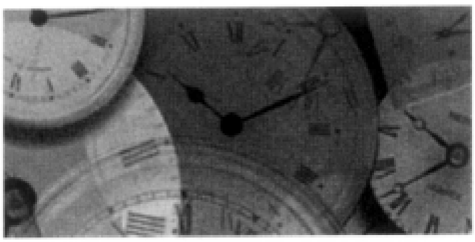
Radioisotopes in Medicine

A history of nuclear medicine

The first use of radioisotopes in medicine pro-dated the discipline of nuclear medicine. Work began in the late 1930s, when scientists used radioactive iodine to assess how much of a dose of administered radioactive iodine localised in the thyroid. This gland, located near the trachea, was known to concentrate iodide from the circulation. A Geiger counter was used to measure radiation emitted from the neck in the region of the thyroid after administration of a dose of radio-iodine.



Early developments

By 1948, scientists had discovered that gamma rays could be detected using photomultiplier tubes. This finding resulted in instrumentation which allowed the thyroid gland to be mapped on a 400-point grid over about one and a half hours.

During the 1950s, pharmaceuticals labelled with radioactivity were developed that allowed the study of other organs including the heart, liver, kidneys and bone. These advances, together with production of new instrumentation, enabled more precise detection of gamma rays.

Recent advances

Radiopharmacouticals

It was not until the mid 1970s that new radioactive nuclides became widely available. These materials, and especially technetium-99m, dramatically changed the practice of nuclear medicine. For the first time, this radionuclide provided a means whereby inactive pharmaceuticals could be conveniently labelled on the hospital premises using a technetium generator (see below), rather than obtaining radionuclides from a reactor. Technetium-99m is much more 'patient friendly' than radionuclides used previously, since it has a short half-life of about six hours and it delivers a relatively low radiation-dose per emitted gamma ray. Its emissions are also of suitable energy to be easily and accurately detected by modern gamma cameras.

Tochnetium generator

The short half-life of technetium-99m would normally pose shipment and distribution difficulties for other than local areas. So the way it is distributed is in a 'generator' which permits technetium-99m to be eluted in sterile solution on demand.

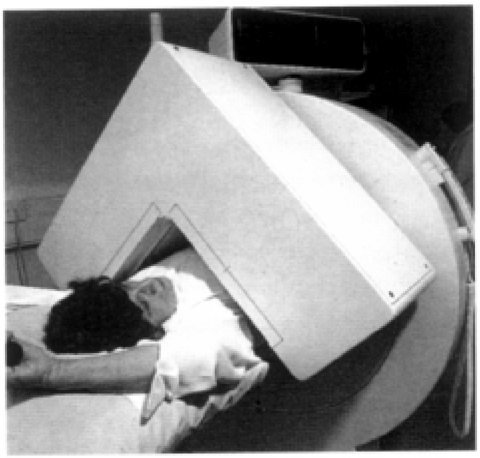
The technetium generator contains molybdenum-99. This is produced in a reactor and is adsorbed onto a short alumina column which is placed into a shielded casing within a portable instrument. Molybdenum-99 decays to technetium-99m (the 'm' stands for metastable). Because the daughter element is chemically different from its parent, it is therefore not bound to the column, and it accumulates in the solvent. Elution of the column washes technetium-99m into the collection vial.

Tochnetium labelling

The chemistry of technetium allows it to form a stable complex with a relatively wide range of chemical chelation agents. If the vial contains a pharmaceutical agent capable of chelating technetium, then the reaction occurs almost instantaneously without further processing. The pharmaceutical agent is thus labelled with the radionuclide. A chromatographic check on the purity of the complex is made before this material is injected into a patient.

A typical technetium generator, with a pack containing vials of scanning agent on the left and a shielded container on the right into which a vial is placed before adding technetium-99m eluate from the generator.

Nuclear medicine instrumentation



A patient under a gamma camera

The 1980s brought the use of computers integrated within gamma cameras that allowed improved processing and quantification of emitted radioactivity. By 1990, the development of high performance single photon emission computer tomography (SPECT, or sometimes just SPET) systems provided imaging of good quality and detail. Nuclear medicine images usually provide information about the function of tissues or organs within the human body. This is because the radiopharmaceutical is imaged as it enters an organ or tumour site. It is then transported or metabolised in the body, as are most drug substances.

Despite competition from other imaging modalities, such as magnetic resonance imaging (MRI), xray computer assisted tomography (CT) and ultrasound scanning, the market for radionuclide imaging equipment in the United States has expanded rapidly. In 1987, the market was worth approximately $US 225 million, and by 1991 this had increased to $US 450 million. The projected value for 1996 is $US 650 million.

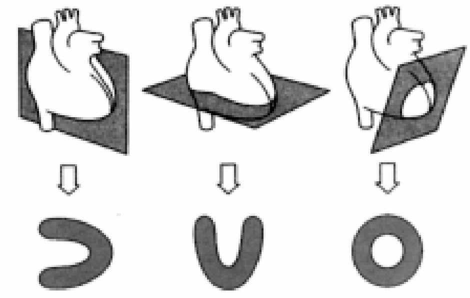
Nuclear medicine today

Nuclear medicine techniques have developed important tools with a very great potential for cost-effective and convenient diagnostic imaging around the world. In addition to the older studies on thyroid, adrenal, kidney, liver and bone function, diagnostic imaging in nuclear medicine is being extended to examine cardiovascular, inflammatory and neurological disorders.

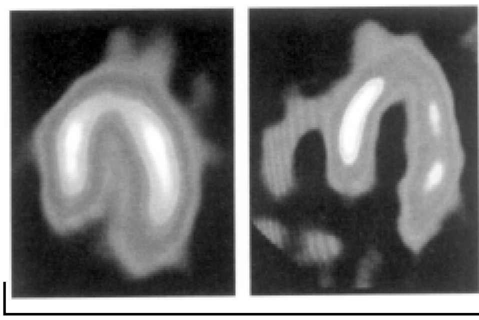
A brain scan at Loyola University Hospital, Illinois, USA

With the increased prevalence of heart disease in western countries, there is now an increase in the number of nuclear cardiology procedures available. Powerful new radiopharmaceuticals are also available, and there is a greater awareness of the diagnostic advantages of functional imaging, as opposed to structural imaging. Other imaging modalities, such as magnetic resonance imaging or computer assisted tomography, visualise anatomical structures within the body, not organ function or blood flow.

Heart function, as revealed by a technetium heart-agent scan, can differentiate between normal and abnormal blood flow. An image, representing a section in a plane through the heart may be formed, and it is examined as one of a series of sections through the organ, as shown below:



Heart Sections

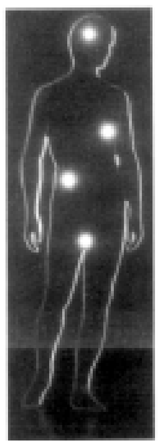


Normal blood-flow Abnormal blood-flow

Cancer therapy

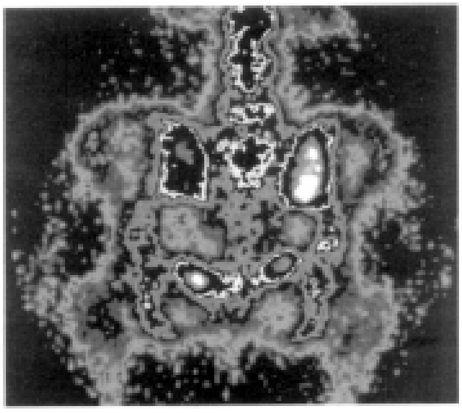
Cancer is a disease that poses one of the greatest medical and research challenges. The earlier a tumour is discovered, the better the chance of successful therapy. Diagnosis and therapy go hand in hand because of the need to understand the cellular mechanisms of cancer growth. The term oncology, which is the study of cancer, is now relatively familiar to most people.

Tumours and metastases



Diagrammatic representation of metastases in different sites around the body

A tumour is a mass of cells that is growing out of control: a tumour may be either benign or malignant. Unfortunately, in many cases the malignant tumour cells have another disastrous property the ability to spread to other parts of the body. This is known as metastasis, and a cell or group of cells will move to another part of the body and start growing there. Sometimes, when an individual with a tumour presents in the clinic for the first time, the cancer has already spread extensively and there can be a large number of secondary tumours. When a tumour has spread to different parts of the body then treatment may differ from the approach when the cancer is confined to a single location. It is important to have good diagnostic methods available to permit detection of metastases.



Pelvic scan which shows secondary metastases

Tumour visualisation

A primary tumour can often be visualised by a number of different methods; these include nuclear medicine imaging, computer assisted tomography (CT), ultrasound imaging and magnetic resonance imaging (MRI). Nuclear medicine is frequently more useful than the other modalities in detecting metastases which are small in size.

Radiotherapy of cancer

External-beam radiotherapy

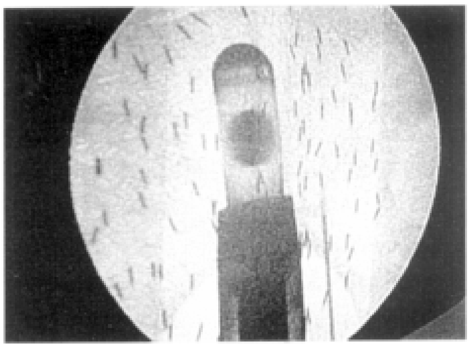
Many hospitals have access to beam radiotherapy equipment, in which is housed a shielded source of xrays, gamma rays or an electron beam. A radioactive source, such as cobalt-60, is located within a special enclosure. This source is used with suitable collimation to focus the beam of gamma rays on a discrete area, for example the size of a pea in irradiation of a pituitary tumour. More general irradiation, such as half (hemi-) body irradiation, is used for patients with extensive secondary (metastatic) tumours which may be difficult to localise.

Secondary metastases and bone pain

The use of a radiopharmaceutical to bring about pain relief for patients with metastatic tumours in the bone has been another success story. Cancer of the prostate is the commonest cancer in men in the western world, and one in ten American men will develop the disease at some point in their lives according to the American Cancer Society, which estimates that 244,000 new cases of prostate cancer will be diagnosed in 1996. In the UK, 7,500 men die from this disease each year.

More than half of patients presenting with symptoms of prostatic cancer have advanced disease with metastases in the bone at the time of diagnosis. These secondary deposits of tumour can be devastating to the patient's quality of life because of the great pain that they cause. Strontium-89 is a radioisotope which mimics calcium in the body and localises in bone. On injection into the bloodstream, it is selectively taken up by, and hence irradiates, all tumour sites in the bone simultaneously. It also delays the development of new pain in existing, but clinically silent, metastases. Improved pain control is reported by up to eighty per cent of treated patients, of whom twenty per cent claim complete pain relief. A single injection is usually effective for up to six months, after which treatment can be repeated, if required.

Implant radiotherapy



A radiograph of a cancerous prostate with implanted iodine seeds and ultrasound probe in position

Implants of radium needles as a treatment for tumours was recognised as being successful and was used routinely from the late 1930s.

There are several methods of treatment currently available for early stage, localised prostate cancer. Choosing the treatment option that is best suited to any particular individual involves close consultation and discussion with the physician. As an example, a successful alternative treatment has been the use of radioactive iodine125 seed implants. These seeds, each smaller than a grain of rice, are held in fine needles and inserted directly into the prostate gland using an ultrasound scanner for guidance. Once implanted, they deliver two to three times as much radiation to the tumour as could be provided by conventional external beam radiation therapy. The benefits to the patient are that symptoms of incontinence and impotence, which are associated with some other treatments, are reduced.

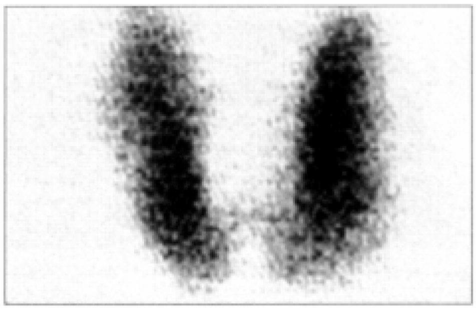
Tumour imaging in nuclear medicine

One of the areas of current interest is to devise more sensitive and reliable ways to detect small metastases that are located at a distance from the primary tumour. This is likely to be important in monitoring the response of a tumour to therapy. The clinical oncologist needs to know how much residual tumour is present after each stage of therapy and this is difficult to achieve at present.

A strength of nuclear medicine is that functional imaging is possible. Here, rather than the impressively detailed anatomical images produced by magnetic resonance imaging and computer assisted tomography scanning, a radiopharmaceutical can be designed to image specific biochemical elements of a tumour, so that it preferentially targets a particular receptor or enzyme location.

Radioactive iodine

As was mentioned previously, radioactive iodide131 was one of the first successes in radiopharmaceutical medicine. Thyroid disease is the second most prevalent endocrine disorder after diabetes. This gland takes up iodine preferentially from the blood stream, and radioiodine is used as a diagnostic agent to assess thyroid function, and also for ablation therapy. Using low doses of radionuclide, the tumour can be imaged with a gamma camera to obtain diagnostic information. A higher, therapeutic dose of radioiodine can be given to the patient to treat a benign or malignant tumour.



A typical thyroid scan:

Future treatments

There are still a number of tumours for which there is little available in the way of conventional chemotherapy. Many drugs and treatment regimes have been tried but none has had any significant effect. If radioisotopes could be delivered selectively to these tumours then some therapeutic benefit should result.

It is important to recognise that complete cures for cancer may not be with us for some years, and so there is an urgent need to identify ways of slowing the progression of the disease and of reducing the painful symptoms associated with many cancers.