

## 13 Radiation in Medicine

The greatest source of man-made radiation exposure to both the general public (cf. Table 3-1) and to workers arises from medical uses of radiation. While a nuclear reactor may have millions of curies of radioactivity, shielding and other engineering controls reduces the average public exposure to less than 1 mrem per year and the total work force involved is relatively small. Radioactive materials are also used in medical clinics such as nuclear medicine, cardiology, endocrinology, and radiation therapy. These medical clinics employ more than 100,000 radiation workers and annually provide radiation services to more than 50,000,000 people in the US.

The biggest source of this clinical radiation exposure remains medical x-rays which comprises 80% to 90% of all imaging procedures. Besides radiology, which we discussed in Chapter 10, diagnostic x-rays are also found in such clinics as cardiology, urology, orthopedics, gastrology, and dental. It is estimated that in 1990, there were approximately 294,000,000 medical imaging procedures performed on a US population of 249,000,000. The patient's dose from diagnostic x-ray procedures depends upon the number of x-ray exposures made and the physical size or density of the patient at the site of interest. While most patient whole-body exposures are very low, skin damage resulting from high skin exposures have been reported. The population exposure from medical x-rays contributes approximately 13% of the average annual population dose.

Cancer patients are often treated by surgery, chemotherapy and/or radiation. In many malignancies combined approaches of radiation therapy and surgery can often improve the results of surgery alone. When using radiation therapy, it is important to use an appropriate radiation energy. Low energy photons deposit their energy non-uniformly through a tissue, more of the radiation is deposited near the surface, so it works best with shallow tumors. High energy photons are more uniformly distributed throughout the tissue, making it possible to uniformly irradiate deep tumors. Since penetrating power is essential, treatment of deep tumors uses very high energy ( $E > 6$  MeV) x-rays. The high energy x-rays are produced when high energy electrons are stopped in a target material such as tungsten. Instead of producing x-rays, the electrons themselves may be used directly to treat superficial cancers. Thus, the type of cancer therapy may depend upon the location of the tumor and may dictate the energy of radiation to use. Deep tumors (cervical cancer, Hodgkin's disease, lung cancer, etc.) respond well to high energy ( $> 6$  MeV) photons. More superficial tumors (breast cancer, etc.) respond well to medium to low energy ( $< 2$  MeV) photons,  $^{60}\text{Co}$   $\gamma$ -rays, and high-energy electron beams. Superficial cancers (lip, etc.) respond well to electron beams.

### 13.1 Nuclear Medicine

Diagnostic radiology is a static exam.

Radiation generated from outside the body is directed at an area of interest. The low energy (i.e.,  $E_{\text{max}} < 120$  kVp) x-rays are attenuated differently by different densities of body tissue (e.g., bone is more dense than muscle which is more dense than the lungs). The radiation that penetrates completely through the body is allowed to produce an image on a photographic film, a TV input phosphor, an array of radiation detectors, etc. The difference in absorption is then interpreted by the radiologist leading to a diagnosis. It is important that the image be crisp. To reduce image blurring, radiology personnel are often heard advising patients to, "...take a deep breath, hold it ...". Even for exams which view the dynamics of a system (e.g., IVP, angiography, upper GI) the concept is unchanged; only a radiopaque substance (e.g., iodine, barium) is used to enhance the soft tissue contrast.

Nuclear Medicine is a scientific and clinical discipline of medicine utilizing radioactive drugs, usually called radiopharmaceuticals, for diagnosis and/or treatment of diseases. In 1993 there were approximately 8,202,000 nuclear medicine procedures performed in the US providing approximately 14 mrem per person to the average population dose. Over 36,000 diagnostic procedures using medical isotopes are carried out each day, over 50,000 therapeutic doses are administered each year and nearly 100,000,000 in vitro laboratory tests use isotopes each year. Figure 13-1 provides a breakdown of the 13,000,000 nuclear medicine procedures carried out in 1996. The number

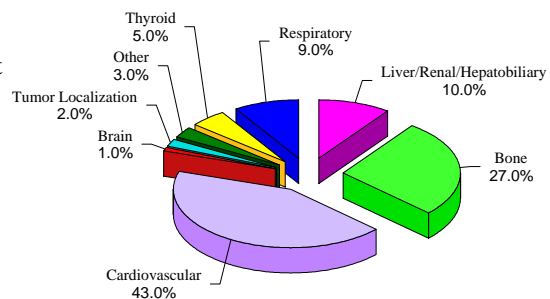


Figure 13-1. 1996 Nuclear Medicine Studies

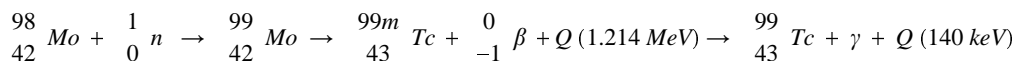
of studies performed increases annually (e.g., a 7% increase from 1995) and the distribution of studies varies (e.g., cardiovascular studies increased from 36% in 1993 to 43% in 1996) according to medical demand.

Nuclear medicine studies are also dynamic studies of metabolic processes. The radiopharmaceutical selected for a particular study is designed so a greater proportion of the drug is concentrated in the organ of interest. The radiopharmaceutical can be either a gas, liquid, or solid and can be administered to the patient orally, intravenously, by inhalation, or may be chemically bound to a patient's bodily fluid sample after the sample is withdrawn from the body (RIA). Technetium-99m ( $^{99m}\text{Tc}$ ) is the radionuclide most commonly used in nuclear medicine because it can be compounded into many different radiopharmaceuticals that target different organs. All drugs must be approved by the Food and Drug Administration. Examples of these drugs include:  $\text{Na}^{99m}\text{TcO}_4$ ,  $^{99m}\text{Tc}$ -sulfur colloid,  $^{67}\text{Ga}$ -Citrate,  $^{133}\text{Xe}$  gas,  $\text{Na}^{131}\text{I}$ . Other uses normally require approval from FDA before each use.

The quantity of radioactivity in the organ is measured or "imaged" by using a large scintillation detector or an array of scintillation detectors which detect the gamma rays (i.e., beta particles do not penetrate from inside the body) emitted during radioactive decay. Diagnosis is made by viewing the concentration and distribution of the radiopharmaceutical within the organ, noting such things as whether there are "hot" or "cold" spots or whether the material is distributed uniformly.

### 13.1.a Nuclear Medicine Radiopharmaceuticals

Radionuclides can be produced either as a byproduct of nuclear reactor use or by activating stable materials in some sort of accelerator (e.g., cyclotron, van de Graaff, etc.). The core of a nuclear reactor (see **Chapter 11**) consists of material (usually uranium) undergoing nuclear fission. Because of the many fission events in the volume surrounding this core, there is a very high neutron flux. It is possible to produce radionuclides by irradiation of a target material within this neutron flux (e.g.,  $^{98}\text{Mo}(n,\gamma)^{99}\text{Mo}$ ;  $^{14}\text{N}(n,p)^{14}\text{C}$ ; etc.) or by separation of the byproducts produced by the nuclear fission events (e.g.,  $^{133}\text{Xe}$ ,  $^{131}\text{I}$ ). The most common radiopharmaceutical is  $^{99m}\text{Tc}$  and it is produced via:



Accelerators are devices that accelerate charged particles or ions (see **Chapter 12**). Although accelerators of heavy ions have been developed, those used for radionuclide production are generally linear accelerators and cyclotrons, which accelerate beams of protons ( ${}_1^1\text{p}$  or  ${}_1^1\text{H}^1$ ), deuterons, ( ${}_1^2\text{d}$  or  ${}_1^2\text{H}^2$ ), helium-3 ions ( ${}_2^3\text{He}^3$ ) and alpha particles ( $\alpha$  or  ${}_2^4\text{He}^4$ ) or electron accelerators which produce beams of high energy electrons. Examples of these types of reactions include:  $^{18}\text{O}({}_1^1\text{p},n)^{18}\text{F}$ ;  $^{130}\text{Te}({}_1^2\text{d},n)^{131}\text{I}$ ; and  $^{127}\text{I}({}_1^1\text{p},5n)^{123}\text{Xe}$ .

### 13.1.b Nuclear Pharmacy

The hub of the UW Nuclear Medicine Clinic is the nuclear pharmacy or *hot lab*. The hot lab is staffed by a nuclear pharmacist and a pharmacy technician who compound radiopharmaceuticals for diagnostic imaging and therapy. Like other pharmacies, the hot lab compounds pharmaceuticals containing diagnostic or therapeutic agents requested by the physician, according to the needs of the individual patient. Unlike other pharmacies, the use of radioactive material in the compounding of radiopharmaceuticals also requires compliance with radiation safety regulations related to their medical use.

Radioactive materials are delivered to the pharmacy daily and their receipt requires monitoring and record keeping as detailed in **Chapter 8**. Products delivered may include  $^{99}\text{Mo}/^{99m}\text{Tc}$  generators,  $^{201}\text{Tl}$ -thallous chloride,  $^{67}\text{Ga}$ -gallium citrate,  $^{131}\text{I}$ -sodium iodide, etc.

The hot lab primarily compounds and dispenses prescriptions for  $^{99m}\text{Tc}$ -labeled radiopharmaceuticals. Because the half-life of  $^{99m}\text{Tc}$  is only 6 hours, these radiopharmaceuticals must be compounded only a few hours before they are administered to the patient. As the  $^{99m}\text{Tc}$ -labeled radiopharmaceuticals are compounded, appropriate quality control samples are taken to verify proper labeling. The hot lab also compounds/dispenses individual prescriptions for patients requiring diagnostic and therapeutic  $^{131}\text{I}$ -sodium iodide solution and dispenses various diagnostic products containing  $^{201}\text{Tl}$ ,  $^{67}\text{Ga}$ ,  $^{111}\text{In}$  and  $^{123}\text{I}$ . Most compounding and quality control procedures take place in the early morning hours so that each patient's dose may be available before the patient arrives for the scan. The rest of the day in the hot lab is dedicated to radiation safety surveys, preparing emergency prescriptions and performing specialized procedures such as autologous leukocyte labeling.

Most radiopharmaceuticals employed in nuclear medicine are chelates of organic or inorganic chemicals compounded with  $^{99m}\text{Tc}$  sodium pertechnetate obtained from a  $^{99}\text{Mo}/^{99m}\text{Tc}$  generator. The nuclear pharmacy usually maintains several of these generators in various stages of decay to provide the necessary concentration of activity needed to effectively compound the required patient doses. Usually the oldest generator is used to supply  $^{99m}\text{Tc}$  for scans required after normal operating hours.

A **generator** is a device in which a short-lived *daughter* radionuclide is periodically separated chemically from a longer-lived *parent* radionuclide. The parent is usually adsorbed on an inorganic resin and the short-lived daughter is separated from the parent by drawing a saline solution through the generator column in a process called **milking** the generator. Although there are many kinds of generators, the  $^{99}\text{Mo}/^{99m}\text{Tc}$  generator (Figure 13-2) is the most common. This generator consists of a heavily shielded ion exchange column of alumina ( $\text{Al}_2\text{O}_3$ ) which has been tightly bound with a calibrated amount of  $^{99}\text{Mo}$  sodium molybdate and sterilized before shipment. Modern generator systems yield high-quality eluates of  $^{99m}\text{Tc}$  sodium pertechnetate that are essentially free of most radionuclidic and chemical contaminants.

Two types of generators are available from manufacturers, wet and dry column generators. The **wet column generator** contains a permanently installed reservoir of sterile sodium chloride solution as the eluant. As the  $^{99}\text{Mo}$  decays, successively smaller evacuated vials are employed to yield elutions of more or less constant specific concentration. The **dry column generator** uses a small vial of sterile sodium chloride solution as the eluant. Eluates of varying specific concentrations may be obtained by selecting the volume of the eluant. Generator eluates are collected in sterile, shielded, evacuated vials which may be easily handled during the compounding process. Before use, the elution must pass several nuclide and chemical purity tests.

The  $^{99}\text{Mo}$  sodium molybdate is tightly bound to the ion exchange column, but small amounts of this compound may be eluted with the  $^{99m}\text{Tc}$  sodium pertechnetate in normal use. This **moly breakthrough** is normally more pronounced with the first elution of a new generator and is expressed as a ratio of activities of  $^{99}\text{Mo}$  to  $^{99m}\text{Tc}$ . Because  $^{99}\text{Mo}$  decays to  $^{99m}\text{Tc}$  by  $\beta$  emission, unnecessary patient radiation dose could result from the use of a product prepared from an elution containing an excessively high ratio of  $^{99}\text{Mo}/^{99m}\text{Tc}$ . For this reason, the allowable amount of  $^{99}\text{Mo}$  is strictly limited to a maximum of  $0.15 \mu\text{Ci } ^{99}\text{Mo}$  per  $\text{mCi } ^{99m}\text{Tc}$  (0.015%) at the time of administration to the patient. The pharmacist tests each elution for  $^{99}\text{Mo}$  breakthrough and determines if the  $^{99}\text{Mo}:^{99m}\text{Tc}$  ratio of the elution is within acceptable limits and will remain so for the life of the products compounded from it. Because  $^{99m}\text{Tc}$  decays considerably faster than  $^{99}\text{Mo}$ , the  $^{99}\text{Mo}:^{99m}\text{Tc}$  ratio increases with time and at the 12-hour expiration time of the elution, one-quarter of the original  $^{99m}\text{Tc}$  remains while the  $^{99}\text{Mo}$  activity is nearly the same as its original activity.

Another test of the generator eluate determines if excess aluminum ion ( $\text{Al}^+$ ) is eluted from the ion exchange column. Because  $\text{Al}^+$  may interfere with certain compounding reactions, elutions of  $^{99m}\text{Tc}$  sodium pertechnetate must not contain more than 10 micrograms of  $\text{Al}^{3+}$  per milliliter of eluate. The presence of aluminum ion is tested with a colorimetric, semiquantitative method, utilizing indicator paper.

For many radiopharmaceuticals, compounding involves the introduction of sterile, non-pyrogenic  $^{99m}\text{Tc}$  sodium pertechnetate into vials of non-radioactive reagents to form  $^{99m}\text{Tc}$ -labeled products. The  $^{99m}\text{Tc}$  sodium pertechnetate ( $\text{Na}^{99m}\text{TcO}_4$ ), contains  $^{99m}\text{Tc}$  in the 7+ oxidation state, or  $^{99m}\text{Tc}$  (VII). To successfully form most radiopharmaceutical chelates, the  $^{99m}\text{Tc}$  (VII) must be reduced to a lower oxidation state. This is accomplished by the inclusion of a small amount of tin, usually as stannous chloride, as a reducing agent. Commonly used radiopharmaceuticals and their indications are summarized in Table 13-1.

All  $^{99m}\text{Tc}$ -labeled radiopharmaceuticals compounded in the pharmacy which are intended for human administration are tested for radiochemical purity. Two types of radiochemical impurity may be found in compounded  $^{99m}\text{Tc}$ -labeled radiopharmaceuticals: free (unbound)  $^{99m}\text{Tc}$  pertechnetate and hydrolyzed-reduced  $^{99m}\text{Tc}$ . These impurities may accumulate in unintended organ systems, possibly confusing the interpretation of the image. For example, properly compounded  $^{99m}\text{Tc}$  medronate (MDP) localizes in the skeleton. Undesirable free (unbound) pertechnetate is localized in the thyroid, salivary glands and stomach, while hydrolyzed-reduced  $^{99m}\text{Tc}$  may appear in the liver. The majority of the compounded products are tested with miniaturized paper chromatography or instant

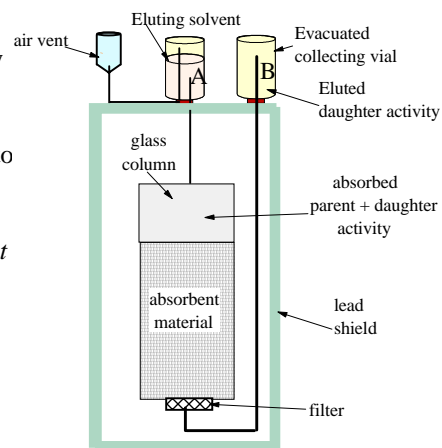


Figure 13-2. Generator System

thin layer chromatography (ITLC). The concept is fairly simple: separation of compounds is based on the relative affinity of the compound for the support (stationary phase) or the solvent (mobile phase). Various combinations of stationary and mobile phases are chosen depending on the product being tested. Standardized markings are used on the stationary phase strips for consistency in analysis. Each radiopharmaceutical utilizes a chromatography system that maximizes the detection of radiochemical impurities.

All individual doses (with a few licensed exceptions for manufacturer-packaged radiopharmaceuticals) are assayed in a dose calibrator before dispensing. Utilizing a syringe shield, the nuclear pharmacist withdraws a specific volume from the shielded vial of radiopharmaceutical and assays the activity in the dose calibrator. The activity of the dose is decayed to the prescribed calibration time, either by calculation or automatically by the dose calibrator. If the activity of the dose at calibration time is within  $\pm 10\%$  of that which is ordered, it may be dispensed. The actual calibrated activity is written on the prescription label and initialed by the pharmacist, then dispensed for a Nuclear Medicine Technologist to use for a study.

Table 13-1. Common Nuclear Medicine Studies

### 13.1.c Nuclear Medicine Studies

Radiopharmaceutical use is continually increasing and new applications continue to appear. There are more than 100 different nuclear medicine exams; however about seven types of studies (Figure 13-1) account for nearly 90% of the work. This section will review several common scans, the concepts and clinical indications involved. Table 13-1 lists common diagnostic studies. The patient is normally injected with the radiopharmaceutical and must then wait for the radionuclide to be absorbed in the desired organ before scanning can begin.

**Bone imaging** is performed to evaluate areas of bone injury or bone disease. The areas usually associated with ongoing bone repair experience increased metabolic activity and increased blood flow. Radiopharmaceuticals which mimic the metabolic behavior of bone constituents will localize in these regions of bone repair in increased concentration relative to normal bone. Bone scans are often used in the staging of malignant disease, evaluation of primary bone neoplasm, diagnosis of early skeleton inflammatory disease, evaluation of elevated alkaline phosphatase of undetermined origin, and determination of bone viability.

**Brain imaging** is difficult because vasculature of the brain normally excludes most ionic materials from the brain, but the vascular integrity can be damaged in many ways (e.g., actual injury / contusion or ischemic injury from a stroke) which then disrupts the "blood-brain barrier." When such injury is present, material can penetrate from the blood stream into the extracellular spaces in the damaged area. If radioactive materials are present in the blood, they will appear in the extracellular space in abnormal concentrations. A brain scan then visualizes a hot spot against a cold background, making this procedure unusually sensitive for the diagnosis of brain tumors, vascular lesions, trauma, inflammation, cystic lesions, and extra-cortical lesions.

**Cardiac imaging** takes on several specialty areas. In gated cardiac blood flow/pool, radiolabeled tracers can be used to visualize areas containing large quantities or pools of blood (e.g., chambers of the heart or aortic aneurysms) and can thus be used to study left ventricular ejection fraction or left ventricular wall motion. Normally,

Radiopharmaceutical	Use
$^{99m}\text{Tc}$ macroaggregated albumin (MAA)	pulmonary perfusion imaging
$^{99m}\text{Tc}$ pentetate	renal perfusion imaging
$^{99m}\text{Tc}$ mebrofenin	hepatobiliary imaging
$^{99m}\text{Tc}$ mertiatid	renal perfusion, anatomical imaging
$^{99m}\text{Tc}$ sestamibi	myocardial imaging
$^{99m}\text{Tc}$ medronate (MDP)	bone imaging
$^{99m}\text{Tc}$ sulfur colloid (SC)	hepatic and bone marrow imaging, gastric emptying studies
$^{99m}\text{Tc}$ bicisate	cerebral perfusion imaging
$^{99m}\text{Tc}$ exametazime	cerebral perfusion imaging, leukocyte labeling
$^{99m}\text{Tc}$ pyrophosphate (PYP)	myocardial infarct imaging, RBC labeling for ejection fraction (MUGA)
$^{14}\text{C}$	helicobacter pylori diagnosis
$^{32}\text{P}$	therapy
$^{67}\text{Ga}$ gallium citrate	tumor imaging
$^{89}\text{Sr}$ or $^{153}\text{Sm}$	metastatic bone palliative therapy
$^{111}\text{In}$ oxyquinoline	leukocyte labeling
$^{123}\text{I}$ sodium iodide	thyroid uptake, imaging
$^{131}\text{I}$ sodium iodide	thyroid uptake, imaging and therapy
$^{133}\text{Xe}$ xenon gas	pulmonary ventilation studies
$^{201}\text{Tl}$ thallous chloride	myocardial imaging

perfused myocardium has a high concentration of intracellular potassium. A myocardial perfusion study images the myocardium by using radioactive potassium or an element that behaves similarly in the body (e.g., rubidium, cesium, or thallium). Myocardial perfusion imaging is performed to detect the regional distribution of the coronary arterial blood flow. Thallus ion ( $Tl^+$ ) has been shown to become distributed in tissues in a manner almost identical to that of the potassium ion. As mentioned above,  $^{99m}Tc$ -labeled bone seeking radiopharmaceuticals localize in areas of ischemic tissue damage. These areas are also damaged in myocardial infarcts. The tracer can localize areas of myocardial damage or dysfunction.

**Liver / spleen imaging** is performed using  $^{99m}Tc$  sulfur colloid administered IV. The sulfur colloid particles are removed from the body by phagocytosis. These cells are normally found uniformly distributed in the liver (85%) and spleen (5 - 10 %) and the radioactive colloid will be uniformly distributed throughout these organs. Disease disrupts the normal architecture and the area of disruption will be displaced or damaged and will usually image as a cold spot. The study can be used to evaluate the size, shape, function and location of the liver and spleen (structure) or to diagnose metastatic cancer which has spread to the liver, other primary tumors and cirrhosis.

**Liver / biliary system** scanning relies on the fact that certain tracers are selectively removed from the blood and excreted in the bile. These can be used to image the pattern of bile excretion via the gallbladder to help differentiate obstructions due to liver causes (jaundice) as opposed to biliary system obstructions.

**Lung studies** may be one of several types of examinations. Perfusion studies use small particulate material (20 - 50  $\mu m$ ) called macroaggregated albumin or MAA that is injected into the bloodstream and is filtered out and entrapped at the first downstream capillary bed it encounters. If injected into a vein, the filtration occurs in the lungs. Using a radioparticle, it is possible to outline those areas of the lung where there is blood flow down to the capillary level. Areas of obstruction (e.g., embolism), shunting (e.g., near pneumonia or atelectasis), or areas absent of capillaries (e.g., blebs) appear non-radioactive as no particle trapping occurs. Perfusion studies to evaluate the distribution of pulmonary arterial blood flow for pulmonary embolism or chronic lung disease diagnosis is normally performed after a pulmonary function test. The MAA particles are trapped in the capillary vessels of the lung like an embolism. The particle blocks fewer than 1 in 1000 pulmonary arterioles and no pulmonary function abnormalities have been demonstrated from such an injection.

**Perfusion scanning** is usually done to screen for pulmonary embolization. However, emphysema, chronic bronchitis, pneumonia, atelectasis, and carcinoma can produce perfusion defects which are indistinguishable from those caused by emboli. Combining a display of regional pulmonary ventilation with the perfusion scan eliminates much of the uncertainty. Ventilation / lung function studies evaluate the ventilation of the lung for pulmonary determination (embolism or tumor), chronic obstruction lung disease, etc. Many formerly involved imaging while the patient breathed radioactive  $^{133}Xe$ , the trend is toward the use of nonradioactive xenon or  $^{99m}Tc$  DTPA aerosol.

**Thyroid imaging** is used to image solitary or multiple thyroid nodules, assess thyroid size and function and aid in management of thyroid cancer. The thyroid traps and concentrates iodine from the blood plasma. In the gland the iodine is organically incorporated and stored as thyroglobulin. This high concentration and prolonged storage permits easy visualization via radioiodine. Pertechnetate ( $^{99m}Tc$ ) ions are also trapped, but not organified, so they can be used to obtain a satisfactory scan. Imaging studies normally use NaI of some sort (e.g.,  $^{123}I$ ,  $^{131}I$ ), however, if the imaging is performed rapidly enough after administration, then  $^{99m}Tc$  can be used. Depending upon agent used, large radiation dose to the thyroid is possible.

Table 13-2 lists some of the activity-dose relationships for different imaging agents.

Some tumors and non-neoplastic lesions (e.g., abscesses) have a high affinity for gallium accumulating in lysosomes and lysosome-like cytoplasmic granules of viable cells. For inflammatory and soft tissue tumors,  $^{67}Ga$  Citrate aids in evaluating areas for possible localized infection and major areas like bacterial endocarditis, lung abscesses, pelvis and intra-abdominal abscesses. For abscesses (only)  $^{111}In$  labeled white cells are normally used.

Numerous drugs are cleared and/or bound by the kidney. Some pharmaceuticals are removed from the blood by cells of the proximal renal tubules and held-up or excreted over time. Thus, renal studies are able to provide both kidney functioning and urinary excretion information; evaluate renal pelvis, ureters and urinary bladder; estimate the effective renal plasma flow; and conduct an evaluation of sequential images of the renal system. The

Table 13-2. Thyroid Doses

Radionuclide	Activity	Thyroid Dose <sup>1</sup> (mrad/ $\mu Ci$ )
$^{123}I$	100 - 400 $\mu Ci$	7.5
$^{125}I$	100 - 400 $\mu Ci$	450
$^{131}I$	1.4 $\mu Ci$	800
$^{99m}Tc$	1 - 2 mCi	0.2

<sup>1</sup>based upon normal (20 - 30%) thyroid uptake

renal function study (renogram) is a graphic expression of the flow of a radiopharmaceutical through the kidneys. Ortho-iodohippurate is cleared from the kidneys by glomerular filtration (20%) and tubular secretion (80%). Static images can be performed to evaluate position, size and shape of the kidney. Tumors, cysts and abscesses (which do not contain tubular cells) or parts of the kidney that are deprived of their blood supply (infarction) or are injured (hematoma) will appear as cold areas.

### 13.1.d Nuclear Medicine Imaging

The two most desirable characteristics of radiopharmaceuticals used for imaging is that they not emit a particle and the energy of the gamma not be too high. Particulate radiation is not very penetrating in tissue and the decay energy will be absorbed within a few millimeters. This energy absorption may result in cellular damage (cf., 2.2) and cannot be used to produce an image. The energy of the gamma photon is also important. If it is too low (e.g., < 50 keV), it will not be able to penetrate completely from within the body. If it is too high, it is difficult to detect it with a scintillation detector. The most desirable energies for detection are between 100 and 150 keV.

For most radiopharmaceuticals, approximately 2 - 4 hours after injection, the patient is ready for the scan. Imaging is performed using a special scintillation detector (cf. 7.4) called a gamma camera. The first types of detectors simply moved over the patient's body measuring the number of gamma photons detected and creating a spot on paper or film corresponding to the intensity of the radiation. These *rectilinear scanners* were too slow for efficient scanning so detectors were made with a collimator enabling an entire organ system to be imaged at once. The two major types of collimators used on radioisotope cameras are multichannel (or parallel-hole) and pinhole collimators (Figure 13-3).

**Multichannel collimators** are the most widely used collimators on gamma cameras. They consist of a series of holes with parallel axes in a plate usually made of lead or some other dense material which stops the gamma rays used in imaging. The holes may be circular, square, or polygonal. The space between the holes should be wide enough and the collimator thick enough so gamma rays traveling at an angle are absorbed. The gamma-ray image at the detector is equal in size to the object observed. The best resolution occurs with the collimator in contact with the object to be imaged and decreases with distance.

**Pinhole collimators** have a single hole in a lead plate. The photons from the source travel through the pinhole and form an inverted image of the object on the detector. If the distance between the hole and the detector is equal to the distance between the object and the detector, the image and the object are of equal size. Because the efficiency of a pinhole system is related to the inverse square of the pinhole-object distance, this type of collimator is best suited for imaging small objects. In clinics, pinhole cameras are primarily used to magnify small objects (e.g., thyroid) or reduced magnification of large objects when the detector is too small to encompass the entire organ (although this use is very inefficient and multichannel collimators should be used).

The scintillation camera (Figure 13-4) is the device used for imaging gamma-ray photons from the scan patient. It consists essentially of a single, cylindrical NaI(Tl) crystal (typically ½-inch thick) optically coupled to a hexagonal array of photomultiplier tubes (PMT). The PMTs are connected to an electronic circuit which determines the position of the flash of light generated within the crystal as a result of gamma-ray interaction. This positioning is accomplished on the basis of the relative amount of light sensed by each photomultiplier tube. Even if a scintillation is produced between the photomultiplier tubes, its position can still be determined because of the proportionate division of the light among the tubes. The total signal from the PMT is summed, and the computer rejects light signals that do not fall within the photopeak of the  $\gamma$ -ray photon being imaged (e.g., 140 keV for  $^{99m}\text{Tc}$ ).

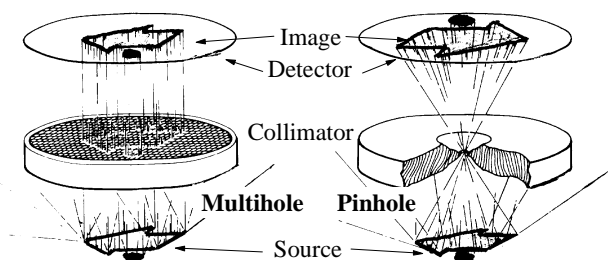


Figure 13-3. Gamma Camera Collimators

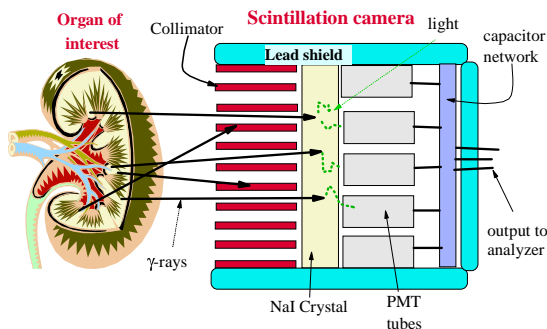


Figure 13-4. Collimated Camera

### 13.1.e Single Photon Emission Computed Tomography (SPECT)

While nuclear medicine is advantageous for dynamic imaging, it suffers the same limitation of diagnostic radiology and fluoroscopy; specifically the output is two-dimensional. Initially this flat image consisted of varying grades of brightness on a regular (single emulsion) x-ray film. As technology progressed, color was added so physicians could quantify the brightness by the various shades of color. However, two dimensions is a limitation.

The introduction of Single Photon Emission Computed Tomography (SPECT) cameras, initially used to perform brain imaging, added another dimension to nuclear medicine. The SPECT system (Figure 13-5) usually consists of 2 (or more) cameras which are angled (e.g., 90°, 180°, etc.) about the patient's target organ. SPECT results in better image quality than single-camera imaging because the sources of activity are not superimposed upon each other; hence the signal-to-noise-ratio (i.e. the contrast between the target and the background activity) is increased.

The primary advantage of this system is its high sensitivity, resulting in high spatial resolution and rapid imaging of the organ. For example, SPECT perfusion images (of the brain) can be obtained with a spatial resolution of 10 mm in the plane of the slice. In addition, the high collection efficiency of the multidetector system makes rapid scanning of an entire slice possible.

Although rotating-type gamma cameras are readily available they have a lower sensitivity than the multidetector camera. With the rotating gamma camera, data is collected from multiple views obtained as the sodium iodide detector rotates about the patient's organ of interest. Because spatial resolution and image quality depend upon the total number of primary, unscattered photons recorded by the detector, gamma cameras have been designed with multiple detectors to improve instrument sensitivity. Three and four-head cameras have been introduced and they have a marked improvement in spatial resolution (6 to 10 mm) compared with 14 to 17 mm for a single head systems without any increase in examination time. Special purpose, ring-type imaging systems were also designed to maximize the amount of detector recording activity from the target organ. These use multiple detectors or a single sodium iodide ring and collect activity simultaneously from either single or multiple slices (multidetector systems) or from all regions of the brain (annular detectors). Special purpose systems produce high quality images with a spatial resolution of 5 to 6 mm. The volume imaging capacity of most SPECT systems permits reconstruction at any angle, and, with some systems, images can be merged with MRI and CT, creating a single image that combines anatomy and physiology (morphological and functional correlation).



Figure 13-5. SPECT Camera

### 13.1.f Positron Emission Tomography (PET)

Most nuclear medicine studies, including PET, are "functional imaging" procedures in contrast to x-rays, CT, MRI or ultrasound procedures which produce static anatomical images. While anatomical studies are vital for many conditions, changes in metabolism, blood flow or receptor status frequently predate and may appear much earlier than the physical changes in the anatomical appearance of a tissue or organ.

Conceptually PET is similar to Nuclear Medicine. It is an imaging technique which uses small amounts of radioactivity for physiological studies. The pharmaceuticals are introduced into the body, either by injection or inhalation of a gas, and a PET scanner is used to produce an image showing the distribution of the pharmaceutical in the body. The difference is that PET radiopharmaceuticals emit positrons ( $\beta^+$ ) rather than the photons ( $\gamma$ ) used in conventional nuclear medicine studies. These positrons travel a short distance (1 - 2 mm) in tissue, before colliding with an electron. This "annihilation reaction" results in the emission of two 511 keV gamma rays traveling in opposite directions (Figure 13-6).

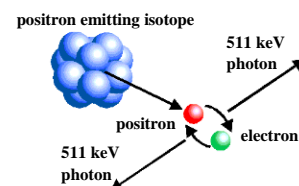


Figure 13-6. Positron Emission

The radioactive material used in PET is produced in an accelerator (see **Chapter 12**) which takes ions (either protons or deuterons), accelerates them and directs them toward "targets." Through nuclear reactions some

atoms are transformed into the desired positron-emitting radioisotopes. The most common radioisotopes used in PET have a half-life between 75 seconds and 110 minutes. The positron-emitting isotopes are transferred from the accelerator target to a chemical synthesis laboratory and labeled to pharmaceuticals for the physiological study.

Labeling is the process of attaching some kind of identifying tag to a compound which will allow the physician to identify where the compound has gone. One of the big advantages of PET is that some of the atoms which can be labeled (turned into positron emitters) are the same atoms which naturally comprise the organic molecules used in the body. Among these atoms are oxygen, carbon and nitrogen. Since these atoms occur naturally in organic compounds, replacing the naturally occurring atoms in a compound with a labeled atom produces a compound that is chemically and biologically identical to the original. It will behave in a manner identical to its unlabeled counterpart and is also traceable. It is possible to label both naturally occurring compounds such as neurotransmitters, sugars, etc., and synthesized compounds (such as drugs) and follow them through the body.

PET is able to provide physicians with information about the body's chemistry that is not always available through other procedures. Unlike CT or MRI, which look at anatomy or body form, PET studies metabolic activity or body function. Some PET uses include:

- Tumors -- PET imaging is very accurate in differentiating malignant from benign growths, as well as showing the spread of malignant tumors. PET imaging can help detect recurrent brain tumors and tumors of the lung, colon, breast, lymph nodes, skin, and other organs. Information from PET imaging can be used to determine what combination of treatment is most likely to be successful in managing a patient's tumor.
- Coronary Artery Disease -- PET imaging is unique in its ability to determine whether a patient's heart muscle will benefit from coronary artery bypass surgery. An image of a heart which has had a myocardial infarction (heart attack) can identify areas that have been damaged by the attack, indicating healthy and dead myocardial tissue and can therefore, identify which patients will not benefit from heart surgery but for whom other forms of treatment will be more beneficial.
- Diseases of the Brain -- PET imaging can provide information to pinpoint and evaluate diseases of the brain. PET imaging can show the region of the brain that is causing a patient's seizures and is useful in evaluating degenerative brain diseases such as Alzheimer's, Huntington's, and Parkinson's. Additionally, within the first few hours of a stroke, PET imaging may be useful in determining treatment therapies.

Because many PET radiopharmaceuticals are chemically equivalent to or close analogs of naturally occurring compounds, it is possible for PET to provide functional images of the human body. Some of the more common PET radiopharmaceuticals and their uses include:

- <sup>11</sup>C -- Acetate as a radiopharmaceutical is primarily used in the heart to measure the oxidative metabolism rate.
- Methionine is used in tumor protein synthesis studies.
- Amitriptyline is used in tricyclic antidepressant studies.
- <sup>13</sup>N -- Ammonia labeled with <sup>13</sup>N is used in cardiac blood flow studies to measure perfusion in the myocardium. The half-life of 10 minutes allows both at-rest and stress studies to be performed in one session.
- <sup>15</sup>O -- Water is used to measure blood flow and in brain research studies.
- <sup>18</sup>F -- Fluoride is used in bone scanning studies.
- Fluorodeoxyglucose (FDG) is similar in structure to glucose and is the compound most widely used in PET due to the ubiquitous use of glucose by the human body. It is used to detect and evaluate tumors, to assess myocardial viability, and in diagnosing of a number of different neurological conditions.
- DOPA is a tracer that measures L-dopa uptake and can give a measure of dopamine synthesis rates.
- Fluoromisonidazole (FMISO) is a hypoxic agent which is metabolically trapped by viable cells according to their degree of hypoxia.
- <sup>82</sup>Rb -- A cardiac blood flow tracer with a very short half-life (75 seconds) that allows for rapid serial studies.

In addition, there are literally hundreds of other positron-emitting compounds that have been synthesized to study various physiological processes in the body.

A PET scan usually takes between one to two hours to perform and requires the patient to lie completely still. Just as in a CT (Figure 10-9), the patient lies on a table that slides into the middle of the scanner. If a brain scan is being performed the patient's head is placed in a special head rest and immobilized using foam blocks or a special mold individually shaped for each patient. After the preparation is completed the patient is placed on the scanner and positioned as accurately and as comfortably as possible for the scan. One or two short scans are taken

prior to administration of the pharmaceutical so the patient will not be startled by the scanning process. It is vitally important that the patient remain absolutely still throughout the entire procedure.

Within the scanner are rings of scintillation detectors (see 7.4). The positron annihilation photons are detected as pairs in coincidence by this series of detectors arranged in a ring around the patient (Figure 13-7). This insures that single gamma photons can be eliminated from the scan. The scanner's electronics record these detected photons and map an image of the area where the radiopharmaceutical is located. Most systems are capable of resolutions of about 5 mm. Because the energies of the positrons are greater than the gamma-ray energy used in nuclear medicine (i.e., 511 keV versus 150 keV), denser scintillation detectors are usually employed. Some of the crystals being investigated are bismuth germanate oxide (BGO) and lutetium oxyorthosilicate (LSO). Recall that denser materials stop gamma rays better than light materials. Sodium iodide, the crystal used in nuclear medicine, has a molecular weight of 149.8 gm/mole. Bismuth germanate oxide and lutetium oxyorthosilicate have molecular weights in the region of 298 gm/mole and 219 gm/mole, respectively, so they are more ideal for photon detection within the positron range of energies.

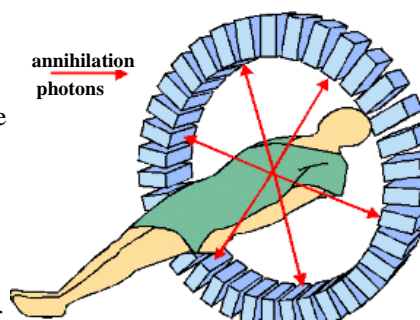


Figure 13-7. PET Scanner

## 13.2 Radiopharmaceutical Therapy

Radiopharmaceuticals are used in both diagnosis and therapy. The therapeutic uses are primarily directed against cancerous tissues utilizing the concept of tissue radiosensitivity as outlined by Bergonie and Tribondeau (i.e., rapidly dividing cells are more radiosensitive). Cancer tissue dies rather quickly after receiving a large dose of radiation. The goal of the therapy is to use radiation to destroy diseased or cancerous tissue while sparing adjacent, healthy tissue. Besides  $^{131}\text{I}$ , therapies have used  $^{32}\text{P}$ ,  $^{89}\text{Sr}$ ,  $^{153}\text{Sm}$ ,  $^{186}\text{Re}$  and  $^{198}\text{Au}$ . Often a much higher dose of radioactivity is administered in a therapeutic situation than in a diagnostic one, so the therapeutic radiopharmaceutical must have a high affinity for the diseased tissue and the pharmacist must follow detailed protocols. The precautions followed depend both upon the type and quantity of radioisotope. The quantity of radiopharmaceutical administered determines hospitalization and the type determines preparation of the inpatient area.

Certain chemical compounds, when absorbed by the body, concentrate in one or several organs. In radiation protection the organ which has a high affinity for a radionuclide is called the **critical organ**. In therapy the critical organ is usually called the **target organ** for the therapy. The **organ uptake** or **uptake** tells how much, or what percent, of an administered radiopharmaceutical will actually be absorbed, metabolized and stored in the target organ. Some factors which influence uptake are: (1) how much of the chemical is already in the organ, (2) how well the organ is vasculated, (3) how the pharmaceutical is administered.

The attending physician will prescribe a quantity of radiopharmaceutical based upon the uptake of the organ and the radiation dose needed to perform the therapy. The normal procedure is to administer a high specific activity radiopharmaceutical to the patient either orally or intravenously. The radiopharmaceutical is metabolized and taken up by the target organ. Most of these radiopharmaceuticals tend to decay by  $\beta$  emission although in the past  $\alpha$ -emitters have been used. The  $\beta$  has only a limited range in tissue and will deposit all its energy in the immediate vicinity of the organ. This deposition is measured in gray (rad) and dose to the organ is usually given in Gy/MBq (rad/mCi) or Gy/kBq (rad/ $\mu$ Ci) either administered or taken up by the organ. The radiation deposition destroys the cells in the target organ. With much of the organ destroyed, patients may then be required to take drugs as replacement for hormones or metabolics produced by that organ.

### 13.2.a $^{32}\text{P}$ Therapy

In treating ascites (excessive accumulation of fluid in the abdomen) with  $^{32}\text{P}$ , normally 111 - 185 MBq (3 - 5 mCi) is injected directly (through butterfly) into the peritoneum. Additionally, though less popular now, 3 - 5 mCi may be administered IV for polycythemia vera where the  $^{32}\text{P}$  concentrates in the bone marrow essentially reducing the number of red blood cells produced.

The  $^{32}\text{P}$  therapies are usually performed in the Nuclear Medicine Clinic on an outpatient basis. The area where the injection is to take place is draped with absorbent paper to prevent any drops of  $^{32}\text{P}$  contaminating the area.

Clinical staff wear gloves and utilize Lucite shielding when carrying the dose. Usually leaded syringe shields are used in the clinic. Because of bremsstrahlung, Lucite shields may be better for  $^{32}\text{P}$ . TLD rings are also mandated. After the injection, the staff surveys the application area with a thin-window GM probe. Syringe and tubing are placed in the clinic's radioactive waste, absorbent paper with no detectable  $^{32}\text{P}$  is not considered radioactive waste.

### 13.2.b Palliative ( $^{32}\text{P}$ , $^{89}\text{Sr}$ , $^{153}\text{Sm}$ , $^{186}\text{Re}$ ) Therapy

One increasing common therapeutic application is the use of radiopharmaceuticals for the relief of pain for patients with disseminated bone cancer and other joint disorders (e.g., hemophilic arthropathy). Intravenous injections of certain  $\beta$ -emitting bone seekers ( $^{89}\text{Sr}$ ,  $^{153}\text{Sm}$ ,  $^{186}\text{Re}$ ) will spare the patient much pain and degradation by numbing the neural ends in the bone. Injection of high-energy  $\beta$ -emitters directly into a joint will retard joint degradation and reduce pain. Because these radiopharmaceuticals emit high-energy  $\beta$  particles, there is very little radiation exposure from the patient and very little contamination. Medical staff normally use the same precautions for palliative therapy as they follow for  $^{32}\text{P}$  therapy.

### 13.2.c $^{131}\text{I}$ Therapy

Iodine-131 is administered orally for both Graves Disease (hyperthyroidism) and thyroid carcinoma. The dosage regimen depends upon the therapy desired and thyroid's uptake. Because of a high uptake, Graves Disease is normally treated with 370 - 1110 MBq (10 - 30 mCi) while thyroid carcinoma and thyroid ablations, which usually have a low uptake, may be treated with between 925 - 5,550 MBq (25 and 150 mCi).

Therapies involving radiopharmaceutical doses less than 1,220 MBq (33 mCi) are usually performed in the Nuclear Medicine Clinic on an outpatient basis. The  $^{131}\text{I}$  may come encapsulated in gel caps (expensive) or as a liquid (inexpensive). Capsules are easily administered and pose little cleanup problem. Administration of a capsule is usually by hand, similar to any capsule. Liquid administration is more complicated. The liquid vial must first be vented in a fume hood to eliminate any  $^{131}\text{I}$  vapor buildup. The administration area is covered with absorbent paper, the patient sits in front of the prepared area and sips the liquid  $^{131}\text{I}$  through a straw. The vial is flushed several times with sterile water to insure a maximum amount of  $^{131}\text{I}$  is ingested. Because the  $^{131}\text{I}$  has an 8 day effective half-life, emits beta particles and gamma rays, and can easily be ingested by other family members, the patient is counseled regarding their personal actions after they leave the clinic. Specific instructions include: maintain distance from young children, use of disposable utensils, dishes, etc., personal hygiene, restrict over-affectionate embraces. When the patient departs, the administration area is surveyed and waste is properly disposed.

The NRC presently requires that, unless more restrictive than normal precautions are followed by the patient or multistage excretory models are utilized by the clinic, all patients who are administered more than 1,220 MBq (33 mCi) of radioiodine be hospitalized until the quantity of radioactive material in their body is reduced to below 1,220 MBq (33 mCi). This requirement is based on the need to maintain exposures to all members of the general public below 0.1 mSv (100 mrem) and to specific members of the general public (e.g., family members) below 0.5 mSv (500 mrem). Therefore, some  $^{131}\text{I}$  thyroid therapy patients must be hospitalized. These patients are usually healthy and able to care for themselves with no bedside nursing. These therapies are routinely given after the patient has had their thyroid surgically removed, the  $^{131}\text{I}$  is used to destroy (i.e., ablate) any residual thyroid tissue. Because the remainder of the thyroid is small and poorly vasculated, uptakes of iodine are generally low requiring larger doses, normally 3,700 - 5,550 MBq (100 - 150 mCi). Multiple therapy doses in the range of 9,250 MBq (250 mCi) require the staff observe the patients blood counts for signs of bone marrow depletion.

If the clinic considers excretory data, then a 3-compartment model can be applied by substituting values from those found in Table 13-3 into the accepted equation:

$$D(t) = \frac{34.6 \Gamma Q_0}{(100 \text{ cm})^2} \left\{ E_1 T_p (0.8) \left( 1 - e^{-\frac{0.693(0.33)}{T_p}} \right) + E_2 F_1 T_{1\text{eff}} \left( e^{-\frac{0.693(0.33)}{T_p}} \right) + E_2 F_2 T_{2\text{eff}} \left( e^{-\frac{0.693(0.33)}{T_p}} \right) \right\}$$

If this method is used, the dose must be calculated and placed in the patient's record. The required entry for a hyperthyroid therapy would be exposure dose (mrem) = 8.843 x (administered activity) mCi and for a thyroidectomy the equation exposure dose (mrem) = 2.267 x (administered activity) mCi would be used. For example, a 29.9 mCi dose for hyperthyroidism has a calculated exposure of 264 mrem and a 150 mCi dose for thyroidectomy has a calculated exposure of 340 mrem. These values would be included in appropriate sections of the consent form.

Table 13-3. Uptake Fractions and Effective Half-Lives for Iodine-131 Treatments

Medical Condition	Extrathyroidal Component		Thyroidal Component	
	Uptake Fraction F <sub>1</sub>	Effective Half-Life T <sub>1eff</sub> (day)	Uptake Fraction F <sub>2</sub>	Effective Half-Life T <sub>2eff</sub> (day)
Hyperthyroidism	0.20	0.32	0.80	5.2
Postthyroidectomy for Thyroid Cancer	0.95	0.32	0.05	7.3

Other considerations for performing <sup>131</sup>I in-patient therapies are:

- Liquid <sup>131</sup>I is stored in a fume hood and vented by the Nuclear Medicine radiopharmacist immediately prior to actual ingestion.
- Room preparation is designed to reduce the risk of contamination
  - ✓ Patient is given a room with private bathroom, preferably away from entrance and egress points
  - ✓ Absorbent paper (Kraft paper in 5 ft rolls is adequate) is placed on floor creating a walkway to door, bathroom, and between the bed. It is also placed on the bathroom floor where the patient may stand and on tray tops where they eat.
  - ✓ Plastic gloves are placed on items patient may touch such as faucet handles, door handles, nurse call button, light switch, etc.
  - ✓ Two waste boxes are placed in room, one for trash and one for linen
  - ✓ Closet is furnished with 3 or 4 linen exchanges (to include pajamas, robes, slippers, etc.)
  - ✓ Signs posted on the door include **Caution - Radioactive Materials**, sketch of room with dose rates, nursing precautions, and sign-in register.
- Patient is counseled regarding actual procedure, length of stay, procedures to follow while an inpatient, and precautions when released, <sup>131</sup>I contamination, it's sources and precautions to take to reduce the spread.
- The dose is administered in a similar fashion to the Graves Disease patient, however administration is performed in the patient's room with physician and Nuclear Medicine personnel present. After the dose is administered, the tubing, straws, etc. are surveyed prior to leaving. The activity administered is entered on the visitor precaution sign on the door and the patient room is surveyed at 1 meter from patient, at bedside, at the visitors chair, at doorway, and on the other side of all accessible walls. Exposure results are indicated on survey sheet.
- The patients record is annotated, "Radioactive" labels are affixed, one on the outside and one in the history section indicating the dose and exposure rate for nurses. Dosimeters, sign-up sheet, and nursing instructions are given to chief ward nurse with whatever verbal instructions are appropriate
- Patient must remain hospitalized until the activity remaining in their body is below 1220 MBq (33 mCi). This can be determined in several ways:
  - ✓ Collection and assay of urine to determine how much has been excreted. This method is probably not done at many facilities since the urine of these patients is normally exempt from radioactive waste precautions unless collected.
  - ✓ Activity - Exposure Ratio. The exposure from the patient is measured 1 hour after dosing. This dose rate, D<sub>i</sub>, is the initial dose and corresponds to the administered dose, A<sub>i</sub>. The patient is monitored twice daily until the final dose rate, D<sub>F</sub>, corresponds to 33 mCi. Use the ratio:
 
$$D_F = 33 \cdot \frac{D_i}{A_i}$$
  - ✓ Exposure Rate. The exposure rate at 1 meter from the patient's thyroid is measured twice daily (AM, PM). An exposure rate of 6.6 mR/hr at 1 meter indicates that the patient has about 30 mCi (1.8 mR/hr = 8 mCi, 11 mR/hr = 50 mCi; Table 4, NCRP 37).

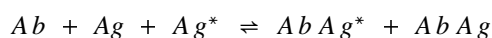
When the radiation restrictions are removed, the chief ward nurse is informed that the patient may go home when the attending Nuclear Medicine physician releases him/her. The patient's record is annotated with the final dose rate and the precaution label on the record is removed. The patient is counseled to bathe/shower and dress, close the door, and see the chief nurse about moving to another room or going home.

The room cleanup follows patient discharge. Absorbent paper and plastic gloves are removed and placed in trash box. Linen is removed and placed in linen box. The room is surveyed with a thin-window GM to ascertain

spread of contamination. Hot spots or areas of suspected contamination are cleaned with soap and water and resurveyed. It is common to find hot spots in the bathroom around the toilet (males should be directed to sit when urinating), the bed rails, bedside cabinet, etc. Trash and linen is removed and held for 10 half-lives (i.e. 80 days) before being disposed of or laundered, as appropriate. The final survey is performed using wipes and counting on a sensitive system (e.g., auto-gamma counter, liquid scintillation counter). Results are recorded on the survey form. If additional cleaning is required, the contaminated spots are again cleaned and resurveyed. When room is finally released to nursing, the chief ward nurse is informed and all signs and markings removed from door.

### 13.3 Clinical Lab Procedures (RIA)

Radioimmunoassay is a technique involving the use of labeled compounds to measure the concentration of hormones or other compounds in the plasma or other body fluids (e.g., urine). In theory, RIA is based on the radionuclide dilution principle, along with the use of a specific antibody to bind a portion of a substance to be measured. If an antigen or hormone, Ag, is mixed with a specific antibody, Ab, to that antigen an interaction will occur, forming an antigen/antibody complex, AgAb, that is chemically different from either the antigen or antibody.



If there is not enough antibody to complex all the antigen present, mixing of the antibody with a known amount of radionuclide labeled antigen (Ag\*) along with an unknown amount of unlabeled antigen or hormone allows quantification of the unlabeled antigen. If the amount of radioactive labeled antigen is a known quantity, then by competitive binding the amount of Ag\*Ab complex formed will be inversely dependent on the amount of unlabeled antigen (hormone etc.) present.

The basic procedure followed in RIA is: mix patient sample and radioactive labeled antigen (less than 0.01  $\mu$ Ci) in a test tube, add antibody (Ab), mix contents - vortex, incubate the reaction mixture (minutes to day), separate the complex (AbAg | AbAg\*) from the free antigen (Ag | Ag\*), measure free antigen or complex (count the radiation in sample). To measure the unknown concentration of antigen, a series of known antigen concentrations (or standards) must be measured along with the unknown.

The choice of a radionuclide for labeling purposes is dictated mostly by the availability of a suitable procedure to tag the antigen under study. Radionuclide half-life, specific activity, availability and cost are other items that must be considered. For most studies  $^{125}\text{I}$  is the isotope of choice because: (1) the counting efficiency for  $^{125}\text{I}$  is higher than for  $^{131}\text{I}$ ; (2) the lower  $\gamma$ -ray energy of  $^{125}\text{I}$ ; (3) the longer half-life of  $^{125}\text{I}$  (60 days) compared with that of  $^{131}\text{I}$  (8.05 days) prolongs shelf-life; and (4) the handling of  $^{125}\text{I}$  presents a lesser radiation hazard than  $^{131}\text{I}$ . The activity in these clinical kits is very small, so they are usually exempt from Department of Transportation regulations and pose no radiation hazard to coworkers.

Table 13-4. RIA Radionuclides

Radionuclide	Application
$^3\text{H}$ , $^{14}\text{C}$	steroid analysis
$^{56}\text{Co}$ / $^{57}\text{Co}$	$\text{B}_{12}$
$^{125}\text{I}$ , $^{131}\text{I}$	peptide hormones, viral antigens, drugs

### 13.4 Brachytherapy

The word **brachytherapy** means *short therapy* appropriately implying that the radiation is limited to short distances. In brachytherapy, a sealed (i.e., encapsulated) source in the form of seeds, needles, or wires is inserted directly into the tumor (i.e., interstitial implant) or near a tumor (i.e., intracavitary therapy, mold therapy) where it will deliver gamma or beta radiation at a distance up to a few centimeters. Such short-range therapy results in decreased toxicity and allows the escalation of radiation dose. Brachytherapy for treating cancerous tumors was first used in the 1940s and was originally carried out using radium sources. Now artificially produced radionuclides are more commonly used. Some of the isotopes used are  $^{103}\text{Pd}$ ,  $^{125}\text{I}$ ,  $^{137}\text{Cs}$ ,  $^{192}\text{Ir}$  and  $^{90}\text{Sr}$  (beta therapy). Brachytherapy can be used in situations where surgery is not possible or not optimal or in situations where prior dose-limiting external-beam (see 13.5) has already been given. The fundamental objective of the use of specially constructed sealed sources (see Figure 9-8) is to obtain maximum therapeutic effect with minimum exposure to the patient's surrounding healthy tissue, the patient, the hospital staff and the general population.

Initially,  $^{226}\text{Ra}$  and  $^{222}\text{Rn}$  were the only sources used for brachytherapy. Because of this widespread use of radium, a system of specifying source strength in terms of **milligram-radium equivalent (mg-Ra eq)** developed and many clinics still prescribe source strengths in this unit. The equivalence is usually obtain by comparing the

exposure rates at a particular point from a given source and a radium source placed at the same distance. Because of the wide range of energies and filtrations now encountered in brachytherapy sources, the National Council on Radiation Protection and Measurement (NCRP) has recommended that the exposure rate be measured in terms of the *effective* equivalent mass of radium. This conversion is made by dividing the exposure rate of the source at 1 meter by the exposure rate constant of radium (encapsulated in a container with a specified wall thickness) at 1 meter. However, the best way to calibrate and specify brachytherapy sources is in terms of exposure rate at a distance of 1 meter. The effective mg-Ra eq activity should be used only to provide an approximate output comparison with radium sources.

### 13.4.a Low-Dose Rate (LDR) Afterloading

Low-dose rate therapy uses low activities (1850 - 7400 MBq; [50 - 200 mCi]) of  $^{103}\text{Pd}$ ,  $^{125}\text{I}$ ,  $^{137}\text{Cs}$ , or  $^{192}\text{Ir}$  to bombard the tumor volume usually for a 2 - 5 day period of time, although some therapies are performed where the sealed sources are permanently left within the tumor. Afterloading, one of the most common types of brachytherapy, uses stainless steel applicators in which the radioactive sources are loaded after all dose calculations are performed. The applicator, without the sources, is surgically implanted in the patient. After recovering from the anesthetic, the patient is x-rayed with simulated (or dummy) sources placed in the applicators to determine the geometry of the sources in relation to the tumor. The therapy physician has prescribed a certain radiation dose to the tumor. The source strength (Gy/hr @ 1 meter or mg Ra equivalent) and geometry will determine the length of time to reach the prescribed dose. Often (e.g., therapy of the cervix), dose to several other body parts in proximity to the cervix (e.g., bladder, rectum) is also determined and may be the limiting dose factor. After the simulation, the patient is transported to their room where the actual radioactive sources are inserted into the hardware.

Because the patient remains hospitalized with a significant quantity of radioactivity, surveys and monitoring are required. The patient's room and surrounding areas are monitored as soon as practicable after loading the sources into the patient. Exposure rates are measured at one meter from the patient's implant area, the implant site, the patient's bed side, one meter from the bed, the entrance to the room, in adjacent rooms (even if unoccupied), other outside areas, and in the hallway, particularly if the hall is adjacent to patients bed. Warning signs are placed on the door along with a list of precautions for staff and visitors to observe. Additionally, radiation stickers are usually placed on the patients record for the duration of the therapy.

Two to three days after insertion (based on source strength, geometry, and prescribed dose), the sources are removed by a radiation therapy physician and the applicators are then removed by surgical staff. After all of the sources have been removed and inventoried, a survey of the patient is performed to verify that all sources have indeed been removed. The therapy staff brings the sources to their storage room and replaces them in the vault, taking care to inventory and log the sources which insures none have been lost. With the sources removed, the patient no longer presents a radiation exposure hazard and all warning signs may be removed.

### 13.4.b Low-Dose Rate (LDR) Permanent Implant

Some low-dose rate therapy uses sealed sources (e.g.,  $^{103}\text{Pd}$ ,  $^{125}\text{I}$ ) that are permanently implanted within a tumor and which bombard the tumor volume for the active life of the source. The type of radiation source is selected because it has a low energy (e.g.,  $^{103}\text{Pd}$  - 22 keV x-ray;  $^{125}\text{I}$  - 35 keV  $\gamma$ -ray) which allows treatment of the organ without excessive radiation dose to normal tissue surrounding the tumor nor to members of the general public.

Currently, this type of therapy is most commonly used to treat cancer of the prostate. The sources, called *seeds* (Figure 13-8), are very small, some measure only 4.5 mm x 0.8 mm (0.177 inch x 0.032 inch). The physician typically implants from 40 to 100 seeds into the cancer site using ultrasound or a scope for guidance. The seeds are usually implanted by inserting a thin needle into a template and pushing a prescribed number of seeds into the organ at that point. The procedure takes approximately 1 hour to perform and patients have been treated on essentially an outpatient basis. The seeds slowly decay over their physical half-life (e.g.,  $^{103}\text{Pd}$  - 17 days;  $^{125}\text{I}$  - 60.1 days) and remain in the organ permanently.

This type of therapy has been conducted with very few reports of complications. In prostate therapy, one or two of the seeds may be excreted and pass out when the patient urinates and some patients report slight bleeding or



Figure 13-8.  $^{103}\text{Pd}$  seeds

blood in the urine for the first week or so. While not required, it is prudent to have the patient collect any seeds found in the linen, place them in a vial and return them to the therapy clinic.

### 13.4.c High-Dose Rate (HDR) Afterloading

High-dose rate afterloading (Figure 13-9) uses a high activity (185 - 370 GBq [5 - 10 Ci]) source of  $^{192}\text{Ir}$  to traverse in and around the tumor volume following a series of preprogrammed steps, irradiating the tumor with a very high dose rate (235 - 469 Gy/hr @ 1 cm) in a short period of time (typically 5 - 15 minutes per treatment). The HDR can be used to treat a cancer at virtually any accessible body site. Typically the patient receives between 3 to 6 treatments over a one to two week period. The benefits of this type of therapy include: (1) patients may receive this treatment as outpatients (improving patient comfort and quality of life), (2) training of nursing staff is minimal (when compared to in-patient services), (3) the device may be used to treat several patients in one day, and (4) more elaborate treatment plans (e.g., external beam followed by HDR and then more external beam) may be employed insuring a higher probability of cure.

Because of the high exposure, the treatment room is specially shielded and the staff must exert great care to insure that the treatment plan is followed to insure that no misadministration of dose occurs. Also,  $^{192}\text{Ir}$  has a 73.83-day half-life, so the source is replaced at 3-month intervals. The HDR device is computer controlled and guides the operator through the treatment process, reducing the chance of error and improving throughput. For example, once the treatment plan is established for a patient, that plan may be recorded on a magnetic, patient treatment card which can be used to set the HDR up for subsequent treatments of the same patient.

There are other types of remote afterloading devices, although currently not used by the UW. Two units similar to the HDR are a Pulsed-Dose Rate (PDR) brachytherapy system and a Low-Dose Rate (LDR) remote system. In these devices, the patient is treated in an in-patient status. Low energy sources (i.e., 18.5 - 37 GBq [0.5 - 1 Ci]) are automatically inserted into the tumor periodically (e.g., for 10 minutes each hour) and then withdrawn into the shielded device. In this manner, nursing service personnel can attend the patient without being exposed to the treatment radiation.



Figure 13-9. HDR  
used to set the HDR up for

### 13.5 External Beam Therapy (Teletherapy)

While brachytherapy is effective in treating patients, use of these sealed sources is both labor and resource intensive. Most source afterloading devices must be inserted surgically. Each patient requires his/her own room during therapy. The in-patient brachytherapy may require several treatments, each lasting 2 - 3 days. Such intensive demand is impractical when the basic goal of radiation therapy is to periodically irradiate the tumor volume with a total dose of between 50 to 70 gray (5000 to 7000 rad) over a several week period. In many cases, this same radiation dose can be delivered by high energy photon beams.

Before the nuclear age, the only source of high energy photons were x-ray machines. These *orthovoltage therapy* systems were limited by technology to approximately 150 - 500 kV and treatments normally were performed at 200 - 300 kV and 10 - 20 mA. While these systems were capable of delivering the required radiation dosage, their low potential (kV) meant that much of the radiation energy was absorbed by tissues in front of the cancer and consequently their success rate was not very good for deep-seated tumors or tumors surrounded by bone.

Because of the high penetrating power of the gamma-ray from  $^{60}\text{Co}$  ( $E_{\gamma} = 1.173$  and  $1.332$  MeV) and  $^{137}\text{Cs}$  ( $E_{\gamma} = 0.662$  MeV) and the ability to generate high radiation doses in a controlled setting,  $^{60}\text{Co} / ^{137}\text{Cs}$  *teletherapy* units began making widespread appearances. The results of these systems in treating deep tumors was much better than the 300 keV x-ray systems because higher energies are more deeply penetrating and tend to deposit their energy more uniformly along the radiation path.

The post World War II years saw progress in the quest for higher energy x-ray beams. *High voltage* or *supervoltage* therapy systems in the range of 500 - 1000 kV were researched. The major problem encountered was insulating the high voltage transformer. Resonant transformer units were developed to generate x-ray from 300 to 2000 kV. The 1950s saw the introduction of *megavoltage* (i.e., energy > 1 MV) systems such as the Van de Graaff

generator capable of producing 2MV x-rays. Ultimately high energy linear accelerators (linac) using the traveling wave principle (cf. Figure 12-7) were developed to irradiate tumors via *external beam therapy*. Accelerators are seeing greater medical and industrial use as they replace lower energy  $^{60}\text{Co}$  systems.

### 13.5.a Medical Linear Accelerators

As noted in Chapter 12, a linac has much in common with an x-ray machine. The electron source arises from a hot filament or cathode in an evacuated tube. There is an accelerating voltage between the cathode and the target or anode. In diagnostic generators, this voltage is adjustable from about 30 kV to 150 kV. In a linac, the accelerating voltages are fixed for a particular system and they normally range from about 4 MV to 35 MV. Diagnostic exposures often involve a single (0.001 to 10 sec) pulse with a 60 Hz to 720 (i.e., 12 pulse) Hz frequency, while linac radiation consists of short bursts (duration about 5  $\mu\text{sec}$  or 0.000 005 second) repeated several hundred times per second, each burst has a 3000 MHz frequency. Both systems employ collimators to shape the beam (although these are much thicker in linacs). Because the energy of the linac is much higher than the energy used in diagnostic x-rays, thick concrete walls are used for shielding instead of the relatively thin sheets of lead (1/16 inch) hidden in the walls of diagnostic x-ray rooms. High-energy linacs ( $E > 7 \text{ MeV}$ ) have the potential to generate neutrons from interaction with heavy metals found in the target material, walls of the accelerator structure, wave-guide, filters, collimators. While neutron activation of the air around the patient and of the patient is possible, it is very little and only of minor concern. A maze is usually incorporated in the room design to prevent neutron scatter from reaching the control console. Additional shielding using borated (5%) polyethylene can be used to attenuate neutrons when a sufficient thickness of concrete is not possible.

Because all medical linacs serve the same purpose, they tend to have similar components. Some of the major components in a linac are (Figure 13-10) the gantry, the stand, the control console, and the treatment couch. The two major structural components are the stand and the gantry. The *stand* is anchored firmly to the floor and the *gantry* rotates on bearings in the stand. The operational accelerator structure is housed in the gantry and rotates about a horizontal axis fixed by the stand. Other major components include:

The *klystron* is the source of microwave power used to accelerate the electrons. This power is conveyed to the accelerator structure in the gantry by a *wave-guide* and there is a *circulator* inserted in the wave-guide which isolates the klystron from any microwaves reflected back from the accelerator. The circulator diverts these reflected microwaves so they won't damage the klystron.

A *cooling system* is used to cool the various components that experience heat buildup and insures stable operating temperature sufficiently above room temperature to prevent condensation of moisture from the air.

The *accelerator structure* is the component where electron acceleration takes place. It consists of a copper tube with its interior divided by copper disks or diaphragms of varying aperture and spacing (Figure 12-7) and is kept under a high vacuum. Electrons are injected into the accelerator structure with an initial energy of about 50 keV by the *electron gun* (i.e., cathode) and are energized by the microwaves emitted by the klystron.

The high energy electrons emerge from the window of the accelerator structure in the form of a pencil-thin beam about 3 mm in diameter. In low energy linacs ( $E < 6 \text{ MV}$ ) the electrons strike the tungsten target to produce x-rays. In high-energy linacs, the accelerator structure is so long that the electrons are sent through the field of a

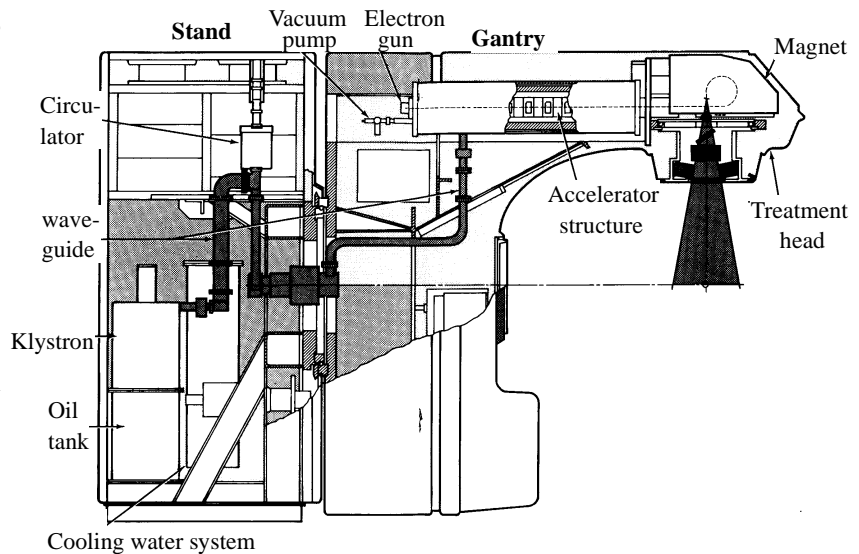


Figure 13-10. Medical Linac

**bending magnet** in the treatment head which deflects the electrons in a loop (usually 90° or 270°) before they can strike the target and produce x-rays or be used for electron treatment. The **treatment head** also contains beam shaping and monitoring devices.

X-rays are produced when the electrons hit a tungsten target. The target is water cooled and thick enough to absorb most of the electrons. The average photon energy of the beam is about one-third of the maximum electron energy. Directly opposite the collimator and extending from the bottom of the gantry may be a **beam stopper**. This is a large absorber which reduces room shielding requirements because it absorbs the radiation beam that emerges from the patient.

Some linacs are also capable of producing electron beams for therapy. The electrons produced in an accelerator are usually monoenergetic, consequently their energy is designated in units of million electron volts (e.g., 10 MeV), whereas the x-ray beam is more heterogeneous and designated in units of megavolts (e.g., 18 MV).

### 13.5.b Electron versus X-ray Beam Therapy Systems

Not all tumors are deep. Some are either on the surface or just beneath the surface. Shallow tumors are often treated with electrons generated from the linac. Figure 13-11 compares the treatment head arrangement for an electron beam versus an x-ray beam. As the electrons exit the accelerator structure, the beam is pencil thin. For electron therapy, instead of striking a tungsten target, the beam of electrons is made to strike an electron **scattering foil** in order to spread the beam as well as get a uniform electron density throughout the treatment field. This foil is most often a thin lead foil which scatters the electron beam without producing a significant number of bremsstrahlung x-rays.

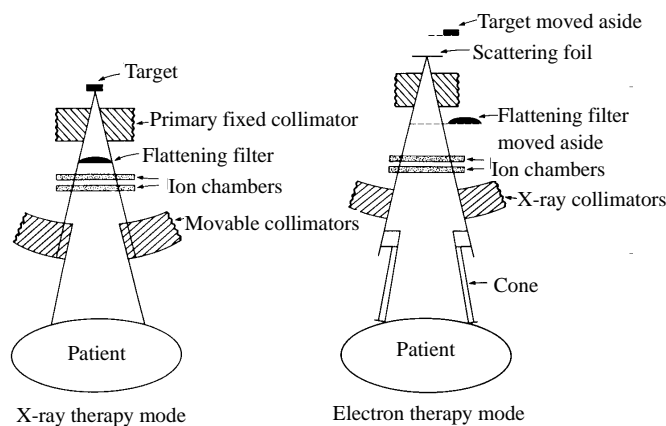


Figure 13-11. Treatment Head Configuration

Electrons are desirable for treating superficial tumors (< 5 cm deep). The types of tumors suitable for electron therapy are skin and lip cancers, chest wall irradiation in breast cancer, boost doses to lymph nodes, and head and neck cancers. Electron beam therapy is desirable because it produces a uniform dose in the target volume and minimizes dose to deeper tissues.

### 13.5.c Isotopic (<sup>60</sup>Co) Teletherapy Systems

Although several different radioisotopes (e.g., <sup>137</sup>Cs, <sup>226</sup>Ra) have been employed in teletherapy, it is <sup>60</sup>Co which has proven to be the most suitable for external beam therapy. The reason for this selection include:

- ✓ higher possible specific activity (curies per gram).
- ✓ greater radiation output per curie (<sup>60</sup>Co has 2 photons per decay).
- ✓ higher average photon energy ( $E_{avg} \approx 1.2$  MeV).

Isotopic teletherapy systems are different in construction than a linac because the radiation is emitted from the decay of <sup>60</sup>Co. The source typically has approximately 1.85 - 5.55 PBq (5,000 - 15,000 Ci) of <sup>60</sup>Co welded into a 1.0 - 2.0 cm diameter (Figure 9-8) cylinder positioned in the head of the teletherapy machine with the circular end facing the patient. Because radiation is always emitted, the **source head** is made with several inches of lead (or other dense metal) to shield the radiation during nonuse periods when the source is in the **off** or shielded position. The source is actually a **sealed source** and is accompanied by paperwork indicating it has been tested to the more stringent (transportation and durability) standards required of sealed sources.

For treatment, the isotopic source is advanced pneumatically (i.e., by air pressure) or mechanically to the treatment position. Per treatment, the tumor is usually given a dose of approximately 2.50 to 3.50 Gy (250 - 300 rad). The treatment distance is normally about 100 - 200 cm from the source. For <sup>60</sup>Co, the exposure rate at 1 m for a 5000 Ci source would be approximately 0.90 Gy/min (90 rad/min) and double that for a 10,000 Ci source. Because of the high radiation levels, the treatment room must be designed to shield the rest of the clinic from the radiation

(both main beam and scatter). Normally, lead and/or concrete is used. The energy of the  $^{60}\text{Co}$  gamma rays is only 1.173 and 1.332 MeV and some of the energy is absorbed while passing through healthy tissue. Consequently, the dose distribution is not quite as uniform as a 4 MV linac. Because of this somewhat non-uniform depth dose distribution and regulations pertaining to byproduct materials, these systems are slowly being replaced by linacs.

### 13.5.d Radiation Protection Factors of Particle Accelerators and Teletherapy Systems

Radiation levels from linac photon and electron and teletherapy units can be very high. The tumor treatment dose rate is on the order of 3 Gy/min (300 rad/min). Accidental exposure is a potential hazard which must be integrated in the design and installation of the system. Consequently, a multitude of safety systems are utilized to protect both the patients and staff from unnecessary exposure.

- Interlocks - entry into the treatment room during an exposure opens a switch causing automatic termination of the beam.
- Emergency off button - both the control panel and the treatment room have a large, red *emergency off* button which either cuts the klystron current or retracts the radiation source into the source-head.
- Warning systems
  - ✓ Flashing or rotating lights or overhead light dimmer/flasher
  - ✓ Warning signs (e.g., **[Grave] Danger - [Very] High Radiation Area**)
  - ✓ Audible signal
  - ✓ Radiation barriers
- Operating systems
  - ✓ Key switch (cannot activate without key in place)
  - ✓ Interlock circuits (usually tested at least once per day)
  - ✓ Clearance procedure / spot checks (depending on type of radiation)
- Area radiation and video monitoring in any area accessible to people.
  - ✓ Capable of measuring all types of radiation
  - ✓ Video camera in the treatment room connected to remote monitor at control panel
  - ✓ Sealed source leak test at least semiannually
- Training - Operators are trained in the safe use of the irradiator system, to identify hazards and to test warning lights and interlocks before use. Operators also receive refresher training periodically to discuss regulations, accidents, emergency procedures.
- Operators and staff members wear dosimeters (cf. 7.2.d).

In some systems the collimators are made of depleted uranium. These can emit low energy photons which might appear as skin doses on the dosimetry report. A clear sheet of Plexiglas can be placed over the end of the collimator to absorb these low energy radiations. Because high-energy linacs ( $E > 7$  MeV) have the potential to generate neutrons from interaction with heavy metals found in the target material, walls of the accelerator structure, wave-guides, filters and collimators, there is a maze designed to prevent neutron scatter from reaching the control console or additional shielding using borated (5%) polyethylene incorporated in the room design. Because radiation exposures are higher near the door, personnel should be cautioned not to stand too near the room's door when the linac is operating.

## 13.6 Veterinary Medicine Program

Animals can get many of the same types of diseases as people and these maladies are capable of being diagnosed and treated using the same modalities (e.g., bone, brain, and renal scintigraphy; feline hyperthyroidism, etc.) The School of Veterinary Medicine (SVM) has both radiation therapy and nuclear medicine capabilities.

### 13.6.a Veterinary Radiation Therapy

The SVM has a Theratronics 780 teletherapy unit used to eradicate cancer in companion animals. The current  $^{60}\text{Co}$  ( $T_{1/2} = 5.271$  years) source was installed with an activity of 293.6 TBq (7934 Ci) as of 22 January 1999. Cobalt-60 is the preferred source for radiation therapy because each decay results in two high-energy gamma rays (1.173 MeV and 1.332 MeV) and, unlike linear accelerators (linac), there is very little down time. The unshielded exposure at one meter from this source would be about 10,500 R/hr (175 R/min). Because of the high exposure, the

room is extensively shielded. The walls and ceiling are made thick (i.e., 3 - 4 feet) reinforced concrete and steel plating to help insure radiation exposures outside the room are essentially background.

Several safety devices are installed to reduce the risk of unexpected exposure. The door is posted with a **Grave Danger - Very High Radiation Area** sign. There is a radiation alarm within the room, the door is interlocked to the control panel so exposures can not be made with the door open, there is an in-room video camera and monitor, and there is an emergency shutoff within the room. Additionally, there is a 30-second alarming delay switch on the door which sounds a bell and prevents exposures for 30 seconds after the door is fully closed. The operator uses a GM to measure radiation levels at the door before entering to insure the source is not stuck in the expose position.

While these safety devices are normally sufficient to keep exposures ALARA, because of the potential for high exposures in the unlikely event of an accident, all persons entering the room must receive training sufficient to insure they will not be inadvertently exposed. Custodians and maintenance personnel receive relatively brief training to allow them to recognize emergency situations. Operators receive extensive training, must pass a test on the system, and then must receive annual training about the system, rules and regulations, and emergency response.

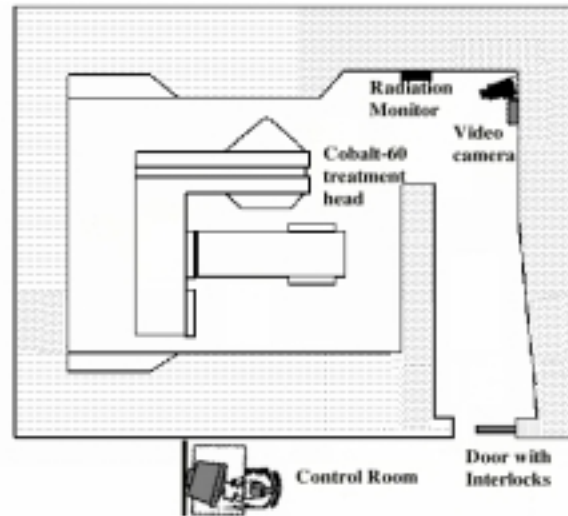


Figure 13-12.  $^{60}\text{Co}$  Treatment Room

### 13.6.b Veterinary Nuclear Medicine

The Veterinary Clinic uses radiopharmaceuticals in ways similar to clinical human nuclear medicine, the major difference is the administered activity since the patients range in mass from 5 kg to 500 kg. In fact, the radioactive drugs used are compounded in the UW Hospital's Nuclear Medicine Clinic.

Administration of radiopharmaceuticals to people is usually done on an outpatient basis. Each patient is given instructions on ways to keep exposures to others ALARA (e.g., time, distance). Because veterinary patients are animals, control of potential contamination is a major concern. Additionally, the magnitude of the radioactivity involved may pose an exposure hazard. For example, human  $^{99\text{m}}\text{Tc}$  doses typically range from 370 to 1110 MBq (10 to 30 mCi); the same dose for a horse may be as much as 7400 MBq (200 mCi). For that reason, following administration of radioactive material, the patients are normally housed in a designated area that can contain and/or facilitate disposal of contaminated material, has the appropriate radiation postings / notifications and access is controlled. Each small animal is tagged with a bright collar bearing the radiation warning symbol and **Caution - Radioactive Materials**. Large animals have a similar warning tag affixed to their halter. Additionally, the patient's record is labeled to indicate the patient has received radioactive material and to whom to direct questions.

The maximum exposure rate at 1 meter from the approximate center of the target organ(s) is measured immediately after administration of the radiopharmaceutical and is normally recorded on the patient's chart. Because some radiopharmaceuticals are rapidly metabolized and excreted, when redistribution or significant excretion of the radionuclide is anticipated, the exposure rate is remeasured and recorded at appropriate intervals. The exposure rate is the basis for determining the length of time which an attendant staff member may spend near the patient. In general, the pet owners are not allowed to visit patients during the period of confinement.

Most of the nuclear medicine radionuclides are short-lived (e.g., for  $^{99\text{m}}\text{Tc}$ ,  $T_{1/2} = 6.01$  hour). Syringes and contaminated bedding is processed by half-life decay and final disposal as normal syringes or animal excreta, as appropriate. Because of species differences as well as tests and quantities use in the study, each animal is housed and treated differently

Horses are housed in the large animal holding area. To reduce the risk of spreading contamination, the preferred stall is the one nearest the imaging area; however, all stalls are similar and the controls implemented will be similar. Diagnostic doses are usually based on body weight and horse doses on the order of 5.5 - 7.4 GBq (150 - 200 mCi) are not unusual. Extra heavy, wood shaving bedding is used to completely absorb urine. The sex of the horse actually determines the possible locations for urination; males in the center of the stall, females around the

perimeter. Drains should not be located inside the stall since the absorption of urine should occur within the stall with no leakage to the environment. The stall is routinely labeled with **Caution - Radioactive Materials**. A radiation area exists if exposures exceed 5 mR/hr at 30 cm from a source or the surface of an animal. While it is unlikely that a radiation area will exist for horse stalls, if a radiation area does exist, the stall must be labeled with a **Caution - Radiation Area** sign. After the patient is released, the stall is tagged as contaminated along with the date after which the bedding can be handled as non-contaminated by animal care workers.

Dogs are housed in cages which share a common drain at the rear corner of the dog run. The drain is blocked so urine from a dog injected with the radiopharmaceutical does not get to the sewer system. Some animals refuse to urinate in cages. In these instances, trained animal care workers accompany the animal to a specially designated and marked (grass/dirt) fenced-in area outside where dogs may urinate. Animals are tagged as radioactive and only specifically trained individuals will be allowed to assist in the animal's care. After the patient is released, the cage will be tagged as contaminated along with the date after which it can be hosed down by animal care workers.

In some ways, cats are the easiest animal to care for. Cat litter is handled as radioactive waste. The cats are carried to and from imaging rooms in animal carriers or upon carts. After the patient is released, the cage will be tagged as contaminated along with the date after which it can be cleaned by animal care workers. Additionally, some cats receive large doses of radioiodine for thyroid problems. Older cats have a relatively high risk for feline hyperthyroidism which responds well to a therapeutic (74 - 296 MBq [2 - 8 mCi])  $^{131}\text{I}$  dose (cf. **Section 13.2.c**). Considerations in these  $^{131}\text{I}$  therapy cases include:

- ✓ Only specially trained personnel may be involved.
- ✓ The cage is labeled (**Caution - Radioactive Materials**) and the cat wears a yellow/magenta tape collar and is housed in relative isolation. The floor in front of the cage is covered in absorbent paper.
- ✓ The cat is monitored daily and the results of this monitoring are used to determine release.
- ✓ The room in which the animal cage is located has good ventilation negating the need for air monitoring.
- ✓ The workers involved in treating and caring for these felines routinely receive thyroid bioassays.

To reduce the risk of contamination, when transporting the animal to the imaging area, the shortest route should be taken and trained animal care workers survey the route from the area the animal is housed to the imaging area to insure any contamination which occurs is within defined limits or decontaminated. Decontamination supplies are available and personnel are informed of the location of these supplies and decontamination procedures.

Because the radionuclides used usually have short half-lives, the primary mechanism to be employed for contamination is decay-in-storage. Absorbent material in the large animal stalls is allowed to decay a minimum of 10-half-lives and is then monitored prior to disposal as not radioactive waste. In the event of patient death before release, the body will be handled and disposed under conditions of the UW's license.

Release of patients to owners or other clinical wards follows exposure guidelines found in NUREG-1492, *Regulatory Analysis on Criteria for the Release of Patients Administered Radioactive Material* and DG-8015, *Release of Patients Administered Radioactive Materials* to insure doses to members of the general public are maintained below 100 mrem. Patients may be released when **all** the following criteria have been met.

- ✓ The total integrated dose that could be accumulated by any individual in close association (1 meter) with the patient for an infinite period of time ( $D_\infty$ ) is less than 100 mrem. This dose can be calculated by the equation at the right.
- ✓ If the effective half-life is unknown (or as a worst case example), then the physical half-life may be used to calculate the maximum exposure. For our purposes, examples of allowable exposure rates at the time of release for some of the common diagnostic and therapeutic radioisotopes are listed in Table 13-6.

Table 13-6. Nuclear Medicine Exposure Rates

Nuclide	$T_{1/2}$	mR/hr per mCi	mR/hr @ 1 m
$^{67}\text{Ga}$	3.25 day	0.11	0.9
$^{99\text{m}}\text{Tc}$	0.25 day	0.07	11.6
$^{111}\text{In}$	2.81 day	0.48	1
$^{113\text{m}}\text{In}$	0.07 day	0.23	40.4
$^{123}\text{I}$	0.55 day	0.07	5.22
$^{131}\text{I}$	8.04 day	0.22	0.36
$^{201}\text{Tl}$	3.8 day	0.09	0.94

$$\frac{mR}{hr} = \frac{100 mR}{1.44 \times T_{\frac{1}{2} eff}}$$

✓ Additionally, the minimum confinement period based on the half-life of the administered radioisotope has been satisfied in the UW's license. These minimum periods are usually sufficient to allow at least one half-life period to occur before release and allow for excretion of radioactive urine and feces for those radiopharmaceuticals with a significant rate of excretion. The confinement period for most radioisotopes is listed in Table 13-7.

Table 13-7. Confinement Periods

Half-life	Confinement Period
< 12 hr	1 physical half-life
12 - 24 hr	24 hr
> 24 hr	48 hr

Because the nuclear medicine facility is used infrequently, the clinic is required to survey the rooms each day that radionuclides are used and weekly for all rooms in which radioactive materials are stored. The action levels are:

- ✓ if  $^{99m}\text{Tc}$  exposures exceed 1 mR/hr at 1 cm or  $^{131}\text{I}$  exposures exceed 0.6 mR/hr at 1 cm, the area must be cleaned, shielded, or posted as appropriate.
- ✓ if  $^{99m}\text{Tc}$  contamination surveys exceed 2000 dpm/100 cm<sup>2</sup> or  $^{131}\text{I}$  contamination surveys exceed 200 dpm/100 cm<sup>2</sup>, the area must be cleaned, shielded, or posted as appropriate.

In the spirit of ALARA, the owner of the patient is provided detailed instructions which explain the hazards and precautions relative to their stewardship of the patient during the period of potential exposure and environmental contamination (10 half-lives).

### 13.7 Review Questions - Fill-in or select the correct response

1. The radionuclide most commonly used in nuclear medicine is \_\_\_\_\_.
2. Nuclear medicine diagnosis is made by reviewing the concentration of the radiopharmaceutical within an organ, noting whether there are \_\_\_\_\_ or \_\_\_\_\_ spots.
3. If a patient receives a therapy dose of 100 mCi of which 25 mCi is absorbed by the target organ, then the organ uptake is \_\_\_\_\_ percent.
4. Radiopharmaceutical therapy administrations require more controls than diagnostic radiopharmaceutical administrations. **true / false**
5. Brachytherapy is performed by inserting sealed radioactive sources within a patient's body. **true / false**
6. The accelerating voltage in a linac may range from about \_\_\_\_\_ to \_\_\_\_\_.
7. A  $^{60}\text{Co}$  teletherapy system is as effective as a 4 MV linac. **true / false**
8. The average population dose from nuclear medicine is approximately \_\_\_\_\_  $\mu\text{Sv}$  or \_\_\_\_\_ mrem.
9. A device in which a short-lived daughter radionuclide is separated chemically and periodically from a longer-lived parent radionuclide is a \_\_\_\_\_.
10. The most widely used collimator on gamma cameras is the \_\_\_\_\_.
11. A positron produces annihilation radiation resulting in the emission of two \_\_\_\_\_ MeV photons.
12. The PET scanner detects annihilation photons as pairs in coincidence. **true / false**
13. The type of radiation therapy in which a sealed source of radioactivity is inserted directly into the tumor where it will deliver radiation at a distance of a few centimeters is called \_\_\_\_\_.
14. \_\_\_\_\_ are brachytherapy implants designed to remain permanently within the organ.
15. Electron beam therapy is desirable for treating superficial tumors. **true / false**

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