Regional Cerebral Blood Flow in Stroke by $^{133}$Xenon Inhalation and Emission Tomography

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SUMMARY  A rapidly rotating single-photon emission tomograph was used to study regional cerebral blood flow by $^{133}$Xenon inhalation. Using a rotation speed of 180°/5 sec a tomographic picture of the average Xenon concentration in 3 slices is obtained. By taking a sequence of 4 one-minute tomograms during and after a one-minute $^{133}$Xenon inhalation period, a flow-dependent variation in local isotope concentration is seen. This sequence is used for calculating CBF by a deconvolution procedure. The CBF maps have a spatial resolution of approximately 1.7 cm (FWHM).

This preliminary study comprises normal subjects and 10 unselected patients with stroke. The CBF tomograms localized appropriate ischemic areas in all 10 patients. In one patient the conventional x-ray tomogram was negative, while the flow tomogram clearly showed a decreased flow in consonance with the clinical findings.

Regional cerebral blood flow measured tomographically by $^{133}$Xenon inhalation circumvents the extra-cranial contamination and the superposition of intracranial tissues that hamper $^{133}$Xenon inhalation flow studies using stationary detectors.

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THE RATE of uptake and wash-out of $^{133}$Xenon recorded by stationary detectors has for several years been used to measure regional cerebral blood flow (rCBF). This yields 2-dimensional flow maps. With intra-carotid injection a high count rate can be reached, so that many small, highly collimated scintillation detectors can be used. The 254 detector Dynamic Gamma Camera developed for such studies yields a good resolution, FWHM of approximately 1.5 cm, in the plane. Yet the depth resolution is poor due to superposition of the labelled tissues in the hemisphere counted from.

With inhalation or i.v. injection of $^{133}$Xenon an atraumatic technique is obtained. The lower count rate means that the field of view of each detector must be larger. This reduces the resolution in the plane. And, due to the simultaneous labelling of both hemispheres and of extracranial tissues, the depth resolution is even poorer than with $^{133}$Xenon i.a. injection.

In this study we present the first clinical results using a rapidly rotating single photon tomograph, Tomomatic 64,* for rCBF with $^{133}$Xenon inhalation. This method circumvents superposition of tissue layers since the 3-dimensional isotope distribution is reconstructed by the computer in the same way as with conventional x-ray tomography (CT-scanning). The results show that $^{133}$Xenon tomography yields CBF maps ("slices") that clearly display areas of tissue ischemia. This is important as many clinical problems are concerned with the detection of, and treatment of, brain ischemia.

The Tomograph

A detailed description of the tomograph has recently been published. The rapid rotation of the detector head of 180°/5 sec implies that all the projections are taken "practically simultaneously." In order to accumulate a sufficient number of counts for reconstruction of an image, a sufficient number of turns are accumulated. We use an integration time of one minute per picture and take a sequence of 4 one-minute pictures. In each picture this represents a map of the distribution of the time-averaged $^{133}$Xenon concentration. With the concentration of $^{133}$Xenon used (10 mCi/l), the counting rate is about 600,000 counts per minute in the second one-minute period, in which the counting rate is at its maximum. At this counting rate the spatial resolution is about 1.7 cm (FWHM).

The instrument records from 3 slices simultaneously, each 2 cm in thickness (FWHM) and with an interslice distance of 2 cm. This is accomplished by each of the 64 detectors (16 in each of the 4 banks) consisting of a narrow 14 cm long sodium iodide crystal. Three photomultipliers "look" at each crystal and position the photons as in a conventional Anger type gamma camera. The instrument is set so that only the high energy photons of $^{133}$Xenon (81 KeV) are recorded. This is done in order to reduce Compton scatter effects.

The tomographic images are reconstructed from the observed projections using a filtered back projection algorithm. An attenuation coefficient was used to compensate for the tissue absorption of the radiation. This coefficient is set so that a uniform source (a water filled plastic bucket) gives a uniform image.

$^{133}$Xenon Administration and the Air Curve

The $^{133}$Xenon gas was administered from a closed recirculating system in which the concentration could be monitored. We have used a concentration of 10 mCi/liter for 1 minute. This results in a radiation exposure of the lung, the target organ, of 0.36 rad/study as calculated for the gamma and beta radiation. The gonadal dose is approximately 0.005 rad/study.

The air curve was monitored over the right lung using a single collimated probe positioned at a distance of 30 cm in order to reduce the effect of chest wall
movements. The air curve was synchronized to the
tomograph in that 8 data periods per second were
transferred to the core memory of the computer.

Calculations

In a recent paper Kanno and Lassen proposed 2
different approaches for calculating regional cerebral
blood flow (rCBF) from tomographic 133Xenon pictures.
The "4 step method" is based on the sequence of
4 one-minute pictures in that the count rate in each
pixel is followed in the 4 pictures: an increasing and
subsequently decreasing concentration is recorded and
this pattern is compared to the theoretically expected
profiles assuming monoeponential step functions (of
known time constants $k = 1/\lambda$ min$^{-1}$). The "initial pic-
ture method" is based on the bolus distribution prin-
ciple: a low count rate in the sum of 1st and 2nd one-
minute tomograms is taken to indicate a low flow.
The algorithm used for calculating rCBF in the
present study makes use of both methods. As described
elsewhere in some detail the 4-step method is used to
estimate the absolute flow levels in pixels with high
count rates. With this estimate the initial picture
method can be scaled in absolute units of $rCBF = \frac{100}{f}$
in ml/100 g/min. It is assumed that the partition
coefficient $\lambda$ has the same value of 0.85 ml/g in all
areas. Since all our conclusions in patients with stroke
are based on side-to-side asymmetries the exact value
of $\lambda$ is not essential. No correction was made for
Compton scatter.

Results

In normal man the tomographic CBF map is
symmetrical with a cortical flow level of about 60 to
80 ml/100 g/min. The 3 slices usually studied were the
OM + 2 cm, OM + 6 cm and OM + 10 cm. Their
patterns varied somewhat with the size of the brain.
The OM + 2 cm slice showed in most cases an area of
high flow anteriorly in the midline, a reflection of
Compton scatter from 133Xenon in the nasal sinuses.
In the OM + 0 cm slice this artifact is readily seen as
well as the cerebellum. The OM + 6 cm slice typically
showed a high flow region in the midline posteriorly
(striate cortex) and anteriorly (mesial frontal cortex)
as well as in both lateral Sylvian regions. The centrum
semiovale white matter low flow region was not well
demarcated. The OM + 10 cm slice usually showed a
fairly even high flow field.

In the 10 patients with stroke who were studied,
asymmetry of rCBF was seen with the low flow areas
agreeing well with the localization suggested by the
clinical symptoms. In all of these patients x-ray
tomography was made by the Department of Neuro-
radiology, Rigshospitalet, Copenhagen. In 9 patients
infarcts were seen as low density regions localized
where the rCBF tomograms showed low flow (one
with a smaller deep x-ray lesion showed larger rCBF
ischemia, see patient 2). In the 10th patient (see
patient 6 below) with a left-sided hemiparesis mainly
affecting the hand, the x-ray tomography made was
negative, while the rCBF map showed a low flow

Patient Histories

1. Completed Stroke (A.H.)

A 69-year-old woman, 5 days before had the sudden
onset of right-sided hemiparesis and severe aphasia
with no remission. X-ray tomography showed an ex-
tensive left hemisphere infarct. The CBF tomogram
showed ischemia of entire left hemisphere.

2. Completed Stroke (E.F.)

A 71-year-old woman, 8 days before had the sudden
onset of right-sided hemiparesis and aphasia with no
remission. X-ray tomogram shows a deep infarct on
the left side — in the anterior part of the internal cap-
sule and centrum semi ovale. The rCBF tomogram
showed a larger ischemic area including an area of
cortical flow reduction on the left side anteriorly both
in upper (OM 10 cm) and middle (OM 6 cm) slice.

3. Completed Stroke (B.T.)

A 47-year-old man, 2 weeks before suddenly had
slight right-sided hemiparesis and right-sided
hemianopsia, with no remission. CBF and x-ray
tomography both showed an extensive defect in the
posterior part of left hemisphere.

4. Multiple Completed Stroke (J.P.)

A 63-year-old man, 4 months earlier, had sustained
a left-sided hemiparesis and left hemianopsia of
sudden onset with no remission. Arteriography
revealed no vessel occlusions. rCBF and x-ray tomog-
raphy showed infarcts in both hemispheres (most ex-
tensive in the right side).

5. Completed Stroke (G.H.)

A 55-year-old man had a left-sided hemiparesis
with onset 1 month previously. Angiograms revealed a
total occlusion of the right internal carotid artery. X-
ray and CBF tomography showed 2 infarcts in the
right hemisphere (near the anterior horn and in the oc-
cipital lobe).

6. Completed Stroke (E.C.)

A 45-year-old woman had a slight left-sided
hemiparesis mainly of the hand of sudden onset 4
months previously. X-ray tomography was negative.
CBF tomogram showed a large (ca. 5 x 5 cm)
ischemic area in the right parieto-central region in an
upper slice OM + 10 cm, the cerebral blood of flow
level in the ischemia area was about 30 ml/100 g/min.

7. TIA (B.E.)

A 41-year-old man with multiple transient ischemic
attacks characterized by right-sided hemiparesis and
aphasia. Angiograms showed a total occlusion of the
left internal carotid artery. X-ray tomography showed a small left parietal infarct. CBF tomography showed a larger left-sided parietal ischemic region and a lesser flow reduction anteriorly in the same hemisphere.

8. Completed Stroke (B.J.)
A 62-year-old-man, 4 months before, had the sudden onset of expressive aphasia and slight right-sided hemiparesis, no remission. X-ray tomogram
showed an infarct in the left parieto-central region. CBF tomograms show an even larger left-sided low flow area extending into the left frontal lobe.

9. Completed Stroke Following Subarachnoid Hemorrhage (A.J.)

A 56-year-old woman, 10 months before, had a subarachnoid hemorrhage (no aneurysm was found); she had slight aphasia and right-sided plantar extensor reflex, pronounced apathy and aspontaneity. X-ray tomogram showed bifrontal mesial infarcts, and CBF tomogram showed low flow in same regions.

10. Completed Stroke (B.E.)

A 29-year-old woman, 1 month before, developed left-sided hemiparesis and hemianopsia of sudden onset, with no remission. X-ray tomogram showed a right-sided thalamic infarct. CBF map showed slight reduction of flow in right parieto-occipital and in right frontal regions. The angiogram was normal.

Discussion

The "raw" $^{133}$Xenon concentration images used for calculating the flow maps and obtained over the 4 one-minute integration periods, show clearly that dynamic tomographic pictures can be obtained with $^{133}$Xenon with a spatial resolution of ca. 1.7 cm using the medium resolution collimator.\(^4\)

The low flow regions — ischemic areas — were clearly seen. In our 10 patients comprising an unselected sequentially studied series of strokes with clearcut focal symptoms, ischemic areas were found. The ischemia seen typically had flow values of approximately 20 ml/100 g/min as compared to 50 to 60 in other cortical areas. The ischemic areas were extensive and tended to be homogeneous. They were easy to recognize and no statistical evaluation was needed to ascertain their significance. In one patient, #10, there was a moderate asymmetry of the CBF map in the cortex which was considered evidence of the disease process. This patient had an x-ray-proven thalamic infarct and an ipsilateral cortical flow reduction to approximately 40 ml/100 g/min as compared to 50–55 ml/100 g/min on the opposite side. This may reflect a state of deafferentiation.

The rapidly rotating tomograph circumvents the superposition of tissues that invalidates the conventional stationary detectors with regard to detection of ischemic areas.

Comparing the flow tomograms to the x-ray tomograms (conventional CT scanning) the following points can be made: a) The parameters studied differ, viz. tissue blood flow versus tissue density. The low flow areas tended to be larger than the hypodense areas. This suggests that incomplete ischemia may impair normal neuronal function without destroying the tissue. Patient 6 with normal x-ray tomograms is particularly interesting in this context. b) The spatial resolution of the flow tomograms is very coarse compared to that of the x-ray tomograms. The low flow areas are often larger than the hypodense ones. c) Negative x-ray tomograms are regularly found in the first hours after a stroke. There are reasons to expect that in the early phase the flow maps will be positive in those reported here, where flow defects were found days to weeks after symptom onset. d) Function related changes in the flow map can be expected. We have studied the effect of hand movement in 2 normal subjects (including one of the authors, N.A.L.). In both about 20% flow increase in the contralateral central cortex was seen in the upper slice, OM + 10 cm.

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References

Accuracy of Bedside Diagnosis in Stroke

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SUMMARY The clinical diagnosis of the type of acute cerebrovascular diseases is often considered unreliable, although this has not been validated prospectively in representative patients. The accuracy of bedside diagnosis was, therefore, tested in 206 patients consecutively admitted to the Stroke Unit of the Serafimerlasarettet in Stockholm. Bedside diagnosis turned out to be correct in 69%. In 24% the diagnoses were altered after hospital investigation and in the remaining 7% no defined preliminary and/or final diagnosis could be made. When the diagnoses were considered “fairly certain” they were accurate in 87%, compared to 53% when regarded as only “probable”. The diagnostic accuracy improved during the period studied. Sensitivity in identifying hemorrhages was much lower (39%) than for cerebral infarctions (83%). It is suggested that new investigational methods should be compared with what can be accomplished with bedside methods alone.

Specific acute and secondary preventive therapy has become available for some forms of cerebrovascular diseases (CBVD). It is, therefore, important not only to differentiate between hemorrhagic and ischemic disorders but also to separate the subgroups within these entities.

Many qualified methods for investigating stroke have, accordingly, come into use. Some are associated with great costs and require equipment not available in all hospitals or for all patients. The benefit of such specific investigations for the aged patient has also been questioned. Although many authors support the value of new diagnostic examinations with the observation that bedside diagnosis is not reliable in CBVD, there is no prospective validation of this idea in a living patient population. Therefore, we have evaluated the accuracy of diagnoses at the bedside made on clinical grounds alone. The present study, over 2 years, was aimed at answering the following questions:

1) How often can we correctly identify the type of stroke with bedside methods only?
2) Are the bedside diagnoses more often correct when initially considered “certain” than when considered “probable”?
3) Which clinical factors guided our preliminary judgement and which factors were involved in the final diagnoses?
4) Did our diagnostic ability improve during the two year study period in the Stroke Unit?

Patients and Methods

Serafimerlasarettet is a university hospital of the Karolinska Institute. It serves a defined population of 120,000 inhabitants in greater Stockholm. Two hundred and six patients (97 men and 109 women, mean age 73 years) were consecutively admitted from the Emergency Ward to the Stroke Unit of the Medical Department during the period October 1976 to July 1978. Criteria for admission to the Stroke Unit were: acute to subacute appearance of focal neurological deficit, either as transitory ischemic attacks (TIA) within the last month or as persistent symptoms within the last week. Doctors on duty were informed about the study and checked that the patients fulfilled these criteria. The patients were then sent to the Stroke Unit if there was a bed available. The admission procedure has been described and evaluated earlier as well as the general organization of the Stroke Unit.

Bedside Diagnoses

The patients arrived in the Stroke Unit with a mean delay of 16 hours after the onset of symptoms. A bedside diagnosis was made and irretrievably designated...
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