Technetium-99m

Technetium-99m (99mTc) is a generator-produced isotope that is readily available and has a number of advantages over 201Tl for gamma camera imaging.

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Imaging in Drug Development

James Nairne, ... Andreas Meijer, in Progress in Medicinal Chemistry, 2015

3.1.1 Technetium-99m Tracers

Technetium-99m is produced relatively inexpensively using a generator. Molybdenum-99 suspended on an alumina column decays ($t_{1/2}$ = 66 h) to form technetium-99m. The singly charged $^{99m}TcO_4^-$ is eluted in preference to the doubly charged 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 , 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.

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 ^{99m}Tc-Sestamibi (Cardiolite) and ^{99m}Tc-Tetrofosmin (Myoview) (Figure 6) primarily for imaging myocardial perfusion and ^{99m}Tc-MDP (methylenediphosphonate) for imaging bone metastases. The delivery of these tracers to the organ of interest is based on a non-target specific localisation mechanism.

^{99m}Tc-Sestamibi and ^{99m}Tc-Tetrofosmin are also both transport substrates recognised by the multidrug resistance (MDR) P-glycoprotein (Pgp). Pgp can confer resistance to many cytotoxic cancer therapeutics. ^{99m}Tc-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 ^{99m}Tc-Sestamibi initial uptake in tumours were found to be less likely to respond to chemotherapy. The sensitivity,

specificity and accuracy of ^{99m}Tc-Sestamibi in identifying chemotherapy responders were 94%, 90% and 92%, respectively [20].

Thyroid, Parathyroid, and Salivary Glands

Fred A. MettlerJr. MD, MPH, Milton J. Guiberteau MD, in Essentials of Nuclear Medicine Imaging (Sixth Edition), 2012

Technetium-99m

Technetium-99m pertechnetate is trapped by the thyroid in the same manner as iodides but is not organified; therefore, it is released over time as unaltered pertechnetate (^{99m}TcO4–) ion. Its short physical half-life of 6 hours and principal gamma energy of 140 keV are ideal for gamma camera imaging (greater than 90% efficiency with a ½-inch-thick crystal). These physical characteristics and its ready availability are distinct advantages for thyroid scanning. In addition, the low absorbed dose to the thyroid permits administration of higher doses and therefore allows for more rapid imaging of the gland with minimal motion artifact. Only 1% to 5% of administered ^{99m}Tc-pertechnetate is normally trapped by the thyroid, so image background levels are higher than those with radioiodine. On a ^{99m}Tc-pertechnetate scan, the salivary glands are usually well seen in addition to the thyroid. As a result, unless a patient is hyperthyroid, a ^{99m}Tc scan can usually be distinguished from an ^{123}I scan by excellent visualization of the salivary glands. Technetium-99m pertechnetate is preferred over radioiodine when the patient has recently received thyroid-blocking agents (such as iodinated contrast agents) or is unable to take medication orally or when the study must be completed in less than 2 hours.

Genitourinary System and Adrenal Glands

Fred A. MettlerJr. MD, MPH, Milton J. Guiberteau MD, in Essentials of Nuclear Medicine Imaging (Sixth Edition), 2012

Glomerular Filtration Agents

Technetium-99m diethylenetriamine pentaacetic acid (DTPA) is the radiopharmaceutical used for the evaluation of glomerular filtration function. As the DTPA complex is cleared by the renal glomeruli, serial images may be obtained that demonstrate sequential visualization of the kidneys and collecting systems, ureters, and bladder. Measurement of its excretion can also provide an accurate estimate of the glomerular filtration rate (GFR). The normal GFR is 125 mL/min. Because a small amount (≈5% to 10%) of injected DTPA is bound to plasma proteins, it tends to underestimate the GFR slightly. For routine clinical applications, however, this is generally not significant. About 20% of ^{99m}Tc-DTPA is extracted from the blood with each pass through the kidney (extraction fraction), so that about 90% of DTPA is filtered by simple exchange or diffusion into the urine within 4 hours. This makes it an inexpensive agent for renal imaging and as a substitute for contrasted CT in patients who are allergic to radiographic contrast and if ultrasound or MRI are not available. Because the nephrogram phase of the examination is brief, however, it is not an ideal agent for demonstrating intraparenchymal renal lesions. In addition, it may not be the agent of choice in patients with obstruction or impaired renal function in whom tubular agents with higher extraction efficiencies allow for increased excretion and better renal visualization. Technetium-99m DTPA is normally administered in activities of 10 to 20 mCi (370 to 740 MBq).

Cardiovascular System

Fred A. MettlerJr. MD, MPH, Milton J. Guiberteau MD, in Essentials of Nuclear Medicine Imaging (Sixth Edition), 2012

Technetium-99m Tetrofosmin

Technetium-99m tetrofosmin

Technetium-99m tetrofosmin (Myoview) is a cationic diphosphine with good myocardial uptake (1% to 2% of the injected dose with a first-pass extraction efficiency of ≈50%) and retention with little redistribution from the myocardium over time. Tetrofosmin underestimates myocardial blood flow at high flow rates (about two times baseline flow). There is rapid clearance of background activity from the blood pool. Similar to sestamibi, its cellular localization involves binding to cytoplasmic mitochondria. Its biokinetics are also in many ways similar to those of ^{99m}Tc-sestamibi. Less hepatic uptake and more rapid clearance from the liver after exercise, however, make imaging possible within 30 minutes of intravenous injection and minimizes the likelihood of artifacts associated with overlapping hepatic activity.

Shoulder Pain

Scott David Martin, ... Thomas S. Thornhill, in Kelley and Firestein's Textbook of Rheumatology (Tenth Edition), 2017

Scintigraphy

Technetium 99m (Tc 99m) methyl diphosphonate (MDP) or gallium may be of diagnostic help in evaluating skeletal lesions in the area of the shoulder joint. Bone scans generally are not helpful in the diagnosis of non-neoplastic or noninfectious shoulder disease.

Scintigraphy may have a role in identifying patients with complete rotator cuff tears that evolved to cuff-tear arthropathy. This distinction is important because patients with complete rotator cuff tears may do well, whereas patients who experience progressive changes of cuff-tear arthropathy have progressive arthritis, pain, and significant functional impairment. Synovitis or calcium pyrophosphate deposition disease may be an important factor in the pathogenesis of cuff-tear arthropathy. In such cases, scintigraphy may show the increased blood flow and blood pooling associated with chronic synovitis.

Liver resection in cirrhosis

Norihiro Kokudo, Kiyoshi Hasegawa, in Blumgart's Surgery of the Liver, Biliary Tract and Pancreas, 2-Volume Set (Sixth Edition), 2017

Other Tools to Assess Liver Function

Technetium-99m (^{99m}Tc)-galactosyl serum albumin liver scintigraphy (Kwon et al, 1997) and ^{99m}Tc-mebrofenin hepatobiliary scintigraphy (Bennink et al, 2004) are additional useful tools to assess the liver function reserve. However, they have practical problems such as cost and the availability of equipment needed for scintigraphy. Monoethylglycinexylidide (MEGX) test (Oellerich & Armstrong, 2001), galactose elimination capacity test (Ranek et al, 1976), and ^{13}C–liver function breath test (Afolabi et al, 2013) are also available and useful as liver function assessment tools, although these are complicated and time-consuming procedures. The application of these tools is not widespread and presently limited to a few cases in which other tests, including the ICG test, cannot be used.

Lumbar spine disorders

Zacharia Isaac, Jeffrey N. Katz, in Rheumatology (Sixth Edition), 2015

Radionuclide bone scintigraphy

Technetium-99m diphosphonate scans are useful in assessing for infection, tumors, inflammatory arthritis, and

fractures.[37] The sensitivity of bone scanning is generally equal to that of MRI (90% vs. 96%), but it is less specific, for example, in detecting vertebral osteomyelitis (78% vs. 92%). Gallium and indium scans increase the specificity when used with a technetium scan but are less sensitive when used alone. Bone scintigraphy is better than MRI when evaluation of the whole skeleton is required, such as in patients with metastatic disease who may have unsuspected bone lesions in other parts of the skeleton (Fig. 72.3). The addition of single-photon emission computed tomography of bone can be useful for identifying facet pathology and predicting patients who will respond to intraarticular facet injection.[38]

Endocrine System

In Nuclear Medicine (Fourth Edition), 2014

Technetium-99m Pertechnetate

Technetium-99m pertechnetate has been used as an alternative to I-123 for thyroid scintigraphy because of its ready availability from molybdenum99/Tc-99m generators and its low patient radiation dose.

Physics

The 140-keV photopeak of Tc-99m (89% abundance) is ideally suited for use with a gamma camera. It has a short 6-hour half-life and no particulate emissions (Table 6-1).

Pharmacokinetics

In contrast to oral administration of radioiodine, Tc-99m pertechnetate is administered intravenously. It is trapped by the thyroid by the same mechanism as iodine but is not organified nor incorporated into thyroid hormone. Thus it is not retained in the thyroid and imaging must be performed early, usually at peak uptake, 20 to 30 minutes after injection.

Dosimetry

The lack of particulate emissions and short 6-hour half-life result in relatively low radiation absorption by the thyroid (Table 6-2). The administered activity of Tc-99m pertechnetate (3-5 mCi) is considerably higher than that for I-123 for routine thyroid scans (200-400 μCi). The resulting large photon flux allows for high-quality images.

Hepatobiliary System

In Nuclear Medicine (Fourth Edition), 2014

Radiopharmaceuticals

Technetium-99m–labeled hepatobiliary radiopharmaceuticals became available in the early 1980s; because of their superior image and diagnostic quality they replaced iodine-123 rose bengal.

Three hepatobiliary radiopharmaceuticals have been approved by the U.S. Food and Drug Administration (FDA) for clinical use in the United States (Fig. 8-2). The first was Tc-99m dimethyl iminodiacetic acid (IDA), which was referred to as hepatic IDA (HIDA). Although it is no longer used, HIDA has become a generic term for all Tc-99m IDA radiopharmaceuticals. The two agents in clinical use today in the United States are shown in Table 8-2.

Table 8-2. Technetium-99m Hepatobiliary Agent Names

Chemical	FDA	Commercial
Tc-99m diisopropyl IDA (DISIDA)	Disofenin	Hepatolite
Tc-99m bromotriethyl IDA	Mebrofenin	Choletec

FDA, U.S. Food and Drug Administration.

Chemistry

Tc-99m serves as a bridging atom between two IDA ligand molecules (Fig. 8-2). Both IDA molecules bind to an acetanilide analog of lidocaine. The latter determines the radiopharmaceutical's biological and pharmacokinetic properties.

Minor structural changes in the phenyl ring (N substitutions) result in significant alterations in the pharmacokinetics of IDA radiopharmaceuticals (Table 8-3). Many Tc-99m HIDA analogs with different aromatic ring chemical substitutions have been investigated, with generic names of BIDA, DIDA, EIDA, PIPIDA, and so forth; however, most were found to have less uptake and slower clearance than the approved commercially available agents.

Table 8-3. Normal Pharmacokinetics of Technetium-99m Hepatobiliary Iminodiacetic Acid Radiopharmaceuticals

Agent	Hepatic uptake (%)	Clearance half-time (min)	2-hr renal excretion (%)
Tc-99m disofenin (DISIDA)	88	19	<9
Tc-99m mebrofenin (BrIDA)	98	17	<1

Radioactivity, Radionuclides, and Radiopharmaceuticals

Fred A. MettlerJr. MD, MPH, Milton J. Guiberteau MD, in Essentials of Nuclear Medicine Imaging (Sixth Edition), 2012

Technetium-99m

Technetium-99m fulfills many of the criteria of an ideal radionuclide and is used in more than 80% of nuclear imaging procedures in the United States. It has no particulate emission, a 6-hour half-life, and a predominant (98%) 140-keV photon with only a small amount (10%) of internal conversion.

Technetium-99m is obtained by separating it from the parent ^{99}Mo (67-hour half-life) in a generator system. Molybdenum-99 for generators is generally produced by neutron irradiation of ^{98}Mo or by chemical separation of ^{235}U fission products. In the latter case, ^{99}Mo is nearly carrier free and has a high specific activity. In the alumina generator system, the molybdenum activity is absorbed on an alumina column. By passing physiologic saline over the column, ^{99m}Tc is eluted or washed off as sodium pertechnetate (Na $^{99m}TcO_4^-$).

Technetium can exist in a variety of valence states, ranging from –1 to +7. When eluted from an alumina column generator, ^{99m}Tc is present primarily as heptavalent (+7) pertechnetate (TcO_4^-). In the preparation of radiopharmaceuticals, ^{99m}Tc pertechnetate can be reduced from +7 to a lower valence state, usually +4, to permit the labeling of various chelates. This is generally accomplished with stannous (tin) ions.

As pertechnetate, the technetium ion is a singly charged anion and is similar in size to the iodide ion. After intravenous injection, ^{99m}Tc pertechnetate is loosely bound to protein and rapidly leaves the plasma compartment. More than half leaves the plasma within several minutes and is distributed in the extracellular fluid. It rapidly concentrates in the salivary glands, choroid plexus, thyroid gland, gastric mucosa, and functioning breast tissue; during pregnancy, it crosses the placenta.

Excretion is by the gastrointestinal and renal routes. Although ^{99m}Tc pertechnetate is excreted by glomerular filtration, it is partially reabsorbed by the renal tubules; as a result, only 30% is eliminated in the urine during the first day. The ion is

also secreted directly into the stomach and colon, with a much smaller amount coming from the small bowel. The colon is the critical organ and receives about 1 to 2 rad/10 mCi (0.04 mGy/MBq) of ^{99m}Tc pertechnetate administered. The biodistribution of ^{99m}Tc pertechnetate is shown in Figure 1-6. The principal emission (140-keV photon) of ^{99m}Tc has a half-value layer (HVL) of 0.028 cm in lead and 4.5 cm in water. Because tissue is close to water in terms of attenuation characteristics, it is clear that about 2 inches of tissue between the radionuclide and the detector removes about half of the photons of interest, and 4 inches removes about three fourths.