

## How to optimize carotid artery stenting

R. UFLACKER

Interventional Radiology  
Medical University of South Carolina  
Charleston, SC, USA

Carotid angioplasty and stenting is now an alternative to surgical endarterectomy to treat carotid occlusive disease and is becoming mainstream in medical practice. However, the information available, the procedure techniques and the technologies are still evolving and several issues are still being discussed. Mandatory training, familiarity with the indications and contraindications, knowledge of the technology and devices are paramount for the success, however, the devices for carotid stenting are still under development. The impact of stent design seems to be greater than previously appreciated. Carotid plaque morphology may be important for the indication of the procedure. The pre, trans, and postprocedure patient management of the patient is essential for reducing morbidity and mortality. Due to the devastating potential complications, compared with other endovascular and minimally invasive procedures, carotid stenting requires a much more strict scrutiny of the operators training and outcomes, since the improvement in the learning curve is accompanied by a comparative reduction in the complication rates. This article presents a review of the information available on how to optimize carotid stenting.

**KEY WORDS:** Carotid artery diseases - Stents - Balloon angioplasty.

### Importance of carotid occlusive disease and risk of stroke

There are approximately 700 000 new stroke patients per year in United States. Stroke is the third leading cause of death in the United States. The mortality rate is about 10% to 35%. Thirty percent of stroke patients die within 12 months of the event. About 400 000 of the patients are supposedly asymptomatic before the event.

There are 2 million/year handicapped patients by stroke in United States, at a cost of more than US\$ 50 billion.<sup>1</sup> Eighty percent of the strokes are ischemic, and 30% are related to extracranial carotid artery occlusive disease<sup>2</sup> and the incidence increases with age. Thirty-three percent of the patients are younger than 45 years and 80% of the patients are older than 50 years.<sup>3</sup>

African Americans, who comprise over 20% of the United States population, have heart disease and stroke death rates that are approximately 1<sup>1</sup>/<sub>2</sub> to 2 times higher than the white population.<sup>4</sup> About 30% of patients with stroke will develop an acute myocardial infarct within 30 days of the neurologic event, showing the close correlation between the two problems. The recognized major risk factors for heart disease and stroke are high blood pressure, high blood cholesterol, diabetes, tobacco use, physical inactivity, poor nutrition, and obesity, allowing ample prevention opportunities. Since it is a potentially correctable problem, carotid artery occlusive disease screening should be more widely used. The detection and treatment of carotid disease can prevent a significant number of strokes. In asymptomatic patients, one has to treat 80 patients to avoid one stroke within one year, but in symptomatic patients with stenosis greater than 70%, one has to treat only 6 patients to avoid one stroke within 2 years.<sup>5</sup> In other words, patients with an 80% asymptomatic stenosis will run a 1-2% per year stroke risk, and patients with an 80% symptomatic stenosis will run a 10-20% risk of stroke in the first year.<sup>5, 6</sup> However, more than 80% of the strokes relat-

Address reprint requests to: R. Uflacker, MD, Interventional Radiology, Medical University of South Carolina, 609 Ashley Avenue, Main Hospital, Charleston, SC 29425, USA. E-mail: uflacker@musc.edu

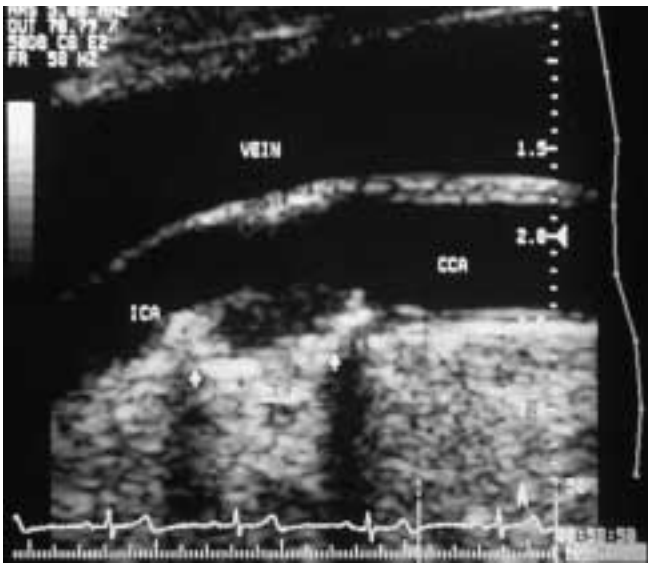


Figure 1.—Doppler ultrasound of the carotid showing atheromatous plaque.

ed to carotid occlusive disease will not present with red flags or recognizable symptoms before the stroke event.

Traditional method of treating carotid stenosis includes medical and surgical therapy. Symptomatic patients with moderate to severe or asymptomatic patients with severe cervical carotid stenosis have been very successfully treated with carotid endarterectomy (CEA) based on the results of the two pivotal studies from the 1990's, NASCET and ACAS.<sup>5,7</sup> Medical therapy with aspirin and more recently with clopidogrel has been reserved for mild-to-moderate (asymptomatic) carotid stenosis or noncervical carotid stenosis. The results of recent trials indicate that statin treatment reduces not only the risk of coronary heart disease, but also the risk of stroke, in patients with existing heart disease. Mechanisms for risk reduction include the retardation of plaque progression, plaque stabilization, and reducing the risk of coronary events.<sup>8</sup>

Carotid artery stenting (CAS) has, until recently,

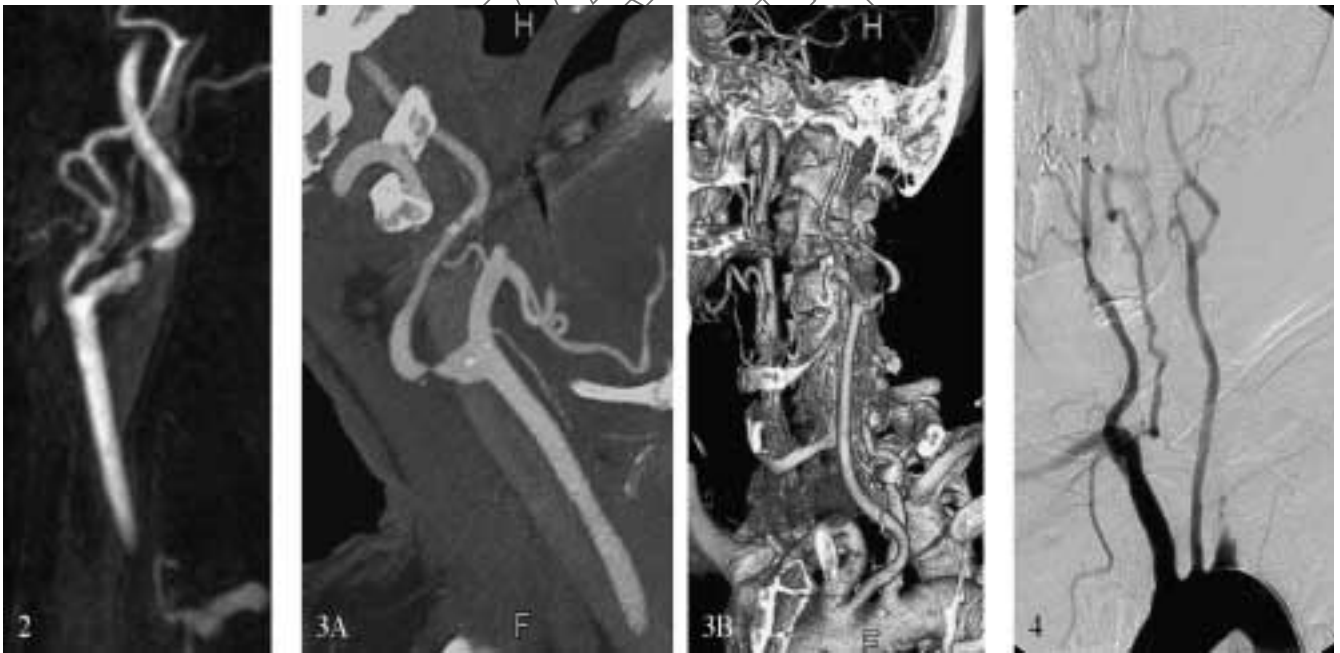


Figure 2.—Magnetic resonance of the proximal left internal carotid showing an eccentric severe stenosis with deep ulceration. Figure 3.—A) Maximum intensity reconstruction (MIP) CT angiography (CTA) of the left carotid showing a 90% stenosis with some calcification. Note the excessive tortuosity of the internal carotid artery. B) Volume rendering with 3D reconstruction of the carotid CTA showing the 90% stenosis of the left carotid stenosis. Note the tortuosity of the proximal common carotid artery, the common origin of the carotid and the brachiocephalic trunk. The aortic arch is a Type III elongated. Figure 4.—Aortic arch angiogram showing a Type I arch, with moderate stenosis of both internal carotid arteries, and diffuse disease of the right vertebral artery. Note occlusion of the left subclavian artery. Late phase showed reversed flow in the left vertebral artery and some degree of reconstitution of the subclavian artery (not shown).

been only a footnote in the management of carotid artery disease, mostly because it was performed at only a handful of institutions, for a few selected indications and was non reimbursable by insurance carriers.<sup>9</sup> With the perfecting of angioplasty techniques, improvement of stent devices, and more recently the development of distal embolic protection devices (EPD), CAS has become a viable alternative for the treatment of carotid artery occlusive disease, demonstrated by the trials SAPHIRE,<sup>10</sup> ARCHeR,<sup>11</sup> SECuRITY, BEACH, CAVATAS<sup>12</sup> and CABERNET which provided level 1 and 2 evidence for the safety, effectiveness and durability of CAS comparable to CEA. However, two more recent trials the EVA-3S<sup>13</sup> and the SPACE trial,<sup>14</sup> showed CAS to have more complications than CEA in the first in the hands of less trained interventional operators showing the need for cautious training and credentialing processes and failed to prove noninferiority of CAS compared to CEA in the latter.

**Diagnosis of carotid artery occlusive disease**

The diagnosis of carotid artery occlusive disease should start by screening widely the population above 60 years of age, particularly the ones at higher risk for peripheral and coronary artery disease, such as family history of stroke, coronary artery disease, hypercholesterolemia, tobacco use, and inadequate diet.

In asymptomatic patients clinical exam with palpation and auscultation of the carotids looking for bruits is the most basic screening tool, followed by a Duplex ultrasound scan of the carotids (Figure 1). If a significant bruit and/or stenosis of more than 50% are identified, a carotid artery magnetic resonance angiography (MRA) should be obtained for further evaluation (Figure 2). If the MRA is nonconclusive or unfeasible, a computed tomography angiography (CTA) of the extracranial carotids should be obtained (Figure 3). In asymptomatic patients, catheter angiography should not be used as a screening tool and indicated only when there is a question on the MRA or CTA, or when assessment for stenting treatment is planned in a patient with stenosis of 80% or more (Figure 4). Catheter carotid angiography carries a low risk of complications in experienced hands, however, may reach up to 1.2% complication rate as showed in the ACAS trial.<sup>7</sup>

In symptomatic patients, the assessment should start by clinical exam and Duplex ultrasound scan of

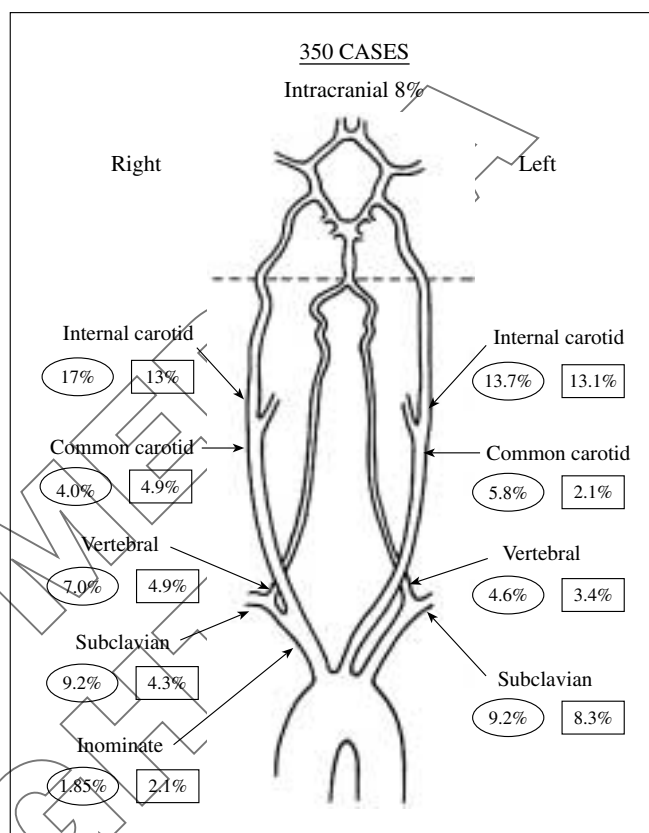


Figure 5.—Schematic drawing of the craniocervical vessels showing the incidence of stenosis (circle) and occlusions (square) in 350 cases (Modified from Johnsrude).<sup>15</sup>

the carotids. In our opinion, MRA should be acquired in all patients, including images of the aortic arch, for planning of stenting procedure. Due to the frequent association of renal function deficit in this population, CTAs should be indicated only when the MRA is nondiagnostic or not feasible. However, operators should have in mind the public health advisory issued by the Food and Drug Administration (FDA), to notify healthcare professionals that cases of nephrogenic fibrosing dermopathy may occur in patients with moderate to end-stage kidney disease after they have had a MRI or MRA scan with a gadolinium-based contrast agent (<http://www.fda.gov/cder/drug/infopage/gcca/default.htm>). Carotid angiography may be used more liberally in this group of patients, in the context of further evaluation to answer some of the questions, such as location and severity of ulcerations, and anatomic planning, immediately before stenting, despite the

TABLE I.—*Specific symptoms related to carotid TIAs.*

Ophthalmic	Visual loss in a single eye, in cortin Transient monocular blindness “ <i>amaurosis fugax</i> ”
Hemispheric	Acute transitory hemiparesis/hemiplegia, mostly brachial Sudden transitory global aphasia

TABLE II.—*Neurologic events nonspecific for carotid related TIAs.*

Symptoms	Description
Syncope	Loss of consciousness
Nausea - Vertigo	Dizziness
Headaches	Recurrent, persistent
Concentric monocular visual loss <i>Hemianopsia fugax</i> <i>Diplopia fugax</i>	Binocular transitory blindness
Ataxia	Loss of balance
Seizures	
Transitory confusion	

risks of worsening renal function. Hydration, small volume of low osmolar nonionic contrast material, and vitamin C should be used to protect the renal function, and have been proved helpful.

In 350 cases with atherosclerosis of the brachiocephalic vessels, Johnsrude<sup>15</sup> identified 13% of stenosis >60% and 17% of occlusion of the proximal right internal carotid artery (ICA), and 13.7% of stenosis >60% and 13.1% of occlusion of the proximal left ICA. The common carotid arteries (CCA) were much less frequently involved, either with significant stenosis or with occlusions<sup>15</sup> (Figure 5).

**Neurologic events related to carotid transient ischemic attacks**

Neurologic events related to carotid disease may be specific and nonspecific.

Specific symptoms are more clearly related to transient ischemic attacks (TIAs), and include ophthalmic (*amaurosis fugax*) and hemispheric events (transitory hemiparesis/hemiplegia, global aphasia) (Table I), while nonspecific symptoms can be a combination of multiple events, and not necessarily transient (syncope, ataxia, headache, confusion, loss of memory, diplopia) (Table II). Neurocognitive deficits are just now starting to be considered as significant in the selection of patients for treatment of carotid occlusive disease.<sup>16</sup>

TABLE III.—*Cervical levels of carotid bifurcation and the percent of incidence.*

Cervical level of carotid bifurcation	Incidence %
C1-C2	0.3
C2-C3	3.7
C3-C4	34.2
C4-C5	46.3
C5-C6	13.0
C6-C7	0.15

**Indication and contraindication analysis for carotid artery stenting**

CAS is currently indicated in the following situations:

1. unilateral or bilateral symptomatic *de novo* atherosclerotic carotid lesion.
2. Restenotic lesions in native carotid arteries post-CEA.
3. Neurologic symptoms plus stenosis:
  - a. >50% stenosis according to the NASCET criteria, and used in most CAS trials;
  - b. >70% stenosis, according to the CMS/Medicare reimbursement criteria in the USA.
4. No neurologic symptoms plus stenosis:
  - a. >80% according to the NASCET criteria, and used in most CAS trials;
  - b. no indication for treatment according to the CMS/Medicare reimbursement criteria.
5. High carotid bifurcation (Table III).
6. Contralateral occlusion.
7. High risk criteria for CEA:
  - a. congestive heart failure (CHF);
  - b. severe coronary artery disease, recent myocardial infarct;
  - c. severe chronic obstructive pulmonary disease;
  - d. contralateral carotid occlusion;
  - e. contralateral laryngeal nerve palsy;
  - f. radical neck surgery for cancer and radiation therapy;
  - g. recurrent stenosis after CEA;
  - h. hostile neck (previous surgery, radiation therapy, neck cancer, tracheostomy) (Figure 6);
  - i. patient older than 80 years of age (changing indication, more recently described at higher risk for complications with carotid stenting as well).

CAS is not indicated or relatively contraindicated in the following situations:



Figure 6.—A) Good indication for carotid stenting. Hostile neck with multiple surgeries for neck cancer and permanent tracheostomy. B) Postradiation therapy left carotid 90% stenosis showed in the selective angiogram. C) Angiogram of the carotid artery following balloon angioplasty and stenting. The patient had bilateral severe carotid occlusive disease which was treated by CAS in separate procedures.

1. In tandem lesions:
  - a. stenosis in the ICA and CCA;
  - b. association of intracranial stenosis;
2. Need of more than one stent in long lesions.
3. Unfavorable anatomy (may be relative contraindication depending of the experience of interventional operator). The Delphi Consensus Committee (C. Schonholz, Personal communication) is currently organizing the unfavorable anatomy classification:
  - a. excessive tortuosity of the internal carotid;
  - b. excessive elongation and tortuosity of the aortic arch (type III);
  - c. bovine arch in association with other significant tortuosities;
  - d. heavily calcified plaques.
4. Presence of intracranial aneurysm with more than 9 mm in diameter.
5. Stroke within previous 48 h.
6. Intraluminal thrombus (reversal of flow technique may be an option).
7. Total occlusion.
8. Bleeding disorder (coagulopathy).
9. Thrombophilia.
10. Short life expectancy, <1 year.

11. Concomitant ostial lesion of CCA or brachiocephalic trunk (relative contraindication).

#### **Anatomy of the aortic arch, carotid arteries, and lesion characteristics**

The type and length of the aortic arch has always been a limitation for safe and fast catheterization of the brachiocephalic vessels. This difficulty just got more significant for successful carotid stenting. On top of the arch unfavorable anatomy, excessive tortuosity of the common and internal carotids may produce an insurmountable obstacle for safe carotid stenting. The classification of the arch in three types has been helpful in defining who may be treated according to the experience of the operator. In type III, aortic arches with bovine configuration, special guiding catheters, and buddy wires may have to be used for additional stability. In excessive tortuous arches and carotids, the 0.014-inch filter wire may not support the degree of tracking necessary for advancing the stent. Complex aortic arch is the most common cause for failure and excessive manipulation within a difficult arch may cause embolization to the target territory and even to

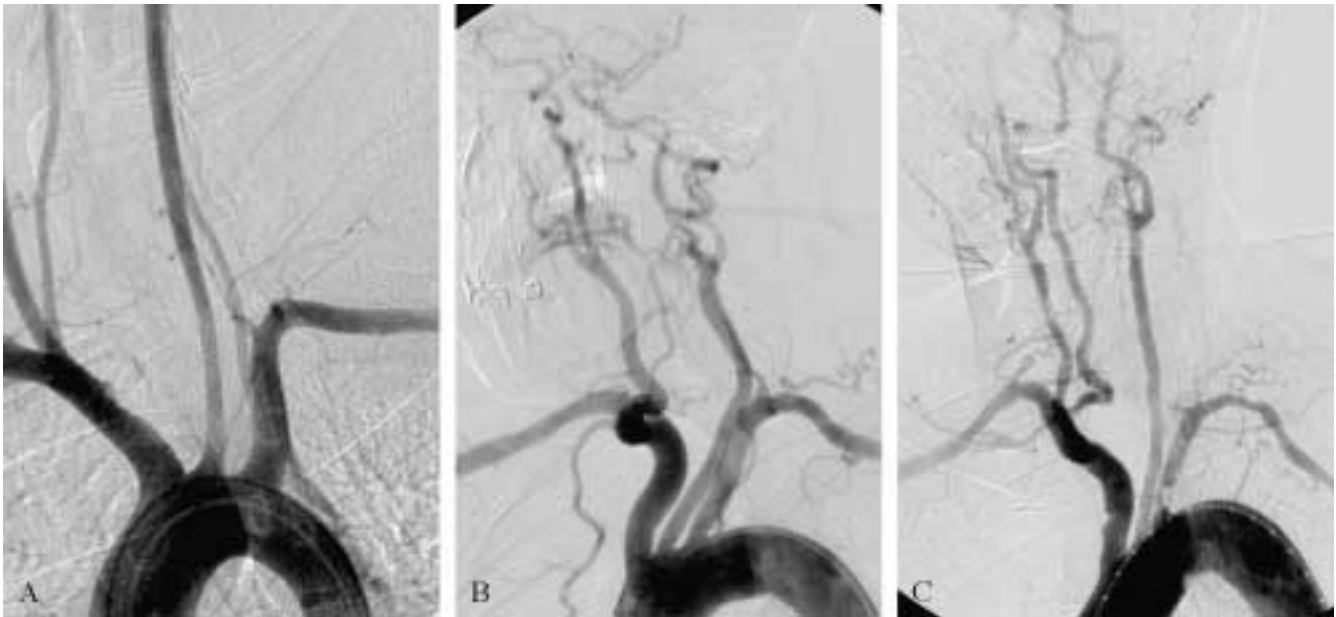


Figure 7.—A) Angiogram of the aortic arch showing a Type I arch. B) Type II. C) Type III.

the contralateral carotid territory, being responsible for up to 30% of the strokes in the postmarket trials CAPTURE and EXACT 900.<sup>17</sup> Technical failure is acceptable, but technical failure with a stroke is not. In some cases, the brachial approach is a viable alternative to the femoral approach in difficult arch situation and may allow safe catheterization.

Types of aortic arch (Figure 7):

Type I. — conventional arch anatomy with three main brachiocephalic branches at the same plane level, without significant elongation;

Type II. — conventional arch anatomy with three main brachiocephalic branches with origins at different plane level, with the brachiocephalic trunk moved in the direction of the anterior mediastinum and lower than the left subclavia with a length equivalent of at least one vessel diameter;

Type III. — conventional arch anatomy with three main brachiocephalic branches with origins at different plane level, with the brachiocephalic trunk moved in the direction of the anterior mediastinum and lower than the left subclavia with a length equivalent of more than one vessel diameter. More recently, a Type IV arch has been added to the classification, which includes dilatation and excessive elongation of the aortic arch.

Types of aortic arch according to the number and position of the brachiocephalic branches (Figure 8):

— normal distribution: three brachiocephalic branches;

— bovine arch variation: common variation where the left CCA originates from the brachiocephalic trunk;

— combination of a variety of patterns.

Target lesion characteristics (Figure 9):<sup>18</sup>

— Type A:  $\geq 80\%$   $< 1.5$  cm nonulcerative, ostium spared, concentric.

It is recommended that when beginning carotid stenting, the operator should initially choose 20 or so patients with Type A lesions to perform CAS.

— Type B:  $\geq 85\%$   $> 1.5$  cm may be ulcerative and/or eccentric – CCA may be involved.

Operators should approach Type B carotid lesions after experience with about 20 patients with type A lesions.

— Type C:  $> 85\%$   $> 2$  cm ulcerative, tandem lesions may be present CCA involved.

Only experienced operators should treat Type C lesions. Special care should be exercised with the presence of major ulceration and suspicion of clot within the stenosis. When differentiation of clot *versus* plaque cannot be made angiographically or with intravascular ultrasound (IVUS) and virtual

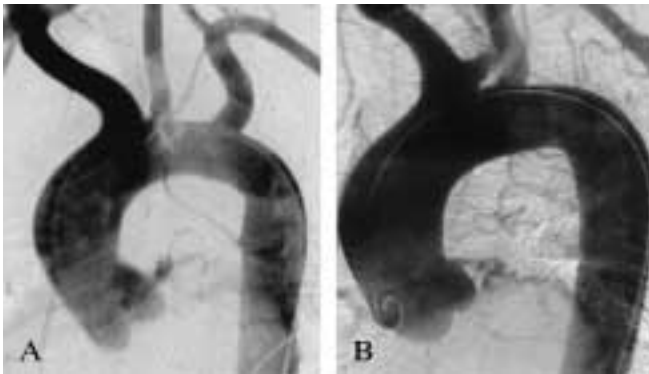


Figure 8.—Most common presentations of aortic arch and origin of the cervical branches. A) Usual presentation, 65%. B) Left common carotid sharing the brachiocephalic trunk with the right subclavian and right common carotid artery, 27% (Bovine arch).

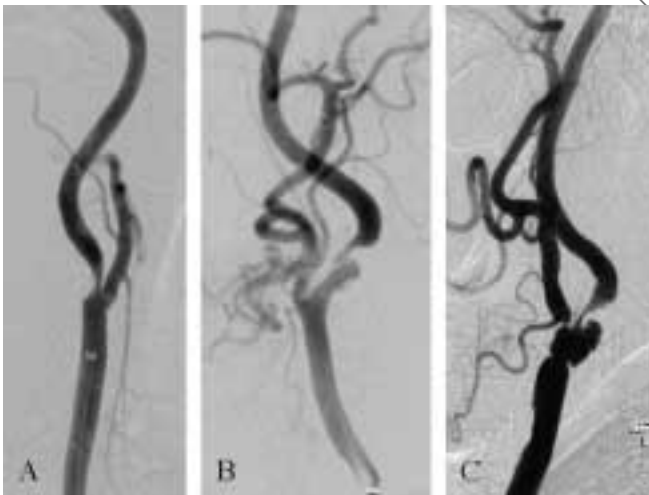


Figure 9.—Types of carotid artery stenosis. A) Type A: >80% <1.5 cm nonulcerative, ostium spared, concentric. B) Type B: >85% >1.5 cm may be ulcerative and/or eccentric—CCA may be involved. C) Type C: >85% >2 cm ulcerative, tandem lesions may be present. CCA involved.

histology (VH), the procedure may have to be abandoned and the patient sent for CEA. The use of a reversal of flow device may be an option in selected cases.

*Carotid artery plaque composition*

Carotid plaque composition is still an unsettled issue and, in fact, may represent similar risk related to the vulnerability concept present in the coronary artery cir-

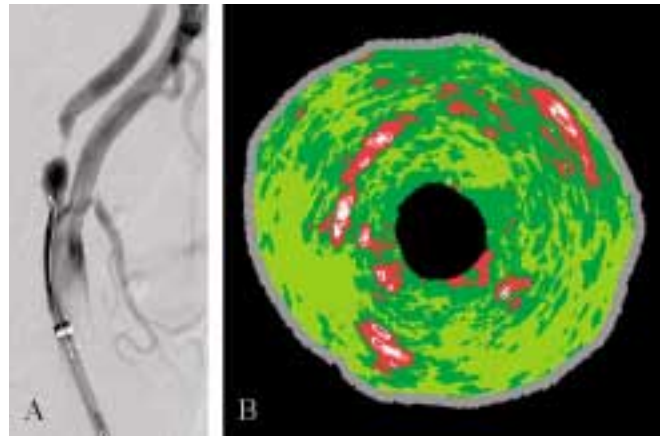


Figure 10.—A) Carotid angiogram showing a concentric 90% internal carotid stenosis. B) Virtual histology showing predominance of fibrous (green) and fibrous-lipidic (yellow) material in the plaque. The lipidic necrotic material (red) and calcium (white) are less prominent in this case, making a good candidate for stenting. If red and white are dominant the patient probably should be referred for endarterectomy.

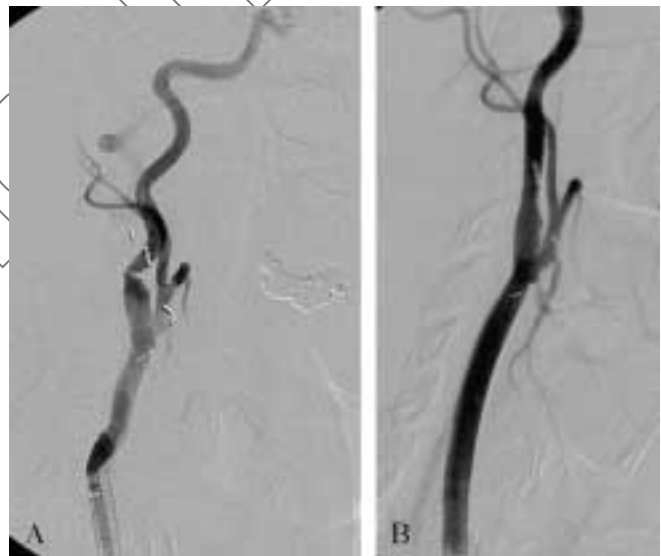


Figure 11.—A) Carotid angiogram through the introducer sheath. Note the area of dissection in the common carotid artery and the tight postendarterectomy internal carotid artery stenosis. B) Angiogram poststent placement in the internal carotid artery and in the common carotid artery to fix the dissection area.

ulation.<sup>18, 19</sup> To understand the plaque composition some operators have incorporated IVUS with VH to the procedure of CAS, which provides quantitative analysis of plaque characteristics, including amount of

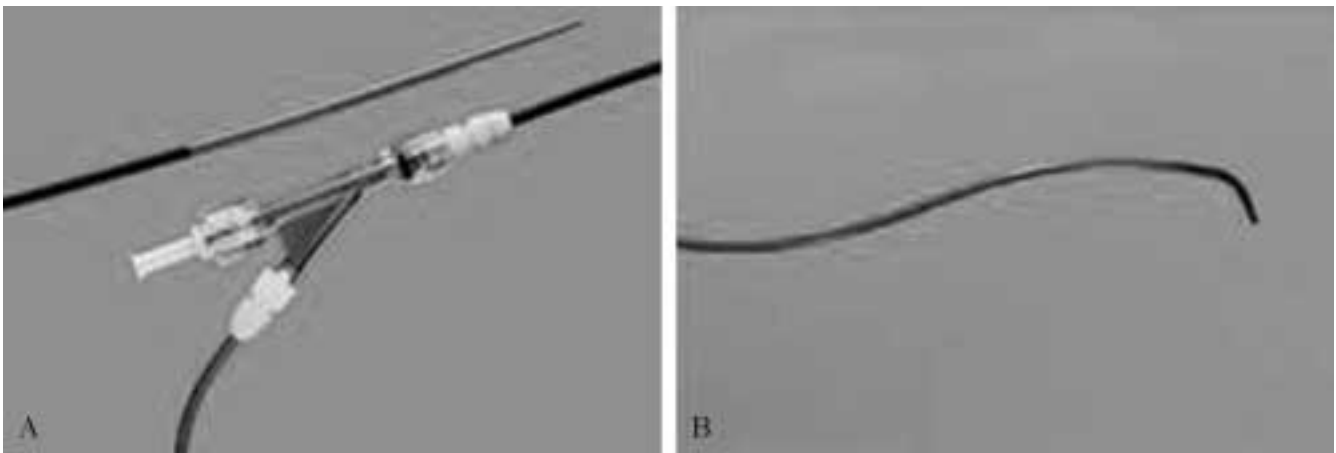


Figure 12.—A) Shuttle introducer sheath, with Tuohy Borst adaptor. B) Slip-Cath Select Beacon Tip Catheter.



Figure 13.—A) Carotid angiogram showing an 85% internal carotid stenosis. B) Angiogram after carotid stenting done under cerebral protection.

fibrosis, necrotic, calcific and lipid components of the plaque. From this analysis, it is expected that the operators will be able to define which patients will be better suited for stenting *versus* open surgery.

The Volcano system uses a 45MHz, 3.2F catheter/transducer called Revolution, which is placed across

the stenosis over the wire. The demonstration of a significant necrotic core, dystrophic calcifications and changes of unstable plaque, may render the patient more suitable for CEA (Figure 10).

### Selection of devices

Selection of the access system to the carotid is of paramount importance due to the natural anatomic difficulties of the aortic arches of the elderly and patients with advanced atherosclerosis. The first situation is overcoming the tortuosity of the Type II and III aortic arches, which if not accomplished will represent failure of the procedure. The combination of a flexible but strong sheath is necessary, to progress the system into the CCA and stay there for the duration of the procedure. The selective hydrophilic catheter certainly facilitates the advancement of the sheath hopefully minimizing manipulation and the risks of contralateral and ipsilateral strokes. The second situation to be considered is the safe access to the carotid without trauma to the artery wall. Main risk involved is dissection of the common carotid, particularly if the vessel is tortuous (Figure 11).

### Sheath and guidewire systems

#### COOK SYSTEM

— Shuttle Select Guiding Sheath (6 Fr-7 Fr) (Figure 12A).

Flexor design, atraumatic tip, hydrophilic coating

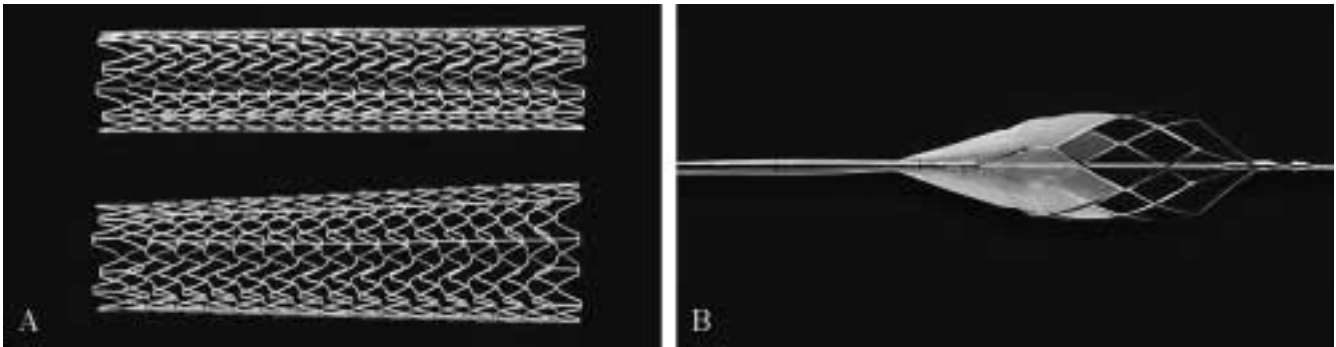


Figure 14.—A) Acculink carotid stent. Straight and tapered configurations. B) AccUNET cerebral protection device.

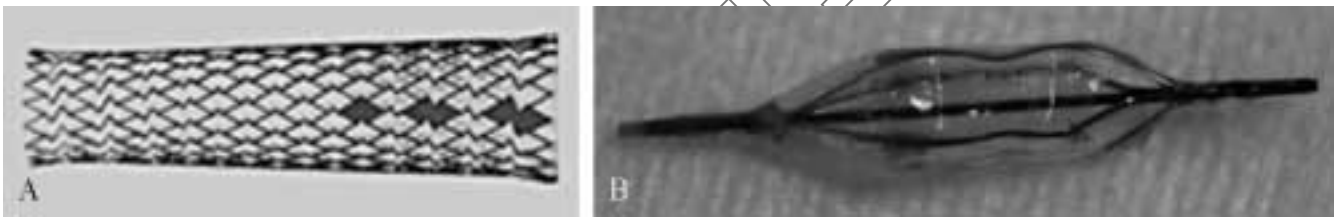


Figure 15.—A) Xact carotid stent. Note the cell design and small size. The stents are available in straight and tapered configurations. B) The EnboShield cerebral protection device with a nitinol frame.

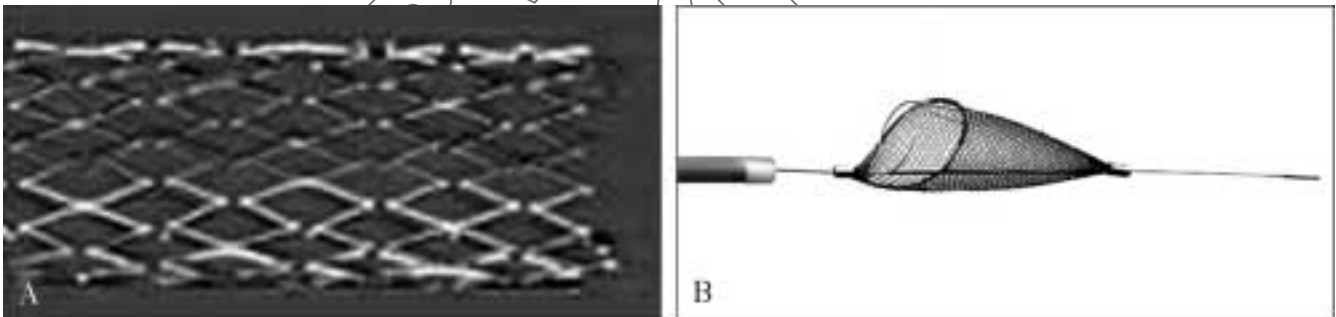


Figure 16.—A) Protégé stent. B) SpiderX device. Note the metallic net and the nitinol skeleton. This device allows the use of a regular guidewire to cross the stenosis and after advancing the delivery system the device is deployed.

(top 50 cm), distal tip marker, 90 cm long, Tuohy-Borst valve.

— Slip-Cath Select Beacon Tip Catheter (H1, JB1, JB2, Simmons, VTK) 6.5 Fr (Figure 12B).

Nylon braided torque catheter shaft, beacon soft tip, hydrophilic coating (top 60 cm), and 125 cm long.

— HiWire Hydrophilic 0.035-inch wire.

Hydrophilic, stiff, medium stiffness, and floppy, 180-260 cm long.

TERUMO SYSTEM

— Destination Sheath (6 Fr-7 Fr).

Flexible, unkinkable, atraumatic tip, hydrophilic coating (top 15 cm), distal tip marker, 90 cm long, Tuohy-Borst adaptor, or hemostatic valve.

— Terumo Hydrophilic Glidewire 0.035-inch wire.

Hydrophilic stiff and regular stiffness shaft 180-260 cm.

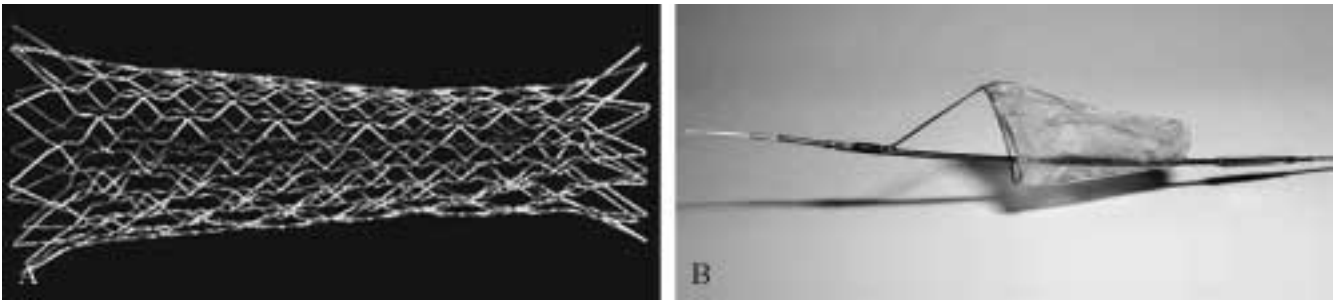


Figure 17.—A) Picture of the NewStent. This stent is a wrapped nitinol sheet with a locking mechanism when expanded with a balloon, assuming the diameters of the internal carotid and the common carotid, according to the balloon size used. B) FilterWire EZ showing some captured plaque debris.

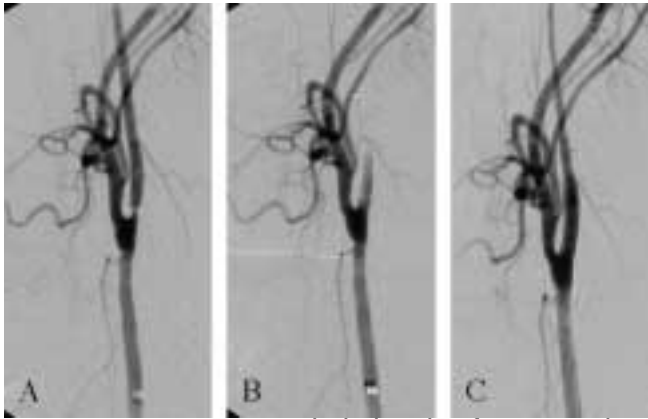


Figure 18.—A) Carotid angiogram showing a tight recurrent stenosis of the proximal internal carotid, postendarterectomy. B) Postangioplasty angiogram showing improvement in the stenosis site, but complete occlusion of the distal internal carotid artery by spasm produced by the AccUNET cerebral protection device. C) Completion angiogram performed after stenting and quick removal of the filter. Some spasm is still seen but the flow is free. Intracerebral circulation was normal.

#### GUIDING CATHETERS

Despite the multitude of devices available for access to the carotid for carotid stenting, including guiding catheters and introducer sheaths, the sheaths are proving to be more versatile and friendly when treating patients with excessive tortuosity of the aortic arch and proximal carotids. The sheaths are more stable and flexible with atraumatic tips for the antegrade approach.

Recently, Invacev *et al.*<sup>20</sup> described a new access technique to facilitate the management of patients with excessive tortuosity of the arch and carotids. The technique uses surgical exposure of the ipsilateral temporal artery and catheterization with a micro-

catheter loaded with a 0.014-inch wire. The system is introduced through the external carotid artery into the CCA and into the aorta where the 300 cm long, 0.014-inch wire is snared and passed through the 6 F, 80 cm long carotid sheath previously placed in the femoral artery, establishing a through-and-through access from the temporal artery to the femoral artery. Using the small wire the introducer is advanced within the sheath and the system is advanced into the CCA. The CAS procedure proceeds with the small wire left in place as a “buddy wire” to stabilize the sheath, while the procedure is performed in the standard fashion with the protection device.

#### Cerebral protection devices

Due to the variable nature of the embolic material potentially breaking off from atheromatous plaques during a carotid procedure, it was realized early on that mucopolysaccharide components and necrotic core of lipid-laden debris,<sup>21, 22</sup> in addition to blood clots, could make a large component of the debris embolizing the brain. Therefore, pharmacologic strategies to reduce platelet aggregation and inhibit clot formation will not effectively prevent cerebral embolization in all cases, making some sort of filtration or downstream cerebral protection necessary.<sup>23-29</sup> With time, three types of technologies were developed for embolic cerebral protection as follows: 1) distal occlusion devices; 2) distal filtration devices; 3) proximal occlusion/reversal of flow devices.

#### DISTAL OCCLUSION DEVICES

Concept based on the blockage of the distal blood flow to the brain by placing a balloon within the

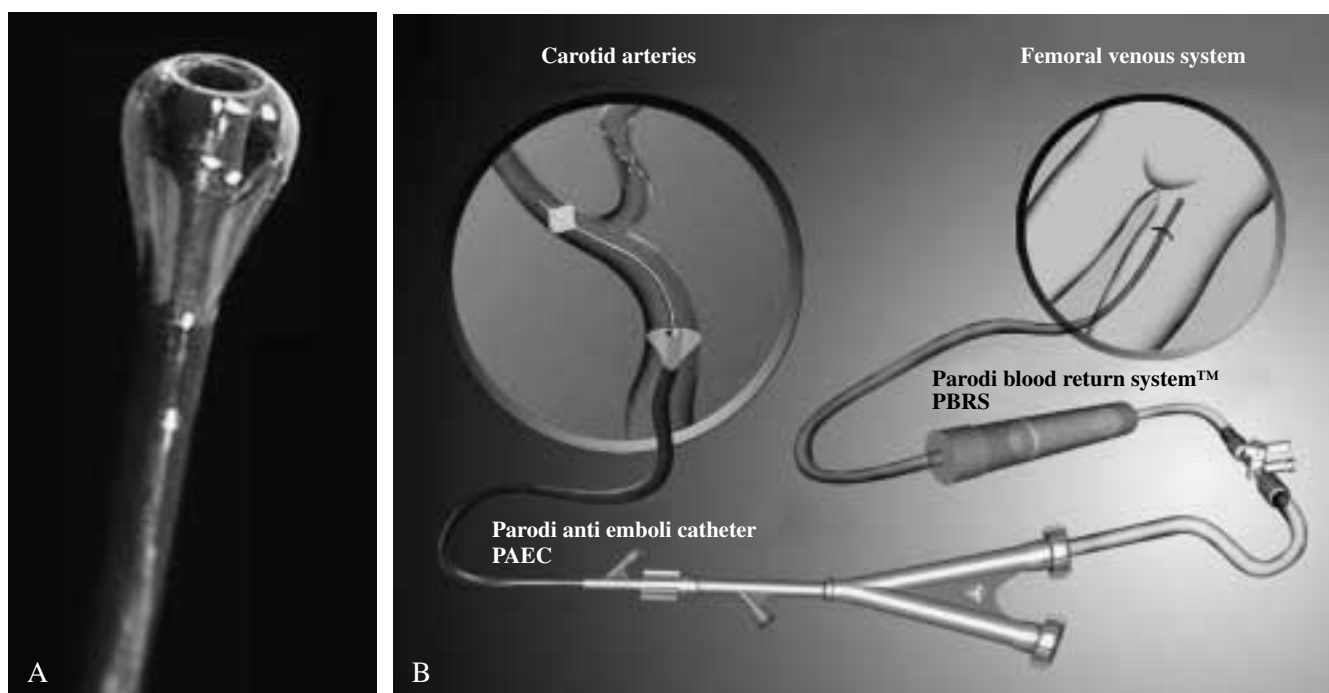


Figure 19.—Reversal of flow device. A) Guiding sheath with the occlusion balloon at the tip. B) Schematic disposition of the devices used for the reversal of flow in the treated carotid. Note the occlusion balloon in the external carotid artery, the occlusion of the common carotid artery by the guiding catheter. The main lumen is connected to the contralateral femoral vein, through the filter system, or blood return system.

ICA, during the carotid intervention. The idea is to arrest the flow in the internal carotid during the procedure, trapping the embolic debris from the plaque, and removing the debris by aspiration through the guiding catheter/sheath. Jack Theron developed the distal occlusion concept, in 1989.<sup>30</sup> There are three distal occlusion devices designed for carotid stenting, one is called PercuSurge GuardWire (Medtronic, Inc., Santa Rosa, CA), the other one is the TriActiv FX embolic protection system (Kensey Nash, Exton, PA) (approved for saphenous vein graft and rapidly inflated by CO<sub>2</sub>), both consisting of a hypo tube with an inflatable balloon attached at the end. The hypo tube serves as the interventional guidewire, which is used to cross the stenosis and the balloon is inflated to 1 to 3 atm, occluding the carotid flow. Following the completion of the procedure the stagnant blood within the occluded carotid is aspirated using the PercuSurge Export catheter (Medtronic) or a distal saline infusion catheter (Flushcath, Kensey-Nash) to remove the existing debris. The other occlusive device is the GuardDog (Possis Medical Inc., Minneapolis, MN)

(approved for peripheral use) and consists of a 0.035-inch guidewire with a compliant balloon attached at the tip, and the debris can be removed using the AngioJet device (Possis Medical Inc., Minneapolis, MN). Obvious advantages of the occlusion devices is the low profile (<3 F), quick inflation and deflation, short landing zone, and these devices trap all particles including the smaller than 100  $\mu$ , lower limit of most of the filter devices. Disadvantages are mostly related to the potential cerebral ischemia during occlusion time, and if complete occlusion is not achieved, debris can pass the device and embolize the brain. Despite careful aspiration and flushing of the area around the balloon, some debris may still remain in the stagnant column of blood and embolize into the brain during balloon deflation. Additionally, the external carotid circulation is not protected and potential brain embolism can still occur through intracranial anastomosis.<sup>22</sup> In one publication, 15% of the patients treated with an occlusive protection device presented complications, suggesting the risks of the technique.<sup>31</sup>

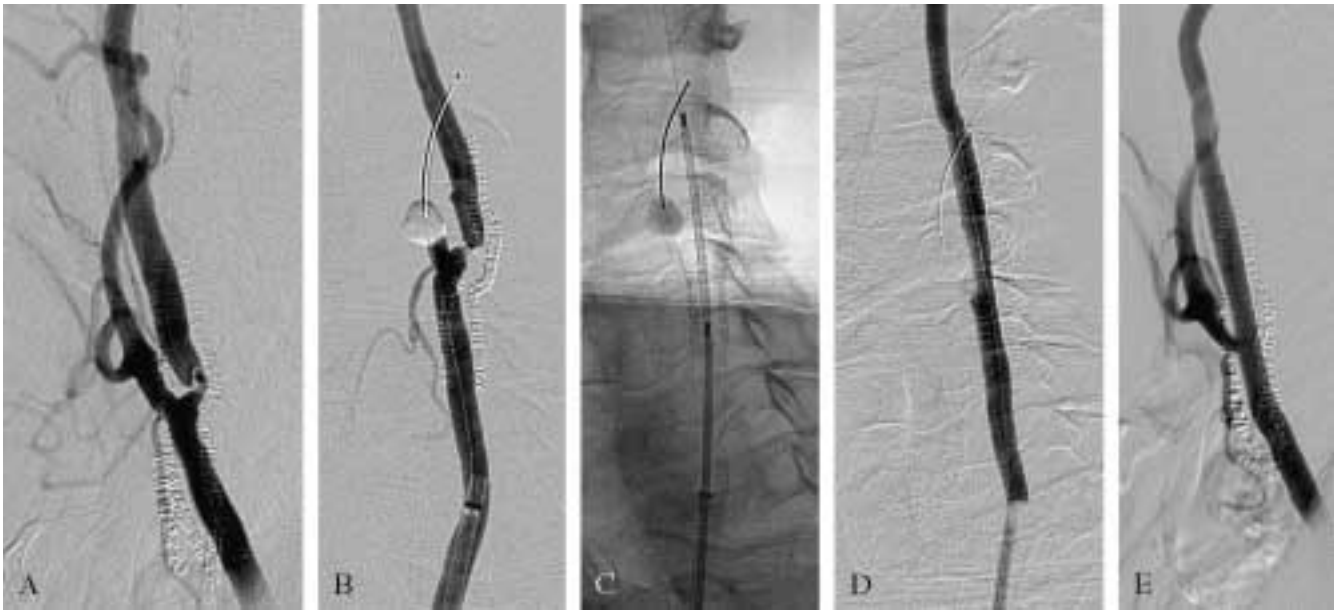


Figure 20.—A) Carotid angiogram showing a 90% recurrent internal carotid artery stenosis with a filling defect. Note the metal clips used with the carotid patch from previous endarterectomy. B) Angiogram after occlusion of the external carotid angiogram. The common carotid is not occluded yet. C) Following external carotid and common carotid occlusion with establishment of reversal of flow the stenosis was crossed, followed by balloon plasty and stenting. Note the stent just before deployment. D) Angiogram still under reversal of flow showing the stent in place. E) Conclusion angiogram showing resolution of the carotid stenosis, and patent external carotid. No complications were observed.

#### DISTAL FILTER CEREBRAL PROTECTION DEVICES

Filtering cerebral protection devices are the most commonly used systems to prevent cerebral embolism during carotid stenting procedures<sup>23-29</sup> (Figure 13). The devices are in general sophisticated in construction, but the protection is based on a simple concept of trapping downstream larger particles of debris capable of causing cerebral ischemia. Most of the devices are calibrated to filter particles larger than 100  $\mu$ , allowing blood flow to continue during the procedure. At the time of this written there are four FDA approved filtering devices for carotid stenting in the United States, the Angioguard (Cordis Corporation, Miami, FL), Accunet (Guidant/Abbot Vascular, Abbot Park, IL) (Figure 14), EnboShield Pro, (Mednova/Abbott, Galway, Ireland) (Figure 15) and SpideRX (ev3, Inc. Minneapolis, MN) (Figure 16). The FilterWire EX and EZ (EPI/Boston Scientific Corporation, Natick, MA) has two versions and is approved by the FDA for coronary venous grafts, but has been used extensively in Europe for carotid stenting and was recent-

ly approved by the FDA, together with the NextStent (Endotex/BSC) (Figure 17).

The Angioguard, the Accunet, and the FilterWire have the filters attached to the working wire, while in the other devices the filter is deployed over the wire already in place. The filter devices are deployed above the stenosis after passing through the lesion and apposed to the ICA wall. Following the procedure, a recovery sheath recaptures the filters. The carotid flow is maintained throughout the procedure allowing test injections to identify the location of the lesion and proper stent placement. A potential shortcoming of the filter protection technique is the need to cross beyond the stenosis unprotected, and some of the filters have larger crossing profile than the occlusion balloons, potentially increasing the risks. Most of the filters need a longer landing zone above the lesion, which can be problematic in tortuous internal carotids and distal lesions, reducing apposition to the vessel wall, which may lead to embolism around the device. In addition, concerns for embolism during recapture and retrieval of the filter should be assessed. The filters can pro-

mote spasm and/or dissection of the artery or may become occluded by the excessive volume of debris, as they are small devices with limited volumetric capacity<sup>22-25, 29</sup> (Figure 18).

#### PROXIMAL OCCLUSION AND FLOW REVERSAL DEVICES

The main theoretical advantage of the proximal occlusion or flow reversal devices is establishing protection through occlusion of the blood flow to the intracranial circulation, before the lesion is crossed.<sup>32, 33</sup> The two main devices available are the proximal occlusion system MoMa Device (Invatec, Brescia, Italy) not approved in the United States, but extensively used in Europe<sup>32, 33</sup> and the true reversal of flow system Gore Neuro Protection System (previously known as the Parodi Antiembolic Device)<sup>34, 35</sup> (Gore & Associates, Flagstaff, AZ) currently undergoing clinical trial in USA (Figures 19, 20).

The MoMa Device is a 9 F, five lumen catheter with a 2.12 mm working channel. It has two compliant balloons attached to the same catheter, one for the external carotid artery and one for the CCA. It allows carotid occlusion and intermittent aspiration of the stagnant column of blood within the carotid, but does not establish true reversal of flow. The crossing of the lesion is done by a steerable guidewire while the blood flow is stopped for complete protection. Intolerance to flow blockage is encountered in 5.7% to 7.6% of the patients. The Gore Neuro Protection System (GNPS) is a 9 F catheter with a compliant balloon attached to the tip, used for occlusion of the CCA. The external carotid artery is catheterized with a separate occlusion balloon on the wire, and occluded. The working lumen of the main catheter is connected to the contralateral femoral venous circulation through a filter, establishing the reversal of the flow when the occlusion balloon is inflated within the CCA. Once the reversal of flow is established, the lesion can be crossed with minimal risk. Main advantages are related to difficult lesions, with tortuous ICAs above the stenosis, and the presence of intravascular thrombus. An "Air-Bag and Seat-Belt" technique<sup>23</sup> has been described using the GNPS system and a filter protection device, especially useful when the patient may not tolerate the continuous reversal of flow, which happens in up to 8% of the cases. The reversal of flow is established while the filter is used to cross the lesion and deployed above the stenosis,

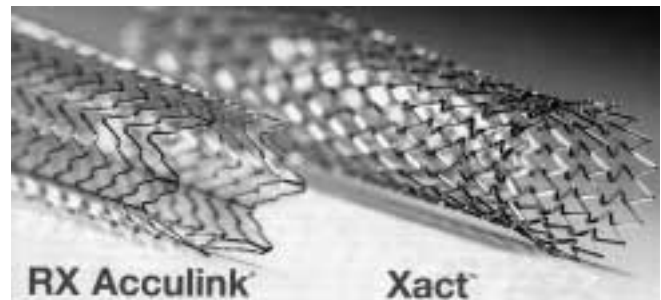


Figure 21.—Comparative picture of the Acculink stent with large cell size and the Xact stent with small cell size.

allowing full protection even when the reversal of flow is discontinued.

#### *Angioplasty balloons and stents for carotids*

##### BALLOONS

There are several low profile balloons used for carotid angioplasty, ranging from 2 to 6 mm in diameter and 15 to 20 mm in length. The 2 and 3 mm balloons are used for predilatation of the stenosis and the 4 to 6 mm balloons are used for poststenting dilatation. Low profile rapid exchange (monorail) balloon catheters are mandatory, and short inflation times are required.

##### STENTS

There are five carotid stents currently approved by the FDA for clinical use in the United States. The Acculink and Xact carotid stent (Guidant/Abbott Vascular) (Figures 14, 15), the Precise stent (Cordis Endovascular, Inc) and the recently approved NexStent (EndoTex/Boston Scientific, Natick, MA) and the Protégé (ev3 Inc., Minneapolis, MN) (Figures 17, 18). These are all self-expandable devices, and with the exception of the Precise stent, available in tapered configuration and in a monorail delivery system. The tapered configuration is advantageous in reducing the oversizing of the stent in the ICA, when there is a significant discrepancy in size between the internal and the external carotid artery, which is the rule. The NexStent is a nitinol sheet, wrapped around the delivery system with selfexpandable capabilities and can acquire the tapered configuration of the vessel, but due to the specific design, it requires balloon dilation to lock in the device in place. The Carotid Wallstent (BSC), the Vivexx (Bard peripheral), and Exponent RX

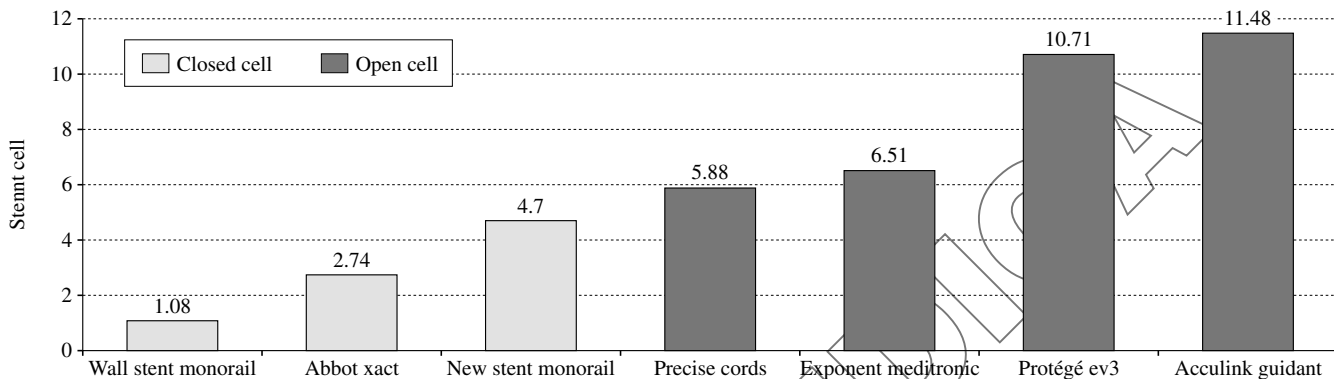


Figure 22.—The area of the stent cell is expressed in square millimeters.

(Medtronic Inc.) are currently undergoing clinical trials in the US or pending PMA revision by the FDA at the time of this written. However, the Wallstent has been used successfully for many years in the USA and Europe as a carotid stent.

More recently, it has been described that device characteristics may affect outcomes in CAS. Particularly, in symptomatic patients or with echolucent lesions, closed-cell design and eccentric filters seem superior.<sup>36</sup> Postprocedural event rate was 1.3% for closed cell and 3.4% for open-cell stents. All these differences were highly significant among symptomatic patients ( $P < 0.0001$ ), but not in asymptomatic individuals (Figure 21). After carotid stenting, complication rates vary according to stent type, free cell area and cell design. In the symptomatic population postprocedural complication rates are highest for the open cell types of stents and increase with larger free cell area<sup>37, 38</sup> (Figure 22).

### Cerebral protection, complications, and Bailout techniques

It has been showed that carotid manipulation promotes migration of emboli and microemboli to the cerebral circulation.<sup>29</sup> Emboli to the brain circulation may consist of organized clots from the surface of the plaque, debris, plaque fragments, and a mixture of fibrin, cholesterol clefts, red and white cell aggregates.<sup>21</sup> High intensity transient signals (HITS) on the transcranial Doppler US (TDUS), with and without cerebral protection are observed. Although some of the HITS observed during cerebral protection may

be due to microemboli, a significant component of the HITS may be actually related to air trapped in the deployed devices and delivery systems (Figure 23). The literature emphasizes, however, that cerebral protection is beneficial, from experimental data<sup>29</sup> and clinical data.<sup>23</sup> Acute carotid thrombosis after carotid stenting is a difficult problem to manage and has been treated with surgery and rheolytic thrombectomy.<sup>39, 40</sup>

### Thrombolytic therapy

Thrombolytic therapy plays an important role in the reopening of intracranial branches occluded by a clot embolus.<sup>41</sup> Urokinase used at a rate of 500 000 to 5 000 000 U/h infused with a microcatheter directly within the clot should be able to take care of a small clot within the middle cerebral artery (Figure 24). More recently, rt-PA has been used for the same purpose with a bolus of 5 mg of Alteplase (rt-PA), or at a rate of 1 mg/h up to 4 h. Retavase has been used at 1 U into the clot. It is important, however, to note that the thrombolytic drug will not act upon an atheromatous embolus, but may reduce associated clots or clot propagation. A bolus of 2 000 U of heparin is given, upon confirmation of the clot, followed by 500 U/h until the end of the lytic infusion. Abciximab has been proposed at a standard dose of 0.25 mg/kg, followed by a 12-h infusion of 0.125 mg/kg/min, but the risks of intracranial bleeding are greater.<sup>42</sup>

### Concentric Merci device

The Merci device is a bail out system for embolism of the middle cerebral artery (Figure 25). The device

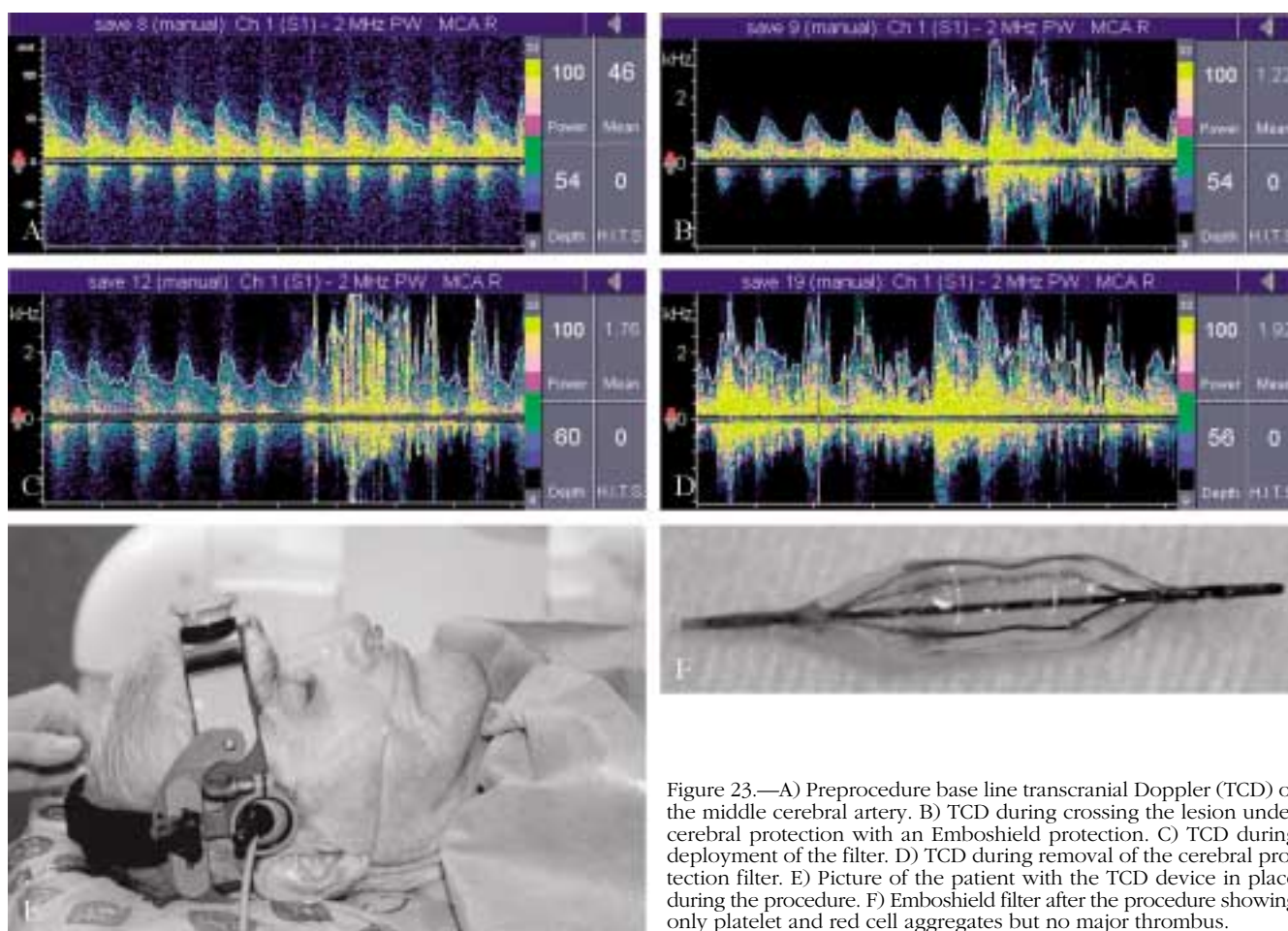


Figure 23.—A) Preprocedure base line transcranial Doppler (TCD) of the middle cerebral artery. B) TCD during crossing the lesion under cerebral protection with an Emboshield protection. C) TCD during deployment of the filter. D) TCD during removal of the cerebral protection filter. E) Picture of the patient with the TCD device in place during the procedure. F) Emboshield filter after the procedure showing only platelet and red cell aggregates but no major thrombus.

is used from the femoral approach reaching the CCA. The introducer system is an aspiration large bore catheter with an occlusive balloon at the tip. Once the system is in place, the mechanical thrombectomy device is advanced and deployed through a microcatheter using standard technique, across the site of the occlusion in the middle cerebral artery. Once deployed the device is gently pulled back and torqued to engage the clot. Once the clot is engaged, occlusion of the flow is established and continuous suction is applied to the delivery system with a large syringe, as the engaged clot is pulled out through the sheath. A follow-up angiogram is performed and the occluded vessel carefully evaluated. Risks of the device are arterial spasm, arterial wall laceration/perforation, and reperfusion bleeding into the brain.

### Pharmacological management of the patient for carotid artery stenting and pre and postprocedure care

It has been shown that carotid stenting should be performed following premedication with aspirin and clopidogrel, to reduce the incidence of thrombus and platelet build up on the surface of the plaque, particularly if ulcerations are present. More recently, a retrospective review of more than 1 000 patients undergoing CEA it was observed that patients using statins for more than one week suffered less strokes, less TIAS and presented less mortality than untreated patients.<sup>43</sup> Although the available data pertains to CEA treated patients, it is reasonable to assume that patients for CAS will benefit as well.

Heparinization is important during the procedure,

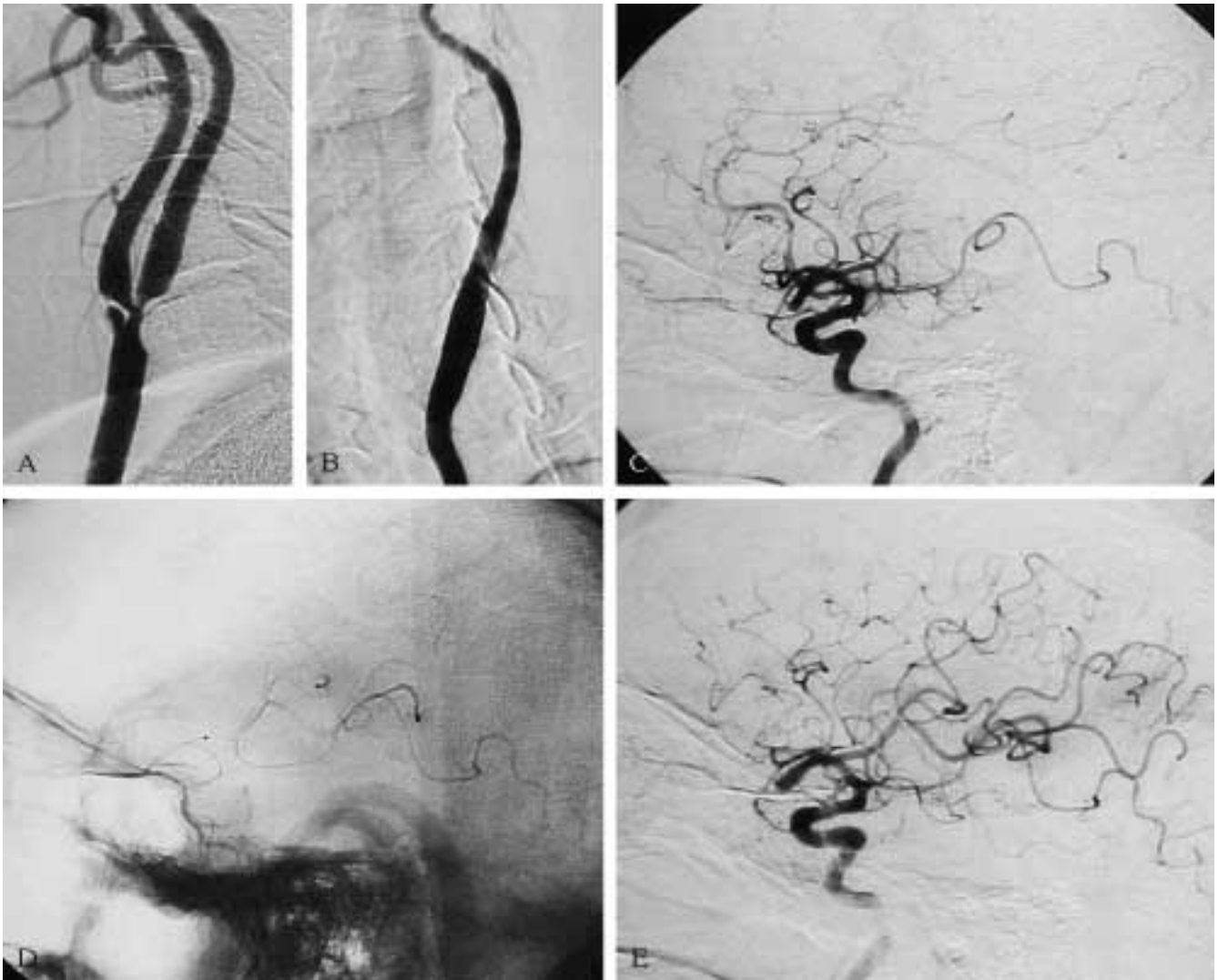


Figure 24.—A) Angiogram of a tight complex carotid artery stenosis, extending from the internal carotid to the common carotid and to the external carotid. B) Angiogram following carotid stenting showing a patent internal carotid, but occluded external carotid. C) Intracranial angiogram showed occlusion of the middle cerebral artery. D) A microcatheter was advanced into the middle cerebral artery and 500 000 IU of UK were infused. E) Completion intracranial angiogram showing patency of the middle cerebral artery. A CT of the brain did not show any changes.

to reduce clot formation within and around the instruments and catheters used. Activated clotting time (ACT) should be maintained at about 250 s (reference value ACT range 70-189 s). IIB/IIIA inhibitors are not currently recommended during or after carotid stenting. Foley catheter may be necessary to reduce discomfort during the procedure and monitor diuresis.

Atropin should be used to treat bradycardia or asy-

tole during carotid angioplasty and stent placement.<sup>43</sup> It seems that there is no advantage of prophylactic use of atropin. The operator should be careful with patients taking  $\beta$ -blockers, because these patients will start the procedure with a much lower heart rate and may not respond as well to atropin as other patients not taking the medication.

In the postprocedure phase, if the patient persists with bradycardia and low blood pressure, dopamine

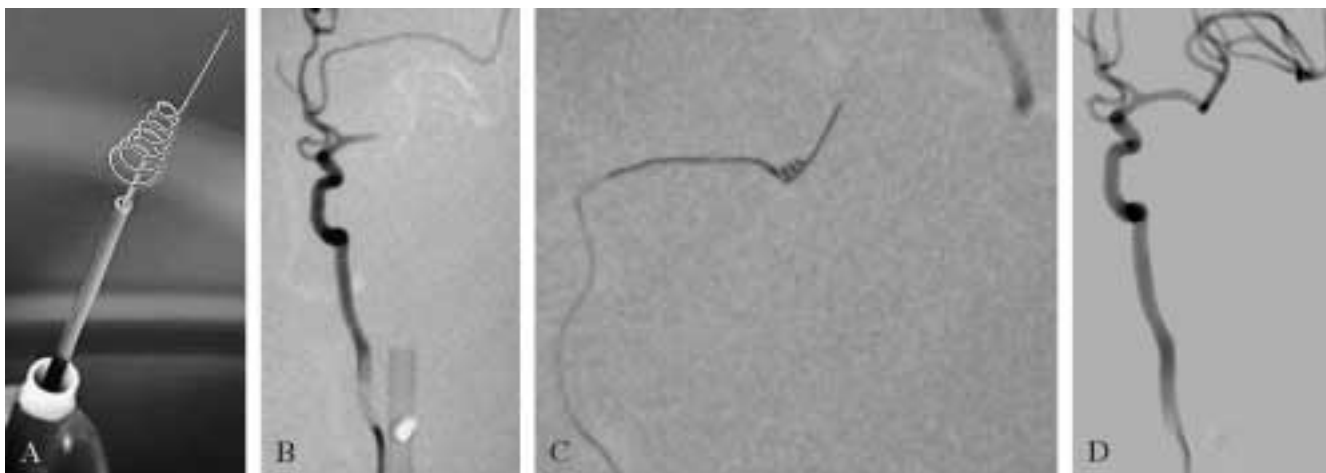


Figure 25.—A) The Merci device. Note the large delivery system with a balloon at the tip for occlusion and aspiration. B) Carotid angiogram on a bench model showing occlusion of the middle cerebral artery. C) The Merci device deployed within the middle cerebral artery across the occluding thrombus. D) Conclusion angiogram showing restored patency of the middle cerebral artery.

infusion may be used as necessary. Cardiac, and blood pressure monitoring is mandatory in those cases. The patient should be admitted to acute inpatient care unit. Close vital surveillance is necessary, q 15 min until stable, then q 30 min x 4, then q 2 h; i.v. fluids D 51/2 NS + 20 meq KCl/L at 50 mL/h until oral diet tolerated. Atropine should be used in case of bradycardia and hypotension, 0.5 gm i.v. q 15 min, *p.r.n.* h. A temporary pacemaker may be necessary in rare patients.<sup>44</sup> Pain medication should be available, as well as medication for nausea. Clopidogrel should be continued in the postprocedure recovery and continue as suggested below.

Long-term medication after carotid stenting should include clopidogrel for at least one month and aspirin for the rest of the patient's life.

#### Pharmacologic protocol

- Before the procedure:
  - aspirin (100-325 mg/*die*);
  - clopidogrel (Plavix) (75 mg/*die* for 2-3 days);
  - statins used for one week before procedure;
- during the procedure:
  - heparin i.v. (70-100 IU/kg) with ACT between 250-300 s (wait 3 to 5 min before approaching the arch branches);
  - atropine 0.5-1 mg/i.v. (after dilation/stenting if bradycardia and/or hypotension),
  - careful with patients taking  $\beta$ -blockers;

— postprocedure:

- i.v. hydration;
- dopamine (infusion pump available);
- atropine 0.5 mg i.v. q 15 min. *p.r.n.* h;
- hold blood pressure medication;
- long-term medication:
  - clopidogrel (Plavix) (75 mg/day/1 month);
  - aspirin used for long term (only aspirin, if followed by coronary bypass surgery).

#### Discussion

CAS is one of the most controversial minimally invasive endovascular procedures ever developed. The start was slow and took a significant amount of time, but development, and refining of the instruments allowed the achievement of adequate results, comparable to CEA. Despite the obvious advances, particularly in the last few years, a number of issues are still pending resolution. Significant controversy was generated by the discussion of the most prepared operator to perform CAS safely and effectively. Training in carotid catheterization is essential for CAS, since the procedure is not feasible if proper, safe, and stable catheterization is not achieved. Now it is becoming clearer that operators with more experience, previous training with catheter/wire procedures and doing more than 25-50 cases per year do it safely. The recognition of the anatomic difficulties from the

aortic arch anatomy, carotid tortuosity and plaque characteristics for the success of the procedure is a more recent realization and still unsettled. Device selection is a matter of training and familiarity, which should match the anatomic characteristics of the particular patient. In US, the number of approved devices is still small and limits the selection of devices for some specific lesions. The stent cell geometry is a relatively recent discussion, and it seems that there is strong evidence that the closed-cell geometry is safer, reducing the number of stroke and TIA events post-procedure. In longer deep ulcerations, it seems that the braided monofilament alloy stents, such as the Wallstent, are advantageous. As of this writing, no such stent has been approved for CAS in the US. On the other hand, tortuous internal carotids may require a more flexible open-cell geometry stent. The open-cell stents, however, may penetrate the intima of the artery due to the "fish scale" effect, creating a potential restenosis site, or a fracture point due to the stress upon the metal. The internal carotid to common carotid discrepancy in diameter is another potential problem, which some available straight stents does not address properly. Therefore, selection of the right stent for the proper anatomy is an essential part of the procedure. Cerebral protection has been showed to be of benefit for the safety of the procedure,<sup>45</sup> however, the available protection devices do have some potential drawbacks, and one device does not solve all the problems. In general, the filtering capabilities are variable and the pore size range from 100 to 120  $\mu$ . The smaller the pore size, the higher the chances of flow obstruction if the filter in fact captures particles. The larger cerebral protection devices, with bigger metal frame, are potentially more prone to produce arterial spasm. Some cerebral protection devices, however, are designed to remain motionless within the ICA during catheter exchange, reducing the risk of spasm. The reversal of flow devices has a clear indication in highly complex lesions with ulcerations where clots and platelet clusters may be present. However, the patient has to have an open external carotid artery and up to 8% of the patients may not tolerate the occlusion and reversal of flow within the ICA, limiting the utilization of the device. There is still a very unclear situation regarding the use of carotid stenting in the elderly population. It is becoming of concern, however, that patients with more than 80 years of age may be at higher risk for stroke complications following CAS.<sup>16, 45</sup> It is not clear, however, why that

would be the case. It is very likely that more advanced disease, as well as unfriendly anatomy of the arch and carotids may be the problem, and if that is taken in consideration in the patient's selection process, it may be an avoidable problem. Another pending issue is the understanding of the significance of the presence of vulnerable carotid plaques. It seems that patients with softer plaques with more lipids and ulcerations are more embologenic and the complication rates of these patients are higher. The use of IVUS with virtual histology may help in selecting these patients, excluding them from CAS. After CAS, neurocognitive and memory performance may improve, however it is not consistently demonstrated or understood.<sup>16</sup> In summary, CAS is still evolving and we are learning that selection of the patient is still the most important issue in the consideration for treatment of the patients with carotid occlusive artery disease.

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