Myocardial Perfusion Scintigraphy

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Coronary atherosclerosis determines an altered vasoreactivity to vasodilator stimuli. As a result, impaired coronary flow reserve is one of the earliest signs of coronary artery disease (CAD), which can be assessed scintigraphically.

Myocardial perfusion scintigraphy (MPS) involves intravenous (IV) administration of a small quantity of a radioactive substance, which is avidly extracted by the myocardium in relation to myocardial blood flow (MBF) and viability. Images showing myocardial regional distribution of radioactivity are subsequently obtained, and relative MBF differences are detectable. If there is a decrease in relative regional perfusion, as seen in hemodynamically significant CAD, or loss of cell viability, as seen in myocardial infarction (MI), a reduced signal is collected scintigraphically. Usually, MPS is performed at rest and during some form of cardiovascular stress. Absence of uptake on stress images may represent areas of significantly decreased flow or areas without viable myocardium. Persistent or fixed defects on resting or baseline images depict scar. Complete defect resolution represents viable myocardium rendered ischemic during stress. Partial defect resolution is observed in areas with a mixture of scar and ischemia.

The diagnosis of CAD remains a common application of MPS, but it is increasingly being used for prognosis assessment in patients with known CAD, and for selection for revascularization and assessment of suspected acute coronary syndromes (ACS).
1. Principles of Radionuclide Imaging

Radionuclide imaging is based on the introduction into the organism of a substance with unstable atoms which emit photons, usually gamma rays and/or X-rays, when the nucleus of these atoms change from one energy level to a lower one. Thus, the body is imaged “from the inside out” by recording the distribution of radioactivity coming from internally administered radionuclides using special devices.

Radiopharmaceuticals are radionuclides that, combined or not with a chemical molecule, meet legal requirements for being administered to subjects. Radiopharmaceuticals are also known as tracers or radiotracers because they have specific organ location and no functional consequences (when given for diagnostic purposes), allowing studying or following a process without disturbing it. The radionuclide fraction of the radiopharmaceutical permits external detection, and the chemical portion is responsible for the biodistribution. For a few agents, the radionuclide itself confers the desired location properties to the radiopharmaceutical.

1.1 Gamma Scintillation Camera or Anger Camera

The scintillation camera is a device capable of detecting the radioactivity coming from organs containing radiotracers, allowing the temporal and spatial location required to generate scintigraphic images. The gamma camera consists of a radiation detector, a signal processor/event locator, and an image recording system.\(^1\)

The detector is made from transparent sodium iodide crystal containing thallium impurities (thallium-activated sodium iodide crystal – NaI[Tl]). When gamma or X-rays enter the crystal, they impart energy to the electrons of the crystal, which give off photons of light to return to the baseline state.\(^1\)

NaI[Tl] crystals are relatively inexpensive and afford great flexibility in size and shape. They have a good stopping power (complete energy absorption of radiation arising from the crystal) at the energy range of radiation used in clinical nuclear medicine (70–364 keV, optimally at 100–200 keV range).\(^2\) However, they are fragile and highly hydroscopic, requiring air-tight hermetrical containers, which usually consist of thin aluminum on three sides and quartz on the fourth side. This quartz window permits the light photons to reach and interact with the photocathode of a photomultiplier tube (PMT), dislodging some electrons, which are subsequently accelerated by a series of electrodes (dynodes) at gradual higher potential. As electrons are accelerated toward each dynode, they gain sufficient kinetic energy to eject several electrons at impact, with increasing the number of electrons finally collected at the anode of the PMT.\(^1\) The multiplication factor is approximately 3–6 per dynode stage and up to several million overall. All these components are mounted on a platform made of lead or tungsten to shield them from stray radiation.

The electrical output is further amplified and the voltage pulse is processed through positioning and energy circuitries. The positioning circuitry determines the spatial location of the radiation event detected (X and Y pulses), and the energy circuitry calculates the energy deposited in the crystal (Z pulse). The location of the event in the crystal is estimated so that each tube may be thought of as having X and Y coordinates in a cartesian plane. Tubes closest to the event collect the greatest number of light photons, with lesser contributions for more remote tubes. Additionally, the output from all of the PMTs is summed and referred to as the Z pulse, which through a pulse height analyzer is used to determine whether the detected event is within the desired energy range and should be accepted in the formation of the image or whether it is of lower or higher energy and should be discriminated against and rejected.

The height of the electrical pulse recorded is proportional to the energy of the radiation initially dissipated in the crystal.\(^1,2\) This allows discrimination between photons directly coming from the organ of interest without any previous disturbance (primary photons) and those that have undergone scatter before detection (secondary photons, less energetic than the primary photons, with lower pulse heights). Additionally, this permits distinction of radiation coming from different radionuclides, with different energies.

For image generation, only primary photons with completely perpendicular direction to the crystal detector need to be registered. Registration of secondary photons is restricted by the pulse height analyzer with an energy window setting (usually symmetrically centered at the
energy peak of the radionuclide being used), and by placement of a collimator in front of the crystal detector.

The collimator is a lead foil with multiple and uniformly distributed holes, which limits the interaction of the radiation photons with the crystal to only those photons traveling parallel to the longitudinal axes of the holes, selectively absorbing the photons that strike obliquely.1

1.2 Creation of the Digital Image

When a radiation event is accepted for storage, it is recorded using an analog-to-digital converter on dedicated computer systems. Data recorded may be thought of as superimposed on a grid or matrix of pixels, where each X and Y pairs determine the coordinates of the event location. Each pixel of the matrix has a number corresponding to the total events accumulated during the acquisition period. The larger the matrix, the better the spatial resolution but the longer the time required to achieve adequate counting statistics in each pixel.3 Most studies in cardiac current practice are obtained in a 64 × 64 or 128 × 128 matrix.

If time information is desired, additional time markers such as the R wave on the electrocardiogram (ECG) can be used to synchronize data collection as in gated cardiac studies. Each R-R interval is divided into a preset number of subintervals, usually 8–16. The R wave triggers data acquisition into a frame corresponding to the first subinterval. At the end of each subinterval time, data collection is switched to a frame corresponding to the next subinterval time. A new R wave will restart the cycle with data collection into the first frame of the series. The sum of data collected over several hundred cardiac cycles generates a series of images that represents a single, average cycle (representative cycle), which allows the survey of cardiac function and the assessment of wall thickening and motion when reviewed in cinematic mode. However, the presence of a fairly regular cardiac rhythm is essential.4,5

1.3 Data Analysis and Display

Several types of analyses can be applied to digitized images and a variety of calculations on the pixels in a “region of interest” can be performed, including the area, the total count, maximal and minimal counts, and the average counts per pixel.

With the development of computers, these devices have gained an integral role not only for image acquisition and processing but also for image management.

2. MPS Radiopharmaceuticals

Characteristics of the ideal radiopharmaceutical for MPS are summarized in Table 4.1. Currently available photon emission tracers used for MPS are divided into two groups: thallium-201 (201Tl) and technetium-99m (99mTc) labeled agents.

2.1 Thallium-201

Thallium is a metallic element in group III-A of the periodic table of elements. The isotope 201 of thallium is generated in cyclotron. 201Tl has a physical half-life of 73 hours and a main radioactive energy of emission of 69–83 keV (88% abundance). It is administered in the form of thallous chloride. The initial myocardial uptake of 201Tl after IV administration depends on both MBF and the myocardial extraction fraction for 201Tl.6–8 Under conditions of normal flow, approximately 85% of 201Tl is removed by myocardium in a single pass. Because myocardium receives 5% of the cardiac output, 4% of the total dose is taken up by myocardium (Table 4.2). 201Tl myocardial uptake is proportional to regional perfusion over a wide range of flow rates. However, as flow increases, more of the tracer passes through the capillary without being extracted and will reach a plateau when flow is increased >3.5–4 times the baseline values (Figure 4.1).9 Therefore, the uptake of 201Tl at high flow rates underestimates the true

Table 4.1. Characteristics of the ideal radiopharmaceutical for MPS

<table>
<thead>
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<th>Characteristic</th>
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<tr>
<td>Myocardial uptake in proportion to blood flow over the range of values experienced in health and disease</td>
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<td>Efficient myocardial extraction from the blood on the first passage through the heart</td>
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<td>Stable retention within the myocardium during image acquisition</td>
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<td>High photon flux at an energy between 100 and 200 keV and short half-life</td>
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<td>Rapid elimination allowing repeat studies under different conditions</td>
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<td>Ready availability</td>
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<td>Low cost</td>
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myocardial flow. Additionally, at very low flow rates, the $^{201}\text{Tl}$ extraction fraction efficiency increases in viable cardiomyocytes because $^{201}\text{Tl}$ spends more time in contact with the capillary membrane, resulting in higher extraction. More than 60% of myocardial $^{201}\text{Tl}$ uptake occurs via the $\text{Na}^+\text{,K}^+\text{–adenosine triphosphatase}$ active transport membrane pump, thus it cannot be removed by nonviable cardiomyocytes.$^2$($^10$)

Maximum myocardial $^{201}\text{Tl}$ uptake occurs at 10–20 minutes after IV injection, which correlates with rapid clearance of the tracer from the blood pool. The half-life of elimination from myocardium is approximately 7 hours. $^{201}\text{Tl}$ is principally excreted by the renal system, having a biological half-life of approximately 10 days.

There is a dynamic changing (redistribution) between the intracellular and intravascular content of $^{201}\text{Tl}$ along time. MPS performed early after injection reflects the MBF conditions at the time of $^{201}\text{Tl}$ administration. However, after the initial cellular extraction phase, $^{201}\text{Tl}$ continually exchanges between both compartments to meet the equilibrium. Thus, images obtained several hours after remaining at rest reflect resting MBF conditions. Redistribution results from combined effects of differential myocardial $^{201}\text{Tl}$ washout, which is proportional to the rate of MBF, and late $^{201}\text{Tl}$ uptake in hypoperfused but still viable myocardium.$^2$($^10$) Once the exercise test has been completed, image acquisition should commence within 5–10 minutes of injection, as soon as the patient’s heart rate has returned to near baseline values. This prevents motion artifacts caused by the shifting position of the heart during the period of image acquisition secondary to the different amplitude of diaphragmatic excursion while recovering from the exertion (“upward creep” phenomena) and at the same time.
time minimizes $^{201}$Tl redistribution. This short delay also maximizes the ability to detect transient left ventricular dysfunction.

The major limitation of MPS with $^{201}$Tl is the absence of an ideal photopeak of energy emission, which results in poor-quality images in obese patients and problems in distinguishing attenuation artifacts from defects caused by underlying CAD. Moreover, imaging must be performed very close to the stress testing because of redistribution, which also precludes repetition of image acquisition when artifacts appear.\(^\text{10}\)

### 2.2 $^{99m}$Tc-Technetium-labeled Agents

$^{99m}$Tc has become the most frequently used radionuclide for clinical imaging because of its availability, the energy characteristics (140 keV) of its principal emission, and its favorable dosimetry that is related to its short half life. $^{99m}$Tc is obtained from $^{99m}$molybdenum ($^{99m}$Mo)/$^{99m}$Tc generator systems, which consist of a longer-lived radionuclide parent ($^{99m}$Mo, physical half-life of 66 hours), practical for the commercial shipment, and a shorter-lived radionuclide daughter ($^{99m}$Tc, physical half-life of 6 hours), useful for clinical applications. $^{99m}$Mo, produced by the fission reaction of $^{235}$Uranium, is chemically purified and passed on to an anion exchange column of alumina, which binds the $^{99m}$Mo ions. The column is placed in a lead container with tubing attached at each end. Elution of the column with normal saline solution through a vacuum system provides $^{99m}$Tc-pertechnetate. The amount of $^{99m}$Tc available from a generator decreases each day as a result of decay of the $^{99m}$Mo parent. However, the long physical half-life of $^{99m}$Mo permits the same generator to be used for at least 1 week.

The short physical half-life of $^{99m}$Tc allows the administration of 10-fold-larger doses of $^{99m}$Tc-radiopharmaceuticals than of $^{201}$Tl. Moreover, because of the energy of the gamma rays given off by $^{99m}$Tc, its photons experience less scatter and attenuation than photons emitted by $^{201}$Tl, which results in superior image quality. Commercially available $^{99m}$Tc agents for MPS include sestamibi (hexakis 2-methoxyisobutyl isonitrile) and tetrofosmin (1,2-bis[bis(2-ethoxyethyl) phosphino]ethane). $^{99m}$Tc-sestamibi is a monovalent cation in which $^{99m}$Tc is surrounded by six isonitrile ligands. $^{99m}$Tc-tetrofosmin is a diphosphine. Both are prepared from a kit, but only the former requires boiling for labeling. Both agents are lipophilic cations that passively diffuse into cardiomyocytes along an electropotential gradient and are actively trapped in mitochondrias. Myocardial fixing after injection depends on both MBF and mitochondrial retention. Myocardial extraction fraction is approximately 30% in a single pass under conditions of normal MBF, lower than that of $^{201}$Tl (Table 4.2).\(^\text{9}\) As with $^{201}$Tl, myocardial uptake experiences a similar roll-off phenomenon, which occurs at lower high rates of MBF, when flow increases >2.5 times the baseline values. Additionally, flow is also overestimated at low flow rates (Figure 4.1).\(^\text{8,9}\) $^{99m}$Tc agents are cleared from the blood rapidly, with hepatobiliary and renal excretion, without being secondarily released back into the blood (minimal or null redistribution). Uptake in myocardium is also rapid, but imaging requires a long delay in order to allow adequate hepatobiliary clearance of the tracer. The required imaging time after $^{99m}$Tc-tetrofosmin and $^{99m}$Tc-sestamibi injection is $\geq 10$–$15$ minutes for exercise studies, $\geq 30$–$45$ minutes for rest studies, and 45–60 minutes for pharmacologic stress studies. Because there is minimal redistribution, images can be obtained several hours after tracer injection depending on the laboratory logistics. Likewise, image acquisition can be repeated with no repercussion on image quality when artifacts are considered to be responsible for the production of a perfusion defect. The absence of redistribution, however, requires injection of tracer twice, once during stress and once at rest.\(^\text{10,11}\)

### 3. Image Acquisition

Planar and tomographic imaging can be performed. Comparative studies between both methodologies showed substantially higher sensitivity with tomography for the detection of CAD. Nevertheless, the prognostic power of a normal planar scintigraphy is excellent, suggesting that the coronary lesions missed by this modality may not be prognostically significant.

#### 3.1 Planar Imaging

Planar imaging is a two-dimensional (2D) image representation of the 3D distribution of an
emitting radiation body. This compression of a 3D image into a 2D one containing the radioactivity coming from above and below the organ being imagined (background activity) results in a reduction of contrast, with decreased ability to discriminate between areas of a specific organ with normal and abnormal radioactivity count levels.

Heart anatomy is sufficiently simple to allow planar imaging to assess the location and extent of defects from several projections (or views) without need of computer reconstruction. In fact, planar imaging has good resolution and it can be the solution for patients unable to remain immobile during longer acquisition times, which is essential for single photon emission computed tomography (SPECT) studies, or for those who are very obese. An advantage of planar imaging is that a scan can be quickly repeated if the patient moves during the acquisition.

In planar MPS, it is crucial to reproduce the same position on initial and delayed images. The standard planar views are supine anterior, supine 45° left anterior oblique, and a right side decubitus 90° left lateral. The 90° left lateral view is difficult to reproduce and can be substituted by the supine 70° left anterior oblique position, which frequently is suboptimal because of occurrence of attenuation artifacts.12,13

In ECG gated acquisition, no beat rejection should be used in order to preserve statistical counting, because the multiple frames (usually 16) of the gated images can be summed to produce a single static planar image for conventional visual and quantitative analysis of myocardial perfusion.

Image acquisition begins by setting the energy window size. For 99mTc agents, it is symmetrically centered to 20% of 140 keV, and for 201Tl to 30% of 72 keV and 167 keV. Images should contain >500 000 counts per view, which takes approximately 10 minutes for 201Tl and 5 minutes for 99mTc agents. When ECG gating is used, imaging time increases by approximately 3 minutes.

### 3.2 SPECT Imaging

SPECT is a method that uses photon emission radionuclides for producing image sections of the body displayed as 2D images. It is considered the state-of-the-art for MPS, and it is based on a computer collection of multiple planar images obtained by the rotating scintillation detector, 180° or 360° around an underlying radiation emitting body. Transaxial, sagittal, and coronal slices are generated by computer from the 3D distribution of the tracer in the body, thus removing overlying structures that may obscure an abnormality, improving image contrast.14 The resolution in SPECT is determined by the same mechanisms as in planar images: the collimator, the photon energy, the distance from the source to the detector, and the duration of the acquisition.

Usually, SPECT is performed with the patient lying in the supine position with elevation of the left arm above the head. Prone imaging can be added when doubts arise about possible diaphragmatic and/or breast/lateral chest-wall fat attenuation (Table 4.3).

Energy window setting is the same as that used in planar imaging. On systems with improved energy resolution, window size could be reduced, resulting in decreased scatter and improved image resolution, but increasing imaging times. 201Tl SPECT uses low-energy parallel hole collimators of high sensitivity (all-purpose collimators, LEAP), whereas 99mTc agents SPECT use low-energy parallel hole collimators of high resolution (LEHR). LEHR collimators have longer bores, thinner septa, and smaller holes, as compared with LEAP collimators, which provide better resolution at the expense of reduced sensitivity.

Matrices of $64 \times 64$ pixels, with pixel size of 6.4 ± 0.2 mm, offer sufficient contrast and resolution for cardiac SPECT imaging. An orbit of 180° (from the 45° right anterior oblique to the 45° left posterior oblique) yields better contrast and spatial resolution and less attenuation than an orbit of 360°, because of avoiding the noise coming from the posterior projections in which the heart is fairly distant to the detector. Orbits of 360° yields better field uniformity, and for multiple detector systems, may generate similar image quality as 180° once scatter, attenuation, and variable resolution effects are corrected. Circular orbits have been widely used, although maintenance of a fixed radius of rotation results in the detector not being close to the patient, with worse spatial resolution. Recently, non-circular orbits have proliferated in conjunction with attenuation correction algorithms. Patient-contoured orbits bring the detector closer to the heart, improving spatial resolution. However, the potential of artifact production at reconstruction exists because of higher variation in spatial
resolution resulting from the increased variation of source-to-detector distance.\textsuperscript{12,14,15} Often, the detector acquires photons throughout the orbit at preselected angles while motionless for a predetermined time, after which the detector moves to the next angular position, in a tomographic acquisition mode called “step-and-shoot.” No counts are recorded as the detector moves. This process is repeated until the total number of preselected views is acquired. The optimal number of views depends on matching the number of projections to the resolution of the system. For $^{201}$TI SPECT studies, which are acquired using LEAP collimators and thus having relatively low resolution, 30 projections over an orbit of 180° are sufficient. For higher-resolution studies, such as those with $^{99m}$Tc agents, acquired using LEHR collimators, $\geq$60 projections over an orbit of 180° are required to prevent loss of resolution.\textsuperscript{2,12,13,16} Double number of projections is necessary when imaging throughout 360° orbits. Less widespread mode is “continuous” acquisition, for which the detector moves continuously while collecting photons, which allows increase of the number of collected counts for the same whole acquisition time. However, there is some spatial resolution loss associated with this “continuous” acquisition. A third mode is “continuous step-and-shoot” acquisition, for which the detector does not interrupt the collection of photons during its movement from one angle to the next in the step-and-shoot mode. This yields in increased counting statistics compared with the standard step-and-shoot mode while reducing most of the blurring associated with continuous acquisition.\textsuperscript{12}

The total time for acquisition is based on the need to collect sufficient counts, but should not

<table>
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<tr>
<th>Image variants and artifacts</th>
<th>Presumed explanation</th>
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<tbody>
<tr>
<td>1. Apical defect</td>
<td>Physiologic “apical thinning” (exaggerated by attenuation correction and elliptical orbits)</td>
</tr>
<tr>
<td>2. Basal septal defect</td>
<td>Physiologic membranous tissue in atrioventricular valve plane</td>
</tr>
<tr>
<td>3. Fixed/reversible anterior and/or lateral defect</td>
<td>Attenuation by the left breast/lateral chest wall fat</td>
</tr>
<tr>
<td>4. Fixed inferior or inferolateral defect</td>
<td>Attenuation by the left hemidiaphragm (mainly in men)</td>
</tr>
<tr>
<td>5. Diffusely reduced myocardial uptake</td>
<td>Normalization to noncardiac maximal activity</td>
</tr>
<tr>
<td>6. Fixed/reversible defects confined to the septum</td>
<td>LB8B causes asynchronous relaxation of the septum, resulting in shortened diastolic myocardial perfusion period in this region</td>
</tr>
<tr>
<td>7. Fixed basal inferolateral defect</td>
<td>Depth-dependent attenuation in obese patients</td>
</tr>
<tr>
<td>8. Anterosetal and inferoseptal linear defects</td>
<td>Attenuation at the insertion points of the free wall of the RV (“11 and 7 o’clock defects”). The 11 o’clock defect is usually more marked in circular acquisition orbits of 180°</td>
</tr>
<tr>
<td>9. Opposed defects in contralateral walls</td>
<td>Flood field nonuniformity</td>
</tr>
<tr>
<td>10. Basal defects and apical hot spot</td>
<td>Truncation</td>
</tr>
<tr>
<td>11. Anterior defect and normal/increased inferior uptake</td>
<td>Scatter from subdiaphragmatic tracer accumulation artifactually increases inferior wall count density, which is erroneously taken as the reference region for image normalization (exaggerated by attenuation correction)</td>
</tr>
<tr>
<td>12. Inferior defect and increased anterior uptake</td>
<td>Intense subdiaphragmatic activity adjacent to the inferior wall, which is removed together with count density of the inferior wall when ramp-filtering</td>
</tr>
<tr>
<td>13. Loss of detail and contrast resolution</td>
<td>Increased detector-to-patient distance</td>
</tr>
<tr>
<td>14. Excessive noise</td>
<td>Decreased critical frequency of processing filter</td>
</tr>
<tr>
<td>15. Decrease in the lateral-to-septal wall tracer activity</td>
<td>LV hypertrophy</td>
</tr>
<tr>
<td>16. Hot spots in the anterolateral and inferolateral walls</td>
<td>Hypertension with hypertrophy of papillary muscles</td>
</tr>
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LV, left ventricle; LB8B, left bundle branch block; RV, right ventricle.
surpass 30 minutes, which is readily accomplished with dual-headed systems for the usual administered doses. A dual-headed system has the detectors separated by 90°, completing a 180° orbit by rotating through 90° angle, in half time compared with single-detector systems.

Images may be recorded with attenuation correction, using either an X-ray or radionuclide source for the acquisition of a transmission scan that is used to generate a reference map of the attenuation factors for the patient. Transmission images can be obtained sequentially or simultaneously to emission images.

ECG gating acquisition is frequently applied in clinical practice. Usually, data are collected in 8 or 16 time bins per cardiac cycle.4,5

After data acquisition, collected planar views should be reviewed in cinematic mode to identify possible source of artifacts (Table 4.3), such as breast shadow caused by attenuation, photopenic area in the fundus of the stomach caused by diaphragmatic attenuation, superimposed abdominal visceral activity, “upward creep,” and patient motion, giving attention to even small variations in arm position as possible origin of shifting breast shadow artifacts. For gated studies, a full display of all time bins for each projection is required to detect gating errors, although, when the assessment is performed in the sum of all gated tomograms, most types of gating errors will become apparent as a “flashing” of image counts.

4. Image Processing

Planar MPS does not generally need any image reconstruction, but there are different quantitative programs available to quantify regional myocardial perfusion to provide a more objective means of analysis. In fact, all quantitative attempts in single photon emission imaging, either planar or SPECT, are semiquantitative, because they determine relative rather than absolute perfusion in each region of the myocardium. Hence, to determine if an individual patient’s MPS is normal or abnormal, the patient’s data must be compared with that of normal population.

Quantitative programs in planar MPS apply a background subtraction, which is essential in this type of image because the relative tissue distribution of the tracer at rest and after exercise may be markedly different. The software also aligns initial and delayed images, and generates a graphic displaying regional myocardial activity, generally involving a circumferential count distribution profile. This method provides a single-curve display of counts sampled around the myocardial perimeter. When compared with a normal database from “normal” subjects or normalized to each other, these profiles allow detection of the severity and extent of perfusion abnormality, and the degree of reversibility.17

SPECT imaging is based on the reconstruction of tomographic images from projection images. Until recently, this reconstruction has been performed by filtered backprojection. Each source of radioactivity creates spikes in the count activity profiles seen by the detector as it rotates around the patient. The counts in each profile are assumed to correspond to uniformly distributed activity perpendicular to the profile. Therefore, linear superimposition of the profiles at each projection angle back across the reconstruction matrix results in the tomographic image, but with loss of resolution and contrast as well as generation of a star artifact. Filtered backprojection solves these drawbacks of standard backprojection by filtering each profile before it is backprojected.14,18 Currently, improvements in computer power have made possible other reconstruction approaches based on algebraic techniques that also use the projection images as input to find the mathematic solution to the problem of activity distribution in the field of view. Because the exact solution to this problem is not possible when matrix dimensions are not very small, an approximated iterative method is used instead. In iterative reconstruction, the value of all pixels is initially guessed using filtered backprojection, then successive slight transformations (iterations) of those initial values result in a tomogram consistent with the available count profiles. The iterative reconstruction makes it possible to integrate correction for many physical effects such as attenuation, scatter, variation of spatial resolution as function of depth, etc.14,19,20

Whether the reconstruction method is filtered backprojection or iterative, smoothing or low-pass filters are always applied to projection images before reconstruction so as to reduce statistical noise early in the processing chain. In filtered backprojection, a high-pass filter (ramp-filter) is subsequently applied to minimize the star artifact.
Tomographic reconstruction of projection images generates transaxial images, i.e., images perpendicular to the long axis of the patient. Because the orientation of the heart relative to the patient's long axis varies from patient to patient, the reconstruction process is followed by reorientation of transaxial data into the long axis of the individual patient's heart, which extends from the center of the mitral valve plane to the apex. The transaxial image data set is then resampled to generate a vertical long-axis image, on which the same operation is repeated. Then the left ventricle (LV) is successively cut through these long-axis planes, generating vertical long-axis slices (extending from the septum to the lateral wall) and horizontal long-axis slices (extending from the inferior wall to the anterior wall). Finally, sections perpendicular to both long-axis planes generate short-axis slices (extending from the apex to the base). Therefore, each plane of section is oriented at 90° angles relative to each other (Figure 4.2). Reorientation should be comparable at rest and stress studies.

Stress and rest tomographic series should be displayed normalized at peak count density within the myocardium for each set, side-by-side, appropriately aligned, and using the same color continuous scale for ready comparison of corresponding tomograms.

SPECT semiquantification of regional perfusion is achieved by commercial software programs which usually provide an average of tracer uptake throughout myocardial walls. Values obtained are normalized to the highest myocardial counts. By assuming that this maximum represents the “most normal” perfusion zone, the relative reduction of activity can be used to demarcate perfusion abnormalities. Results are displayed in a 2D circular plot referred to as a polar map or bull's eye (Figures 4.2 and 4.3; see color section). Separate databases have been used for male and female patients, but with the advent of different data sampling approaches and attenuation corrections, new normal databases are being tested.²¹

If images have been acquired by ECG gating, the individual frames of the study can be summed to create a composite data set similar to that of a nongated study, with important regional and global LV function information added, such as regional wall motion and thickening, end-diastolic (ED) and end-systolic (ES) volumes and LV ejection fraction (LVEF). Functional assessment can be both qualitative and quantitative. It is based on the changes in cavity dimensions and in count density between ED and ES frames. There are several types of well-validated and reproducible commercial software for these purposes, which have showed good agreement with other imaging techniques for the assessment of LVEF as well as for the assessment of wall motion and thickening. LV volume measurements have been less widely validated and may vary with the tracer used (²⁰¹TI or ⁹⁹ᵐTc agents), and reconstruction methods (filter characteristics).²¹ Potential sources of error in gated SPECT LVEF calculations are listed in Table 4.4. Global and regional LV function quantification are calculated separately using different methods based either on the detection of endocardial and epicardial edges and making geometric assumptions to estimate LV volumes, or based on peak counts measured at ED and ES to estimate thickening fractions, avoiding edge detection. Newer programs are usually a hybrid of both methods.⁴³

5. Image Interpretation

Computer screen image assessment of the three tomographic planes is recommended to interpret correctly SPECT imaging. It permits use of cinematic displays and adjustment of the contrast, brightness, and color scales optimized to the myocardium. Initial review of the images should be performed without reference to clinical information in order to decide on major features, and then to modify the impression and decide on minor features if necessary, after review of the clinical information.

MPS may show different appearances of normally perfused myocardium on account of scatter, attenuation, and the nonuniform thickness of myocardial walls. Therefore, qualitative interpretation of MPS requires expertise for the correct evaluation of myocardial tracer distribution, including recognition of normal variants and artifacts (Table 4.3) as well as correlation of abnormalities with the known vascular territories of the three major coronary arteries. Moreover, interpretation of MPS should involve the pretest probability of CAD apart from the result of the test itself. Homogeneous LV myocardial tracer uptake indicates normally perfused and viable myocardium. The LV looks like a horseshoe on long-axis SPECT slices and on planar views (the latter may also have an ellipsoidal appearance), and it has a doughnut appearance.
on short-axis SPECT slices. The SPECT tomo-
grams and polar map appearance are best explained by referring to Figure 4.2, which also shows the recommended nomenclature of the 17 LV segments with their coronary artery territory assignment. In short-axis SPECT slices, the most intense activity is usually seen in the lateral wall, because it is the region closest to the detector (Figure 4.3; see color section). The right ventricle (RV) may not be seen, especially on resting
be present in two or more consecutive slices and two or more axes to be considered significant. The standard variables extracted from MPS are the extent (amount of segments), severity (intensity), and reversibility of defects of tracer uptake. Each of these variables has proven diagnostic and prognostic value. Different polar maps may be strikingly visible in cases of RV hypertrophy. Mild lung uptake may be seen, but when it is increased, one should consider the presence of severe CAD and/or LV dysfunction or underlying lung disease. Liver and/or bowel tracer activity may obscure LV inferior wall.

Because blood flow is diverted from the splanchnic bed to exercising muscles during dynamic exercise, exercise stress images usually show better heart to background signal than rest images and especially than pharmacologic stress images, which increases splanchnic blood flow. A defect of myocardial tracer uptake in the stress images that shows an improvement or normalization of the uptake in the rest images (a reversible defect) indicates inducible myocardial ischemia. A defect of myocardial tracer uptake in both stress and rest images (a fixed defect) indicates MI. On SPECT studies, defects must be present in two or more consecutive slices and two or more axes to be considered significant. The standard variables extracted from MPS are the extent (amount of segments), severity (intensity), and reversibility of defects of tracer uptake. Each of these variables has proven diagnostic and prognostic value. Different polar maps may be strikingly visible in cases of RV hypertrophy. Mild lung uptake may be seen, but when it is increased, one should consider the presence of severe CAD and/or LV dysfunction or underlying lung disease. Liver and/or bowel tracer activity may obscure LV inferior wall.

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showing relative counts as well as defect extent, severity, and reversibility may help visual assessment. Polar maps display the LV in a circular plot of successive annular rings, where myocardium extends from apex in the center to base in the outer ring (Figure 4.2). These plots are advantageous because they display all ventricular activity on a single image. However, they generate a mapping distortion similar to that produced by a polar projection map of the earth, which hampers visual estimation of defect extent. To solve this, polar maps can be scaled accordingly either to the distance from apex to base (distance weighted) or to the different thickness of the myocardium at each level from apex to base (volume weighted). Distance-weighted and volume-weighted polar maps can yield accurate defect location and extent, respectively. It is also possible to display 3D representations of perfusion maps, which provide a visual appreciation of the magnitude and orientation of areas of myocardial scar or ischemia specific to the actual shape of each patient’s LV (Figure 4.4; see color section).12,15

Other variables that can be derived from MPS are washout (clearance) of ²⁰¹TI from the myocardium, which is related to local myocardial perfusion, and LV cavity dilatation at stress in comparison with rest, or transient ischemic dilatation, which reflects diffuse subendocardial ischemia and indicates severe and extensive CAD.25

Although attenuation correction algorithms are very attractive, they sometimes result in artifacts, which forces review of both uncorrected and corrected data to minimize the likelihood of misinterpretation.26

Functional gated planar imaging should be evaluated qualitatively because images include background activity, which impedes clear differentiation between the apparent and real endocardial edge to get precise measures of regional or global wall motion. Gated SPECT data are usually summarized with a moving five-slice display (apical, mid-ventricular, and basal short axis, along with mid-ventricular vertical and horizontal long-axis tomograms). It is important to display the computer-generated contours to

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Figure 4.4. Different angle views, under stress and rest conditions, of three-dimensional left ventricle perfusion display corresponding to a woman with severe and extensive ischemia in the LAD territory. There is a reversible defect in the apex and mid apical anterior wall.
ensure that automatic edge detection has been correctly defined. Paper copies display an ED and ES set of images, scaled on the same intensity. Polar plots of wall motion and thickening, LV volume curve, and results of different computations are also available. Most new systems include moving 3D displays of surface-shaded representations of “beating” endocardial and epicardial surfaces, with or without a superimposed grid of the ED reference surface, which are useful for the assessment of different ventricular wall displacements during the cardiac cycle as well as for the assessment of ventricular shape (Figure 4.5; see color section). LV wall motion is best assessed in continuous gray scale, whereas wall thickening is best analyzed in continuous color scale. This latter evaluation offers better insight in the survey of functionality in areas of reduced tracer uptake, because it clearly manifests by striking increase in image brightness (Figure 4.5; see color section). Assessment of regional LV function improves the specificity of MPS for the detection of CAD by differentiating attenuation artifacts from MI, and may also be helpful for viability detection within perfusion defects. Moreover, the evaluation of tracer distribution in the ED frame may also improve the sensitivity of the test, particularly in patients with LV hypertrophy by reducing the blurring effect of wall motion during heart contraction. In addition, recent reports indicate that the detection of poststress stunning by gated SPECT acquired 15–30 minutes after stress increases the sensitivity of MPS for the detection of CAD (Figure 4.5; see color section).

6. Exercise and Pharmacologic Modalities Used in Stress MPS

Indications of MPS include the diagnosis of patients with an intermediate likelihood of CAD and/or risk stratification of patients with an intermediate or high likelihood of CAD, with different levels of supporting evidence (Table 4.5).
Different stress testing modalities of MPS yield comparable diagnostic value, but exercise provides additional prognostic information based on physical capacity and exercise-induced arrhythmias.

7. Exercise Stress

The preferred stress test in patients who can exercise to an adequate workload and do not have a left bundle branch block (LBBB) or elec-
tronically paced ventricular rhythm is dynamic exercise. Otherwise, pharmacologic stress should be performed. Adequate exercise is most important if the aim of the study is to detect CAD. Exercise increases myocardial oxygen demand, which, by autoregulation, increases MBF (approximately 2.5-fold above the resting condition) in normal coronary arteries, but not in arteries with fixed coronary stenoses, which can be depicted with perfusion tracers. In patients with mild and moderate CAD, MBF may become abnormal only at high heart rates [≥85% of age maximal predicted heart rate (MPHR), which is calculated as 220 – years of age] or at high double products (≥25,000). At lower heart rates, MBF may be normal and perfusion images will be correspondingly normal. In patients with known CAD who are being evaluated for extent and severity of inducible myocardial ischemia, submaximal exercise can provide clinically relevant information.

8. Pharmacological Stress

Pharmacological stress is the preferred stress modality in patients who cannot achieve an adequate heart rate and blood pressure response to exercise because of mental or physical limitations (pulmonary, peripheral vascular, or musculoskeletal abnormalities) or lack of motivation. It has the advantages of speed, reliability, and reproducibility, but the disadvantages that it is difficult to assess the adequacy of stress and it is not equivalent to the physiologic stress of everyday life.

8.1 Adenosine

Adenosine is a natural endogenous molecule normally produced in myocardial vascular smooth muscle and endothelial cells. It is shortly present in the extracellular space, yet it has an extremely short half-life (<10 seconds) where it may bind to A2A membrane cell adenosine receptors producing direct arteriolar vasodilator. In normal coronary arteries, there is an increase in MBF of approximately 4.5 fold compared to baseline, but it is of lesser magnitude through stenotic arteries, creating a flow differential and inhomogeneous distribution of perfusion tracers. However, depending on the severity of coronary stenosis and coronary flow reserve limitation, true ischemia can occur because of a coronary steal phenomenon, principally in collateral flow-dependent arteries.

In addition to the common indications of pharmacologic stress testing, vasodilator stressors such as adenosine and dipyridamole are also indicated in patients with LBBB or paced ventricular rhythm and patients with very recent AMI (<3 days) or recent (<2 weeks) angioplasty/stenting.

Adenosine should be administered through an IV line with dual-port Y-connector using an infusion pump at a rate of 140 μg/kg/min over 4–5 or 6 (standard protocol) minutes. Mild increase in heart rate and modest decrease in blood pressure result from adenosine infusion. The injection of the tracer (through the Y-connector) should be performed after 2 minutes (with 4- to 5-minute infusion protocol) or after 3 minutes (with 6-minute protocol) of the beginning of the infusion, which should be continued for another 3 minutes. The infusion may start at a lower dose (70 μg/kg/min) for patients considered to be at a higher risk for complications (recent ischemic event, borderline hypotension, inadequately controlled asthma). If this dose is well tolerated for 1 minute, the infusion rate should be increased gradually to
140 µg/kg/min and continued for 4 minutes. The tracer should be injected 1 minute after starting the 140 µg/kg/min dose.12

Table 4.7 summarizes side effects attributable to different pharmacologic stressors. Those associated with adenosine usually resolve in a few seconds after discontinuation of the infusion, and only rarely is the administration of the antagonist drug (aminophylline 75–250 mg IV) required. Supplementation of adenosine infusion with low-level exercise minimizes the side effects of adenosine and improves the image quality by decreasing the artifacts caused by high hepatic tracer uptake, which is common with pharmacologic stress.37–39 However, the low-level exercise supplementation should not be used in patients with LBBB, because, in this abnormality, it is desirable not to increase the heart rate.2,12,13,16 First clinical trials with selective A2A receptor agonists are promising, resulting in images of similar quality to those obtained with adenosine, but allowing a bolus administration

| Table 4.6. Contraindications of stress testing and indications for early test termination |
|----------------------------------------------------|------------------------|------------------------|
| Absolutely contraindications | Relative contraindications | Indications for early termination |
| Dynamic exercise | 1. AMI within 2 d | 1. Severe angina |
| | 2. Uncontrolled unstable angina | 2. Ataxia, dizziness, near-syncope, marked dyspnea, or fatigue |
| | 3. Uncontrolled cardiac arrhythmias with symptoms or hemodynamic compromise | 3. Signs of poor perfusion (cyanosis or pallor) |
| | 4. Uncontrolled heart failure | 4. ST elevation of ≥1 mm in leads without pathologic Q waves |
| | 5. Symptomatic severe aortic stenosis | 5. Horizontal or downsloping ST depression (>2 mm) |
| | 6. Acute pulmonary embolus/infarction | 6. Decrease in systolic blood pressure of ≥10 mm Hg from baseline |
| | 7. Acute myocarditis/pericarditis | 7. Sustained supraventricular tachycardia |
| | 8. Acute aortic dissection | 8. Hypertensive response (≥250 systolic or 115 mm Hg diastolic) |
| | 9. Severe pulmonary hypertension | 9. Impossibility of ECG or blood pressure control |
| Adenosine | 1. Asthma with ongoing wheezing | 1. Severe sinus bradycardia (<40 bpm) |
| | 2. Heart block >first degree without a pacemaker | 2. Recent cerebral ischemia or infarction |
| | 3. Sick sinus syndrome | 3. Development of symptomatic persistent second-degree or complete heart block |
| | 4. Systolic blood pressure >90 mm Hg | 4. Wheezing |
| | 5. Hypersensitivity to dipyridamole or adenosine | 5. Development of symptomatic persistent second-degree or complete heart block |
| | 6. Use of dipyridamole >24 h | 5. Sustained supraventricular tachycardia |
| | 7. Use of xanthines (e.g., aminophylline, caffeine) <12 h | 6. Decrease in systolic blood pressure of ≥10 mm Hg from baseline |
| | | 7. Hypersensitivity to dipyridamole or adenosine |
| | | 8. Use of xanthines (e.g., aminophylline, caffeine) <12 h |
| Dipyridamole | As for adenosine | As for adenosine |
| Dobutamine | As for adenosine | As for adenosine |
| | 1. AMI <1 wk | As for dynamic exercise, Hypokalemia |
| | 2. Unstable angina | As for dynamic exercise, Hypokalemia |
| | 3. Hemodynamically significant LV outflow tract obstruction | Termination for ventricular tachycardia or ST segment elevation is more likely with dobutamine than with other pharmacologic stressors. |
| | 4. Critical aortic stenosis | Termination for ventricular tachycardia or ST segment elevation is more likely with dobutamine than with other pharmacologic stressors. |
| | 5. Atrial tachyarrhythmias with uncontrolled ventricular response | 5. Atrial tachyarrhythmias with uncontrolled ventricular response |
| | 7. Uncontrolled hypertension | 7. Uncontrolled hypertension |
| | 8. Aortic dissection or large aortic aneurysm | 8. Aortic dissection or large aortic aneurysm |
| | 9. β-Blockers treatment (block heart rate response) | 9. β-Blockers treatment (block heart rate response) |

AMI, acute myocardial infarction; AV, atrioventricular.
and having less incidence and severity of side effects.\textsuperscript{40,41}

### 8.2 Dipyridamole

Dipyridamole produces coronary arteriolar vasodilation increasing adenosine tissue levels by preventing its intracellular reuptake and deamination. The increment in coronary flow produced by dipyridamole does not differ significantly from that produced by adenosine. However, coronary hyperemia induced with dipyridamole is somewhat less predictable and lasts longer (>15 minutes) than that induced by adenosine due to the longer half-life (30 minutes) of dipyridamole.\textsuperscript{2,12,13,16,33} Both drugs have similar indications and contraindications (Table 4.6).

Dipyridamole is administered manually as a continuous infusion at a rate of 0.56 mg/kg IV over 4 minutes. This results in a modest increase in heart rate and a modest decrease in blood pressure. The tracer is injected 3–4 minutes after the completion of dipyridamole infusion, which obviates the need for a Y-connector.

Side effects with dipyridamole (Table 4.7) are less frequent than with adenosine, but more prolonged.\textsuperscript{33,42} They can be readily reversed with aminophylline (75–250 mg IV), although can reappear later because the half-life of dipyridamole is longer. Supplementation of dipyridamole infusion with low-level exercise for 4–6 minutes soon after the end of dipyridamole infusion, injecting the tracer during the performance of exercise, reduces the side effects of the vasodilator and improves image quality.\textsuperscript{43} As with adenosine, low-level exercise supplementation is not recommended for patients with LBBB.

### 8.3 Dobutamine

Dobutamine is a $\beta_1$-, $\beta_2$-, and $\alpha_1$-adrenergic agonist with positive inotropic and chronotropic effects, which increases myocardial oxygen demand secondarily to dose-related increase in myocardial contractility, heart rate, and blood pressure. High doses of dobutamine result in a secondary increase in MBF only within normal vascular beds (approximately three-fold increase), with the potential to provoke ischemia in vascular beds supplied by significantly stenosed arteries.\textsuperscript{2,33}

Dobutamine stress testing is indicated in patients who cannot undergo exercise stress and have contraindications to pharmacologic vasodilator stress. It has not been studied as extensively as adenosine or dipyridamole in the evaluation and prognostication of patients with CAD.

Gradually increasing doses of dobutamine are administered through an IV line with a dual-port Y-connector using an infusion pump, starting at 5 $\mu$g/kg/min and followed by 10, 15, 20, 30, and 40 $\mu$g/kg/min, every 3–5 minutes. The tracer should be injected at $\geq$85% MPHR or at 1 minute into the dose of 40 $\mu$g/kg/min, continuing the infusion $\geq$1 minute. Atropine administration (0.25–1 mg IV) may be required to increase the heart rate response >120 beats/min with the maximum dose of dobutamine. Severe side effects (Table 4.7) may require IV administration of a short-acting $\beta$-blocker (Esmolol).

### 9. Currently Used Protocols

Protocols for MPS vary with regard to the radiopharmaceutical administrated, the type of stress performed (if any), and the clinical indication of the test.\textsuperscript{44} The latter can include the diagnosis or prognosis of myocardial ischemia, the assessment of patients with suspected ACS in the

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**Table 4.7. Side effects (%) attributable to different pharmacologic stressors**

<table>
<thead>
<tr>
<th></th>
<th>Adenosine</th>
<th>Dipyridamole</th>
<th>Dobutamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>45\textsuperscript{*}</td>
<td>20</td>
<td>39</td>
</tr>
<tr>
<td>Flushing</td>
<td>35</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>33</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Dizziness</td>
<td>9</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Gastrointestinal discomfort</td>
<td>15</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Headache</td>
<td>30</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Hypotension</td>
<td>2</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>3</td>
<td>5</td>
<td>45</td>
</tr>
<tr>
<td>High-degree AV block</td>
<td>7</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>STE†</td>
<td>6†</td>
<td>8</td>
<td>30</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>0.1</td>
<td>0.15</td>
<td>0</td>
</tr>
<tr>
<td>Fatal AMI/cardiac death</td>
<td>0</td>
<td>0.05</td>
<td>0</td>
</tr>
<tr>
<td>Nonfatal ACS</td>
<td>0.01</td>
<td>0.05</td>
<td>0.3</td>
</tr>
<tr>
<td>Any adverse effect</td>
<td>80</td>
<td>50</td>
<td>75</td>
</tr>
</tbody>
</table>

From References 2, 16, 33, 40.

AMI, acute myocardial infarction; AV, atrioventricular.

\textsuperscript{*} Chest pain is nonspecific and not necessarily indicative of the presence of CAD.

\textsuperscript{†} ST segment depression (1 mm) is indicative of significant CAD.
emergency department, and the identification of myocardial viability.

A fast of ≥4 hours is recommended before MPS. Cardiac medications, if not contraindicated, should be suspended 24 hours before the stress MPS if imaging is performed for diagnostic purposes, especially drugs such as calcium channel blockers and β-blockers that may reduce the heart rate and blood pressure response to exercise and dobutamine stress. Additionally, caffeine and methylxanthine-containing drugs, foods or beverages, should be discontinued 24 hours before both the exercise testing and pharmacologic vasodilator testing. By preparing patients in this manner, if they are not able to achieve an acceptable exercise workload, pharmacologic vasodilator testing can be undertaken. Patients taking dipyridamole should stop the drug for ≥24 hours before pharmacologic vasodilator testing.2,12,13,16 Sublingual nitroglycerine (0.4–0.8 μg) or isosorbide dinitrate (10–20 mg) can be administered 5 minutes before tracer injection for resting studies in order to increase regional MBF and enhance detection of ischemic but still viable myocardium.45,46

During the stress testing, the tracer should be injected at peak of the stress effect. Usual administered activity is 80–111 MBq for studies with 201Tl and 300–925 MBq for studies with 99mTc agents. Tracer doses should be adjusted for heavier patients (0.04 mCi/kg for 201Tl and by 0.31 mCi/kg for 99mTc agents). ECG should be monitored continuously and heart rate and blood pressure recorded at baseline and at the end of each stage of the stress test (or every 2 minutes). Monitoring should continue for ≥5 minutes after the termination of the stress or until patient stabilizes.

The value of giving a fatty meal between tracer injection and imaging to facilitate clearance of tracer from the liver and gall bladder is uncertain. It can result in abundant radioactivity in the upper gastrointestinal tract, which may interfere significantly with the interpretation of the inferior LV wall. Thoracic radiopaque objects should be removed before image acquisition. Registration of the patient body habitus and implanted prostheses in the thorax is also advisable.

The duration of acquisition at each stop (30–40 seconds for dual detector systems) depends on the protocol, type, and activity of radiopharmaceutical administered, patient size, gated or ungated study, and tolerance of the patient to rest without moving under the gamma camera. Total imaging time should be ≤30 minutes. Gated-SPECT acquisitions using 201Tl may require increased imaging times or use of multidetector systems to collect an adequate number of counts. When using 99mTc agents, gated acquisition should be performed in both stress and rest studies, providing that there is adequate count density, particularly with regard to the lower dose acquisitions of 1-day protocols, because there is increasing evidence that post-stress global and regional LV function are not representative of basal LV function in patients with stress-induced ischemia.28

In the reconstruction process of SPECT data, correct filter selection is critical and depends on the specific radioisotope and protocol used. The aim of filtering is to find the optimal balance for smoothing the image while preserving its spatial resolution.47 It is recommended that standardized filters be used for all patients undergoing the same imaging protocol.

9.1 201Tl Stress-redistribution Imaging Protocol

201Tl (111 MBq) is IV administered at peak of stress. Stress imaging should begin within 5–10 minutes of injection and should be completed within 30 minutes to minimize the effects of redistribution, so that images acquired during this period reflect myocardial perfusion at peak stress despite the cessation of exercise. Redistribution imaging is usually performed 4 hours after the exercise images.

9.2 201Tl Rest-redistribution Imaging Protocol

201Tl (111 MBq) is IV administered at rest, beginning image acquisition within 15 minutes. Redistribution imaging is performed ≥3 hours after the initial resting images. Additional delayed imaging at 24 hours after injection may be helpful to establish more completely redistribution in myocardial regions, which appear to have significant tracer uptake but little or no redistribution by 4 hours.

This protocol is generally considered in patients with known LV dysfunction in whom viability of a ventricular segment distal to a severe coronary artery stenosis is the clinical question to be addressed.
allows the higher dose to be given during stress, which provides optimum imaging of stress-induced defects and may improve detection of defect reversibility compared with the alternative stress–rest sequence. However, neither the imaging sequence nor the minimum interval time between the two tracer injections is fully settled. In overweight patients (>90 kg), a low dose of 99mTc agent may result in suboptimal images; therefore, a 2-day imaging protocol is preferable. Because pharmacologic stress perfusion imaging results in higher hepatic and gastrointestinal tracer uptake with slower clearance compared with exercise studies, a rest–stress imaging sequence may offer an advantage.

9.3 201Tl Stress-redistribution-reinjection Protocol

A second dose of 201Tl (37 MBq) is reinjected after redistribution images are complete (the same day of the stress or the day after), and a third set of images is obtained 15 minutes later. This may enhance the amount of uptake in an initially severe defect, which shows no redistribution on delayed imaging. Repeat imaging at 24 hours after reinjection may further enhance the detection of redistribution in severe defects.

9.4 99mTc-agent Two-day Imaging Protocol (Stress–rest or Rest–stress)

99mTc agent (925 MBq) is IV administered at peak of stress. Imaging begins 15 or ≥45 minutes after tracer injection depending on the type of stress performed (exercise or pharmacologic, respectively). The day after stress imaging, the same dose of 99mTc agents is given at rest, beginning imaging ≥45 minutes later. The sequence stress–rest can be inverted to rest–stress. In patients with known CAD or with high likelihood of CAD, both imaging sequences are equally acceptable. In patients with a relatively low likelihood of CAD, it is preferable to start with stress imaging first, and if it is completely normal, rest imaging may be unnecessary.

9.5 99mTc-agent One-day Imaging Protocol (Rest–stress or Stress–rest)

99mTc agent (250–300 MBq) is IV administered at rest, beginning imaging ≥45 minutes after tracer injection. Three hours later (to allow time for hepatobiliary and gastrointestinal clearance of the tracer from previous injection), a further injection of 99mTc agents (750–925 MBq) is administered at peak of stress. Imaging acquisition is performed 15 or ≥45 minutes after tracer injection depending on the type of stress performed (exercise or pharmacologic, respectively).

As with the previous protocol, the sequence rest–stress can be inverted. The three-times-higher dose given for the second test yields an adequate image quality without the need for subtracting the residual activity from the low dose of the first test. The rest–stress sequence

9.6 One-day Dual Tracer Imaging Protocol (201Tl Rest–99mTc-agent Stress)

201Tl (111 MBq) is IV administered for initial rest study, imaging within 15 minutes, and 99mTc agent (925 MBq) is IV administered for stress study, imaging 15 or ≥45 minutes after tracer injection, depending on the type of stress performed (exercise or vasodilator, respectively).

This strategy allows a shorter duration of the entire imaging protocol and takes advantage of the myocardial viability properties of 201Tl and the higher energy quality imaging characteristics of 99mTc agents. If fixed defects are present, additional imaging 24 hours later, centered at 201Tl photopeaks, may be helpful for better detection of defect reversibility secondary to delayed redistribution. However, because of the differences between 201Tl and 99mTc in terms of physical properties, this protocol requires somewhat greater experience for image interpretation. Furthermore, the approach may not be ideal for a patient population with a low likelihood of CAD, who may not require the rest study.

References


35. O’Keefe JH, Bateman TM, BARNHART CS. Adenosine thallium-201 is superior to exercise thallium-201 for detecting coronary artery disease in patients with left


