Radiopharmaceuticals — an overview of the basic principles

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Radiopharmaceuticals are medicinal products which, when ready for use, contain one or more radioactive isotopes. When used for diagnosis, radiopharmaceuticals typically elicit no physiological response from the patient. A radiopharmaceutical can be either an isotope combined with a “kit” (see below) or an isotope alone.

In the UK, most large hospitals will have their own dedicated radiopharmacy that prepares radiopharmaceuticals. However, due to the costs of operating a radiopharmacy and a lack of trained staff, many hospitals are now purchasing their supplies from larger commercial or centralised radiopharmacies.

What is a kit?
A kit is a prepacked set of sterile ingredients designed for the preparation of a specific radiopharmaceutical. It contains a mixture of ligand, reductant, antioxidants, buffers and other components that, when mixed with a radioactive isotope, produces the required product.

Kits are commercially available and are the preferred method for the production of radiopharmaceuticals, since they are a “closed” system (ie, neither the ingredients nor the final solution are exposed to the external environment).

The alternative is to make preparations in-house — this can involve complex processes, in which the ingredients or semi-finished products are exposed to the atmosphere (ie, not closed in a vial, syringe or other sealed container). There is therefore a theoretical risk of microbial contamination and spillage.

Technetium 99m
The isotope of choice for routine labelling of kits for diagnostic work is technetium 99m ($^{99m}$Tc). It has a gamma photon emission that is compatible with the requirements of a gamma camera, and no beta emission, so radiation exposure for the patient is minimised. The chemical properties of $^{99m}$Tc also mean that it binds well to the tracers contained in the kits.

The half-life of $^{99m}$Tc is 6.02 hours (ie, the time required for the isotope to decay to one half of its original radioactivity). However, its biological half-life is shorter because it undergoes rapid renal clearance. This is advantageous because any radiopharmaceutical that has not been absorbed by the target organ is cleared from the body and this results in high-quality images.

The dose of $^{99m}$Tc that is administered depends on the radiopharmaceutical kit being used, the organ being imaged and the test performed. Doses are set out in the Advisory Committee’s “Notes for guidance on the clinical administration of radiopharmaceuticals and use of sealed radioactive sources”.

Calculating doses for children requires special consideration since they have a young child’s organ-size-to-body ratio can be different from that of an older child or adult. These factors, along with the possibility of somatic and hereditary adverse effects that can result from small amounts of administered radioactivity, must be balanced against the possible benefits of any investigation. Each department should have a policy that addresses dosing for such patients.

Other radioisotopes are also used (eg, indium 111, iodine 123, selenium 75, fluorine 18) but are outside the scope of this article.

Indications
Various $^{99m}$Tc radiolabelled kits are used for imaging different organs, some of which are outlined below.

Bone
Kits containing bisphosphonates (eg, medronate) that are labelled with $^{99m}$Tc are used to detect areas of rapidly metabolising bone (eg, bone with metastatic growth or undergoing fracture repair).

For a standard bone scan the radiopharmaceutical is usually injected into a peripheral vein and the patient is imaged about two or three hours later. This allows time for the osteoblasts to incorporate the radiolabelled bisphosphonate into the bone.

All bone is in a state of turnover so the whole skeleton will be visible on the bone scan. However, the radiopharmaceutical is preferentially taken up into areas of rapidly metabolising bone so these areas will be more visible on the scan.

Kidneys
There are three main radiopharmaceutical products used to image the kidneys, each used for different indications.

Radiolabelled mercaptoacetyl triglycine (Mag-3; mertiatide) is used to assess renal blood flow and function. In addition to generating pictorial scans, Mag-3 scanning also produces graphical data representing renal function. Mag-3 is excreted mainly via tubular extraction, although some 11% is excreted via glomerular filtration. Blood clearance is rapid and renal excretion is close to 70% after 30 minutes and 94% after three hours. This improves the quality of organs such as the kidneys, heart and brain. Brush up on the basic principles of its use here
of the images (because the target-organ-to-background ratio is better), reduces the
time taken to conduct the scan and
minimises patient exposure to radiation.
Radiolabelled diethyleneetriamine
dipentaacetic acid (DTPA; pentetate) is
excreted via glomerular filtration and it can
therefore be used to measure glomerular
filtration rate. This test is often used to
assess renal function before or during a
course of nephrotoxic chemotherapy, and
to adjust chemotherapy doses if required.

Radiolabelled dimercaptosuccinic acid
(DMSA; succimer) is used for
morphological studies of the renal cortex,
individual kidney function and to locate an
ectopic kidney.

Brain Kits containing 99mTc-labelled
exametazime are used to assess blood flow
within the brain after stroke or in
neurological conditions such as epilepsy,
Alzheimer’s disease and migraine. It is an
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within the brain after stroke or in
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of its low molecular weight, is able to cross
the brain-blood barrier. Maximum uptake of
99mTc-exametazime into the brain occurs
within one minute of injection and, at best,
7% of the injected dose reaches the
brain. Typically, patients require no specific
preparation for this test.

Heart There are two 99mTc-labelled
products that are used commonly in the UK
for cardiac imaging: tetrofosmin and
sestamibi. Such cardiac imaging can be used to
assess the severity of myocardial
infarction and identify the location of areas
of cardiac ischaemia. Images are obtained
when a patient is at rest and after cardiac “stress” (eg, after a patient runs on a
treadmill or after administration of drugs
such as adenosine or dobutamine).

Very little of the injected dose of 99mTc
is taken up into the myocardium — 1.2% of
the administered dose is taken up at rest
and 1.5% during cardiac stress. Irreversibly
damaged myocardial cells do not take up the
radiopharmaceutical and, therefore,
areas of low/no uptake indicate areas of
cardiac damage.

The scan should occur about one hour
after the radiopharmaceutical is injected,
during which time the patient should eat a
light, fatty meal or drink one or two glasses
of milk. This promotes hepatobiliary
-clearance of the radiopharmaceutical,
which results in a better image (because any
radioactivity that is not in the cardiac tissue
will be eliminated).

Before using tetrofosmin or sestamibi
patients must stop taking certain medicines.
Typically nitrates, beta-blockers and
calcium channel blockers should be stopped
at least 24 hours before the test (although
department protocols can vary).

Patients should not consume caffeine-
containing drinks from midnight the day
before the test. This is because caffeine is a
competitive antagonist of adenosine, which
is often used to induce cardiac stress during
the test. If the effect of adenosine on the
myocardium is reduced, the results of the
images obtained will be less accurate.
Accidental consumption of caffeine is a
common reason for these tests being
cancelled at short notice.

Lungs Radiolabelled kits can be used to
collect lung scans that are used to
diagnose pulmonary embolism. A lung scan
comprises two parts — a perfusion scan and
a ventilation scan — and a diagnosis is
made by comparing the two.

The perfusion scan involves injecting
99mTc-labelled macroaggregated albumin
into a peripheral vein. The particles of
macroaggregated albumin are carried to the
capillary tree of the pulmonary artery
system. The particles do not penetrate the
lung tissue but are distributed evenly in the
lung capillary bed and therefore result in an
image that represents lung perfusion —
reduced flow will be represented by areas
with fewer particles and therefore less
radiation. The length of time the particles
remain in the lung depends on the particle
size, with larger particles having a longer
biological half-life.

For the ventilation scan, patients are
scanned during or after inhaling radioactive
krypton gas or an aerosol of 99mTc-labelled
DTPA. The resulting image shows where
air circulates in the lungs. Aerosols of
radio-labelled DTPA tend to be used more
commonly because aerosol generation
devices produce a consistent particle size
and 99mTc is readily available in most
radiopharmacy departments.

Adverse reactions Adverse reactions to radiopharmaceuticals are very rare overall. They can include: dry
mouth; rash on the neck, arms or chest;
urticaria; sore, swollen lips; oedema of the
face and eyes; dizziness; sweating; nausea
and vomiting; headache; and lethargy. Most
reactions that are reported have occurred
with the use of bone imaging preparations,
probably because these are the most
frequently used.

References
1 The Medicines Act 1968 (Application to
3 Administration of Radiopharmaceutical Substances Advisory Committee. Notes for guidance on the clinical
org.uk/notes_for_guidance (accessed 3 June 2011).