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ANSWER

1. A radioactive tracer, radiotracer, or radioactive label, is a [chemical compound](https://en.wikipedia.org/wiki/Chemical_compound) in which one or more atoms have been replaced by a [radionuclide](https://en.wikipedia.org/wiki/Radionuclide) so by virtue of its [radioactive decay](https://en.wikipedia.org/wiki/Radioactive_decay) it can be used to explore the mechanism of chemical reactions by tracing the path that the radioisotope follows from reactants to products. Radiolabeling or radiotracing is thus the radioactive form of [isotopic labeling](https://en.wikipedia.org/wiki/Isotopic_labeling).

Radioisotopes of [hydrogen](https://en.wikipedia.org/wiki/Hydrogen), [carbon](https://en.wikipedia.org/wiki/Carbon), [phosphorus](https://en.wikipedia.org/wiki/Phosphorus), [sulfur](https://en.wikipedia.org/wiki/Sulfur), and [iodine](https://en.wikipedia.org/wiki/Iodine) have been used extensively to trace the path of [biochemical reactions](https://en.wikipedia.org/wiki/Biochemistry). A radioactive tracer can also be used to track the distribution of a substance within a natural system such as a [cell](https://en.wikipedia.org/wiki/Cell_(biology)) or [tissue](https://en.wikipedia.org/wiki/Tissue_(biology)),[[1]](https://en.wikipedia.org/wiki/Radioactive_tracer#cite_note-rennie-99-1) or as a [flow tracer](https://en.wikipedia.org/wiki/Flow_tracer) to track [fluid flow](https://en.wikipedia.org/wiki/Fluid_dynamics). Radioactive tracers are also used to determine the location of fractures created by [hydraulic fracturing](https://en.wikipedia.org/wiki/Hydraulic_fracturing) in natural gas production.[[2]](https://en.wikipedia.org/wiki/Radioactive_tracer#cite_note-Reis_iodine-2) Radioactive tracers form the basis of a variety of imaging systems, such as, [PET scans](https://en.wikipedia.org/wiki/PET_scan), [SPECT scans](https://en.wikipedia.org/wiki/SPECT_scan) and [technetium scans](https://en.wikipedia.org/wiki/Technetium-99m). [Radiocarbon dating](https://en.wikipedia.org/wiki/Radiocarbon_dating) uses the naturally occurring [carbon-14](https://en.wikipedia.org/wiki/Carbon-14) isotope as an [isotopic label](https://en.wikipedia.org/wiki/Isotopic_label).

2. **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.**

The attributes of naturally decaying atoms, known as radioisotopes, give rise to several applications across many aspects of modern day life (see also information paper on [The Many Uses of Nuclear Technology](https://www.world-nuclear.org/information-library/non-power-nuclear-applications/overview/the-many-uses-of-nuclear-technology.aspx)).

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.

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 (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 over 20 million nuclear medicine procedures per year, and in Europe about 10 million. 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.

The global radioisotope market was valued at $9.6 billion in 2016, with medical radioisotopes accounting for about 80% of this, and it is poised to reach about $17 billion by 2021. North America is the dominant market for diagnostic radioisotopes with close to half of the market share, while Europe accounts for about 20%.

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 computerised 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.\*

\* Some Tc-99m is produced in accelerators but it is of lower quality and at higher cost.

## Nuclear medicine diagnosis

Radioisotopes are an essential part of medical diagnostic procedures. In combination with imaging devices which register the gamma rays emitted from within, they can study the dynamic processes taking place in various parts of the body.

In using radiopharmaceuticals for diagnosis, a radioactive dose is given to the patient and the activity in the organ can then be studied either as a two dimensional picture or, using tomography, as a three dimensional picture. 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 earliest technique developed uses single photons 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 on a monitor for indications of abnormal conditions. Single photon emission computerised tomography (SPECT) is the current major scanning technology to diagnose and monitor a wide range of medical 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 indications 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 (PET-CT), enabling 30% better diagnosis than with a 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.

Positioning of the radiation source within (rather than external to) the body is 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.

### Diagnositic 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, whilst the brain consumes quantities of glucose. 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 Tc-99, 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, such as with SPECT. These are:

* It has a half-life of six hours which is long enough to examine metabolic processes yet short enough to minimize the radiation dose to the patient.
* It decays by an 'isomeric' process, which involves the emitting of 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.
* The chemistry of technetium is so versatile it can form tracers by being incorporated into a range of biologically-active substances that ensure 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 (Mo-99), with a half-life of 66 hours, which progressively decays to Tc-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 Tc-99 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 towards 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.

## Nuclear medicine therapy

The uses of radioisotopes in therapy are comparatively few, but nevertheless important. Cancerous growths are 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 used as high-energy X-ray sources (gamma and X-rays are much the same). An external radiation procedure is known as gamma knife radiosurgery, and involves focusing gamma radiation from 201 sources of Co-60 on a precise area of the brain with a cancerous tumour. Worldwide, over 30,000 patients are treated annually, generally as outpatients. Teletherapy is effective in the ablation of tumours rather than their removal; it is not finely tuned.

Internal radionuclide therapy is administered by 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. Permanent implant seeds (40 to 100) of iodine-125 or palladium-103 are used in brachytherapy for early stage prostate cancer. Alternatively, needles with more-radioactive Ir-192 may be inserted for up to 15 minutes, two or three times. Brachytherapy procedures give less overall radiation to the body, are more localized to the target tumour, and are 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.

Lutetium-177 dotatate or octreotate is used to treat tumours such as neuroendocrine ones, and is effective where other treatments fail. A series of four treatments delivers 32 GBq. After about four to six hours, the exposure rate of the patient has fallen to less than 25 microsieverts per hour at one metre and the patients can be discharged from hospital. Lu-177 is essentially a low-energy beta-emitter (with some gamma) and the carrier attaches to the surface of the tumour.

A new field is targeted alpha therapy (TAT) or alpha radioimmunotherapy, especially for the control of dispersed (metastatic) 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 such as a monoclonal antibody has taken the alpha-emitting radionuclide such as bismuth-213 to the areas of concern. Clinical trials for leukaemia, cystic glioma, and melanoma are underway. TAT using lead-212 is increasingly important for treating pancreatic, ovarian, and melanoma cancers.

An experimental development of this is Neutron Capture Enhanced Particle Therapy (NCEPT) which involves injecting a patient with a neutron capture agent shortly before irradiation with protons or heavy ions. This approach boosts the target dose without increasing the dose to healthy tissue and delivers a significant dose to secondary lesions outside the primary treatment area. It uses boron-10 or gadolinium-157 which concentrate in malignant brain tumours. The patient is then irradiated with thermal neutrons or protons 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 more 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.

Treatment may involve significant radioactivity (e.g. 4.4 GBq is quoted as an average dose of I-131 for thyroid ablation, and up to 11 GBq for patients with advanced metastatic disease). According to US regulatory guidelines for I-131, the patient can be released if the activity is below 1.2 GBq, or 0.07 mSv/hr at 1 metre. Meanwhile a lot of I-131 is flushed down the hospital toilet and plumbing needs to be shielded accordingly.

### 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 (e.g. 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 liver cancer, and it is being used more widely, including for arthritis treatment. Lu-177 and Y-90 are becoming the main RNT agents.

Iodine-131, samarium-153, and phosphorus-32 are also used for therapy. I-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. P-32 is used to control this excess.

Caesium-131, palladium-103, and radium-223 are also used for brachytherapy, all being Auger (soft) X-ray emitters, and having half-lives of 9.7 days, 17 days, and 11.4 days, respectively, much less than the 60 days of I-125 which they replace.

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. This is boron neutron capture therapy.

For targeted alpha therapy (TAT), actinium-225 is used, from which the daughter bismuth-213 can be obtained (via three 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 Ac-225 (half-life 10 days) is formed from radioactive decay of radium-225, the decay product of long-lived thorium-229, which is obtained from decay of uranium-233, which in turn is formed from thorium-232 by neutron capture in a nuclear reactor. A Th-229/Ac-225 generator is eluted about eight times per year at ORNL, but output is limited. Ac-225 itself is an alpha-emitter and may be used directly, bonded to a protein or antibody such as PSMA for prostate cancer. Larger quantities of Ac-225 are being produced in Canada by TRIUMF with a high-energy proton beam on a Th-232 target.

Another radionuclide recovered from Th-232, but by natural decay via thorium-228, is Pb-212, with a half-life of 10.6 hours. Pb-212 can be attached to monoclonal antibodies for cancer treatment by TAT. A Ra-224/Pb-212 generator system similar to the Mo-99/Tc-99 one is used to provide Pb-212 from Ra-224 (via Ra-220 and polonium-216 (po-216)). Pb-212 has a half-life of 10.6 hours, and beta decays to Bi-212 (1 hour half-life), then most beta decays to Po-212. The alpha decays of Bi-212 and Po-212 are the active ones destroying cancer cells over a couple of hours. Stable Pb-208 results, via Tl-208 for the bismuth decay.

TAT also uses Ra-223, Th-227, Ac-225 and astatine-211.

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.

## Sterilisation

Many medical products today are sterilised by gamma rays from a Co-60 source, a technique which generally is much cheaper and more effective than steam heat sterilisation. The disposable syringe is an example of a product sterilised by gamma rays. Because it is a 'cold' process radiation can be used to sterilise a range of heat-sensitive items such as powders, ointments, and solutions, as well as biological preparations such as bone, nerve, and skin to be used in tissue grafts. Large-scale irradiation facilities for gamma sterilisation are installed in many countries. Smaller gamma irradiators, often utilising Cs-137, having a longer half-life, are used for treating blood for transfusions and for other medical applications.

Sterilisation by radiation has several benefits. It is safer and cheaper because it can be done after the item is packaged. The sterile shelf-life of the item is then practically indefinite provided the seal is not broken. Apart from syringes, medical products sterilised by radiation include cotton wool, burn dressings, surgical gloves, heart valves, bandages, plastic, and rubber sheets and surgical instruments.