Non Invasive Tomographic Imaging of Cerebral Blood Flow (CBF) and Oxygen Extraction Fraction (OEF) in Superficial Temporal Artery to Middle Cerebral Artery (STA-MCA) Anastomosis.

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Clinical indications for extra-intracranial arterial bypass (EIAB) surgery are still rather ill-defined and are the matter of a randomized trial in progress currently. However, "hemodynamic" transient ischemic attacks (TIAs) are considered at present the clinical entity that should benefit most from this surgical procedure. The contribution of conventional CBF techniques in assessing both the physiological indications and the usefulness of EIAB has been only moderate, though substantial. Clearly, both CBF and regional metabolic data should be obtained, ideally in tomographic representation. We have attempted such study using the 15O continuous inhalation technique in a small number of instructive patients. Two different patterns of the CBF-OEF relationship have been defined that could be of some importance in respect to both the underlying mechanisms of "hemodynamic" TIAs and to the rational bases for EIAB procedures.

Patients and methods: We have applied to Positron Emission Tomography the non-invasive 15O Inhalation Technique. The method has been described in detail elsewhere. It briefly consists of continuous inhalation to equilibrium of the short-lived positron-emitter 15O in the form of C15O2 and 15O2 consecutively. For each brain level studied, a set of 3 tomographic images is obtained: 1) a 15O2 image that represents CBF; 2) a 15O2 image that represents both oxygen metabolism and CBF; 3) a 15O2/C15O2 ratio image that is linearly proportional to the OEF. Absolute quantitation of CBF and OEF by this technique still presents difficulties, and was therefore not attempted here. On the images obtained, the side-to-side differences in count-rate were calculated for various regions of interest, and the values found were then compared to normal ranges.

Five patients underwent EIAB surgery for clinical reasons. The clinical data are summarized in Table 1 and detailed below. All five patients had both pre- and postoperative 15O studies at approximately the same brain levels. In all cases, the anastomosis was proven to be patent and functional by both Doppler studies and angiography.

### Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>ICA Oc.</th>
<th>ICA Sten.</th>
<th>Post Oc. T:As</th>
<th>Infarct.</th>
<th>EIAB</th>
<th>EIAB Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R</td>
<td>L. Siphon</td>
<td>+</td>
<td>R+L W.</td>
<td>L+R</td>
<td>++</td>
</tr>
<tr>
<td>2</td>
<td>L</td>
<td>0</td>
<td>+</td>
<td>O</td>
<td>L</td>
<td>++</td>
</tr>
<tr>
<td>3</td>
<td>R</td>
<td>L cervical</td>
<td>+</td>
<td>R W.</td>
<td>R</td>
<td>++</td>
</tr>
<tr>
<td>4</td>
<td>L</td>
<td>0</td>
<td>+</td>
<td>L W.</td>
<td>L</td>
<td>++</td>
</tr>
<tr>
<td>5</td>
<td>L</td>
<td>R. plaque</td>
<td>0</td>
<td>L insula</td>
<td>L</td>
<td>++</td>
</tr>
</tbody>
</table>

### Clinical data and results (Table 2)

<table>
<thead>
<tr>
<th>Case</th>
<th>Side</th>
<th>Preoperative findings</th>
<th>Postoperative findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R</td>
<td>( \times ) decreased, ( \times ) increased, N = Normal</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>L</td>
<td>( \times )</td>
<td>( \times )</td>
</tr>
<tr>
<td>3</td>
<td>R</td>
<td>( \times )</td>
<td>( \times )</td>
</tr>
<tr>
<td>4</td>
<td>L</td>
<td>( \times )</td>
<td>( \times )</td>
</tr>
<tr>
<td>5</td>
<td>L</td>
<td>( \times + N )</td>
<td>( \times )</td>
</tr>
</tbody>
</table>

Case 1: a 65 y.o. man had suffered since 1974 from repeated TIAs involving the left or right hemisphere and retinae, as well as a progressive permanent weakness.
of both hands an diffuse mental impairment. Four-vessel angiogram in 1978 showed an occlusion of the right cervical internal carotid artery (ICA) and a severe stenosis of the left ICA siphon. The right MCA filled only through the contralateral ICA. A C.T. Scan showed a bilateral infarction of the cortical watershed areas. The TIAs continued and he underwent bilateral EIAB in March and April 1979. In July, he had a single left hemisphere TIA. When last seen in April 1980, he had not had any further TIAs and his mental status had improved. Angiographic and Doppler studies showed excellent functioning of both EIABs. The pre-operative $^{15}O$ study disclosed, in addition to the old bilateral watershed infarct, a significant increase in the ratio value over the right upper MCA territory associated with a decreased $^{15}O_2$ activity (Fig. 1). The post-operative $^{15}O$ study showed disappearance of the above-mentioned abnormalities.

Case 2 will be detailed in a separate report (in preparation). A 65 y.o. man suffered repeated TIAs distal to an occluded left ICA and triggered by orthostatic hypotension. These attacks were alleviated by a left EIAB. The pre-operative $^{15}O$ study showed a decreased $^{15}O_2$ count rate associated with an increased ratio value over the left MCA territory, particularly at the parieto-occipital watershed area. Following surgery, the repeat $^{15}O$ study showed complete resolution of these abnormalities. Control angiogram showed excellent functioning of the anastomosis.

Case 3 : a 73 y.o. man was evaluated in 1975 for repeated attacks involving the left hand and face, and a permanent sensory-motor deficit of the left upper limb. An angiogram showed occlusion of the right cervical ICA and a mild stenosis of the cervical left ICA. The TIAs continued for a while and then stopped for the next 4 years. In January 1980, the left hemisphere TIAs recurred, and the permanent left hand deficit increased and fluctuated, involving now the left lower limb. Repeat angiogram disclosed a pseudo-occlusive stenosis of the left cervical ICA. A C.T. Scan showed an old right hemisphere watershed infarct. On 25/7/1980, a right EIAB and a left ICA endarterectomy were performed. Post-operatively, the TIAs stopped and the permanent left hemiparesis dramatically improved to the point that the deficit was now clearly milder than what it had been for the past 4 years. A control angiogram showed a patent anastomosis with complete filling of all the MCA branches. The pre-operative $^{15}O$ study showed a significant decrease of $^{15}O_2$ count-rate over the right upper MCA territory with a normal ratio value (Fig. 2). Post-operatively, the previous asymmetry had totally disappeared.

Case 4 : a 57 y.o. man had in 1967 a few left hemisphere TIAs. In November 1978, he suffered a left lateral medullary syndrome which recovered well, but there was also a pyramidal deficit of the right hand. Four-vessel angiography showed an occlusion of the cervical left ICA and a marked stenosis of the terminal left vertebral artery. The left MCA filled exclusively through the latter. A C.T. Scan revealed an old left parieto-occipital watershed infarct. A left EIAB (performed in May 1979) was thought justified in view of the dependance of the left MCA on the stenotic left vertebral artery. A control angiogram 9 months later showed a patent anastomosis which filled almost all branches of the left MCA. The pre-operative $^{15}O$ study showed just anterior to the old infarct previously mentioned, a circumscribed area of significantly decreased $^{15}O_2$ count-rate without change in the ratio value. Post-operatively, this area now had an increased $^{15}O_2$ count-rate with normal ratio value.

Case 5 : in 1958, a then 45 y.o. man had a rapidly regressive left hemiparesis. Starting in 1976, he suffered repeated left hemisphere and retina TIAs. On 3/2/79, he had the sudden onset of a right hemiplegia with aphasia that regressed within 24 hours, leaving only a minimal dysphasia. A C.T. Scan showed a 2 cm recent infarct in the left insula. An angiogram revealed an occlusion of the cervical left ICA, and a mild but ulcerated plaque at the origin of the right ICA; the latter filled the left MCA. A right ICA endarterectomy was decided, but a prior left EIAB was considered a justified precaution. The patient underwent both operations in March and April 1979. A control angiogram showed a patent anastomosis that fed most of the left MCA branches. The pre-operative $^{15}O$ study (20/2/1979) disclosed changes corresponding to the recent insular infarct, as well as a slight increase in $^{15}O_2$ count-rate over the upper left MCA territory. Post-operatively, the repeat study (19/6/1979) showed disappearance of the latter asymmetry.

Discussion : Although only semi-quantitative, our findings appear to carry patho-physiological significance since 1) the abnormalities found pre-operatively were topographically correlated with both the clinical symptoms and the side of
the ICA occlusion, and 2) the post-operative reversal of such abnormalities was also
well correlated to both clinical improvement and good bypass graft function.

Of the 5 patients reported here, one (case 5) will not be further mentioned in
the discussion because 1) the occurrence of a recent infarct renders interpretation
of the $^15$O findings difficult, and 2) the EIAB was solely justified as a protection
during contralateral ICA endarterectomy. Of the remaining 4 patients, the indication
for EIAB in the first three cases was based on the clinical problem of “hemodynamic”
TIAs (with fluctuating permanent deficit in case 3), and in case 4 as a means to
protect the brain from potential hemodynamic failure.

In these 4 patients, CBF was focally decreased in the MCA territory distal to the
ICA occlusion, and the CBF reduction appeared more marked over the watershed terri­
itories. Post-operatively, however, CBF returned to symmetrical values. These findings
are consistent with previous reports indicating a return of CBF towards normal va­
values following either carotid endarterectomy or EIAB in patients with TIAs and
carotid artery stenosis or occlusion$^2,6,9,10,11$.

However, the metabolic correlate of this focal CBF decrease was strikingly diffe­
rent in cases 1 and 2 and in cases 3 and 4 where the OEF was respectively increased
and normal. The first type, the one showing OEF increase, suggests a focal mismatch
between perfusion and metabolism where perfusion is insufficient relative to the
metabolic requirements of the tissue: it has been jocularly termed the “misery-
perfusion syndrome” because it represents the situation radically converse to “luxury
perfusion syndrome”. The “misery-perfusion syndrome” indicates an increase in the
oxygen arterio-venous difference, which is commonplace in a number of low-flow state;
of the brain secondary to either focal or generalized severe reductions in perfusion
pressure, or to hyperventilation. Misery-perfusion has also been reported in cere­
bral infarction$^1,5$. In the two present cases, the surgical revascularization re­sulted in a dramatic reversal of this condition. Using the $^{15}$O intra-carotid in­
jection technique, Grubb et al$^7$ also reported 3 cases very similar to ours with
respect to both the pre-operative findings and the effects of surgery.

The second type of abnormalities (cases 3 and 4) indicates a matched decrease
in CBF and oxygen metabolism, with a post-operative increase in both parameters.
Grubb et al$^7$ and Thomas et al$^{12}$ each reported two patients with similar findings.

The reason(s) for there being two possible CBF-OEF patterns of abnormalities
in roughly similar clinical situations is still unclear. However, they both showed
potential reversibility. This suggests that, paralleling the clinical results,
EIAB was physiologically useful in these patients, and that, as suggested previously
both patterns of abnormalities may constitute rational indications for this type
of surgical procedure.

Noteworthy is the fact that, in these cases of continuing neurological events
following ICA occlusion, the maximum CBF decrease (associated with either normal
or decreased OEF) was located at the watershed territories. In such areas, EIAB
reversed this state of chronically impaired CBF and metabolism and perhaps prevented
impending watershed necrosis. This would also apply to some watershed infarcts the
borders of which are chronically malfunctioning and threatened by extending neuronal
decay.

References:

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Fig. 1: $^{15}\text{O}$ Inhalation Studies (case 1). The upper and lower rows are the pre and post-operative images respectively. The left-hand side, middle, and right-hand side images are the $\text{C}^{15}\text{O}_2$, $\text{O}_2$ and ratio images respectively. Pre-operatively, there is a decreased $\text{C}^{15}\text{O}_2$ count-rate over the right upper convexity (straight arrow) with increased ratio value (arrowframe). Post-operatively, these abnormalities have disappeared. The curved arrows indicate the right watershed infarct.

Fig. 2: $^{15}\text{O}$ Inhalation Studies (case 3). Display in same as Fig. 1. Pre-operatively, there is a decreased $\text{C}^{15}\text{O}_2$ (arrows) and $\text{O}_2$ (arrowheads) over the right upper convexity, with normal ratio image. Post-operatively, these asymmetries have disappeared. The arrowframe points to an artifactual ratio value over the surgical scalp area.