Radioiodine Whole-Body Imaging

11

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Introduction

Radioiodine imaging is an important diagnostic modality for the evaluation of differentiated thyroid carcinoma. A basic understanding of the physics, radioisotopes, equipment, and imaging techniques will help the physician fully comprehend the logistics, interpretation, strengths, and weaknesses of this diagnostic tool. This chapter presents a primer of the subjects noted in Table 11.1.

Overview of Atoms and Isotopes

An atom is made up of a central core (nucleus) and electrons, which circle around the nucleus in nearly the same way as satellites orbit the earth. A particular atom is designated by one or two letters, such as "I" for iodine, and is a distinct chemical element. The nucleus is composed of two types of particles, namely, protons and neutrons. The total number of protons and neutrons equals the mass number, which is labeled as "A." The number of protons is called the "atomic number" and is labeled as "Z." These qualifying labels are usually placed above and below the letter or letters used to designate the chemical element as noted in Fig. 11.1.

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This label is often shortened to include only the mass number (e.g., ^{131}I). In this case, the "I" identifies the element (iodine), and the "131" indicates the total number of protons and neutrons in the atom.

Although a given chemical element must always have the same number of protons, the number of neutrons may vary. In other words, the atomic number (*Z*) must always be the same, but the mass number (*A*) will change as the number of neutrons in the nucleus changes. When only the number of neutrons differs, those atoms of the same element are called isotopes. ^{131}I, ^{123}I, ^{124}I, and ^{127}I are all isotopes of the same chemical element, iodine, and are different because of the different number of neutrons in the nucleus. While all have 53 protons, ^{131}I has 78 neutrons, ^{123}I has 70 neutrons, ^{124}I has 71 neutrons, and ^{127}I has 74 neutrons. The number of neutrons affects the isotope's physical characteristics, which include the half-life and decay (see below), but the neutrons have no effect on its chemical behavior. Two isotopes—^{131}I and ^{123}I—are used routinely, and a third, namely, ^{124}I, has recently become available and is being evaluated for the diagnosis of thyroid carcinoma.

An important and distinct characteristic of the various isotopes of radioiodine is how that particular radioiodine releases its energy as it transforms from one iodine to another more stable element. This release of energy is called "decay," but this terminology is misleading. Although decay suggests deterioration, nothing is being destroyed. The element is only changing to another form with the release of energy.

The several types of decay have been discussed in "Radiation and Radioactivity" (see Chap. 55). One method involves releasing a wave. These waves are similar to light but cannot be seen by the human eye and can pass through tissue. These "waves of energy" are γ (gamma) *waves* or *rays* and can be seen only by special devices: γ *cameras*. Just as there are different types of light, there are different types of γ waves. The γ cameras used by the nuclear medicine physician or nuclear radiologist not only have the ability to see the γ waves but also have the ability to identify the types of γ wave.

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Table 11.1 Overview of Topics in This Chapter

Overview of atoms and isotopes
Advantages and disadvantages of radioiodine isotopes
Overview of the γ camera
Nuclear medicine imaging techniques and systems
Types of whole-body scintigraphy
Selection of radioisotope and prescribed activity
Utility of whole-body scanning

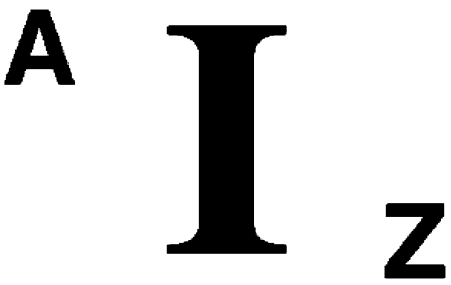

Fig. 11.1 Notation of an element. "I" represents the element. The superscript "A" represents the atomic weight, which is the total number of protons and neutrons. The subscript "Z"is the atomic number, which is the number of protons and determines the element iodine. Alternative forms might be written without the superscripts and subscripts, such as 131-I or I-131

Another way of releasing energy is in the form of a particle, which is similar to those particles that comprise the current that flows to and through a light bulb. The particle could be negatively or positively charged and is referred to as a β particle. The negatively charged β particles are identical to *electrons*, whereas the positively charged particles are called *positrons*. With this form of radioactive decay, energy is released by the nucleus as it "throws off" an electron or positron.

The methods of energy release are shown schematically in Fig. 11.2 (^{131}I) and Fig. 11.3 (^{123}I). The decay of ^{124}I is complex and beyond the scope of this chapter; however, a simplified decay scheme is shown in Fig. 11.4. When ^{123}I decays, it releases γ waves. When ^{131}I decays, it releases several types of γ waves, as well as a β particle. When ^{124}I decays, it releases energy in many different ways; the diagnostically important method is by the release of a positron. This positron collides with an electron, and both the positron and electron disintegrate or annihilate each other with the conversion of mass into two γ waves of the same energy which are released 180° apart.

Another important characteristic of any radionuclide is its half-life, which is the time it takes for half of the atoms to decay. The half-life could be seconds, minutes, hours, or days, but it is the same for all atoms of a given isotope. For example, for 100 atoms of ^{131}I, it would take 8.06 days for 50 of the atoms to transform into the element, xenon. For 100 atoms of ^{123}I, this same process would take 11.3 h for 50 atoms to transform into tellurium, and for ^{124}I, it would take 4.2 days. A summary of the decay mode, half-life, γ energy, production method, and typical prescribed activity is noted in Table 11.2.

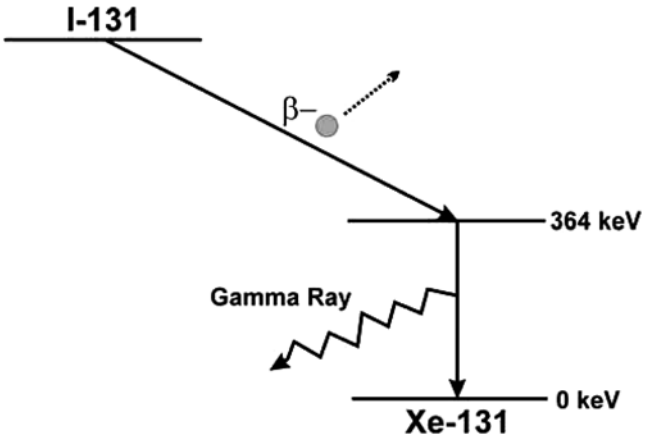

Fig. 11.2 β-decay for ^{131}I. This is a very simplified visual representation of the decay of ^{131}I, which does so by a process known as β-emission. β-emission is a mode of radioactive decay by which an unstable nucleus, one containing too few positively charged particles or protons, can become more stable. In this case, one of the neutral particles in the nucleus, i.e., the neutron, transforms into a proton. As this particle was originally neutral before changing to a positively charged particle, it must then also form a negatively charged particle so that the two charges cancel each other. The negatively charged particle produced is identical to the electrons that are the constituents of matter. However, because the electron does not belong within the confines of the nucleus, it is forcefully ejected during the transformation process. To identify this particle as having originated from within the nucleus, "β,"is used—β particle. Following the emission of the β particle, the nucleus usually emits a γ ray, in this case one that carries 364 keV of energy

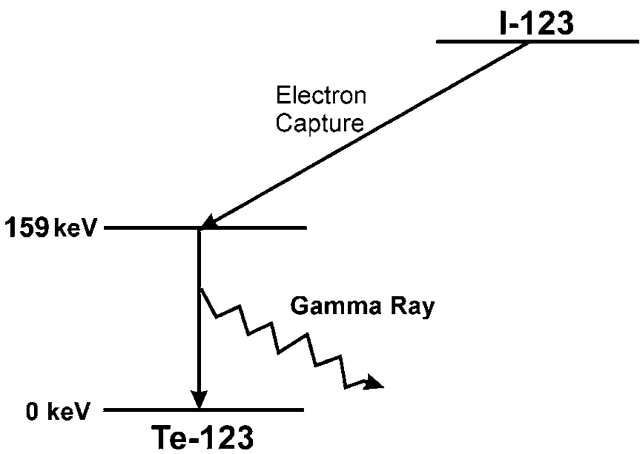

Fig. 11.3 Electron capture decay for ^{123}I. This is a simplified visual representation of the decay of ^{123}I, which does so by a process known as electron capture. In an unstable nucleus that contains too many positively charged particles or protons, electron capture is a mode of radioactive decay in which one of the protons in the nucleus captures one of the atom's orbital electrons. These two particles combine in such a way that the negative charge of the electron and positive charge of the proton effectively cancel each other out to produce a neutral particle, a neutron, which remains in the nucleus. Following the capture, the nucleus usually emits a γ ray

Advantages and Disadvantages of Radioiodine Isotopes of ^{123}I, ^{131}I, and ^{124}I

Some advantages and disadvantages of ^{123}I, ^{131}I, and ^{124}I are summarized in Table 11.3. The contents of this table are likely to change over time as a result of fluctuations in the cost of these isotopes or as new information becomes available.

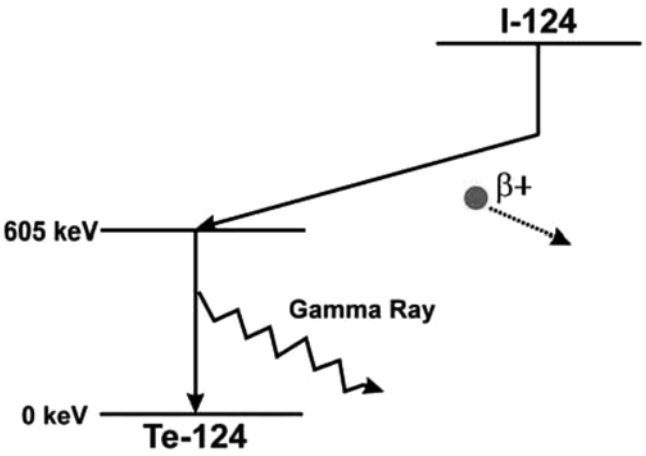

Fig. 11.4 Positron emission (β+) decay for ^{124}I. This is a simplified visual representation of the decay of ^{124}I, which does so by a process known as positron emission. Positron emission, like electron capture, is a mode of radioactive decay for an unstable nucleus that contains too many protons. In this case, to get rid of the excess positive charge, the proton transforms into a neutron and ejects a particle, which has the same mass as an electron except that it is positively charged. This positively charged electron is a positron or a β+ particle. Particles of this type are referred to as antiparticles. The ultimate fate of the positron is that after it loses most of its energy traveling through several millimeters of surrounding matter, the positron will combine with an electron. The two particles will annihilate each other with the subsequent production of two γ rays each with 511 keV of energy that travel in nearly opposite directions from the site of annihilation. It is these annihilation γ rays that are imaged using a PET scanner, which also exploits their simultaneous production and directionality of the two γ rays to form the image

Overview of the γ Camera

As noted above, the basic instrument used in nuclear medicine to form an image of the radionuclide distribution within a patient is the γ camera. This terminology is derived from the fact that it generates a two-dimensional (2D) image of an object (like a photographic camera) by detecting γ radiation, a particular type of radiation that is emitted from the tracer within the patient. Although there are numerous designs and configurations of γ cameras, most have one important component in common: the type of radiation detector used to measure the γ radiation. The device is a *scintillation detector*, as it is based on measuring a small burst of light that is produced by the γ radiation as it passes through the detector. For this reason, a γ camera is also frequently referred to as a *scintillation camera*. The technology is not new; in fact, the γ camera has been used in medical imaging since its invention by Hal Anger in the early 1960s. Since the γ camera was introduced, its design and performance have evolved considerably into the sophisticated device that is in widespread use today. Although there are numerous commercial versions of γ cameras currently available on the market, four components are common to virtually all of them: a collimator, scintillation crystal, photomultiplier tubes, and the electronics/computers to process and display the image. These components are shown in Fig. 11.5.

Collimator

The γ rays produced by the radioiodine within a patient are emitted randomly in all directions. However, to form an image requires knowledge or information about the direction that the γ rays are traveling. Because it is not possible to determine this directly, a collimator is used instead. The

Table 11.2 Radioiodines used for imaging of thyroid diseases

	Decay mode	Half-life	Gamma energy (keV)	Production method	Typical prescribed activity MBq (mCi)
^{123}I	Electron capture	13.6 h	159	Cyclotron methods. One method, referred to as a (p,5n), produces ^{123}I with no ^{124}I contamination and little ^{125}I The other approach, referred to as (p,2n), has a number of impurities that have high-energy γ's and long half-lives. These contaminations reduce image quality and increase the radiation exposure of the patient	15–148.8 (0.4–4.0)
^{124}I	Positron emission	4.2 days	511	Cyclotron	74–148 (2–4)
^{125}I	Electron capture	60.2 days	35	Cyclotron. Not used for imaging because the γ energy is too low. Also, the long half-life results in a significant radiation burden to the patient. This has primarily been used for radioimmunoassays and other in vitro laboratory tests	Not used for imaging owing to long half-life and low energy of γ ray
^{127}I	Stable	–	–	Naturally occurring	N/A
^{131}I	β-decay	8.02 days	364	Reactor produced either from direct bombardment of a target by neutrons or from the reprocessing of spent fuel rods from a nuclear power plant	Uptakes: 0.185 (0.005) Imaging: 37–185 (1–5) Treatment :1.07–37 GBq (29–1,000)

Table 11.3 Comparison of ^{123}I, ^{124}I, and ^{131}I

	^{123}I	^{124}I	^{131}I
Expense	$$	$$$	$
Readily available	Y (In some countries)	Just becoming available	Y
Reimbursed by insurance	Y	N	Y
Useful in the treatment of differentiated thyroid carcinoma	N	Y[a]	Y
Useful for dosimetry (blood/bone marrow)	Possibly	Y	Y
Useful for dosimetry (lesion)	Limited	Y	Limited
Stunning	No	Possibly	Possibly
Risk to personnel handling patient and radionuclide	Low	Medium	Medium
Necessity of radiation safety precautions for patient and public	N	Y	Y
Image quality	Good	Excellent	Fair
Delayed imaging (>48 h)	N[b]	Y	Y
PET scanner required	N	Y	N
Tomographic images (routinely)	N[c]	Y	N[c]
Image fusion with other modalities	N[c]	Y	N[c]

[a]The energy of the positron and half-life of ^{124}I would make it technically feasible for this radioiodine to be used for the treatment of differentiated thyroid carcinoma. However, even if sufficient quantities could be produced in today's market, the cost would be prohibitive

[b]Multiple studies have demonstrated the ability to obtain images at 48 h after administration of ^{123}I, and with higher prescribed activity, further delayed imaging may be possible

[c]With the development of single photon emission tomography (SPECT) tomographic images that can be fused with images obtained from other imaging modalities can be performed. However, this is not available at all facilities, and even if available, SPECT images of the whole body are not routinely performed because of significant increased time and expense

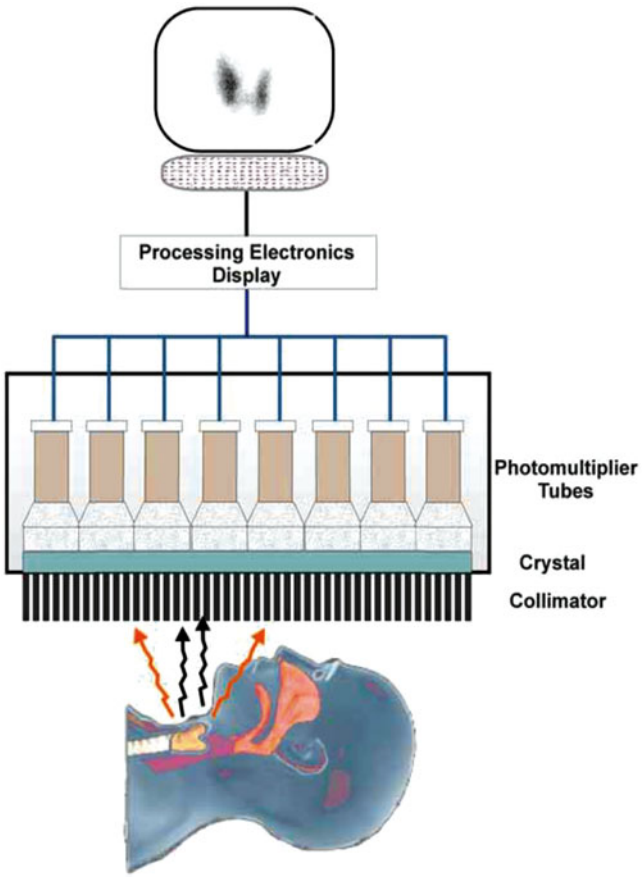

Fig. 11.5 Components of a γ camera. See text for discussion

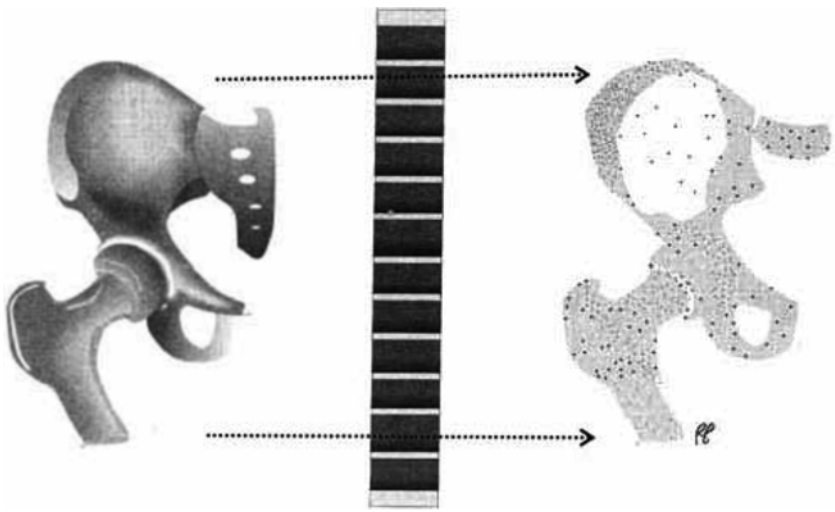

Fig. 11.6 Parallel-hole collimator. The collimator is an essential component of the γ camera. One type shown in this figure is a parallel-hole collimator because each channel through which the γ rays must pass before they can be recorded in the image is parallel to all of the other channels or holes. See text for more discussion (Reproduced with permission from Essentials of Nuclear Medicine Physics, Blackwell Publishers, Inc)

most common design of a γ camera collimator is shown in Fig. 11.6. It usually consists of a set of holes or channels (typically several thousand) in a block of lead, each of which is parallel to all the others. Hence, it is referred to as a *parallel-hole* collimator. γ rays that are traveling in a direction that pass through the channel will make it to the opposite side and enter the detector. Most γ rays that would cross from one channel to another will be absorbed in the lead that separates the holes and will not be recorded in the image. As a result, the γ rays that pass through the collimator form a distribution on its exit side, which is a representation of the radionuclide's spatial distribution within the patient.

To form an accurate representation of the distribution of radioiodine within the patient, it is important that as few γ rays as possible that have crossed between channels reach the detector. The γ rays that do are referred to as *penetration radiation*. Because of the nature of the passage of γ rays through material, it is not possible to completely stop all penetration, but it can be minimized through appropriate design and construction.

Several variables could be used to characterize the design of such a collimator and will have an impact on the quality of the image formed. These variables include the diameter of the hole, thickness of the collimator, and spacing between holes. By making the channel or hole wider, more γ rays will pass through the collimator and will be recorded in the image. Therefore, the statistical noise* in the image will be reduced. The importance of counts on the overall image quality is illustrated in Fig. 11.7.

However, the larger hole is less selective about the direction that the γ ray is traveling; therefore, the uncertainty about where the γ ray originated from within the patient is greater. Thus, larger channels will produce images with less statistical noise but also less sharpness or detail, i.e., greater blurring of images. The thickness of the material that separates one channel from an adjacent channel affects the amount of radiation that "penetrates" the collimator. Increasing this thickness reduces the penetration but also reduces the number of γ rays recorded in the image. Once again, the statistical noise can become a limiting factor. Furthermore, if it is too thick (>3 mm), the pattern of the holes or channels in the collimator can be visualized as it is superimposed on the patient's image. To compensate for this effect, the collimators can be increased in total height to maintain the spacing between channels at acceptable values.

Another important characteristic of γ rays is that the higher the energy of the photon, the more difficult it is to stop or absorb that radiation. This factor has a major impact on collimator design. Consequently, collimators are designed specifically for certain energy ranges. A typical and important rule followed in collimator design is that the number of γ rays that penetrate the collimator septa should be less than approx 5 % of the total number that pass through the collimator. Because ^{131}I emits a relatively high-energy γ ray (364 keV), it is important to use a collimator that has been designed for high-energy imaging. Usually, the penetration radiation is spread out diffusely over the entire patient image, but if there is a small intense area of ^{131}I concentration in the patient, it will be manifested as a star-like artifact, with rays projecting outward from the center like the points on a star. The number of points and shape of this artifact depend on the layout of the

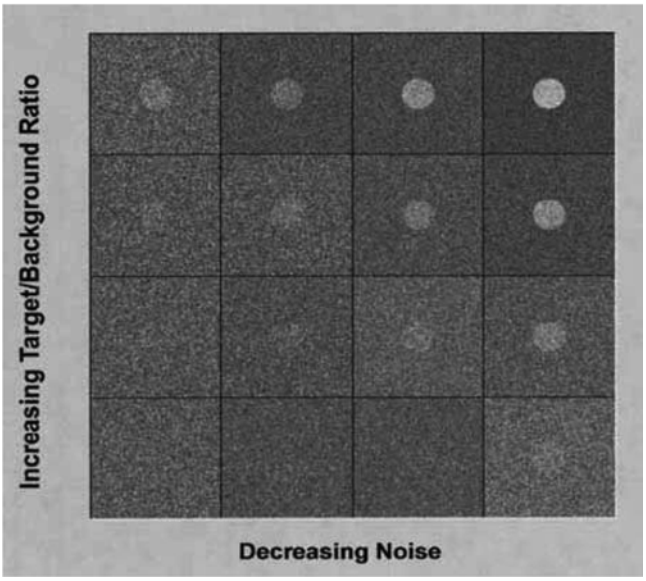

Fig. 11.7 Relationships of spatial resolution and detected events. This figure illustrates the importance of both counts (the number of γ rays recorded in the image) and the contrast (the relative ability of the tissue to concentrate the radionuclide compared to its surrounding tissues) on the ability to "detect" a lesion. The lesion in this case is a circular area in a uniform background. Along each row of this grid, the contrast is a constant value but increases progressively from the *bottom* to the *top*. Likewise, the statistical variations in the image (called "noise") are the same along a given column but decrease progressively from *left* to *right*. The *box* at the *lower left* has the lowest lesion contrast and the greatest noise level, whereas the *box* in the *upper right* corner has the highest lesion contrast and the least noise level. If you examine the bottom row, you will probably only be confident that the lesion is present in the *last box*. However, the lesion is present in every *box*; it is just obscured by the noise. For the second row from the *bottom*, the lesion is probably just detectable in the next to the *last box*. Similarly, for the next row up, the lesion is detectable in the last three *boxes*. This illustrates that as the contrast increases, the lesion can be detected in the presence of greater noise levels. The contrast depends on a number of physiological parameters that affect the ability of the metastatic thyroid tissue to concentrate the radioiodine relative to surrounding background tissues. One common way for the nuclear medicine physician to try and increase the lesion contrast is to delay the time of imaging an additional 24 h or longer. This takes advantage of the fact that non-protein-bound iodine is generally cleared or eliminated from normal tissues faster than it is from functioning thyroid metastasis. As a result, the contrast may increase over time, which would be equivalent to moving to a higher row in this image. What can also be observed in this figure is that even low-contrast lesions can be "seen" if the statistical noise is small enough. Noise can be reduced by recording more γ rays in the image. There are a variety of ways in which the number of detected γ rays can be increased. The simplest is to increase the imaging time. Another option might be to increase the administered prescribed activity. However, in the case of ^{131}I, this might increase the risk of stunning. The patient could be imaged sooner after the administration of the radioiodine while there is more activity in the patient, but this would result in a smaller lesion contrast as noted above

Fig. 11.8 Star artifact on radioiodine whole-body scan. See text and Chap. 12 for discussion

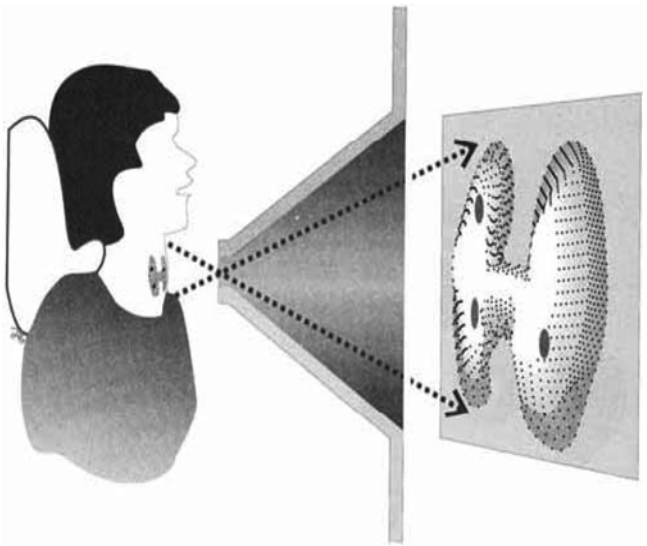

Fig. 11.9 Pinhole collimator. See text for discussion (Reproduced with permission from Essentials of Nuclear Medicine Physics, Blackwell Publishers, Inc)

channels and shape of the hole in the collimator. Basically, the projections are along paths where the material that separates one hole from its neighbor is the thinnest. An example is shown in Fig. 11.8.

The parallel-hole collimator is the most widely used type in nuclear medicine, but the pinhole collimator is another particularly useful design in imaging small organs like the thyroid gland.

The pinhole collimator is much simpler than the parallel-hole collimator in terms of its design and construction. The bulk of this collimator consists of a large lead conical shell with the tip cut off. The base of the cone will cover a large portion of the γ camera crystal. The purpose of this shell is to shield the detector from the γ rays that do not pass through the collimator itself. As implied by the name, the pinhole collimator itself consists of a single small hole (often referred to as an *aperture*) in the truncated tip of the cone. The diameter of this aperture is typically several millimeters. Ideally, the only γ rays that can reach the detector and contribute to the image are those that are emitted from the patient, pass through the pinhole, and strike the crystal. As γ rays travel along a straight line, each point on the crystal would then correspond to a small volume within the patient. This is illustrated in Fig. 11.9.

How well defined the patient's image is depends partly on how large the pinhole is. If it is too large, then γ rays from a broader region of the organ being imaged can pass through the aperture and strike the same location on the crystal. As a result, the image is not sharp. Alternatively, if the aperture is too small, then very few γ rays will pass through the opening, and the image (although sharp) will be of poor quality because of statistical limitations of low counts. For this reason, pinhole collimators are usually designed so that the aperture is changeable to accommodate different imaging conditions and requirements. A typical set of pinholes might include a diameter range of 2, 4, 6, and 8 mm. Generally, for lower-energy γ and higher administered activities (e.g., ^{99m}Tc pertechnetate), the smaller 2–4-mm pinhole is used; for higher energies (e.g., ^{131}I), a larger 6–8-mm pinhole is used.

Just as for parallel-hole collimators, penetration of the collimator by γ waves is also a problem for pinhole collimators. For this reason, the insert assembly is often manufactured using Tungsten, which is a strong metal that can be machined and is about 1.5 times more than the density of lead. Consequently, it is even more effective than lead at reducing the penetration radiation. Another advantage is its strength. Lead is a soft metal and can be easily damaged. For some research applications, an even denser metal has been used, i.e., *depleted uranium*. Naturally occurring uranium consists of a mixture by weight of three radionuclides of uranium: ^{238}U (99.27 %), ^{235}U (0.72 %), and ^{234}U (0.0054 %). The uranium used in nuclear power plants requires an "enriched" form in which the fraction of ^{235}U has been increased from 0.72 % to about 1.5–3 %. Depleted uranium is the uranium remaining after the enrichment process and

contains only about 0.2 % of the fissionable ^{235}U. This material is even denser than tungsten and is about two times greater than the density of lead.

There are a number of important differences between pinhole and parallel-hole collimators. One is the *field of view* (FOV), which is how large an area of the patient the γ camera can image. For the parallel-hole collimator, the size of the FOV is essentially the physical size of the detector itself (aside from dead space around the periphery). However, for pinhole collimators, the area of an organ that can be imaged depends on how far the organ is from the pinhole. For objects only about 5 cm from the pinhole, the FOV is about one fourth to one third of the dimensions of the detector. As the object moves closer to the pinhole, the FOV decreases. In addition, as objects move away from the pinhole collimator, the number of γ rays that can pass through the pinhole falls off rapidly. Consequently, pinhole collimators are used to image small organs, such as the thyroid gland and neck bed, which can be positioned close to the collimator.

Fig. 11.10 Photomultiplier tube. The left end of the tube is coupled to the crystal. See text for discussion

Scintillation Crystal

Once the γ ray passes through the collimator, it must then be detected. This involves the use of a special type of material that will produce a brief flash of light (*scintillation*) when a γ ray interacts. This flash itself only lasts less than a 1/1,000,000 of a second. Although not all materials possess this capability, many that do are in a physical form, which we refer to as a "crystal," i.e., the atoms are lined up in a regular periodic structure. There are many different scintillation crystals, but the most commonly used for γ cameras is sodium iodide (NaI). The primary reasons for using NaI are the natural abundance of the raw materials and relative ease of growing the large crystals needed for this application. Both of these factors contribute to a relatively low cost for this component of the imaging system. The usual representation of the sodium iodide crystal is NaI(Tl). This indicates that a small amount (~0.1 %) of thallium (Tl) has been intentionally included in the growth of this scintillation crystal. A small amount of this impurity has been found to significantly increase the amount of light produced in the crystal by the radiation. When a γ ray interacts in the crystal, two important features help in the imaging process: (1) the light emanates from the point at which the γ interacts, and (2) the intensity of the light is proportional to the energy of the γ ray. The first factor allows an image of the location of the γ ray to be generated (i.e., where it came from in the patient), and the second factor allows the discrimination of γ rays of different energies, which then allows the discrimination of different radionuclides and γ wave scatter within the patient. Most γ cameras use a single, rectangular, large-area scintillation crystal that is capable of imaging a substantial portion of the patient at one time. Typical FOV are 20 in. wide by 15 in. in length.

Photomultiplier Tubes (PMT)

These electronic devices are designed for a single purpose—to detect and measure small amounts of light in a short period of time. The γ camera consists of an array of photomultipliers (PMTs) (see Fig. 11.10), which cover the surface of the scintillation crystal. Generally 2–3-in. diameter PMTs are used so that 50–100 of these devices are required. Each time a scintillation event occurs in the crystal (a γ ray is detected), some resultant light is detected by the PMT, and an electrical signal is produced. The more light that is "seen" by a PMT, the greater the signal it produces. Although "photomultiplier" implies the multiplication of photos (see Fig. 11.11), the PMT multiplies the electrical signal.

Processing Electronics and Image Display

The last component in the γ camera imaging chain is associated with the processing of the electrical signals from the PMTs and conversion of this information into an image. The closer a PMT is to the source of the light (i.e., the point in the crystal where the γ ray was absorbed), the more light it sees. Hence, the greater the electrical signal, the closer the PMT is to the scintillation event. By examining the signal distribution from a cluster of PMTs surrounding the interaction site, it is possible to determine the location of the γ interaction in the crystal itself with some degree of precision. In fact, despite the PMTs fairly large size (typically about 75 mm in diameter), this approach for localization can determine the site with a precision of about ±2.0 mm. Finally, the information from each detected event is stored in a 2D array, and each element of the array (called a pixel for picture element) contains the

Fig. 11.11 See text (Photo was reproduced with permission of the Dr. Claus Grupen, the creator)

total number of γ rays that were detected at that location in the crystal during the entire acquisition period. The image displayed on the computer is a representation of the radioactivity distribution in the patient. Usually, the image is displayed in black and white, with the scale or darkness proportional to the number of λ rays that came from that region of the patient.

Nuclear Medicine Imaging Techniques and Systems

Several techniques can be used to image thyroid tissue and differentiated thyroid cancer using the γ camera and other systems.

Static Planar Imaging

The operating principles of the γ camera were described in the previous section. As indicated, this device consists of a large-area crystal to detect the γ rays and a collimator to select the γ rays on the basis of their direction of travel. Usually, the collimator is a parallel-hole design, which means that the γ rays recorded in the image are only those that are traveling (more or less) in a direction that is perpendicular to the crystal. If the detector has a dimension, e.g., of 15 by 20 in., then the area of the patient that would be examined is also approximately the same size. If the area of interest was much smaller than the camera area, such as the thyroid bed, then the detector would not be utilized efficiently. In this case, a different type of collimator might be used instead, i.e., a pinhole collimator, which has improved spatial resolution. Conversely, the FOV of the γ camera may not be large enough to cover all the areas of the patient that needs to be examined. In this instance, a series of images are acquired with the patient repositioned in front of the γ camera. Each image is often referred to as a "static" image or "spot" image since the patient and the γ camera are stationary during the imaging process, which may take 10–20 min.

Whole-Body Imaging (Metastatic Survey)

The whole-body or metastatic survey is a routinely performed imaging procedure to detect the metastatic spread of differentiated thyroid carcinoma. As thyroid cancer can metastasize to regions well outside the thyroid bed, it is necessary to image or *survey* a large portion of the patient's body. Hence, it is often referred to as *whole-body* scanning (WBS). In practice, however, the area scanned usually extends from the head to the knee or just below the knee because thyroid cancer rarely metastasizes more distally than this. The radionuclide used for this purpose is one of the radioisotopes of iodine. In the past, this has been generally ^{131}I; but more recently, ^{123}I has had increased usage, and the positron-emitter ^{124}I may have an important role in the not-too-distant future.

For either ^{123}I or ^{131}I, the device used is the γ camera to generate a 2D image of the radionuclide distribution within the patient, who is really a 3D object. Because some radiation is absorbed within the patient's body, the resulting image will be influenced to a greater extent by the radioiodine that is located closer to the patient's surface on the side that the γ camera is positioned. Thus, concentrations of activity (metastases) that are located posteriorly within the patient

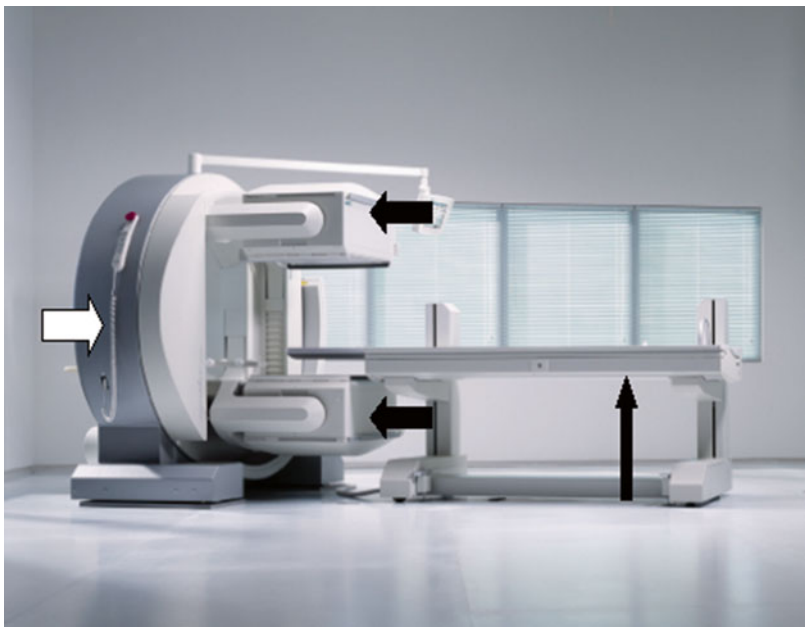

Fig. 11.12 Dual-head nuclear medicine γ camera. The *thick arrows* represent the dual γ camera heads. The *thin vertical arrow* represents the patient table, and the *white arrow* represents the camera gantry (Photo courtesy of Siemens Medical Solutions USA, Inc)

might not be visualized when viewed anteriorly and vice versa. Images are therefore obtained routinely from both the anterior and posterior projections.

To reduce imaging time, most systems currently employ two γ cameras that are mounted on a gantry, allowing the detectors to be positioned directly opposite each other, with the patient located between them (see Fig. 11.12). In this case, the anterior and posterior images can be acquired simultaneously. Furthermore, because the FOV along the length of the patient is typically only approx 15 in., multiple sets of images need to be acquired to cover or survey the patient's whole body. Although this could be accomplished by imaging each section of the patient individually, with some slight overlap between sections, this is a time-consuming approach for the patient and the technologist. Ultimately, the nuclear medicine physician must deal with assembling these images from all the different sections into the proper presentation. To facilitate the imaging of a substantial length of the patient, most imaging systems also have the capability of continuously scanning over the length of the patient as the data are collected. This scanning can either involve the patient's bed moving between the detectors or the camera gantry traversing along a track. In either case, the imaging system has been designed to incorporate the relative position of the γ cameras and table to generate a single image from each detector over the entire length that was scanned.

SPECT Imaging

One limitation of the imaging methods discussed so far is that these techniques all produce a 2D projection (image) of the radioiodine distribution within the patient, much like that of a conventional X-ray. As a result, the depth of a focal region of uptake cannot be determined from a single image. Since γ rays are absorbed or attenuated as they pass through tissue, the difference in the intensity of an area of interest between the anterior and posterior images, or any opposing views, can provide a clue as to whether the structure is closer to one surface or another, but this is not very precise. Static images from other orientations, such as a lateral projection, could provide more details. Regardless, the fact that each location in the image is a reflection of the superposition of the activity along a line through the patient, then overlying and/or underlying normal physiologic structures might obscure an abnormal area of radioiodine uptake. One approach to this limitation is that of SPECT (single photon emission computed tomography). This involves collecting a number of 2D images using the same γ camera described in this chapter over a set of angles that completely encircles the patient. Typically this set of images is acquired every 3–6° around the patient. Each of these images provides a different perspective of the internal distribution of the radioactivity within the patient. Using computer processing similar to that employed in conventional X-ray CT scanners, it is possible to construct a set of 2D transaxial sections of the activity within the patient. If we stack all of these slices up, we now have the 3D representation of the activity within the patient. Depth and overlying normal physiologic structures are no longer a problem. Clinical applications of SPECT imaging are discussed in Chap. 14. Although SPECT images may provide more information than whole-body or static images, there are several drawbacks. In order to produce high-quality, statistically useful SPECT studies, more γ rays need to be detected. However, this results in relatively longer imaging times (typically 30–45 min for a complete 360° set of images). In addition,

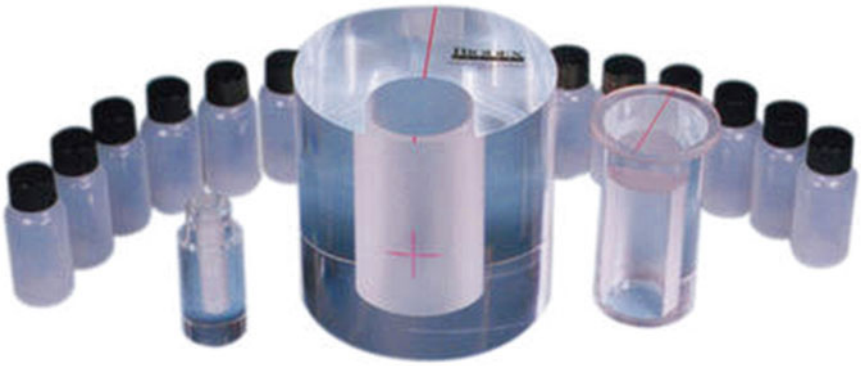

Fig. 11.13 Thyroid phantom. See text for discussion

this set of images will only cover a length of the patient equal to the height of the detector, which is typically in the order of 40 cm. Unfortunately, to survey the entire length of the patient would typically not be practical. Hence, the use of SPECT imaging in this setting might be to better evaluate areas of known metastatic disease or suspicious areas identified on the whole-body or static images. While SPECT imaging can improve lesion detectability and provide 3D localization, there are still farther limitations. Since γ rays are absorbed as they pass through tissue (for ^{131}I about 50 % for every 6 cm of tissue), there can be artifacts due to this attenuation as well as quantitative inaccuracies. Furthermore, there may be ambiguities in the anatomical localization of focal areas of uptake. To address these issues, the SPECT system may actually be a hybrid device that incorporates a CT scanner (or similar device) that can provide both the anatomical information and the necessary corrections to account for attenuation.

Radioiodine Uptake

An important factor often used to help select the prescribed activity for ablation or treatment of well-differentiated thyroid cancer with radioiodine is the *uptake*. Uptake is a measure of the fraction (usually expressed as a percentage) of the administered radioiodine present in some specific tissue at the time of measurement—usually 24 h after dosing. The tissue in question could be the thyroid gland, thyroid remnant left after near-total thyroidectomy, or metastatic thyroid carcinoma. The uptake is a significant parameter because it will directly impact the radiation dose that can be delivered to the tissue targeted for treatment and, hence, the potential effectiveness of the radioiodine therapy. The calculation itself is relatively simple:

$$\text{Uptake}\ (\%) = \text{radio activity in tissue} \times 100 \,/\, \text{administered activity}$$

Although the radioactivity in the tissue is measured at a specific time after the administration, the value used in this equation is what it would have been at the time of administration. Thus, this value is corrected for the decay of the radionuclide between the time of administration and measurement. If ^{123}I is being used for this measurement, then this amounts to a correction factor of about 3.4 for a 24-h period.

At issue is how to determine the activity in the tissue. There are basically two approaches to measure the uptake and use different instrumentation: an uptake probe and a γ camera. As the radiation detectors count γ rays while the patient is given an amount of radioiodine measured in units of *activity*, i.e., mega-Becquerel (MBq) or millicuries (mCi), then some conversion of the counts into radioactivity would be needed. In addition, because the thyroid gland is at some depth, albeit small, within the patient's neck, some loss of γ rays is from their absorption within the patient. Consequently, a separate measurement of a known amount of radioactivity (calibration source) of the radioiodine used for the uptake is also measured using the same device. In this case, the calibration source is (1) placed inside a phantom designed to mimic a typical neck size and tissue depth, and (2) the phantom is positioned in front of the uptake probe or the γ camera in the same manner as the patient would be. In order to achieve some measure of consistency, the neck phantom has been standardized by the International Atomic Energy Agency and is shown in Fig. 11.13.

A solid plastic cylinder simulates the neck of a patient approximately 5 in. in diameter by 5 in. in height with a cylindrical hole that extends partially through the phantom and is offset toward the "anterior" surface. If capsules containing the standard radioiodine are used, they are placed inside the plastic insert shown just to the left of the neck phantom. This insert is then placed inside the holder to the right of the neck, and the assembly is inserted into the hole in the phantom. If liquids are used instead of capsules, then one of the vials is filled with the radioiodine and placed into the insert. Frequently, the same capsule(s) to be administered to the patient are used for the calibration. The denominator in the equation above is simply the counts recorded using this measurement; no additional corrections are required.

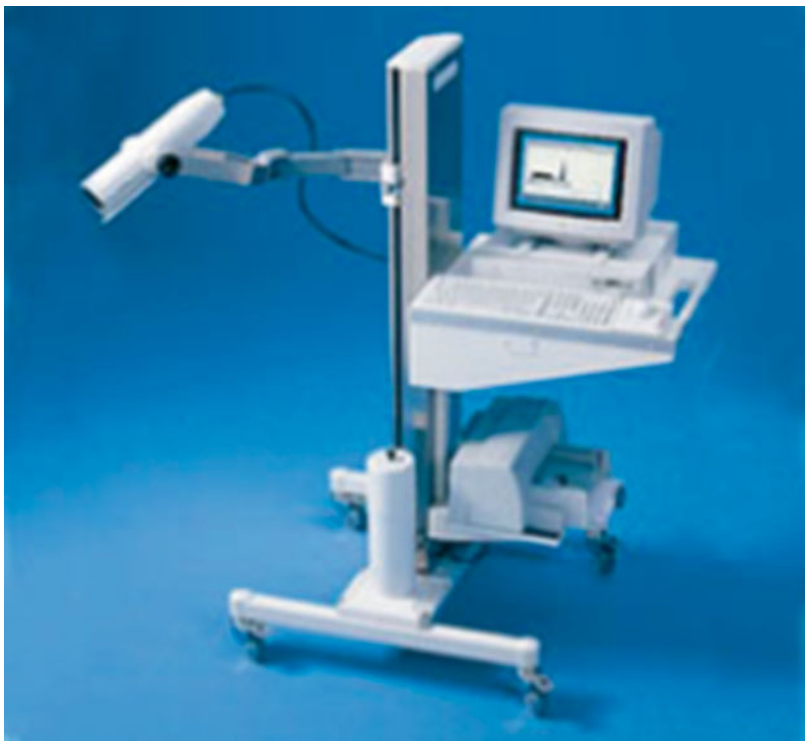

Fig. 11.14 Thyroid uptake probe. See text for discussion

Uptake Probe

The uptake probe typically uses a single small NaI (Tl) radiation detector that is mounted onto an articulating arm. The diameter of this detector is generally between 1 and 2 in. A collimator is in front of the detector and is a slightly tapered, cylindrical, lead-based shell of about 5 in. in length that blocks γ rays from striking the detector, unless they originate from a reasonably small volume at the end of the collimator. Because γ rays travel along straight lines, the size of the sensitive volume gradually increases with distance from the detector. Systems specifically designed as thyroid uptake probes are commercially available, and an example is shown in Fig. 11.14.

The arm holding the probe can move vertically along the counterbalanced stand to allow easy positioning over the anterior surface of the thyroid bed of the seated patient. The γ radiation emanating from the patient is then counted for about 1–5 min. As the number of γ rays that would strike the detector depends strongly on the distance of the source from the probe, there is also a movable device mounted on the side of the probe that allows the patient to be positioned at a consistent and reproducible distance about 3 in. from the collimator.

Acquisition Parameters and Technique

Scintigraphic protocols for imaging differentiated thyroid cancer depend on which radioiodine was administered and the mode of operation of the γ camera. To evaluate the patient for metastatic spread of the thyroid cancer, a large portion of the body must be imaged from the head to the knees. Although this can be accomplished in different ways, the most common technique is a whole-body scan, which was discussed earlier in this chapter. Today, most scintillation cameras are mounted on a gantry that enables either the patient bed to continuously translate the patient through the imaging field or the gantry and camera to "scan" along the length of the patient. In either case, a single image can be produced in which the width is equal to the camera's active width, whereas the height of the image corresponds to the distance that was scanned. Typically, the maximum length that can be scanned is approximately 200 cm. Furthermore, many scintillation camera systems currently have two detectors, such that anterior and posterior projections can be acquired simultaneously, thereby reducing the overall imaging time. If the imaging system is not capable of whole-body scanning, then separate overlapping images that span the appropriate length of the patient can be used. The whole-body scan or survey is an indispensable diagnostic tool; nevertheless, the image quality is not quite as good as that obtained from a static or "spot" view of a particular area of the patient. Table 11.4 lists typical acquisition parameters that might be used to acquire each image for the different modes of operation (whole-body scanning, static images, and pinhole images) for ^{123}I and ^{131}I. For some parameters, the values listed are guidelines and might differ somewhat between facilities. Additional information is also available from the Society of Nuclear Medicine [1].

Table 11.4 Typical acquisition parameters

Whole-body scanning					
Radionuclide	*Collimator*	*Peak (keV)*	*Window*	*Speed*	*Matrix*
^{123}I	Low energy	159	15–20 %	4–6 cm/min	512×1024
^{131}I	High energy	362	15–20 %	4–6 cm/min	512×1024
Static imaging					
Radionuclide	*Collimator*	*Peak (keV)*	*Window*	*Time/view*	*Matrix*
^{123}I	Low energy	159	15–20 %	10–20 min	256×256
^{131}I	High energy	362	15–20 %	10–20 min	256×256
Pinhole imaging					
Radionuclide	*Pinhole insert*	*Peak (keV)*	*Window*	*Time*	*Matrix*
^{123}I	4 mm	159	15–20 %	10–20 min	256×256
^{131}I	6 mm	362	15–20 %	10–20 min	256×256

Positron Emission Tomography (PET) Scanner

Because ^{124}I is a position-emitting radionuclide, a different device is required to image this radioiodine, the PET scanner, which is discussed further in Chap. 103.

Types of Whole-Body Scintigraphy

Understanding the different types of radioiodine whole-body scanning can be confusing because a whole-body scan can be performed many different ways, and the terminology varies between imaging facilities and also within the same facility. To aid the understanding and communication of the many different types of radioiodine whole-body scans, three factors are typically included in the name (see Table 11.5).

Table 11.5 Factors for describing radioiodine whole-body scan

The point in time during the patient's medical care when the scan is performed
The type of thyroid stimulation used in preparation for the scan
The specific radioiodine used

Time Points of Scanning

Scans may be typically performed at five time points during the patient's medical care.

Time Point 1: Pre-ablation Scan

The first scan is performed typically 4–6 weeks after the patient's initial thyroid surgery and before the first radioiodine ablation, hence, the terms *pre-ablation scan*, *first diagnostic scan*, or *postoperative* scan.

The objectives of this scan are:

1. To visually assess the extent and distribution of normal thyroid tissue still remaining after the thyroidectomy
2. To qualitatively demonstrate and quantitatively measure (uptake probe) the amount of radioiodine in the thyroid bed, which could affect the empiric, ablative prescribed activity of ^{131}I
3. To evaluate the presence of metastasis (e.g., cervical lymph nodes, bones, lungs, or brain) that may alter the immediate management of the patient

Although a large portion of facilities perform these pre-ablation scans, many facilities have eliminated them [2, 3]. These facilities typically use a single empiric prescribed activity of ^{131}I for all initial ablations in adults regardless of the results from the initial pre-ablation scan. The controversy of performing or not performing radioiodine scans before ^{131}I ablation is discussed further in Chaps. 14, 15, and 19. However, this author (dvn) believes that these scans are valuable for the reasons noted above and in Table 11.6. For the minor inconvenience to the patient and a cost equivalent to about one computed tomography (CT) scan, the information obtained is useful and could alter the physician's management of the patient.

Time Point 2: Follow-Up as a Screen for Recurrent Cancer (Surveillance Scan)

As part of the follow-up and screening for recurrent well-differentiated thyroid cancer in patients who have had a thyroidectomy and radioiodine ablation, a radioiodine whole-body scan may be used, and this is frequently called a *surveillance scan*. These scans may be performed as soon as 6 months or possibly as long as 2 years after the patient's initial ablation. Most surveillance scans are performed at approx 6 months to 1 year after remnant ablation or adjuvant treatment. However, with the availability of both thyroglobulin blood levels that can be used as a tumor marker and ultrasound, many facilities have stopped performing routine surveillance scans as part of the patient's routine follow-up

Table 11.6 Utility of the pre-ablation scan

Demonstration of the pattern and percent uptake of iodine in the thyroid bed or neck area that could, in turn, alter the patient's management, the amount of therapeutic ^{131}I prescribed activity, or both. Examples include:
1. A single area of significant uptake, such as 5–30 %, which suggests considering additional surgery or modifying the empiric prescribed activity of ^{131}I
2. A single area of low uptake such as <1 %, which suggests modifying the empiric prescribed activity of ^{131}I[a]
3. A pattern of radioiodine uptake consistent with cervical metastasis that may suggest (1) further evaluation with ultrasound or MR; (2) additional fine-needle aspiration, surgery, or both; and/or (3) the use of a larger empiric prescribed activity of ^{131}I
Demonstration of distant metastasis that may alter the evaluation and/or the management of the patient prior to ^{131}I therapy. Examples include:
1. Focal or diffuse uptake in lung that may warrant further evaluation with CT, pulmonary function tests, and dosimetry to determine the maximum tolerated prescribed activity without exceeding 48-h retained whole-body. The latter may increase or decrease prescribed activity relative to an empiric prescribed activity and may help minimize the potential for acute radiation pneumonitis and pulmonary fibrosis
2. Focal area suggesting bone metastasis that may need further evaluation with CT, larger empiric prescribed activity, dosimetry, and/or coordination of other treatment modalities such as metastasectomy, subsequent external radiotherapy, or radiofrequency ablation, to name a few
3. Focal uptake in the head that may warrant an MR exam of the brain. If the focal area is a brain metastasis, then consideration of surgery, external radiation therapy (i.e., gamma knife), reduction of the empiric prescribed activity, and/or treatment with steroids, glycerol, and/or mannitol prior to treatment with ^{131}I

[a]Various reports suggest that the prescribed activity for residual thyroid tissue in the thyroid bed be increased or decreased based upon the radioiodine uptake (see Chap. 58, Refs. [32–36])

and monitoring [4–7]. Nevertheless, surveillance scans may be of value in selected patients. Surveillance scans and follow-up baseline scans are discussed further in Chap. 41.

Time Point 3: Follow-Up Baseline

A scan may be performed 6–18 months after initial131I therapy in order to establish a new baseline scan, and this scan can be used for comparison should a subsequent scan be performed for evaluation of possible recurrence (See Chap. 41).

Time Point 4: When Metastasis Is Suspected

A scan may also be performed when recurrence of thyroid cancer is already known to be present or is suggested based on an elevated or rising thyroglobulin blood level, positive cytology obtained by fine-needle aspiration of a lymph node, a new mass on physical exam, and/or findings suggesting recurrence on CT, ultrasound, magnetic resonance (MR), or positron emission tomography (PET). Although some facilities also refer to this as a surveillance scan, the objective of this scan is no longer for surveillance. Rather, the objective of this scan depends on the patient's clinical situation. For example, if the patient's serum thyroglobulin level is rising, the objective of the scan may be to try to localize the site of the recurrent cancer for possible surgery, to determine whether the thyroid cancer has radioiodine uptake and could benefit from ^{131}I treatment or both. However, if a new mass is present, and its cytology by fine-needle aspiration is positive, the objective of the scan may be to determine whether it can be potentially treated with ^{131}I and/or if there are other sites of metastasis, which may alter management.

Time Point 5: Post-therapy Scan

This scan is typically performed between 3 and 7 days after the patient's ^{131}I ablation or treatment. Post-therapy scans have a particular advantage over the other scans discussed because of the much higher prescribed activity of ^{131}I used for the patient's ablation or treatment. As a result, these scans may demonstrate thyroid tissue or metastases that could not be detected on the postoperative or preablation scans. Although the information provided by the post-therapy scan typically does not alter the patient's immediate management, it could have an impact on subsequent follow-up and evaluation. This is discussed in more detail later in this chapter.

Method of Thyroid Stimulation

Patients may be prepared either by withdrawing their thyroid hormone to elevate their endogenous thyrotropin (TSH) level or by administering recombinant TSH. In regard to withdrawal, Hilt et al. [8] evaluated serial TSH levels after T3 withdrawal or thyroidectomy. After T3 was substituted for levothyroxine and then the T3 discontinued 4 weeks later, Hilt et al. reported a doubling time of 2 days until at least a TSH level of 40 uIU/ml was reached with a maximum at 20 days. The mean time required to reach a level of 50 uIU/ml was 11 days, and they suggested 11 days for TSH determination before I-131 imaging. After total thyroidectomy the dou-

Table 11.7 Terminology of radioiodine whole-body scanning

^{123}I postoperative withdrawal scan
^{123}I postoperative rhTSH scan
^{123}I pre-ablation withdrawal scan
^{123}I pre-ablation rhTSH scan
^{123}I first-time withdrawal scan
^{123}I first-time rhTSH scan
^{131}I postoperative withdrawal scan
^{131}I postoperative rhTSH scan
^{131}I pre-ablation withdrawal scan
^{131}I pre-ablation rhTSH scan
^{131}I first-time withdrawal scan
^{131}I first-time rhTSH scan
^{123}I surveillance or baseline withdrawal scan
^{123}I surveillance or baseline rhTSH scan
^{131}I surveillance or baseline withdrawal scan
^{131}I surveillance or baseline rhTSH scan
^{131}I withdrawal scan and dosimetry
^{131}I rhTSH scan and dosimetry
Post-therapy scan

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bling time was more variable with a mean doubling time of 7.6 days. The use of thyroid hormone withdrawal and administration of rhTSH injections for preparation prior to ^{131}I therapy are discussed in further detail in Chaps. 34, 57, and 60.

Type of Radioiodine

As already discussed earlier in this chapter, the whole-body scan is performed with ^{123}I, ^{131}I, or ^{124}I.

Thus, by knowing these previous three factors, e.g., time, preparation, and type of radioiodine, the physician has a better understanding of the wide spectrum of terms that are used, types of whole-body scans available, and which whole-body scan may have been performed for their patients. Examples of terminology are shown in Table 11.7.

Selection of Radioisotope

As already noted in the Introduction, radioiodine whole-body scintigraphy is a valuable diagnostic tool in the assessment of patients with thyroid cancer. Two of the most controversial areas of radioiodine whole-body scanning involve the (1) selection of the radioisotope and (2) the prescribed activity to administer. The choices of radioiodine isotopes are ^{131}I, ^{123}I, and ^{124}I, and the physical characteristics of each have already been discussed earlier in this chapter. This section presents an overview of the choices of ^{131}I, ^{123}I, and ^{124}I. Further discussion regarding thyroid hormone withdrawal vs recombinant human (rh) TSH injections can be found in Chaps. 34, 57, and 60. Additional information regarding ^{124}I is also available in Chap. 103.

^{131}I

The most frequently used radiopharmaceutical to date is ^{131}I [9, 10]. Its major advantages are its long historical use, availability, reasonable cost, and half-life. ^{131}I has been used for clinical imaging for over 50 year, is readily available, and is relatively inexpensive for a diagnostic radiopharmaceutical. The half-life is approx 8 days, which allows additional delayed imaging to be performed as long as 3 or 4 days, and possibly even longer after administering ^{131}I. The value of delayed scanning is to allow significantly more time for the patient's background radioactivity to clear. Although the radioactivity of the normal or abnormal thyroid tissue may also have clearance over time, this decrease in radioactivity within the thyroid tissue or metastasis is typically less than the reduction of the whole-body background radioactivity. This causes increasing thyroid tissue-to-background ratios of radioactivity, thereby increasing the detection of functioning normal and abnormal thyroid tissue. The long half-life of ^{131}I also allows dosimetry to be performed, including whole-body counting, blood specimens, and urine specimens to be obtained and measured 5 days and even longer after radioiodine administration.

The major disadvantage of ^{131}I is the potential of "stunning." The concept and arguments for and against "stunning" are discussed in Chaps. 16, 17, and 18. In brief, stunning is the short-term reduction of radioiodine uptake after diagnostic amounts of prescribed activities of ^{131}I secondary to the radiation dose to the tissue. Again, as discussed elsewhere, this can potentially reduce the therapeutic effect of an ^{131}I treatment when administered shortly after a diagnostic ^{131}I study.

^{123}I

As an alternative to ^{131}I, ^{123}I has been used, and its advantages and disadvantages have been previously noted in Table 11.3. No documented stunning has been reported using ^{123}I, and given the relatively small estimated radiation doses from diagnostic amounts of ^{123}I, thyroid stunning of any significant degree is highly unlikely. Although frequently Hilditch et al.'s study [11] has been referenced as possibly indicating some stunning with ^{123}I, the authors suggest that the reduction of uptake after a therapeutic administration of ^{131}I is unlikely to be stunning from ^{123}I but rather a therapeutic effect from the therapeutic ^{131}I. ^{123}I also has better imaging characteristics than ^{131}I, resulting in

high-quality images, and ^{123}I does not require a high- or medium-energy collimator. This allows great flexibility for obtaining images by various γ cameras within a nuclear medicine facility. Although the availability and cost for ^{123}I were previously problematic, ^{123}I has becoming more widely available in more countries, and the cost of ^{123}I has decreased as its use has increased.

Studies Involving ^{123}I

In evaluating (1) the prescribed activity of ^{123}I, (2) the time of imaging after dosing ^{123}I, and (3) the detection of thyroid tissue and thyroid cancer metastasis with ^{123}I relative to ^{131}I, multiple studies have been reported [12–17, 19–24].

Naddaf [13] compared 13 ^{123}I scans in 10 patients with post-therapy ^{131}I scans. The ^{123}I scans were performed 4, 24, and 48 h after the oral administration of 370 MBq (10 mCi) of ^{123}I. Anterior and posterior whole-body images were obtained for 60 min. The post-therapy scans were performed 5–7 days after 2.78–8 GBq (75–217 mCi) of ^{131}I. Of functioning thyroid tissue, 27 sites were identified on the post-therapy ^{131}I scans, and 24 of the 27 sites were identified on the ^{123}I scan. No comment was made regarding the relative utility of imaging ^{123}I at 4, 24, and 48 h.

Mandel et al. [10] evaluated 14 patients in whom the ^{123}I scans were obtained 5 h after administration of 48–56 MBq (1.3–1.5 mCi) ^{123}I. The ^{131}I scans were obtained at 48 h after the administration of 111 MBq (3 mCi) of ^{131}I. These scans were then compared with post-therapy scans performed 7 days after ^{131}I therapy. There were 35 foci identified, and ^{123}I images demonstrated that all 35 foci were in the thyroid bed and neck, whereas only 32 of 35 foci (91 %) were seen on the pre-therapy ^{131}I scan. Mandel et al. concluded that ^{123}I resulted in improved quality of images relative to ^{131}I in patients undergoing thyroid remnant ablation.

Berbano [14] reported that 15 of 16 patients had concordant findings on the ^{123}I scans relative to the ^{131}I scans. Only one patient had an additional site identified on the ^{131}I scan, which was not identified on the ^{123}I scan, and this was a patient with metastatic disease. The prescribed activity of ^{123}I was 370 MBq (10 mCi). The ^{131}I scans were performed after radioiodine therapy, with prescribed activities ranging from 75 to 2.8–7.4 GBq (200 mCi). Berbano [14] also evaluated ^{123}I scans at 24 and 48 h after dosing. He reported no advantage for imaging at 48 h in comparison to 24 h.

Maxon [15] evaluated 13 administrations of ^{123}I in 11 patients. The average prescribed activity of ^{123}I was 743 MBq (20.1 mCi); the ^{123}I scans were compared with scans performed 2–3 days after ^{131}I therapy. He reported no false-negative ^{123}I scans when those scans were imaged at 18–24 h after administration of ^{123}I. Scans performed 2 h after ^{123}I administration had a false-negative rate of 38 % (5/13). Pre-therapy scans with ^{131}I were performed with 74 MBq (2 mCi) of ^{131}I, and the results of analyzing the ^{123}I scans with ^{131}I scans were not reported.

Yaakob [16] examined 13 patients with ^{123}I with prescribed activities of 30–37 MBq (0.8–1.0 mCi). Images were obtained 24 h after ^{123}I administration and compared with scans performed 7–10 day after ^{131}I therapy. There were 11 ^{123}I scans that correlated with the post-therapy scan. One patient had an additional area detected on the ^{131}I post-therapy scan that was not detected on ^{123}I scan, and one patient had an additional area detected on the ^{123}I scan that was not seen on the ^{131}I post-therapy scan. The latter was attributed to physiologic esophageal activity.

Shankar [17] compared ^{123}I and ^{131}I scans in 26 patients. The ^{123}I scans were performed 4 h after the administration of 55.5 MBq (1.5 mCi) of ^{123}I, and the ^{131}I scans were performed 48 h after the administration of 111 MBq (3 mCi) of ^{131}I. ^{123}I scans identified 56 foci of activity, whereas the ^{131}I scan demonstrated only 44 of the 56 foci seen on the ^{123}I scan. All 56 foci of activity were seen on the post-therapy ^{131}I scan, and the post-therapy ^{131}I scan showed one additional area not seen on the ^{123}I scan. Of the 56 foci, 54 foci were in the neck and thyroid bed, with one focus each in the mediastinum and lung. In a separate report, Shankar et al. [18] demonstrated that the imaging with ^{123}I was superior at 24 h relative to 5 h after administration of the ^{123}I.

In a comparison of ^{123}I scans with post-therapy ^{131}I scans, Gerard et al. [19] identified 37 sites on post-therapy scan; 26 were identified with ^{123}I for a sensitivity of 70 %. Of the 11 sites missed by ^{123}I, 7 were seen on the post-therapy scan relative to the early scan. A total of ten patients had 48-h ^{123}I scans, and eight were of good quality. Lesion detection was improved on the 48-h scans. ^{123}I scans after withdrawal of thyroid hormone were performed with 3–5 mCi 111–185 MBq (3–5 mCi) of ^{123}I at 6, 24, and 48 h.

Alzahrani et al. [20] had 238 pairs of pre-therapy ^{123}I scans and post-therapy ^{131}I scans with a concordance rate of 94 %. Siddiqi [21] compared ^{123}I whole-body scans to post-therapy ^{131}I scans in 12 patients who had elevated serum thyroglobulin levels and previous negative ^{131}I whole-body scans. On subsequent evaluations, the ^{123}I dose was 185 MBq (5 mCi), and images were obtained at 2 and 24 h after administration of ^{123}I. The post-therapy scans were performed 4–7 days after the therapy with 150 mCi 5.55 GBq (150 mCi). The ^{123}I scans were concordant with the ^{131}I post-therapy scan in 11 of 12 patients.

Sarkar et al. [22] compared ^{123}I and ^{131}I in 12 patients, and both revealed residual disease in nine patients. ^{131}I detected metastases in five studies of four patients. In four of the five studies, ^{123}I missed metastases shown by ^{131}I in eight body regions including the neck, mediastinum, lungs, and bone and detected three other sites of metastasis only in retrospect. No lesion was better seen with ^{123}I than ^{131}I. Although ^{123}I is adequate for imaging residual disease, it appears to be less sensitive than ^{131}I for minimal thyroid cancer metastasis.

Khan et al. [23] compared ^{123}I scans with prescribed activity of 5.55–111 MBq (1.5–3.0 mCi) with post-therapy ^{131}I in

183 patients, showing a similar number of lesions in similar locations in 91 %, but the time of imaging was not noted. Nine patients (4.5 %) had more lesions detected in the ^{123}I scan when compared to the 7-day post-therapy ^{131}I scan. Likewise, nine patients had more lesions detected on the 7-day post-therapy scan. Post-therapy scans were obtained 7 days after 2.22–7.4 GBq (60–200 mCi). It is assumed that some of these lesions were included in earlier reports from the same institution [10, 17].

Anderson et al. [24] evaluated 101 consecutive ^{123}I and 101 consecutive ^{131}I scans after preparation with rhTSH injections. There were 96 patients in the ^{131}I group and 98 patients in the ^{123}I group who had received previous ^{131}I ablations or treatments. They used 111 MBq (3 mCi) of ^{123}I and 148 MBq (4 mCi) of ^{131}I, and images were obtained 24 h after ^{123}I and 48 h after ^{131}I. The rhTSH-stimulated ^{123}I scans and thyroglobulin levels were concordant in 90 % (91/101) of patients; the results of rhTSH-stimulated ^{131}I scans and thyroglobulin levels were concordant in 84 % (85/101) of patients. ^{123}I whole-body scans detected nine foci of disease in six patients, and ^{131}I whole-body scans detected ten foci of disease in nine patients. Anderson proposed that rhTSH-stimulated ^{123}I scans might prove to be as sensitive as rhTSH-stimulated ^{131}I scans for the detection of metastatic disease.

^{124}I

^{124}Is a positron-emitting radioisotope and has recently become commercially available for research studies. The advantages and disadvantages of ^{124}I have been previously noted in Table 11.3 and include superior image quality, tomographic images, bone marrow and metastatic lesion dosimetry, and the ability to fuse the tomographic images with CT, MR, or both. The physical half-life of ^{124}I is approx 4 days, which is sufficiently long enough to allow delayed imaging and dosimetry. The major disadvantages of ^{124}I are its availability (production sites are limited), cost, and requirement for a PET imaging system, and it is not approved by the FDA. Another potential disadvantage of ^{124}I is stunning, as the radiation-absorbed dose is about half that of a comparable prescribed activity of ^{131}I. A few studies have already been reported using ^{124}I [25, 26], and ^{124}I has been discussed further in Chap. 103.

^{99m}Tc Pertechnetate

Multiple studies have been published evaluating ^{99m}Tc pertechnetate (^{99m}Tc04) as an alternative radioisotope to evaluation patients with differentiated thyroid cancer postoperatively and pre-^{131}I therapy [27–30]. ^{99m}Tc04 would avoid the issue of stunning from ^{131}I. However, because of higher background radioactivity, the negative predictive value of ^{99m}Tc04 does not appear as good as radioisotopes of iodine [28].

Table 11.8 Factors that affect scanning and radioisotope selection

Time of the whole-body scintigraphy
First scan, which is performed after initial diagnosis, thyroidectomy, and prior to radioiodine remnant ablation or adjuvant treatment
Surveillance scan[a]
Follow-up baseline scan
Pretreatment scan[a]
Patient preparation
Thyroid hormone withdrawal
rhTSH injections
Whether thyroglobulin levels are obtained before or simultaneously with radioiodine scan
Presence or absence of increased thyroglobulin blood levels when suppressed or stimulated prior to whole-body scanning
Physician's belief in the potential for stunning
Physician's approach to the selection of prescribed activities for first-radioiodine remnant ablation or adjuvant treatment (e.g., fixed or variable empiric prescribed activity or dosimetrically determined prescribed activity)
Physician's approach to subsequent selection of prescribed activities for treatment (e.g., recurrence and/or distant metastases) of differentiated metastatic thyroid carcinoma (e.g., "blind treatment," empiric vs dosimetrically determined prescribed activity for treatments)

[a]Defined in text

Utility of Whole-Body Scanning: Pre-ablation, Surveillance, Pre-treatment, and Post-therapy

So, should one scan or not, and if one scans, what isotope of radioiodine does one use? The choice depends on multiple factors, such as those shown in Table 11.8, as well as the factor(s) that the physician and/or patients consider the most important. Four of the more common situations are discussed briefly below and the reader is referred to the chapters that discuss these situations in more detail.

Pre-ablation Scan

For those facilities that administer a standard empiric prescribed activity for remnant ablation or adjuvant treatment and would not alter their ^{131}I therapy based on any radioiodine scan finding, a scan is obviously unnecessary. For those facilities that believe that a radioiodine scan offers useful information prior to the first therapy, the use of ^{123}I is an excellent choice. Not only does this author believe that pre-therapy scans are useful (as already discussed above, in Table 11.6, and in Chap. 19), but this author also believes that if ^{123}I is available, it is the radioisotope of choice. At the time of this publication, ^{123}I is a reasonably cost-effective isotope that can demonstrate both the pattern and percent uptake of radioiodine activity in the thyroid bed. In addition, its sensitivity is as good or at least comparable to ^{131}I to show functioning metastasis that would result in altering management of anticipated initial ^{131}I therapy. Although ^{123}I may arguably miss a small focus with low uptake in residual thyroid disease or

metastasis, the failure to detect these small or low-uptake foci will be infrequent. In addition, regardless of whether or not ^{131}I may cause significant stunning, ^{123}I virtually eliminates the possibility and consideration of stunning (see Chaps. 16, 17, and 18). In regard to ^{124}I, this radioisotope is not approved for use within the United States (see Chap. 103).

Surveillance Scan (to Be Distinguished from a Follow-Up Baseline Scan or Pre-treatment Scan)

The term, "surveillance scan," has been used in a number of contexts, which has been discussed earlier and in more detail in Chap. 41. In brief, a surveillance scan is a radioiodine scan performed at some routine interval, which is typically every year beginning 6 months to 1–2 years after ablation or treatment. The objective of this scan is to *screen* for recurrent and/or metastatic functioning differentiated thyroid cancer in patients who are in otherwise clinical remission. Clinical remission is defined here as no evidence of disease on physical exam, undetectable serum thyroglobulin levels on thyroid hormone suppression or stimulation, and no evidence by any other imaging modalities such as ultrasound that has been performed.

As defined above, a surveillance scan should be differentiated from a "pre-therapy scan," which is a radioiodine scan performed in "anticipation" of ^{131}I therapy in patients in whom the physician is suspicious of recurrent local thyroid cancer or metastases or patients who have documented recurrence or metastatic disease. A surveillance scan should also be differentiated from a follow-up "baseline scan." A baseline scan is performed after an ^{131}I therapy such as remnant ablation, adjuvant treatment, or treatment for locoregional and/or distant metastases in order to establish a new baseline scan to be used for any future comparison (see Chap. 41).

Although surveillance scans in the past have been frequently performed every 6 months to 1 or 2 years after the initial therapy of residual thyroid tissue or adjuvant treatment, the utility and cost-effectiveness of such a surveillance scan in patients who are in a low-risk group or clinical remission is no longer warranted [4–7]. This fact is especially true when the patient must undergo a prolonged period of hypothyroidism during thyroid hormone withdrawal. Again, surveillance scans are discussed further with proposed recommendations from various organization groups and societies in Chap. 41.

However, if a physician believes a surveillance scan is still valuable for his or her patients, then which isotope should be used? Again, either ^{123}I or ^{131}I may be used when the patient is prepared with thyroid hormone withdrawal. For those patients who are prepared with injection of rhTSH, many facilities use ^{131}I because ^{131}I was the radioisotope used in the initial studies with rhTSH. However, ^{123}I may also be used. To our knowledge, no prospective study is available comparing ^{123}I and ^{131}I scans after rhTSH preparation for surveillance scanning.

Pre-treatment Scan

(A) *Before therapy when an empiric prescribed activity of ^{131}I is planned for adjuvant treatment of suspected residual cancer or treatment of known recurrent or metastatic disease*:
The *preferred* radioiodine isotope in the opinion of this author is ^{123}I if the patient has known or highly suspected recurrent or metastatic disease and the physician anticipates treating with an empiric prescribed activity of ^{131}I. This choice is again based on the objective of the scan, namely, identification of findings that would potentially alter management. The findings are similar to some already noted in Table 11.4.

B) *Before therapy when dosimetrically determined prescribed activity of ^{131}I is planned in suspected or known recurrent or metastatic disease*:
The preferred radioiodine isotope is ^{131}I. Although the prescribed activity used in different facilities may vary from 37 to 148 MBq (1–4 mCi), this author recommend the lowest prescribed activity that still allows the performance of dosimetry while attempting to minimize the likelihood of stunning. In the author's facility, this ranges from 37 to 74 MBq (1–2 mCi). For ^{123}I, high-prescribed activities up to 740 MBq] (20 mCi) have been used [15], and further study is warranted using high diagnostic prescribed activity of ^{123}I for dosimetry. Initial studies have already demonstrated the potential of ^{124}I for dosimetry [25, 26], but additional research is needed regarding its potential for stunning. Table 11.9 summarizes several proposed recommendation for the use of first-time pre-ablation scans, surveillance scans, and pre-therapy scans.

Post-therapy Scans

Post-therapy scans image the ^{131}I administered for the radiotherapy, and this scan is performed between 3 and 7 days after radioiodine remnant ablation or adjuvant treatment and has been shown to be useful and is routinely performed [3, 31–37]. Fatourechi et al. [35] reported that 13 % of (17/117) post-therapy scans demonstrated an abnormal foci of ^{131}I that was originally undetected on the pre-therapy scan. The areas of newly detected abnormal uptake were located in the neck (5), lung (5), mediastinum (4), bone (2), and adrenal (1). The prescribed activity of the pre-therapy scan was 111 MBq (3 mCi) of ^{131}I, and post-therapy images were obtained between 1 and 5 days after therapy. The likelihood of detecting new

Table 11.9

First-time pre-remnant ablation or adjuvant treatment scan	
After thyroid hormone withdrawal After rhTSH injection	• ^{123}I using 74–148 MBq (2–4 mCi) with imaging at 24 h • Consider ^{123}I using 74–148 MBq (2–4 mCi) with injection after the second injection of rhTSH with imaging at 24 h followed by ^{131}I therapy later that day
Surveillance scan[a]	
After thyroid hormone withdrawal After rhTSH injections	• ^{123}I using 74–148 MBq (2–4 mCi) with imaging at 24 h • ^{131}I with 148 MBq (4 mCi) and imaging at 48 h • Consider ^{123}I using 74–148 MBq (2–4 mCi) with injection after the second injection of rhTSH with imaging at 24 h
Pre-therapy scan[a] with the intent to treat with an empiric prescribed activity of ^{131}I for recurrent and/or metastatic differentiated thyroid cancer	• ^{123}I using 74–148 MBq (2–4 mCi) with imaging at 24 h
Pre-therapy scan[a] with the intent to treat with dosimetrically determined prescribed activity of ^{131}I for recurrent and/or differentiated thyroid cancer	• ^{131}I using the lowest prescribed activity possible to perform dosimetry and to minimizing potential of stunning (typically 37–74 MBq [1–2 mCi])

[a]Defined in text and see Chap. 41

Table 11.10 Post-therapy radioiodine scans

Reference	Patients	Pair scans	Days on which scans were performed	Recommend scanning time
Bourgeois [39]	43	49	3 vs 6	Early and late
Chong [42]	52	52	3 vs 7	Late
Hung [41]	239	717	3–4 vs 5–6 vs 10–11	Early
Khan [38]	18	18	2 vs 7	Late
Lee [43]	81	81	3 vs 10	Early
Oliveira [40]	164	164	2 vs 7	Low risk: early
				High risk: early and late
Salvatori [45]	134	134	3 vs 7	Early
Wakabayisha[44]	42	42	3 vs 7	Early SPECT-CT

uptake on the post-therapy scans decreases after each successive therapy. Sherman et al. [33] reported that 22 % (31/143) new lesions were detected on the post-therapy scan that were not seen on the pre-therapy scan. They used 74–185 MBq (2–5 mCi) for the pre-therapy scan, and the post-therapy scan was performed between 5 and 12 days after therapy. In regard to the effects of post-therapy scans on management strategies, Fatourechi et al. [35] reported that 9 % of scans affected management (e.g., future decisions about plans for diagnostic scanning or ^{131}I therapy) or changed the patient's risk-group category. Post-therapy scans are widely performed and accepted as useful.

However, when post-therapy scans should be performed is more controversial, and multiple authors have evaluated this issue [38–45] (see Table 11.10). Hung et al. [41] evaluated 239 patients evaluating three sequential radioiodine whole-body scans at 3–4 days, 5–6 days, and 10–11 days after ^{131}I therapy. For remnants, imaging at 3–4 days, 5–6 days, and 10–11 days missed 1.1 % (2/170), 1.8 % (3/170), and 5.4 % (9/170) foci, respectively. For metastases, imaging at 3–4 days, 5–6 days, and 10–11 days missed 6.3 % (7/112), 2.5 % (3/112), and 25 % (28/112) areas, respectively. The trend was that earlier imaging was better than later imaging in order to identify remnant thyroid tissue and metastases.

Salvatori et al. [39] evaluated 124 patients that were performed on the third (early) and seventh (late) day. The early and late scans were concordant in 80.5 % (108/134) of patients. However, 7.5 % (10/134) of the early scans demonstrated lymph nodes (seven patients) and distant metastatic uptake (three patients) that were not seen on the late scan. In addition, in 12 % (16/134) of the patients, the late scan showed thyroid remnants (4), lymph nodes (7), and distant metastases (5) that were not seen on the early scan. Bourgeois et al. [38] suggested considering performing both scans, whereas Oliveira et al. [39] suggested early scanning for low-risk patients and early and late scans for high-risk patients. Salvatori et al. proposed that performing the early scan yields highly accurate results while saving the expense of a second scan and avoiding an additional visit to the imaging facility for the patient. However, in this case, one could miss up to 12.5 % of other foci.

Based on my interpretation of Salvatori et al.'s data, the early and late scans were either completely concordant, positive on the early scan and negative on the late scan, or negative on the early scan and positive on the late scan. No patient showed some lesions on the early and different lesions on the late scan. If correct, then I would propose that one may wish to consider performing an early scan at 3–4 days, and if that scan is negative, then consider performing a late scan at 7 days. This would result in only 12.5 % of the patients requiring a second scan.

In closing this section, two caveats are appropriate. First, if one is performing only an early 3-day scan or only a late 7-day scan and that scan is negative, then that does not necessarily mean that the patient's differentiated thyroid cancer no longer takes up radioiodine. Based on Salvatori et al.'s data, one would miscategorize that patient as radioiodine-negative in 7.5–12.5 % of the patients. Salvatori et al.'s paper also provokes an interesting question regarding stunning. Although Salvatori et al. did not report performing pre-ablation scans, if a focus of radioiodine uptake was observed on a pre-ablation scan but not observed on the post-therapy scan, that is not in of itself indicative of stunning. It may indicate that only a 3-day or only a 7-day scan was performed and missed the foci and that the foci were not stunned. Clearly, further study is warranted.

Summary

Radioiodine whole-body scans are important diagnostic tools in the evaluation of patients with differentiated thyroid carcinoma. With a basic understanding of such factors as radioelements, scientific notation, decay, physical half-life, γ cameras, and protocols, the physician will have a better understanding of how the radioiodine whole-body scans are performed, as well as their utility and controversial aspects. The next chapter presents a primer and atlas for the basic interpretation of radioiodine whole-body scans.

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