Analysis of the Gamma Ray Spectra Recorded in the Use of Xenon-133 for Cerebral Blood Flow Studies


SUMMARY A problem in the measurement of cerebral blood flow with \( ^{133} \)Xenon is the presence of extracerebral counts in the total counts recorded with a collimated gamma ray detector looking at the brain. A method of studying qualitatively the contribution of this extra-cranial component in patients is described. This entails the sequential accumulation of gamma ray spectra recorded during the clearance phase of \( ^{133} \)Xenon from the brain. It is shown that different CBF indices are obtained for various regions of the recorded gamma ray spectra. The principal component of the extracerebral counts at 15 minutes post-injection appears to be intra-cranial, and not the scalp as assumed previously in the spectrum subtraction method.

**THE CLEARANCE OF \( ^{133} \)XENON from the brain is the most commonly used method for measuring regional cerebral blood flow in man. The radioactive gas is introduced into the brain by inhalation,\(^1\) internal carotid injection,\(^2\) or recently by intravenous injection.\(^3\) The clearance of Xenon is usually analysed by the Obrist two-compartment analysis programme,\(^4\) although for clinical use, two alternative methods of deriving a cerebral blood flow index have been applied: the two minute slope\(^5\) and the initial slope index.\(^6\)

Problems in measuring cerebral blood flow arise from the method of introducing \( ^{133} \)Xenon, from extracerebral contamination, and in choosing a method of analysis. The various cerebral and extra-cerebral compartments are loaded with the Xenon at different rates, and their degree of saturation depends on the method of administration. The proportion of counts measured from each compartment is therefore affected, and this probably affects the shape of the clearance curve, which, in turn, influences the calculated CBF value.

Risberg et al.\(^7\) have applied the spectrum subtraction method proposed by Crawley and Veall\(^8\) to remove the scalp contribution from slow clearing extra-cerebral tissues. Phantom studies indicate that the spectrum subtraction method used overestimates the Xenon in the scalp for two reasons. Firstly, multiple scattering of 80 keV photons results in a significant proportion of counts in the 30 keV energy window defined with a single channel analyser (SCA). Secondly, the skull does not act as a perfect filter for the 30 keV photons emanating from Xenon in the cerebral tissue.

An attempt is made in this paper to study some of the problems associated with extra-cerebral and, in particular, extracranial contamination, and to examine the changes in the CBF values that result. The method entails analysis of the changes in the recorded gamma ray spectrum during the clearance of Xenon. The contribution of the scalp counts at any time during the clearance phase can only be estimated if the skull thickness could be determined.
Method

For these cerebral blood flow studies, 2 mCi of $^{133}$Xe in less than 2 ml was administered by intravenous injection. To ensure good transfer of Xenon to the blood the patient was asked to hold his/her breath for about 10 to 15 seconds during and after the injection. End-expired pCO$_2$ and the expired air count rate were continuously recorded.

Two opposed 4 cm diameter NaI detectors 3 cm thick with 5 cm long and 2.5 cm diameter single hole parallel collimators were used. The counters were placed with the posterior edge of each collimator just in front of the appropriate parietal eminence so that the field of view defined was the middle cerebral region. The pulse height output of each detector was connected to an 800 channel Nokia MCA through a mixer router module with the gain set to approximately 1 keV per channel. The counting rate over the whole gamma ray spectrum was usually less than 1000 cps so that the corresponding dead time of the analyser using a 20 MHZ clock rate ADC was less than 5%.

Sequential gamma ray spectra were simultaneously recorded during the uptake and clearance of Xenon for the cerebral volumes 'seen' by each detector for 6 seconds clock time in the two holes of the 800 channel analyzer memory every 30 seconds. The readout of the 800 channel spectrum after each 6 second accumulation took less than 24 seconds. Therefore, over 15 minutes 30 spectra were recorded for subsequent gamma ray spectral analysis and cerebral blood flow computation. The data from the cassette tape was then transferred to a PDP 11/10 computer, with which the spectra could be examined for integration, normalisation, subtracting, comparison, etc. The counts using the normal single channel analyser windows for the 30 keV and 81 keV peaks were used for two compartment analysis. The so-called true 30 keV peak counts were obtained by linear interpolation of the background below this peak using the mean of 5 points below the 20 keV channel and 5 points above the 40 keV channel.

Phantom Studies

To estimate the contribution of Xenon in the scalp to the total counts, a pure scalp source was obtained by spraying Xenon in saline on the temporal area of a subject's scalp and promptly recording the gamma ray spectra recorded using a thin plane source made of perspex (4 mm thick x 15 cm square) filled with $^{133}$Xe placed with the posterior edge of each collimator just in front of the appropriate parietal eminence of the subject's head. There was no significant difference between the two spectra.

To study the change in the spectra with the depth of $^{133}$Xe in the brain, the scalp phantom was placed in a water tank (20 x 25 x 30 cm) and a hemisphere of human skull placed between the tank and the collimated detector. The gamma ray spectra recorded with the plane source at various depths confirmed that the skull does not act as a perfect filter for the 30 keV X-rays of Xenon-133 and even with a source 10 cm depth which would represent the midline in the patient's cerebrum, the proportion of counts in the 30 keV peak recorded with an SCA would represent more than 15% of the 80 keV counts. Also, as expected, the proportion of scattered radiation from 40 keV to 70 keV was found to increase steadily with depth.

Results

Typical gamma ray spectra recorded over 6 second intervals during a 15 minute clearance phase of Xenon from the brain are shown in figure 1. The energy window used with an SCA to record the 30 keV X-rays, therefore, includes a significant proportion of scattered 80 keV photons that originate from both intra- and extra-cranial Xenon (inside and outside the field of view of the detector). The true 30 keV counts are, therefore, superimposed on a background that changes shape and relative intensity with time. Clearly inspection of these spectra demonstrates that subtraction of the 30 keV counts recorded with an SCA would result in a gross overestimate of the Xenon seen in the brain. Also, the 65-95 keV energy window normally used with an SCA in CBF studies to measure the 80 keV photons from $^{133}$Xe includes a significant proportion of scattered photons.

Typical cerebral blood flow indices calculated using the variable metric algorithm method of analysis (Obrist et al.) with a start fit time of 120 seconds and a total measuring time of 15.5 minutes are depicted in table 1 for various energy windows of the gamma ray spectra recorded from a patient study. The largest difference in the indices appears in the relative weights, although the differences in the CBF indices for the 80 keV peak and the total gamma ray spectrum was less than 10%. However, the CBF values for the 30 keV SCA counts and true peak counts differ from the 80 keV peak values. These differences and trends in the CBF indices were found to be consistent in the 5 patient studies undertaken using this method of spectral analysis.

![Gamma ray spectra recorded for 6 seconds from the brain at various times during the clearance phase. The spectrum obtained at the maximum count rate from the brain is assigned time zero.](http://stroke.ahajournals.org/)

**Figure 1.** Gamma ray spectra recorded for 6 seconds from the brain at various times during the clearance phase. The spectrum obtained at the maximum count rate from the brain is assigned time zero.
**Table 1. Typical Cerebral Blood Flow Values for Various Energy Regions using a Two-Compartmental Model (Start Fit Time 120 sec, Total Measuring Time 15.5 min)**

<table>
<thead>
<tr>
<th>Energy window</th>
<th>$K_1$ (min⁻¹)</th>
<th>$F_1$ (ml/100 g/min)</th>
<th>FF1</th>
<th>W1</th>
<th>$K_2$ (min⁻¹)</th>
<th>$F_2$ (ml/100 g/min)</th>
<th>MF (ml/100 g/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 keV peak (60-95 keV)</td>
<td>0.928</td>
<td>70.2</td>
<td>0.75</td>
<td>0.47</td>
<td>0.134</td>
<td>20.0</td>
<td>43.4</td>
</tr>
<tr>
<td>Total (20-100 keV)</td>
<td>0.906</td>
<td>72.5</td>
<td>0.74</td>
<td>0.43</td>
<td>0.129</td>
<td>19.4</td>
<td>42.5</td>
</tr>
<tr>
<td>30 keV SCA (20-40 keV)</td>
<td>0.880</td>
<td>64.5</td>
<td>0.71</td>
<td>0.36</td>
<td>0.100</td>
<td>15.0</td>
<td>32.8</td>
</tr>
<tr>
<td>30 keV True (20-40 keV)</td>
<td>0.765</td>
<td>63.6</td>
<td>0.67</td>
<td>0.30</td>
<td>0.091</td>
<td>13.7</td>
<td>28.8</td>
</tr>
</tbody>
</table>

**Figure 2.** Comparison of the spectrum from the scalp phantom and the in vivo spectra recorded at various times during the clearance phase, normalised to the height of the 80 keV photopeak.

Figure 2 compares the gamma ray spectrum obtained from the scalp phantom study and two spectra recorded during the clearance phase. The spectra have been normalised for the same 80 keV peak height. The secondary peak at about 70 keV probably corresponds to scattered photons from Xenon in the air passages and face mask. The proportion of these scattered photons changes with time and their presence will be more likely to influence the cerebral blood flow values derived using a short start fit time.

**Discussion**

This study demonstrates that a reasonable proportion of the counts recorded by a detector placed over the middle cerebral region for cerebral blood flow measurements using $^{133}$Xenon arises from sources outside the field of view. Obrist et al. have studied the effect of this scattered radiation on the computed blood flow values, and most non-invasive techniques seek to remove contamination from this source by choosing a longer start fit time that allows the isotope concentration in the expired air to reach a relatively low level.

Comparison of the scalp and patient spectra also demonstrates that even after 15 minutes of the clearance phase there are marked differences between them. The scalp component influences but does not dominate the early or late in vivo spectra.

In conclusion, the simple SCA spectrum subtraction method proposed by Crawley and Veall overestimates the scalp contribution, leads to poor statistics and an underestimate of Xenon in the brain. Quantitation of the proportion of scalp counts in the recorded gamma ray spectra is difficult because the skull does not act as a perfect filter for the 30 keV photons emanating from Xenon in the brain. Dynamic brain scintigraphy studies have estimated this to be of the order of 30%. Even at 15 minutes post injection the principal component of extra-cerebral counts appears to be intracranial.

**References**

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