Atraumatic CBF Measurement With the Scintillation Camera

Comparison with Intracarotid rCBF Values

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SUMMARY A scintillation camera connected to a dedicated computer system was employed for atraumatic CBF measurements in 43 patients after intravenous injection of 35 to 55 mCi $^{133}$Xe in saline solution. To validate this method results were compared to flow values in the same patients measured after intracarotid Xe injection. While the correlation between i.c. and i.v. values was not satisfactory when a high resolution collimator was used, a high sensitivity collimator improved count rates and yielded CBF values after i.v. injection in 43 patients of whom 32 suffered from organic disease of the central nervous system in whom CBF was studied only after intravenous Xe injection. The usual technology applies multiple detectors and automated data analysis with a dedicated computer system. As scintillation cameras are available in every nuclear medicine department, efforts have been repeatedly undertaken to use this equipment for atraumatic CBF measurement. However, previously published results with the camera have shown no satisfying correlation with flow values obtained after intracarotid Xe injection. With slight modification of the technique, count rates have been improved and the results of atraumatic CBF measurements compare well with data from intracarotid Xe injection. The results reported here indicate that the scintillation camera is a useful tool for clinical CBF studies.

Methods

Data were obtained from 49 patients (aged 16 to 74 years); among them were 6 healthy subjects without organic disease of the central nervous system in whom CBF was studied only after intravenous Xe injection to show normal values. Cerebral blood flow (CBF) measurements in 43 patients after intravenous injection of 35 to 55 mCi $^{133}$Xe in saline solution. To obtain comparable views for i.e. and i.v. studies the camera head was accurately repositioned. The reproducibility of the view could be proved by the scintiphotos taken from the camera oscilloscope after Xe injection. In 24 patients a high resolution collimator (thickess 31.8 mm, FWHM in 100 mm: 8.1 mm, sensitivity absolute 280 cpm/mCi, relative: 1.0) and in 19 patients a new collimator with high efficiency for low energies and moderate resolving capacity (thickness 17.3 mm, FWHM in 100 mm: 13.9 mm, sensitivity absolute: 924 cpm/mCi, relative 3.3) was used (fig. 1). The activity over the head was recorded in 6 sec sampling periods for 11 min and stored on disc for later analysis. The concentrations of CO$_2$ and Xe in the respired air were registered with a separate system (single probe, ratemeter, recorder, capnograph).

After termination of each study the stored data
were analyzed. Thirteen regions of interest were selected using the same scheme for each patient (fig. 2) and time activity curves were derived for these regions and for the total hemisphere. The values of the Xe air curve were typed in. Xe curves were deconvoluted and flow values calculated using a modified version of the computer program developed by Obrist et al. From previous experience6 the starting point for the fit of the head curve was selected when the air curve had decayed to 10–5% of its maximum; this corresponded to 89 ± 6% of the peak of the head curve so that most of the airway artefacts were avoided.1 The following flow values were printed out for each clearance function: MF: mean flow, in ml/100 g/min; FF: fractional flow of fast compartment in %; IS: initial slope index; F1: flow of fast compartment; F2: flow of slow com-

**Fig. 1.** Regression analysis of hemispheric flow values obtained after intravenous (MF) and intracarotid (fB) Xe injection with high resolution and high efficiency collimator. Limits of confidence are given for regression line and for 2 standard deviations of MF for a given fB.

**Fig. 2.** Range of hemispheric and regional peak count rates (cps) after intravenous Xe injection recorded with high resolution (upper row) and high efficiency collimator (lower row of each recording area).
partment in ml/100 g/min; $W_i$; relative weight of fast compartment in %. Different symbols were used for the parameters calculated from clearance curves recorded after intracarotid or intravenous Xe injection to make it easier to distinguish them in the text and figures.

The relationship between hemispheric and regional flow values obtained after intracarotid and intravenous Xe administration was tested by calculating PM correlation coefficients. For the correlation of regional values intracarotid $r$CBF maps had to be transformed into 13 regions identical in size and location to the intravenous studies. Additionally, areas were selected with pathologically decreased or increased flow in relation to the hemisphere and the flow values were compared.

**Results**

**Hemispheric Flow Values**

Tables 1 and 2 summarize the results obtained by the intracarotid and intravenous methods using the 2 different collimators. As shown, the mean values were comparable in both samples: $f_B$ was similar to MF; FF, IS and $F_t$ gave close estimates of $f_B$ and, also, the mean flow of the slowly perfused compartment and the mean compartmental weight were similar with both techniques. As shown in the correlation coefficients, the comparability of the 2 methods was much improved with the new collimator. As expected, the new collimator yielded better count rates (total over the hemisphere of 10000-30000 cps at maximum) but these count rates were still low when compared to those recorded after intracarotid Xe injection (total over the hemisphere of 527-2016 cps compared to 270-1423 cps at maximum) but these count rates were still low when compared to those recorded after intracarotid Xe injection (total over the hemisphere of 10000-30000 cps at maximum without extracerebral contamination). For the high resolution collimator correlation coefficients with $p < 0.001$ (table 1) were found for $f_B \times MF$ ($MF = -1.3 + 0.98 f_B$, fig. 1), $f_B \times IS$ ($IS = -8.1 + 1.2 f_B$) and $f_B \times IS$ ($IS = -6.2 + 0.95 f_B$); the correlation coefficient for $f_B \times F_t$ ($F_t = 8.8 + 0.78 f_B$) reached $p < 0.05$, while no significant relationships were found between $F_B \times FF$ ($FF = 57.1 + 0.30 f_B$), $f_B \times FF$ ($FF = 50.2 + 0.29 f_B$), $f_t \times F_t$ ($F_t = 13.9 + 0.28 f_B$) and $w_i \times W_i$ ($W_i = 52.1 - 0.18 w_i$). The high variability is also demonstrated in the high standard deviation ($w \times x$) for the prediction of the $y$-value (i.v. study) from the $x$-value (i.c. study).

For the new collimator with high efficiency, correlation coefficients with $p < 0.001$ were obtained for $f_B \times MF$ ($MF = 0.2 + 0.95 f_B$, fig. 1), $f_B \times IS$ ($IS = -10.9 + 1.56 f_B$) and $f_t \times IS$ ($IS = -8.6 + 0.93 f_t$) and $p < 0.01$ for $f_t \times F_t$ ($F_t = -2.4 + 0.94 f_t$), while the relationships $f_B \times FF$ ($FF = 48.5 + 0.43 f_B$), $f_t \times FF$ ($FF = 59.3 + 0.09 f_t$), $f_t \times F_t$ ($F_t = 25.2 - 0.19 f_t$) and $w_i \times W_i$ ($W_i = 45.2 + 0.01 w_i$) did not reach a level of significance. The improved reliability is also expressed in the lower $w_i \times x$, which was especially good for $f_B \times MF$ ($w_i \times x = 2.93$).

**Regional Flow Values**

As expected, the count rates achieved with the high efficiency collimator were higher than those with the high resolution collimator (fig. 2). For the analysis of relationships between regional values obtained after intracarotid and intravenous Xe administration, a comparison between $f_B$ and MF values was performed, since the hemispheric studies showed the best correlation between these 2 values. Means of the i.c. and i.v. values in the recorded regions, the correlation coefficients between i.c. and i.v. values and the estimated standard deviation of the i.v. values from the i.c. values ($w \times x$) are shown in figure 3 (high resolution collimator) and figure 4 (high efficiency
FIG. 3. Mean values and standard deviation of regional flow values after intracarotid (first line) and intravenous Xe injection (second line in each area) as obtained with high resolution collimator. Slope (B) and intercept (A) of regression lines, the correlation coefficient (r) and its level of significance (p) and the standard deviation of MF for a given fB (sy-x) are given for each region.

**FIGURE 4.** Mean values and standard deviations of regional flow values after intracarotid (first line) and intravenous Xe injection (second line in each area) as obtained with high efficiency collimator. Results from regression analysis of regional flow data as in figure 3.
collimator). As for hemispheric results, the mean values obtained by the 2 methods were similar, but the correlation between the values was better with the new collimator. With this collimator, a significant correlation was found in all regions, while no significant relationship was obtained in 4 regions with the high resolution collimator. The correlation coefficients obtained from measurements with the high efficiency collimator were all higher than with the high resolution collimator, and the standard deviations (sy • x) were lower. In the figures the mean values and standard deviations of the i.e. (fB) and i.v. study (MF), the slope (b) and intercept (a) of the regression lines, the correlation coefficient (r) and its level of significance (p) and the standard deviation of MF for a given fB (sy • x) are given. Values and regression lines from one representative region as measured with the 2 methods and different collimators are shown in figure 5.

Flow in Abnormally Perfused Regions

In the 24 patients studied with the high resolution collimator 22 ischemic regions were observed. These regions could be distinguished from the surrounding, better-perfused brain tissue in both i.e. and i.v. measurements. The mean flow value in these regions was 31.4 ± 5.9 in the i.e. and 35.0 ± 9.8 ml/100 g/min in the i.v. study. The calculated regression (MF = 0.02 + 1.11 fB) demonstrated the significant relationship (r = 0.677, p < 0.001, sy • x = 7.39). Results with the high efficiency collimator were again better: 18 ischemic and 1 pathologic hyperemic areas were well defined in i.e. and i.v. measurements. Again, the mean value for the i.e. study (30.8 ± 7.4) was lower than for the i.v. study (34.6 ± 9.8 ml/100 g/min), but the regression analysis demonstrated the good relationship (MF = 1.5 + 1.1 fB, r = 0.809, sy • x = 5.91). The quality of the distinction of an ischemic

focus may be seen in figure 6, where the focus is numerically recorded for the i.e. study and color coded for the i.v. study.
Normal Flow Values

Six volunteers (aged 11–39 years), who were investigated with the atraumatic method only, had mean flow values of MF $51.7 \pm 7.2$ ml/100 g/min, FF $74.6 \pm 4.3\%$, IS $81.5 \pm 11.0$, $F_1 = 83.6 \pm 9.6$ ml/100 g/min, $F_2 = 23.2 \pm 4.1$ and $W_t = 45.1 \pm 4.7\%$, which were comparable to the normal values reported in other studies with multidetector equipment. Regional MF values did not reveal significant differences of flow between various brain areas (fig. 7).

Discussion

Since the scintillation camera has been applied successfully for rCBF measurement with intracarotid Xe injection,11–19 several authors have tried to use the scintillation camera for rCBF studies using atraumatic Xe administration. Klassen et al.2–3 utilized inhaled $^{133}$Xe to evaluate hemispheric circulation in control subjects and patients with cerebrovascular disease. However, their atraumatic values did not compare well with results from intracarotid measurements, and the Xe dosage necessary for regional flow was rather high (50–150 mCi) which limited the clinical usefulness. In studies performed by Wyper et al.19 single probes were superior to the scintillation camera in detecting ischemic regions, and, therefore, the application of the camera for flow studies was discontinued. Only Philippou et al.4 attained satisfying results from 8 to 12 regions over the brain with total peak count rates of 50,000 cpm; however, they did not validate their technique by comparison with other methods.

As shown in our results with 2 different collimators, an increase in count rates improves the reliability of the flow values after intravenous Xe injection. However, the achieved count rates do not satisfy the postulated peak rates of 800 to 1000 cps required for adequate statistics1 but they are close to the count rates reached with small probes, which also yielded reliable flow measurements (review in Ref. 20). The results with the camera could be further improved by constructing a collimator with still higher efficiency and a spatial resolution just tolerable for this type of study. For the rather large recording areas ($3 \times 3$ cm) the resolution of the high efficiency collimator was still too good (FWHM of 13.9 mm at 10 cm distance). The application of a collimator with less resolution capacity could further improve the count rates.

Despite the low count rates achieved after i.v. Xe injection our results with the high efficiency collimator show comparable flow values from both i.c. and i.v. measurements and significant correlation coefficients for several hemispheric values and for flow ($f_0 \times MF$) in all 13 regions. The correlation coefficients and the standard deviation of the i.v. value from a given i.c. value were comparable to those reported by Reivich et al.21 ($r = 0.96$ for mean hemispheric fast flow, $r = 0.90$ for regional fast flow of 11 patients), Wyper et al.19 ($r = 0.87 - 0.91$ in 16 measurements), Austin et al.20 (0.86 for grey matter flow, 0.2 for white matter flow in 7 patients), and Thomas et al.22 ($r = 0.976, sy \cdot x = 4.87$ calculated from the given data of 6 patients). Our correlations are based on data obtained with the camera for total hemispheres and 13 regions while the previous studies were carried out with single probes in 7–15 regions,21 2 regions over one hemisphere,22 2 regions over each hemisphere,23 and 3 regions over each hemisphere.24 Some of our discrepancies, e.g. low correlation coefficients among FF and i.c. values, may be due to the start fit point below 10% of air curve maximum, by which the fast compartment might be underestimated. However, a start fit point between 20 and 10% of air curve maximum often corresponded to the plateau of the head curve still contaminated by scattered radiation from air passages. This disagreement with other investigations might be due to the
usage of an i.v. bolus instead of 1 min inhalation of 133Xe.

While the low count rates can be overcome with collimators of better efficiency, the disadvantage of the camera, namely that measurements of both hemispheres cannot be performed in one study, could be solved by simultaneous application of 2 camera heads. On the other hand, the camera is independent of a predefined position as is the case with single detectors and allows selection of areas of interest from which flow values can be calculated. These areas can be repeatedly chosen after the study and their location, size and configuration may be varied. Irrespective of their irregular shape such areas can be treated as individual recording fields. Thus pathologically perfused regions can be exactly defined and compared to the flow in the surrounding brain. By decreasing the number of recording fields the count statistics in the interesting areas are improved without loss of clinical information. When repeated studies are performed, comparison of flow in corresponding regions is facilitated.

All 2-dimensional techniques for rCBF measurements with radioisotopes suffer from certain limitations, mainly inclusion of activity not originating in the tissue volume of interest and inadequate resolution of badly perfused brain regions when overprojected by tissue with high blood flow, commonly referred to as the "look through" phenomenon. A scintillation camera technique has some further disadvantages. However, as shown in our results, rCBF can be reliably determined with the scintillation camera. This technique is applicable in all the clinical conditions where atraumatic rCBF measurements have been shown to be of clinical value.

References
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