, or recently has been, in use in the vicinity of a balloon.
- 2) emboli, consistent with air emboli in character are detected.
- 3) the pattern of embolisation are short, bursts of air emboli coinciding with each systolic pulse.

These phenomena were detected in each of the two cases, approximately 4-5 systolic beats prior to the backflow of blood around the deflating balloon into the operative site. This was followed shortly after by the displacement of the shunt by the pressure of blood. The recognition of these TCD criteria would prevent reinsertion of the shunt and attempted reinflation of the punctured balloon. Instead the ICA and the shunt should be clamped and the distal balloon reinflated under vision to test for puncture and replaced if necessary.

Immediate postoperative carotid thrombosis was the cause of two permanent deficits and one temporary deficit. These cases have already been described in detail in chapter 5 but are outlined again here as they can be considered as technical defects even though no surgical error was identified. In their large retrospective study of 3062 CEAs Riles and colleagues identified that early postoperative thrombosis of the operated artery was the remaining largest cause of perioperative strokes in their series [Riles *et al*, 1994]. Also, while the incidence of ischaemic stroke had declined over the years with the increased use of shunts, the incidence of stroke secondary to thrombo-embolism had remained unchanged [Riles *et al*, 1994]. The new finding from this study that

TCD: Quality Control

TCD monitoring can detect this complication at an early stage enabling early operative intervention to prevent neurological deficits may prove to be an important method to reduce perioperative strokes.

TCD monitoring detected each case of carotid thrombosis at an early stage and having established the criteria necessary to make a diagnosis, based on the experience of the first two cases, it was possible to avoid a permanent neurological deficit in the final patient by immediate operative intervention. Interestingly, none of the thrombosed arteries were technically compromised suggesting that some patients are at risk of thrombosis even in the absence of technical error. This finding is in contrast to those of Riles and colleagues who found that postoperative carotid thrombosis was usually associated with the presence of uncorrected technical imperfections at the endarterectomy site e.g. clamp injuries, kinks, ledges at the end of endarterectomy, stenosis, rough endarterectomy surfaces and thrombus forming on artificial patch material. However, in a number of cases no specific cause could be found [Riles *et al*, 1994]. The underlying factors responsible for thrombosis in cases where no identifiable technical error can be found are uncertain, however it is known that carotid endarterectomy can be associated with enhanced platelet activation, especially at the endarterectomy site [Stratton *et al*, 1988]. The investigation of these haematological factors may be the subject of future research.

14.5 Summary

Evidence has been provided to support the role of TCD monitoring as a continuous quality control technique, detecting errors of surgical technique during the operation and detecting carotid artery thrombosis in the immediate postoperative period. In particular four types of technical error were identified by TCD monitoring which provide the surgeon with an early warning enabling correction of the defect before possible adverse clinical effects. Potentially harmful particulate embolisation from unstable carotid plaque is caused by manipulation during the initial dissection of the carotid bifurcation and may be detected by TCD monitoring. In cases of persistent embolisation early clamping of the carotid artery prevents further embolisation.

TCD monitoring detected occlusion of blood flow through an intraluminal shunt in 13% of cases and enabled immediate correction and re-establishment of flow. In two cases, TCD monitoring detected puncture of the distal retaining

TCD: Quality Control

balloon of the intraluminal shunt. The TCD criteria to diagnose this complication have been described.

TCD detected early postoperative carotid artery thrombosis in 3 cases enabling correction. As a result of this study the TCD criteria for diagnosing this phenomena have been established (Chapter 5).

CHAPTER 15
DISCUSSION OF QUALITY CONTROL

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Discussion of Quality Control

15.1 Discussion of Quality Control

In the introduction to this section the ideal quality control technique was described as being able to detect all technical defects known to be associated with adverse clinical outcome; be easy to apply and interpret and be easily incorporated into the routine intraoperative situation; and finally be safe and not contribute to the operative morbidity/mortality and have a low number of false positives leading to unnecessary and possibly hazardous re-explorations.

Of the techniques employed to detect completion defects angiography had significant advantages over BMU and CWD and came closest to the ideal characteristics.

Angiography proved to be a simple technique to perform enabling the surgeon to operate independently of technicians and the magnified images of the arterial lumen viewed on colour monitors required little specialised knowledge for interpretation. Angiography proved a sensitive technique for the detection of intimal flaps and fragments of intraluminal thrombus. A major advantage of angiography is that defects are detected and corrected prior to restoration of flow, avoiding the need to reopen the artery. This is particularly important with regard to fragments of intraluminal thrombus which may be dislodged as soon as flow is restored and therefore, never detected by methods applied after this stage. In addition, the detection of small fragments of thrombus by ultrasound is unreliable as platelet aggregates are echopoor [Lane, 1980].

Angiography enabled a full assessment in 98% of patients while BMU achieved only 76% due to difficulty insonating the distal ICA end-point, because of the dimensions of the probe, and poor penetration of artificial patch material. BMU required a vascular technologist in attendance to obtain adequate images and help with interpretation of sonographic images. The low number of adequate examinations achieved with this technique would severely limit its routine application. In addition the occurrence of two false positive re-explorations based on BMU images indicating stenosis reduced the surgeons' confidence in the technique. This resulted in a true stenosis not being re explored and corrected, however this was not associated with an adverse clinical outcome.

In previous studies, BMU has demonstrated intimal flaps down to 1mm in size both in vitro and in vivo, but in this study no additional intimal flaps were

Discussion of Quality Control

detected by BMU indicating a low incidence of false negatives with angioscopy [Coehlo *et al*, 1981].

Difficulty examining the distal end-point was also experienced with CWD in 9% of cases and difficulty with signal interpretation also occurred. In previous studies subjective changes in acoustic frequency were used to indicate the presence of technical abnormalities which were then investigated further by intraoperative angiography [Seifert, Blackshear, 1985]. In this study an attempt to improve the reliability of the technique was made by standardising the angle of insonation and obtaining objective velocity readings. However, isolated velocity spectra was considered by the surgeons to be a limited amount of information on which to base clinical decisions and indicates that CWD applied alone has a limited role as a quality control technique in CEA.

Duplex ultrasound overcomes the difficulty of interpreting the significance of isolated velocity spectra by also providing B-mode images of the artery. This enables more accurate sampling of velocity spectra from areas of interest identified by the B-mode images. Both conventional and colour coded Duplex ultrasound have been used to assess the result of CEA with good results, however the difficulties of probe access to insonate high distal end-points still occurred [Schwartz *et al*, 1988; Harris, Horrocks, 1995]. A further disadvantage of this technique is the difficulty of obtaining the use of the scanner for routine intra-operative assessments when this expensive technology is heavily utilised for diagnostic procedures. This factor would generally preclude the use of this method in the majority of hospitals.

The postoperative Duplex scan at 6 weeks identified a number of defects which were either not detected intraoperatively or developed in the postoperative period. These consisted of two arterial kinks, a 75% stenoses due to intimal hyperplasia at the distal endpoint and two asymptomatic carotid artery occlusions. No new defects developed between 6 weeks and 6 months. After careful review of the intraoperative recordings of the angioscopic and B-mode images and the CWD velocity profiles the most likely conclusion was that the defects developed in the postoperative period. The evidence to support this conclusion was that in each case good images had been obtained with the intraoperative B-mode scans, including the area of artery where the defect eventually developed and the defect was not present. These results would suggest that the configuration of the operated artery, although acceptable at

Discussion of Quality Control

the time of intraoperative assessment, may undergo change in the hours or days following the operation resulting in the development of technical errors. Therefore, one may conclude that although completion quality control techniques are useful in detecting technical errors which may occur within the operation, these techniques may not ensure the elimination of all arterial defects, because some develop in the postoperative period.

Further evidence for the development of technical defects postoperatively was provided by the TCD detection of 3 cases of carotid artery thrombosis in the immediate postoperative period. In each of these cases thrombosis was not associated with the presence of a technical error. Thrombus formed on a normal endarterectomy surface of the ICA just distal to the bifurcation. Each of these cases were associated with the development of neurological deficits (2 permanent, 1 temporary) but the 6 week postoperative Duplex scan identified two other cases of asymptomatic carotid artery occlusion. The time of carotid artery occlusion in these cases is uncertain but most probably developed in the postoperative period after TCD monitoring had ceased (30 minutes after clamp release. Both of the patients had non stenosed contralateral carotid arteries and good collateral cerebral blood flow indicated by a high MCAV during ipsilateral carotid clamping. Therefore, neither was at risk from an haemodynamic stroke as a result of carotid occlusion but whether significant embolisation occurred is unknown. Riles and colleagues described 4 carotid artery thromboses which occurred within 10 hours of the operation [Riles *et al*, 1994]. An extension of the postoperative monitoring time with TCD may have detected these cases and this would appear a promising area for future research. However Riles also described two cases of thrombosis occurring on the 6th and 14th postoperative day and obviously extending the TCD monitoring time to this extent is unfeasible. Therefore, there may be some late carotid occlusions which are unavoidable.

In combination with angiography TCD monitoring would appear to have a role as quality control method. Angioscopy was the most accurate of the completion techniques and the easiest to apply routinely. If used as an alternative technique to completion angiography, angioscopy would avoid the complications associated with performance of the angiography [Hankey *et al*, 1990], the need to use potentially hazardous ionising radiation and avoid the injection of contrast material. Evidence from lower limb arterial studies would

Discussion of Quality Control

suggest that more technical errors would be detected with angioscopy [Miller *et al*, 1994].

TCD has been proposed as a monitoring technique for detecting intraoperative ischaemia and indicating the need for an intraluminal shunt [Halsey *et al*, 1992]. The results of this study would suggest that TCD has a much wider role as a continuous quality control measure detecting errors of operative technique as they occur during the operation and detecting thrombosis of the endarterectomised artery in the early post-operative period (Table 15.1). The ability of TCD to identify carotid thrombosis in the early postoperative period, prior to detection of neurological signs enabling early surgical intervention to avoid neurological deficit, is an important new clinical application of this technique.

The combination of TCD and completion angioscopy offered the maximum positive yield in identifying technical error and detecting significant causes of perioperative morbidity during CEA in this study. In addition this combination would appear to have the potential to detect the majority of operation related factors known to be associated with perioperative strokes. Riles and colleagues identified over 20 different mechanisms of perioperative stroke in their review of 3062 CEAs performed in their centre [Riles *et al*, 1994]. A combination of TCD and angioscopy has the potential to detect and prevent many of them

Other mechanisms of stroke identified by Riles would not be affected by TCD and angioscopy such as wound infection with carotid haemorrhage, suture disruption with carotid haemorrhage, global anoxia due to premature extubation and strokes occurring in other vascular territories [Riles *et al* 1994]. However, these causes tended to be single occurrences and therefore less significant than carotid artery thrombosis which occurred in 15 patients [Riles *et al*, 1994]

The question that further study needs to answer is whether the increased detection and correction of technical errors by angioscopy and TCD would lead to an improvement in perioperative morbidity and mortality? Two previous controlled trials of quality control techniques have failed to show a clear benefit. Miller compared angioscopy and angiography for assessment of lower limb arterial reconstructions and found that, although angioscopy detected many more technical errors than angiography this did not have a statistically significant effect on 30 day graft survival rates [Miller *et al*, 1992].

Discussion of Quality Control

Mechanism of Stroke	Role of TCD and Angioscopy
Difficulty placing shunt	TCD detects ischaemia during clamping
Hypotension-shunt in place	TCD detects inadequate cerebral blood flow during shunting
Bradycardia no shunt	TCD detects inadequate cerebral blood flow during clamping
Occlusion of contralateral ICA, stroke contralateral	No known role
Intracranial haemorrhage	TCD detects cerebral hyperperfusion prior to haemorrhage
Embolism during dissection	TCD detects embolism during dissection
Embolism during clamp release	Angioscopy detects intraluminal thrombus prior to clamp release TCD detects embolisation after clamp release
Carotid artery thrombosis	TCD detects carotid artery thrombosis prior to the development of neurological deficit.
Carotid artery embolus	TCD detects intraoperative embolisation
Atheroemboli from aortic arch	TCD detects intraoperative embolisation
Cardiac embolus	TCD detects intraoperative embolisation
Cerebral angiography	Angioscopy avoids the need to perform angiography

Table 15.1 Operation related defects [Riles *et al*, 1994] detectable by a combination of TCD monitoring and completion angioscopy.

Similarly, Lane compared B-mode ultrasound assessment of CEA with no assessment in 380 operations. Once again BMU detected a significant number of technical defects which were corrected intraoperatively but there was no statistically significant effect on the incidence of postoperative

Discussion of Quality Control

morbidity/mortality in the two groups [Lane, Appleberg 1982]. The definitive answer to this question would be provided by a controlled clinical trial. However, the problem with carotid surgery research is that the number of patients suffering postoperative strokes is relatively small while the causes of these strokes are many and varied. In their study of 3062 CEAs Riles and colleagues identified over 20 different mechanisms of perioperative stroke [Riles *et al*, 1994]. Therefore, it is unlikely that any one method of monitoring or quality control would eliminate all these causes. The results of this study would indicate that a combination of TCD monitoring and completion angiography may detect many of the causes of perioperative stroke and therefore may have a significant effect on perioperative morbidity and mortality.

PART FOUR : CHAPTER 16

**DESCRIPTION AND DISCUSSION OF MAJOR MORBIDITY AND
MORTALITY OCCURRING DURING THE STUDY**

CHAPTER 16

Mortality, Morbidity and Postoperative Complications

In this study 5% of patients had a stroke or died within 30 days of surgery. Three deaths occurred as a result of patch angioplasty disruption, one patient died as a result of a stroke (NIH = 11; RDS = 4) secondary to early postoperative carotid artery thrombosis and one patient experienced a permanent right hand monoparesis (NIH = 1; RDS = 2) also secondary to early postoperative carotid artery thrombosis

No new neurological deficits or deaths occurred between the 30 day postoperative period and the final Duplex carotid artery scan at six months.

Four patients experienced intraoperative neurological deficits of which 2 were permanent and 2 were temporary. The two permanent deficits consisted of a right sided hemiplegia (NIH = 11; RDS = 4) and a right hand monoparesis (NIH = 1; RDS = 2) resulting from gross particulate embolisation in the immediate postoperative period associated with incipient carotid artery thrombosis. One of these patients later died. One temporary right hand monoparesis (NIH = 1; RDS = 1) also resulted from carotid artery thrombosis but TCD monitoring enabled an early diagnosis and correction of the defect based on the experience of the previous two cases. The remaining temporary deficit resulted from an episode of gross air embolisation caused by the rupture of the distal retaining balloon of an intraluminal shunt and repeated attempts at reinflation. This caused a temporary worsening of a pre-existing hemiparesis which resolved completely within three days (NIH deterioration from 2 to 3; RDS 1 to 2).

The major cause of mortality in the study was patch angioplasty disruption which resulted in a rapidly expanding neck haematoma causing stridor and eventually haemorrhage from the neck wound. Two cases occurred on the 5th and 7th postoperative day, after discharge from hospital and both patients died. Another two cases occurred in hospital. In one patient the haematoma was controlled and immediate reoperation prevented any neurological deficit however in the other case rapid haemorrhage resulted in the death of the patient despite attempts at resuscitation. Post-mortems were obtained on each of the patients who died and in addition the carotid specimens were saved for further investigation by the surgical team.

Morbidity and Mortality

Examination of the carotid specimens revealed the cause of rupture in each case and enabled operative technique to be modified to prevent further ruptures. In one case rupture was due to central vein patch necrosis. This a rare but well recognised complication of using vein patches however this is only the second case reported where rupture has occurred from the use of upper thigh long saphenous vein [White et al, 1995].

One case of rupture was due to fraying of a Dacron patch resulting in separation of the patch from the arterial wall. This is the first reported case of this complication and will be described in more detail in chapter 17.

The two remaining cases resulted in separation of vein patch from the arterial wall. Examination revealed that the suture material was missing altogether from a short segment on the medial side of the patch, opposite the origin of the external carotid artery. This segment coincided with the site where the angioscope was inserted at the end of the operation. Further investigations and experiments were performed to explain this phenomena and these studies will be described in more detail in chapter 18. As a result of these investigations the suturing technique around this area was modified and further ruptures have been avoided.

CHAPTER 17

SUTURE LINE DISRUPTION

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17.1 Introduction

Patch angioplasty rupture is a sudden and often fatal complication occurring several days after an apparently successful operation. Recent investigations into the cause have revealed that central necrosis of a vein patch, especially when harvested from the ankle was responsible for the majority of cases [Riles et al, 1990]. This could largely be avoided by the use of upper thigh vein which was more resistant to rupture [Archie, 1991].

In this centre it was routine practice to close the carotid arteriotomy with a vein patch angioplasty derived from the upper thigh long saphenous vein. This technique had been successfully applied for over 4 years with no vein patch ruptures. However, in the course of this study two ruptures occurred in the space of one month which did not conform to the usual pattern associated with rupture. Instead of rupture through the centre of a necrotic vein patch, rupture had occurred through a suture line defect between the vein and arterial wall. One case occurred on the seventh postoperative day after discharge from hospital and the patient died at home. The other case occurred in hospital was immediately operated on and the patient survived with no residual neurological deficit. A post-mortem examination on the first patient, operative findings in the second patient and subsequent experiments revealed an unusual and previously unreported cause.

The case reports of both these patients be described followed by a description of the experiments that were performed to elucidate the cause.

17.2 Case Report One

A 63 year old man was admitted with a history of amaurosis fugax of the right eye and transient ischaemic attacks affecting the left arm and hand. The right carotid artery was 60% stenosed and the contralateral artery was 40% stenosed. A right carotid endarterectomy was performed during which TCD monitoring of the right MCA was performed. Arteriotomy revealed a stenosing, ulcerated plaque at the carotid bifurcation which was removed by endarterectomy. The 7 cm long arteriotomy was closed using a vein patch derived from the long saphenous vein of the thigh. Just prior to final suturing of the patch the endarterectomy site was inspected by insertion of a 2.8mm angioscope. A knot was tied in the superior running suture of 6/0 Prolene to

leave a gap of approximately 1cm for insertion of the angioscope. After the angioscope was removed the running suture was continued from the knot to complete suturing of the 1cm gap and tied to the inferior running suture. Therefore, there were three knots around the patch angioplasty, one at the superior apex of the patch and two on the medial side of the patch 1cm apart.

During angioscopic examination, some residual luminal thrombus was detected and removed. Blood flow was restored through the endarterectomised artery and this was then inspected with both B-mode ultrasonography and continuous wave Doppler scanning. No abnormalities were detected and carotid artery blood-flow velocities were within normal limits.



Figure 17.1. Post-mortem specimen showing suture line defect on the medial side of the vein patch angioplasty.

Post-operatively the patient quickly regained consciousness and there was no detectable postoperative cognitive or neurological deficit. The patient was discharged home on the fifth postoperative day. Two days later the patient suffered a sudden haemorrhage from neck wound. The patient quickly lost consciousness and was dead on arrival at hospital.

A post-mortem examination was performed which revealed that the haemorrhage was derived from the operated artery. The vein patch

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angioplasty was intact, however, the suture line was deficient for a 1cm long gap between the two knots on the medial side of the patch. Both knots were intact. The cause of death was attributed to haemorrhage through the gap between the vein patch and arterial wall on the medial side of the artery.

17.3 Case Report Two

A 62 year old sales representative was admitted with frequent left carotid territory transient ischaemic attacks. The left carotid artery was 90% stenosed and the contralateral artery was 40% stenosed. A left carotid endarterectomy was performed and the atheromatous plaque successfully removed from the carotid bifurcation. The arteriotomy was closed with a vein patch harvested from the upper thigh long saphenous vein. Suturing of the patch was performed in the same manner as case one with one knot at the superior apex of the patch and two knots on the medial side to leave a 1 cm gap for insertion of the angioscope. After removal of the angioscope, the running suture attached to the upper knot was continued to complete the suturing of the patch and tied to the lower running suture to leave three knots as previously described.

Postoperatively the patient quickly regained consciousness and there was no detectable neurological or cognitive deficit. On the third postoperative day the patient experienced a sudden swelling of the neck on the side of the operation. The patient was quickly returned to theatre, intubated and ventilated and the wound reexplored. Haemorrhage was originating from a gap between the vein patch and the arterial wall between the two medial knots. Suture material found within the wound was retrieved for further investigation. The vein patch was resutured from the superior apex of the patch to leave just two knots. Post exploration the patient made a full recovery and no neurological or cognitive deficit was apparent. Postoperative CT scan revealed no new infarction.

17.4 Discussion

Prior to using angioscopy as a quality control method, closure of the vein patch angioplasty consisted of using a single, double-ended 6/0 Prolene suture with one knot to secure the suture at the apex of the patch and a further knot on the medial side of the patch.

When angioscopy was introduced, several surgeons tried to prevent unravelling of the upper suture during insertion of the angioscope by tying a knot in continuity with the suture and the needle. When the angioscope was removed, the attached needle and suture was continued to close the remaining defect in the patch. However, the evidence from these two cases suggested that these two knots on the medial side of the patch were a weak point of the repair. Previous descriptions of anastomotic line failures have identified only two possibilities, either the suture material breaks or the knots slip [Brouwers et al, 1991]. Initially it appeared the knot slippage was unlikely as all these operations had been performed by experienced vascular surgeons.

Suture material obtained from the wound in case two underwent careful analysis at the laboratories of Ethicon UK Ltd. The suture material was carefully labelled and examined using scanning electron microscopy (figure 17.3) Three lengths of suture were obtained and labelled A, B and C and the ends of each length were labelled 1 and 2. Examination of the lengths of suture material revealed several possible defects. The middle of length A had a spiral deformity consistent with participation in a knot and a partial cut, possibly caused by a scalpel. End A1 was a sharp cut consistent with being made with a scalpel blade. End A2 was a double ridged deformity consistent with a cut using scissors. The middle of piece B had a deformity consistent with having been grasped with forceps. End B1 was severely deformed in three places consistent with being crushed in forceps. End B2 had a double ridged deformity consistent with a cut using scissors. The middle of piece C had three moderate deformities along its length consistent with either crushing with instruments or possibly participation in a knot. End C1 was consistent with a scissors cut and C2 was consistent with a tension break. However, it was impossible to distinguish which defects were caused at the original CEA and which defects were caused during the emergency re-exploration.

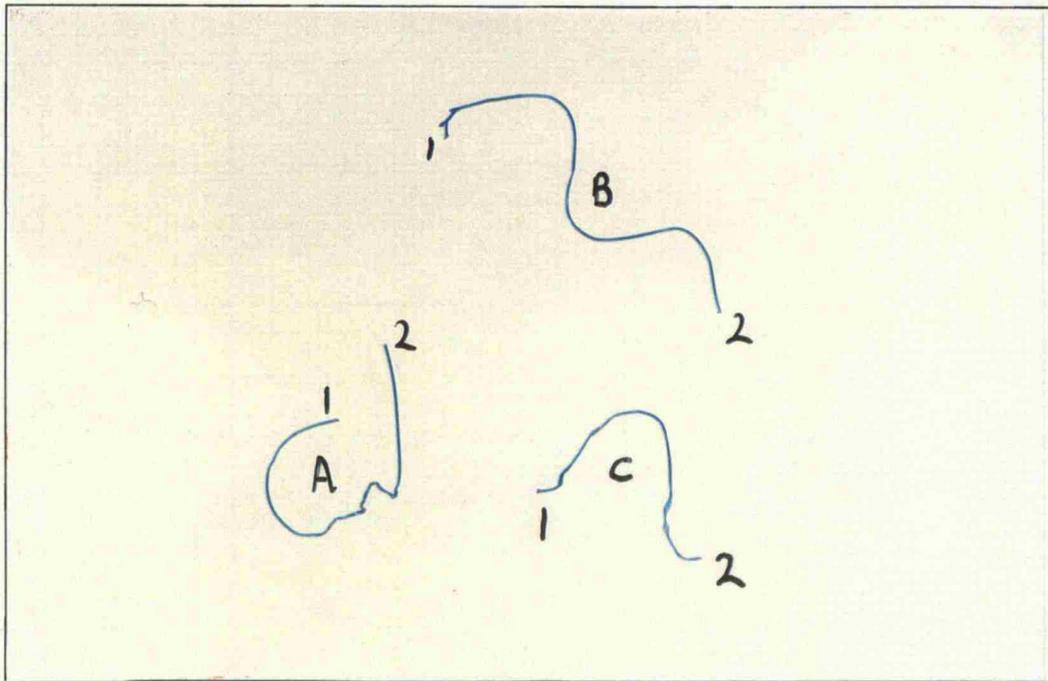


Figure 17.2: Picture illustrating the three pieces of suture material obtained from patient two at reoperation. Each piece has been labelled A, B and C. and each end labelled 1 and 2 to enable identification.



Figure 17.3: Scanning electron micrograph of middle of piece A: an unravelled knot.



Figure 17.4: Scanning electron micrograph of end A1: A scalpel cut.

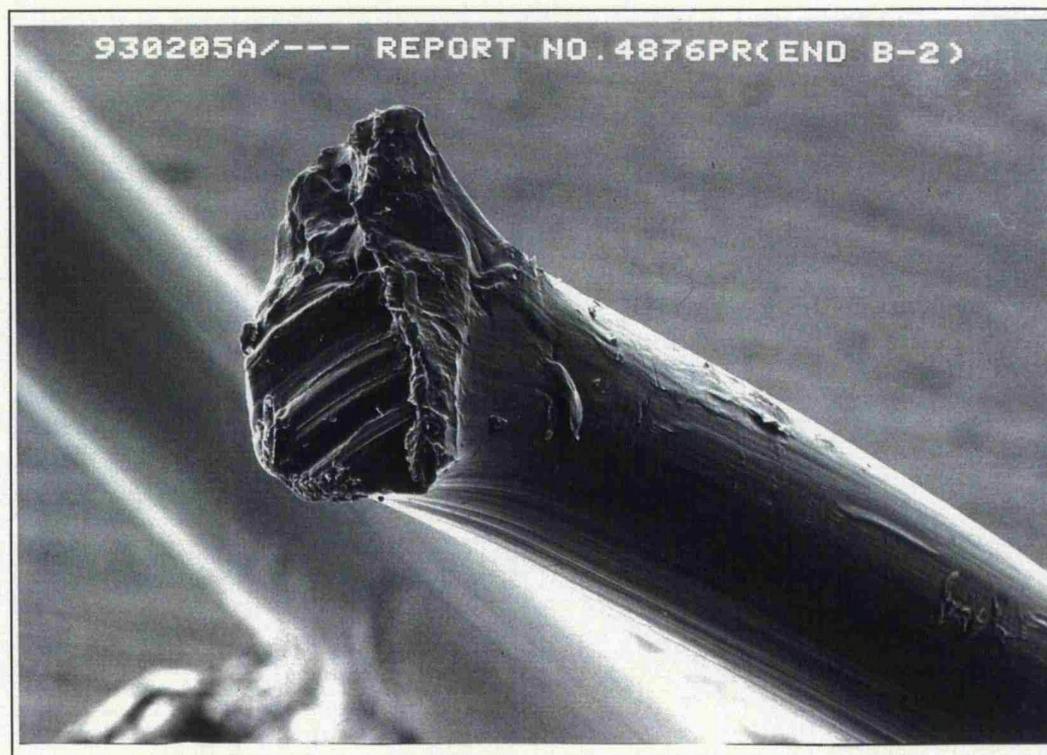


Figure 17.5: Scanning electron micrograph of end B2: A scissors cut.

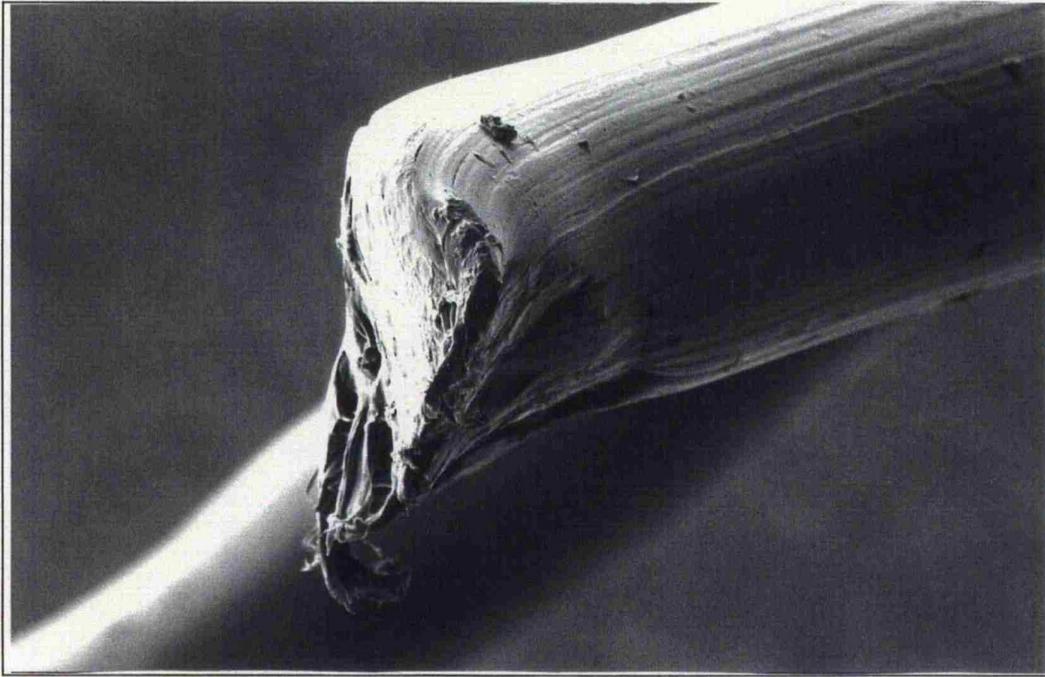


Figure 17.6: Scanning electron micrograph of end A2: A tension break.

Therefore, it was decided to design experiments to test new, undamaged lengths of 6/0 Prolene suture material to investigate both possibilities of either suture disruption or knot slippage in the context of carotid patch angioplasty.

17.5 Investigation of stress on a 6/0 Prolene suture used to close a vein patch angioplasty of the carotid artery.

Introduction

It was proposed that insertion of an extra knot on the medial side of the vein patch angioplasty had altered the distribution of stress on the suture around the patch producing an area of high stress between the two knots resulting in fracture of the 6/0 Prolene suture.

The suture 6/0 Prolene is a very fine non-absorbable suture with a cross-sectional area of $6.82 \times 10^{-5} \text{ cm}^2$ (Ethicon, UK). Prior to angioplasty, a single length of this suture, with a small round bodied needle (size BV-1) at either end had been used to close the vein patch angioplasty and had invariably proved reliable. The technique used was to tie a knot at the superior apex of the patch angioplasty and arteriotomy to leave a relatively long end and a relatively short end. The long end was used to sew the patch to the artery down the medial

lateral side of the patch, around the lower apex and half way up the medial side. The short end was used to sew the medial side until the two ends of the suture met and a knot tied to complete closure of the patch.

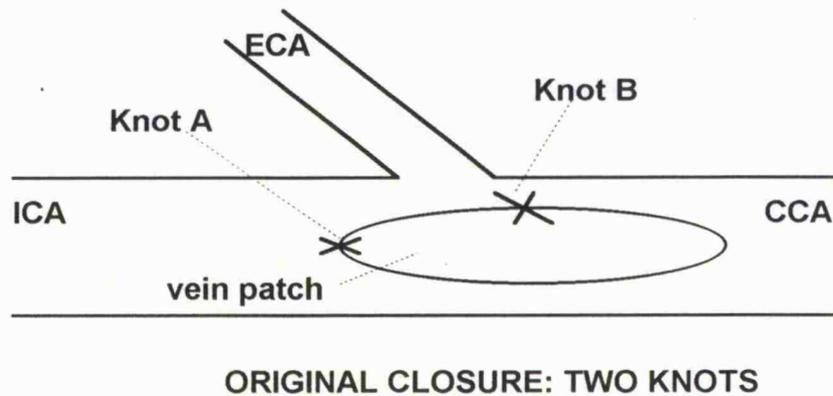
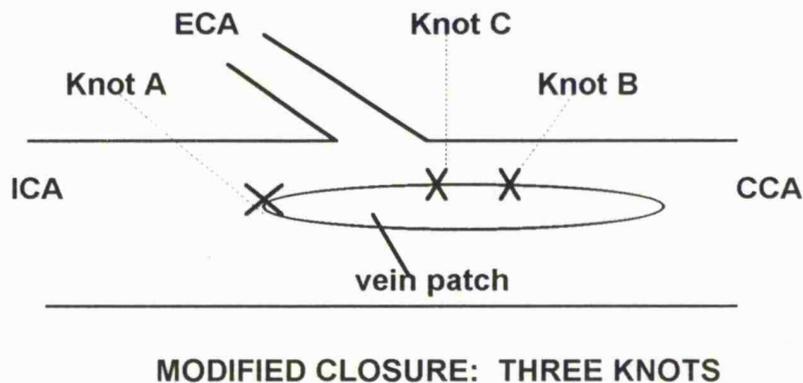


Figure 17.7 Diagram illustrating the original method of suturing the vein patch angioplasty using two knots

In the modified technique, the long end was sutured as normal, but the short end was tied 1 cm from the meeting point to leave a gap for insertion of the angioscope.



17.8 Diagram illustrating the modified method of suturing the vein patch angioplasty using three knots

The knot was tied with a loop of suture in one hand and the remaining single strand and attached needle in the other. After removal of the angioscope the

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single strand and needle was used to complete closure of the patch and tied to the lower strand.

Clamp release and restoration of blood flow causes a distension of the endarterectomy site and the vein patch imposing a lateral and longitudinal strain on the suture material. The use of a continuous running suture allows a small degree of slip and stretch of the suture material so that the stress is redistributed around the patch. However, it was proposed that the introduction of a third knot had created a fixed point, concentrating stress in the 1cm of suture material between the two medial knots. The short length of suture between the two knots was not able to stretch or slip in response to increasing tension and was therefore under greater stress than the suture at other points around the patch. It was proposed that this increased stress was sufficient to break the suture at this point leading to failure of the patch.

To test this theory it was proposed to recreate the situation on a flow rig and subject the suture to appropriate stress and see if fracture occurred.

Materials and Methods

The in-vivo situation was recreated by setting up an in-vitro flow rig. Lengths of fresh lyophilised, gamma irradiated bovine carotid artery and bovine internal jugular vein (Ethicon UK. Ltd, Edinburgh) were reconstituted in water for four hours. A 7cm long longitudinal arteriotomy was made in one wall of the artery and arteriotomy was closed with a bovine jugular vein patch using 6/0 Prolene double-ended suture (Ethicon UK. Ltd, Edinburgh). The 1cm fixed segment was recreated but to exclude knot slippage six throws of suture were used to tie each square knot.

The arteries were transported to the department of medical physics, Edinburgh Royal Infirmary and connected to a computer controlled flow device capable of simulating the blood flow patterns and pressures present in a carotid artery [Hoskins et al, 1989]. Fluid was pumped around the circuit using a gear pump driven by a stepping motor. The flow rate was determined by the rotational speed of the motor, which was controlled by a computer to simulate the pulsatile carotid artery blood flow from an heart beating at 60 beats per minute.

The fluid consisted of 42% solution of glycerol by volume. This has a viscosity of 0.004 kg/m²/sec at 20°C which is the same as blood at 37°C [Hoskins et al,

1989]. The conduit vessels around the flow rig consisted of PVC tubing to which the test artery with patch was connected (Fig. 17.3). Fluid pressure was monitored using a medical barometer (HP78342A) and a cardiac pressure catheter to ensure accurate simulation of human carotid systolic and diastolic conditions. The pressure waveform was adjusted to produce a peak (systolic) pressure of 200mmHg and a minimum (diastolic) pressure of 150mmHg.

A total of five patch repairs were tested. In each case the flow device ran continuously for seven days.

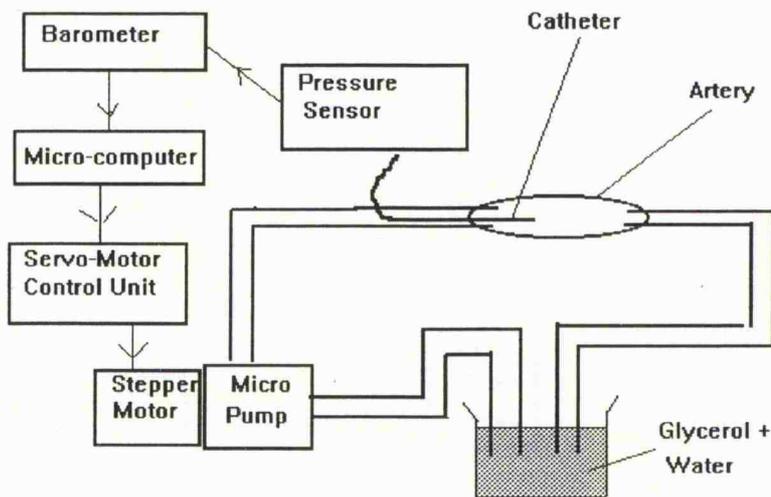


Figure 17.9 Diagram illustrating the Flow Rig used to test the rupture pressure of 6/0 Prolene suture used to close carotid vein patch angioplasty.

Results

Successfully continuous runs were obtained for each artery for the full seven days.

There was no evidence of either patch repair dehiscence nor tensile strength failure of the sutures in any of the samples evaluated

Discussion

Ideally, a greater number of experiments would have been performed but logistical difficulties occurred with the transport of specimens from Leicester, where the suturing of the patch occurred, to Edinburgh, where the flow rig was situated. However, the quality of Prolene sutures varies very little and the aim of the experiment was to investigate whether the suturing method used placed excessive stress on 6/0 Prolene suture material in general [Dobrin, 1988]. Therefore, it may be assumed that the suture material used in the five experiments underwent a rigorous test and was representative of 6/0 Prolene material in general.

The validated intraluminal pressures obtained on the flow rig are higher than one would expect in the clinical situation. Therefore, although the consistency of lyophilised bovine carotid artery only approximates the human artery one can be confident that the pressures exerted on the suture material are of the order necessary to demonstrate disruption if this was going to occur. The fact that rupture did not occur is reassuring.

However, clinical cases of the apparent fracture of Prolene suture material have been reported and these cases have been the basis for laboratory based investigation. Much work has been performed on 6/0 Prolene suture material by Philip Dobrin of Loyola University Medical Center, USA. Dobrin investigated the factors which lead to a reduction in the tensile strength of 6/0 Prolene suture. Knotting, kinking or mild stretching did not significantly reduce the tensile strength of the suture, however, the presence of a stray knot reduced tensile strength by 17% and grasping the suture material with forceps causing deformity significantly reduced tensile strength in a dose-dependent fashion [Dobrin, 1989].

When 6/0 Prolene is used to close a linear carotid arteriotomy in an artery of 5mm radius and the vessel is pressurised to 100mmHg the stress is 32% of the sutures breaking stress representing a safety factor of 3.12 [Dobrin, 1988]. However, suture stress is increased by hypertension and a large vessel radius [Dobrin, 1988]. In our clinical situation, the normal blood pressure experienced by the majority of patients undergoing CEA exceeds 100mmHg which is consistent with expected range of blood pressure for this age range. In addition, patients experience arterial blood pressure in excess of 100mmHg especially during and immediately after CEA. Although strenuous efforts are

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made to maintain normotensive conditions it is not unusual for a patient to experience temporary periods of hypertension and systolic pressures in the region of 180-200mmHg in the immediate postoperative period, may occur due to an imbalance in baroreceptor function associated with CEA. In addition, the use of patch angioplasty tends to increase the vessel diameter greater than normal and may also add to tensile stress the suture and reducing the safety factor for fracture [Dobrin 1988].

Dobrin states that in the laboratory, sutures usually break at a knot, because at this point the filament crosses over itself, creasing its outer surface where the majority of its tensile strength resides (Figure 17.3). When a filament is passed through living tissue in a running fashion, the filament breaks at the region of highest concentration of stress, provided that the local load exceeds the tensile strength of the filament [Dobrin, 1989]. Therefore, theoretically it may be reasonable to speculate that the introduction of an extra knot prevented an even distribution of stress around the suture line, as well as introducing a point of weakness. This, combined with the effect of hypertension and an increased vessel diameter caused by the patch angioplasty, resulted in an excessive local load which resulted in the fracture of the 6/0 Prolene suture.

However, our experimental model which attempted to recreate these conditions failed to result in fracture of the suture material and support the hypothesis. However, an important additional factor in the clinical situation, which has not been excluded by this experiment, is the presence of unrecognised damage to the suture material. This further factor, in addition to the others already described may have been sufficient to exceed the tensile strength of the suture. However, the conclusion from this part of the study is that the results from the flow rig failed to support the hypothesis that fracture of the suture occurred. Therefore, one may assume that new, undamaged lengths of 6/0 Prolene suture material are strong enough to resist fracture when used to secure a carotid patch angioplasty.

The alternative to fracture of the suture is that the knot tied between a double and single strand of the same suture slipped. The experiments performed to test this hypothesis will be described in the next section.

17.6 Investigation of the stress placed on the knots around the patch angioplasty.

Introduction

The findings of the patch after rupture suggested that the introduction of a third knot was the cause of the patch rupture in these cases. The question to be answered was whether the formation of the knot itself was a weak point.

The knot at the apex of the patch, Knot 'A' is a secure knot because it consists of a single strand tied to another single strand of the same suture, using three throws and the stresses are equal on each strand and serve to tighten the knot further. Knot 'B' is formed by the tying of a single strand onto another single strand using three throws. Although a potential site for slippage this knot had been used frequently and there was no reported incidence of knot slippage at this knot. The new knot 'C' was formed by tying a loop consisting of one strand originating from either side of the vein and artery and a single strand originating on the arterial side and consisting of three throws.

It was proposed that the tying of a knot using a loop of suture straddling the defect to tie to a single strand of the same suture end is a weak knot and prone to slippage.

Therefore a series of knot tying experiments were organised to test this theory.

Materials and Methods

These experiments were performed at the Ethicon Research Institute, Edinburgh.

Newly manufactured lengths of 6/0 double ended Prolene of different batches were obtained. Each suture was divided two thirds along its length. the longer end was formed into a loop while the shorter end was left as a single strand. The loop was tied to the single strand using either three throws, four throws or five throws to form the knot. Twenty examples of each knot were formed by the same operator.

For comparison, 20 examples of each knot formed again but this time using a single strand onto another single strand. The suture knot complex was then subjected to tensile test using an Instron Corporation, series IX automated

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materials testing system v4.03e. The purpose of this test was to test whether suture fracture occurred before the knot slipped. The loop end and the single strand end were placed in different jaws of the machine. The pull commenced using a pull rate of 20/second and a crosshead speed of 300mm/min. The load necessary to break the suture was measured in Newtons [N]. Humidity was 50% and room temperature was 24°C

Results

A loop tied to a single strand using 3 throws to form a square knot resulted in 6 out of 20 knots slipping. A loop tied to a single strand using four throws to form a square knot resulted in 3 out of 20 knots slipping. A loop tied to a single strand using 5 throws to form a square knot resulted in 0 out of 20 knots slipping.

There was no statistical difference in the mean load in Newtons [N] required to break the suture if slippage did not occur.

A single strand tied to another single strand using 3 throws resulted in 0 out of 20 knots slipping. The same results were obtained for 4 throws and therefore 5 throws was not performed.

Number of Throws per Knot	Number of sutures	Number of knot slips	Mean Load (95% CI) at suture breakage
3 throws	20	6	3.637 N (2.573 to 4.701)
4 throws	20	3	3.566 N (2.139 to 4.394)
5 throws	20	0	3.621 N (2.625 to 4.352)

Table 17.1 Table illustrating the number of knots slipping before the suture broke for 3, 4 and 5 throws used to form a square knot from a loop onto a single strand.

Discussion

The ability to tie secure knots is fundamental to the safe practice of surgery. This is particularly the case in vascular surgery where fine monofilament, low

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friction sutures are used in anatomical sites subjected to repeated stresses at arterial pressures. During the course of an arterial procedure a surgeon may tie many knots all of which are required to function perfectly to ensure a successful outcome. The failure of just one knot may result in disaster, therefore the association of any knotting technique with slippage is absolutely unacceptable. Therefore, it was disconcerting to discover that the customary knotting technique of applying three throws to form a square knot performed in this situation of tying a loop to a single strand was so unreliable. The use of four throws was more reliable but slippage still occurred and therefore was unacceptable. Only the use of five knots was absolutely secure in this experiment.

One must be cautious not to transpose the results of this experiment directly to the clinical situation. These sutures are manufactured to break at loads much higher than they would be exposed to in the clinical situation [Dobrin, 1988]. Therefore, the load at which these knots slipped may occur only rarely in the clinical situation and in the majority of cases are adequate. However, the safest situation for most surgeons may be that they would prefer a situation where the suture would break before the knot slipped. The results of this experiment would suggest that the use of five knots to form a square knot is the only technique which ensures this level of safety when tying a loop onto a single strand.

The use of three throws to tie a square knot was reliable when tying two single strands.

One should consider that these results relate to the knotting ability of one surgeon. It is hoped that in further experiments the knotting ability of other surgeons may be tested in a similar way.

17.7 Conclusions

The results of these experiments would suggest that the cause of the patch disruptions in these two cases was knot slippage although suture breakage as a cause cannot be completely discounted. Since the occurrence of these two cases the suturing technique has been modified to eliminate knot C altogether. Instead of tying a knot while the angioscope was inserted the suture is held under tension and then suturing continued once the angioscope is removed

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and knot B is formed as in the original situation. No further patch disruptions have been encountered. Therefore, it is possible to avoid the position of tying a loop onto a single strand of the same suture and this is to be recommended. However, if such a situation is unavoidable, the results of this study would suggest that at least five throws are needed to form a secure square knot.

CHAPTER 18
PATCH FRAYING

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18.1 Introduction

In chapter seventeen I described how the cause of two patch angioplasty ruptures was attributed to the insertion of an extra knot on the medial side of the arteriotomy to enable insertion of the angioscope. As a result of the findings of that investigation operative technique was modified to exclude the presence of a third knot. Therefore, this had returned the suturing of the patch angioplasty to a situation where only two knots were present around the patch, a technique which had been used in many hundreds of carotid endarterectomy without patch rupture.

I was surprised, therefore, when our routine follow-up of the patients in this study, discovered that another patient had died of patch rupture even though the original suturing method had been used. Difficulty in ascertaining the cause of this rupture was encountered because the patient had died at his home in Preston, Lancashire. Fortunately, I was able to contact the pathologist prior to performance of the post-mortem and direct him to the area of interest. As a result, the post-mortem findings revealed yet another unusual and interesting cause of this complication.

18.2 Case Report

A 67 year old man was admitted with a history of a minor stroke and amaurosis fugax attributable to the territory of the left carotid artery. The left carotid artery was 90% stenosed and the contralateral artery was occluded. A left carotid endarterectomy was performed and the atheromatous plaque was successfully removed from the carotid bifurcation. In the absence of suitable vein the arteriotomy was closed with a Dacron patch. To do this a suitably shaped length of patch was cut from woven Dacron aortic tube graft.

Suturing of the patch with 6/0 Prolene commenced at the superior apex of the patch with a knot tied to anchor the suture. From this knot a continuous running suture was taken down the lateral side around the inferior apex of the patch and one third of the way up the medial side. The short end of the suture was run down the medial side until a 1 cm gap existed between the two suture ends. The suture ends were held under tension as the angioscope was inserted and once removed the upper suture was continued and tied end-to-

end with the lower suture. Therefore the angioplasty was completed with a total of two knots.

Post-operatively the patient quickly regained consciousness and no neurological or cognitive deficit was detected. The patient was discharged from hospital on the fourth post-operative day to his home in Lancashire. Our routine telephone follow-up of patients discovered that the patient had been found dead at home on the seventh postoperative day. The patient's General Practitioner had attended the scene and informed me that the cause of death appeared to be haemorrhage from the operative site. However, a post-mortem examination was scheduled to take place the following day at the local hospital.

Fortunately, I was able to discuss the case with the pathologist prior to the post-mortem and inform him of our area of interest. The pathologist kindly agreed to send me the pathological specimen of the carotid artery once the Coroner's inquest was complete.



Figure 18.1: Photograph of a post-mortem carotid endarterectomy specimen showing the fraying of Dacron patch angioplasty leading to fatal haemorrhage

Patch Fraying

Examination of the specimen revealed that the haemorrhage had originated from the operated artery. However in this case the suture line was intact. Instead, the Dacron patch material had frayed near the edge of the patch and therefore blood had ruptured through the patch.

18.3 Discussion

Dacron patches are available which are specially manufactured for use as carotid patches. The manufacture of these patches enables the material to be cut to size without the risk of fraying of the cut edge. However aortic tube graft is designed to be used as a tube replacing the lumen of the diseased aorta. Therefore tube graft is designed to be cut transversely without fraying but is not manufactured to be cut longitudinally because in aortic surgery this would never be performed. This fact was unknown to the surgeon who having used this technique several times before without incident did not suspect a problem.

However, on this occasion, suturing may have been performed too close to the cut edge of the Dacron material and the tendency for this material to fray was exposed after the repeated stress of carotid arterial pulsation.

This case highlights the importance of using a specific material for a specific purpose and not assuming that material manufactured for one purpose can be modified in theatre for use in another.

CHAPTER 19

CONCLUSIONS AND PROSPECTS FOR FUTURE RESEARCH

Conclusions and Prospects for Future Research

CONCLUSIONS AND PROSPECTS FOR FUTURE RESEARCH

In the first part of this thesis I described how intraoperative embolisation had been determined as the major cause of perioperative morbidity and mortality during carotid endarterectomy. This assumed further significance when the results of the European Carotid Surgery Trial and the North American Symptomatic Carotid Endarterectomy Trial studies were published showing that carotid endarterectomy was significantly better than medical therapy alone at preventing disabling strokes in patients with severe carotid artery stenosis. This meant that an increased number of patients would be referred for operation, however, the authors of both studies emphasised that the benefit of carotid endarterectomy was dependent on a low rate of perioperative neurological deficits. Therefore, the detection and elimination of perioperative complications became paramount.

Several large retrospective studies identified a wide range of different mechanisms by which perioperative strokes could occur. The two main strategies that developed to reduce perioperative strokes were intraoperative monitoring and completion quality control. Transcranial Doppler ultrasound was a new method which was proposed as a monitoring technique because it enabled both an estimation of cerebral blood supply and the detection of intraoperative cerebral emboli. Several studies demonstrated that TCD could detect intraoperative emboli, but the incidence of embolisation appeared much higher than the incidence of neurological deficits. However, because none of these studies was set up to specifically examine clinical outcome, the exact clinical relevance of these TCD detected emboli remained uncertain.

The main aim of the second part of this thesis was to determine the incidence and clinical relevance of TCD detected intraoperative embolisation during carotid endarterectomy. The strategy adopted to achieve this consisted of dividing the operation into its constituent stages and determining the incidence and character of emboli for each stage. Emboli were characterised into air or particulate and the clinical relevance of the emboli was established by pre- and postoperative investigations consisting of neurology and cognitive function tests; retinal fundoscopy and automated visual fields; CT and MRI brain scans.

Chapter 5 describes the number and character of emboli occurring in each operative stage. The majority of intraoperative emboli occurring during carotid

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endarterectomy were characteristic of air, however, emboli occurring during the dissection and recovery stages were characteristic of particulate emboli. The results from the neurological and cognitive function tests in chapter 6 established that air emboli, in the volumes normally associated with carotid endarterectomy were not associated with the development of cognitive or neurological deficits. However, more than 10 particulate emboli occurring during dissection was associated with a significant deterioration in cognitive function. Gross, persistent particulate embolisation during the recovery phase of the operation heralded the thrombosis of the operated artery and was associated with the development of major neurological deficits. The TCD detection of particulate emboli during this phase occurred before the development of neurological signs and immediate operative intervention to correct the defect, based on the TCD evidence, had the potential to avoid permanent neurological deficits.

A major component of the study was the differentiation of emboli into air and particulate based on existing TCD criteria in combination with an assessment of the likely nature of the emboli based on the phase of the operation in progress at the time of detection. Although, probably imprecise, this approach has yielded a clinically useful method of assessing TCD emboli occurring during carotid endarterectomy and has already been adopted into clinical practice. However, this method is less reliable during other stages of the operation when the two forms of emboli may occur together. However, in this study no significant neurological deficits were associated with these other stages of the operation, although there were a number of unexplained cognitive deficits which may be explained by more specific identification of embolic character. A more precise method of differentiation based on Wigner spectral analysis of TCD signals is currently under investigation at our centre and early results are encouraging but further work needs to be done before this is clinically applicable.

Another important factor in the study was the use of several different clinical methods to assess outcome in the same cohort of patients. In particular the negative results from the ophthalmological study and the CT and MRI brain scans were reassuring that no significant clinical episodes had been missed and added strength to the positive findings. In the ophthalmology study there was no significant association between TCD detected embolisation and new retinal infarcts or visual field deficits. It is possible that transient retinal

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embolisation occurred before the postoperative examinations were performed, but the main aim of the study was to detect clinically significant defects and these did not occur. Evidence from the preoperative funduscopy and visual field findings suggest that only emboli causing the occlusion of major retinal blood vessels have a significant effect on visual field scores. However, a number of patients had evidence of 'silent' retinal embolisation on funduscopy but no symptoms of either amaurosis fugax or retinal infarction. Previous studies have established that fundoscopic evidence of retinal emboli is associated with a poorer prognosis and has been advocated as an indication for performing carotid endarterectomy. The fact that these patients with silent retinal emboli had presented with embolic symptoms, other than in the eye, would appear to support this. Therefore it may be justified to consider these patients in the same prognostic group as patients with silent brain infarction. This may be an interesting field for future research.

In this study silent cerebral infarction was not detected by either CT or MRI scanning. Infarcts were only associated with the three patients experiencing gross particulate embolisation during the recovery phase. Therefore, one may conclude that TCD detected embolisation is not associated with silent brain infarction. The CT findings were confirmed by the more sensitive technique of MRI scanning which would have been expected to detect early infarcts if they had occurred.

The third part of the thesis was concerned with a comparison of quality control techniques in the same cohort of patients. Quality control can be described as the application of methods to detect errors of surgical technique and the ideal technique would detect all known errors, be simple to apply and interpret and not be associated with any adverse complications. Problems with applying completion angiography at this site had prompted a search for alternative techniques and among those proposed were angioscopy, B-mode ultrasound and continuous wave Doppler. However, in the absence of a comparative study using these techniques in the same cohort of patients, assessment as to the most appropriate technique to apply to carotid endarterectomy remained unresolved. Therefore, the aim of this study was to apply these three techniques to assess the same cohort of patients and compare their suitability for routine use in carotid endarterectomy. In addition, the potential of TCD as a quality control technique was investigated. Although individual instances of TCD monitoring detecting errors of surgical technique had been described, no

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study had been performed to quantify and qualify the number of cases when TCD provided clinically useful information. Therefore, in addition to the completion methods described above, this study aimed to investigate the role of TCD as a continuous quality control measure detecting errors of operative technique as they occurred during the operation.

Chapter 11 describes how angioscopy proved to be a reliable and simple method to apply, detecting intimal flaps and fragments of intraluminal thrombus in a significant proportion of patients. The main advantage of angioscopy was the detection and correction of defects prior to restoration of blood flow. In particular this prevented the distal embolisation of the fragments of thrombus which may have occurred on clamp release.

In contrast, B-mode ultrasound and continuous wave Doppler detected no additional intimal flaps or thrombus and were technically unsatisfactory in 24% and 9% of patients respectively. In addition both techniques produced a significant number of false positives leading to unnecessary re-explorations and a decline in the surgeons' confidence in the techniques.

TCD proved to be useful in detecting technical error in addition to the detection of particulate emboli during dissection and recovery described above. In particular, TCD was useful in detecting shunt malfunction especially shunt kinking and occlusion which occurred in 13 patients. TCD also detected puncture of the distal retaining balloon in two cases and the criteria for diagnosing this error have been described.

In conclusion, a combination of TCD monitoring and completion angioscopy provided the highest yield in detecting technical error and determining the cause of perioperative morbidity and mortality. In particular, the ability of TCD to provide an early warning of thrombosis of the operated artery in the immediate postoperative period may have a significant role in reducing the morbidity and mortality resulting from this serious complication.

However, the main question arising from this work consists of whether the routine application of continuous intraoperative TCD monitoring and completion angioscopy during carotid endarterectomy would significantly reduce perioperative morbidity and mortality? The answer to this question may be

Conclusions and Prospects for Future Research

provided by a randomised controlled trial and this will form the next phase of research to be undertaken in this area.

APPENDIX ONE

Neurologic and Cognitive Tests

NEUROLOGIC AND PSYCHOMETRIC TESTS

NEUROLOGY

Medical Research Council Grading of Muscle Weakness [Clarke, 1987]

Grade	Definition
0	No contraction
1	Flicker of contraction
2	Active movement with gravity eliminated
3	Active movement against gravity
4	Active movement against gravity and resistance
5	Normal power

The National Institute of Health (NIH) Stroke Scale

1a. Level of Consciousness

0 = Alert, keenly responsive.

1 = Not alert, but rousable by minor stimulation to obey, answer or respond

2 = Not alert, requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not Stereotyped).

3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, areflexic.

1b. LOC Questions

0 = Answers both questions correctly

1 = Answers one question correctly

2 = Answers neither question correctly

1c. LOC Commands

0 = performs both tasks correctly

1 = performs one task correctly

2 = performs neither task correctly

Neurologic and Cognitive Tests

2. Best Gaze

0 = Normal

1 = Partial gaze palsy.

2 = Forced deviation, or total gaze paresis not overcome by the oculocephalic maneuver.

3. Visual

0 = no visual loss

1 = partial hemianopia

2 = complete hemianopia

3 = bilateral hemianopia (blind including cortical blindness)

4. Facial Palsy

0 = normal symmetrical movement

1 = minor paralysis (flattened nasolabial fold, asymmetry on smiling)

2 = partial paralysis (total or near total paralysis of lower face).

3 = complete paralysis of one or both sides.

5. Motor Arm

0 = no drift, limb hold 90 (or 45) degrees for full 10 seconds

1 = drift before 10 seconds but does not hit bed or other support

2 = some effort against gravity but cannot get to or maintain (if cued) 90 or 45 degrees.

3 = no effort against gravity, limb falls.

4 = no movement

9 = amputation or joint fusion.

6. Motor Leg

0 = no drift, holds leg at 30 degrees for 5 seconds

1 = drift, leg falls but does not hit bed before 5 seconds

2 = some effort against gravity; leg falls to bed within 5 seconds.

3 = no effort against gravity, leg falls immediately

4 = no movement

9 = amputation, joint fusion.

7. Limb Ataxia

0 = absent

1 = present in one limb

2 = present in two limbs. Describe arm or leg.

8. Sensory

0 = normal no sensory loss

1 = mild to moderate sensory loss; feels pinprick less sharp on affected side.

2 = severe to total sensory loss; not aware of being touched.

Neurologic and Cognitive Tests

9. Best Language

- 0 = no aphasia; normal
- 1 = mild to moderate aphasia
- 2 = severe aphasia; fragmentary expression.
- 3 = mute

10. Dysarthria

- 0 = normal
- 1 = mild to moderate; slurs some words.
- 2 = severe, unintelligible, mute/anarthic.

11. Extinction and inattention

- 0 = no abnormality
- 1 = visual, tactile, auditory, spatial or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities.
- 2 = profound hemi-inattention or hemi-inattention to more than one modality

12. Distal Motor Function.

- 0 = normal (no flexion after 5 seconds)
- 1 = some extension after 5 seconds.
- 2 = No voluntary extension after 5 seconds.

A significant deterioration was considered to be an increase in score by 2 points.

Rankin Disability Scale (RDS) : to be scored at detection of defect and 7 days postoperatively or discharge if earlier [Rankin, 1957].

0 =	no neurological deficit
1 =	minor symptoms, not interfering with lifestyle
2 =	minor handicap - symptoms may lead to some restriction of lifestyle but do not interfere with independence.
3 =	moderate handicap - symptoms significantly restrict patients lifestyle and/or prevent total independence.
4 =	moderately severe handicap - symptoms prevent an independent existence but the patient does not require constant supervision
5 =	severe handicap - patient totally dependent and requires constant supervision night and day

Neurologic and Cognitive Tests

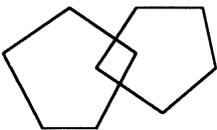
COGNITIVE FUNCTION TESTS

30 Point General Cognitive Assessment

1. What is the (Year, Season, Month, Date, Day) ? -Max = 5 points
2. Where are we (Country, County, Town, House No. and Street) or home address. Max = 5 points
3. Name 3 objects: ask the patient to repeat all 3 - Repeat until patient knows all 3. Max = 3 points
4. Either: ask the patient to count backwards from 100 in 7's or ask the patient to spell WORLD backwards. Max = 5 points
5. Ask the patient to name the objects in (3) above. Max = 3 points
6. Ask the patient to name a pencil and a watch as you point to them. Max = 2 points
7. Ask the patient to repeat ' No ifs, ands or buts'. Max = 1 point
8. Ask the patient to follow a 3 stage command: 'Take the paper in your right hand. Fold it in half. Put it on the floor'. Max = 3 points
9. Ask the patient to read and obey:- 'CLOSE YOUR EYES' Max = 1 point
10. Ask the patient to write a sentence below

Max = 1 point

11. Ask the patient to copy the design. Max = 1 point.



Maximum score = 30 points.

Neurologic and Cognitive Tests

Wechsler Cognitive Function Tests

1. Wechsler orientation Version A and B.

A. Personal and Current Information Max = 4

1. Age
2. When born
3. Prime minister
4. Previous

B. Orientation Max = 5

1. Year
2. Month.
3. Day
4. Where now
5. City in

Wechsler Concentration version A

1. (30") 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1.

Count backwards from 20 to 1. Record errors and time in seconds. Time limit is 30 seconds. Score 2 points if no errors within time limit. Score 1 point if 1 error within time limit. Score extra point if no errors and completes within 10 seconds. Max = 3.

2. (30") A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P, Q, R, S, T, U, V, W, X, Y, Z.

Record time and errors. Time limit is 30 seconds.

Score 2 points if no errors, 1 point if 1 error and 1 extra point if no errors and completed within 10 seconds. Max = 3

3. (45") 1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40.

Record time and errors in time limit of 45 seconds.

Score 2 points if no errors, 1 point if 1 error and 1 extra point if no errors and completed within 20 seconds. Max = 3.

Wechsler Concentration- Version B

1 and 2 are the same tasks.

3. (45") 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53.

Same scoring as version A.

Wechsler Logical Memory-Version A

A. Anna Thompson/ of south/ Leeds/ employed/ as a cleaner/ in an office building/ reported/ at the police station/ that she had been held up/ on Boar Lane/ the night before/ and robbed/ of fifteen pounds/. She had four/ little children/ the rent/ was due/ and they had not eaten/ for two days/. The officers/ touched by the womans story/ made up a purse for her/.

Score for A = number of memories

Neurologic and Cognitive Tests

B. The American/ liner/ New York/ struck a mine/ near Liverpool/ Monday/ evening/. In spite of a blinding snowstorm/ and darkness/ the sixty/ passengers including 18/ women/ were all rescued/ though the boats/ were tossed about/ like corks/ in the heavy sea/. They were brought into port/ the next day/ by a British steamer/.

Score for B = Number of memories.

Average Score = (A+B)/2=?

Wechsler Logical Memory - Version B

A. Dogs/ are trained/ to find/ the wounded/ in war time/. Police dogs/ are also trained/ to rescue/ drowning people/. Instead of running/ down to the water/ and striking out/ they are taught/ to make / a flying leap/ by which they save/ many swimming strokes/ and valuable/ seconds of time/. The European sheep dog/ makes the best/ police/ dog/.

B. Many/ school/ children/ in northern/ France/ were killed/ or fatally hurt/ and others/ seriously injured/ when a shell/ wrecked/ the schoolhouse/ in their village/. The children/ were thrown/ down a hillside/ ans across/ a ravine/ a long distance/ from the schoolhouse/. Only two/ children/ escaped uninjured.

Version B was scored the same as Version A.

Wechsler Digit Span - Version A.

Digits Forward	Score	Digits Backward	Score
6.4.3.9.	4	2.8.3.	3
7.2.8.6.	4	4.1.5.	3
4.2.7.3.1.	5	3.2.7.9.	4
7.5.8.3.6.	5	4.9.6.8.	4
6.1.9.4.7.3.	6	1.5.2.8.6.	5
3.9.2.4.8.7.	6	6.1.8.4.3.	5
5.9.1.7.4.2.3.	7	5.3.9.4.1.8.	6
4.1.7.9.3.8.5.	7	7.2.4.8.5.6.	6
5.8.1.9.2.6.4.7.	8	8.1.2.9.3.6.5.	7
3.8.2.9.5.1.7.4.	8	4.7.3.9.1.2.8.	7

Score = Forward score + Backward score.

Neurologic and Cognitive Tests

Wechsler Digit Span - Version B

Digits Forward	Score	Digits Backward	Score
2.8.6.1.	4	7.5.1.	3
5.3.9.4.	4	2.9.6.	3
7.4.2.9.6.	5	3.5.8.2.	4
8.5.1.6.4.	5	9.6.1.7.	4
7.2.9.5.3.6.	6	4.7.1.8.6.	5
8.4.2.7.5.1.	6	3.9.2.6.1.	5
7.4.8.2.5.9.1.	7	6.3.9.1.5.8.	6
8.3.9.6.1.5.2.	7	4.8.1.6.3.7.	6
2.6.9.5.8.3.7.1.	8	5.4.9.2.7.3.6.	7
3.7.2.9.4.1.5.8.	8	2.5.1.9.4.7.3.	7

Version B scored the same as Version A.

Wechsler Paired Associate - Version A

First	Present- ation	Second	Present- ation	Third	Present- ation
metal -	iron	rose -	flower	baby -	cries
baby -	cries	obey -	inch	obey -	inch
crush -	dark	north -	south	north -	south
north -	south	cabbage-	pen	school -	grocery
school -	grocery	up -	down	rose -	flower
rose -	flower	fruit -	apple	cabbage-	pen
up -	down	school -	grocery	up -	down
obey -	inch	metal -	iron	fruit -	apple
fruit -	apple	crush -	dark	crush -	dark
cabbage-	pen	baby -	cries	metal -	iron

first recall	easy	hard	second recall	easy	hard	third recall	easy	hard
north			cabbage			obey		
fruit			baby			fruit		
obey			metal			baby		
rose			school			metal		
baby			up			crush		
up			rose			school		
cabbage			obey			rose		
metal			fruit			north		
school			crush			cabbage		
crush			north			up		

Neurologic and Cognitive Tests

After reading the first presentation , the first recall was tested after allowing 5 seconds to pass. After the first recall was completed the second presentation was read after a 10 second rest.

Scoring. One point was scored for a correct response within 5 seconds. The final score was obtained as follows: All points obtained on the easy association were added together and halved. This total was then added to the total number of points scored on the hard associations to give the final score.

Wechsler Paired Associate - Version B

First	Present- ation	Second	Present- ation	Third	Present- ation
Come -	Go	Knife -	Sharp	Country -	France
Lead -	Pencil	Jury -	Eagle	Necktie -	Cracker
In -	Although	Country -	France	Murder -	Crime
Country -	France	Lead -	Pencil	Dig -	Guilty
Dig -	Guilty	Necktie -	Cracker	Come -	Go
Lock -	Door	Murder -	Crime	In -	Although
Jury -	Eagle	Lock -	Door	Lock -	Door
Murder -	Crime	Come -	Go	Jury -	Eagle
Knife -	Sharp	Dig -	Guilty	Lead -	Pencil
Necktie -	Cracker	In -	Although	Knife -	Sharp

First Recall	Easy	Hard	Second Recall	Easy	Hard	Third Recall	Easy	Hard
Knife			Lock			Lead		
Lead			Dig			Lock		
Jury			Come			Necktie		
Country			Jury			Come		
In			Knife			Dig		
Murder			Country			Country		
Necktie			In			Jury		
Lock			Murder			Knife		
Come			Necktie			In		
Dig			Lead			Murder		

Version B was scored using the same method as Version A.

APPENDIX TWO : PATIENT RECORD

Appendix 2 : Patient Record

LEICESTER VASCULAR RECORD - CAROTID ENDARTERECTOMY

NAME	DOB	GP
ADDRESS	No.	SURGERY
ADMISSION DATE ___/___/___	CONSULTANT	WARD

ADMISSION INFORMATION

ADMISSION SOURCE (ring answers)	1 waiting list 2 accident and emergency 3 outpatients 4 GP 5 internal hospital referral consultant = 6 external hospital referral consultant =
ADMISSION TYPE	1 elective 2 emergency 3 urgent

DISCHARGE INFORMATION

DISCHARGE DATE ___/___/___	to	1 home :
OPERATION AND FINAL DIAGNOSIS		2 internal transfer to ward :
		3 external transfer to :

PATIENT OUTCOME	1 improved 2 same 3 worse 4 died cause =
-----------------	--

OUTPATIENT APPOINTMENT	Y / N	in ___ weeks / months	___/___/___
Drugs on discharge	:		
Complications	Y / N	(see back page for details)	

Appendix 2 : Patient Record

PRESENTING COMPLAINT

LEFT CAROTID TERRITORY SYMPTOMS (circle and complete)

	DURATION OF SYMPTOMS	DATE OF MOST RECENT EPISODE	NUMBER OF EPISODES
ASYMPTOMATIC			
AMAUROSIS FUGAX			
CRAO			
TIA			
STROKE WITH RECOVERY			
STROKE WITH RESID DEFICIT			

RIGHT CAROTID TERRITORY SYMPTOMS (circle and complete)

	DURATION OF SYMPTOMS	DATE OF MOST RECENT EPISODE	NUMBER OF EPISODES
ASYMPTOMATIC			
AMAUROSIS FUGAX			
CRAO			
TIA			
STROKE WITH RECOVERY			
STROKE WITH RESIDUAL DEFICIT			

HISTORY OF PRESENTING COMPLAINT

Appendix 2 : Patient Record

PAST MEDICAL HISTORY

DIABETES	YES / NO duration insulin/oral diet	HYPERTENSION	YES / NO on treatment
		CLAUDICATION	YES / NO
CARDIAC	previous MI YES/ NO dates angina YES / NO	SMOKING	YES / NO / EX cigarettes / cigar / pipe how many____ how long____ how long since stopped

MAJOR ILLNESSES IN PAST

PREVIOUS OPERATIONS, ANGIOPLASTIES AND ANGIOGRAMS

SYSTEMIC ENQUIRY

CARDIOVASCULAR	RESPIRATORY
GASTROINTESTINAL	GENITOURINARY
FAMILY HISTORY	NEUROLOGICAL
SOCIAL HISTORY	
ALLERGIES	MEDICATIONS

Appendix 2 : Patient Record

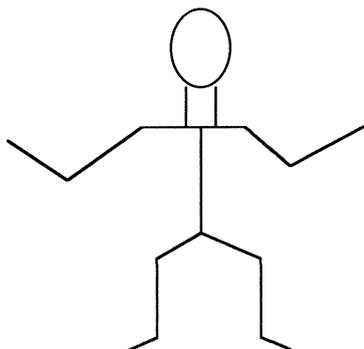
GENERAL PHYSICAL EXAMINATION

Appendix 2 : Patient Record

VASCULAR EXAMINATION

PULSE	BRUIT
FULL ++	
WEAK +	SOFT 1
ABSENT -	LOUD 2

COMMENTS



NEUROLOGICAL EXAMINATION (and see separate neurological and cognitive function tests)

Neurological deficits

NIH Stroke Scale Score _____

Rankin Disability Scale _____

SUMMARY OF CLINICAL FINDINGS

Appendix 2 : Patient Record

PRE-OPERATIVE DUPLEX SCAN ASSESSMENT

LEFT CAROTID	PROXIMAL CCA	DISTAL CCA	ICA	ECA
% STENOSIS				
PLAQUE MORPHOLOGY				

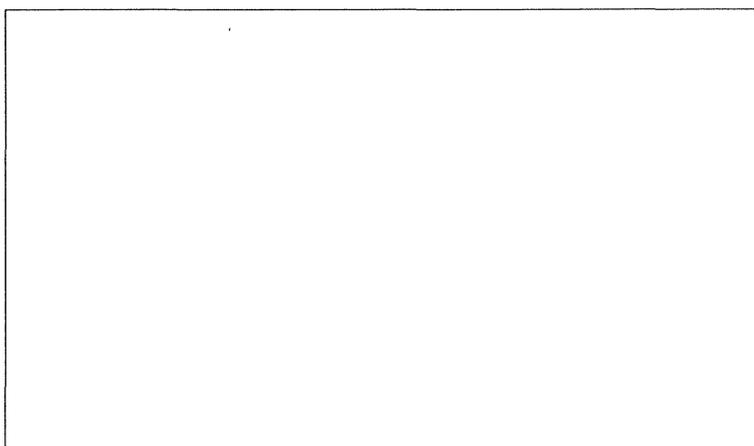
PLAQUE MORPHOLOGY :

Plaque surface : 1 = smooth, 2 = irregular, 3 = ulcerated, 4 = ulcerated +thrombus, 5 = thrombus (not ulcerated).

Plaque composition : 1 = echolucent, 2 = predominantly echolucent, 3 = predominantly echogenic, 4 = echogenic.

RIGHT CAROTID	PROXIMAL CCA	DISTAL CCA	ICA	ECA
% STENOSIS				
PLAQUE MORPHOLOGY				

DIAGRAM OF SYMPTOMATIC BIFURCATION



ANY CHANGE FROM FIRST ULTRASOUND SCAN

Appendix 2 : Patient Record

OPERATION 1 (CAROTID ENDARTERECTOMY)

DATE ___/___/___ SURGEON _____ CON / SR
 ASSISTANT (S) _____
 ANAESTHETIST _____
 OPERATION SIDE LEFT / RIGHT _____
 ELECTIVE/ EMERGENCY/ URGENT _____

OPERATION DETAILS

CAROTID SINUS BLOCK	Y / N	ARTERIOTOMY LENGTH	cm
SHUNT UTILISED	Y / N	TOTAL BLOOD LOSS	ml
SHUNT TIME	_____ mins	RE-EXPLORATION NECESSARY	YES / NO
CLAMP TIMES	___ & ___ mins	REASON	
VEIN PATCH	Y / N	EASE OF ENDARTERECTOMY	DIFF / AVERAGE / EASY
PTFE PATCH	Y / N	LEVEL OF BIFURCATION	HIGH/ NORMAL / LOW
DACRON PATCH	Y / N	INTIMAL TACKING SUTURES	PROX / MID / DISTAL
HEPARIN	Y / N	PLAQUE MORPHOLOGY	
PROTAMINE	Y / N	TIME FOR HAEMOSTASIS	

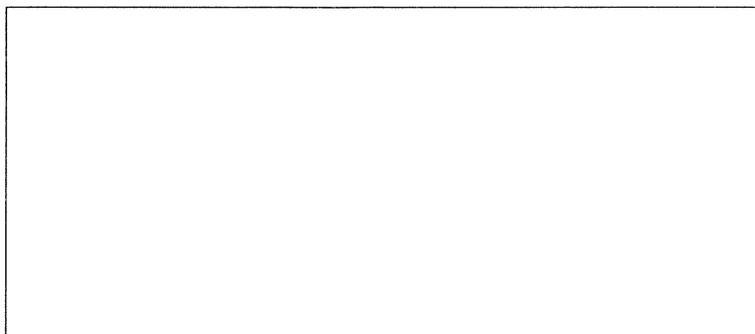


DIAGRAM OF OPERATIVE PROCEDURE

COMMENTS :

Appendix 2 : Patient Record

PERIOPERATIVE MONITORING

TRANSCRANIAL DOPPLER

detection of shunt kinking or malposition YES / NO

DETECTION OF INTRA-OPERATIVE EMBOLI

DISSECTION	SHUNT OPENING	DURING SHUNTING	ECA FLOW	ICA FLOW	MANIPULA TION	RECOVERY

COMMENTS :

ANGIOSCOPY FINDINGS

CCA	PROXIMAL END-POINT	MIDPOINT	ECA	DISTAL END-POINT	ICA

0 = normal 3 = major thrombus > 3mm 6 = stenosis < 30%
 1 = fixed fronds 4 = intimal flap < 3 mm 7 = stenosis > 30%
 2 = minor thrombus < 3 mm 5 = intimal flap > 3 mm 8 = occlusion

COMMENTS :

INTRA-OPERATIVE B-MODE ULTRASOUND

CCA	PROXIMAL END-POINT	MIDPOINT	ECA	DISTAL END-POINT	ICA

0 = normal 3 = major thrombus > 3mm 6 = stenosis < 30%
 1 = fixed fronds 4 = intimal flap < 3 mm 7 = stenosis > 30%
 2 = minor thrombus < 3 mm 5 = intimal flap > 3 mm 8 = occlusion

COMMENTS :

Appendix 2 : Patient Record

PERI-OPERATIVE MONITORING

CONTINUOUS WAVE DOPPLER (peak systolic velocity in cm/sec measured at 60o to plane of artery)

CCA	PROXIMAL END-POINT	MIDPOINT	ECA	DISTAL END-POINT	ICA

MEAN PEAK VELOCITY READINGS ABOVE 125 cm/sec CONSIDER FOR RE-EXPLORATION.

COMMENTS :

INTRAVASCULAR ULTRASOUND

CCA	PROXIMAL END-POINT	MIDPOINT	ECA	DISTAL END-POINT	ICA

- | | | |
|---------------------------|--------------------------|--------------------|
| 0 = normal | 3 = major thrombus > 3mm | 6 = stenosis < 30% |
| 1 = fixed fronds | 4 = intimal flap < 3 mm | 7 = stenosis > 30% |
| 2 = minor thrombus < 3 mm | 5 = intimal flap > 3 mm | 8 = occlusion |

WALL THICKNESS AT EACH POINT

COMMENTS :

Appendix 2 : Patient Record

IMMEDIATE POSTOPERATIVE NEUROLOGICAL EXAMINATION

INTRA-OPERATIVE NEUROLOGICAL DEFICIT YES / NO
POST-OPERATIVE NEUROLOGICAL DEFICIT YES / NO
(time after clamp release when deficit developed) _____

NEUROLOGICAL DEFICITS

NIH STROKE SCALE SCORE _____

RANKIN DISABILITY SCALE SCORE _____

Appendix 2 : Patient Record

POST-OPERATIVE PROGRESS

Appendix 2 : Patient Record

POST-OPERATIVE PROGRESS

Appendix 2 : Patient Record

COMPLICATIONS

SURGICAL (specify)	
GENERAL	<p>CARDIAC</p> <p>arrhythmia angina heart failure myocardial infarct cardiac arrest</p>
	<p>RESPIRATORY</p> <p>chest infection/pneumonia pulmonary embolism pneumothorax respiratory failure</p>
	<p>RENAL</p> <p>urinary tract infection retention of urine renal failure</p>
	<p>CEREBRAL</p> <p>TIA stroke</p>
	<p>GASTROINTESTINAL</p> <p>prolonged ileus bleeding perforation obstruction</p>
	<p>OTHER</p> <p>septicaemia coagulopathy DVT other _____</p>

NIH STROKE SCALE SCORE _____

RANKIN DISABILITY SCALE SCORE _____

APPENDIX THREE

INTRAOPERATIVE TRANSCRANIAL DOPPLER MONITORING

NAME

DATE

TAPE READING	OPERATIVE EVENT	MCA VELOCITY	B.P.	CO2	EMBOLI

OPHTHALMIC CHART

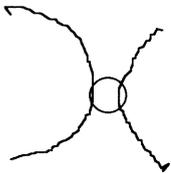
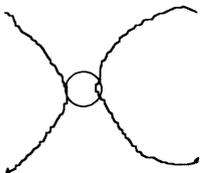
NAME

CAROTID ENDARTERECTOMY STUDY

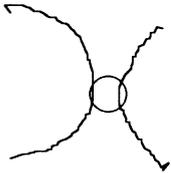
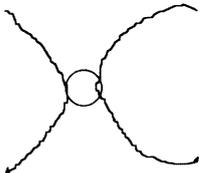
Pre-op

	RIGHT	LEFT
VISUAL ACUITY		
PREVIOUS OCULAR HISTORY	YES / NO / SPECIFY	YES / NO / SPECIFY
AMAUROSIS FUGAX	YES / NO / EQUIVOCAL	YES / NO / EQUIVOCAL

SLIT LAMP EXAMINATION

	0-----1-----2-----3	0-----1-----2-----3
CORNEAL LENS OPACITIES		
INTRAOCULAR PRESSURE		
FUNDI		
FIELDS (HUMPHREY 120 pt 3 level)		
COMMENTS		

Post-op

VISUAL ACUITY		
FUNDI		
FIELDS (Humphrey 120 pt 3 level)		
change in fields		
COMMENTS		

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