Quantification of Regional Cerebral Blood Flow With IMP-SPECT

Reproducibility and Clinical Relevance of Flow Values

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Single-photon emission computed tomography with \(^{123}\)I-isopropyl-p-iodoamphetamine (IMP-SPECT) was performed in 14 normal volunteers (seven men and seven women aged 25.1\(\pm\)5.3 years) and 29 patients with cerebrovascular disease (18 men and 11 women aged 54.1\(\pm\)13.7 years). The fluid microsphere model was used to estimate cerebral blood flow (CBF). Normal subjects were scanned twice, 1 week apart, to determine the reproducibility of the CBF estimates. Hemispheric blood flow (hCBF) was calculated as the mean of regional cerebral blood flow (rCBF) values in 16 gray matter regions per hemisphere. In normal subjects mean hCBF was 68 ml/100 g/min. The highest rCBF was found in the occipital cortex, followed by the frontal, temporal, and parietal cortices. CBF values were reproducible (p<0.001 except the right thalamic region, where p<0.01). Intraindividual variation ranged between 0.3% and 15%. Women exhibited significantly higher (16%, p<0.02) CBF than men. Patients were subdivided into groups with reversible (n=19) and persistent (n=10) symptoms. Significant hCBF differences between the affected and the contralateral hemispheres were recorded only in the group with reversible symptoms (p<0.005), whereas the group with persistent symptoms showed a significant bilateral decrease of hCBF compared with normal subjects and patients with reversible symptoms. Focal CBF was significantly lower in patients with completed stroke than in patients with transient symptoms (p<0.001). Our results indicate that IMP-SPECT can be used for the routine estimation of CBF in normal and pathologic states. (Stroke 1989; 20:183–191)

In the last few years new tracers, such as \(^{123}\)I-isopropyl-p-iodoamphetamine (IMP)\(^{1,2}\) and \(^{99m}\)Tc-hexamethylpropyleneamine oxime (Tc-99m-HMPAO),\(^{3,4}\) for visualizing cerebral blood flow (CBF) using single-photon emission computed tomography (SPECT) have been synthesized. It is generally accepted that the distribution of both tracers in the brain during the first 2 hours after their administration reflects regional cerebral blood flow (rCBF). However, quantification of CBF with Tc-99m-HMPAO seems to be at present rather difficult due to partially unknown tracer kinetics. Single attempts to quantify CBF from IMP-SPECT images have been undertaken,\(^{5,6}\) but the reproducibility and clinical reliability of the obtained values has never been investigated. Our purpose is to describe the possibility of CBF quantification with IMP-SPECT using a rotating gamma camera. Furthermore, we report the reproducibility of CBF values obtained in normal volunteers as well as the relation between calculated CBF values and the duration of neurologic impairment in patients with cerebrovascular disease (CVD).

Subjects and Methods

The reproducibility of known concentrations of iodine-123 in SPECT images was investigated by an approach similar to that described by Kuhl et al.\(^7\) First, a Lucite cylinder 200 mm in diameter (the phantom) filled with 0.5 \(\mu\)Ci/ml of an iodine-123 solution was scanned as for patient investigations (see below). The average number of counts per voxel (count density) in the reconstructed image was then converted into microcuries per voxel. Then, 19 cylindrical plastic bottles 29 mm in diameter (approximately twice full-width half-maximum [FWHM]\(^8\) were placed in a concentric arrangement inside the phantom. Fourteen bottles contained solutions of different iodine-123 assays, while five bottles were filled with water (Figure 1) to investi-
gate the efficiency of the applied scatter correction in depth.

CBF was quantified using the fluid microsphere model proposed by Kuhl et al., in which $\text{CBF} = \frac{R \times \text{Cb}}{O}$ and $R =$ constant withdrawal rate of arterialized venous blood in milliliters per minute, $\text{Cb} =$ local tracer concentration in microcuries per 100 grams trapped by the brain in the first 5 minutes, and $O =$ octanol extraction of the (true) tracer concentration in the withdrawn blood in microcuries.

For SPECT, we used a dual-head rotating scintillation camera (Siemens Gammasonics, Uithoorn, The Netherlands, Dual Rota ZLC37) connected to a computer (Nodecrest Micas 2000). Due to low sensitivity, fast SPECT scans cannot be performed with this instrumentation. Therefore, the total amount of tracer trapped by the brain 1–5 minutes after intravenous bolus injection of 5–6 mCi IMP (iodine-123 produced by the $p, \gamma$ reaction and free of iodine-124) had to be estimated by conventional scanning (anteroposterior projection) during this period. To maintain the method nearly noninvasive, arterialized venous blood (hand placed in a 44°C water bath) was withdrawn constantly ($R = 1 \text{ ml/min}$) from a vein in the hand at the same time. Thirty minutes after IMP injection, when brain tracer concentration was constant, another static scan of the head (anteroposterior projection) during 5 minutes was obtained. Immediately thereafter, SPECT scanning was started. The scanning modalities and image processing have been reported in detail, and here we give just a brief description. Sixty projections ($2 \times 30$ angles; $100 \text{ sec/angle}$) with a sampling distance of $3.125 \text{ mm}$ were achieved. The camera heads were equipped with low-energy all-purpose (LEAP) collimators (FWHM 1.4 cm in the reconstructional plane). The subject was placed on a reclining dentist’s chair with a special head support to reduce the diameter of rotation to 250 mm. Scatter correction was performed using a multiple energy window technique. Projections were filtered with a filter of variable shape and size for reduction of Poisson noise, and data were reorganized in a sinogram. After attenuation correction, 3.125-mm-thick cross sections were reconstructed by filtered back projection in $128 \times 128$ matrices. Consecutive summation of seven sections gave a set of $21.9$-mm-thick transverse slices. Regions of interest (ROIs) were drawn on four adjacent cross sections. The correct position of these cross sections was established on anteroposterior and lateral projections (Figure 2).

Since the obtained SPECT images represent IMP distribution 35–85 minutes after tracer administration (during the stable phase), they must be time-corrected to show total tracer uptake during the inflow phase (i.e., 1–5 minutes after intravenous injection of IMP). This correction is performed as follows: ROIs are placed over each hemisphere on the early (1–5 minutes) and late (30–35 minutes) anteroposterior scan, and total counting rates are obtained in these ROIs. The subsequent calculations are made for each hemispheric ROI. The total counting rate in the late stable-phase anteroposterior scan (LScts) is proportional to the total tracer amount ($\text{LP\%}, 100\%$) delivered to the brain between 1 and 30 minutes after IMP injection. Therefore, $\text{LP\%} = \text{EP\%} + \text{CP\%}$, where $\text{EP\%}$ is the count density in the early anteroposterior scan expressed as percent ($\text{EP\%} = 100\% \times \text{EScts/LScts}$), $\text{EScts}$ is the counting rate in the early anteroposterior scan, and $\text{CP\%}$ is the unknown percentage of tracer delivered to the brain between 6 and 29 minutes. $\text{CP\%}$ is therefore $\text{CP\%} = \text{LP\%} - \text{EP\%}$ (mean ± SD $\text{CP\%}$ in normal volunteers was 34.5 ± 6.2%). Since the late anteropos-
FIGURE 2. Top: For anatomic orientation, position of four transverse single-photon emission computed tomography slices (second row) is displayed on anteroposterior (A-P) and left lateral (L-LAT) projections. Third row: Region of interest scheme used: SF, mesiofrontal; MF, lateralfrontal; IF, inferior lateralfrontal (also containing Broca's area); C, central; SP+IP, superior and inferior parietal; SO, superior occipital; IO, inferior occipital; ST, superior temporal; IT, inferior temporal; BG, anterior basal ganglia (caudate+lentiform nucleus); TH, thalamus; HI, hippocampal structures.

terior scan and the SPECT study were both performed during the stable phase, the SPECT image ROI can be time-corrected by a proportionate reduction in counts, corresponding to the hemispheric CP%. This gives the counting rate that would result from a 50-minute SPECT recording of a brain that contains the amount of tracer trapped in the first 5 minutes.

For estimation of normal CBF and the reproducibility of the estimates, 14 controls (normal volunteers, seven men and seven women aged 19-40 [mean±SD 25.1±5.3] years) were scanned twice, 1 week apart, after they had given written informed consent. In addition, 29 patients (18 men and 11 women aged 27-72 [mean±SD 54.1±13.7] years) suffering from CVD were investigated. SPECT was performed 1-3 weeks after the ischemic attack. Four patients had had a transient ischemic attack (TIA), 15 a reversible ischemic neurologic deficit (RIND), and 10 a completed stroke (CS). No SPECT study showed a luxury perfusion. End-tidal PCO₂ was in the normal range (controls: first measurement mean±SD 38.0±2.2 mm Hg, second measurement 38.2±2.1 mm Hg; patients: 37.8±2.5 mm Hg). Subjects were studied with their eyes closed and their ears unplugged. The room was dimly lit, and background noise originated from cooling fans.

Results

Figure 1 shows a schematic representation of the phantom used and the plot of the calculated correlation and regression analysis of true and measured tracer concentrations. Iodine-123 concentrations in the phantom were similar to those found in normal or ischemic brain tissue when 5-6 mCi of IMP are applied. Despite these low isotope concentrations, the measured values were highly reproducible in volumes of 14.5 ml (r=0.984, p<0.001; y=0.045 +0.867x). The slope of the regression line was somewhat decreased by the effect of Compton radiation in bottles containing water and placed in the center of the phantom (Bottles 2, 3, and 4).

Controls

Table 1 shows the calculated hemispheric cerebral blood flow (hCBF) and rCBF values obtained from controls in the two measurements. The means were comparable for both measurements. As shown by the correlation coefficient (r), hCBF and rCBF values were reproducible (p<0.001 for all regions except the right laterofrontal and right thalamic regions, where p<0.01). The intraindividual variation between the measurements ranged from 0.3% to 15% (mean 6.2%). The regression analysis of hCBF is shown in Figure 3. By calculating the mean for each lobe, the highest rCBF was found in the occipital lobe (left [L] 73.2, right [R] 72.0 ml/100 g/min), followed by the frontal lobe (L 67.9, R 67.9 ml/100 g/min), temporal lobe (L 66.7, R 66.5 ml/100 g/min), and parietal lobe (L 63.3, R 62.8 ml/100 g/min). Since central cortex regions cover tissue pertaining to the frontal and parietal lobes, they were treated separately and showed the lowest rCBF (L 60.6, R 61.0 ml/100 g/min).

When hCBF of male and female controls were compared using the two-tailed independent t test, differences were found between the sexes. Women showed significantly higher (16%; p<0.02) hCBF...
TABLE 1. Correlation and Regression Analysis of Reproducibility of Two Cerebral Blood Flow Values Measured 1 Week Apart in 14 Normal Volunteers Using IMP-SPECT

<table>
<thead>
<tr>
<th>Hemispheric flow</th>
<th>Left</th>
<th>Right</th>
<th>1M</th>
<th>2M</th>
<th>r</th>
<th>b</th>
<th>m</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>58.8±9.9</td>
<td>60.5±9.0</td>
<td>0.866*</td>
<td>14.20</td>
<td>0.79</td>
<td>57.7±10.0</td>
<td>59.6±10.0</td>
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<td>2</td>
<td>70.4±11.2</td>
<td>71.0±10.8</td>
<td>0.841*</td>
<td>13.71</td>
<td>0.81</td>
<td>68.6±11.1</td>
<td>68.8±10.4</td>
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<td>3</td>
<td>71.7±9.4</td>
<td>73.3±10.3</td>
<td>0.872*</td>
<td>4.59</td>
<td>0.96</td>
<td>71.5±9.3</td>
<td>71.2±9.8</td>
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<td>MF</td>
<td>67.1±10.5</td>
<td>67.2±9.8</td>
<td>0.850*</td>
<td>13.79</td>
<td>0.80</td>
<td>68.9±10.9</td>
<td>68.5±10.6</td>
</tr>
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<td>IF</td>
<td>71.5±10.5</td>
<td>72.3±9.9</td>
<td>0.819*</td>
<td>17.17</td>
<td>0.77</td>
<td>72.8±10.9</td>
<td>72.9±10.4</td>
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<td>C</td>
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<td>58.3±8.2</td>
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<td>0.73</td>
<td>56.5±8.7</td>
<td>57.1±8.4</td>
</tr>
<tr>
<td>2</td>
<td>63.7±9.5</td>
<td>63.8±9.8</td>
<td>0.844*</td>
<td>8.58</td>
<td>0.87</td>
<td>65.4±9.9</td>
<td>65.6±9.7</td>
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<tr>
<td>SP</td>
<td>59.2±8.8</td>
<td>60.1±9.2</td>
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<td>6.62</td>
<td>0.90</td>
<td>58.7±9.3</td>
<td>60.2±9.1</td>
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<tr>
<td>IP</td>
<td>67.3±10.1</td>
<td>66.6±10.0</td>
<td>0.833*</td>
<td>11.09</td>
<td>0.83</td>
<td>66.8±10.3</td>
<td>67.4±9.1</td>
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<tr>
<td>SO</td>
<td>74.3±12.2</td>
<td>74.3±11.0</td>
<td>0.802*</td>
<td>20.75</td>
<td>0.72</td>
<td>73.4±11.2</td>
<td>74.6±10.4</td>
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<tr>
<td>IO</td>
<td>72.1±11.1</td>
<td>72.7±9.8</td>
<td>0.844*</td>
<td>18.63</td>
<td>0.75</td>
<td>70.5±11.1</td>
<td>72.7±10.8</td>
</tr>
<tr>
<td>ST</td>
<td>68.7±10.7</td>
<td>69.6±10.9</td>
<td>0.843*</td>
<td>10.51</td>
<td>0.86</td>
<td>70.1±10.9</td>
<td>70.8±10.4</td>
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<td>IT</td>
<td>64.8±10.0</td>
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<td>0.844*</td>
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<td>0.73</td>
<td>66.1±9.0</td>
<td>67.1±8.7</td>
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<td>HI</td>
<td>66.4±9.2</td>
<td>66.8±9.6</td>
<td>0.794*</td>
<td>12.03</td>
<td>0.83</td>
<td>63.3±9.2</td>
<td>64.5±10.3</td>
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<td>BG</td>
<td>75.8±13.9</td>
<td>74.9±9.4</td>
<td>0.880*</td>
<td>29.74</td>
<td>0.60</td>
<td>70.2±9.5</td>
<td>72.1±10.5</td>
</tr>
<tr>
<td>TH</td>
<td>76.4±11.4</td>
<td>77.4±11.4</td>
<td>0.866*</td>
<td>11.21</td>
<td>0.88</td>
<td>74.8±11.4</td>
<td>74.4±11.1</td>
</tr>
</tbody>
</table>

Data are mean±SD ml/100 g min. IMP-SPECT, single-photon emission computed tomography with N-isopropyl[123I]; p-iodoamphetamine; 1M, first measurement; 2M, second measurement; r, correlation coefficient; b, intercept; m, slope. SF, mesiofrontal; MF, laterofrontal; IP, inferior parietal (also containing Broca’s area); C, central; SP, superior parietal; IO, inferior occipital; ST, superior temporal; IT, inferior temporal; BG, basal ganglia (caudate + lentiform nucleus); TH, thalamus; HI, mesiotemporal parts of limbic system. Numerals refer to transverse slices (see Figure 2).

*tp<0.001, p<0.01, respectively.

than men in both measurements (first measurement mean±SD for L hCBF: women 73.9±11.3, men 61.8±3.4 ml/100 g min [t=2.73]; R hCBF: women 73.0±10.8, men 61.3±3.5 ml/100 g min [t=2.71]).

No significant intraindividual rCBF changes were found between the two measurements using the two-tailed paired t test. When rCBF values for the first measurement were compared between hemispheres, significant side-to-side differences were found (mesiofrontal in first slice, L>R, t=2.42, p<0.05; mesiofrontal in the second slice, L>R, t=3.31, p<0.01; laterofrontal R>L, t=3.13, p<0.01; central cortex in second slice, R>L, t=3.36, p<0.01; anterior basal ganglia, L>R, t=3.62, p<0.01; inferior occipital L>R, t=2.37, p<0.05; hippocampal L>R, t=3.61, p<0.01).

Patients

hCBF of the 29 CVD patients was significantly lower by two-tailed independent t test than hCBF of the controls (L: 55.6±17.7 ml/100 g/min, t=2.39, p<0.025; R: 58.7±16.1 ml/100 g/min, t=2.08, p<0.05. Mean±SD hCBF values of the control group are given in Table 1).

CVD patients were divided into a subgroup of 19 patients with reversible symptoms (TIA and RIND) and a subgroup of 10 patients with persistent neurologic deficit (CS). hCBF values of both subgroups were compared with those of the controls by one-way analysis of variance (Table 2). hCBF of the subgroup with reversible symptoms did not differ from that of controls despite significantly higher age, whereas hCBF of the subgroup with persistent neurologic deficit was significantly lower than that of the controls and of the subgroup with reversible symptoms (Newman-Keuls test, p<0.01).

Table 3 shows the comparison of hCBF values between the affected and contralateral hemispheres of the 29 CVD patients. hCBF in the affected hemisphere was significantly lower than that in the contralateral hemisphere by two-tailed paired t test (t=3.059, p<0.005) due to a significant interhemispheric difference in hCBF in the subgroup with reversible symptoms (t=3.234, p<0.005). No significant difference was obtained in the subgroup with persistent neurologic deficit (t=2.043) since hCBF was decreased in both hemispheres.

When rCBF side-to-side percentage differences of the control group were estimated, the mean±2SD for each ROI did not exceed 12%. Therefore, ischemic regions were defined as those with rCBF values that were 15% (probability of correct definition of >95%) lower than those of their contralateral counterpart. If ischemia extended over several
TABLE 2. Comparison of Hemispheric Cerebral Blood Flow Measured Using IMP-SPECT in Normal Volunteers and Patients With Cerebrovascular Disease

<table>
<thead>
<tr>
<th>Hemisphere</th>
<th>n</th>
<th>Affected</th>
<th>Contralateral</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total group</td>
<td>29</td>
<td>55.4±17.2</td>
<td>58.9±16.6</td>
<td>-3.059</td>
<td>&lt;0.005</td>
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<tr>
<td>TIA+RIND</td>
<td>19</td>
<td>63.5±14.0</td>
<td>65.7±15.7</td>
<td>-3.234</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>CS</td>
<td>10</td>
<td>39.8±10.9</td>
<td>46.1±9.2</td>
<td>-2.043</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are mean±SD ml/100 g/min. IMP-SPECT, single-photon emission computed tomography using N-isopropyl-[123I]-p-iodoamphetamine. TIA+RIND, reversible symptoms; CS, persistent neurologic deficit. r value obtained from paired t test. NS, not significant.

significant difference in rCBF between the two subgroups was also found in ROIs contralateral to those demonstrating ischemia (t=3.413, p<0.005). The interhemispheric difference of these rCBF values was less pronounced in the CS subgroup by two-tailed paired t test (t=4.393, p<0.005) than in the subgroup with TIA or RIND (t=6.956, p<0.001). Figure 4 shows SPECT studies and rCBF values recorded in a control, in a patient suffering from a RIND, and in a CS patient with an occlusion of the left middle cerebral artery.

Discussion

Continuous improvement of the SPECT technique has led to a wide clinical application of this method for the detection of impaired CBF in various neurologic diseases. Lassen et al13 introduced a fast rotating multidetector system and a model14 suitable for the determination of CBF with xenon-133 SPECT.

Opinions concerning CBF measurement with IMP-SPECT are rather divergent. Kuhl et al5 quantified CBF from IMP-SPECT images using the Mark IV scanner and obtained an overall mean±SD CBF value of 47.2±5.4 ml/100 g/min in five normal subjects applying the microsphere model. Other authors1516 described a redistribution of IMP in ischemic lesions that occurs 3-5 hours after tracer administration. From these observations, it was postulated that quantification of CBF is not possible

TABLE 3. Comparison of Hemispheric Cerebral Blood Flow Measured Using IMP-SPECT in Patients With Cerebrovascular Disease

<table>
<thead>
<tr>
<th>Hemisphere</th>
<th>n</th>
<th>Affected</th>
<th>Contralateral</th>
<th>t</th>
<th>p</th>
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<tr>
<td>Total group</td>
<td>29</td>
<td>55.4±17.2</td>
<td>58.9±16.6</td>
<td>-3.059</td>
<td>&lt;0.005</td>
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<tr>
<td>TIA+RIND</td>
<td>19</td>
<td>63.5±14.0</td>
<td>65.7±15.7</td>
<td>-3.234</td>
<td>&lt;0.005</td>
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<tr>
<td>CS</td>
<td>10</td>
<td>39.8±10.9</td>
<td>46.1±9.2</td>
<td>-2.043</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are mean±SD ml/100 g/min. IMP-SPECT, single-photon emission computed tomography using N-isopropyl-[123I]-p-iodoamphetamine. TIA+RIND, reversible symptoms; CS, persistent neurologic deficit. r value obtained from paired t test. NS, not significant.

TABLE 4. Comparison of Focal and Contralateral Cerebral Blood Flow Measured Using IMP-SPECT in Patients With Reversible Symptoms or Persistent Neurologic Deficit

<table>
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<tr>
<th>Hemisphere</th>
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<th>Focal</th>
<th>Contralateral</th>
<th>t*</th>
<th>p</th>
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<tr>
<td>Total group</td>
<td>17</td>
<td>47.7±16.2</td>
<td>60.3±12.3</td>
<td>-6.023</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TIA+RIND</td>
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<td>58.8±9.8</td>
<td>67.8±10.6</td>
<td>-6.956</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CS</td>
<td>8</td>
<td>35.2±12.3</td>
<td>51.9±8.0</td>
<td>-4.393</td>
<td>&lt;0.005</td>
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</table>
| t* from paired t test for interhemispheric comparison. | | t* from independent t test for comparison of TIA+RIND and CS subgroups.

Data are mean±SD ml/100 g/min. IMP-SPECT, single-photon emission computed tomography using N-isopropyl-[123I]-p-iodoamphetamine. TIA+RIND, reversible symptoms; CS, persistent neurologic deficit.

* from paired t test for interhemispheric comparison.

† from independent t test for comparison of TIA+RIND and CS subgroups.
since IMP distribution in the brain changes with time and might be related to specific binding of the tracer to aminergic receptors. To our knowledge, no conclusive or convincing investigation has yet been performed that could fully elucidate the cause of this late tracer redistribution.

In applying the described method for CBF quantification we expected the following: 1) the equip-
ment and image processing used should show linear sensitivity to known isotope concentrations; 2) the calculated hCBF and rCBF values in normal volunteers should be comparable with those obtained with other, already established methods; 3) repeated measurements in the same subject should give comparable results if significant tracer washout or redistribution occurs during SPECT scanning [i.e., 35-85 minutes after IMP administration], reproducibility would be seriously affected; 4) the intrahemispheric variation should be similar to that of cerebral metabolic values obtained with positron emission tomography (PET) in the same subject when repeated measurements are not performed in the same session; and 5) in stroke patients CBF values should reflect the degree of CVD and should be related to the degree of neurologic impairment.

As shown, the response of the scanning system used to iodine-123 concentrations that are usually detected in the human brain after intravenous injection of 5-6 mCi IMP is linear. Only in deep ischemic lesions can somewhat overestimated CBF values due to incompletely corrected scatter radiation be expected. Looking at the measured concentrations of iodine-123 of Bottles 12, 13, 14, and 15 in Figure 1, doubts about the proper positioning of the attenuation matrix may arise since these values are to some extent overestimated. If this is the case, then the measured values in Bottles 18 and 19 should be higher. In our opinion, these inconsistencies are caused by adsorption of iodine-123 to particles in the phantom fluid, which may affect the uniformity of tracer distribution.

Employing PET to measure CBF, the following normal mean±SD gray matter flow values have been reported: 65±17 ml/100 g/min,17 59±11 ml/100 g/min,18 65±7 ml/100 g/min,19 and 74±10 ml/100 g/min.20 Devous et al21 found a mean±SD gray matter blood flow of 71±12 ml/100 g/min using xenon-133 SPECT. Our calculated mean (67-68 ml/100 g/min) and standard deviations of gray matter blood flow closely resemble those obtained with established three-dimensional techniques.

Analyzing the cortical rCBF distribution in our controls, the highest value was found in the occipital and frontal lobes, followed by that in the temporal and parietal lobes. Comparison with reported rCBF values is rather difficult since different investigators use different regional schemes, depending on the spatial resolution of the system employed. However, high rCBF values in the visual cortex have been reported by several groups,21-23 and "hyperfrontality" is commonly known from the xenon-133 clearance technique.24 If rCBF and regional glucose metabolism (CMRglu) is proportionally distributed in normal brain tissue, then our findings are further supported by metabolic PET measurements.25-28

It must be considered that our time correction of SPECT images had to be based on the tracer input function of the whole hemisphere and not on single regional input functions. Since the hemispheric input curve represents the mean of all regional input functions, high CBF might be somewhat underestimated and low CBF somewhat overestimated if large differences in regional tracer arrival time during the first 5 minutes of measurement occur. However, this possible source of error seems not to play a major role since a similar normal distribution pattern of CBF was found with other techniques.

Measurements of hCBF and rCBF in controls were reproducible. Intraindividual rCBF values did not differ significantly between the SPECT studies. The intraindividual variation ranged between 0.3% and 15%, which compares well with that found by Phelps et al29 for paired studies separated by 1-8 days.

An unexpected result was the significant difference in CBF between sexes. We found few articles in the literature reporting a similar finding. Using the xenon-133 inhalation technique, Gur et al30 and Shaw et al31 observed significantly higher values in women than in men. In the subjects investigated by Devous et al,21 females of different ages had higher hCBF and rCBF values than age-matched males; significant differences were found in the 20-29- and the 30-39-year-old groups. Yoshii et al32 reported significantly higher CMRglu in young and elderly females than males. Besides physiologic explanations such as hematocrit variations or a brain-volume-dependent regional tracer uptake,33 this finding could be related to a different attenuation of photons by the skulls of females and males.

In comparing interhemispheric rCBF differences of controls, we expected a rightward shift that could be related to increased attention or anxiety of subjects during scanning. The significance level of interhemispheric rCBF differences found in our controls was rather low but consistent in the two measurements. Since controls were accurately positioned for scanning, side-to-side rCBF differences were not due to a partial volume effect. When correction for sequential testing was performed, the level of significance was >95%. Recently, Perlmuter et al34 reported significantly higher right rCBF in nine brain regions of 32 normal subjects. Thus, it seems that rCBF is not symmetrically distributed in the two hemispheres during scanning in the resting state.

The recorded CBF values in the CS patients reflected the degree of their neurologic impairment. The subgroup of patients with reversible symptoms showed normal hCBF in both hemispheres; hCBF in the affected hemisphere was only slightly decreased compared with that in the contralateral hemisphere. In contrast, the CS subgroup exhibited a marked decrease of hCBF in both hemispheres. The high mean difference in hCBF between the affected and contralateral hemispheres in this subgroup was caused by hCBF values of two patients with large infarcts in the territory supplied by the middle cerebral artery (interhemispheric differences...
56.43% and 40.09%), while the other eight CS patients showed relatively small interhemispheric differences (range −14.6% to 5.5% of hCBF in the contralateral hemisphere, mean ± SD −3.5 ± 5.9%). Due to the small number of CS patients and the large intraindividual variability of hCBF differences in this subgroup, side-to-side comparison did not yield a statistically reliable result.

A clear-cut difference in focal CBF was found between the two patient subgroups. The results are in good agreement with previously reported CBF findings in CVD patients. Heiss et al found a clear relation between the long-term prognosis of stroke patients and hCBF. Meyer et al recorded decreased hCBF in the nonaffected hemisphere ("dischisis") of stroke patients.

Considering the range of the obtained CBF values, their reproducibility, and the clinical results, IMP-SPECT seems to be suitable for the routine determination of CBF under normal and clinical conditions. The IMP we used was free of iodine-124 (main energy peak 603 keV) and thereby dosages of 5-6 mCi are commonly administered. Scatter radiation is substantially decreased by the absence of iodine-124 (main energy peak 603 keV) and thereby the signal-to-noise ratio in SPECT images can be improved. Kuhl et al calculated the radiation exposure for a 70-kg human (administration of 5 mCi IMP containing 4% iodine-124, assumed average half-life for washout from all tissues 66 hours) to be 0.7 rad in the brain, 4.9 rad in the lungs, 4.1 rad in the liver, and 0.45 rad for the whole body. Approximately half of the radiation exposure is due to the iodine-124 contaminant. Considering this radiation exposure, repeated CBF measurements cannot be performed in the same session (as is possible with xenon-133 SPECT) but must be separated by 7 or more days. The higher spatial resolution inherent to stable tracer techniques may compensate for this disadvantage.

References
23. Amamo T, Meyer JS, Okabe T, Shaw T, Mortel KF: Stable xenon CT cerebral blood flow measurements computed by a

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Quantification of regional cerebral blood flow with IMP-SPECT. Reproducibility and clinical relevance of flow values.
I Podreka, C Baumgartner, E Suess, C Müller, T Brücke, W Lang, F Holzner, M Steiner and L Deecke

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