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Medical Applications of Radioisotopes

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ABSTRACT: Nuclear medicine uses radiation to provide diagnostic information about the functioning of a person's specific organs, or to treat them. Diagnostic procedures using radioisotopes are now routine. Radiotherapy can be used to treat some medical conditions, especially cancer, using radiation to weaken or destroy particular targeted cells. Over 40 million nuclear medicine procedures are performed each year, and demand for radioisotopes is increasing at up to 5% annually. Sterilization of medical equipment is also an important use of radioisotopes.[1]

The attributes of naturally decaying atoms, known as radioisotopes, give rise to several applications across many aspects of modern day life .

There is widespread awareness of the use of radiation and radioisotopes in medicine, particularly for diagnosis (identification) and therapy (treatment) of various medical conditions. In developed countries (a quarter of the world population) about one person in 50 uses diagnostic nuclear medicine each year, and the frequency of therapy with radioisotopes is about one-tenth of this.

Nuclear medicine 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 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 closely involved with the use of radioactive tracers in medicine.[2,3]

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 (Tc-99), with some 40 million procedures per year, accounting for about 80% of all nuclear medicine procedures and 85% of diagnostic scans in nuclear medicine worldwide. In developed countries (about one-quarter 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 over 20 million nuclear medicine procedures per year, and in Europe about 10 million, with 2 million of these being therapeutic. In Australia there are about 560,000 per year, 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 PET/CT (positron emission tomography with computerized tomography) procedures have become established, increasing the role of accelerators in radioisotope production. However, the main radioisotopes such as Tc-99m cannot effectively be produced without reactors.

KEYWORDS : nuclear medicine, radioisotopes, radiation, radiotherapy, medical

I. INTRODUCTION

Nuclear medicine uses radioactive isotopes in a variety of ways. One of the more common uses is as a tracer in which a radioisotope, such as technetium-99m, is taken orally or is injected or is inhaled into the body. The radioisotope then circulates through the body or is taken up only by certain tissues. Its distribution can be tracked according to the radiation it gives off. The emitted radiation can be captured by various imaging techniques, such as single photon emission computed tomography (SPECT) or positron emission tomography (PET), depending on the radioisotope used. Through such imaging, physicians are able to examine blood flow to specific organs and assess organ function or bone growth. Radioisotopes typically have short half-lives and typically decay before their emitted radioactivity can cause damage to the patient's body.

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Therapeutic applications of radioisotopes typically are intended to destroy the targeted cells. This approach forms the basis of radiotherapy, which is commonly used to treat cancer and other conditions involving abnormal tissue growth, such as hyperthyroidism. In radiation therapy for cancer, the patient's tumor is bombarded with ionizing radiation, typically in the form of beams of subatomic particles, such as protons, neutrons, or alpha or beta particles, which directly disrupt the atomic or molecular structure of the targeted tissue. Ionizing radiation introduces breaks in the double-stranded DNA molecule, causing the cancer cells to die and thereby preventing their replication. While radiotherapy is associated with unpleasant side effects, it generally is effective in slowing cancer progression or, in some cases, even prompting the regression of malignant disease.[4,5]

Table: Medical applications of radioisotopes

Radioactive Isotope	Applications in Medicine
Cobalt-60	Radiation therapy to prevent cancer
Iodine-131	Locate brain tumors, monitor cardiac, liver and thyroid activity
Carbon-14	Study metabolism changes for patients with diabetes, gout and anemia
Carbon-11	Tagged onto glucose to monitor organs during a PET scan
Sodium-24	Study blood circulation
Thallium-201	Determine damage in heart tissue, detection of tumors
Technetium-99m	Locate brain tumors and damaged heart cells, radiotracer in medical diagnostics (imaging of organs and blood flow studies)

II. OBSERVATIONS

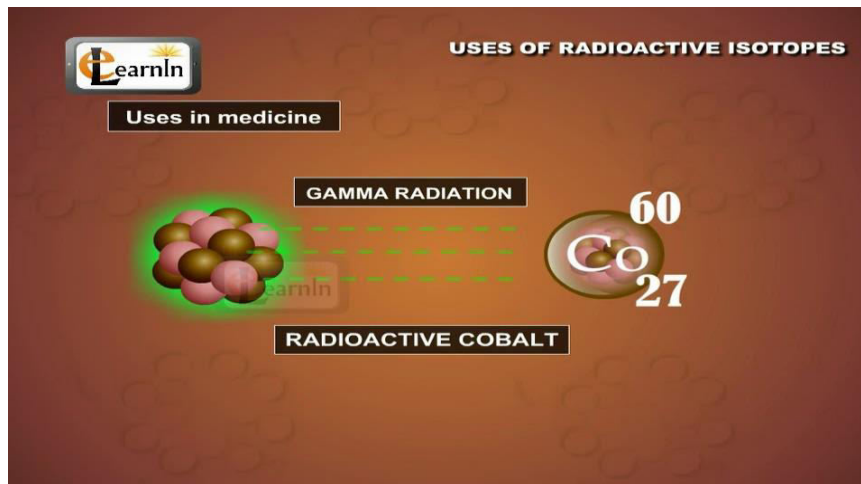
A large number of radionuclides used in nuclear medicine are also produced in nuclear reactors. Nuclear reactor is a device in which the nuclear fission chain reaction takes place, in a controlled manner, for the production of energy and neutrons. Most of the reactor produced radionuclides available for biomedical usages are produced either through the recovery of fission products or by neutron activation of the specific targets. In nuclear fission several radioisotopes and stable isotopes of different elements are produced and very elaborate and extensive processing facilities are required to ensure the production of a particular radioisotope with high radionuclidic purity. The most important advantage of this method is that, several medically useful radionuclides can be obtained with higher specific activity than that obtainable from corresponding neutron activation method. However, the need of highly sophisticated processing facilities with remote handling equipments and good infrastructure for highly active and long-lived waste disposal increases the cost of the radionuclide. In the neutron activation method, the target nucleus first absorbs a neutron and then emits either a gamma photon or a charged particle depending upon the energetics of the reaction. In some cases, multistage neutron capture process involving successive neutron capture also takes place, though this route is of limited utility owing to the production of radionuclide with very low specific activity.

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On the other hand, neutron capture followed by particle emission type reactions has the advantage of involving transmutations thereby providing radionuclides [6,7] with very high specific activity. However, the most common route employed for the production of γ radionuclides used in radiopharmaceuticals is the (n, γ) reaction. The advantage of this method is its inherent simplicity and almost all the elements undergo this reaction, though with varying probabilities. However, specific activity of the radioisotopes obtained by this method is relatively low as the target and product are the isotopes of same element and hence, cannot be separated by any easy means. Many bio-medically important radionuclides, such as, ^{24}Na , ^{99}Mo , ^{153}Sm , ^{165}Dy , ^{166}Ho , ^{177}Lu , ^{186}Re , ^{192}Ir and ^{198}Au) reaction. γ are produced by using the (n, γ) Use of radionuclide generator system is also a popular route for obtaining some of the short-lived radionuclides at the hospital radiopharmacies. Radionuclide generators may be defined as a device containing a longer-lived parent nuclide in equilibrium with its daughter nuclide from which the daughter nuclide with a shorter half-life can be obtained at regular intervals. The radionuclide generator is the most convenient method of making short-lived radionuclides available at long distances from the production site.



Medical radioisotopes

In a longer-lived parent - shorter-lived daughter chain, a fraction of the daughter atoms that undergo radioactive decay is replaced by new daughter atoms formed from the radioactive decay of the parent. The net result of this combination

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of continual growth and decay on the part of the daughter is that the activity of the daughter, while in the presence of the regenerating parent, decreases at a slower rate than in the absence of the parent. Therefore, the apparent half-life of the shorter-lived daughter is increased and in equilibrium mixture equals that of the parent. This provides more time for shipment, permits a longer shelf-life and results in a continuous source of the daughter radionuclide within the user's laboratory. Applications of radioisotopes in human health care are extensively wide-spread and cover both the diagnostic and therapeutic domains. The diagnostic procedures could be performed either by in-vivo use of radiopharmaceuticals or by in-vitro use of radioimmunoassay. On the other hand, therapeutic procedures could be effected either by using the sealed sources or by the systematic administration of radiopharmaceuticals.[8,9]

IV. DISCUSSION

An isotope of iodine (I-131) is used in both the diagnosis and treatment of thyroid cancer. The thyroid will normally absorb iodine to produce the iodine-containing thyroid hormones. An overactive thyroid gland will absorb the radioactive material which can then destroy excess thyroid tissue or any cancer of the thyroid. The material is sometimes used to image cancers in other parts of the body.[10,11]

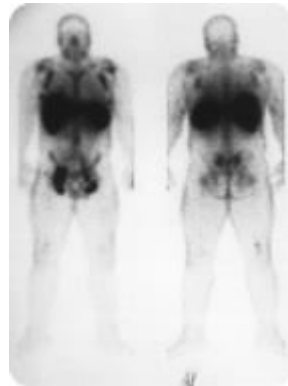


Figure 1. Radioisotope scan to detect tumors.

Technetium-99m is perhaps the most widely used radioisotope in diagnosis and treatment (the "m" stands for metastable). This isotope decays to Tc-99 and a gamma emission of low intensity, making the radiation damage fairly negligible. The half-life is about six hours, so it will remain in the body for some time. Tc-99m can be used to look at cardiac damage. The isotope flows in the blood stream; if there is less blood flow in the heart, there will be less isotope concentrated in the heart muscle. Similar information can be obtained for blood flow in the brain.

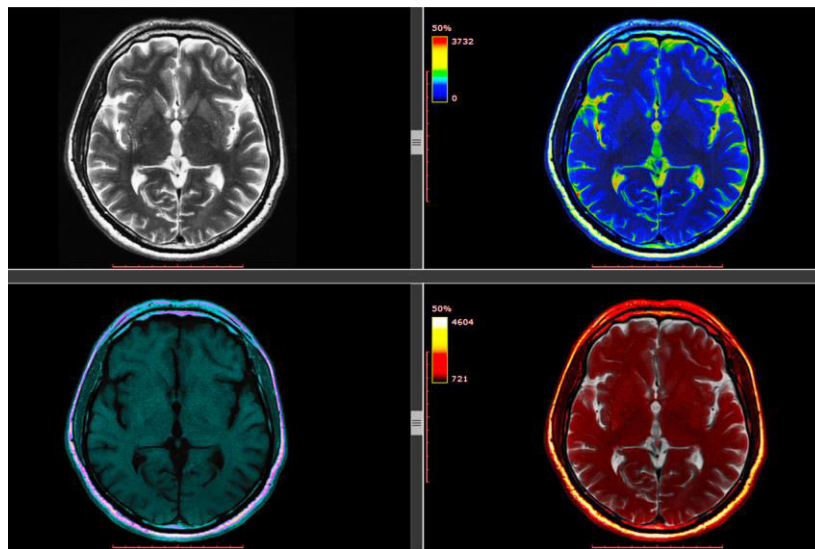
Isotopes can be very useful in scans to locate cancer cells. This patient has multiple tumors that have spread (metastasized) from the main tumor. A radioisotope has been attached to antibodies that bind to specific cancer cells. The very dark spots in the armpits, neck, and groin represent areas where tumor cells exist.[12,13]

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CT Scan

Table: Radioisotopes Employed in Diagnosis and/or Treatment

Isotope	Half-Life	Application
Cr-51	28 days	labeling red blood cells
Fe-59	446 days	study iron metabolism in spleen
Xe-133	5 days	study lung function
Ho-166	26 hours	cancer treatment

V. RESULTS

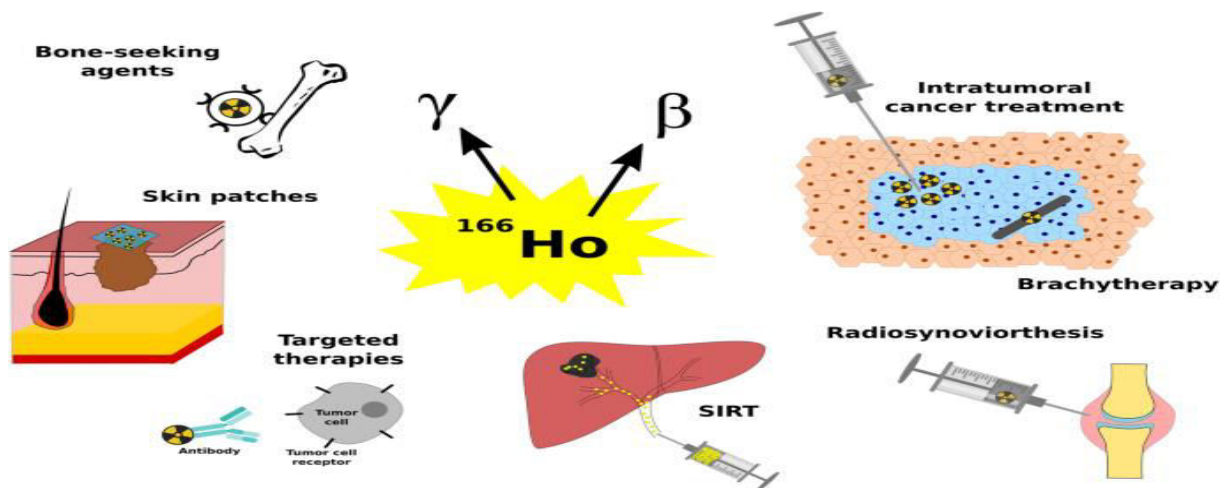
Diagnostic techniques in nuclear medicine use radioactive tracers which emit gamma rays from within the body. These tracers are generally short-lived isotopes linked to chemical compounds which permit specific physiological processes to be scrutinized. They can be given by injection, inhalation or orally. 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.[14,15]

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Application of holmium

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.[16]

New procedures combine PET with CT scans to give co-registration of the two images, enabling 30% better diagnosis than with traditional gamma camera alone.

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.

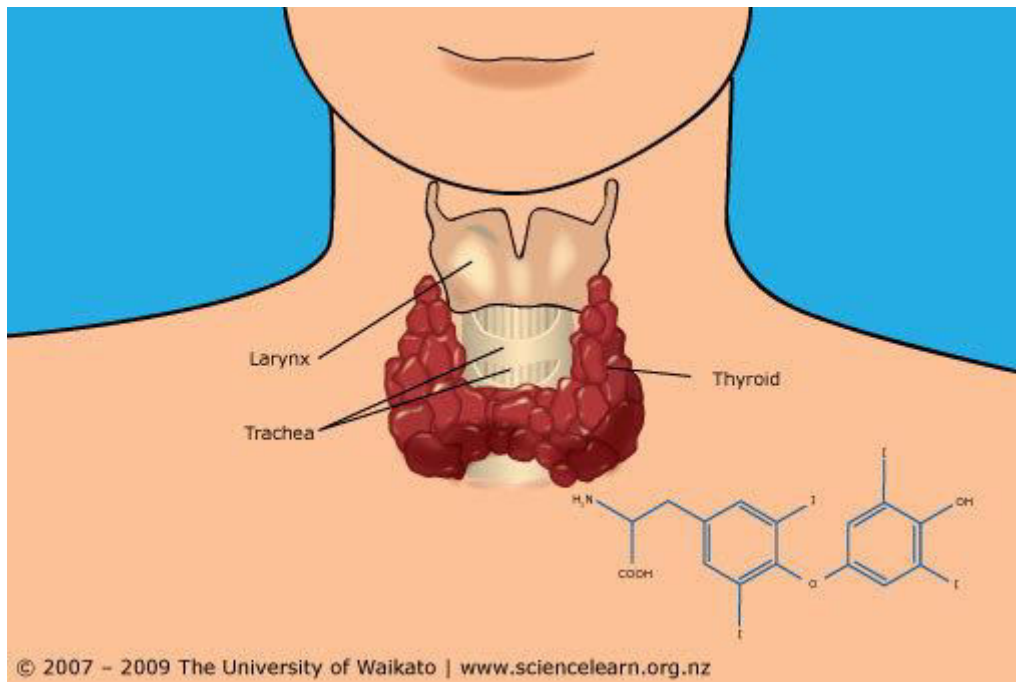
A distinct advantage of nuclear imaging over x-ray techniques is that both bone and soft tissue can be imaged very successfully. This has led to its common use in developed countries where the probability of anyone having such a test is about one in two and rising. The mean effective dose is 4.6 mSv per diagnostic procedure.

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Use of radioisotopes as tracers

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 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).[17]

Internal radiotherapy is by administering or planting a small radiation source, usually a gamma or beta emitter, in the target area. 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.

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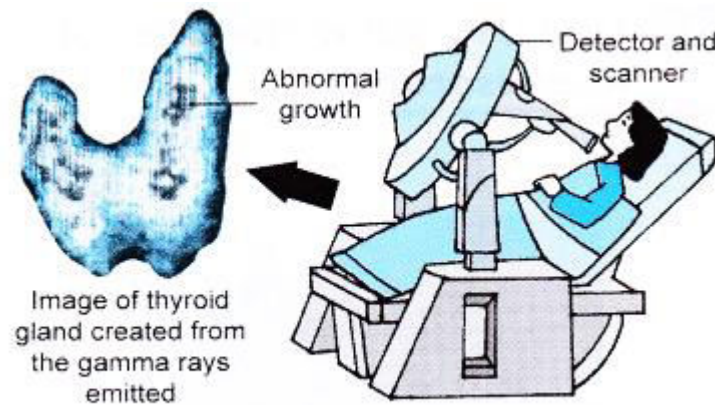
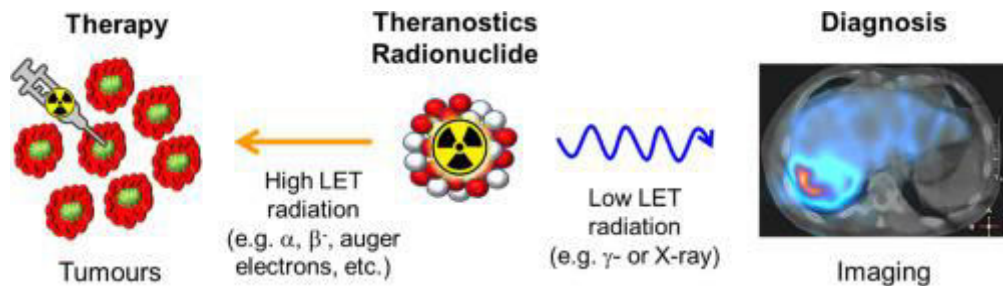


Figure *Imaging of a diseased thyroid gland*

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 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.

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.

VI. CONCLUSIONS

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

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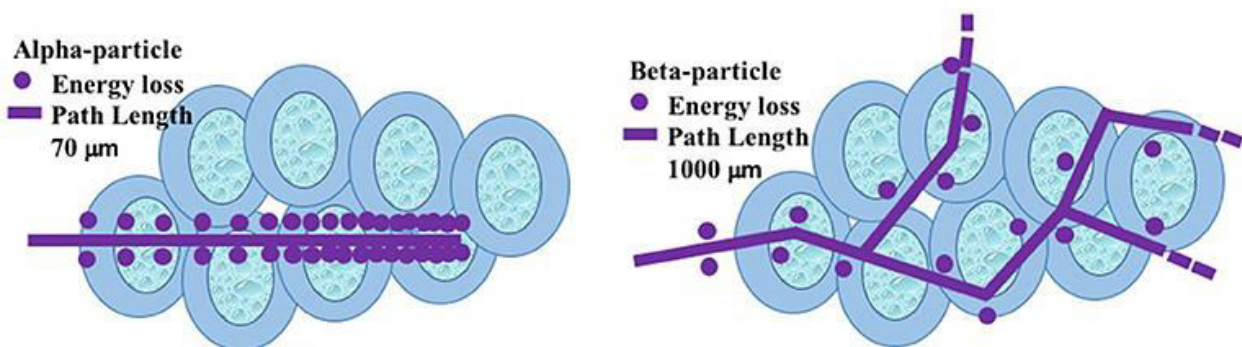
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results. Every organ in our bodies acts differently from a chemical point of view. Doctors and chemists have identified a number of chemicals which are absorbed by specific organs. The thyroid, for example, takes up iodine, the brain consumes quantities 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.[18,19]

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.



Theranostic

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. 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 minimized.

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.

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Radiation studies

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.

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 of a cyclotron.

VII. FUTURE SCOPE

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 radiotherapy. Short-range radiotherapy is known as brachytherapy.

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 beta emitter with just enough gamma to enable imaging, eg lutetium-177.

Iodine-131 and phosphorus-32 are examples of two radioisotopes 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.[20]

A new and still experimental procedure uses boron-10 which concentrates in the tumor. The patient is then irradiated

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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 now, from which the daughter Bi-213 can be obtained (via 3 alpha decays) to label targeting molecules.

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.

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