Redistribution of Cerebral Blood Flow Following STA-MCA By-Pass in Patients With Hemispheric Ischemia

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SUMMARY Regional cerebral blood flow and vasomotor reactivity were measured in 33 patients with surgically remediable hemispheric ischemia by the 133Xe inhalation method prior to superficial temporal to middle cerebral arterial by-pass. Thirteen patients also underwent LCBF and \( L \lambda \) measurements by the stable xenon CT method for comparison. Twenty-four had proximal occlusion of one or both internal carotid arteries, 9 had intracranial occlusive disease (4 internal carotid, 5 middle cerebral). Measurements were repeated at intervals up to 30 months following surgery and compared to measurements in a similar group (N = 13) treated medically. In the surgically treated group 22 patients had recurrent TIAs, of whom 12 also had minor residual neurological deficits from recent small cerebral infarctions with potential for recovery (RINDs) while the remaining 11 had RINDs without TIAs.

After surgery 28 improved with cessation of TIAs and/or neurological recovery, 3 remained unchanged, 2 cases worsened. Compared to age-matched normal hemispheric F\(_1\) (gray matter) values, pre-operative F\(_1\) values in the STA-MCA group were reduced in both ischemic and opposite hemispheres. Ischemic regions showed impaired vasomotor reactivity to 5% CO\(_2\) or 100% O\(_2\) inhalation. After surgery, mean hemispheric F\(_1\) values increased +12.8% on the by-pass side and +10.5% on the contralateral side. Mean F\(_1\) increases reached a maximum 3 months after by-pass, most evident in ipsilateral frontal regions (+24.2%). Vasomotor reactivity did not significantly improve. Medically treated cases did not show similar F\(_1\) increases. Thirteen with carotid occlusive disease (8 with TIAs, 5 with small recent infarcts) underwent CT LCBF and \( L \lambda \) measurements before and after STA-MCA by-pass. Cases with recent infarcts showed reduced LCBF and \( L \lambda \) values which increased significantly after STA-MCA by-pass, however the total group operated upon showed only trends for CBF increases, probably due to large standard deviations encountered in serial measurements.

EXTRACRANIAL TO INTRACRANIAL arterial by-pass procedures, using microsurgical techniques are now commonly carried out at medical centers throughout the world after the technical feasibility of these procedures was first established.

Information is incomplete, however, concerning long-term hemodynamic results of such procedures, which patients may be expected to benefit and how such benefit is brought about. Clinical and arteriographic indications are currently being assessed by randomized clinical trials to assess long-term effectiveness. There is a paucity of information concerning serial measurements made by the 133Xe inhalation method of regional cerebral blood flow (rCBF) supplying both hemispheres before and after superficial temporal artery to middle cerebral arterial by-pass. Those reported, so far, show trends for rCBF increases which correlate with clinical and psychological improvement. There have been a number of reports of serial rCBF measurements made using the intracarotid 133Xe injection method before and after extracranial-intracranial by-pass but in such patients the intra-carotid injection of a bolus of 133Xe is less suitable than the inhalation method of 133Xe administration. The injectate must be inserted via the occluded or contralateral carotid artery, a method which favors the injectioned hemisphere and may overlook collateral circulation via the vertebrobasilar arterial system. There are also ethical problems if invasive techniques are considered for long-term sequential studies. Intraoperative, pre-and post by-pass rCBF measurements, made with miniature detectors placed on the cortical surface combined with fluoresceinangiography clearly demonstrated local redistributions of flow within the ipsilateral hemisphere after by-pass.

The 133Xe inhalation technique is better suited for prospective measurements before and after STA-MCA by-pass, because the entire circulation to the brain is measured including the vertebro-basilar contribution as well as any rCBF changes affecting both hemispheres. Furthermore, comparable groups of patients who have been treated medically can undergo similar prospective measurements for purposes of comparison. Another advantage of the 133Xe inhalation method is that comparisons can be made, not only of F\(_1\) values before and after surgery, but also with age-matched normal controls. Advantages of the 133Xe inhalation method are that resolution is poor due to Compton Scatter and tissue overlap and local partition coefficients (\( L \lambda \)) of ischemic or infarcted brain are assumed rather than measured. The stable xenon inhalation method does not have these limitations.
In the present study, rCBF, LCBF and Lx measurements were made by both $^{133}$Xe and stable xenon CT methods, which are both non-invasive methods. The results of both methods were compared and appear to provide information concerning flow reductions of the contralateral hemisphere as well as the ipsilateral hemisphere, due to intracranial steal prior to surgery. After by-pass there were highly significant flow increases and resolution of the inter-hemispheric steal which were measurable for several months after the surgical procedure. Cerebral vasomotor reactivity showed trends toward improvement but was not significantly altered following the operation. At present, preliminary results are reported, but longitudinal analysis completed so far for 30 months after surgery does not appear to show sustained rCBF increases after this time interval. Compared to a medically treated group, both show comparable age-related declines in CBF between the 6th and 30th month. It is planned to increase the number of subjects admitted to the study and to continue to conduct the longitudinal follow-up for several years.

Patients

Patients Undergoing $^{133}$Xe CBF Measurements

Patients who underwent STA-MCA by-pass in this series were referred by neurosurgeons who are expert in the STA-MCA by-pass procedure. The majority of surgical procedures were carried out by three of the co-authors (JL, RL, RJ) and angiographic procedures by two others (RC, YYL). As shown in table 1 (part 1), all patients had complete occlusion of the internal carotid artery in the neck or stenosis of its intracranial portion. All had recurrent transient ischemic attacks (TIAs) or putative reversible ischemic neurologic deficits (RINDs) resulting from presumed small cerebral infarctions with small low density lesions by CT scanning. Results were compared with a non-operated control group of 13 patients with occlusive disease in the carotid and/or middle cerebral arteries who had a mean age of 54.5 ± 8.9 years. They were comparable in all respects except that they or their physicians elected non-surgical treatment, which consisted of control of hypertension plus two aspirin tablets a day to minimize recurrent TIAs.

Clinical symptoms, risk factors for atherosclerosis, general medical and neurological examination, CT and angiographic findings of each patient were reviewed and checked by two neurologists on the first visit, and patients were reexamined on subsequent visits. The group selected from all patients undergoing STA-MCA by-pass operation consisted of 33 consecutive patients from a group of 36, whose postoperative angiograms showed that the by-pass remained patent (table 1, part 1). Three patients were excluded because post-operative angiograms did not show patency of the by-pass. During follow-up visits, which were scheduled at intervals of 3-6 months, each patient was questioned about recurrent TIAs, RINDs, stroke and any change in cerebral symptomatology as well as undergoing a medical and neurological examination and repeat rCBF measurements. The patient’s hematocrit values did not alter before and after surgery in a manner to significantly alter mean CBF values.

As shown in table 1 (part 1), 10 patients had TIAs without any evidence of low density lesion by CT.

### TABLE 1 Case Material

<table>
<thead>
<tr>
<th>Clinical symptoms</th>
<th>Case numbers</th>
<th>Age mean ± SD</th>
<th>Sex</th>
<th>Extracranial occlusion</th>
<th>Intra-cranial occlusion</th>
<th>Affected hemisphere</th>
<th>Risk factors†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>F</td>
<td>M</td>
<td>L</td>
<td>R</td>
<td></td>
</tr>
<tr>
<td>Part 1. rCBF measurements made by $^{133}$Xe inhalation method</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I. TIA without cerebral infarction</td>
<td>10</td>
<td>56.7 ± 7.7</td>
<td>1</td>
<td>9</td>
<td>7</td>
<td>3 (2)</td>
<td>5</td>
</tr>
<tr>
<td>II. TIA with recent or remote cerebral infarction</td>
<td>12</td>
<td>53.3 ± 9.9</td>
<td>1</td>
<td>11</td>
<td>8</td>
<td>4 (1)</td>
<td>6</td>
</tr>
<tr>
<td>III. Small cerebral infarction, recent, without TIAs</td>
<td>11</td>
<td>52.4 ± 6.2</td>
<td>1</td>
<td>10</td>
<td>9</td>
<td>2 (2)</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>54.0 ± 8.4</td>
<td>3</td>
<td>30</td>
<td>24</td>
<td>9 (5)</td>
<td>17</td>
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<tr>
<td>Part 2. LCBF and Lx measurements made by stable xenon inhalation during CT scanning</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>I. TIA without cerebral infarction</td>
<td>4</td>
<td>57.0 ± 5.2</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>2</td>
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<td>II. TIA with recent or remote cerebral infarction</td>
<td>4</td>
<td>58.0 ± 1.0</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>3 (1)</td>
<td>3</td>
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<tr>
<td>III. Small cerebral infarction, recent, without TIAs</td>
<td>5</td>
<td>58.4 ± 2.3</td>
<td>0</td>
<td>5</td>
<td>4</td>
<td>1 (1)</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>57.5 ± 4.0</td>
<td>0</td>
<td>13</td>
<td>8</td>
<td>5 (2)</td>
<td>6</td>
</tr>
</tbody>
</table>

*Extracranial occlusions showed complete ICA thrombosis in the neck. Intracranial occlusions showed either severe stenosis of intracranial ICA or complete occlusion or stenosis of MCA.
†Risk factors for stroke include hypertension, hyperlipidemia, heart disease and diabetes mellitus.
‡Indicates which series included single cases with fibromuscular dysplasia involving the internal carotid artery in the neck. (N) Parentheses indicate the numbers of cases with MCA occlusion or stenosis.
scans and 12 patients had TIAs plus RINDs and showed low density lesions by CT scan and are listed in table 1 as TIAs with recent or remote cerebral infarction. The remaining 11 patients in this group had no TIAs but had RINDs with small low density areas on CT scan and are listed in table 1 as small, recent cerebral infarctions without TIAs. The mean age of the operated group was 54.0 ± 8.4 years. Twenty-four patients had internal carotid artery occlusion in the neck on the appropriate side for ischemic symptoms. Four patients had marked intracranial ICA stenosis, which were inaccessible for carotid endarterectomy and 5 had MCA occlusion or severe stenosis. Seventeen patients had occlusive disease of the left carotid and 16 of the right carotid arteries. Twenty-five patients had risk factors for atherosclerotic infarction such as hypertension, hyperlipidemia, heart disease and diabetes mellitus. Eight patients had no risk factors and 2 had fibromuscular dysplasia involving both internal carotid arteries. In post-operative follow-up, 28 patients showed cessation of TIAs or improvement of neurological symptoms such as increased motor function of the limbs and/or improvement of speech and mentation. Three patients with RIND and residual minor neurological deficit showed no further neurological improvement and two cases had temporary worsening of dysphasia, hemiparesis and hemisensory loss with subsequent partial improvement. For purposes of comparison a similar group of patients (table 2) with occlusive disease of the carotid-middle cerebral arterial system who were treated medically underwent comparable prospective clinical and CBF evaluations.

Cases Undergoing Stable Xenon Contrast
CT CBF Measurements

As shown in table 1 (part 2) a series of 13 patients with occlusive disease of the carotid artery underwent measurements of local cerebral blood flow (LCBF) and local partition coefficients (LA), before and after STA-MCA by-pass, measured by inhalation of 35% stable xenon during CT scanning11-13 in addition to the 133Xe measurements for purposes of comparison. In all cases, the by-pass was shown to be patent by arteriography. Eleven patients had risk factors for cerebral arteriosclerosis, one had fibromuscular dysplasia and one had occlusive disease of the internal carotid, cause undetermined. There were 8 patients with TIAs and 5 with RINDs. Their mean age was 57.5 ± 4 years of age. Eight cases had occlusion of the internal carotid artery in the neck and 5 had surgically inaccessible intracranial stenosis of the internal carotid artery or complete occlusion or stenosis of MCA. The same levels for CT scanning of the brain were selected for stable xenon measurements before and after surgery, by matching pre-operative and post-operative scans in the CT room during the second visit. Four patients had TIAs without evidence of cerebral infarction on CT scans, 4 patients had both TIAs and a history of remote cerebral infarction which was recognized as a low density lesion on CT scan, and 5 patients had RINDs along with recent small cerebral infarctions appearing as small low density lesions on CT scanning, with good clinical recovery. All patients having stable xenon CT CBF measurements also had 133Xe measurements within 24 hours for purposes of comparison.

Informed Consent

Consent forms, which were approved by the institutional review boards of the VA Medical Center and Baylor College of Medicine, for both methods of cerebral blood flow measurements, were signed by all patients prior to each procedure.

Methods

rCBF Measurements By The 133Xe Inhalation Method

Regional cerebral blood flow was measured by the 133Xe inhalation method14 modified after Obrist et al.15 Briefly, 16 suitably collimated thallium activated NaI crystal scintillation detectors were mounted in a radial array over both hemispheres including frontal, precen-

| Table 2 Age-matched Control Group with Carotid-middle Cerebral Arterial Oclusive Disease Treated Medically |
|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Clinical symptoms | Case numbers | Age (mean ± SD) | Sex | Extra-cr | Intracr |
| | | | | cranial occlusion | cranial occlusion |
| I. TIAs without cerebral infarction | 3 | 54.7 ± 3.4 | 0 | 3 | 3 | 0 | 1 | 2 | 3 | 0 |
| II. TIAs with recent or remote cerebral infarction | 4 | 57.5 ± 7.5 | 0 | 4 | 1 | 3 | (2) | 2 | 2 | 3 | 1 |
| III. Small cerebral infarction, recent, without TIAs | 6 | 52.5 ± 10.9 | 1 | 5 | 3 | 38 (3) | 4 | 2 | 3 | 3 |
| Total | 13 | 54.5 ± 8.9 | 1 | 12 | 7 | 6 (5) | 7 | 6 | 9 | 4 |

*This medically treated group had symptoms similar to the STA-MCA by-pass treated group and followed at intervals between 1 week to 48 months. 3 cases improved, 8 cases showed no change and 2 cases deteriorated.
*Extra-cr Intracr indicates either severe stenosis of intracranial ICA or occlusion or stenosis of MCA. Risk factors for stroke including hypertension, hyperlipidemia, heart disease and diabetes mellitus (+ = present, - = absent).
*Indicates single cases were included diagnosed by clinical signs, symptoms, bruises etc., but arteriography was deferred. (N) Parentheses indicate numbers of cases with MCA occlusion or stenosis.
Results of $^{133}$Xe Inhalation Measurements of Regional CBF

Effects of STA-MCA By-Pass

Average hemispheric $F_{i}$ values were analyzed for both the ischemic and contralateral hemispheres before and after by-pass, and compared with mean $F_{i}$ for age-matched normal healthy volunteers (fig. 1). There were no significant changes in PECO$_2$ or blood pressure before or after surgery and hematocrit and hemoglobin values remained within normal limits before and after surgery. Compared to normal control values of $76 \pm 10$ ml/100g brain/min., preoperative $F_{i}$ values were reduced significantly for both the ischemic hemisphere ($61.1 \pm 11.2$ ml/100g/min, $p < 0.001$) and the contralateral hemisphere ($64.6 \pm 10$ ml/100g/min, $p < 0.001$).

Changes in all regional $F_{i}$ values, for both hemispheres and brainstem-cerebellar regions, before and after STA-MCA by-pass are illustrated in figure 2. Significant regional flow increases were observed in frontal, precentral and occipital areas for the ipsilateral hemisphere. Percentage increases in these regions were $+11.5$ to $+24.2\%$ and were most evident in frontal regions. Significant regional flow increases were also observed in frontal, precentral, parietal, occipital and inferior temporal regions of the opposite hemisphere ($+9.4$ to $+14.4\%$). Similar patterns of regional flow increases were noted when analyzed by regional ISI, and CBF=$v$ values.

Percentage reduction of regional $F_{i}$ values before and after operation were then compared to values for age-matched normal controls and the results are shown in figure 3. Reduction of pre-operative flow values were maximal in the distribution of the occluded carotid artery and its middle cerebral territory. Maximal flow reductions were measured in precentral areas ($-24.8\%$) and sylvian-opercular areas ($-20.2\%$) of the hemisphere supplied by the occluded carotid artery. Following surgery the flow values increased toward normal, however, regions of maximal pre-operative ischemia in the precentral region still showed significant flow reductions compared to control values.

Effects of STA-MCA By-Pass On Cerebral Vasomotor Responsiveness

Prior to operation, (fig. 4) mean hemispheric vasodilator responsiveness to 5% carbon dioxide inhalation was slightly reduced ($+2.5 \pm 2.9$ $\Delta F_{i}/\Delta mmHg$ PECO$_2$) compared to values for age-matched normal volunteers ($+3.5 \pm 1.7\%$). This impairment of vasodilator responsiveness was not significantly improved after the by-pass operation. Compared to normal volunteers, vasoconstrictive responses to 100% oxygen inhalation were slightly impaired prior to the by-pass operation without significant improvement after surgery.

Longitudinal Effects of STA-MCA By-Pass on Cerebral Perfusion Compared To Non-Surgically Treated Patients

Results of longitudinal analysis of rCBF measure-
COMPARISON OF PRE AND POST-OPERATIVE HEMISPHERIC GRAY MATTER FLOW (F₁) VALUES IN PATIENTS WITH PATENT STA-MCA BY-PASS PROCEDURES PERFORMED FOR STENOSIS OR OCCLUSION OF THE INTERNAL CAROTID ARTERY WITH CEREBRAL ISCHEMIC EPISODES AND NORMAL OR SMALL LOW DENSITY LESIONS BY CT SCAN

Age-Matched Normal Controls
(N=33, age 54.8±11.5 yrs. old)

Patients Undergoing STA-MCA By-pass
(N=33, age 54.0±8.4 yrs. old)

Figure 1. To show results of cross-sectional analysis of average hemispheric F₁ values (measured by ¹³³Xe inhalation) of both operated and contralateral hemispheres in patients with STA-MCA by-pass procedures (N = 33, mean age 54.0 ± 7.2 years) compared to values for age-matched normal controls. 1–2 weeks after surgery, hemispheric flow values increased significantly by +12.8% on the by-pass side and 10.5% on the contralateral side.

Results of Stable Xenon CT Measurements of LCBF and Lλ

Mean Bihemispheric LCBF and Lλ Changes After STA-MCA By-Pass

Pre-operative and post-operative values for LCBF and Lλ measurements in patients undergoing the by-pass procedure were compared to normal values measured in healthy volunteers as illustrated in table 3. In general, results measured by the two methods were in good agreement. In table 3, all LCBF and Lλ values, from symmetrically cursored areas of both hemispheres, were pooled for both normal and patient groups and for pre- and post-surgical comparisons. In table 3, cursored areas were selected from areas showing normal CT appearances. Results in low density areas in patients with RIND (shown in table 4) will be...
TO SHOW PERCENTAGE CHANGES IN REGIONAL $F_1$ VALUES AFTER STA-MCA BY-PASS PROCEDURES IN PATIENTS WITH HEMISPHERIC ISCHEMIC EPISODES

$N=33$ Age 54.0 ± 8.4 years old

<table>
<thead>
<tr>
<th></th>
<th>preop</th>
<th>postop</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{CO_2}$</td>
<td>37.6 ± 3.9</td>
<td>37.8 ± 4.8 mmHg</td>
</tr>
<tr>
<td>MABP</td>
<td>97.3 ± 9.2</td>
<td>95.9 ± 14.3 mmHg</td>
</tr>
</tbody>
</table>

Hemisphere Undergoing By-pass
hemispheric average $F_1$
preop 61.1 ± 11.2 ml/100g/min
postop 68.9 ± 11.4

% Change after by-pass
20% Increase
$F_1$ values before by-pass

Contralateral Hemisphere
hemispheric average $F_1$
preop 64.6 ± 10.0 ml/100g/min
postop 71.4 ± 10.0

FIGURE 2. To show percentage increases of regional $F_1$ values (measured by $^{133}$Xe inhalation) after by-pass operation compared to the values before by-pass. Significant regional flow increases were observed in the frontal precentral, parietal and occipital areas in the hemisphere undergoing by-pass operation. In the contralateral hemisphere, significant flow increases were observed in the frontal, precentral, parietal, occipital and inferior temporal areas.

FIGURE 3. To show the percentage reduction of regional $F_1$ values in patients undergoing STA-MCA by-pass, compared to values of age-matched normal controls. Before by-pass operation, as shown in open bars, maximum regional flow reduction was observed in the precentral area of the hemisphere undergoing by-pass. After by-pass, flow reduction rates decreased toward normal as shown in solid bars.
Effects of STA-MCA bypass on cerebral vasomotor responsiveness in patients with hemispheric ischemia

Vasodilator Response to 5% Carbon Dioxide Inhalation

<table>
<thead>
<tr>
<th>Patients</th>
<th>Normal</th>
<th>N=8</th>
<th>(Mean Age 51.6±6.5)</th>
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<tbody>
<tr>
<td></td>
<td>Volunteers</td>
<td>N=10 Before</td>
<td>After</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Mean Age 61.3±6.9)</td>
<td>Bypass Bypass</td>
</tr>
</tbody>
</table>

Vasoconstrictor Response to 100% Oxygen Inhalation

<table>
<thead>
<tr>
<th>Patients</th>
<th>Normal</th>
<th>N=16</th>
<th>(Mean Age 52.4±9.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Volunteers</td>
<td>N=20 Before</td>
<td>After</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Mean Age 54.9±11.4)</td>
<td>Bypass Bypass</td>
</tr>
</tbody>
</table>

Figure 4. To show the effects of bypass operation on cerebral vasomotor responsiveness to 5% carbon dioxide and 100% oxygen inhalation. Vasodilator responsiveness to hypercapnia before bypass showed a trend to be reduced compared to normals, and some trend toward improvement after operation but these differences were not statistically significant. Vasoconstrictive responses during 100% oxygen inhalation were significantly impaired prior to bypass compared with normals (p < 0.001) but trends toward normalization after surgery are not statistically significant for the preliminary data so far available.

Compared to normal values, pre-operative gray matter LCBF values in patients with unilateral carotid occlusive disease were reduced in both hemispheres for both cortex and basal ganglia. Average L values for both gray and white matter were not significantly reduced. When LCBF and L values measurements were repeated 1 to 60 weeks (mean 5.8 weeks) after STA-MCA bypass, LCBF values showed a tendency to increase for both frontal and temporal cortex. Likewise, caudate nuclei, lentiform nuclei and thalamus showed trends toward LCBF increases after surgery. Flow reductions were maximal in the middle cerebral territory, ipsilateral to the occluded carotid artery. Average flow increases were +10% for gray matter and +10.7% for white matter. These trends toward flow increases were not quite significant at the p < 0.05 level, because of the large standard deviation on serial measurements with the stable xenon CT method.

LCBF and L changes in low density regions by CT scanning

LCBF and L values were also measured in the low density regions considered to be anatomically appropriate and responsible for the recent cerebral ischemic neurological deficits (RINDs). This was achieved satisfactorily in six cases as shown in Table 4. Pre-operative LCBF and L values for gray matter in the low density zones showed moderate but significant reductions compared to normal values. Furthermore, these low CBF-low L values showed significant improvements in L values, as well as flow, after bypass. Pre-operative LCBF and L values for low density lesions of white matter, likewise showed that both mean val-
PERCENTAGE DEVIATION OF F1 VALUES FROM PRE-OPERATIVE OR INITIAL CBF MEASUREMENTS MADE OVER A 30 MONTH INTERVAL IN TWO GROUPS OF PATIENTS WITH HEMISPHERIC ISCHEMIA DUE TO CAROTID-MIDDLE CEREBRAL ARTERIAL OCCLUSIVE DISEASE WITH TIAS AND RIND. ONE GROUP UNDERWENT STA-MCA BY-PASS, THE OTHER WAS TREATED ONLY WITH OPTIMAL MEDICAL THERAPY.

<table>
<thead>
<tr>
<th>Time Interval in Months</th>
<th>Case Numbers</th>
<th>Age in Years</th>
<th>Initial Mean Hemispheric F1</th>
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</thead>
<tbody>
<tr>
<td>1-3 months</td>
<td>N = 5</td>
<td>54.5 ± 8.9</td>
<td>64.0 ± 11.3 ml/100g brain/min</td>
</tr>
<tr>
<td>4-6 months</td>
<td>N = 28</td>
<td>54.0 ± 8.4</td>
<td>64.2 ± 11.8</td>
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<tr>
<td>7-18 months</td>
<td>N = 5</td>
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<td>19-30 months</td>
<td>N = 7</td>
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</tr>
<tr>
<td></td>
<td>N = 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 5</td>
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</tr>
</tbody>
</table>

Group differences between limited numbers examined are not significant using non-paired t-test.

FIGURE 5. To compare percentage deviations for F1 values between preoperative or initial measurements and repeated measurements over a 30 month interval in two groups of patients with chronic hemispheric ischemia. One group underwent STA-MCA by-pass and the other was treated medically. In the operated group, flow increases maximally within the first 3 months after operation. In the non-operated patients, flow values generally remained lower than for the initial visit during the entire follow-up period. Differences for flow values were not significant between the medically and surgically treated groups measured at each interval for preliminary data so far available.

Discussion

Most authors agree that patients most likely to benefit from STA-MCA by-pass, are those with cerebral hemodynamic ischemic symptoms (including TIA's and RINDs), associated with occlusion of the internal carotid artery in the neck or marked stenosis or occlusion of its intracranial segments; which are surgically inaccessible. Stenosis or occlusion of the middle cerebral artery, vertebrobasilar arterial lesions and giant aneurysms with compromised cerebral circulation are well-defined indications for extracranial-intracranial by-pass. In all these indications, a major aim of surgery is to supplement an inadequate collateral circulation. Occlusive disease requiring STA-MCA bypass, is usually due to atherosclerosis, but rarely there are other indications including inflammation of arteries, developmental disorders such as fibromuscular dysplasia, congenital stenosis, dissecting aneurysm and finally compromise of the cerebral circulation due to tumor or aneurysm.

In the present series two patients had fibromuscular dysplasia. Symptoms most likely to benefit after STA-MCA by-pass appear to be TIA's and RINDs due to complete occlusion of the carotid artery in the neck. Occlusive disease of the intracranial carotid or middle
cerebral arteries appeared to show less predictable hemodynamic and clinical benefit. RINDs are usually identifiable by CT scanning as minor infarctions revealed as small, low density lesions. Another less common indication for STA-MCA by-pass appears to be diffuse low perfusion syndromes of the brain due to occlusive disease of multiple intracranial and extracranial arteries (e.g., both carotids) although experience here is limited to a few cases. Surgical intervention in acute thrombotic stroke with severe brain edema is contraindicated and such cases were not edema is contraindicated.

Are Xenon CBF Measurements Helpful In Screening Patients For STA-MCA By-pass?

According to experience gained from the present study, consonant with earlier observations already cited, measuring rCBF values by $^{133}$Xe inhalation and the use of multiple external probes are helpful in evaluating patients with cerebral ischemia, and identifying patients with interhemispheric steal, due to carotid occlusive disease who are likely to benefit from STA-MCA by-pass. In such cases, major infarction has not occurred, and changes in LA do not alter flow values, so that the technical disadvantages of the $^{133}$Xe method do not distort the results. In fact, results obtained by the stable xenon method, where LA was measured, were in good agreement with $^{133}$Xe measurements. As described earlier the pattern of gray matter flow reduction in the middle cerebral territory, with reduced gray matter flow in the occipital regions of the contralateral hemisphere was found to be characteristic of interhemispheric steal, due to carotid occlusive disease. In the present study, the preoperative mean hemispheric $F_c$ values, measured by either $^{133}$Xe or stable xenon with CT scanning, were significantly reduced in the middle cerebral territory of the ischemic hemi-

### Table 3
3 Dimensional Measurements of Local CBF (LCBF) and Local $\lambda$ ($\lambda_A$) by Scanning During Xenon Inhalation in Normal Healthy Volunteers (n = 9) and Patients (n = 13) Undergoing STA-MCA By-pass

<table>
<thead>
<tr>
<th>Regions measured</th>
<th>LCBF</th>
<th>($\lambda_A$)</th>
<th>LCBF</th>
<th>($\lambda_A$)</th>
<th>LCBF</th>
<th>($\lambda_A$)</th>
<th>Δ% LCBF change after by-pass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal volunteers</td>
<td>(n = 9, age 38.3 ± 10.8 years)</td>
<td></td>
<td>Pre-operation</td>
<td>Post-operation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(LA)</td>
<td></td>
<td>(LA)</td>
<td></td>
<td>(LA)</td>
<td></td>
</tr>
<tr>
<td>Frontal cortex</td>
<td>31</td>
<td>82.3 ± 8.5</td>
<td>(0.87 ± 0.09)</td>
<td>13</td>
<td>54.3 ± 12.2*</td>
<td>(0.94 ± 0.07)</td>
<td>58.2 ± 12.7</td>
</tr>
<tr>
<td>Temporal cortex</td>
<td>35</td>
<td>81.5 ± 8.8</td>
<td>(0.85 ± 0.07)</td>
<td>20</td>
<td>60.0 ± 15.9*</td>
<td>(0.86 ± 0.09)</td>
<td>68.8 ± 13.9</td>
</tr>
<tr>
<td>Lateral occipital cortex</td>
<td>16</td>
<td>84.8 ± 7.0</td>
<td>(0.84 ± 0.08)</td>
<td>9</td>
<td>65.7 ± 12.2*</td>
<td>(0.95 ± 0.10)</td>
<td>63.9 ± 18.7</td>
</tr>
<tr>
<td>Striate cortex</td>
<td>12</td>
<td>86.0 ± 7.9</td>
<td>(0.88 ± 0.08)</td>
<td>10</td>
<td>64.0 ± 14.3*</td>
<td>(0.90 ± 0.10)</td>
<td>72.9 ± 10.8</td>
</tr>
<tr>
<td>Caudate nucleus</td>
<td>8</td>
<td>88.3 ± 4.4</td>
<td>(0.91 ± 0.07)</td>
<td>16</td>
<td>66.2 ± 10.7*</td>
<td>(0.90 ± 0.07)</td>
<td>68.3 ± 15.4</td>
</tr>
<tr>
<td>Lentiform nucleus</td>
<td>7</td>
<td>85.1 ± 10.5</td>
<td>(0.94 ± 0.11)</td>
<td>13</td>
<td>60.1 ± 15.1*</td>
<td>(0.92 ± 0.10)</td>
<td>63.9 ± 17.4</td>
</tr>
<tr>
<td>Thalamus</td>
<td>27</td>
<td>85.8 ± 8.0</td>
<td>(0.90 ± 0.07)</td>
<td>21</td>
<td>65.9 ± 9.8*</td>
<td>(0.92 ± 0.10)</td>
<td>68.7 ± 13.1</td>
</tr>
<tr>
<td>Average gray matter</td>
<td>136</td>
<td>83.0 ± 8.2</td>
<td>(0.87 ± 0.08)</td>
<td>102</td>
<td>62.4 ± 13.6*</td>
<td>(0.91 ± 0.09)</td>
<td>66.7 ± 15.1</td>
</tr>
<tr>
<td>Average white matter</td>
<td>49</td>
<td>29.2 ± 5.9</td>
<td>(1.34 ± 0.1)</td>
<td>48</td>
<td>26.0 ± 7.0*</td>
<td>(1.30 ± 0.14)</td>
<td>27.1 ± 7.5</td>
</tr>
</tbody>
</table>

*Post-operative measurements were done 1–3 weeks after by-pass operation except one case who was measured 15 months after operation.

Pre-operative and post-operative Δ%LCBF changes are not significant.

### Table 4
Post STA-MCA By-pass Changes in Regions of Low Perfusion-low $\lambda$. Values Measured by Xe $\lambda$ CT Scans in Patients with RIND (n = 6)

<table>
<thead>
<tr>
<th>Regions measured</th>
<th>Pre-operation LCBF</th>
<th>$\lambda$</th>
<th>Post-operation LCBF</th>
<th>$\lambda$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gray matter</td>
<td>51.4 ± 11.0‡</td>
<td>0.75 ± 0.05‡</td>
<td>68.7 ± 12.7†</td>
<td>0.92 ± 0.13‡</td>
</tr>
<tr>
<td>White matter</td>
<td>20.0 ± 2.6‡</td>
<td>1.14 ± 0.06‡</td>
<td>30.1 ± 6.6†</td>
<td>1.31 ± 0.17*</td>
</tr>
</tbody>
</table>

* or † indicates significantly increased values compared to pre-operative measurements. (*$p < 0.05$, †$p < 0.01$)‡Indicates significantly reduced values compared to normal values at $p < 0.01$ level.
sphere and in the contralateral occipital and frontal regions due to hemispheric steal. The reduction in the contralateral hemisphere was clearly due to steal, since it was reversed toward normal for several months after surgery by the by-pass operation, and pre-operative flow reductions correlated with angiographic evidence of interhemispheric steal from the contralateral posterior and anterior cerebral arteries to the middle cerebral territory. Furthermore, similar patterns of bilateral hemispheric increase of flow after surgery were measured by the stable xenon CT CBF method, which is devoid of potential artifacts using the $^{133}$Xe method (such as poor resolution due to Compton Scatter and changes in local $\lambda$), that might conceivably give rise to spurious reduction of flow in the contralateral hemisphere. The bihemispheric increases (10%) of gray matter flow measured by the stable xenon CT method after STA-MCA by-pass were in good agreement with the $^{133}$Xe data.

Maximal reductions of rCBF in the frontal area, in the distribution of the occluded carotid, were in the order of −20%, which is consonant with the data reported by Austin et al. using the $^{133}$Xe intravenous bolus method.

Regional flow reductions due to steal were significantly improved in the contralateral frontal, precentral, parietal, inferior temporal and occipital regions after by-pass operation. These results indicate, that after successful STA-MCA by-pass procedures, blood flow to both hemispheres is significantly improved. This agrees with experimental data showing that after occlusion of a major vessel, interhemispheric collateral circulation is established via the circle of Willis to supply the ischemic hemisphere by accommodating to its lower perfusion pressure.

Results of the present study, showing highly significant mean increases of hemispheric $F_v$ values by +12.8% on the by-passed side, and +8% on the contralateral side, for several months after surgery, are in good agreement with results of +10.5% on the operated side and +8% on the non-operated side, reported in a smaller series of cases by Halsey et al. using the $^{133}$Xe inhalation method, and +13% on the by-passed side reported by Hungerbuhler et al. Between the 6th to the 30th month, both STA-MCA by-passed cases and medically treated cases, show similar progressive CBF declines which appear to be age-related.

It has been reported previously that cerebral vasomotor reactivity is impaired in patients with acutely ischemic brain when tested by inducing hypocapnia, hypercapnia, or hyperoxia. It was hoped that these impaired vasomotor responses would be restored toward normal by the STA-MCA by-pass procedure, indicating that ischemia itself was responsible for the impaired vasomotor activity, possibly by impairing prostacyclin synthesis of the vessel walls. However, trends toward improvement after surgery were not significant. It has been shown previously that in acute stroke cerebral autoregulation and vasomotor reactivity are impaired. In the past, this impairment has been attributed to factors such as damage to the vessel wall, brain edema, pH change, and diachisis. Halsey et al. reported improvement in rCBF responses to hypocapnia in their series of patients following the by-pass operation.

The present series of patients showed reduction in frequency and sometimes total cessation of TIAs after STA-MCA by-pass. It seems unlikely that enhancing the cerebral collateral circulation will prevent emboli formation. It appears more likely that, enhanced collateral blood supply to marginally ischemic areas, provided by the STA-MCA by-pass, prevents regional hemodynamic crises of ischemia. This view is supported by other evidence. In animal experiments, it has been shown that STA-MCA anastomosis prior to MCA embolization provides protection from the severity of the neurological deficit and reduces the size of cerebral infarction compared to embolized control groups.

In the present study, a limited number of patients have been followed longitudinally for an interval of 30 months. Those cases undergoing STA-MCA by-pass showed increased hemispheric flow values which reached a maximum within three months, and remained augmented for up to 30 months. This was not seen in a comparable group of cases treated over the same interval of time without the by-pass procedure. These rCBF increases correlated with gradual increases in the diameter of the superficial temporal artery observed by arteriography.

Patients with RIND due to small recent cerebral infarctions showed improvement of their neurological deficits, co-incident with increases of LCBF and $L/\lambda$ values toward normal, in the areas of low density by CT scanning. This could be due to the natural history of the disease or to the surgical augmentation of the collateral circulation. The normalization of the $L/\lambda$ values is taken as indirect evidence of improved tissue function, since the change in tissue solubility can only reflect some physical or chemical alteration in tissue, such as a reduction of edema or changes in lipid or amino acid synthesis in the low density area observed by CT scanning. The reduction of $L/\lambda$ values could not be attributed to severe flow reduction with diffusion limitation, since the reduced $L/\lambda$ values were measured in regions where LCBF values were not cortically reduced and were comparable to LCBF values in other ischemic regions of brain where $L/\lambda$ values were within normal limits.

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