NUCLEAR MEDICINE – RECENT PROGRESS AND POSSIBLE FUTURE ADVANCES

Bill Wall, Consultant Radiologist, Lancaster and Kendal Hospitals

INTRODUCTION

Nuclear medicine is sometimes seen as the Cinderella of the X-ray department. In terms of anatomical resolution it is easily surpassed by computed tomography (CT) or magnetic resonance (MR). It does, however, have a unique role to play in many areas by virtue of its ability to demonstrate disorders of function (pathophysiology) as well as anatomy. In this way it is frequently able to answer a specific question that cannot be given by other imaging techniques. This may, however, be a drawback. It requires the clinician to decide exactly what is wanted from a test, which may result in under-utilization.

The challenges for the nuclear medicine department are to ensure that it keeps up in a continuously evolving field, introduces new techniques that become available, and updates those tests already of proven value. Developments are taking place in equipment and in the field of radiopharmaceuticals. The major development in equipment has been the introduction of single photon emission computed tomography (SPECT). This uses a programmed, moving detection camera (Fig 1) which rotates around the patient (to produce tomograms) instead of a static camera. Information from the count rates detected is processed by a computer in a similar way to a CT scanner. Images are produced as a series of slices which may be cross-sectional or in different planes through the patient. This improves the quality of the image with better anatomical detail and contrast. The clinical application of a SPECT camera is described later in more detail. It is relevant to our service in Lancaster, especially in view of Phase III.

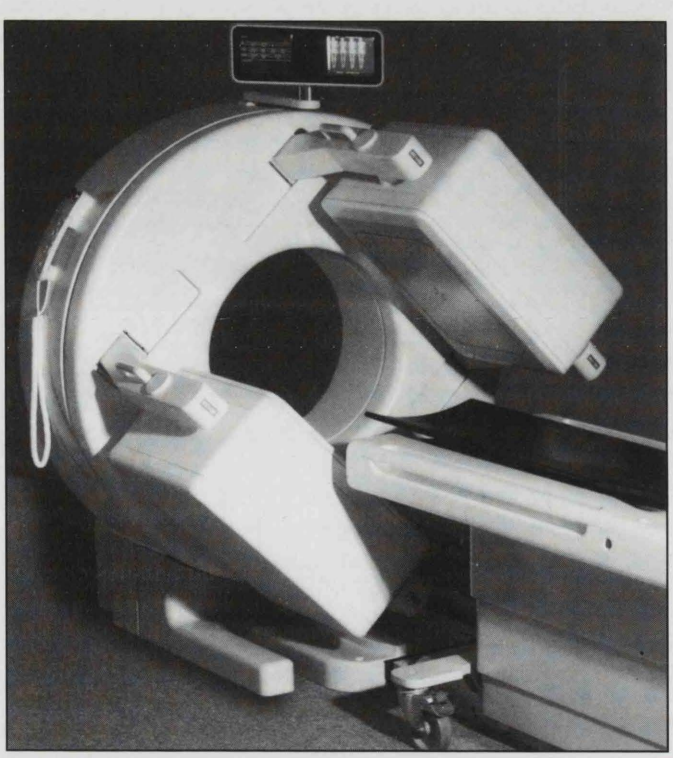

Figure 1

RECENT DEVELOPMENTS IN LANCASTER

The major recent developments in the department have been in cardiac work and in developing V/Q scans for pulmonary embolic disease.

1. Cardiac studies

Isotope left ventricular ejection fraction studies (LVEF) are now performed on the majority of patients after myocardial infarction. Large recent studies in the United States have shown that the decision to treat with ACE inhibitors should be based on the LVEF. Those with an LVEF of 35% or less benefit from treatment. We use an in-vivo red blood cell (RBC) labelling technique. An intravenous injection of stannous pyrophosphate is given at the start, followed 30 minutes later by i.v. ^{99m}Tc pertechnetate. The stannous pyrophosphate acts as a complexing agent making the ^{99m}Tc adhere to the red cells. Images are obtained from the left anterior oblique position to separate the two ventricles. ECG gated count rates and images are produced over a period of approximately 45 minutes with the aid of the computer. A region of interest is drawn around the left ventricle in systole and diastole. Irregular beats are rejected by the computer, background activity is subtracted and the LVEF is calculated by the formula $\text{LVEF} = \frac{\text{EDC - ESC}}{\text{EDC}}$ where EDC = end diastolic counts and ESC = end systolic counts. It is expressed as a percentage figure.

2. Pulmonary V/Q scans

Ideally we should have V/Q scanning available on a daily basis to investigate pulmonary embolic disease. A normal perfusion scan soon after onset of symptoms virtually excludes embolic disease. A classical positive scan will show multiple segmental, wedge-shaped perfusion defects in both lungs. These show a ventilation/perfusion mismatch, ie normal ventilation in the areas of absent perfusion. If the chest X-ray shows areas of consolidation, matched V/Q defects may be seen in these areas provided there is mismatching elsewhere. Patients with other forms of pulmonary pathology, whether visible on the chest X-ray (pneumonia, heart failure) or not visible (chronic airway disease) may have perfusion defects but these will all be matched by ventilation defects.

Not all cases are clear cut; several scoring systems exist to try to classify equivocal cases (Biello, PIOPED). We provide a daily 'perfusion only' service during the week. If the scan is normal, there is no need to proceed further but if it shows

defects a follow-up V/Q scan is performed the next Wednesday.

We use krypton gas for ventilation studies. ^{81m}Kr has many advantages and its very short half life of 13 seconds gives low dose. No special gas extraction equipment is required, and because the activity does not persist in the lungs a true ventilation image is obtained. Multiple views of the lungs can be taken. In addition, the imaging energy of 190 keV is suitable for the camera. The gas is eluted from a rubidium generator which we share with Royal Preston Hospital. It is prepared overnight in a cyclotron in Birmingham and sent up by train for use in Preston in the morning. It is then brought by road to Lancaster for the afternoon. Other options exist for ventilation scanning. Aerosols have the advantage of daily availability but give poor distribution to the periphery of the lungs. Xenon is difficult to use because of its long half life (^{133}Xe = 5.3 days) and low energy level. The high initial capital costs of some techniques make them expensive.

3. Infection

Another development has been scanning for infection, particularly of orthopaedic prostheses. Gallium (^{67}Ga citrate) is transported in blood bound to the iron-carrying protein transferrin. It concentrates in abscesses by direct leakage of plasma proteins through inflamed permeable capillaries, by concentration in lactoferrin in neutrophils and by direct concentration in bacteria. It has been largely superseded for abdominal work because of the delay in uptake (24-48 hours) and the fact that it is excreted by the kidneys and into the bowel which may obscure an abscess. It is still useful in hip or other limb infections.

FUTURE DEVELOPMENTS

1. A SPECT scanner

Future developments will depend on the facilities available, especially, as previously mentioned, SPECT scanning. This will open up new possibilities, particularly myocardial imaging of patients with ischaemic heart disease. This can be done using either thallium or ^{99m}Tc MIBI. Thallium (^{201}Tl) is a cycloton-produced isotope that is distributed in the body in a similar way to potassium. About 85% of thallium is extracted from the coronary arteries at first pass so myocardial uptake is proportional to the blood flow. The heart is stressed before injection of thallium either by physical exercise or by drugs (i.v. dipyridamole). Cardiac monitoring is important at this stage. Scans are done immediately, and further delayed scans at four hours. Infarcts are seen as persistent cold defects on both scans. Areas of ischaemia induced by stress but without infarction are seen as reversible defects – cold on the stress scan but filled in normally by redistribution of thallium on the delayed scan. Thallium does have disadvantages: the low energy of most of the emitted rays at 68-80 KeV is not ideal for the camera and the long half life of 72 hours results in higher patient radiation. Because of this, a technetium-based isonitrile radiopharmaceutical (^{99m}Tc MIBI) has been introduced which produces better quality images resulting in greater accuracy of results and lower dose. The stress and non-stress scans require separate injections with MIBI. A combination of SPECT with MIBI would produce significantly more accurate results than with the older planar scans (figures of 90% sensitivity and 5% specificity are quoted). They will never equal the precise information given by coronary angiography but are non-invasive and could have a very useful place in cardiac investigation.

Another possibility is cerebral imaging with SPECT. The 'old' brain scans were performed using a product that collected in areas where the blood-brain barrier had broken down and showed only large lesions (tumour, infarct etc) as hot foci.

Modern scans are performed using ^{99m}Tc HMPAO, a lipophilic agent that crosses the blood-brain barrier and binds in normal brain cells. There is approximately 80% extraction from cerebral blood at the first pass. Good images of the brain, particularly the cortex, can be obtained and uptake is proportional to blood flow. The technique is very useful for early detection of ischaemia, being more sensitive than CT, and in recent work has been shown to be useful in distinguishing different forms of dementia.

The tomographic facility of the SPECT scanner would have other uses, eg for precise localisation of a hot spot seen on a bone scan.

These are significant improvements and for all these reasons we ought to have a SPECT scanner in Phase III.

2. Labelled white cells

In addition to SPECT, another possible development would be the use of labelled white cells to improve identification of foci of infection. Blood is taken from the patient, the white cells are separated out and labelled with an isotope, usually indium (^{111}In) and re-injected to localise in foci of infection. This is a well proven technique but we do not have a radiopharmacy here and it would require close liaison between us and the pharmacy at Preston.

RADIATION DOSE AND COST

In the light of these advances and possible future developments it is worth considering briefly some radiation doses and costs. Radiation doses for studies using technetium are quite small and compare favourably with other radiological examinations. Use of gallium, radio-iodine or thallium involve higher dose. Care must be taken with products that concentrate in specific organs, eg iodine in the thryoid, technetium, iodine and gallium in breast milk. Table 1 below gives comparisons of effective dose equivalents for a range of investigations. For comparison, the normal background radiation is 2.5 mSv per annum, a chest

RADIONUCLIDE	ACTIVITY GIVEN MBq	EFFECTIVE DOSE EQUIVALENT mSv
^{99m}Tc Pertechnetate (for thyroid)	40	0.5
^{99m}Tc MAG 3 (renal study)	40	0.4
^{99m}Tc HAA (lung perfusion)	75	0.75
^{99m}Tc Pertechnetate (cardiac LVEF)	600	5.0
^{99m}Tc MIBI (myocaridal perfusion)	300	3.0
^{201}Tl (myocardial perfusion)	80	20.0
^{67}Ga	75	9.0
^{81m} Kr (ventilation lung scan)	—	0.1

Table 1 Effective dose equivalents of selected radionuclides

radiograph is 0.02 mSv and a CT scan of the abdomen is 8.0 mSv per annum.

Costs are quite reasonable for well-established examinations but are higher for recently-introduced radiopharmaceuticals.

^{99m}Tc Pertechnetate (thyroid scan)	£19.50
^{99m}Tc HDP (bone scan	£25.90
^{99m}Tc MAG 3 (renal scan)	£59.50
^{99m}Tc MAA (perfusion lung scan)	£26.40
201 Thallium (cardiac)	£50.00
67 Gallium (infection)	£80.00
^{99}Tc MIBI (myocardial)	£100 – £150

Table 2 The costs of some radiopharmaceuticals

These prices are for a single examination. Cost is often significantly less if several are done at the same session, eg a second bone scan costs £6.50 extra.

For ventilation lung scans we share the cost of the generator with Preston. Our share is £86 for one half day's use (4-6 patients).

The long term future for any imaging method is speculative. There are hopes for monoclonal antibody labelling to target malignant lesions but so far the technology has not been perfected. Whatever the future, the aim must be to detect pathology at the earliest possible stage whether foci of infection, early malignancy or vascular disease. Nuclear medicine is noninvasive and involves little discomfort to the patient. If, either by tagging an isotope to a specific cell or chemical it is possible to identify a lesion when it is still at the microscopic stage, or by detecting alteration in function it is possible to identify disease before morphological changes become apparent, then nuclear medicine will hold a key role in the future of medical imaging.

ANSWERS TO QUIZ ON PAGE 10

1. It comes from two Greek roots, orthos (straight) and paedeia (rearing of children). It was created in 1741 by Nicholas André who published a book on musculoskeletal deformities in children.
2. Hippocrates.
3. In Rome. It was the main sewage outlet into the Tiber in the first century A.D.
4. Celsus. He was not a medical practitioner but was the first medical author to be printed in morable type (1478) after Gutenberg's invention of the printing press.
5. The thermometer.
6. The use of digitalis in the treatment of dropsy.
7. His gastic fistula. It was created by a gunshot wound and observed by William Beaumont in his classic study of gastric physiology in 1833 'Experiments and Observations on the gastric juice and the Physiology of Digestion'.
8. He found the Red Cross.
9. Louis Pasteur (1822 - 1895).
10. Marie Curie (1867 - 1934).

This quiz was derived from 'Medicine, an Illustrated History'.

Lyons & Petrucelli, Abradale Press, New York.