Radionuclidic Imaging Procedures in the Diagnosis of Cancer *

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Radionuclide is a comprehensive term which includes isotopes, isobars, isotones and isomers. The obsolescence of the designation "radioisotope" for all scanning agents is only one indication of the changes in Nuclear Medicine during the past few years. Progress in this field has been so extensive that the Joint Committee on the Accreditation of Hospitals now requires that all approved hospitals have convenient access to Nuclear Medicine diagnostic procedures.

Of the 25 different radionuclides used in diagnostic procedures, only a few are valuable in diagnosing cancer. The choice of one of these agents is dictated by the organ or system under study, the method of biological transport of the radionuclide and its degree of concentration within the organ. The radionuclide should have the least potential for damage to the target organ or system, and the shortest possible half-life consistent with diagnosis.

*These tables are an up-to-date revision of the work by Dr. Norman R. Ackerman, "Use of Radioisotopic Agents in the Diagnosis of Cancer," published by the American Cancer Society, Inc., in 1965.

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Once the appropriate radionuclide is chosen it is added to a pharmaceutical compound (such as the chemical form of the nuclide in a saline solution). When the radiopharmaceutical enters the body, it behaves like the chemical the organ normally metabolizes so that the organ tissue "takes up" the radionuclide (for example, radioactive iodine which concentrates in the thyroid just as stable iodine does).

Radionuclides localize cancer in one of two ways: either the tumor (1) concentrates the radionuclide from the rest of the organ and shows up as a "hot spot" on the scan or camera recording, or (2) it does not concentrate the compound and is seen as a "cold spot" on the surrounding normal tissue which has concentrated the radionuclide. It is easier to detect the hot lesions than the cold because the higher background surrounding cold lesions is more difficult to resolve with currently available detectors. The diagnostic accuracy of the scans which show active pickup in tumor such as brain, bone and functioning thyroid metastases exceeds 90 percent. Those studies where the absence of activity indicates disease are less accurate; for example, in liver imaging for possible metastases the scans are positive in less than 80 percent of cases.

There are two types of detectors currently in use for radionuclidic imaging. One is the rectilinear scanner which moves back and forth across the area, charting the concentration of radioactivity within or around the tumor by means of parallel lines. This technique requires 5 to 45 minutes to produce a complete "picture," depending on the dose of the radionuclide, the energy of its radiation, the size of the scintillation crystal, etc.

The other device is a stationary scanner or "camera" which produces a rapid complete image of the entire organ or system at one time. The camera's speed of imaging is an advantage especially if the patient is uncooperative or unable to remain immobile for the time necessary to obtain a rectilinear scan. The camera also provides a better picture of the features near the surface of the organ; however, the rectilinear scanner achieves a better resolution at depth which makes it more useful in certain situations, despite the longer exposure time.

To date, radionuclidic imaging has proved quite useful in diagnosing cancer of several sites. It is now used routinely in detecting tumors of thyroid and primary or metastatic tumors of the bone, brain and liver or spleen. Efforts are currently directed towards screening for metastases in cases where a primary tumor is proven or strongly suspected. The brain and bone scans are most useful in detecting metastases from carcinoma of the breast, colon and lung. Because the liver scan has detected only 75 to 80 percent of known metastases, it is more useful as a confirmatory procedure in cases of suspected metastases than as a screening technique.

Newer radionuclides are becoming available through the expanded use of medical cyclotrons. For example, Gallium-67 citrate has been used experimentally in the staging of lymphoma and shows a great deal of promise, as does fluorine-18 in bone scanning. Many of these newer agents have very short physical half lives. Because the radioactivity disintegrates within the body at a faster rate, and many of these nuclides are pure gamma emitters, larger doses may be tolerated and the quality of the image improved without risking excessive patient irradiation.

Several radiopharmaceuticals which are not on the Atomic Energy Commission's list of generally accepted radionuclides or procedures are included in these tables because they are promising and, in many instances, will be used routinely in the near future.
# Radionuclides in the Diagnosis of Cancer

| Radionuclide     | Pharmaceutical Name | Physical Half-Life | Dose          | Detection Method                      |
|------------------|---------------------|--------------------|---------------|---------------------------------------|
| **Thyroid**      |                     |                    |               |                                       |
| Iodine-123       | Sodium Iodide       | 13.3 hours         | 50-100 µCi   | Scan 24 hours after injection         |
| (¹²³I)           |                     |                    |               |                                       |
| Technetium-99m   | Sodium Pertechnetate| 6 hours            | 1-3 mCi      | Scan 30-60 minutes after injection    |
| (⁹⁹ᵐTc)          |                     |                    |               |                                       |
| Iodine-125       | Sodium Iodide       | 60 days            | 50-100 µCi   | Scan 24 hours after injection         |
| (¹²⁵I)           |                     |                    |               |                                       |
| Iodine-131       | Sodium Iodide       | 8.1 days           | 50-100 µCi   | Scan 24 hours after injection         |
| (¹³¹I)           |                     |                    |               |                                       |
| **Parathyroid**  |                     |                    |               |                                       |
| Selenium-75      | Selenomethionine    | 120 days           | 250 µCi      | Serial imaging during first hour      |
| (⁷⁵Se)           |                     |                    | (IV or IA)   |                                       |
| **Spleen**       |                     |                    |               |                                       |
| Technetium-99m   | Technetium sulfur   | 6 hours            | 1-2 mCi      | Imaging 1-2 hours after injection     |
| (⁹⁹ᵐTc)          | colloid             |                    |               |                                       |
| Indium-113m      | Indium colloid      | 1-7 hours          | 1-2 mCi      | Imaging 1-2 hours after injection     |
| (¹¹³mIn)         |                     |                    |               |                                       |
| Technetium-99m   | Crenated            | 6 hours            | 1-2 mCi      | Imaging 1-2 hours after injection     |
| (⁹⁹ᵐTc)          | Technetium tagged   |                    |               |                                       |
| Chromium-51      | Crenated            | 27.8 days          | 150-300 µCi  | Imaging 1-2 hours after injection     |
| (⁵¹Cr)           | Chromium tagged     |                    |               |                                       |
| **Lymph Nodes**  |                     |                    |               |                                       |
| Gold-198         | Gold colloid        | 2.7 days           | 50 µCi       | Imaging 4-24 hours after intralymphatic injection |
| (¹⁹⁸Au)          |                     |                    |               |                                       |
| Technetium-99m   | Technetium sulfur   | 6 hours            | 1-5 mCi      | Imaging 4-24 hours after intralymphatic injection |
| (⁹⁹ᵐTc)          | colloid             |                    |               |                                       |
| Rationale                                                                 | Application                                                                 |
|---------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Incorporated into thyroid hormogenesis                                     | Evaluation of functional status of nodules. High cancer probability in single nonfunctioning nodules in young adults |
| Trapped by the thyroid                                                    | Some tumors, benign or malignant, retain trapping function but cannot organify. |
| Incorporated into thyroid hormogenesis                                     | Evaluation of functional status of nodules. High cancer probability in single nonfunctioning nodules in young adults |
| Incorporated into thyroid hormogenesis                                     | Evaluation of functional status of nodules. High cancer probability in single nonfunctioning nodules in young adults |
| Locates in active anabolic structures                                     | Location of parathyroid adenomas                                           |
| Reticuloendothelial system of spleen removes about 10% of injected colloid| Determination of size and presence of masses in the spleen                 |
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| Spleen removes damaged red cells.                                         | Determination of size and presence of masses in the spleen                 |
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| Lymph nodes act as a filter to the colloid                                | Determination of patency of lymphatic chains                               |
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| Radionuclide        | Pharmaceutical Name                  | Physical Half-Life | Dose     | Detection Method                              |
|---------------------|-------------------------------------|-------------------|----------|----------------------------------------------|
| **Kidney**          |                                     |                   |          |                                              |
| Technetium-99m (Tc) | Technetium Diethylentriaminepenta-acetic Acid | 6 hours           | 2-10 mCi | Serial camera or scanning images immediately to hours after injection |
| Iodine-131 (I)      | Sodium orthiodohippurate             | 8 days            | 15-300 µCi | Serial camera or scanning images immediately to hours after injection |
| Mercury-197 (Hg)    | Chloromerodrin                       | 2.7 days          | 70-200 µCi | Camera or scan image 0.5-24 hours post injection |
| Mercury-203 (Hg)    | Chloromerodrin                       | 47.9 days         | 50-200 µCi | Camera or scan image 0.5-24 hours post injection |
| Ytterbium-169 (Yb) | Ytterbium Diethylentriaminepenta-acetic Acid | 32 days           | 2-10 mCi | Serial camera or scan images immediately to hours after injection |
| Technetium-99m (Tc) | Pertechnetate or technetium labeled human serum albumin | 6 hours           | 5-20 mCi | Camera images during bolus injection |
| **Brain**           |                                     |                   |          |                                              |
| Technetium-99m (Tc) | Sodium Pertechnetate                 | 6 hours           | 10-20 mCi (IV) | Scan or camera images immediately to 4 hours after injection |
| Technetium-99m (Tc) | Technetium labeled human serum albumin | 6 hours           | 5-15 mCi (IV) | Scan or camera images immediately to 6 hours |
| Indium-113m (In)    | Indium-Diethylentriaminepenta-acetic Acid (DTPA) | 1.7 hours         | 10-15 mCi | Scan or camera images immediately to 4 hours |
| Ytterbium-169 (Yb) | Ytterbium Diethylentriaminepenta-acetic Acid (DTPA) | 32 days           | 5-10 mCi (IV) | Scan or camera images 30-60 minutes |
| **Spinal Cord and Ventrices** |                                     |                   |          |                                              |
| Iodine-131 (I)      | Iodinated human serum albumin (High specific activity) | 8.1 days          | 50-100 µCi intrathecal | Image 4 to 72 hours after injection |
| Technetium-99m (Tc) | Technetium labeled human serum albumin | 6 hours           | 0.5-1 mCi intrathecal | Image 4-24 hours |
| Rationale                                                                 | Application                                      |
|--------------------------------------------------------------------------|--------------------------------------------------|
| Cleared from kidneys by glomerular filtration                            | Evaluation of renal structure and function       |
| Cleared from the kidney mainly by tubular secretion (about 20% by glomerular filtration) | Evaluation of renal structure and function       |
| Locates in functioning renal tubules                                     | Evaluation of renal structure and function       |
| Locates in functioning renal tubules                                     | Evaluation of renal structure and function       |
| Cleared from kidney by glomerular filtration                             | Evaluation of renal structure and function       |
| Blood pool agent                                                         | Evaluation of vascularity of known renal masses   |
| Disruption in the blood brain barrier, which normally keeps these agents out of the brain, permits intracerebral concentration | To screen for or confirm a variety of intracranial neoplastic or non-neoplastic conditions |
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| Follows the normal cerebrospinal fluid flow                              | Used to diagnose low pressure hydrocephalus, location CSF leaks and confirm CSF blocks |
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| Radionuclide     | Pharmaceutical Name | Physical Half-Life | Dose     | Detection Method                                      |
|------------------|---------------------|-------------------|----------|------------------------------------------------------|
| Phosphorus-32 ($^{32}$P) | Sodium Phosphate | 14.3 days | 250-750 μCi (IV) | Semiconductor counting at surgery 1-12 hours after injection |
| Technetium-99m ($^{99m}$Tc) | Technetium Sulfur Colloid | 6 hours | 1-5 mCi (IV) | Image 30-90 minutes after injection |
| Indium-113m ($^{113m}$In) | Indium Colloid | 1.7 hours | 1-2 mCi (IV) | Image 30-90 minutes after injection |
| Gold-198 ($^{198}$Au) | Gold Colloid | 2.7 days | 50-200 μCi (IV) | Image 30-90 minutes after injection |
| Iodine-131 ($^{131}$I) | Iodinated Micro-aggregated human serum albumin | 8.1 days | 150-300 μCi (IV) | Image 0.5-4 hours after injection |
| Iodine-131 ($^{131}$I) | Iodinated Rose Bengal | 8.1 days | 25-250 μCi (IV) | Image 0.5, 4 and 24 hours after injection |
| Selenium-75 ($^{75}$Se) | Selenomethionine | 127 days | 150-250 μCi | Image serially up to 2 hours after injection |
| Technetium-99m ($^{99m}$Tc) | Technetium labeled human serum albumin microspheres | 6 hours | 1-4 mCi (IV) | Image immediately after injection |
| Iodine-131 ($^{131}$I) | Iodine Macro-aggregated human serum albumin | 8.1 days | 50-300 μCi | Image immediately after injection |
| Indium-113m ($^{113m}$In) | Indium Ferric Hydroxide Macro-aggregates | 1.7 hours | 1-4 mCi | Image immediately after injection |
| Technetium-99m ($^{99m}$Tc) | a) Macroaggregated Technetium labeled human serum albumin. b) Ferrous hydroxide macroaggregates | 6 hours | 1-4 mCi | Image immediately after injection |
| Rationale                                                                 | Application                                                                                           |
|--------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| Increased uptake in tumors of the eye                                     | Separate benign from malignant conditions of the eye both of which may cause retinal detachment       |
| Colloid cleared by reticuloendothelial system                            | Detection of hepatic neoplasia, abscesses, cirrhosis and trauma.                                       |
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| Dye excreted in bile duct after clearance by polygonal cells             | Separation of obstructive from nonobstructive jaundice in children and adults                          |
| Selenomethionine, an analog of Methionine, is picked up in the active anabolic tissues, including the pancreas and liver. | To detect pancreatic tumors or to exclude acute pancreatitis. The finding of a normal pancreas scan has a 90% probability of excluding pancreatic carcinoma. Hepatomegaly interferes with pancreatic imaging. |
| Held up in first capillary bed                                           | To assess integrity of pulmonary capillary bed. Especially useful in cases of pulmonary emboli, carcinoma and intracardiac shunting. |
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| Radionuclide | Pharmaceutical Name | Physical Half-Life | Dose | Detection Method |
|--------------|---------------------|-------------------|------|------------------|
| Technetium-99m (\(^{99m}\)Tc) | Technetium Sulfur Colloid | 1-5 mCi | Image 6-24 hours after inhalation thru positive pressure or ultrasonic nebulizer |
| Technetium-99m (\(^{99m}\)Tc) | Technetium labeled human serum albumin | 1-5 mCi | Image 6-24 hours after inhalation thru positive pressure or ultrasonic nebulizer |
| Gold-198 (\(^{198}\)Au) | Gold Colloid | 250 μCi | Image 6-24 hours after inhalation thru positive pressure or ultrasonic nebulizer |
| Fluorine-18 (\(^{18}\)F) | Sodium Fluoride | 1.87 hours | 1-4 (PO or IV) | Scan or camera images after 1-4 hours |
| Strontium-85 (\(^{85}\)Sr) | Strontium Chloride or Nitrate | 65 days | 75-100 μCi (IV) | Scan or camera images at 5-7 days |
| Strontium-87m (\(^{87m}\)Sr) | Strontium Chloride | 2.8 hours | 1-3 mCi (IV) | Scan or camera images 2-6 hours after injection |
| Technetium-99m (\(^{99m}\)Tc) | Technetium phosphates | 6 hours | 1-5 mCi (IV) | Scan or camera images 2-24 hours after injection |
| Gallium-67 (\(^{67}\)Ga) | Gallium Citrate | 78 hours | 1-4 mCi | Serial imaging 48-96 hours after injection |
| Indium-111 (\(^{111}\)In) | Indium Chloride | 2.8 days | 0.5-2 mCi | Serial imaging 48-96 hours after injection |
| Selenium-75 (\(^{75}\)Se) | Selenomethionine | 120 days | 250 μCi | Serial imaging 0.5-2 hours after injection |
| Iodine-131 (\(^{131}\)I) | 19-Radioiodocholesterol | 8.1 days | 2 mCi | Imaging 48 hours after injection |
| Iodine-125 (\(^{125}\)I) | 4-(3-dimethylaminopropylamino)-7-radio-iodoquinoline | 60 days | 2 mCi | Imaging 24-96 hours after injection |
| Rationale                                                                 | Application                                                                 |
|------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Deposited along areas of bronchial patency                             | Used to locate or confirm areas of intrabronchial obstruction in lung tumor suspects |
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| Deposited along areas of bronchial patency                             | Used to locate or confirm areas of intrabronchial obstruction in lung tumor suspects |
| Localizes in actively metabolizing bone and bone tumors                 | Detection of metastases to bone                                              |
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| Localizes in actively metabolizing bone and bone tumors                 | Detection of metastases to bone                                              |
| Localizes in actively metabolizing bone and bone tumors                 | Detection of metastases to bone                                              |
| Selective concentration in certain malignancies, especially lymphoma   | Staging of lymphoma cases.                                                  |
| Selective concentration in certain malignancies, especially lymphoma   | Staging of lymphoma cases.                                                  |
| Locates in active anabolic tissue                                       | Detection of Thymoma as in patients with myasthenia gravis                  |
| Locates in adrenal cortex                                               | Visualization of adrenal glands                                             |
| Selective concentration in pigmented tissues                            | Detection of melanoma metastases                                            |