No Absolutes in Neuromonitoring for Carotid Endarterectomy

Edwin M. Nemoto

Stroke 1999;30;895-
Stroke is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0039-2499. Online ISSN: 1524-4628

Letters to the Editor

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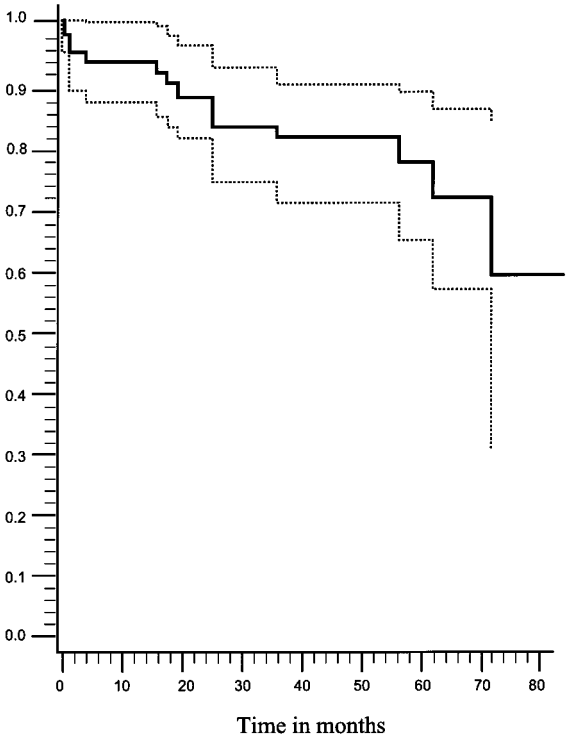
Ischemic Stroke in Poland and the United States

To the Editor:

We, as neurologists, read with interest the report of Massing et al[1] on stroke mortality trends in Poland and the United States. The authors found different stroke mortality trends in the 2 countries (a decrease in the United States, an increase in Poland), a difference that was more pronounced in younger groups of patients. They concluded that the difference could have resulted from the effects of lifestyles and socioenvironmental and medical care determinants.

Our study on stroke in young adult patients has led us to similar conclusions. Between 1988 and 1995 in the Department of Neurology of the Medical Academy in Warsaw, we saw 71 patients (38 men and 33 women) aged 18 to 45 years (mean, 36.89±6.77 years) with a diagnosis of first-ever ischemic stroke. Four of our patients died within 28 days. All the deaths were atributed to the stroke. To assess long-term prognosis among this group of patients, we performed a follow-up study. We obtained precise information on 66 of 67 patients (98.5%) who survived the first stroke episode. The observation times varied from 4 months to 7 years (mean, 45.85±21.84 months). Two of the patients died during the observation time (both vascular deaths), and 9 others experienced a second ischemic stroke between 1 month and 6 years after the first (see the Figure).

Calculated 28-day mortality in our group was 5.6%; the incidence of vascular death or recurrent stroke was 5.6%/y (95% CI, 3.2 to 9.7), and after 24 months it was 10.9% (95% CI, 7 to 14.8).



Kaplan-Meier curve for combined vascular death and second, nonfatal stroke.

The 28-day mortality rate, regarded as one of the methods to judge hospital performance,[2] was similar in our group to the data in the literature (3.65% to 7%).[3–5] It could suggest that acute care in stroke in our center is similar to that in others. Quite to the contrary, recurrent stroke and vascular deaths appeared in our data twice as often as in the literature. In the similar group described by Kappelle et al,[4] the risk of vascular death, stroke, or nonfatal myocardial infarction was 2.6%/y; in the study of Hier et al,[6] 5.2% of the patients (of similar age) experienced recurrent stroke within 24 months after the first-ever stroke. As far as risk factors are concerned, we found cigarette smoking in 63% of our patients and hypertension in 44%. These results are also different compared with published data. Rohr et al[7] found cigarette smoking among young stroke patients (in 40% of whites and 52% of blacks). Kapelle et al[4] noticed this risk factor in 57% of their patients (mainly white Americans), but the data were collected between 1977 and 1992. As far as hypertension is concerned, it was present in 44% of the patients in our group whereas in similar groups in the literature 19% to 33% were hypertensive.[3,4,8] Rohr et al[7] found hypertension present in 60% of the black young adults in their study.

Our results confirm, although indirectly, the conclusion formed by Massing et al[1] in their study. Both the high rate of recurrent strokes in our study and the mortality trends found in that of Massing et al could be the effects of lifestyle and socioenvironmental determinants.

Jaroslaw Pniewski, MD, PhD
Neurology Department
Medical Research Centre
Polish Academy of Sciences

Beata Szyluk, MD
Department of Neurology
Warsaw Medical School
Warsaw, Poland

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No Absolutes in Neuromonitoring for Carotid Endarterectomy

To the Editor:

I have some concerns about the recently published study by Beese et al.[1] While I applaud the number of patients they studied, they misled the readers regarding the reliability of somatosensory evoked potentials (SEP) for carotid endarterectomies. I question the validity of their data because of their description of sensor location, inadequate data presentation, and conclusions that are not warranted by their results. I also disagree with some of the points raised in their discussion.

To their credit, the authors addressed some of these concerns, but inadequately, I believe. My 5-year experience with near-infrared spectroscopy (NIRS), the NIRO 500, and the INVOS 3100A and 4100 convinces me that the INVOS accurately measures brain hemoglobin oxygenation even in pathological states. Understanding what is being measured and how best to apply it in its many potential and untested uses is the challenge before us.

First, the authors tacitly imply that SEP monitoring is 100% sensitive and specific by stating that the avalidity of SEP has been established. In fact, previous studies involving 200 to 500 patients report sensitivity of 60% to 100% and specificity of 94% to 100%.[2–4] No neuromonitoring technique monitors the entire brain. SEP monitors the somatosensory strip over the postcentral gyrus. The middle cerebral artery feeds most of the cerebral cortex and is most likely to be affected by carotid clamping. Frontal placement of the sensor monitors part of the ACA and MCA arterial distributions.

The authors also chose the aloss of SEP, where the N20 and P25 are not discernible, to call for a shunt. Shunts are usually called with a P25 amplitude reduction of $\geq$50%. In our study,[5] any changes in SEP, even decreases of $<$50%, were correlated with rSO_2 decreases of $\geq$10 units.

Second, if comparisons are to be made with median SEP, some portion of the middle cerebral artery territory should be in the view of the sensor. The sensor should be placed as close to the hairline as possible, with the detectors and light-emitting diode (LED) parallel to and about 0.5 to 1.0 cm from the hairline and as far lateral as possible over the temporal lobe. Patients with a high hairline or who are bald allow placement of the detectors and LED parallel to the sagittal sinus and over the watershed zone. Additionally, avoidance of the frontal sinus is essential. If the inferior aspect of the sensor is placed immediately above the eyebrow, the optodes can be over the frontal sinus. The uncertainty of sensor placement renders the entire study subject to question.

It is important to know what is being "seen" by the sensor. A review of the CT scan, usually available in the operating room, may reveal the presence of an infarct or other anomaly. Infarcted brain could give normal values of oxygenation,[6] likely due to the measurement of sequestered, pooled venous blood in nonmetabolizing tissue. This drives home the fact that cerebral oximetry measures oxygen availability and not cerebral blood flow.

Third, their data presentation makes it impossible for the reader to relate individual rSO_2 change to the loss or persistence of SEP as presented in Figure 1 in their article. Absolute values were not presented except for the median and ranges. If the authors presented the absolute values or the mean and SD, rather than the median and SD, the 95% confidence interval could be calculated.

Fourth, Beese et al cite 13 different articles to support their statement that absolute rSO_2 values are of no value. Of these articles, those reporting poor correlation with jugular venous oxygen saturation in pathological states, such as during carotid cross-clamping, are clearly misguided. Cerebral oximetry should not correlate with jugular venous saturation in pathology because jugular venous saturation is not a reliable indicator of hemispheric ischemia. If blood flow to the ipsilateral hemisphere is completely interrupted by the carotid cross-clamp, the entire outflow is from the opposite hemisphere. In several articles, the validity of cerebral oximetry was questioned because of the lack of correlation with brain blood flow, specifically when blood flow is absent in dead or brain-dead persons. It is critical to understand that the oximeter measures capillary oxyhemoglobin percent saturation and not blood flow.

The INVOS uses the concept of spatial resolution, and the rSO_2 index is actually the ratio of the HbO_2 signal relative to the isobestic point, thereby giving the absolute percentage of oxyhemoglobin or hemoglobin oxygen saturation. It is true that one cannot calculate the absolute oxyhemoglobin concentration without knowing the path length, but the ratio of HbO_2 to total Hb is absolute and valid. In my experience, the normal value in adults ranges between 65 and 75 and in children between 55 and 65, or about 10 points lower than adults. I have not seen values much outside of this range except in patients with pathology. Regarding the variability in anormal people, it is of interest to note that oxygen microelectrodes with tip diameters of 1 μ placed in the cerebral cortex yield values ranging from 0 to arterial PO_2. Could this distribution of values be somehow skewed in some anormal patients? It is also uncertain whether some patients may have AV malformations or other problems that may affect cerebral oximetry readings and still be anormal.

Understanding how best to apply and use this new technology in its many potential applications, not only on the brain but on other organs as well, will help further scientific knowledge and improve patient care and thereby reduce the cost of patient care.

Edwin M. Nemoto, PhD
Department of Neurological Surgery
Presbyterian University Hospital
University of Pittsburgh
Pittsburgh, Pennsylvania

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Comparison of Near-Infrared Spectroscopy and Somatosensory Evoked Potentials for the Detection of Cerebral Ischemia During Carotid Endarterectomy

To the Editor:

When used appropriately, the INVOS 3100A is a valuable tool for monitoring cerebral perfusion during carotid endarterectomy. Over the last 4 years we have monitored over 600 carotid endarterectomies, with a stroke rate of less than 2% and a shunt insertion rate of only 10%. All our patients are monitored with this device.

Beese et al[1] used somatosensory evoked potentials (SEP) to predict shunt requirements. However, no patient suffered perma-

nent neurological injury, and it cannot be assumed that SEP would have forewarned neurological damage.

They experienced "considerable variability" in the oximetry reading using the INVOS 3100A when the probe was placed on the forehead. We demonstrated in 1994[2] that the forehead is inappropriate for this purpose. The sensitivity to hypoxemia is greatly improved (as might be expected) when the probe is placed over the relevant middle cerebral artery territory. With a "correctly" positioned probe in the parietal area, we demonstrated a highly significant ($r=0.92$, $P<0.001$) correlation between jugular venous oxygen saturation and oximetry readings; however, the INVOS 3100A is virtually useless when positioned over the frontal cortex in carotid surgery. We have never experienced a patient refusing to have a small area of scalp shaved for this purpose.

Beese et al have not produced any evidence to invalidate the opposite conclusion: that near-infrared spectroscopy detects cerebral hypoxia during carotid endarterectomy and is the simplest apparatus to use and interpret.

H. Chant, FRCS
G. Riding, FRCS
A. Picton, BSc
C.N. McCollum, MD, FRCS
Department of Surgery
University Hospital of South Manchester
Manchester, UK

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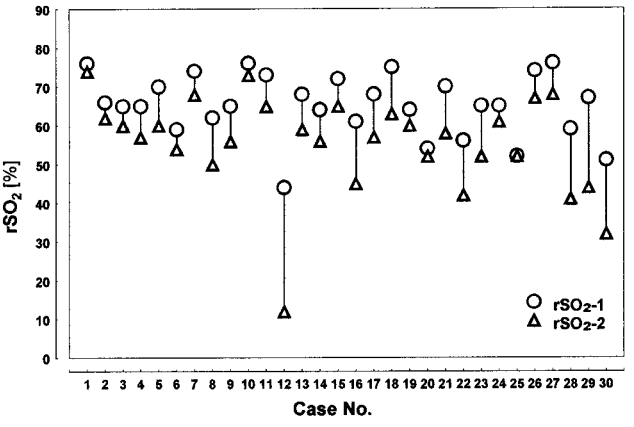
Response

We are grateful for the opportunity to reply to the comments of Nemoto and Chant and collegues on our study.[1] Both letters reflect the heated debate concerning the usefulness of near-infrared spectroscopy (NIRS) in the setting of carotid endarterectomy under general anesthesia. Although Nemoto as well as Chant and collegues are convinced of the clinical value of the INVOS 3100A, they are adding little evidence to support their conviction besides "personal experience." However, one of the basics when introducing a new monitoring device is to answer the question of whether aquisition of data will alter the treatment plan. Therefore, it is essential to define a threshold under which neuronal damage is likely to occur and intervention is appropriate. So far, no threshold values, confirmed by the individual neurological outcome of a sufficient number of patients, were found for the INVOS 3100A. The hypothesis that this device reliably detects cerebral ischemia has yet to be validated. To ask for an invalidation (letter of Chant and collegues) can only thereafter be accomplished.

No single neuromonitoring device will detect all causes of perioperative cerebral damage with a 100% sensitivity and specificity, and we never claimed that this can be accomplished by the monitoring of SEP. However, the loss of cortical waveform after cross-clamping of the internal carotid artery is a reliable marker for severe clamp-related ischemia and the need for placement of an intraluminal shunt.[2,3] Our own preliminary validation study[4] showed that a loss of cortical waveform N20P25 was followed by neurological deficits in 7 of 9 nonshunted patients. The significance of a clamp-related SEP loss was also demonstrated in a study of patients undergoing the same procedure under regional anesthesia.[5] A prospective analysis of our database, including more than 1500 patients, revealed that a preserved cortical SEP predicts uneventful recovery at emergence from general anesthesia in 99.4% of cases (Dinkel, unpublished data). Therefore we believe that SEP is useful as a reference method for new forms of neuromonitoring such as NIRS.



Change of regional cerebral saturation (rSo_2) before (rSo_2-1) and after (rSo_2-2) cross-clamping of the internal carotid artery in patients with loss of cortical SEP during clamping phase. Note the high variability in preclamping values and the differences in magnitude of rSo_2 decrease after cross-clamping.

Nemoto states that there is a correlation between changes in SEP and reduction of "regional cerebral saturation" (rSo_2).[6] It should be noted that in their study only 9 patients were monitored by means of INVOS 3100A. Two patients showed a reduction of SSEP amplitude after carotid cross-clamping, but in only 1 patient did a >50% reduction occur. However, in both patients a decrease of ≈11% in rSo_2 was noted. We have seen patients with rSo_2 changes of >11% without concomittant SEP loss as well as patients with minimal or even no changes with accompanying SEP loss (see the Figure). Nemoto and collegues are merging a complete loss and a <50% reduction of SEP. Although the latter criterion is not recognized as an indicator of cerebral ischemia that requires intervention, they claim that a decrease of >10% of the displayed rSo_2 value should dictate the need for a shunt. Given the few patients studied and the inherent risk of shunt placement, we do not think this recommendation is justified.

We agree with Nemoto and Chant et al that the placement of the sensor is of importance. We stated that the sensor location was "according to the manufacturer instructions over the ipsilateral forehead," and this implies that the lower margin of the sensor was ≈2 cm above the eyebrow, thus not covering the frontal sinus. Chant and collegues were trying to provide evidence that only placement of the sensor over the temporal lobe is correct by correlating the rSo_2 readings with jugular venous oxygen saturation in 14 patients.[7] However, the significance of a good correlation between the readings of the INVOS and jugular venous oximetry is unclear, since the latter form of neuromonitoring is acknowledged as unreliable in carotid surgery.[8] On this point we agree with Nemoto, although we doubt his statement that during cross-clamping of the internal carotid artery the entire venous outflow comes from the other hemisphere. Interestingly, a recently published study[9] provides evidence that lateral placement will not improve the performance of INVOS 3100 in patients with severe cerebral ischemia indicated by clamp-related EEG changes.

Dr Nemoto is correct when he states that blood pools between the sensor and the brain reduce the effectiveness of the INVOS measurement. By means of routinely obtained CT scans prior to surgery, we excluded that artifact.

We did not cite articles concerning jugular venous oximetry for the lack of correlation with NIRS but for the variability of the obtained values for rSo_2 prior to any intervention. We cannot share Dr Nemoto's experience regarding the values he stated as normal in

adults. Although the possibility of unknown underlying pathology cannot be excluded, it seems unlikely that this is true for many patients who will be outside the narrow "normal range" of 65 to 75. It is our concern that a single displayed rSO_2 number will give a false sence of certainity. The fact that a device which claims effective reduction of extracranial contamination will give rSO_2 readings of >70% in cadavers with removed brains renders the interpretation of single numbers questionable.[10]

Due to the various etiologies of neurological damage during and soon after carotid endarterectomy, a multimodal monitoring approach in patients undergoing this procedure under general anesthesia is desirable.[11] There is growing evidence that transcranial Doppler will be a useful adjunct to electrophysiological monitoring.[12] The same will have to be proved for NIRS before implementation of this evolving technology will lead to an improvement of patient care.

Ulrich Beese, MD
Harald Langer, MD
Michael Dinkel, MD
Department of Anaesthesiology

Werner Lang, MD
Department of Surgery
Division of Vascular Surgery
University of Erlangen-Nürnberg
Erlangen, Germany

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Advantages of Transcranial Power Duplex Imaging After Contrast Injection to Detect Low Flow in a Moyamoya Syndrome

To the Editor:

We read with great interest articles recently published in *Stroke* by Nabavi et al,[1] Goertler et al,[2] and Postert et al,[3] who reported an increasing interest for the diagnostic value of contrast-enhanced transcranial color-coded duplex sonography in ischemic cerebrovascular disease. To the best of our knowledge, however, transcranial power duplex imaging (TPDI) after contrast injection has not yet been evaluated in stroke patients.

TPDI is one of the most recent development in neurosonology. Distinct from color duplex flow imaging (CDFI), PDI produces intravascular color signals based on the reflected echo amplitude, depending mainly on the amount of red blood cells within the sample volume. The consequence of this principle, associated with the use of special filter systems for blood/tissue discrimination, is an increased signal-to-noise ratio. PDI provides a more useful diagnosis in complicated, high-grade stenoses of internal carotid arteries (ICAs) than does CDFI,[4] but it has not yet been studied in stenoses of intracranial arteries, even though a superiority of PDI over CDFI has been suggested regarding the depiction of central as well as peripheral segments of intracranial vasculature.[5] Injection of contrast agent for ultrasound results in a significant signal enhancement of the cerebral arteries and improves the diagnostic usefulness[6] of transcranial duplex imaging, but it has not yet been evaluated specifically in severe stenoses of intracranial vasculature. However, a recent study[7] suggests a strong interest in using ultrasound contrast with CDFI in the differential diagnosis between subocclusion and occlusion of ICA, allowing the depiction of slow flow in large vessels. We would like to share our interesting experience of combining these 2 new duplex imaging modalities—TPDI with contrast injection—to improve cerebral artery delineation and to image low flow in a case of moyamoya syndrome.

In October 1996, a 42-year-old man without previous medical history was admitted because he presented with 5 recurrent transient ischemic attacks (TIAs), manifested each time by an isolated left-sided hemiparesis. The motor deficit was completely resolved each time within 24 hours. Brain MRI showed multiple small ischemic lesions without leukoencephalopathy in the white matter of both hemispheres. Conventional cerebral angiography

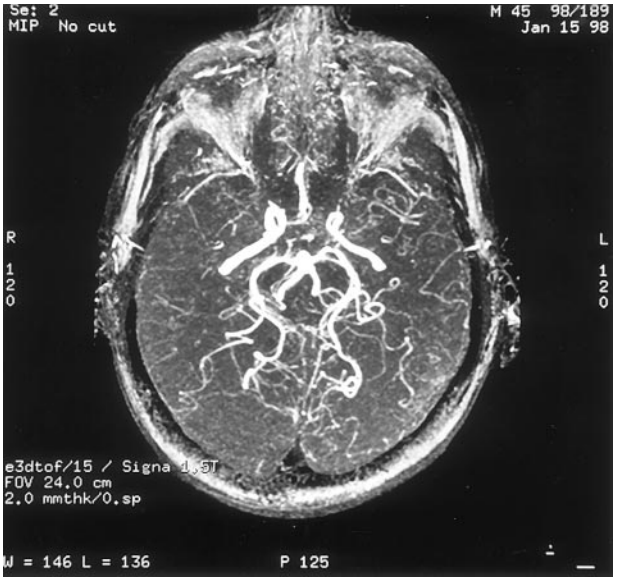

Figure 1. MR angiogram using time-of-flight (TOF) technique and maximum intensity projection image reconstruction algorithm showing severe stenosis of the distal segment of the ICAs, reduced flow in the M2 segment of the left MCA, and absence of detectable flow within the M1 segment of both MCAs as well as within the left ACA. These features led to a presumptive diagnosis of moyamoya disease. (Through the courtesy of Dr T. Duprez and Prof G. Cosnard, Department of Radiology, Université Catholique de Louvain, UCL, Bruxelles, Belgium.)

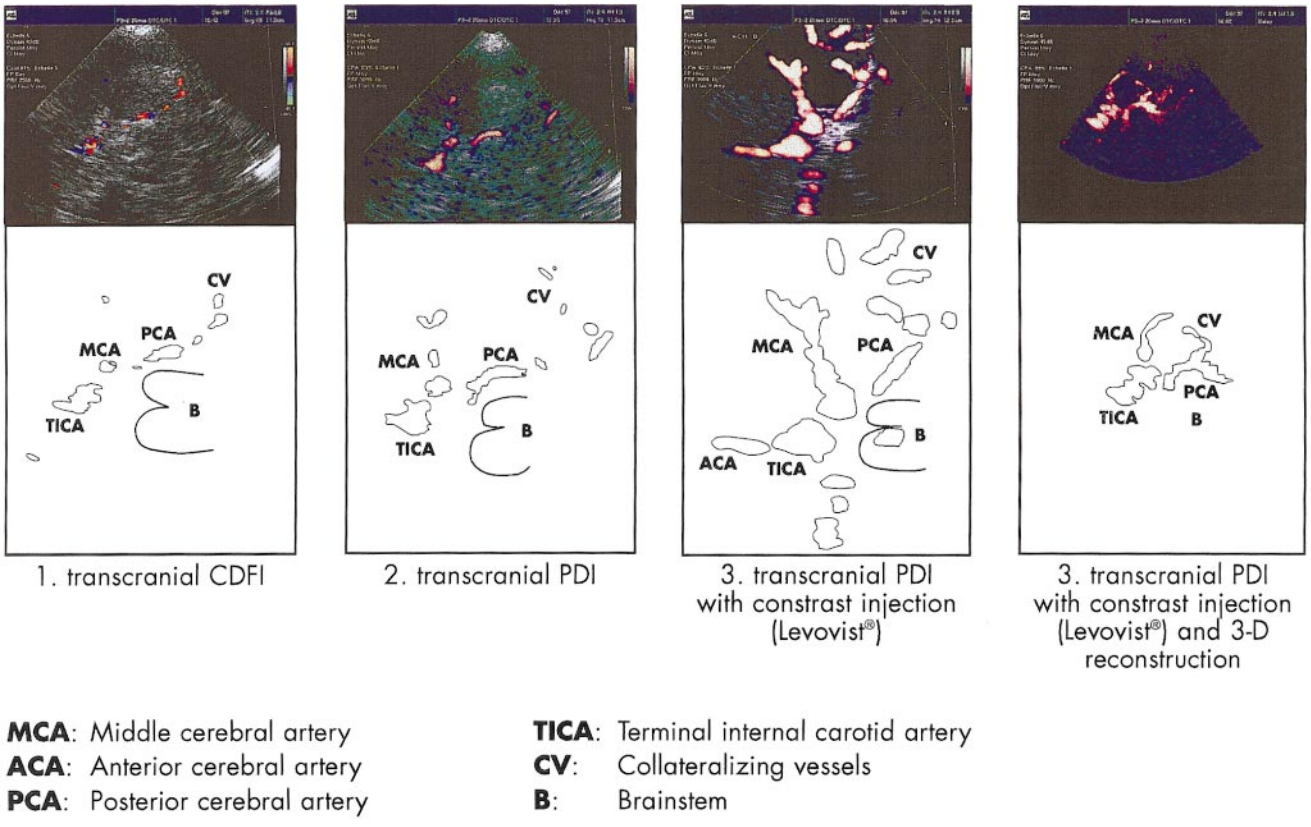

Figure 2. Panel 1, No color signal depicted on the right MCA while an aliasing phenomenon is observed on the right terminal internal carotid artery; small collateralizing vessels and large right PCA observed on TCDFI. 2, In comparison to TCDFI, appearance of small color signals on the right MCA and better visualization of both collateralizing vessels and right PCA with TPDI. 3, TPDI after contrast injection (c-TPDI) reveals the right MCA and a very developed collateral network that converges toward the territory of MCA; the right MCA is clearly visualized, and parts of vessels equivocally interpreted as vessels or artifacts appear as branches or loops of colateralizing vessels on c-TPDI with 3D reconstruction (fourth panel).

revealed bilateral stenosis of the supraclinoid ICA (left>right), subocclusion of the right middle cerebral artery (MCA), severe stenosis at the origin of the left MCA and of the anterior cerebral artery (ACA), and collateralization by the external carotids (middle meningeal/temporal arteries) as well as pial collaterals arising from the branches of the posterior cerebral arteries (PCAs). According these radiological findings and the absence of any other demonstrated cause of TIAs despite an extensive search, we concluded that it was moyamoya syndrome and instaured antiplatelets (300 mg/d of aspirin) as treatment. Three months later, the patient continued to present with TIAs, exhibited as left-sided hemiparesis, and stopped working. At this time, we discussed the opportunity of surgical revascularization because of his poor response to the medical therapy, but the patient refused surgery. In October 1997, he noticed a slight regression of TIA occurrence—always characterized by a left hemiparesis—and continued to take aspirin. He rejected conventional angiography because he was still opposed to surgery, and we performed MR angiography (MRA) as well as a transcranial color Doppler flow imaging (TCDFI) and a TPDI without and after contrast injection (c-TPDI). MRA was performed using both 3D time-of-flight and phase contrast techniques without contrast agent injection on a 1.5-T system. Maximum intensity projection images disclosed severe stenosis of the supraclinoid ICA on both sides (left≫right) and absence of detectable flow within the proximal segment of the 2 MCAs and the left ACA (Figure 1). Slow flow reappeared distally in the left MCA, and a marked collateralization from external carotids arteries and PCAs was observed (Figure 1). The conventional TCD showed peak systolic velocities of 175 and 259 cm/s on the right and left terminal ICAs, respectively, with no Doppler signal recorded on both MCAs and on the left ACA. TCDFI (Figure 2, panel 1) showed a mosaic-like pattern of changing red and blue effects (aliasing) in the region of both terminal ICAs (left≫right), suggestive of stenoses of the terminal ICAs, and no depiction of the 2 MCAs and left ACA. TCDFI detected enlargement of the PCA on both sides and small collateralizing vessels. TPDI without Levovist enhanced (panel 2) the detection of small, atypical collateralizing vessels and showed some signals on both MCAs. TPDI after contrast injection (panel 3) considerably improved the diagnostic usefulness of TPDI: both MCAs were well distinguished by c-TPDI in contrast with previous modalities. Moreover, c-TPDI revealed multiple collateralizing vessels. In our case, we assume that both the neurosonographer and neuroradiologist who performed the MRA were informed of the results of the former conventional angiography (in which patency of intracranial vessels was found) at the moment of their examination. Thus, we believe that the knowledge of the previous intracranial vascular status of the patients as reported by conventional angiography could not logically influence one more than the others.

We agree with Morgenstern et al,[8] who observed in two moyamoya patients that TPDI visualized parts of the intracranial collateral network not possible with TCDFI and allowed a better diagnosis of intracranial vascular pathology than TCDFI. In our case, TPDI also improved the detection of the intracranial collateral network and noted color signals on both MCAs, which was not possible with TCDFI. Meairs and Hennerici[9] recently concluded that although TPDI was an interesting approach, allowing imaging of small vessels (the anterior and posterior

communicating arteries, for instance) as well as identifying low flow after intracranial stenoses or occlusions, clinical evaluation of TPDI was still underway. C-TPDI considerably enhanced the ability to evaluate collateralization as well as low flow in a subocclusive stenosis of intracranial vasculature in our case, just as described by Hennerici[7] for extracranial large arteries. This case report suggests that PDI with contrast could be superior to 3D and phase-contrast MRA to identify very low flow consecutive to a proximal intracranial artery stenosis, but no definite conclusions can be drawn for these single case report findings. Further clinical studies are required to address this issue. It is well known that MRA can overestimate the degree of brain arterial stenosis, particularly in high-grade stenoses, which are visualized as a loss of signal and, in consequence, erroneously interpreted as an occlusion. c-TPDI associated with 3D reconstruction (Figure 2, panel 3) allows a better visualization of the supply from PCA to MCA. With 3D imaging, the small, atypical collateralizing vessels are, in fact, loops or branches of the vessels equivocally identified as vessels or artifacts with TCDFI, TPDI, and c-TPDI. However, despite the fact that no false-positive diagnosis of a nonoccluded intracranial artery by TPDI with contrast has been reported (series have included too few patients), we should take this possibility into account for the following reasons. First, a short application period (10 to 15 seconds) of the echo-contrast agent as applied in our study and others could lead to an increased color "blooming" artifact that could be erroneously interpreted as residual poststenotic flow, even if "blooming" was reduced by decreasing the color Doppler gain. The use of a slower administration of the echo-contrast agent (at least 3 minutes) may reduce color artifacts but has not yet been specifically compared with the short application period. Second, as described by Baumgartner et al,[3] a deep middle cerebral vein that drains toward the insula and the basal vein of Rosenthal provides color Doppler signals showing the same flow directions as those of the MCA and PCA, respectively. Consequently, it is very difficult to discriminate slow arterial flow (poststenotic) from venous flow by means of TPDI without spectral Doppler analysis. This point is still more crucial for TPDI with or without contrast because this duplex modality, by principle, cannot provide information concerning the flow's direction. Even if TPDI and c-TPDI essentially provide a "map" of the intracranial circulation without hemodynamic data about flow velocity and direction (the reason we feel that these techniques must be combined with conventional TCD), we believe that these 2 modalities, particularly c-TPDI, represent a promising technique by which to diagnose subocclusive stenosis of brain arteries characterized by low flow. Further investigations in larger series will be required to establish the reliability of c-TPDI to diagnose low flow in brain circulation.

G. Devuyst, MD
Department of Neurology
CHUV
Lausanne, Switzerland

N. Cals, MD
V. de Borchgrave, MD
P. Bara, MD
M. Vandooren, MD
Department of Neurology
Hôpital de Jolimont
La Louvière, Belgium

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