Scintillation scanning in the diagnosis of neurological disease

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INTRODUCTION

THE CHIEF TYPES of scintillation scanning procedures available in CNS investigation includes

1) Brain scanning
2) Myeloscintigraphy and
3) Radioisotope ventriculography and cisternography.

The brain scan attempts to detect the presence of a brain lesion (SOL), characterise its size, shape and position and finally identification of its nature. It depends on the administration of a radioactive agent which is localised in the lesion, to a higher concentration than the surrounding normal brain, so that it is shown up on scanning or on scintiphotography using a gamma camera. Mode of action of the scan agent has been put down to the following:

1. increased vascularity associated with the lesion
2. uptake in neoplastic cells
3. breakdown in blood brain barrier involving increased capillary permeability and uptake in the increased interstitial space associated with the lesion.

RADIOPHARMACEUTICALS USED

There have been a large variety of radioactive substances used for brain scanning and the desirable properties of such agents includes:

1. ability to be measured when present in small amounts
2. gamma emitter with energy range of 0.1 to 0.5 MEV to allow detection of deep seated lesions and still not offer too many problems due to collimation.
3. Beta emission absent or weak
4. concentration in the tumour compared to normal brain tissue should be as high as possible and maintained during the entire period of scanning.
5. tumour to muscle ratio should also be high to detect lesions in the posterior fossa.
6. Physical and effective half lives should be short to reduce dosage and there should be no areas of prolonged retention with resultant high dosage to this organ.

The chief scan agents in use are:

1. 131I Albumin

Fig. 1: 57-year-old female patient with signs of left frontal lobe SOL. Scan shows area of increased uptake in the posterior frontal area.

Fig. 2: Anterior view of same patient. Note lesion is strictly to the left and does not cross midline. Final diagnosis at surgery meningioma.

2. 203 or 197 Hg Neohydrin
3. 99mTc Pertechnetate
4. 113m Indium DTPA

Most centres, including the Department of Radiotherapy and Nuclear Medicine here, use 99 mTc as the scan agent because it is easily available and very effective. A dosage of 10 to 15 millicuries is used and the whole body radiation dose is 0.18 rads with 1-3 rads to the large bowel. Technetium is milked from a 99Mo generator. The agent could be given orally or parenterally although the latter method is preferable as absorption might be irregular orally and higher dosages may be needed. The majority of SOL are demonstrated, using any one of the several available tracers; however, certain lesions are demonstrated only, or more clearly, by a particular tracer. Chiro (March 68) has pointed out that specific tropism exists towards certain lesions, the classical case being radioiodine for thyroid metastases.

131 HSA for metastases
197 and 203 Hg Chlormerodrin for Gliomas
131 I Antifibrinogen for sarcomatous lesion
labelled albumin tracers AV malformation

Multiple tracer study is justified where strong clinical or neuroradiological evidence exists of a SOL. For routine scans 99mTc is the best. Where a scan is equivocal, it must be repeated with a different agent.

INSTRUMENTATION

There are numerous types of instruments available for scintillation scanning. A single crystal (5 inch) Na I thallium activated detector scanner was used here. Multiple detector scanners make it possible for more than one view to be done at the same time. Position emitters 18F and 68 Ga have been used with special position cameras and dual crystal moving detector scanners – the advantage here being ability to localise the lesion more precisely. The gamma camera has a useful speed advantage over the typical scanner for equivalent quality results. Also the camera for dynamic studies is unrivalled.

ORDER OF INVESTIGATION

The majority of patients referred for brain scans have suspected neoplasms, abscess or cerebrovascular accidents. Routine neurological work is needed in all such cases, and skull X-ray, EEG and LP are needed. However, arteriography and PEG and ventriculography are best done after the scan, one reason for this being they are formidable investigations and may not be needed once the scan is done. Recently, there have been several reports of false positive isotopic

brain scans following arteriography. However, Heinz and his colleagues (Nov. 66) showed that carefully performed angiograms do not produce abnormalities in the brain scan. Scans and angiography define two quite different parameters of brain. The angiogram defines with high spatial resolution and rapidity of flow of opacified blood. The scan is a low resolution map of the blood brain barrier.

METHODS AND MATERIALS

Over the past year, a number of brain scans were done, using a Scintimat scanner with a 5" crystal and a coarse 55-hole collimator. Initially, a fine 163-hole collimator was used; however later, the coarse collimator was found to be more effective. The reduced resolution was more than compensated by the increased count rate obtained. With Technetium – 99m, the patient had 200 mgm of Potassium Perchlorate about ½ hour before the scan to reduce Choroid plexus activity. Where RISA was used, the scans were done shortly after injection to outline the vascular anamolies and repeated in 24-48 hours to show localisation. Iodides were administered 7 days before and after RISA to reduce thyroidal uptake of free 1311. The patient was made comfortable in a recumbent posture on a special scan trolley. Reference was made to the nasion, inion and external auditory meatus. The brain scans were started about 15 minutes after injection, in the case of 99mTc. Usually both laterals and anterior view were obtained. The posterior view was done only in special cases. Special views such as the vertex view (Overton 1965) and the 'angled posterior' view (Witcofski and Roper 1965) were reserved for difficult cases.

A count rate of 10,000 to 30,000 counts/minute were obtained, and the scanning speed varied between 42 to 90 cm/minute. The colour calibration was adjusted so that the range of activity from the superior saggital sinus to the normal brain covered its full range. A line spacing of 2 mm was routine. All the scans were interpreted after the patient's clinical presentation was studied to appraise the problem at hand. They were classed as positive, negative or equivocal. Increased activity should be in 3 consecutive lines for a scan to be classed positive (McAfee and Taxdal 1961).

Results And Discussion

Total number done	44
Positive	14
Negative	28
Equivocal	2

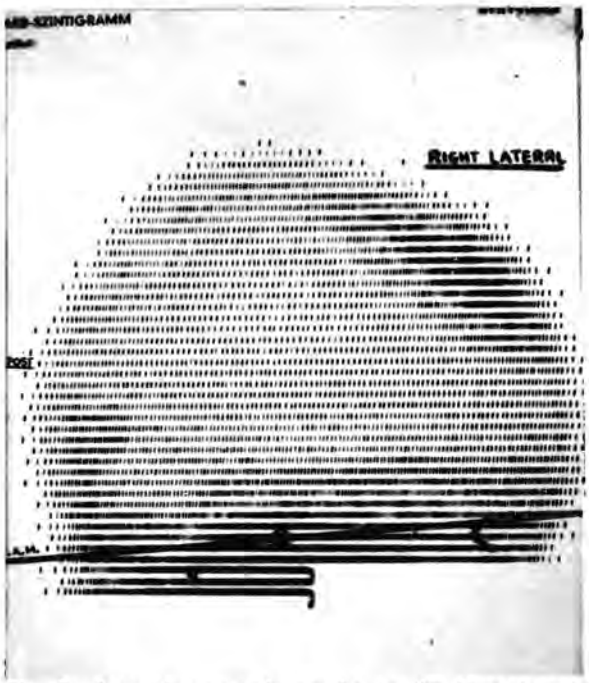

Fig. 3: Area of crescentic uptake in the frontal area. Metastatic deposit from a carcinoma of uterus.

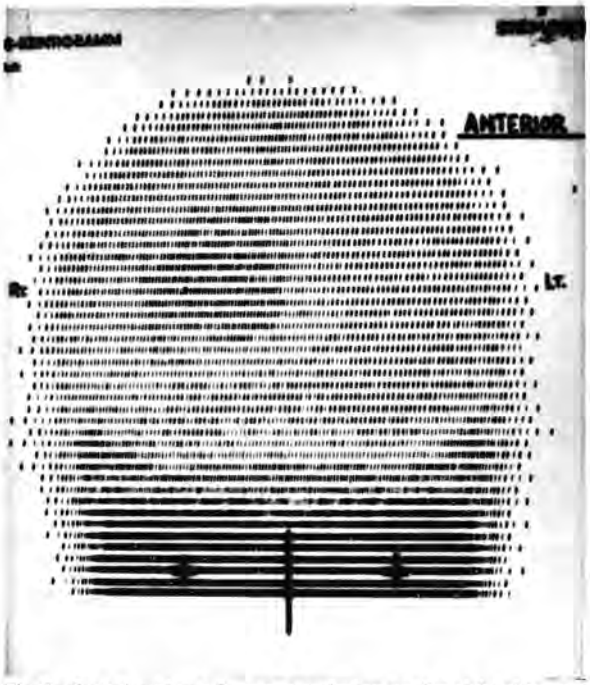

Fig 4: Anterior view of same scan lesion on the right side and solitary.

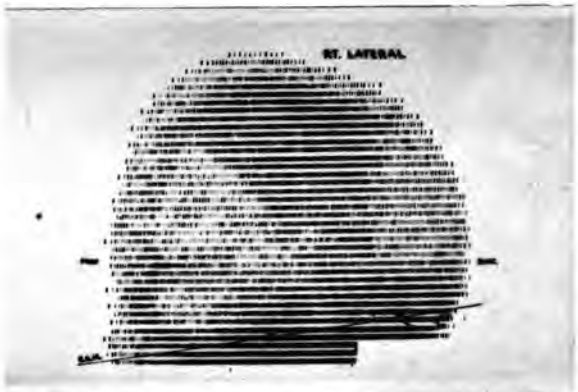

Fig. 5: Positive scan in A/V malformation. Lateral view angiogram confirmed diagnosis.

Fig. 6: Anterior view of AV malformation.

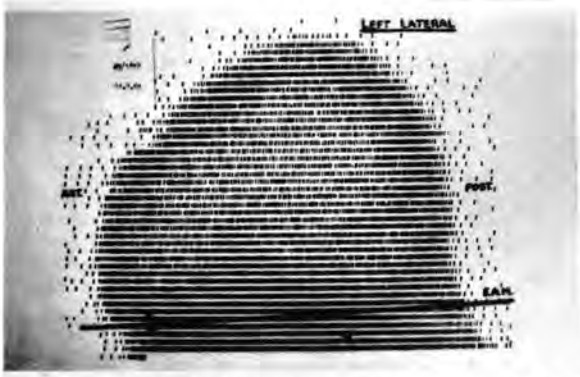

Fig. 7: Scan in craniopharyngioma area of uptake seen in the sellar region. Air studies showed obliteration of the third ventricle.

Equivocal scans are those with assymmetry between the right and left sides in the anterior, posterior and lateral views. Assymmetry was most common in the posterior fossa and around the superior saggital sinus.

Diagnosis in positive scans	
Meningioma	2
Metastases	3
Glioblasoma	1
TB Meningitis	1
A/V malformation	2
Pinealoma	1
Craniopharyngioma	1
Ependymoma	1
Cystic astrocytoma	1
Pituitary tumour	1

Lesions not detected by the scan	
Midline cerebral tumour	1
Pontine Glioma	2
Pituitary tumour	1
Cerebellar sarcoma	1
Intraventricular tumour	1
Diagnosis not known	4

Initially, when scanning was attempted, they were often negative, even in the presence of known lesions. A number of factors are responsible for these false negative scans.

1. **Low count rate:-** Low dose or poor absorption when given orally are important factors. There has been a lot of stress to optimisation of technetium brain scan. Immediately after 99mTc injection, the count rates rise to a maxi in 16 secs., after which they fall to a plateau which lasts for about 8 minutes before declining to reach half its value in 2½ hours time. Too early scanning would miss some lesions (Levy L.M.et al 1966). Early scanning is needed in some cases to detect AV malformations. Delay of ½ hour is optimum as at this stage the tumour/brain ratio is higher and the blood/brain ratio has fallen sufficiently. On delaying the scan too long after injection, the count rates may fall too low to make a good scan – this was common with our earlier cases.
2. **A benign lesion** - Where blood supply and metabolism are of the same degree as normal brain
3. **A small lesion** - This was the case in tumours which are situated in critical locations – for example, a patient with a pinealoma had a scan which was equivocal. However, the air study was conclusive.
   Lesions less than 2 cms may be missed.

4. **An unfavourable site** - Where such a lesion is distant from the scanner, as in deep lesions near the midline or close to areas of high activity such as venous sinuses or the base of the skull. Posterior scans are difficult to interpret for the same reason because of high activity in the nuchal muscles and venous sinuses.
5. **Symmetry** - Bilateral lesions near the surface which are symmetrical may be missed with moderate increases in activity.

The pathology of the lesion cannot be got from the scan unless serial scans are done with long lived isotopes (Planiol 1963). There are, however, clues as to the nature of the lesion from scan appearances.

(a) The relationship to the falx, tentorium, corpus callosum, and the convexity of the dura was stressed by Bull et al (1965). The glioma usually crosses the midline in the region of the corpus callosum while a falx meningloma crossed anterior, posterior or superior to it.

(b) There were three cases which gave a crescentic pattern of activity. One was a glioblastoma multiforme, and the remaining two were metastases. Such patterns are also seen in several other conditions (Heiser, Quinn, and Mollihan, 1966), and includes granular pachymeningitis, Paget's disease of the skull, extracranial haematoma, meningioma en plaque, and subdural haematoma. Metastases in the dura show a localised area of high activity in the lateral scan but subdural haematomas seldom show much increase except in the region of the sylvian fissure.

(c) There were two patients whose history and findings suggested a cerebrovascular accident. One patient had a complete occlusion of the middle cerebral artery as in the angiogram. However, the brain scan was negative in both. Where positive, the scan would show uptake with the shape of a horn rising in the temporal region and curving upwards and backwards, where the middle cerebral or the ant cerebral is occluded. The scan is positive in about 83% of patients in a CVA involving the hemisphere (Williams, 1966). It becomes faintly positive after 3 to 6 days, reaches a peak in 10-14 days and returns to normal after 40-80 days. The intensity of uptake was proportional to the degree of severity of the CVA as assessed clinically. The primary diagnostic use of brain scanning in cerebral infarction is to distinguish it from a neoplasm. A clear positive scan in the first few days after an episode (stroke) makes neoplasm the likely diagnosis. One of our cases had such a positive brain scan after an episode of hemiplegia of sudden onset. Here the diagnosis was cerebral metas-

Fig. 8: Positive scan in pituitary tumour. Interpretation can be difficult because of cavernous sinus activity.

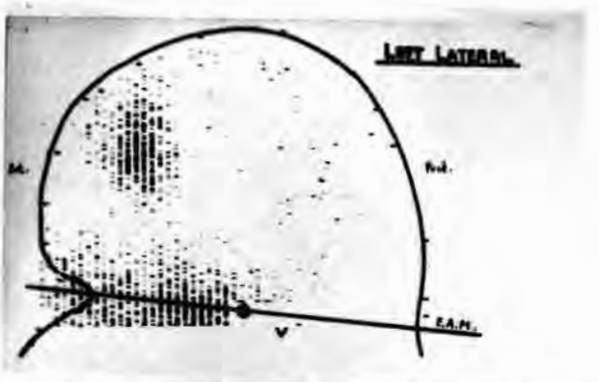

Fig. 9: Risa scan in case of cerebral metastases from a bronchogenic carcinoma. Risa is suitable in showing up metastases.

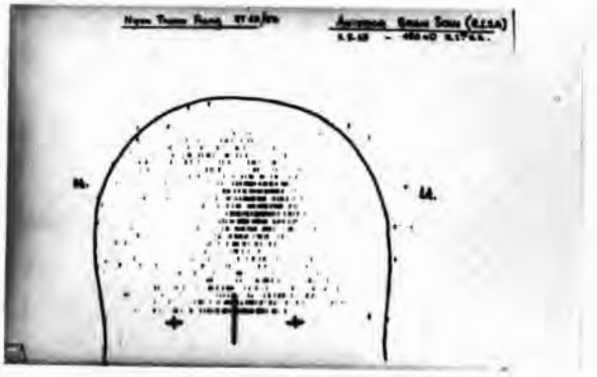

Fig. 10: Anterior view same patient. Lesion on the left but some increased uptake on the right side as well.

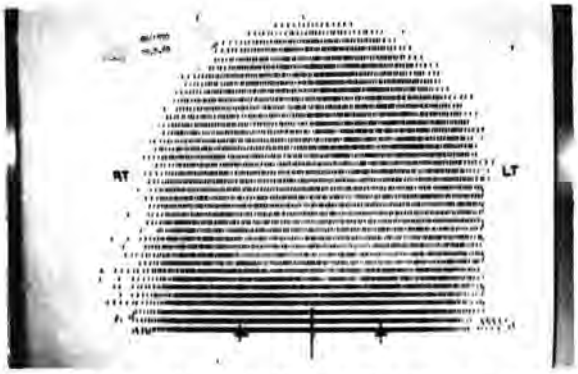

Fig. 11: 36-year-old female Malay with history of fever for 2 weeks, headache and a right hemiplegia. Scan showed uptake in the left posterior frontal area. Angiograms and air studies negative. CSF showed AFB. Cerebritis and ependymitis could give positive uptake in the absence of a SOL.

tases from a carcinoma of the breast.

(d) In the patients with positive scans who had meningioma at operation, the scan showed high activity over the lesion. The degree of uptake correlates well with the vascularity or activity of the lesions. Where the count rates over the lesion is equal to or higher than that over the Superior Saggital Sinus, the lesion was almost always a malignant tumour, a meningioma or an abscess (Forster 1969).

(e) The brain scan image correlates well with the pathology as shown by Bierwaltes (Jan. 66). Apart from the degree of uptake, which was highest for glioblastomas and meningiomas, followed by metastatic carcinoma, meningiomas show sharply demarcated, round concentrations on scanning with characteristic location parasaggital, parasylvian, sphenoid ridge and olfactory groove regions. Astrocytomas usually are small and round with locations in the posterior fossa, in many cases. Glioblastomas were large and irregular with high uptake ratios, whereas metastatic carcinomas were characteristically small and round, often situated in the occipital, posterior parietal, and posterior temporal region, being the commonest cause of more than one positive image in the scan.

Many of the patients have had operations often burr holes for ventriculograms or shunts for relief of hydrocephalous. In all cases, there was increased localisation of isotope in the craniotomy site, for at least 4 weeks. The intensity of localised activity decreased as the postoperative period increased. The localised activity in the operations site is due to the replaced bone rather than the soft tissue, after 4 weeks. In spite of this, scanning is useful after craniotomy 2 to 3 months later to localise a recurrent tumour, a second primary tumour, or possible second metastatic tumour.

Wilkins (August 1967) showed that superficial retention is common in postoperative scans but deep retention was not seen unless there was tumour recurrence. Many patients have had radiotherapy in this series. The scan is not positive after radiotherapy unless there is persistent tumour. The brain scan helps not only in localising the tumour but also following the status after radiotherapy. Where the tumour is located over a less critical area (for example in the frontal lobe) higher doses of radiotherapy could be given; the localisation obtained permits more exact portal placement and intensive treatment could be given without compromising essential cerebral function. In posterior fossa lesions, pituitary and brain stem lesions, and tumours at the base of the brain, the scan is unsatisfactory for this purpose. However, it is of value in localisation and follow-up of glioblastomas and cerebral astrocytomas, (which form 75% of cases of cerebral tumours requiring radiotherapy).

Comparison with other diagnostic procedures.

It is difficult to give any definite figure for merits of scintillation scanning in comparison with other neurological investigations. The LP, Skull X-ray and the EEG are a must in all cases subjected to a scan. The EEG may detect up to 70% of meningiomas and 85% of glioblastomas whereas scintillation scanning detects about 96% of meningiomas and glioblastomas. Obviously in diffuse brain disorders, the EEG is superior. As a screening test, it is best to combine all three and scintillation scanning. The angiogram, and air studies, however, are procedures with a definite mortality and morbidity and could be reserved much later, to provide more information. Besides its role as a screening procedure, the scan may reveal a lesion too small to provide the vascular distortion needed to produce a positive angiogram (Sweet et al).

One of our cases, a 36-year-old female, had a positive brain scan. She had a history of fever and headaches and weakness of the right limbs for about 2 weeks prior to this. The scan showed uptake in the left posterior frontal region. The CSF changes were suspicious of tuberculosis. The angiograms and air studies were, however, negative for a localised space-occupying lesion. It is possible here that there may be a localised process in this area such as a tuberculoma which only the brain scan revealed. However, the diagnosis is unconfirmed.

This second role of scintillation scanning as a more

definitive neurological investigation is bound to increase in importance with further improvements in scan agents, instrumentation and better understanding of the pathophysiology and underlying basis for uptake of radioactive agents by tumours.

SUMMARY

1. The procedure involved in radioisotope scanning is explained, with relative merits of different types of scan agents and instrumentation available.
2. An analysis of experiences with brain scanning at the General Hospital, Kuala Lumpur, is recounted.
3. Pitfalls of scan interpretation, and possibilities for more exact scan diagnosis is explained.
4. Role of scintillation scanning in postoperative evaluation and radiotherapy is discussed.
5. Lastly, the role of scanning as a screening procedure and in relation to other neuro-diagnostic procedures is evaluated.

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