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Quantitative measurement of regional cerebral blood flow with I-123 IMP SPECT: A correction of the microsphere model by global extraction between artery and internal jugular vein

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Quantitative measurements of regional cerebral blood flow with N-isopropyl-(Iodine 123)p-iodoamphetamine (I-123 IMP) as a microsphere model were performed in forty cases. The regional cerebral blood flow values obtained with I-123 IMP were slightly underestimated compared with those of Xe-133 inhalation methods ($y=0.90x-2.1$, $r=0.85$, $p<0.01$). After correction by global extraction (87%) between the artery and internal jugular vein, which was measured in four patients by means of a catheter technique, the underestimation of the values obtained with I-123 IMP was improved ($y=1.0x-2.4$, $r=0.85$, $p<0.01$). Several problems in the accurate quantitative measurement of regional cerebral blood flow with I-123 IMP are discussed.

Key words: regional cerebral blood flow, I-123 IMP, quantitative measurement, extraction, SPECT

INTRODUCTION

QUANTITATIVE MEASUREMENT of regional cerebral blood flow (rCBF) with N-isopropyl-(Iodine 123)p-iodoamphetamine (I-123 IMP)[1] was reported by Kuhl et al.[2] and Matsuda et al.,[3] as resembling a microsphere model. Though I-123 IMP is considered to be a chemical microsphere because of its high first-pass extraction in the brain after injection into the carotid artery, the possibility that the extraction changes when injected intravenously must be considered. We evaluated the quantitative rCBF measurements with I-123 IMP in comparison with Xe-133 inhalation methods and referred to a correction by global extraction measured in patients during scanning.

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MATERIALS AND METHODS

1. Quantitative measurements of rCBF

Forty rCBF measurements were performed on six normal volunteers and thirty-four patients. Normal volunteers were five male and a female aged 24–30 years. Table 1 shows a summary of thirty-four patients aged 25–79 years (mean 57.6).

Patients were examined in the chronic stage. Informed consent was obtained before the examination in each case.

SPECT images were obtained after injection every minute for the first ten minutes by means of a ring type SPECT system (Headtome SET-031, Shimadzu Corp., Japan), with a high sensitivity collimator of which the resolution was 19.8 mm in full width at half maximum (FWHM). At the same time, constant withdrawal of arterial whole blood from the brachial or femoral arteries at 0.9–1.2 m*l*/min for a ten minute period after injection was done with an infusion pump.

The equation for determining rCBF as a microsphere model, reported by Kuhl et al.,[2] is as follows:

$$rCBF=\frac{R \cdot Cb}{N \cdot A} \quad (1)$$

where R is the rate of the constant withdrawal of arterial blood (m*l*/min), Cb is the brain activity concentration (Ci/100 g), A is the total activity in the withdrawn arterial whole blood (Ci), and N is the fraction of the true tracer activity in A, as determined by octanol extraction of arterial whole blood activity.

The cross-calibration factor between reconstructed counts per pixel on SPECT images and a well counter for 100 g water was calculated with a 20 cm diameter cylindrical phantom filled with the I-123 solution. The density of the brain was considered to be equal to that of water. We used the reconstructed counts from ten minute post-injection tomographic images as Cb, and the rCBF values were calculated as follows:

$$rCBF=\frac{R \cdot C_{10} \cdot CF}{N \cdot A} \quad (2)$$

where C_{10} is the reconstructed counts per pixel in the ten minute post-injection images and CF is a cross-calibration factor (well counts per 100 g/ reconstructed counts per pixel). N was determined by octanol extraction in each case.

All cases were also examined by Xe-133 inhalation SPECT studies[4] by means of the same SPECT system with a high sensitivity collimator. Xe-133 gas was administered by rebreathing through a mouthpiece for a minute. During this period and the following 7 minutes of washout, a series of eight consecutive Xe-133 distribution maps of the brain were obtained, each of 1 min duration. The rCBF values were calculated by the sequential picture method and evaluated as the control values.

The intervals between two examinations were 1–14 days (mean 4.5 days). ROIs were placed over both cerebral hemispheres on the slices 55 mm and 90 mm above the orbitomeatal line and the rCBF values for the two methods were evaluated.

2. Calculation of global extraction between artery and jugular vein

In four cases of minor ischemic strokes, 5Fr. angiographic catheters were inserted to the distal segment of the right internal jugular vein via the femoral vein. The catheter tip was placed near the jugular bulb to avoid contamination by external carotid system radioactivity. Constant withdrawal of whole blood from the internal jugular vein, as well as from the brachial or femoral artery was done, for a ten minute period at the same withdrawal rate with a single pump after injection of I-123 IMP as in the quantitative studies.

Table 1 Summary of thirty-four patients

	No. of cases
Cerebral infarction	28
Cerebral hemorrhage	1
Subarachnoid hemorrhage	1
Moya moya disease	1
Spinocerebellar degeneration	2
Head trauma	1
Total	34

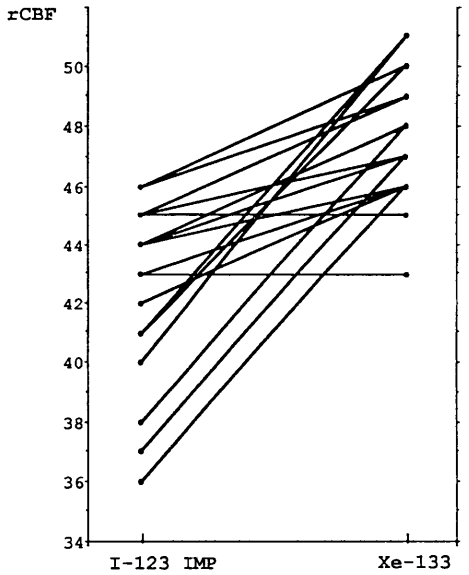

Fig. 1 The relationship between mean rCBF values for the cerebral hemisphere in the two methods in six normal volunteers. The rCBF values as determined by I-123 IMP were slightly lower than those obtained by Xe-133 inhalation methods.

The equation for determining the global extraction of I-123 IMP between artery and internal jugular vein in the first ten minutes after intravenous injection is as follows:

$$E_{10}=\frac{A_{oct.}}{A_{oct.}-V_{oct.}} \times 100(\%) \quad (3)$$

where $A_{oct.}$ (Ci/m*l*) is the fraction of whole arterial blood that has true tracer activity as determined by octanol extraction and $V_{cot.}$ (Ci/m*l*) is the same fraction of whole venous blood from the internal jugular vein. E_{10} is the global extraction in the first ten minutes after injection of I-123 IMP.

RESULTS

In six normal volunteers, the mean rCBF values for the hemisphere (m*l*/100 g/min) obtained with I-123 IMP ranged from 36 to 46 with a mean value of 42.6 ± 3.1, and those by Xe-133 inhalation methods

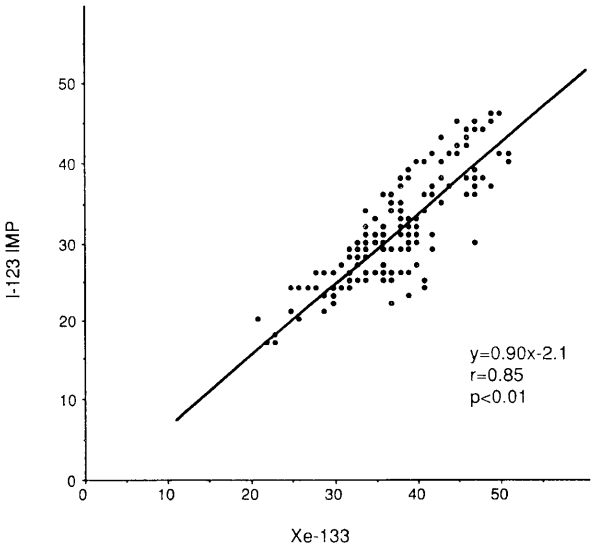

Fig. 2 The relationship between mean rCBF values for the cerebral hemisphere in the two methods in all cases (n=40). The rCBF values measured by I-123 IMP correlated well with the values obtained Xe-133, though the values were slightly underestimated in the measurements with I-123 IMP.

were from 43 to 51 with a mean value of 47.9±2.0. The values by I-123 IMP were slightly lower than those by Xe-133 (Fig. 1).

Figure 2 shows the relationship between rCBF values in the two methods in all cases (n=40). The rCBF values as determined by I-123 IMP correlated well with the values by Xe-133 inhalation methods, although the rCBF values by I-123 IMP were slightly lower than those by Xe-133 ($y=0.90x-2.1$, $r=0.85$, $p<0.01$).

Table 2 shows the global extraction values (E_{10}) between the artery and internal jugular vein and their mean rCBF values for the cerebral hemisphere obtained by an I-123 IMP study in four cases. The mean value for global extraction was found to be 87% and there was no significant correlation between the values for global extraction and rCBF.

DISCUSSION

The first-pass extraction in the brain when I-123 IMP is injected into the carotid artery is reported to be 92% in the monkey according to Kuhl et al.[1] and approximately 90% in man according to Lassen et al.[5] and I-123 IMP is considered to be a chemical microsphere. However it also has a very high first-pass extraction in the lung and is slowly released from the lung to the arterial system when injected intravenously.[6] In quantitative measurements with I-123 IMP as a microsphere model, the actual extraction of I-123 IMP released from the lung to the

Table 2 A list of global extraction values (E_{10}) and rCBF* values

Case	E_{10} (%)	rCBF
1	88	38
2	87	40
3	87	35
4	84	36
Mean	87	37

*rCBF values by I-123 IMP (ml/100 g/min)

brain has not been reported. We evaluated rCBF values obtained with I-123 IMP in contrast with those obtained in Xe-133 inhalation SPECT studies as the reference standard.

Though an Xe-133 inhalation SPECT study has limitations in the measurement of accurate rCBF values because of its low spartial resolution, it is used in many clinical studies and provides a reliable index of rCBF. To reduce the influence of the low spartial resolution as much as possible, ROIs which were large enough for FWHM were placed over the cerebral hemisphere.

In our study, rCBF values measured by I-123 IMP had a significant correlation with the values obtained by Xe-133 inhalation methods, though the rCBF values were slightly underestimated in the measurements with I-123 IMP. The cause of the underestimation is considered to be as follows: Though the first-pass extraction of I-123 IMP in the brain is high enough as a microsphere model, the washout from the brain can not be negligible even in the early period after injection and the net extraction during scanning is possibly lower than that in the first pass. The net extraction is different in each region in the brain because the washout changes in correlation with the rCBF. Therefore it is necessary to correct the rCBF values by the net extraction. Because the measurement of the net extraction in each brain tissue was difficult, the global extraction which is the mean of the net extraction in the whole brain was measured.

In our study of four cases, the global extractions between the artery and internal jugular vein were 84–88% with a mean value of 87%. The relationship between the values for global extraction and rCBF was not clear in the study of a few cases. Correction of the rCBF values by I-123 IMP was done with the global extraction value. If the uptake in the brain of I-123 IMP released from the lung is 87% and there is no release of I-123 IMP trapped in the brain during the first ten minute period after intravenous injection, the equation for correction of the measured rCBF value is as follows:

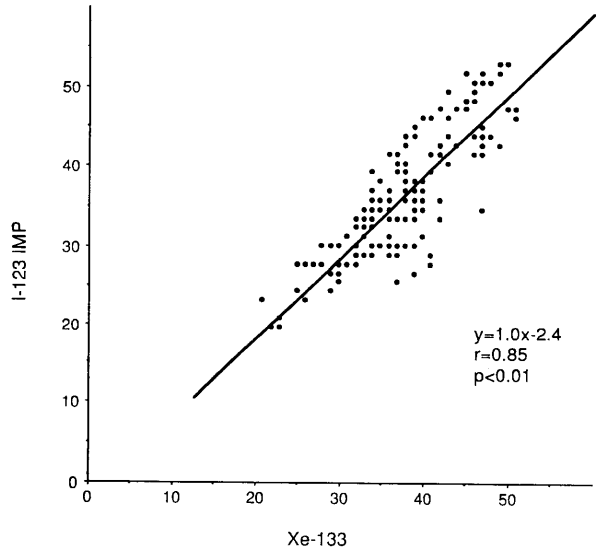

Fig. 3 After correction with equation 4, underestimation of the values measured by I-123 IMP compared to those obtained by Xe-133 inhalation methods was improved and they correlated well.

$$rCBF = \frac{R \cdot C_{10} \cdot CF}{N \cdot A} \times \frac{1}{0.87} \qquad (4)$$

After correction with equation 4, the relationship between the rCBF values obtained by the two methods is shown in Fig. 3. Underestimation of the values measured by I-123 IMP compared to those by Xe-133 inhalation methods is improved and they correlate well ($y=1.0x-2.4$, $r=0.85$, $p<0.01$).

One of the limitations in the quantitative study with a gamma camera rotating type SPECT system is the influence of the washout. As mentioned above, the net extraction modifies the rCBF values and the possibility of underestimation must be noted even in the normal cortex. The washout from hyperemic lesions can not be negligible, even in the early period after injection, because washout occurs more rapidly as perfusion increases.[7] The reconstructed images, which were scanned in the first 20 minutes or more after injection, were often estimated for brain activity with a gamma camera rotating type SPECT system, in which tomographic images in the first ten minutes can not provide adequate counts and data set because of the low sensitivity and low speed. It is possible in such cases that washout from the brain is not negligible and that the distribution of I-123 IMP modifies the rCBF mapping, even if the images are corrected to represent 10 minute reference values with the monitored entire time-activity curve.[3] Washout of I-123 IMP from the each brain tissue is not considered in our concept of the correction and it is important to scan as soon as possible after injection. Another correction with consideration for washout will therefore be necessary for accurate quantitative measurements of rCBF with a gamma camera rotating type SPECT.

CONCLUSIONS

Quantitative measurement using I-123 IMP as a microsphere model is considered to be a reliable method for the evaluation of rCBF values and our correction by global extraction which was determined in this study makes the values closer to the actual rCBF values.

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