“Luxury perfusion” with $^{99m}$Tc-HMPAO and $^{123}$I-IMP SPECT imaging during the subacute phase of stroke

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Abstract. To compare the merits of $^{123}$I-isopropyl-iodoamphetamine ($^{123}$I-IMP) and $^{99m}$Tc-HMPAO in showing abnormal brain uptake distribution during cerebral ischemia, we studied ten patients during the subacute phase of their stroke, a period where metabolism and blood flow are frequently uncoupled. SPECT imaging was performed using both radiopharmaceuticals in the 10 patients from 48 h to 4 weeks after onset of symptoms. Two patients out of the 10 had similar defects with $^{123}$I-IMP and $^{99m}$Tc-HMPAO SPECT, the location of the defects corresponding to the area of infarction observed on CT. Six patients had normal $^{99m}$Tc-HMPAO SPECT and abnormal $^{123}$I-IMP SPECT with defects in the area of infarction shown by CT. The remaining 2 patients had hyperactive abnormalities on $^{99m}$Tc-HMPAO in areas corresponding to defects on the $^{123}$I-IMP images. Two of the patients with SPECT mismatches were studied again more than 1 month after onset. On reexamination, $^{99m}$Tc-HMPAO SPECT which was previously normal or hyperactive became hypoactive with a focal area of decreased activity corresponding to the defect on $^{123}$I-IMP. Crossed cerebellar diaschisis was found in 7 patients with $^{99m}$Tc-HMPAO and was absent for both $^{123}$I-IMP and $^{99m}$Tc-HMPAO in 3. We suggest that SPECT with $^{99m}$Tc-HMPAO could show transient hyperemia not demonstrated by $^{123}$I-IMP whereas in some cases cerebral blood flow in the subacute phase of ischemic lesions, primarily between day 6 and 21 after cerebral infarction (Lenzi et al. 1980). In addition, an early hypaeremic phase has been seen within 72 h of onset of symptoms in 39%-50% of patients (Olsen et al. 1981).

Cerebral $^{123}$I-IMP activity mirrors cerebral blood flow only during the early period after injection and there is a constant redistribution of the radiotracer that becomes evident on delayed imaging (Lassen et al. 1983). The overwhelming consensus is that focal hyperactivity of labeled amines within the 1st h following injection is found only rarely in stroke lesions (Brott et al. 1986; Bushnell et al. 1987) despite the fairly common phenomenon of luxury perfusion (hyperperfusion coupled with decreased oxygen uptake) (Lassen 1966). Also, the redistribution pattern correlates closely with the cerebral metabolic rate of oxygen (CMRO2) (Yonekura et al. 1985) and with clinical outcome (Defer et al. 1987).

$^{123}$I-IMP and other amines have a brain distribution which is related to plasma pH; uptake is also related to the amine sequestration systems within the brain in addition to cerebral blood flow (Kuhl et al. 1982).

On the other hand, the d,l distereoisomer of $^{99m}$Tc-hexamethypropylene amine oxime (HMPAO) (Nowotnik et al. 1985) is a new lipophilic and neutral complex with a high retention time within the brain in animals (Netrincx et al. 1987). Its brain distribution is related to cerebral blood flow when compared to the distribution of labelled microspheres in animals or to $^{133}$Xe inhalation in man (Costa

Introduction

Many investigators have demonstrated the usefulness of SPECT for assessing reversible ischemic (Moretti et al. 1984; Cesaro et al. 1986) and completed strokes (Hill et al. 1982; Lee et al. 1982; Ell et al. 1983; Hill et al. 1986; Bueff et al. 1985) with $^{123}$I-isopropyl iodoamphetamine ($^{123}$I-IMP) (Winchell et al. 1980). PET studies have demonstrated repeatedly the presence of relative hyperperfusion and transient uncoupling between metabolic demand and cerebral blood flow in the subacute phase of ischemic lesions, primarily between day 6 and 21 after cerebral infarction (Lenzi et al. 1980). In addition, an early hypaeremic phase has been seen within 72 h of onset of symptoms in 39%-50% of patients (Olsen et al. 1981).

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Key words: $^{99m}$Tc-HMPAO - $^{123}$I-IMP SPECT - Stroke, luxury perfusion


Offprint requests to: J.L. Moretti, Service de Médecine Nucléaire, Hôpital Avicenne, F-93009 Bobigny, France
et al. 1986; Andersen et al. 1987). The disparity and inci-
dence of luxury perfusion as found with IMP and other ra-
diotracer studies led us to compare brain distribution of
$^{123}$I-IMP with $^{99m}$Tc-HMPAO in 10 patients at least 48 h
after acute cerebral infarction in order to depict increased
tracer uptake related to luxury perfusion.

**Material, methods and patients**

**Radiopharmaceuticals.** $^{99m}$Tc-d$_1$ HMPAO was prepared
from a kit (Ceretec$^1$). Lyophilized d$_1$ HMPAO (0.5 mg)
was reconstituted with 5 ml saline containing not more than
1 GBq $^{99m}$Tc. Incubation time was 2 min at room tempera-
ture. A combination of three TLC chromatographies were
performed to measure the composition of the radioactive
solution giving the percentage of TcO$_2$ and reduced $^{99m}$Tc-
d$_1$ HMPAO $^{99m}$Tc and another less lipophilic complex
of radioactive PAO (Leonard et al. 1986). Because of the
instability of $^{99m}$Tc-d$_1$ HMPAO with time in vitro, all our
preparations were injected within 30 min of labelling. The
preparations contained more than 85% of the HMPAO
complex. The injected dose was 0.4 GBq.

$^{123}$I-IMP was prepared by iodine exchange reaction us-
ing a commercial kit$^2$ as described elsewhere (Moretti et
al. 1983). Each vial containing 10 mg lyophilized IMP and
copper sulfate, and was filled with 0.18 GBq $^{123}$I (p$_2$n)
and acetate buffer (pH 3.6) and heated for 45 min at 130 ° C
to dryness. Chromatography was performed on several
batches with a labelling efficiency greater than 95%.

**Data acquisition.** The imaging studies were carried out with
a conventional tomographic rotating gamma camera. Data
acquisition was performed in 64 projections with a 64 x 64
matrix. The gamma camera was fitted with a high-resolu-
tion, low-energy (140 KeV maximum) collimator for $^{99m}$Tc
studies and with a higher energy (200 KeV maximum) collim-
ator for $^{123}$I studies. The radiopharmaceutical was in-
jected intravenously in a quiet room, with the patient supine
and blindfolded. $^{99m}$Tc-HMPAO began 10 min after the
injection of 0.4 GBq (Sharp et al. 1986). $^{123}$I-IMP SPECT
began 20 min after the injection of 0.18 GBq. The imaging
time was 30 s per projection collecting more than 2.5 mil-

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$^1$ Ceretec, Amersham Pharmaceutical, Amersham, UK

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**Table 1. Neurological manifestation, day of examination and result of CT scan and vascular investigation for each patient**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Neurological symptoms</th>
<th>Day of CT scan</th>
<th>Result (DT)</th>
<th>Cardiac exam +</th>
<th>ANG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>41</td>
<td>Aph + Alex</td>
<td>2 + 75</td>
<td>Left MCA</td>
<td>Aneurysm MCA</td>
<td>(ANG)</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>87</td>
<td>Aph + Alex + RHP</td>
<td>30</td>
<td>Left MCA</td>
<td>Normal</td>
<td>(DU)</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>61</td>
<td>Aph + RHP</td>
<td>1 + 8 + 90</td>
<td>Left MCA</td>
<td>Normal</td>
<td>(DU)</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>57</td>
<td>Aph + RHP</td>
<td>15</td>
<td>Left MCA</td>
<td>Left ICA stenosis</td>
<td>(DU)</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>72</td>
<td>Aph + RHP</td>
<td>15</td>
<td>Normal</td>
<td>Normal</td>
<td>(DU)</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>64</td>
<td>Aph + LH + HRP</td>
<td>30</td>
<td>Normal</td>
<td>Left ICA (10)</td>
<td>(ANG)</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>64</td>
<td>Aph + RHP</td>
<td>3 - 10</td>
<td>Normal</td>
<td>Left ICA stenosis</td>
<td>(DU)</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>69</td>
<td>LHP</td>
<td>8</td>
<td>Right MCA</td>
<td>Right MCA</td>
<td>(DU)</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>69</td>
<td>LHP</td>
<td>13</td>
<td>Normal</td>
<td>Normal</td>
<td>(DU)</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>74</td>
<td>Aph + RHP</td>
<td>1</td>
<td>Normal</td>
<td>Right ICA stenosis</td>
<td>(DU)</td>
</tr>
</tbody>
</table>

*Aph, Aphasia; Alex, Alexia; RHP, right hemiplegia; LHP, left hemiplegia; LH, left lateral homonymous hemianopsia; MCA, middle cerebral artery; ICA, internal carotid artery; DT, damaged territory; DU, doppler ultrasound; ANG, angiography*