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Effective half life of technetium 99m

The radioactive half-life for a given radioisotope is physically determined and unaffected by the physical or chemical conditions around it. However, if that radioisotope is in a living organism it may be excreted so that it no longer is a source of radiation exposure to the organism. For a number of radioisotopes of particular medical interest, the rate of excretion has been cast in the form of an effective biological half-life. The rate of decrease of radiation exposure is then affected by both the physical and biological half-life, giving an effective half-life for the isotope in the body. Though the biological half-life cannot be expected to be as precise as the physical half-life, it is useful compute an effective half-life from 1/TEffective = 1/TPhysical +1/TBiological
Examples of the half-lives show that biological clearing is sometimes dominant and sometimes physical decay is the dominant influence. Isotope Half-lives in days
TPhysicalTBiologicalTEffective
3H4.5 x 1031212
32P14.3115514.1
90Sr1.1 x 1041.8 x 1046.8 x 103
99mTc0.2510.20
Tritium, 3H, has a fairly long physical halflife but clears from the body quickly, lessening the exposure. Phosphorous, 32P, is used for some kinds of bone scans. The phosphorous tends to be held in the bones, leading to a long biological half-life, but its physical half-life is short enough to minimize exposure. Strontium, 90Sr, is very bad news in the environment. It mimics calcium and therefore gets trapped in bone. This gives it a long biological half-life to go with its long physical half-life, making it doubly dangerous. Technetium, 99mTc, is one of the favorites for diagnostic scans because of short physical and biological half-lives. It clears from the body very quickly after the imaging procedures.
Table of Physical, Biological, and Effective Half-lives
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Technetium-99m is a nuclear isomer of Technetium 99. It is a radioactive substance that radiates "Gamma Rays". Technetium 99m Symbol It is symbolized as 99mTc. The metastable state of the nuclear isomer is indicated by the "m". This state is created by exciting the nucleons (neutrons or protons) of an atomic nucleus. Technetium-99m Radiation This nuclear isomer is radioactive and it radiates "Gamma Rays" (γ). When a radioactive substance is undergoing decay, the time it takes to decrease by half is indicated as its half-Life. Technetium 99m undergoes gamma radiation and it takes 6 hours to decrease by half. That means the half-life of this substance is 6 hours. It has a considerably long half-life considering the fact that it emits gamma-ray. Usually, the half-life of radioisotopes undergoing gamma decay is too short. Technetium-99m production
Technetium 99m is not a natural but an artificially produced substance. It is the product of Molybdenum 99 (99Mo) caused by radioactive decay (decay-product). To produce this nuclear isomer, Molybdenum 98(98Mo) is first bombarded with a neutron. This produces 99M that has a half-life of 66 hours. The 99M decays to produce metastable Technetium (Tc) or 99mTc. Producing Technetium 99m in this process is allowed only for medical purposes.
Picture 1 – Technetium-99m Source – faculty.virginia.edu
Technetium 99m Generator
Technetium 99m Generator is the name for the device used to produce metastable Technetium. With the help of this generator, 99mTc is extracted from decaying Molybdenum 99. 99Mo has a long half-life of 66 hours. So, the generator and the 99Mo can easily be carried away to the place where the decay product 99mTc is required.
Technetium-99m Properties
Here are some basic properties of this nuclear isomer:
Atomic Number
The atomic number of Technetium 99m is 43.
Atomic Weight
The atomic weight of this substance is 99.
Physical State
It is a radioactive metal which is silver-grey in color.
Solubility
99mTc is soluble in Nitric Acid, Aqua Regia and concentrated Sulfuric Acid. It is insoluble in Hydrochloric Acid.
Technetium 99m in Nuclear Medicine
Radioactive isotopes are used in Nuclear Medicine. The radioactive decay of the isotopes is relied upon to diagnose and treat the patient. The function of this branch of medicine depends on the concept that the body reacts to substances differently when there is a disease present. To diagnose the disease, the radioactive substance is bound to another chemical substance that can work inside the body without causing any harm. After that, both the chemicals are transported inside the body. As a result, the radioactive isotope can work as a medical tracer from inside the body. It can be detected by special medical equipments. As 99mTc has a much longer half life than other gamma ray radiating isotopes, it is very useful in the field of nuclear medicine.
Technetium 99m in Bone Scan
It is widely used to scan fractures and other problems of bones.
Ligand
Methylene-Diphosphonate (MDP) is a substance that is easily taken up by the bones. So, Technetium 99m is chemically attached to it to be easily transported to the bones via hydroxyapatite for imaging. In this way, the diagnosis of the bones can be easily done.
Technetium 99m Albumin Aggregated (MAA)
It is the name of a radiopharmaceutical substance. It is used in nuclear medicine. The MAA is an injectable substance.
Technetium 99m Medicines
The names of the principal medicines of 99mTc are:
Technetium sestamibi or Cardiolite (trade name)
Technetium tetrofosmin or Myoview (trade name)
Technetium 99m Uses
It is used as a medical tracer in radioactive isotope medical tests. 99mTc is used in the treatment of the following diseases:
Brain Myocardium
Thyroid Lunges
Liver Gallbladder
Kidney Skeleton
Blood Tumors
Technetium-99m Benefits
Some of the main benefits of using this radioactive substance are mentioned below:
The principal benefit of this radioactive substance is its long half life. 6 hours is long enough for various medical examinations to be done. Also, it is short enough for the99mTc to be eliminated from the system without causing any harm. The radiation dose to the patient remains low because 99mTc emits gamma-ray. 99mTc can be tagged or attached to a variety of chemicals so that it can be used for the treatment of various parts of the human body. It emits the 140 keV gamma rays, which is readily detectable. It is one of the most useful radioactive isomers and is widely used in nuclear medicine. It can only be produced artificially for medicinal purposes.
Technetium 99m has great contribution in the advancement of nuclear medicine.
References:
99Mo could be produced by bombarding an enriched 100Mo target with energetic photons (bremsstrahlung), which are produced by bombarding a heavy metal target, such as Ta, W, and Pb, with high-energy electrons in an accelerator (Bennett et al., 1999).From: Comprehensive Biomedical Physics, 2014Tsay-Jung Wu, ... Nenad L. Ignjatović, in Nanotechnologies in Preventive and Regenerative Medicine, 2018Radiolabeling with 99mTc (half-life 6 h) accounts for about 80% of all nuclear medicine procedures worldwide. This can be attributed to its ideal physical properties, such as its half-life, that allow for prolonged in vivo imaging and γ-photon single-energy emission at 140 keV, which is beneficial for effective imaging. The chemical form of 99mTc occurs as 99mTc-pertechnetate Tc99mO4−. In a chemical reaction, it is necessary to reduce its oxidation state to a lower value. Stannous chloride (SnCl2) is the most often used reducing agent. The direct method of 99mTc labeling of NPs is based on the fact that the reduced 99mTcO4 reacts with random groups, such as hydroxyl, carboxylic, and amino groups, present on the surface of the NPs. A direct labeling method was used to label hydroxyapatite nanoparticles (HAPNP).10 as well as astaxanthin-loaded solid lipid NPs. The direct nose-to-brain delivery of the 99mTc-labeled lipid NPs was evident by y-scintigraphy imaging, suggesting their potential use for various neurological diseases.11 Tassano et al. developed another direct labeling procedure via a tricarboxyl precursor Tc99mH2OCCO3+ for radiolabeling dendrimers.12 This method has been proven to be effective for labeling various ligands, such as ethylenediamine-N,N'-diacetate, which have significant tumor uptake exclusively by passive targeting.13 NPs loaded with these compounds have a higher probability for tumor uptake.Radiometals, both diagnostic (64Cu, 68Ga, and 89Zr) and therapeutic (90Y and 177Lu), are best attached to NPs via chelation. The indirect chelator-mediated 99mTc-labeling of NPs has been applied to a variety of NP structures.14 Helbok et al. performed efficient radiolabeling of PEGylated cholesterol liposomes and micelles via an acyclic diethylenetriaminepentaacetic acid (DTPA) chelator.15 Also, poly(ethylene) glycol (PEG) liposomes can be labeled relatively easily and stably with 99mTc after liposome synthesis, using a procedure which includes the conjugation of 99mTc to hexamethyl propyleneamine (HMPAO)16 or hydrazino nicotinamide (HYNIC)17 followed by their encapsulation into liposomes. The HYNIC-based method provides 99mTc-labeled liposomes with a high labeling yield (>95%) and improved in vitro and in vivo characteristics compared to the liposomes labeled via 99mTc-HMPAO. Chitosan (Ch) hydrogel NPs loaded with a vascular endothelial growth factor (a potent angiogenic factor) were efficiently labeled with 99mTc via a DTPA chelator. The quantitative imaging with 99mTc-Ch NPs has been demonstrated to be a valuable strategy that can be combined with an angiogenic therapy to customize the treatment of myocardial ischemia.18 Mercapto acetyl triglycine (MAG3) has been applied to facilitate radiolabeling of morpholinos.19 meso-2,3-Dimercaptosuccinic acid (DMSA) is also a suitable ligand that forms complex compounds with 99mTc, 186/188Re, 166Ho, 177Lu, and 90Y. DMSA enables bidentate binding via two sulfur atoms on silver nanoclusters (Fig. 1.4.4) and additional radiolabeling is possible via the binding of radiometals to DMSA.20Figure 1.4.4. Bidentate-Binding of meso-2,3-Dimercaptosuccinic Acid (DMSA) on Silver Nanoclusters.Reproduced from Zaluzhna O, Brightful L, Allison TC, Tong YJ. Spectroscopic evidence of a bidentate-binding of meso-2,3-dimercaptosuccinic acid on silver nanoclusters. Chem Phys Lett 2011;509(4):148–51.20In some chelating systems it is possible to apply a theranostic approach by substituting the diagnostic radionuclide with a therapeutic one, whereas the chelator and the nanodimensional structure remain. Due to the similar chemical properties of 99mTc for 188Re, the labeling procedure is based on the similar complexation chemistries of two radionuclides with the same vector.Further studies on indirect NP 99mTc-labeling may include the investigation of novel ligands, such as diamino dioxime ligands that form a neutral and lipophilic complex with 99mTc. The specified ligand and those that are chemically similar to it pass easily through the intact blood–brain barrier. Accordingly, they have a high potential in cerebral perfusion imaging.21 Iron oxide nanoparticles (IONPs) may be labeled with a variety of diagnostic and therapeutic radionuclides via direct and indirect, chelator-based radiolabeling techniques. The 99mTc-labeled aminosiolane-coated IONPs may be promising candidates for guided cancer diagnosis and magnetic hyperthermia therapy. Targeting is enabled via the conjugation with a new peptide-based Arg-Gly-Asp (RGD) derivate, which has a high affinity and selectivity for the αvβ3 integrin receptor presented in several tumors. The specific character of 99mTc-NPs-RGD was confirmed in a receptor blocking study, in which the coadministration of an excess amount of the native peptide blocked an experimentally induced U87MG tumor (with an overexpression of the αvβ3 receptors). This resulted in a significantly reduced uptake of 99mTc-NPs-RGD, indicating the specific character of the targeted IONPs (Fig. 1.4.5).22Figure 1.4.5. Active Targeting.Representative planar y images of 99mTc-NPs-[Arg-Gly-Asp (RGD)] (A) nonblocked and (B) blocked] of a U87MG tumor–bearing mouse at 1 h post-injection.Reproduced from Tsiapa I, Efthimiadou EK, Fragogeorgi E, Loudos G, Varvarigou AD, Bouziotis P, et al. 99mTc-labeled aminosiolane-coated iron oxide nanoparticles for molecular imaging of αvβ3-mediated tumor expression and feasibility for hyperthermia treatment. J Colloid Interf Sci 2014;433:163–75.22Simon R. Cherry PhD, ... Michael E. Phelps PhD, in Physics in Nuclear Medicine (Fourth Edition), 2012The 99Mo-99mTc generator produces technetium in the form of . A number of "cold kits" are available that allow different 99mTc complexes to be produced by simply mixing the and the contents of the cold kit together. The cold kit generally contains a reducing agent, usually stannous chloride, which reduces the 99mTc to lower oxidation states, allowing it to bind to a complexing agent (also known as the ligand) to form the radiopharmaceutical. Using these kits, a range of 99mTc-labeled radiopharmaceuticals that are targeted to different organ systems and different biological processes can be prepared quickly and conveniently in the hospital setting. Table 5-5 lists a few examples of 99mTc radiopharmaceuticals that are prepared from kits.K. Hashimoto, Y. Nagai, in Comprehensive Biomedical Physics, 2014Bremsstrahlung and accelerator neutrons have not yet been used to produce medical radionuclides mainly because both bremsstrahlung and neutron fluxes are much lower than the neutron flux in reactors. Recently, however, significant progress has been achieved in both accelerator and target technology, which could allow one to obtain and use high-flux bremsstrahlung and high-intensity accelerator neutrons. These advances provide researchers with the opportunity to develop new techniques to produce medical radionuclides that previously have been produced only in reactors, such as 99Mo and 90Y (Nagai and Hatsukawa, 2009; Ruth, 2009) and also, for example, neutron-depleted positron emitters such as 11C, 13N, and 15O by direct bremsstrahlung irradiation of inactive pharmaca for PET imaging. About 95–99% of all 99Mo, the mother radionuclide of the most widely used SPECT radionuclide 99mTc, is produced by the irradiation of a highly enriched 235U (HEU) target, and less than 5% of the global 99Mo production is derived from the irradiation of a low enriched 235U target. Because most existing reactors, which have been producing 99Mo using HEU, are approaching the ends of their lifetimes, we must seek alternative techniques to produce 99Mo to ensure a constant and reliable supply (Ballinger, 2010). Using an accelerator to produce 99Mo and/or 99mTc is a promising technique, owing to significant advances in accelerator technologies, as mentioned above. In addition, an accelerator production method is in line with the reduced enrichment for research and test reactors program (Goldman et al., 2008). In fact, extensive studies to produce 99Mo and/or 99mTc have been carried out using accelerators, as discussed below.
99Mo production by the 100Mo(γ, n)99Mo reaction or the photofission of 238U99Mo could be produced by bombarding an enriched 100Mo target with energetic photons (bremsstrahlung), which are produced by bombarding a heavy metal target, such as Ta, W, and Pb, with high-energy electrons in an accelerator (Bennett et al., 1999). 99Mo could be also produced by the photofission reaction of depleted uranium, 238U(γ, fission) (Ruth, 2009). Note that processing of fission products is similar to the existing procedure of processing 235U fission products in reactors.
99Mo production by 98Mo(α, n)γ99Mo99Mo may be produced by a neutron capture reaction by a 98Mo target, in which neutrons are produced by bombarding a heavy metal target, such as Pb, Ta, and liquid mercury, with an energetic high-power proton beam (1 GeV 1 mA) via spallation reactions.
99Mo production by the 100Mo(α, n)99Mo reaction99Mo could be produced by the 100Mo(α, n)99Mo reaction using accelerator neutrons (Minato and Nagai, 2010; Nagai and Hatsukawa, 2009). Note that the 100Mo(α, n)99Mo reaction cross-section is as large as about 1.5 barn in the neutron energy range between 12 and 17 MeV, while the 100Mo(α, n)97Zr, 100Mo(α, n)99Nb, and 100Mo(α, n)100Nb reaction cross-sections to produce radioactive impurities are less than a few mbarn at a neutron energy of about 14 MeV. Intense, ~ 14 MeV, neutrons with a flux of 1012 n s− 1 are obtained by bombarding a tritiated Ti target with deuterons. In fact, such neutrons are produced using an accelerator at the Facility of Neutronics Source at the Japan Atomic Energy Agency, as shown in Figure 8. An accelerator to produce intense neutrons with a high flux of 1015 n s− 1 (1014 n cm− 2 s− 1 within 20° with respect to the projectile beam direction) with a most probable energy of 14 MeV is being installed at SPIRAL2 in GANIL in France (Fadil and Rannou, 2008). Neutrons are produced by bombarding a natural carbon target with 40 MeV 5 mA deuterons.
Figure 8. An accelerator at the Facility of Neutronics.Source: Japan Atomic Energy Agency.Sooyoung Oh, in Reference Module in Earth Systems and Environmental Sciences, 2020The RIs being produced in HANARO include 131I, 99mTc by (n,γ) reaction, 192Ir, 166Ho, and so on for the medical and industrial sectors (Park et al., 2010). A target material is encapsulated in an aluminum RI capsule for the irradiation in HANARO. An irradiated capsule is put in a cask and transported to the RI production facility (RIPF). The RIPF has four banks and each bank consists of various number of concrete or lead hot cells. Each bank, except Bank II that is a multi-purpose bank, has a production line dedicated to specific RI products: Bank I for 192Ir source for non-destructive test equipment, Bank III for iodine pharmaceuticals such as 131I metaiodobenzylguanidine (mIBG), and Bank IV for 99m Tc and 188Re generators.The RI-related R&Ds in HANARO extend to radioisotope thermoelectric generators, micro battery, radiolabeled compounds for medical use, and radiotracers and systems for the diagnosis of, for instance, a petro-chemical plant during operation. In addition, HANARO has developed a technology of 99Mo production by fission using a low enriched uranium target. The technology will be implemented in the Kijang research reactor (Park et al., 2014a), which is under construction in Korea.James Nairne, ... Andreas Meijer, in Progress in Medicinal Chemistry, 2015Technetium-99m is produced relatively inexpensively using a generator. Molybdenum-99 suspended on an alumina column decays (t½ = 66 h) to form technetium-99m. The singly charged 99mTcO4− is eluted in preference to the doubly charged 99MoO42− using saline. Commercially available technetium-99m radiotracers are generally prepared by the simple addition of technetium-99m eluted from the generator to a kit vial containing a freeze-dried formulation of the active ingredient. The technetium-99m half-life of 6 h allows time for preparation of the radiotracer, distribution and patient imaging. The energy of the γ-ray emission (140 keV) is ideal for imaging using gamma cameras.Technetium has a rich coordination chemistry with several potential oxidation states [19]. Most nuclear imaging agents contain technetium-99m in the + 5, + 3 or + 1 oxidation states, although it is also present in the + 7 oxidation state in the thyroid imaging agent 99mTcO4−, as formed in the generator. Technetium has good affinity for nitrogen, oxygen, phosphorus and sulphur in the most common oxidation states. The preparation of technetium-99m imaging agents is relatively straightforward (Scheme 1): a kit comprising a reducing agent, usually stannous chloride, a weak chelating agent and the cheland is treated with the generator eluate and the mixture incubated for a short time, often at room temperature, giving a preparation that is ready for injection without purification.Scheme 1. Formation of 99mTc-HMPAO (hexamethylpropyleneamine oxime).Approximately 85% of nuclear medicine diagnostic imaging procedures are still done with technetium-99m. The three most widely used technetium-99m tracers in the USA are 99mTc-Sestamibi (Cardiolite) and 99mTc-Tetrofosmin (Myoview) (Figure 6) primarily for imaging myocardial perfusion and 99mTc-MDP (methyleneidiphosphonate) for imaging bone metastases. The delivery of these tracers to the organ of interest is based on a non-target specific localisation mechanism.
Figure 6. Structures of 99mTc-Sestamibi and 99mTc-Tetrofosmin.99mTc-Sestamibi and 99mTc-Tetrofosmin are also both transport substrates recognised by the multidrug resistance (MDR) P-glycoprotein (Pgp). Pgp can confer resistance to many cytotoxic cancer therapeutics. 99mTc-Sestamibi has been used in cancer clinical trials to predict the response to chemotherapy. In a recent meta-analysis, lung cancer patients who had less 99mTc-Sestamibi initial uptake in tumours were found to be less likely to respond to chemotherapy. The sensitivity, specificity and accuracy of 99mTc-Sestamibi in identifying chemotherapy responders were 94%, 90% and 92%, respectively [20].
Fred A. Mettler Jr. MD, MPH, Milton J. Guiberteau MD, in Essentials of Nuclear Medicine Imaging (Sixth Edition), 2012A licensee may not administer a radiopharmaceutical that contains more than 0.15 μCi (55 kBq) of molybdenum-99 (99Mo) per mCi (MBq) of 99mTc. Persons using 99Mo/99mTc generators are required by the NRC to measure the 99Mo concentration in the first eluate after receiving the generator; however, SNM guidelines indicate this must be done for every elution. Records must include the 99Mo/99mTc ratio, time and date of the measurement, and the name of the individual who made the measurement. The record must be retained for 3 years.Penelope Allisy-Roberts OBE FIPEM FlnstP, Jerry Williams MSc FIPEM, in Farr's Physics for Medical Imaging (Second Edition), 2008This usually involves the simple mixing or shaking at room temperature of the radionuclide (e.g. 99mTc as sodium pertechnetate) with the compound to be labelled (e.g. MDP) and other necessary chemicals. Shielded syringes are used to transfer the components between sterile vials. The manipulations are carried out under sterile conditions in a workstation, for example a glove box or a sterile laminar down-flow cabinet that admits the entry of hands etc. through a curtain of air flowing down across the open face of the cabinet. The cabinet is located in a room that is under a positive pressure of filtered sterile air.All surfaces are impervious: continuous floors, gloss-painted walls, and formica-topped or stainless steel benches. Entry is via an air lock and changing room. Normal sterile procedures are followed. The radiopharmacy must meet the conditions of both the Medicines Act and the Ionising Radiations Regulations in the UK, or the relevant regulations in other countries.With preparation time being necessarily short for PET radiopharmaceuticals, automated synthesis devices using microprocessor control are commonly used. These also greatly reduce the radiation exposure of the staff.Quality control includes testing for:
•radionuclide purity – for example testing for contamination with 99Mo, which would give an unnecessary dose to the patient, by measuring any gamma radiation from 99Mo after blocking off the gamma rays from 99mTcm with 6 mm lead-radiochemical purity – for example testing for free pertechnetate in a labelled 99mTcm compound using chromatography-chemical purity – for example the spot colour test for alumina, which may have come from the 99Mo column and would interfere with labelling-sterility testing and pyrogen testing – the results of which are available only retrospectively, for example after the main part of the eluant has been used•response of the radionuclide calibrator (see section 8.7) – for example to a standard source with a long half-life.Gilles Bignani, in Reference Module in Earth Systems and Environmental Sciences, 2020The JHR objectives for this radioisotope are to be able to produce an annual volume of 25% of European needs on an average basis and up to 50% of European needs in peak production. For this, production must be flexible according to customer's needs.Irradiation capacity for Moly production will be flexible according to customer's orders and may be extended for limited periods as following:
•Weekly maximum capacity: up to 4800 99Mo Curies (Ci)/6-days week
•Yearly maximum capacity: up to 115,200 99Mo Ci/year.The Moly facility has been designed for this production capacity, while integrating safety and operational constraints. From the beginning, the Moly irradiation devices will use Low Enriched Uranium (LEU) targets.The facility is composed of two main parts:•the in-pile part in the reactor pool, which includes four Moly device vessels with the target holder, a movable system, underwater lines up to the piping penetrations and two safety pumps;•the out-of-pile part is composed of the piping penetrations allowing the junction between the in-pile cooling circuit and out-of-pile cooling circuit, equipment for instrumentation and control system (I & C) and power supply.In the JHR beryllium reflector, a reflector sector has been designed to accommodate the four Moly devices and their movable system (Fig. 6 below), in order to provide a large production capacity with the greatest flexibility.
Fig. 6. Implementation of the Moly devices in the JHR reflector.Richard J. Davey, James P. Aubuchon, in Blood Banking and Transfusion Medicine (Second Edition), 200799mTc, which is widely employed as an imaging agent in nuclear medicine, is another useful red cell label. This metastable radionuclide is produced in a molybdenum generator as a product of molybdenum-99 decay. 99mTc decays, in turn, to 99Tc, with a half-life of 6.02 hours. In doing so, 99mTc emits a gamma-photon at 140 keV, which falls within the optimal range of gamma counters. The high yield (90%) of this radionuclide is useful for external imaging. Because of the frequent use of this radionuclide in imaging procedures, many hospitals maintain a generator on site, and thus there is a readily available and inexpensive source of 99mTc for cell labeling applications.99mTc, as pertechnetate, diffuses across the red cell membrane into the cell, where it binds to hemoglobin and other intracellular ligands with a labeling efficiency of about 90%. The short half-life of 99mTc precludes its use for long-term red cell survival studies. In fact, groups of samples must be counted rapidly, and, even with that, a correction must be made for radioactive decay that occurs during the counting procedure. However, because of its short half-life, 99mTc is useful as a red cell label when a series of survival