ESSENTIALS OF NUCLEAR MEDICINE

M.V. Merrick,

ESSENTIALS OF NUCLEAR MEDICINE

M.V. Merrick,
MA, BM BCh, MSc, DMRD, FRCR
Consultant and Head of Department of Nuclear Medicine,
Western General Hospital, Edinburgh;
Part-time Senior Lecturer, University of Edinburgh, UK

Churchill Livingstone
EDINBURGH LONDON MELBOURNE AND NEW YORK 1984

PREFACE

Nuclear medicine has been defined as 'the medical specialty that utilises the nuclear properties of radioactive and stable nucleides to make diagnostic evaluations of the anatomical or physiological conditions of the body, and to provide therapy with unsealed radioactive sources' (Board of Trustees of the Society of Nuclear Medicine, 1983). This book deals with in vivo diagnostic applications of radioactive nucleides, by far the major clinical part of nuclear medicine, impinging on almost every branch of medical practice.

The great strength of nuclear medicine is its ability to measure function noninvasively. However, its weakness is the relatively poor anatomical detail it provides, compared with radiology or ultrasound, and when only anatomical information is required these latter techniques usually give better information. Inferences about function made from anatomical appearances are often misleading—function and structure are of course related, but indirectly. For example, a dilated renal pelvis is not always obstructed, nor is a small heart necessarily a healthy one. Nuclear medicine has been developed to provide the techniques needed to measure, rather than guess, function. However, if reliable clinical results are to be obtained it is necessary to understand the basis of the methods, and their limitations.

In many situations imaging the distribution of the administered radioactivity provides as much information as is necessary for the care of the patient. Correct interpretation nevertheless requires an understanding

of the physiological or biochemical processes responsible for producing the image. Frequently the value or reliability of the information can be increased significantly if a measurement is made of the amount of radioactivity which has been taken up, the rate at which uptake occurs or the rate of discharge. In some cases measurements can be made without imaging.

Imaging and measurement are thus integral interdependent components of the whole, and nuclear medicine cannot be applied properly if they are regarded as mutually exclusive, or one is regarded as ancillary to the other.

In many places nuclear medicine is practised not by full-time specialists but by diagnostic radiologists or physicians who, by virtue of their training, tend to place greater emphasis on one or other of these aspects. The objectives of this volume are to provide radiologists, physicians and others who utilise these techniques with information about the tests which are available, how to perform them and how to interpret the results. Less commonly performed investigations are covered more briefly than those requested more often. Techniques are described concisely, as there is usually more than one way of performing any particular investigation, depending on the available facilities. The objective has been to provide the reader with an understanding of what can or cannot be achieved, and to indicate as a starting point a method which the author has found satisfactory in his experience. Provided that the principles are understood the method can be adapted to local or particular circumstances.

There are many excellent textbooks of physics applied to medicine, physiology and biochemistry, and it will be assumed that the reader is familiar with the relevant aspects of the basic sciences. Where appropriate, attention is drawn to particular points of detail particularly relevant to the subject under discussion.

Used properly, nuclear medicine can provide benefits vastly greater than the minute dangers associated with the very small doses of radiation involved in the majority of tests.

Edinburgh, 1984 M.V.M.

CONTENTS

Chapter One

THE BRAIN AND CENTRAL NERVOUS SYSTEM

CEREBRAL SCINTIGRAPHY

Radiopharmaceuticals

Pertechnetate

Pertechnetate is the most widely used for cerebral scintigraphy. Following intravenous injection about half the administered activity equilibrates with the extravascular, extracellular space, with a half-time of 15 minutes. By 1 hour one third of the pertechnetate left in the blood is associated, rather weakly, with the red cells and the rest principally with albumin. About half the administered activity is excreted within 2 days, equally divided between urine and faeces.

The pertechnetate ion is of similar ionic radius to the iodide ion, and both are bound by the same tissues, namely thyroid, salivary glands, gastric mucosa and

Table 1.1 Absorbed dose from ^{99m}Tc pertechnetate. These figures assume the thyroid has not been blocked. The effect of thyroid blocking agents on absorbed dose has not been published.

	Resting		Non-resting	
	mrad/μCi	μGy/MBq	mrad/μCi	μGy/MBq
Bladder wall	0.053	14	0.085	24
Stomach	0.24	68	0.05	14
Upper larger intestine	0.07	19	0.12	32
Lower large intestine	0.06	18	0.11	30
Ovaries	0.02	6	0.03	8
Red marrow	0.02	6	0.02	6
Testes	0.009	2	0.009	2
Thyroid	0.13	35	0.13	35
Whole body	0.014	4	0.011	3

choroid plexus. Unlike iodide, pertechnetate is not organified, and is therefore exclusively a marker of iodide trapping. Agents which block uptake of iodide, e.g. perchlorate or sodium iodide solution, also block uptake of pertechnetate. Under these circumstances the distribution of pertechnetate most closely resembles that of extracellular water markers such as chloride.

Normal brain contains less extracellular water than most other tissues, or than most pathological processes such as tumours or infarcts that may occur intracranially. Thus once an injected tracer of extracellular fluid has had time to mix, a higher concentration will be found in any abnormal areas than in the normal brain.

Simple diffusion is not the only factor responsible for this distribution. The capillaries of normal brain differ in structure from those in most other tissues. One effect of this difference is that they are less permeable to water-soluble molecules. The capillaries in most abnormalities, and in particular newly formed capillaries around inflammatory or in neoplastic tissue, are more permeable to water-soluble markers than are the normal brain capillaries, allowing diffusion into the extracellular space (which is itself larger than in normal brain) to occur more rapidly. Transfer of molecules across the capillary wall is further accelerated by pinocytosis, a process which is reduced or absent in normal brain capillaries. There is therefore both a more rapid transfer between intravascular and extravascular extracellular water in the abnormal areas than in normal brain and also a larger extracellular fluid volume in the abnormalities.

Thyroid blocking agents should be administered routinely before cerebral scintigraphy with pertechnetate. Although it is sometimes recommended that 200 mg of potassium perchlorate should be given orally 1–2 hours before administration of the pertechnetate, in practice the administration of perchlorate outside the department performing the investigation is erratic. Perchlorate discharges bound pertechnetate from the thyroid, and other tissues to which it is bound, within minutes. It is usually more reliable, and therefore preferable, to administer the perchlorate when the patient attends for scintigraphy. In patients unable to take tablets, 200 mg sodium perchlorate

dissolved in 10 ml water may be administered intravenously at the time of administration of the pertechnetate. Potassium perchlorate cannot be given intravenously because it is poorly soluble, and because of the danger of administering potassium salts intravenously.

Perchlorate also inhibits albumin binding of pertechnetate, and hence accelerates the rate of blood clearance. It is thus helpful in three ways: in preventing visualisation of the choroid plexus; in reducing the absorbed radiation dose to the thyroid and other organs; and in reducing the blood background. The importance of the alteration of absorbed radiation dose to the thyroid is questionable, as this is achieved at the cost of increased absorbed dose to other organs such as the colon which are no less radiosensitive.

Atropine and related drugs, e.g. propantheline, cause vasoconstriction of the mucosa of the mouth, sinuses and musculature. This reduction in blood flow to extracerebral structures gives some improvement in cerebral scintigraphy. The advantages must be balanced against the danger of precipitating glaucoma or urinary retention with these drugs.

Other non-specific agents

Any freely diffusible water soluble tracer may be used, and many have been tried. The only ones worthy of further consideration are ^{99m}Tc DTPA and ^{99m}Tc glucoheptonate.

^{99m}Tc DTPA has the advantage that perchlorate is unnecessary, as the chelated reduced technetium is not bound by iodide trapping tissues. Comparisons of clinical utility with pertechnetate have shown at best a marginal advantage for Tc DTPA in terms of lesion pick-up rate. This is to some extent offset by the much more rapid excretion of Tc DTPA which leads to a very low count rate if imaging is delayed for more than one hour after administration. Particularly in busy departments, such delays are difficult to avoid.

^{99m}Tc glucoheptonate, another agent introduced originally for renal studies, has been shown to have a higher pick-up rate for brain tumours than has pertechnetate. It does not have any advantage when detecting infarcts. The difference is evident only when

imaging is performed more than three hours after injection. In most centres computed transmission tomography is the investigative modality of choice for the detection of intracerebral tumours, whilst scintigraphy is the primary modality when infarction is suspected. The routine use of ^{99m}Tc glucoheptonate is thus justified only if computed transmission tomography is not locally available. It has been suggested that uptake of ^{99m}Tc glucoheptonate is increased by metabolism of the glucoheptonate moiety within the tumour, leaving free reduced technetium which becomes bound locally. The evidence for this is incomplete.

Gallium, given as ^{67}Ga citrate, is taken up by many tumours and many inflammatory lesions. It does have a high uptake in many intracranial tumours, but the cost, the low count rate and the high absorbed radiation dose all render it unsuitable for routine use in cerebral scintigraphy. It is rarely necessary to resort to this radiopharmaceutical for the detection of intracranial tumours.

Technique

The examination is in two parts, a dynamic or flow study which follows the first transit through the cerebral circulation of an intravenously injected bolus, and a subsequent series of static views to demonstrate the distribution of the tracer at equilibrium.

The dynamic study

The patient is positioned in front of a gamma camera with on-line data acquisition facilities. The camera must be fitted with a high sensitivity collimator. If there is good clinical evidence of a solitary lesion placed either anteriorly or posteriorly, the appropriate projection should be chosen. Otherwise a vertex view, which gives the best visualisation of the greatest part of the cerebral cortex, is preferable. A lead collar not less than 2 mm thick and fitting closely around the neck is necessary to prevent scattered radiation from the neck and trunk reducing contrast and obscuring abnormalities of the cerebral circulation.

Data is collected at 4 frames per second, starting just before injection, until the superior sagittal sinus

is clearly filled, usually 5–15 seconds. If the data collection is not started until activity reaches the head the essential early arterial phase, which lasts for less than 2 seconds, will be missed.

There are few counts in each frame of the study. The image quality is correspondingly poor. The visualisation of abnormalities is improved if sets of frames are summed. The optimum timing can be found by initially plotting graphically the total count rate in each frame against time (Fig. 1.1). On this graph the time of arrival of the bolus at the head can easily be identified. The peak of the curve occurs late in the venous phase, when most of the activity is in the superior sagittal sinus.

If the number of frames occurring between arrival and the peak is counted, these can be regrouped into 4 longer frames, the count content and image quality of which is therefore greatly improved compared to the original very short frames. In timing, these frames should correspond approximately to the angiographic phases referred to as arterial, early capillary, late capillary/early venous and late venous. The typical optimum frame length is 1.5 seconds with a range of between 0.5 and 2.5 seconds. Neither the arm to head circulation time nor the cerebral transit time can be predicted with sufficient accuracy in an individual patient.

It is for this reason that recording should be started at or before the time of injection and continued until after the venous phase. If only the short frames are viewed there is a danger that less gross inequalities of circulation will be missed. Because of the poor statis-

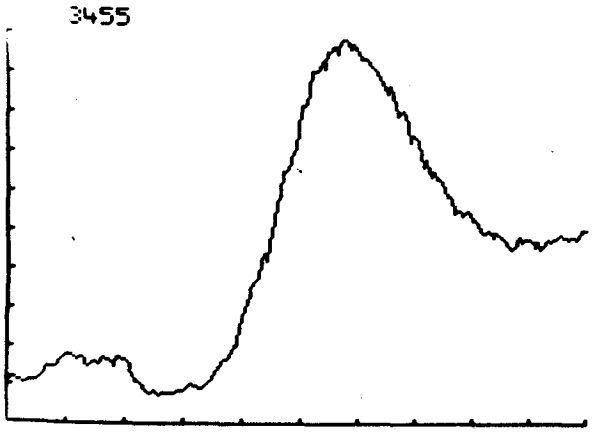

Fig. 1.1 First pass of activity through the brain. The highest count rate occurs late on in the venous phase.

tical content it is always preferable to smooth these frames. A fairly coarse (32 × 32) acquisition matrix is preferable to a finer one giving fewer counts per matrix point and therefore a higher noise content.

An activity of between 600–750 mBq (15–20 mCi) of pertechnetate in a volume not exceeding 2 ml is given as a rapid intravenous bolus into a large vein as centrally as possible. The median or basilic vein in the antecubital fossa is to be preferred, having the most direct route to the superior vena cava. The bolus must be flushed into the right atrium with 10–20 ml of normal saline or 5% dextrose injected immediately after the radioactivity and as rapidly as possible. In young subjects and older ones with a fast peripheral circulation this makes only a marginal difference. However many older subjects have a relatively sluggish peripheral venous circulation. The intravenous bolus is diluted into a large volume which reaches the right atrium over a relatively long period unless flushed in as described.

The technique of injection affects the time taken for the bolus to reach the right atrium but cannot influence its subsequent fate. However if arrival in the right atrium is extended over several seconds the quality of the bolus reaching the head is greatly degraded.

A number of techniques of bolus injection have been described. One simple method is to attach the syringe containing the radioactivity to one inlet of a 3-way tap and a syringe of saline to the second. A needle of 21G or larger is attached firmly to the outlet. Some practice is required to become dextrous, but with experience it is possible to turn the tap from one inlet to the other very rapidly. In this way the pertechnetate is injected and flushed immediately with a bolus of normal saline. The resistance to flow through a tube varies with the square of the length and the fourth power of the radius. Much greater force is thus required to give a rapid bolus through a fine needle than through one of larger diameter.

An alternative technique is to attach a tube, of volume large enough to contain the pertechnetate bolus, between the saline-filled syringe and the needle. The 3-way tap is used to fill the tubing with radioactivity and this plus the saline are then flushed into the vein together. In practice either technique is

acceptable in experienced hands, and choice is purely a matter of individual preference.

An added advantage of either of these bolus injection techniques is that handling of the radioactive syringe is minimised, thereby reducing the radiation dose to the operator.

Another technique often described is to administer the injection before the tourniquet has been removed. In practice this commonly results in an extravasation. This technique is therefore to be discouraged.

A poor bolus injection results in the separate phases merging into a single indistinct and indeterminate blur.

Equilibrium views

When either pertechnetate or glucoheptonate is used these should be obtained not less than one hour and at any time up to 4 hours after injection. When using ^{99m}Tc DTPA, imaging may start after 30 minutes. A longer interval is associated with a low count rate. With all the agents the pick-up rate increases as the interval lengthens. However the difference between pick-up rates at one hour and at any subsequent time is fairly small.

A minimum of four projections must be obtained — anterior, posterior and both laterals. A vertex view is useful to confirm or refute the suggestion of a lesion near the midline, whilst obliques are occasionally helpful to confirm that an apparent abnormality is superficial.

In the anterior projection the patient is positioned with the orbitomeatal line at a right angle to the face of the collimator. The posterior projection requires the head to be flexed as far as possible consistent with contact with the collimator in order to display the posterior fossa. When positioning the patient for the lateral projections care must be taken to include all of the posterior fossa. If acquisition is set for a preset number of counts, the face should be excluded. However if a pre-set time is used this precaution is unnecessary.

When collecting analogue images at least 400 000 counts must be collected in each projection, excluding those coming from the face. It is rarely possible to obtain this number of counts in an acceptable time

when a high resolution collimator is used. If imaging times exceed 3 minutes per view the additional statistics are commonly vitiated by movement, even with fit and cooperative patients. Using digital images which can be smoothed and displayed at optimal contrast, a smaller number of counts is adequate. Images should therefore be collected for a fixed time of 3 minutes.

It has been demonstrated using a rectilinear scanner, without data processing, that a lower resolution focused collimator can detect smaller lesions than a higher resolution collimator of lower sensitivity when imaging times are equal, because the greater statistical noise can conceal lesions in the high-resolution image. There is surprisingly little good information on the effect of data processing on lesion perceptibility. It is clear that the difference between a high count density image obtained with a low resolution collimator and an image containing fewer counts obtained with a high resolution collimator and subsequently smoothed, is small. A very large series would be necessary to demonstrate conclusively which is better.

Normal appearances

A normal 4-frame dynamic study in the vertex projection is shown in Figure 1.2, and the series of shorter duration frames from which it is built up in Figure

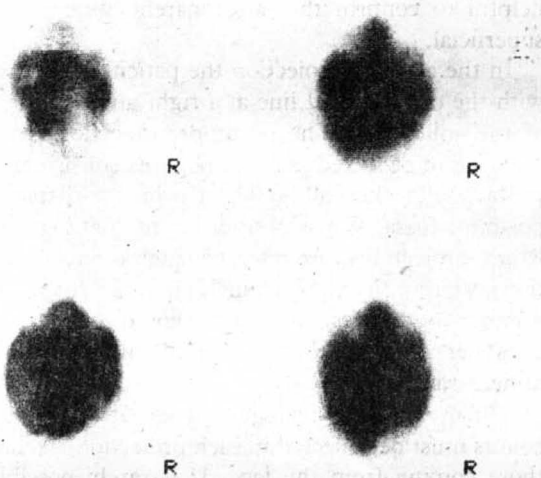

Fig. 1.2 Normal dynamic study 4 consecutive frames, each of 1.5 s.

Fig. 1.3 0.25 s frames from which Fig. 1.2 is built up. Detail is difficult to see because of the poor statistics.

1.3. In effect only the region supplied by the branches of the middle cerebral arteries can be examined. The regions supplied by the anterior cerebral arteries are too close to the midline and to each other to be resolved at the available count rates, whilst the territories of the posterior cerebral arteries are partially obscured by activity in the neck and trunk. The individual territories of the vessels supplying the cerebellum and brain stem are too small to be resolved. Nevertheless this technique is clinically useful because clinical doubt occurs most commonly in lesions in the middle cerebral artery territory.

The initial or arterial frame should show symmetrical activity in the 2 hemispheres. If the patient has been positioned obliquely a higher count rate will be observed from the hemisphere closer to the camera. However, accuracy of positioning can be judged only on the venous frames from the position and shape of the superior sagittal sinus.

Symmetry about the sagittal plane should be maintained throughout the study. The superior sagittal sinus starts to fill in the second or capillary frame, the anterior part filling first. The sinus should be clearly

visible as a straight line in the third or early venous frame, and should stand out clearly against a low background in the final late venous frame.

Apparent curvature or asymmetry of the superior sagittal sinus indicates obliquity of positioning. Any apparent asymmetry of flow must be interpreted with great caution in these cases.

A normal 4-projection equilibrium study is shown in Figure 1.4. This study was obtained with pertechnetate and perchlorate, but the appearance with any other agent is similar. Note that in the anterior projection the orbits are identified, whilst in the posterior view the sigmoid sinus may be symmetrical or asymmetrical. Unilateral hypoplasia or absence of one sigmoid sinus is a common variant of no pathological significance. If the head is well flexed the posterior fossa is seen below the sigmoid sinuses. If the patient cannot flex the head adequately, the posterior fossa is visualised only in the lateral projections.

The vertex projection is not obtained as a routine, but is useful in selected cases. It is preferable that the neck of the patient is extended as far as possible, and a lead collar employed to shield the camera from activity in the trunk, as in the dynamic study. If the projection is obtained by looking directly down onto the unextended head, scattered radiation from the trunk greatly degrades the quality of the image, reducing contrast and thus concealing lesions.

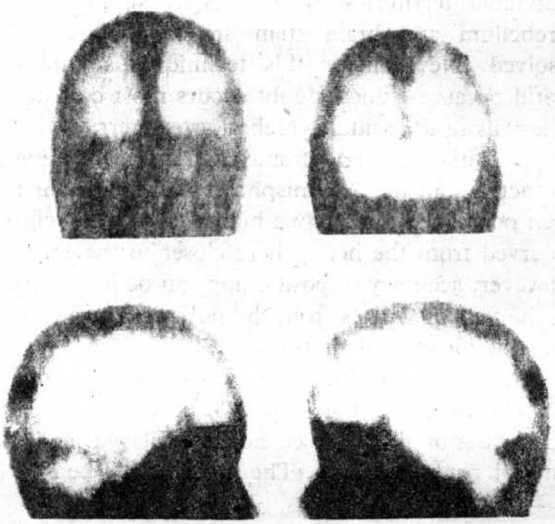

Fig. 1.4 Normal 4-projection brain scintigram, posterior, anterior, right lateral and left lateral.

The abnormal dynamic study

Asymmetry present from the very start of the dynamic study is abnormal. Any asymmetry which does not persist for at least 2 seconds should be disregarded as it may be due to random statistical noise. Asymmetry visible only in the later venous frames is likely to be due to variations in venous anatomy rather than arterial pathology.

It is often not possible to determine from the dynamic study whether the abnormality consists of decreased flow on one side or increased flow on the other. Lateralisation can be obtained either from clinical examination, clinical history or by examination of the later equilibrium views.

Typically an infarct presents with reduced flow. However, acutely, and for the first few weeks, the inflammation and hyperaemia around an infarct may give the appearance of greater flow on the side of the lesion rather than reduced flow. On follow-up increased flow, otherwise called 'luxury perfusion', resolves leaving reduced flow on the affected side. This remains permanently. It may, however, be concealed if infarcts subsequently occur on the contralateral side. This method can demonstrate only relative flow (Fig. 1.5). Thus bilateral abnormalities are not detected.

Highly vascular tumours and arteriovenous malformations may be identified by the presence of early filling of the veins. In these cases the superior sagittal sinus is visualised simultaneously with the earliest

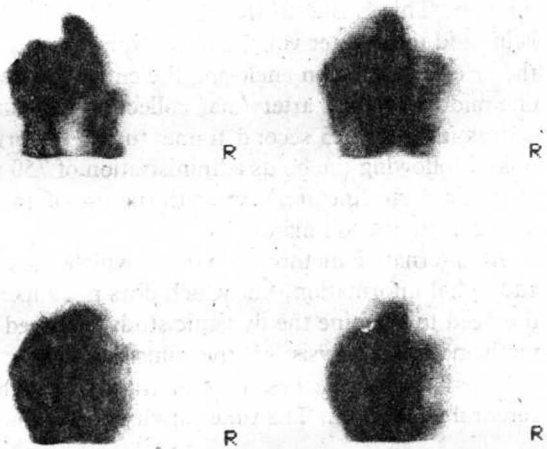

Fig. 1.5 Abnormal dynamic study. Note marked asymmetry of flow.

arterial frame. It is not possible to distinguish between the various types of hypervascular pathology on the basis of radionucleide angiography alone. This is nevertheless a good screening test, especially in patients with minimal physical signs, equivocal or non-specific histories and a relatively low index of suspicion.

The rapidity of flow may be assessed by referring back to the original rapid frames from which the 4-frame study has been built up. Venous filling may be visible as early as a quarter of a second after the first arrival of activity at the head. Indeed, if the delay before the veins are filled is greater than half a second an arteriovenous malformation is unlikely to be present.

Non-filling of the superior sagittal sinus is abnormal. It is rare, but when seen is diagnostic of a superior sagittal sinus thrombosis. With all types of data processing facility it is possible to draw regions of interest, e.g. corresponding to the territories of the middle cerebral arteries on the two sides and the superior sagittal sinus. It is not possible to define the areas of supply of other major arteries either because of overlap or because of the proximity of the two sides. Slight asymmetry of positioning, or an anatomical asymmetry, either of which is readily recognised on the images, will totally invalidate analyses based upon curve symmetry. The curves themselves are always dominated by the count rate in the late venous phase, which is much higher than that found in the arterial phase, even in the presence of massive unilateral infarction. This is due to the slower flow through the veins and the greater volume of blood in them than in the arteries. A region enclosing the entire territory of one middle cerebral artery may collect only about 100 counts in each 0.25 second frame during the arterial phase, following the bolus administration of 750 mBq of ^{99m}Tc pertechnetate, even with the use of an extra high sensitivity collimator.

An alternative method of analysis which does yield additional information, but which does not supersede the need to examine the dynamic study, is based on a mathematical analysis of the time activity curves obtained during the first pass of tracer through the cerebral circulation. The time activity curve obtained