Eur J Vasc Endovasc Surg **21**, 220–226 (2001)
doi:10.1053/ejvs.2000.1308, available online at http://www.idealibrary.com on IDEAL®

Cerebral Blood Flow in Relation to Contralateral Carotid Disease, an MRA and TCD Study*

A. J. de Nie[1], J. D. Blankensteijn†[1], G. H. Visser[2], J. van der Grond[3] and B. C. Eikelboom[1]

[1]*Department of Surgery, Division of Vascular Surgery,* [2]*Department of Clinical Neurophysiology and* [3]*Department of Radiology, University Medical Center Utrecht, PO Box 85500, NL-3508 GA Utrecht, The Netherlands*

Objective: *to describe redistribution of cerebral blood flow in patients with severe internal carotid artery (ICA) stenoses in relation to contralateral ICA disease.*
Methods: *sixty-six patients scheduled for carotid endarterectomy (CEA) were grouped according to severity of contralateral stenosis (<30% [group I]; 30–69% [group II]; 70–99% [group III]; occlusion [group IV]. Transcranial Doppler (TCD) and magnetic resonance angiography (MRA) investigations were performed preoperatively.*
Results: *TCD demonstrated a reversed flow in the contralateral anterior cerebral artery (A_1 segment) and ophthalmic artery in three-quarters of group IV patients ($p<0.0001$). Group IV patients also exhibited decreased blood flow velocity in the contralateral middle cerebral artery ($p=0.001$). MRA showed increased ipsilateral ICA and basilar artery (BA) blood flow volumes (Q-flows) in group IV patients when compared to the other groups ($p<0.001$). No changes in total Q-flow (ICAs + BA) were found.*
Conclusions: *in patients considered for CEA, the severity of the contralateral ICA disease is an important determinant of the pattern of blood flow redistribution through the anterior communicating pathway and ophthalmic artery. Significant flow redistribution through the posterior communicating pathway occurs especially in patients with contralateral ICA occlusion.*

Key Words: Magnetic resonance angiography; Transcranial Doppler; Cerebral arteries; Collateral pathways; Carotid endarterectomy; Cerebrovascular disorders pathophysiology.

Introduction

Severe stenosis of the internal carotid artery (ICA) leads to ischaemic events in some patients, whereas a similar stenosis may be asymptomatic for life in others. The explanation for this symptomatic variety is multifactorial and includes genetic, anatomic, pathological and environmental elements.[1–3]

With respect to the impact of major vessel stenosis or occlusion on cerebral perfusion, a large number of collateral pathways have been described.[3–8] Most studies in this field involve qualitative and morphological measurements. Transcranial Doppler (TCD) and magnetic resonance angiography (MRA) provide quantitative data. TCD investigates blood flow velocities (BFV) in the major intracranial cerebral arteries,[9–11] and with the advent of MRA, volume flow measurement in the major cerebral arteries has become possible.[7,9,11–18]

MRA and TCD proved to provide complementary information when applied to the study of brain haemodynamics in patients with obstructive carotid lesions.[8,11,19] Both techniques have been used to measure intracerebral flow in healthy volunteers and in patients with unilateral carotid stenosis or occlusion.[3,6–8,11,17–22] MRA and TCD data from patients with bilateral carotid disease are currently unavailable. The aim of the present study was to describe patterns of cerebral blood flow redistribution using MRA and TCD in patients with severe stenosis of the internal carotid artery (ICA) in relation to the severity of contralateral ICA disease.

Material and Methods

Study group

From July 1995 through September 1996, 125 patients were scheduled for carotid endarterectomy (CEA) in

† Please address all correspondence to: J. D. Blankensteijn, Department of Surgery, Division of Vascular Surgery, G.04.232, University Medical Center Utrecht University Hospital Utrecht, PO Box 85500, NL-3508 GA Utrecht.
* Presented at the XIth annual meeting of the European Society for Vascular Surgery, 17–20 September 1997, Lisbon, Portugal.

1078–5884/01/030220 + 07 $35.00/0

the University Hospital Utrecht. Only the sixty-six patients (43 men and 23 women) with an angiographic stenosis of at least 70% (NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria)[23] of the internal carotid artery in this group and both MRA and TCD data were included. The remaining 59 patients were excluded because 15 patients had an angiographic stenosis of less than 70%; five patients were claustrophobic, which made an MRA impossible, and in 40 patients MRA and TCD could not be obtained prior to surgery. The mean (range) age was 65 (44–81 years). Forty-eight patients were symptomatic (18 minor stroke, 18 transient ischaemic attacks and 12 ocular) and 18 asymptomatic. Thirteen patients also had contralateral neurological symptoms, 10 of whom had a contralateral ICA occlusion, one a contralateral stenosis >70% and two a <30% contralateral stenosis. Thirty-nine patients were operated on the left side and 27 on the right side.

Patients were grouped according to the severity of the stenosis contralateral to the ICA scheduled for surgery: less than 30% contralateral stenosis (29 patients, group I); 30–69% contralateral stenosis (10 patients, group II); 70–99% contralateral stenosis (14 patients, group III); contralateral occlusion (13 patients, group IV).

TCD sonography

BFV was measured by means of a transcranial Doppler in the middle cerebral artery (MCA), anterior cerebral artery (ACA) A1 segment, posterior cerebral artery (PCA) P1 segment and ophthalmic artery (OA) on both sides and in the basilar artery (BA). Flow direction was assessed in the A1 segments of the ACA and in the OA on both sides. A DWL multidop X device (DWL Elektronische Systeme GmbH, Sipplingen, Germany) with a 2-Mhz pulsed Doppler probe was used. The OA was investigated with a 4-Mhz probe. MCA, ACA and PCA were insonated through the temporal window, the OA through the orbit and the BA through the foramen magnum.

If an intracranial vessel was not found, it was considered as a missing value, and was not included in the statistical analysis. BFV was expressed in cm/s as the mean value of the Doppler velocity spectrum outline (representing maximal flow velocity) over 4.5 s (Vmean). Negative values represent flow velocity in a reversed direction.

The examinations were performed by experienced clinical neurophysiology technicians under direct supervision of an experienced neurophysiologist (GHV).

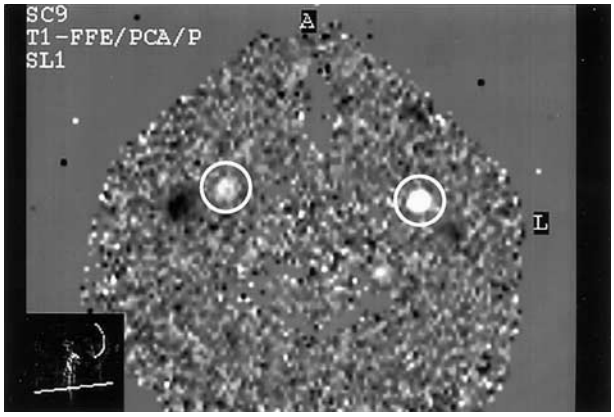

Fig. 1. The MRA slice positioned perpendicular to the CCAs in a patient with a severe stenosis of the right ICA and <30% stenosis of the left ICA. The white circles indicate the manually drawn regions of interest from which volume flow data was obtained. In the lower left corner the orientation of the 2D PC slice is shown in a sagittal plane.

MRA imaging

MR angiography (MRA) studies were performed on a Philips Gyroscan ACS-NT 15 whole body system (Philips Medical Systems, Best, The Netherlands) operating at 1.5 Tesla. Quantitative flow measurements were performed in the common carotid arteries (CCA), in the ICAs, in the BA and in the MCAs. All subjects underwent the same MRA protocol.

First, two non-triggered 2D phase contrast (PC) MR survey scans in coronal and sagittal orientation were performed to visualise the CCAs, the carotid bifurcations, the ICAs, the external carotid arteries (ECAs) and the circle of Willis. In the sagittal orientation two slices were acquired: slice thickness 50 mm, −5 mm slice gap (overcontiguous slices), field-of-view (FOV) 250 × 250 mm, TR/TE (repitition time/echo time) 14/7 ms, flip angle 20°, velocity sensitivity 30 cm/s and four averages. In the coronal orientation we used a single slice (thickness 60 mm) with the same variables. Thereafter, two 2D PC single slices for quantitative flow measurement were positioned. One slice was positioned perpendicular to both CCAs (Fig. 1) and the other slice perpendicular to the C3 segments (precellar segments) of the ICAs and to the basilar artery (Fig. 2) (slice thickness 5 mm, FOV 250 × 250 mm, TR/TE 16/9 ms, flip angle 7.5°, velocity sensitivity 100 cm/s and eight averages). Quantitative flow measurements were performed with previously optimised scan protocols featuring a radio-frequency spoiled gradient echo sequence with full echo sampling.

These measurements were followed by a 3D time of flight (TOF) MRA measurement of the circle of Willis (50 slices, slice thickness 0.6 mm, FOV

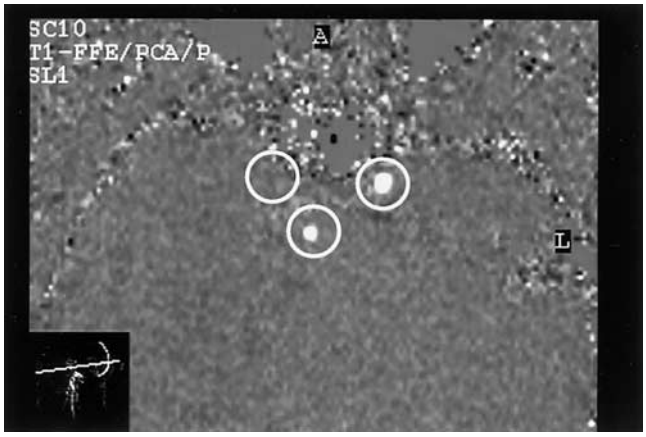

Fig. 2. The MRA slice positioned perpendicular to the ICAs and BA in the same patient as indicated in Fig. 1. The white circles indicate the manually drawn regions of interest from which volume flow data was obtained. In the lower left corner the orientation of the 2D PC slice is shown in a sagittal plane.

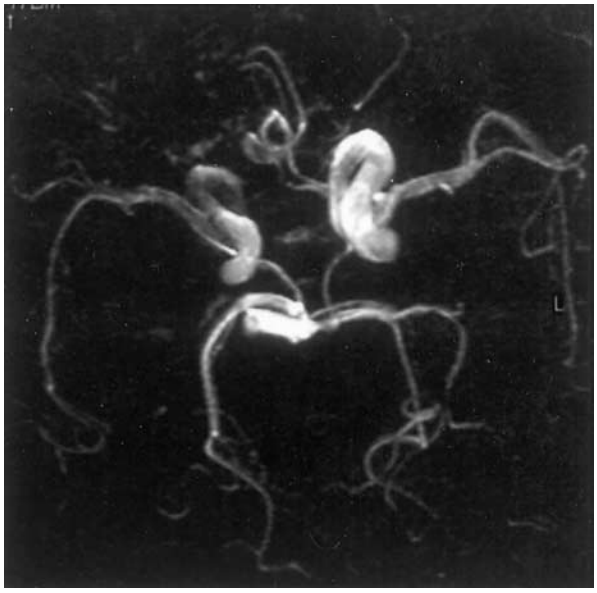

Fig. 3. The results of a 2D time of flight MRA study of the circle of Willis of the same patient as indicated in the previous figures. This figure shows the maximum intensity projection in the transversal direction.

100×100 mm, TR/TE 32/7 ms, flip angle 20° and two averages). On the basis of the reconstruction of the circle of Willis in three directions (Fig. 3), two 2D PC single slices were positioned perpendicular to the left and right MCA (slice thickness 5 mm, FOV 250×250 mm, TR/TE 17/10 ms, flip angle 8°, velocity sensitivity 70 cm/s and 24 averages). The diameters of the anterior and posterior cerebral arteries were too small to perform reliable flow measurements. All volume flow data were obtained by integrating across manually drawn regions of interest enclosing the vessel lumen as closely as possible. The same reader evaluated all images.

Thus we obtained quantitative blood volume flow (Q-flow) in the BA, both MCAs, and in both the ICA scheduled for operation and the contralateral ICA (C-ICA). The sum of the ICA and C-ICA volume flows was expressed as total ICA volume flow (T-ICA). The sum of the T-ICA and BA volume flows was expressed as total volume flow (TOT).

Data analysis

TCD measured BFV values are expressed as cm/s and MRA measured volume flow values as ml/min. All values are given as median with interquartile range (IQ range, 25th–75th percentiles), unless otherwise indicated. For statistical analysis we used non-parametric tests: Mann–Whitney to compare two groups and Kruskal–Wallis to compare more than two groups. For analysis of flow direction in ACA-A_1 and OA, Fisher–Exact and Test for trend were used. A p-value <0.05 was considered statistically significant.

The side of the ICA with a 70–99% stenosis scheduled for surgery was designated the "ipsilateral side", and the "contralateral side" referred to the side contralateral to the ICA scheduled for surgery.

Results

TCD

Table 1 shows the TCD-derived blood flow velocities in the ACA, MCA, PCA, AO and BA, respectively.

In the contralateral occlusion group, group IV, the most important changes in BFV were found. In this group the median BFV in the ipsilateral ACA (I-ACA) ($p<0.001$) was increased. On the contralateral side the median BFV was significantly decreased to a negative value in the ACA (C-ACA) and in the C-OA in the same group ($p<0.005$ and $p<0.001$, respectively). Also in group IV, a decreased BFV was found in the contralateral middle cerebral artery (C-MCA) (median BFV 43 cm/s) as compared with the other groups (median BFV 58 cm/s) ($p=0.001$, Mann–Whitney). In the C-PCA and BA a tendency towards increased BFV with increasing contralateral stenosis was found, although this did not reach statistical significance ($p=0.1$).

Table 2 shows the proportions of patients with reversed flow in the ACA A_1 segment and OA. In

Table 1. Blood flow velocity measured with TCD (in cm/s with the number of observations and the IQ range).

Group	I	II	III	IV
BFV I-ACA (N)	31 (20)	35 (6)	65 (10)	84** (11)
IQ range	9–42	24–48	43–78	72–111
BFV C-ACA (N)	62 (23)	66 (23)	70 (10)	−68* (10)
IQ range	54–82	58–80	55–76	−97–7
BFV I-MCA (N)	54 (27)	53 (10)	66 (13)	65 (12)
IQ range	45–63	51–66	48–76	49–74
BFV C-MCA (N)	56 (29)	56 (10)	68 (13)	43**** (12)
IQ range	50–72	52–71	53–72	37–53
BFV I-PCA (N)	36 (17)	31 (9)	49*** (11)	45 (9)
IQ range	32–42	28–35	42–74	29–58
BFV C-PCA (N)	37 (23)	34 (9)	51 (11)	41 (9)
IQ range	24–46	32–43	38–59	30–74
BFV I-OA (N)	13 (25)	15 (7)	16 (11)	10 (8)
IQ range	7–22	13–22	9–20	−11–14
BFV C-OA (N)	23 (28)	20 (10)	11** (12)	−14** (11)
IQ range	16–28	15–28	1–17	−41–8
BFV BA (N)	44 (26)	40 (9)	50 (13)	53** (11)
IQ range	30–53	35–59	43–74	50–74

* $p<0.005$ Kruskal–Wallis, ** $p<0.001$ Kruskal–Wallis, *** $p=0.01$ Kruskal–Wallis, **** $p=0.001$ Mann–Whitney.

Table 2. Reversed flow in ACA-A_1 segment and AO by TCD (cases/observations).

Group	I-ACA*	C-ACA	I-OA	C-OA
I	5/20	0/23	4/25	0/28
II	1/6	0/9	0/7	0/10
III	1/10	1/10	2/11	3/12
IV	0/11	7/10**	3/8	9/11**

* $\chi^2=3.7$, $p=0.05$ Test for trend, ** $p<0.001$, Fisher–Exact.

group IV, the C-ACA A_1 segment and C-OA showed a reversed flow in three-quarters of cases ($p<0.001$, Fisher–Exact, as compared with the other groups). With increasing severity of contralateral disease (group I through IV) the proportion of reversed ipsilateral ACA A_1-segment flow decreased ($\chi^2=3.7$, $p=0.05$ Test for trend) and the proportion of reversed C-ACA A_1-segment flow increased.

MRA

Table 3 summarises the results of the MRA Q-flow measurements.

The most important findings are an increased Q-flow in the ipsilateral ICA and in the BA in group IV as compared to the other groups ($p=0.01$ and $p<0.005$, respectively) and a decreased T-ICA Q-flow ($p<0.005$) in group IV. Also in group IV a decreased Q-flow was found in the C-MCA ($p=0.01$); in the ipsilateral MCA no significant changes were found. No statistical significant changes in Total Q-flow were found. In group III no significant Q-flow differences were found in the ICA or BA.

Discussion

Severe stenosis or occlusion of the ICA results in a decreased arterial pressure distal to the stenosis. Under normal circumstances, a decrease in regional cerebral perfusion pressure (rCPP) is compensated for by a decrease in peripheral vascular resistance, by means of vasodilatation (autoregulation).[12,24,25] As a result, the cerebral blood flow (rCBF) can be maintained. A second mechanism to maintain rCBF relates to differences in bilateral pressures which promotes recruitment of collateral pathways.[21] Consequently, the net effect of a decrease in CPP due to an ICA stenosis or occlusion on the CBF may be little or none.[26–31]

In some patients there is limited potential for collateral supply, e.g. poor collateral capacity of the circle of Willis or anatomic variations in leptomeningeal vessels. In such a situation a decrease in the CPP directly results in a decreased rCBF if autoregulation has reached its maximum capacity. Kleinschmidt *et al.*[12,32] used acetazolamide-induced vasodilatory stress MRI to show exhaustion of the cerebral autoregulatory reserve capacity in patients with unilateral occlusion of the internal carotid artery. Others showed the same exhaustion using TCD or acetazolamide enhanced single photon emission computed tomography.[12,28–30,33]

In patients with bilateral ICA lesions, there may not be a difference in the bilateral CPP in the anterior circulation. In this case, increased flow through the basilar artery may compensate for the reduced CPP in the anterior circulation.

Because our patients had rather similar ipsilateral stenoses, we can examine the effect of increasing contralateral stenosis. Our study shows that Q-flow in

Table 3. MRA-derived flow volume values.

Group	*n*	Q-flow I-ICA (ml/min) median (IQ range)	Q-flow C-ICA (ml/min) median (IQ range)	Q-flow T-ICA (ml/min) median (IQ range)
I	29	176 (125–213)	317 (238–362)	457 (413–555)
II	10	192 (122–218)	271 (224–316)	427 (393–501)
III	14	167 (142–264)	267 (171–315)	476 (433–519)
IV	13	299 (258–372)*	0***	300 (258–372)**

*** $p<0.001$, ** $p<0.005$, * $p=0.01$, Kruskal–Wallis.

Group	*n*	Q-flow BA (ml/min) median (IQ range)	Q-flow TOT (ml/min) median (IQ range)
I	29	148 (104–192)	646 (573–695)
II	10	141 (107–168)	591 (540–673)
III	14	179 (150–204)	658 (560–738)
IV	13	245 (187–292)**	543 (488–601)

** $p<0.005$.

Group	*n*	Q-flow I-MCA (ml/min) median (IQ range)	Q-flow C-MCA (ml/min) median (IQ range)
I	29	121 (86–160)	133 (92–160)
II	10	85 (68–134)	118 (108–133)
III	14	129 (92–146)	151 (132–163)
IV	13	113 (98–128)	97 (66–101)*

* $p=0.01$, Kruskal–Wallis.

the ipsilateral ICA increases with increasing stenosis on the contralateral side, especially in case of contralateral occlusion, whereas flow in the contralateral ICA tends to decrease. This confirms the capability of a stenosed ICA to contribute to the collateral supply via the circle of Willis, in case of a lower contralateral CPP.

Although we found changes in the relative volume flow contribution in both ICAs, the total ICA flow remained unchanged in all severities of contralateral disease as long as the contralateral ICA was not occluded. In the case of contralateral ICA occlusion (group IV), our combined TCD and MRA results show more severe changes. With no flow through the occluded contralateral ICA, MRA shows a significant increase in ipsilateral ICA flow but also in the BA. This shift towards flow in the posterior circulation suggests that collateral flow in the circle of Willis through the posterior communication arteries is important in the case of contralateral occlusion.

The significant increase in BA Q-flow in group IV, as found by MRA, could not be demonstrated in BFV using TCD. There was a tendency towards an increased BA BFV in group IV but the numbers in this group are small relative to the standard deviation of the measurements.

Despite the anterior to posterior shift, total Q-flow remained unchanged in our groups and is also comparable to figures described for older people in literature.[14,16,21,34]

Of note are the TCD-derived decreased BFVs in the C-ACA and C-OA in group IV. These reached a negative value, which means that the median flow direction is reversed. This corresponds with the increasing number of patients in whom a reversed flow direction is found in C-ACA or C-OA with increasing contralateral ICA stenosis. The reversed flow direction in the C-ACA confirms the capability of a stenosed ICA to contribute to the collateral supply of the circle of Willis. The reversed flow in the OA and C-OA suggests the recruitment of the physiological external-internal carotid artery bypass, as was found by others.[6,8,19]

It is remarkable that, despite the unaltered total Q-flow in group IV, the C-MCA Q-flow and BFV are decreased. This may be a type-II error, but it is tempting to hypothesise that there is recruitment of collateral pathways other than those directly related to the circle of Willis.

The number of TCD observations varies considerably from artery to artery because some are easier to find than others. It is not possible to estimate whether this lack of insonation could be due to low flow or anatomic variation. As the incidence of lack

of insonation was not clearly different between the four groups, this factor was not considered to have an important impact on the measured TCD velocities.

It should be noted that the group of patients we have studied is a selection of patients presented to the vascular surgeon and scheduled and fit for surgery. This is a group of patients who did not suffer from major stroke or death. For this reason we cannot extrapolate our data to all patients with internal carotid occlusive disease.

Conclusion

In patients with severe stenosis of the ICA who are considered for CEA, the severity of the contralateral ICA disease is an important determinant of the pattern of blood flow redistribution through the anterior communicating pathway (MRA and TCD) and OA (TCD). Significant flow redistribution through the posterior communicating pathway occurs, especially in patients with contralateral ICA occlusion (MRA).

Acknowledgements

This study was supported by The Netherlands Heart Foundation, grant D94.012.

References

1 Bock RW, Gray Weale AC, Mock PA *et al*. The natural history of asymptomatic carotid artery disease. *J Vasc Surg* 1993; **17**: 160–169.
2 Eliasziw M, Streifler JY, Spence JD *et al*. Prognosis for patients following a transient ischemic attack with and without a cerebral infarction on brain CT. North American Symptomatic Carotid Endarterectomy Trial (NASCET) Group. *Neurology* 1995; **45**: 428–431.
3 Schromer DF, Marks MP, Steinberg GK *et al*. The anatomy of the posterior communicating artery as a risk factor for ischemic cerebral infarction. *N Engl J Med* 1994; **330**: 1565–1570.
4 Riggs HE, Rupp C. Variation in the circle of Willis. *Arch Neurol* 1963; **8**: 24–30.
5 Nornes H. The role of the circle of Willis in graded occlusion of the internal carotid artery in man. *Acta Neurochir* 1973; **28**: 165–177.
6 Davis WL, Turski PA, Gorbatenko KG, Werber D. Correlation of cine MR velocity measurements in the internal carotid artery with collateral flow in the circle of Willis: preliminary study. *J Magn Reson Imaging* 1993; **3**: 603–609.
7 Edelman R, Mattle H, O'Reilly G *et al*. Magnetic resonance imaging of flow dynamics in the circle of Willis. *Stroke* 1990; **21**: 56–65.
8 Miralles M, Dolz JL, Cotillas J *et al*. The role of circle of Willis in carotid occlusion: assessment with phase contrast MR angiography and transcranial duplex. *Eur J Vasc Endovasc Surg* 1995; **10**: 424–430.
9 Baumgartner RW, Mattle HP, Aaslid R. Transcranial color-coded duplex sonography, magnetic resonance angiography, and computed tomography angiography: methods, applications, advantages, and limitations. *J Clin Ultrasound* 1995; **23**: 89–111.
10 Meairs S, Rother J, Neff W, Hennerici M. New and future developments in cerebrovascular ultrasound, magnetic resonance angiography, and related techniques. *J Clin Ultrasound* 1995; **23**: 139–149.
11 Provinciali L, Minciotti P, Ceravolo MG *et al*. Haemodynamic changes following carotid occlusion: MRI angiography and transcranial Doppler patterns. *Neurol Res* 1992; **14**: 208–210.
12 Turski PA, Levine R, Tunipseed W, Kennell T. MR angiography flow analysis. Neurovascular applications. *Magn Reson Imaging Clin N Am* 1995; **3**: 541–555.
13 Priatna A, Paschal CB. Variable-angle uniform signal excitation (VUSE) for three-dimensional time-of-flight MR angiography. *J Magn Reson Imaging* 1995; **5**: 421–427.
14 Kashimada A, Machida K, Honda N *et al*. Measurement of cerebral flow with two-dimensional cine phase-contrast MR imaging: evaluation of normal subjects and patients with vertigo. *Radiat Med* 1995; **13**: 95–102.
15 Talagala SL, Jungreis CA, Kanal E *et al*. Fast three-dimensional time-of-flight MR angiography of the intra-cranial vasculature. *J Magn Reson Imaging* 1995; **5**: 317–323.
16 Vanninen R, Koivisto K, Tulla H, Manninen H, Partanen K. Hemodynamic effects of carotid endarterectomy by magnetic resonance flow quantification. *Stroke* 1995; **26**: 84–89.
17 Enzmann DR, Ross MR, Marks MP, Pelc NJ. Blood flow in major cerebral arteries measured by phase-contrast cine MR. *AJNR Am J Neuroradiol* 1994; **15**: 123–129.
18 Evans AJ, Iwai F, Grist TA. MR imaging of blood flow with a phase subtraction technique: in vitro and in vivo validation. *Invest Radiol* 1993; **28**: 109–115.
19 Anzola GP, Gasparotti R, Magoni M, Prandini F. Transcranial Doppler sonography and magnetic resonance angiography in the assessment of collateral hemispheric flow in patients with carotid artery disease. *Stroke* 1995; **26**: 214–217.
20 Bendel P, Buonocore E, Bockisch A, Besozzi MC. Blood flow in the carotid arteries: quantification by using phase-sensitive MR imaging. *Am J Roentgenol* 1989; **152**: 1307–1310.
21 Marks MP, Pelc NJ, Ross MR, Enzmann DR. Determination of cerebral blood flow with a phase-contrast cine MR imaging technique: evaluation of normal subjects and patients with arteriovenous malformations. *Radiology* 1992; **182**: 467–476.
22 Levine RL, Turski PA, Holmes KA, Grist TM. Comparison of magnetic resonance volume flow rates, angiography, and carotid Dopplers. Preliminairy results. *Stroke* 1994; **25**: 413–417.
23 North American Symptomatic Carotid Endarterectomy Trial Collaborators. Benificial effect of carotid endarterectomy in symptomatic patients with high-grade stenosis. *N Engl J Med* 1991; **325**: 445–453.
24 Powers WJ. Hemodynamics and metabolism in ischemic cerebrovascular disease. *Neurol Clin* 1992; **10**: 31–48.
25 Powers WJ. Cerebral hemodynamics in ischemic cerebrovascular disease. *Ann Neurol* 1991; **29**: 231–240.
26 Hayashida K, Hirose Y, Kaminaga T *et al*. Detection of postural cerebral hypoperfusion with technetium-99m-HMPAO brain SPECT in patients with cerebrovascular disease. *J Nucl Med* 1993; **34**: 1931–1935.
27 Sacca A, Pedrini L, Vitacchiano G *et al*. Cerebral SPECT with 99mTc-HMPAO in extracranial carotid pathology: evaluation of changes in the ischemic area after carotid endarterectomy. *Int Angiol* 1992; **11**: 117–121.
28 Rozenkranz K, Hierholzer J, Langer R *et al*. Acetazolamide stimulationtest in patients with unilateral internal carotid artery obstructions using transcranial Doppler and 99mTc-HM-PAO-Spect. *Neurol Res* 1992; **14**: 135–138.
29 Cikrit DF, Burt RW, Dalsing MC *et al*. Acetazolamide enhanced single photon emission computed tomography (SPECT) evaluation of cerebral perfusion before and after carotid endarterectomy. *J Vasc Surg* 1992; **15**: 747–753.

30 Burt RW, Witt RM, Cikrit DF, Reddy RV. Carotid artery disease: evaluation with acetazolamide-enhanced HMPAO SPECT. *Radiology* 1992; **182**: 461–466.
31 Algotsson L, Ryding E, Rehncrona S, Messeter K. Cerebral blood flow during carotid endarterectomy determined by three dimensional SPECT measurement; relation to preoperative risk assessment. *Eur J Vasc Surg* 1993; **7**: 46–53.
32 Kleinschmidt A, Steinmetz H, Sitzer M, Merboldt KD, Frahm J. Magnetic resonance imaging of regional cerebral blood oxygenation changes under acetazolamide in carotid occlusive disease. *Stroke* 1995; **26**: 106–110.
33 Visser GH, van Huffelen AC, Wieneke GH, Eikelboom BC. Bilateral Increase in CO2 reactivity after unilateral carotid endarterectomy. *Stroke* 1997; **28**: 899–905.
34 Blankensteijn JD, van der Grond J, Mali WPThM, Eikelboom BC. Flow volume changes in the major cerebral arteries before and after carotid endarterectomy: an MR angiography study. *Eur J Vasc Endovasc Surg* 1997; **14**: 446–450.

Accepted 15 December 2000