

Radioisotopes in Medicine

(Updated January 2011)

- **Nuclear medicine uses radiation to provide diagnostic information about the functioning of a person's specific organs, or to treat them. Diagnostic procedures are now routine.**
- **Radiotherapy can be used to treat some medical conditions, especially cancer, using radiation to weaken or destroy particular targeted cells.**
- **Tens of millions of nuclear medicine procedures are performed each year, and demand for radioisotopes is increasing rapidly.**

Nuclear Medicine

This is a branch of medicine that uses radiation to provide information about the functioning of a person's specific organs or to treat disease. In most cases, the information is used by physicians to make a quick, accurate diagnosis of the patient's illness. The thyroid, bones, heart, liver and many other organs can be easily imaged, and disorders in their function revealed. In some cases radiation can be used to treat diseased organs, or tumours. Five Nobel Laureates have been intimately involved with the use of radioactive tracers in medicine.

Over 10,000 hospitals worldwide use radioisotopes in medicine, and about 90% of the procedures are for diagnosis. The most common radioisotope used in diagnosis is technetium-99, with some 30 million procedures per year, accounting for 80% of all nuclear medicine procedures worldwide.

In developed countries (26% of world population) the frequency of diagnostic nuclear medicine is 1.9% per year, and the frequency of therapy with radioisotopes is about one tenth of this. In the USA there are some 18 million nuclear medicine procedures per year among 305 million people, and in Europe about 10 million among 500 million people. In Australia there are about 560,000 per year among 21 million people, 470,000 of these using reactor isotopes. The use of radiopharmaceuticals in diagnosis is growing at over 10% per year.

Nuclear medicine was developed in the 1950s by physicians with an endocrine emphasis, initially using iodine-131 to diagnose and then treat thyroid disease. In recent years specialists have also come from radiology, as dual CT/PET procedures have become established.

Computed X-ray tomography (CT) scans and nuclear medicine contribute 36% of the total radiation exposure and 75% of the medical exposure to the US population, according to a US National Council on Radiation Protection & Measurements report in 2009. The report showed that Americans' average total yearly radiation exposure had increased from 3.6 millisievert to 6.2 mSv per year since the early 1980s, due to medical-related procedures. (Industrial radiation exposure, including that from nuclear power plants, is less than 0.1% of overall public radiation exposure.)

Diagnostic techniques in nuclear medicine

Diagnostic techniques in nuclear medicine use radioactive tracers which emit gamma rays from within the body. These tracers are generally short-lived isotopes linked to chemical compounds which permit specific physiological processes to be scrutinised. They can be given by injection, inhalation or orally. The first type are where single photons are detected by a gamma camera which

can view organs from many different angles. The camera builds up an image from the points from which radiation is emitted; this image is enhanced by a computer and viewed by a physician on a monitor for indications of abnormal conditions.

A more recent development is Positron Emission Tomography (PET) which is a more precise and sophisticated technique using isotopes produced in a cyclotron. A positron-emitting radionuclide is introduced, usually by injection, and accumulates in the target tissue. As it decays it emits a positron, which promptly combines with a nearby electron resulting in the simultaneous emission of two identifiable gamma rays in opposite directions. These are detected by a PET camera and give very precise indication of their origin. PET's most important clinical role is in oncology, with fluorine-18 as the tracer, since it has proven to be the most accurate non-invasive method of detecting and evaluating most cancers. It is also well used in cardiac and brain imaging.

New procedures combine PET with computed X-ray tomography (CT) scans to give co-registration of the two images (PETCT), enabling 30% better diagnosis than with traditional gamma camera alone. It is a very powerful and significant tool which provides unique information on a wide variety of diseases from dementia to cardiovascular disease and cancer (oncology).

Positioning of the radiation source within the body makes the fundamental difference between nuclear medicine imaging and other imaging techniques such as x-rays. Gamma imaging by either method described provides a view of the position and concentration of the radioisotope within the body. Organ malfunction can be indicated if the isotope is either partially taken up in the organ (cold spot), or taken up in excess (hot spot). If a series of images is taken over a period of time, an unusual pattern or rate of isotope movement could indicate malfunction in the organ.

A distinct advantage of nuclear imaging over x-ray techniques is that both bone and soft tissue can be imaged very successfully. This has led to its common use in developed countries where the probability of anyone having such a test is about one in two and rising.

The mean effective dose is 4.6 mSv per diagnostic procedure.



Radionuclide therapy (RNT)

Rapidly dividing cells are particularly sensitive to damage by radiation. For this reason, some cancerous growths can be controlled or eliminated by irradiating the area containing the growth.

External irradiation (sometimes called teletherapy) can be carried out using a gamma beam from a radioactive cobalt-60 source, though in developed countries the much more versatile linear accelerators are now being utilised as a high-energy x-ray source (gamma and x-rays are much the same). An external radiation procedure is known as the gamma knife radiosurgery, and involves focusing gamma radiation from 201 sources of cobalt-60 sources on a precise area of the brain with a cancerous tumour. Worldwide, over 30,000 patients are treated annually, generally as outpatients.

Internal radionuclide therapy is by administering or planting a small radiation source, usually a gamma or beta emitter, in the target area. Short-range radiotherapy is known as brachytherapy, and this is becoming the main means of treatment. Iodine-131 is commonly used to treat thyroid cancer, probably the most successful kind of cancer treatment. It is also used to treat non-malignant thyroid disorders. Iridium-192 implants are used especially in the head and breast. They are produced in wire form and are introduced through a catheter to the target area. After administering the correct dose, the implant wire is removed to shielded storage. This brachytherapy (short-range) procedure gives less overall radiation to the body, is more localised to the target tumour and is cost effective.

Treating leukaemia may involve a bone marrow transplant, in which case the defective bone marrow will first be killed off with a massive (and otherwise lethal) dose of radiation before being replaced with healthy bone marrow from a donor.

Many therapeutic procedures are palliative, usually to relieve pain. For instance, strontium-89 and (increasingly) samarium 153 are used for the relief of cancer-induced bone pain. Rhenium-186 is a newer product for this.

A new field is Targeted Alpha Therapy (TAT), especially for the control of dispersed cancers. The short range of very energetic alpha emissions in tissue means that a large fraction of that radiative energy goes into the targeted cancer cells, once a carrier has taken the alpha-emitting radionuclide to exactly the right place. Laboratory studies are encouraging and clinical trials for leukaemia, cystic glioma and melanoma are under way.

An experimental development of this is Boron Neutron Capture Therapy using boron-10 which concentrates in malignant brain tumours. The patient is then irradiated with thermal neutrons which are strongly absorbed by the boron, producing high-energy alpha particles which kill the cancer. This requires the patient to be brought to a nuclear reactor, rather than the radioisotopes being taken to the patient.

Radionuclide therapy has progressively become successful in treating persistent disease and doing so with low toxic side-effects. With any therapeutic procedure the aim is to confine the radiation to well-defined target volumes of the patient. The doses per therapeutic procedure are typically 20-60 Gy.

Biochemical Analysis

It is very easy to detect the presence or absence of some radioactive materials even when they exist in very low concentrations. Radioisotopes can therefore be used to label molecules of biological samples in vitro (out of the body). Pathologists have devised hundreds of tests to determine the constituents of blood, serum, urine, hormones, antigens and many drugs by means of associated radioisotopes. These procedures are known as radioimmuno-assays and, although the

biochemistry is complex, kits manufactured for laboratory use are very easy to use and give accurate results. In Europe some 15 million of these in vitro analyses are undertaken each year.

Diagnostic Radiopharmaceuticals

Every organ in our bodies acts differently from a chemical point of view. Doctors and chemists have identified a number of chemicals which are absorbed by specific organs. The thyroid, for example, takes up iodine, the brain consumes quantities of glucose, and so on. With this knowledge, radiopharmacists are able to attach various radioisotopes to biologically active substances. Once a radioactive form of one of these substances enters the body, it is incorporated into the normal biological processes and excreted in the usual ways.

Diagnostic radiopharmaceuticals can be used to examine blood flow to the brain, functioning of the liver, lungs, heart or kidneys, to assess bone growth, and to confirm other diagnostic procedures. Another important use is to predict the effects of surgery and assess changes since treatment.

The amount of the radiopharmaceutical given to a patient is just sufficient to obtain the required information before its decay. The radiation dose received is medically insignificant. The patient experiences no discomfort during the test and after a short time there is no trace that the test was ever done. The non-invasive nature of this technology, together with the ability to observe an organ functioning from outside the body, makes this technique a powerful diagnostic tool.

A radioisotope used for diagnosis must emit gamma rays of sufficient energy to escape from the body and it must have a half-life short enough for it to decay away soon after imaging is completed.

The radioisotope most widely used in medicine is technetium-99m, employed in some 80% of all nuclear medicine procedures - almost 30 million per year (2008), of which 6-7 million are in Europe, 12-15 million in North America, 6-8 million in Asia/Pacific (particularly Japan), and 0.5 million in other regions. It is an isotope of the artificially-produced element technetium and it has almost ideal characteristics for a nuclear medicine scan. These are:

- It has a half-life of six hours which is long enough to examine metabolic processes yet short enough to minimise the radiation dose to the patient.
- Technetium-99m decays by a process called "isomeric"; which emits gamma rays and low energy electrons. Since there is no high energy beta emission the radiation dose to the patient is low.
- The low energy gamma rays it emits easily escape the human body and are accurately detected by a gamma camera. Once again the radiation dose to the patient is minimised.
- The chemistry of technetium is so versatile it can form tracers by being incorporated into a range of biologically-active substances to ensure that it concentrates in the tissue or organ of interest.

Its logistics also favour its use. Technetium generators, a lead pot enclosing a glass tube containing the radioisotope, are supplied to hospitals from the nuclear reactor where the isotopes are made. They contain molybdenum-99, with a half-life of 66 hours, which progressively decays to technetium-99. The Tc-99 is washed out of the lead pot by saline solution when it is required. After two weeks or less the generator is returned for recharging.

A similar generator system is used to produce rubidium-82 for PET imaging from strontium-82 - which has a half-life of 25 days.

Myocardial Perfusion Imaging (MPI) uses thallium-201 chloride or technetium-99m and is important

for detection and prognosis of coronary artery disease.

Canadian 2006 data shows that 56% of Tc-99 use there is in myocardial ischemia perfusion, 17% in bone scans, 7% in liver/hepatobiliary, 4% respiratory, 3% renal, 3% thyroid.

For PET imaging, the main radiopharmaceutical is Fluoro-deoxy glucose (FDG) incorporating F-18 - with a half-life of just under two hours, as a tracer. The FDG is readily incorporated into the cell without being broken down, and is a good indicator of cell metabolism.

In diagnostic medicine, there is a strong trend to using more cyclotron-produced isotopes such as F-18 as PET and CT/PET become more widely available. However, the procedure needs to be undertaken within two hours reach of a cyclotron, which limits their utility compared with Mo/Tc-99.

Therapeutic Radiopharmaceuticals

For some medical conditions, it is useful to destroy or weaken malfunctioning cells using radiation. The radioisotope that generates the radiation can be localised in the required organ in the same way it is used for diagnosis - through a radioactive element following its usual biological path, or through the element being attached to a suitable biological compound. In most cases, it is beta radiation which causes the destruction of the damaged cells. This is radionuclide therapy (RNT) or radiotherapy. Short-range radiotherapy is known as brachytherapy, and this is becoming the main means of treatment.

Although radiotherapy is less common than diagnostic use of radioactive material in medicine, it is nevertheless widespread, important and growing. An ideal therapeutic radioisotope is a strong beta emitter with just enough gamma to enable imaging, eg lutetium-177. This is prepared from ytterbium-176 which is irradiated to become Yb-177 which decays rapidly to Lu-177. Yttrium-90 is used for treatment of cancer, particularly non-Hodgkin's lymphoma, and its more widespread use is envisaged, including for arthritis treatment. Lu-177 and Y-90 are becoming the main RNT agents.

Iodine-131 and phosphorus-32 are also used for therapy. Iodine-131 is used to treat the thyroid for cancers and other abnormal conditions such as hyperthyroidism (over-active thyroid). In a disease called Polycythemia vera, an excess of red blood cells is produced in the bone marrow. Phosphorus-32 is used to control this excess.

A new and still experimental procedure uses boron-10, which concentrates in the tumour. The patient is then irradiated with neutrons which are strongly absorbed by the boron, to produce high-energy alpha particles which kill the cancer.

For targeted alpha therapy (TAT), actinium-225 is readily available, from which the daughter bismuth-213 can be obtained (via 3 alpha decays) to label targeting molecules. The bismuth is obtained by elution from an Ac-225/Bi-213 generator similar to the Mo-99/Tc-99 one. Bi-213 has a 46-minute half-life. The actinium-225 (half-life 10 days) is formed from radioactive decay of radium-226, the decay product of long-lived thorium-232, which is obtained from decay of uranium-238, which is formed from Th-232 by neutron capture in a nuclear reactor.

Considerable medical research is being conducted worldwide into the use of radionuclides attached to highly specific biological chemicals such as immunoglobulin molecules (monoclonal antibodies). The eventual tagging of these cells with a therapeutic dose of radiation may lead to the regression - or even cure - of some diseases.

Radioisotope Poisons

In 2006 Britain witnessed the apparent murder of one of its newer citizens, a former Russian intelligence official, by poisoning with radioactive polonium. His death was slow and excruciating.

Polonium has about 26 isotopes, all of which are radioactive. Webelements periodic table says that it is 250 billion times more toxic than hydrocyanic acid. It is readily soluble in weak acid. (It was the first element discovered by Marie Curie, in 1898, and named after her native Poland. Her daughter Irene was contaminated with polonium in a laboratory accident and died of leukemia at the age of 59.)

Polonium-210 is the penultimate decay product of U-238, before it alpha decays to become stable lead. It results from the beta decay of Pb-210 (in the U-238 decay series) to Bi-210 which rapidly beta decays to Po-210. This gives rise to its occurrence in nature, where uranium is ubiquitous. However, because of its short (138 day) half life, very little Po-210 would be found in uranium ore or mill tailings (Webelements suggests 0.1 mg/tonne). Po-210 levels in soil would be even less, but it is concentrated in tobacco and traces of it can be found in smokers' urine.

Po-210 can also be made by neutron irradiation of Bi-209, and that is most likely source of any significant quantity. Russia has used Po-210 as a heat source in short-life spacecraft and lunar rovers. It also operates reactors using lead-bismuth cooling, which becomes contaminated with Po-210 due to neutron bombardment.

Because its half-life is so short, a gram of Po-210 is about 5000 times as radioactive as a gram of radium - which sets the standard of activity. But at 138 days its half life is long enough for it to be manufactured, transported and administered before it loses its potency. It would not put the carrier at much risk, since alpha radiation is only really a hazard inside the body - a layer of skin is protection. About 10 micrograms (2 GBq) was said to have been used, administered in a cup of tea (it would be warm due to the decay).

However, simply dosing someone with polonium might not have much effect if it simply went in one end and out the other in a day or two without being absorbed from the gut. It would probably need to be complexed on to an organic carrier which would enter the bloodstream and take it to vital organs where it would stay. (This is what happens with targeted alpha therapy (TAT) using very low levels of alpha-active radioisotopes: the carriers take them to dispersed cancerous tissues where they are needed.)

In Mr Litvinenko's case the intense alpha radiation was reportedly in vital organs and sufficient to destroy them over three weeks. It was apparently over one hundred times the dose used in TAT for cancer treatment and the Po-210 is much longer-lived than isotopes used for TAT. It could have been attached to something as simple as a sugar.

Supplies of radioisotopes

Most medical radioisotopes made in nuclear reactors are sourced from relatively few research reactors, including:

- NRU at Chalk River in Canada (supplied via MDS Nordion)
- HFR at Petten in Netherlands (supplied via IRE and Covidien)

- BR-2 at Mol in Belgium (supplied via IRE and Covidien)
- Maria in Poland (supplied via Covidien)
- Osiris & Orphee at Saclay in France (supplied via IRE)
- FRJ-2/ FRM-2 at Julich in Germany (supplied via IRE)
- LWR-15 at Rez in Czech Republic
- HFETR at Chengdu in China
- Safari in South Africa (supplied from NTP)
- Opal in Australia (supplied from ANSTO to domestic market)
- ETRR-2 in Egypt (forthcoming: supplied to domestic market)
- Dimitrovgrad in Russia (Isotop-NIIAR)

Of fission radioisotopes, 40% of Mo-99 (for Tc-99m) comes from MDS Nordion, 25% from Covidien (formerly Tyco), 17% from IRE and 10% from NTP. For I-131, 75% is from IRE, 25% from NTP. Over 90% of the Mo-99 is made in five reactors: NRU in Canada (40%), HFR in Netherlands (30%), BR-2 in Belgium (9%), Osiris in France (5%), and Safari-1 in South Africa (10%). Canadian 2008 data gives 31% for NRU.

World demand for Mo-99 is 23,000 six-day TBq/yr.* It is mostly prepared by fission of U-235 targets in a nuclear research reactor. Most is produced using high-enriched uranium targets which are then processed to separate the Mo-99 and also to recover I-131. Opal, Safari, and increasingly other reactors, are moving to low-enriched uranium targets, which adds about 20% to production costs.

* 23,000 TBq is on basis of activity at 6 days from production reference point, ie 22% of nearly 100,000 TBq required in production processing (given 66 hour half-life). This is still about two days from the end of irradiation, so some 167,000 TBq/yr must be made in the actual reactors to allow for cooling, processing and decay en route to the users.

A number of incidents in 2008 pointed up shortcomings and unreliability in the supply of medical isotopes, particular technetium. As indicated above, most of the world's supply of Mo-99 for this comes from only five reactors, all of them 43 to 52 years old (in mid 2010). The Canadian and Netherlands reactors required major repairs over 2009-10 and were out of action for some time. Osiris is due to shut down in 2015. A major and increasing supply shortfall of Tc-99 is forecast from 2010, and the IAEA is encouraging new producers in Egypt, East Europe and central Asia. During the 2009-10 supply crisis, South Africa's (NECSA) Safari was able to supply 25% of the supply of Mo-99. Australia's Opal reactor has the capacity to produce half the world supply of it, but a much larger Mo production facility would be required. Also the processing and distribution of isotopes is complex and constrained, which can be critical when the isotopes concerned are short-lived. A need for increased production capacity and more reliable distribution is evident. The Mo-99 market is about \$5 billion per year, according to NECSA.

The US Congress has called for all Mo-99 to be supplied by reactors running on low-enriched uranium (LEU), instead of high-enriched uranium (HEU). Also it has called for proposals for an LEU-based supply of Mo-99 for the US market. This supply should reach 111 six-day TBq per week by mid-2013, a quarter of world demand. Tenders for this closed in June 2010.

In January 2009 Babcock & Wilcox (B&W) announced an agreement with international isotope supplier Covidien to produce Mo-99 sufficient for half of US demand, if a new process involving an innovative reactor and separation technology is successful. They plan to use Aqueous Homogeneous Reactor (AHR) technology with low-enriched uranium in small 100-200 kW units where the fuel is mixed with the moderator and the U-235 forms both the fuel and the irradiation target. A single production facility could have four such reactors. B&W and Covidien expect a five-year lead time to first production. (LEU is dissolved in acid then brought to criticality in a 200-litre vessel. As fission proceeds the solution is circulated through an extraction facility to remove the fission products with Mo-99 and then back into the reactor vessel, which is at low temperature and pressure.) At Russia's Kurchatov Institute the 20 kW ARGUS AHR has operated since 1981, and R&D on producing Mo-99 from it is ongoing.

Also in the USA, the University of Missouri is reported to be planning a licence application to NRC in 2010 to produce half of US requirements of Mo-99 at its research reactor using low-enriched uranium targets by 2012.

In Russia, the Research Institute of Atomic Reactors (NIAR or RIAR, with 3 reactors) and Trans-regional Izotop Association (VA Izotop) have established a joint venture, Isotop-NIIAR to produce Mo-99 at Dimitrovgrad from 2010. Phase 1 of the Mo-99 production line with capacity of 1700 TBq/yr was commissioned in December 2010, and Phase 2 will take capacity to 52,000 TBq/yr according to Rosatom, without saying when the activity is measured. (VA Izotop is authorized since 2009 by Rosatom to control all isotope production and radiological devices in Russia.) This JV is aiming to capture 26% of the world market for Mo-99 by 2012. In September 2010 JSC Izotop signed a framework agreement with MDS Nordion to explore commercial opportunities outside Russia on the basis of this Isotop-NIIAR JV, initially over ten years.

Cobalt-60 has mostly come from Candu power reactors by irradiation of Co-59 in special rods, and production is being expanded. Production sites include: Bruce B, Pickering and Gentilly in Canada; Embalse in Argentina; Qinshan Phase III units 1 and 2 in China; Wolsong 1 and 2 in South Korea (all Candu); and Leningrad 1 in Russia (RBMK). These will be joined by the Clinton and Hope Creek BWRs in USA from 2012.

Nuclear Medicine Wastes

The use of radioisotopes for medical diagnosis and treatments results in the generation of mainly Low-Level Waste (LLW). This waste includes paper, rags, tools, clothing and filters, which contain small amounts of mostly short-lived radioactivity. These types of waste often undergo decay storage for periods of months to a few years before being disposed of at urban land-fill sites.

When radiography sources have decayed to a point where they are no longer emitting enough penetrating radiation for use in treatments, they are considered as radioactive waste. Sources such as Co-60 are treated as short-lived Intermediate-Level wastes (ILW). Other sources such as Radium-226, used in cancer therapy, will however require long-term storage and geological disposal as ILW, as a result of their higher level of long-lived radioactivity.

Isotopes used in Medicine

Many radioisotopes are made in nuclear reactors, some in cyclotrons. Generally neutron-rich ones and those resulting from nuclear fission need to be made in reactors, neutron-depleted ones are made in cyclotrons. There are about 40 activation product radioisotopes and five fission product ones made in reactors.

Reactor Radioisotopes (half-life indicated)

Bismuth-213 (46 min): Used for targeted alpha therapy (TAT), especially cancers, as it has a high energy (8.4 MeV).

Chromium-51 (28 d): Used to label red blood cells and quantify gastro-intestinal protein loss.

Cobalt-60 (5.27 yr): Formerly used for external beam radiotherapy, now used more for sterilising

Dysprosium-165 (2 h): Used as an aggregated hydroxide for synovectomy treatment of arthritis.

Erbium-169 (9.4 d): Use for relieving arthritis pain in synovial joints.

Holmium-166 (26 h): Being developed for diagnosis and treatment of liver tumours.

Iodine-125 (60 d): Used in cancer brachytherapy (prostate and brain), also diagnostically to evaluate the filtration rate of kidneys and to diagnose deep vein thrombosis in the leg. It is also widely used in radioimmuno-assays to show the presence of hormones in tiny quantities.

Iodine-131 (8 d)*: Widely used in treating thyroid cancer and in imaging the thyroid; also in diagnosis of abnormal liver function, renal (kidney) blood flow and urinary tract obstruction. A strong gamma emitter, but used for beta therapy.

Iridium-192 (74 d): Supplied in wire form for use as an internal radiotherapy source for cancer treatment (used then removed).

Iron-59 (46 d): Used in studies of iron metabolism in the spleen.

Lutetium-177 (6.7 d): Lu-177 is increasingly important as it emits just enough gamma for imaging while the beta radiation does the therapy on small (eg endocrine) tumours. Its half-life is long enough to allow sophisticated preparation for use. It is usually produced by neutron activation of natural or enriched lutetium-176 targets.

Molybdenum-99 (66 h)*: Used as the 'parent' in a generator to produce technetium-99m.

Palladium-103 (17 d): Used to make brachytherapy permanent implant seeds for early stage prostate cancer.

Phosphorus-32 (14 d): Used in the treatment of polycythemia vera (excess red blood cells). Beta emitter.

Potassium-42 (12 h): Used for the determination of exchangeable potassium in coronary blood flow.

Rhenium-186 (3.8 d): Used for pain relief in bone cancer. Beta emitter with weak gamma for imaging.

Rhenium-188 (17 h): Used to beta irradiate coronary arteries from an angioplasty balloon.

Samarium-153 (47 h): Sm-153 is very effective in relieving the pain of secondary cancers lodged in the bone, sold as Quadramet. Also very effective for prostate and breast cancer. Beta emitter.

Selenium-75 (120 d): Used in the form of seleno-methionine to study the production of digestive enzymes.

Sodium-24 (15 h): For studies of electrolytes within the body.

Strontium-89 (50 d)*: Very effective in reducing the pain of prostate and bone cancer. Beta emitter.

Technetium-99m (6 h): Used in to image the skeleton and heart muscle in particular, but also for brain, thyroid, lungs (perfusion and ventilation), liver, spleen, kidney (structure and filtration rate), gall bladder, bone marrow, salivary and lacrimal glands, heart blood pool, infection and numerous specialised medical studies. Produced from Mo-99 in a generator.

Xenon-133 (5 d)*: Used for pulmonary (lung) ventilation studies.

Ytterbium-169 (32 d): Used for cerebrospinal fluid studies in the brain.

Ytterbium-177 (1.9 h): Progenitor of Lu-177.

Yttrium-90 (64 h)*: Used for cancer brachytherapy and as silicate colloid for the relieving the pain of arthritis in larger synovial joints. Pure beta emitter and of growing significance in therapy.

Radioisotopes of caesium, gold and ruthenium are also used in brachytherapy.

* fission product

Cyclotron Radioisotopes

Carbon-11, Nitrogen-13, Oxygen-15, Fluorine-18: These are positron emitters used in PET for studying brain physiology and pathology, in particular for localising epileptic focus, and in dementia, psychiatry and neuropharmacology studies. They also have a significant role in cardiology. F-18 in FDG (fluorodeoxyglucose) has become very important in detection of cancers and the monitoring of progress in their treatment, using PET.

Cobalt-57 (272 d): Used as a marker to estimate organ size and for in-vitro diagnostic kits.

Copper-64 (13 h): Used to study genetic diseases affecting copper metabolism, such as Wilson's and Menke's diseases, and for PET imaging of tumours, and therapy.

Copper-67 (2.6 d): Beta emitter, used in therapy.

Fluorine-18 as FLT (fluorothymidine), F-miso (fluoromisonidazole), 18F-choline: tracer.

Gallium-67 (78 h): Used for tumour imaging and localisation of inflammatory lesions (infections).

Gallium-68 (68 min): Positron emitter used in PET and PET-CT units. Derived from germanium-68 in a generator.

Germanium-68 (271 d): Used as the 'parent' in a generator to produce Ga-68.

Indium-111 (2.8 d): Used for specialist diagnostic studies, eg brain studies, infection and colon transit studies.

Iodine-123 (13 h): Increasingly used for diagnosis of thyroid function, it is a gamma emitter without the beta radiation of I-131.

Iodine-124: tracer.

Krypton-81m (13 sec) from Rubidium-81 (4.6 h): Kr-81m gas can yield functional images of pulmonary ventilation, e.g. in asthmatic patients, and for the early diagnosis of lung diseases and function.

Rubidium-82 (1.26 min): Convenient PET agent in myocardial perfusion imaging.

Strontium-82 (25 d): Used as the 'parent' in a generator to produce Rb-82.

Thallium-201 (73 h): Used for diagnosis of coronary artery disease other heart conditions such as heart muscle death and for location of low-grade lymphomas.

What are radioisotopes?

Many of the chemical elements have a number of isotopes. The isotopes of an element have the same number of protons in their atoms (atomic number) but different masses due to different numbers of neutrons. In an atom in the neutral state, the number of external electrons also equals the atomic number. These electrons determine the chemistry of the atom. The atomic mass is the sum of the protons and neutrons. There are 82 stable elements and about 275 stable isotopes of these elements.

When a combination of neutrons and protons, which does not already exist in nature, is produced artificially, the atom will be unstable and is called a radioactive isotope or radioisotope. There are also a number of unstable natural isotopes arising from the decay of primordial uranium and thorium. Overall there are some 1800 radioisotopes.

At present there are up to 200 radioisotopes used on a regular basis, and most must be produced artificially.

Radioisotopes can be manufactured in several ways. The most common is by neutron activation in a nuclear reactor. This involves the capture of a neutron by the nucleus of an atom resulting in an excess of neutrons (neutron rich). Some radioisotopes are manufactured in a cyclotron in which protons are introduced to the nucleus resulting in a deficiency of neutrons (proton rich).

The nucleus of a radioisotope usually becomes stable by emitting an alpha and/or beta particle (or positron). These particles may be accompanied by the emission of energy in the form of electromagnetic radiation known as gamma rays. This process is known as radioactive decay.

Radioactive products which are used in medicine are referred to as radiopharmaceuticals.

Appendix to Information Paper 55

Research reactor needed for medical imaging - why cyclotrons cannot do the job

Article from May 1999 edition *Australasian Science Magazine*

Rex Boyd defends the decision to commission a new nuclear reactor (OPAL - now operating)

It is claimed by opponents of the nuclear industry that Australia's demand for medical radioisotopes can be met by cyclotrons. The truth is that any number of cyclotrons will never replace [Australia's need for a reactor](#) .

Australia has two cyclotrons, which use high voltages and electrical fields to accelerate hydrogen atoms through a vacuum chamber. When they collide with a target substance they produce radioactivity.

As a general rule, it is more difficult to make a radioisotope in a cyclotron than in a reactor. Cyclotron reactions are less productive and less predictable than nuclear reactions performed in a reactor.

The cyclotron produces neutron-deficient radioisotopes whereas the reactor produces neutron-rich radioisotopes. Thus the reactor and the cyclotron complement each other in satisfying society's need for a full range of radioisotopes; rarely one acts as a substitute for the other.

A few radioisotopes are exceptions to this rule and can be produced by either facility. One is technetium-99m, currently used in 85% of medical applications. The discovery that technetium-99m can be produced in a cyclotron does not imply that the need for a reactor is disappearing.

The half-life of technetium-99m is 6 hours. This means that this radioisotope must be produced and distributed on a daily basis.

However, when technetium-99m is produced in a reactor it proceeds through a precursor radioisotope, molybdenum-99, which has a half-life of 66 hours. Thus the weekly production of molybdenum-99 generators can meet all the technetium-99m needs of Australian hospitals.

In contrast the cyclotron does not produce molybdenum-99; instead it produces technetium-99m directly. Therefore a network of cyclotrons situated across Australia would be needed to make daily deliveries of technetium-99m to the nation's hospitals. This is one reason why none of the many powerful cyclotrons around the world are used for the manufacture of technetium-99m.

Reliance on cyclotrons for our most frequently used medical isotope would have a serious negative impact on the practice of nuclear medicine. The rapid decay of technetium-99m would limit the number of patients treated in any one day and would preclude the use of nuclear medicine techniques in out-of-hours emergency situations when stocks would be exhausted. Appointments would be subject to technetium-99m availability and patient waiting lists would lengthen.

Economic factors would also militate against cyclotron-produced technetium-99m. The raw materials for reactor production are cheap (a few dollars per kilogram) and readily available, whereas the starting material for the cyclotron-method is a rare form of molybdenum that must be enriched to high levels of isotopic purity (>99%), is not commercially available and would cost millions of dollars per kilogram.

Traces of other molybdenum isotopes in the raw materials can reduce the purity of the technetium-99m. A series of competing nuclear reactions produces undesirable longer-lived technetium radioisotopes, particularly technetium-96, that can accumulate during the day. The level of these impurities may exceed the legal limit and degrade the quality of the scanned image.

Other technetium radioisotopes would expose patients to higher radiation doses. Only 0.1% technetium-96 is necessary before radiation exposure of patients is doubled. Hence before cyclotron-produced technetium-99m could be used, certain regulations governing radiopharmaceutical quality would need changing.

The cyclotron production of technetium-99m is technically feasible but undesirable for all of these reasons.

The frontiers of nuclear medicine now extend beyond the diagnosis of disease with technetium-99m. Other short-lived radioisotopes are being introduced into nuclear medicine with the capability of reducing the pain associated with cancer. Australia must have its own reactor if its community is to have access to these radioisotopes and reap the benefits of the latest advances.

Rex Boyd was formerly the director of the \$20 million National Medical Cyclotron Project at Sydney's Royal Prince Alfred Hospital.