Guidance and Recommendations for the Implementation of Nuclear Cardiology in Developing Countries
Nuclear cardiology represents one of the most widely used non-invasive techniques for the assessment of coronary artery disease (CAD) and other cardiovascular conditions. It has been proven as a cost-effective tool for the management of cardiac patients, usually having a decisive role for diagnosis, prognosis and risk stratification as well as for evaluation of therapy. Clinical scenarios in which nuclear cardiology can be helpful are continuously expanding, with special subgroups of patients being identified as potential beneficiaries of these methods and emerging technological developments in instrumentation and software which tend to enhance the cost-benefit ratio and the reliability of results.

Many developing countries have introduced nuclear cardiology, with increasing utilization of this technique in view of the epidemics of cardiovascular disease that is taking place in most low-to-middle income countries. Longer life expectancy, changes in lifestyle, diabetes, overweight and obesity are thought to be some of the factors at the base of the rapidly growing incidence of this life-threatening condition. Today, cardiovascular diseases are the most common cause of death in adults in most – if not all – countries of the world, showing only different relative weights according to local socio-economic conditions. Thus, proper utilization of available resources such as nuclear cardiology and others is essential to carry out an effective combatting of these diseases.

The practice of nuclear cardiology, however, is not homogeneous worldwide due to differences in technological capabilities, availability of consumables, education and training of human resources, and access to evidence-based medicine, among other reasons. Evidence-based medicine is the judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research. External clinical evidence is constructed by relevant research, especially patient-centred clinical trials evaluating the accuracy and precision of diagnostic tests, the power of prognostic markers, and the efficacy and safety of therapeutic and preventive measures. External clinical evidence often replaces previously accepted diagnostic algorithms and treatments with new ones that are more accurate, more efficacious, and safer.

With the aim of gathering updated information on the current role of nuclear cardiology in cardiovascular disorders, in particular coronary artery disease, and to prepare a practical guidance for nuclear medicine practice focused on developing countries, the IAEA organized a Technical Meeting on Evidence-based Nuclear Cardiology in Ischemic Heart Disease which took place in Vienna, Austria on February 21–25, 2011. The meeting was attended by experts in the field from different countries, who participated in the discussions and contributed to the drafting of the present document. This document is mainly devoted to myocardial perfusion imaging (MPI) and covers all aspects of this modality, from clinical indications to reporting; it is intended to serve for the implementation, homogenization and enhancement of nuclear cardiology practice in Member States, in which the technique is under development, in order to facilitate its rapid upgrade to currently accepted standards and to provide good quality services to the population.

The IAEA technical officers in charge of this publication were Mr Maurizio Dondi and Ms Diana Paez from the Nuclear Medicine Section, Division of Human Health.
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1. INTRODUCTION

1.1. BACKGROUND

Coronary artery disease (CAD) is the leading cause of death in adults in many parts of the western world and increasingly so in low to middle–income countries. In the USA, it accounts for more than 500,000 deaths each year and predictions for 2030 foresee a toll of more than 23 million deaths worldwide. Early diagnosis and treatment can mean the difference between life and death for many. Over the past 20 years, advancements in the field of Cardiology have made use of nuclear techniques to help with the diagnosis and treatment of heart diseases- one of these being the developments in the field of Nuclear Cardiology, which involves the use of specialized imaging processes and radioactive materials to diagnose the health, and functional ability of the heart. Myocardial Perfusion Imaging (MPI) is by far the most widely used of nuclear cardiology techniques, in a variety of clinical conditions. Clinical scenarios where patients are most likely to benefit from single photon emission computed tomography (SPECT) or positron emission tomography (PET) myocardial perfusion imaging (MPI) are clearly identified in Chapter 2. The list is not exclusive, since based on clinical judgment, others can benefit from MPI as well.

1.2. OBJECTIVE

This document is complementary to a previous publication in the same Human Health Series, ‘Role of Nuclear Cardiology in Cost-effective Care’, in which the role of other non-invasive imaging modalities are also discussed, along with MPI. The current publication is directed mainly at nuclear medicine physicians, cardiologists and cardiac surgeons, but also at all other clinical specialists involved in managing and treating CAD. It is intended to serve for the implementation, homogenization and enhancement of nuclear cardiology practice in those Member States where the technique is under development. The aim is also to help strengthen current nuclear cardiology practices where they already exist, in order to facilitate their upgrade to currently accepted standards to provide better quality services to the population.

1.3. SCOPE & STRUCTURE

The current publication is devoted to myocardial perfusion imaging (MPI), and starting from clinical indications, covers all aspects of this modality including comprehensive instructions on the selection of stress tests and acquisition procedures. The reader is provided with guidelines on interpretation of studies and their reporting as well as several images as examples of clinical cases.*

* All images in this publication are courtesy of Dr. Fernando Mut.
2. INDICATIONS FOR MYOCARDIAL PERFUSION IMAGING

Non-invasive cardiac imaging techniques, and in particular stress myocardial perfusion imaging (MPI), have a central role in the diagnostic workup and risk assessment of patients with known or suspected CAD, lowering the cost of managing these patients [2.1, 2.2].

Symptom evaluation is an important component of the decision making involved in the referral for MPI. For the purpose of this document, an ischemic equivalent is defined as a chest pain syndrome, anginal equivalent, electrocardiogram (ECG) abnormalities consistent with ischemia or reduced activity in daily life.

2.1. EVALUATION OF PATIENTS WITH CHEST PAIN OR ISCHEMIC EQUIVALENT [2.3]

— Those with intermediate (≥20% – <50%) or high (≥50%) likelihood of coronary artery disease (CAD)\(^1\).

— Those with low likelihood of CAD (<20%), with un-interpretable resting ECG or unable to exercise.

— Possible acute coronary syndrome/new or recent onset chest pain.

2.2. CLINICAL SITUATIONS OR SYMPTOMS OTHER THAN ISCHEMIC EQUIVALENT

— Cardiac enzyme elevation in conjunction with chest pain and/or ECG abnormalities.

— Patients with abnormal, equivocal or discordant stress testing by ECG or other imaging modality in which the diagnosis of CAD remains a concern.

— Evaluating coronary stenosis of uncertain significance observed on invasive or non-invasive coronary angiography.

— Evaluation of new onset or newly diagnosed heart failure.

— Evaluation of ventricular tachycardia.

— Syncope in patients with an intermediate (≥10%) or high (≥20%) absolute 10-year risk of a cardiac event based on pre-test CAD risk factors\(^2\).

---

\(^1\) Algorithms are available to estimate the likelihood of CAD, including Table 2.1. from Gibbons et al [2.3] and Table 2.2. from Diamond and Forrester [2.7]. However, as the prevalence and age of onset of CAD varies from country to country, these algorithms are most applicable to the population on which they were based and not to all populations.

\(^2\) Algorithms are available to estimate the absolute 10-year risk of a cardiac event (references for the various score, Framingham, PROCAM etc.). Analogous to the likelihood evaluation described above, differences in the prevalence and age of onset of CAD varies from country to country making these algorithms most applicable to the population on which they were based.
2.3. RISK STRATIFICATION AND PROGNOSIS ASSESSMENT [2.4 – 2.6]

— Chest pain syndrome in a patient with high pre-test likelihood of CAD.
— Following myocardial infarction or acute coronary syndrome.
— Monitoring the effects of treatment of CAD, including revascularization and medical therapy.
— Patients with past abnormal coronary angiography or stress imaging study in whom MPI would be expected to alter clinical management.
— Viability assessment in patients with left ventricular (LV) systolic dysfunction in whom this assessment would be expected to alter clinical management.
— Patients undergoing non-cardiac major surgery and with an intermediate (≥20% – <50%) or high (≥50%) likelihood of CAD¹.

2.4. POSSIBLE INDICATIONS FOR ASYMPTOMATIC PATIENTS

— Patients with an intermediate (≥10%, <20%) or high (≥20%) absolute 10-year risk of a cardiac event based on pre-test CAD risk factors².
— Diabetic patients with evidence of a diabetic complication, prolonged duration of diabetes or an additional CAD risk factor, or female diabetic patients.
— Patients with evidence of extra-cardiac atherosclerotic vascular disease.
— Patients with coronary calcium Agatston score of >400 or >100 in diabetics.
— Chronic kidney disease (GFR<30ml).
— Troponin elevation without evidence of acute coronary syndrome.
— Syncope with intermediate to high pre-test likelihood of CAD.

2.5. DEFINITIONS [2.7]∗

— Pretest likelihood is the probability of disease in a patient to be tested.
— Sensitivity is the probability of a positive test result in a patient with disease.
— Specificity is the probability of a negative test result in a patient without disease.
— Post-test likelihood is the probability of disease in a patient showing a given test result. Post-test likelihood is the probability of disease in a patient showing a given test result. Bayes’ Theorem is used to determine the conditional probability by providing a way to calculate the post-test likelihood as a function of pretest likelihood, sensitivity and specificity of the test being applied [2.7].

The following Tables list pre-test and post-test likelihoods of CAD according to symptoms, age and sex (Table 2.1) and stress ECG results (Table 2.2).

### TABLE 2.1. PRE-TEST LIKELIHOOD OF CAD IN SYMPTOMATIC PATIENTS ACCORDING TO AGE AND SEX (Values represent % of patients found to have significant CAD on catheterization) [2,3].

<table>
<thead>
<tr>
<th>Age</th>
<th>Nonanginal chest pain</th>
<th>Atypical angina</th>
<th>Typical angina</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>4</td>
<td>2</td>
<td>34</td>
</tr>
<tr>
<td>40–49</td>
<td>13</td>
<td>3</td>
<td>51</td>
</tr>
<tr>
<td>50–59</td>
<td>20</td>
<td>7</td>
<td>65</td>
</tr>
<tr>
<td>60–69</td>
<td>27</td>
<td>14</td>
<td>72</td>
</tr>
</tbody>
</table>

*From Gibbons et al., Executive summary and recommendations, 1999, modified.*

### TABLE 2.2. POST-TEST LIKELIHOOD OF CAD ACCORDING TO SYMPTOMS, AGE, SEX, AND STRESS-ECG [2,7].

<table>
<thead>
<tr>
<th>AGE</th>
<th>ASYMPTOMATIC</th>
<th>NONANGINAL CHEST PAIN</th>
<th>ST depression ≥ 2.5</th>
<th>ATYPICAL ANGINA</th>
<th>TYPICAL ANGINA</th>
</tr>
</thead>
<tbody>
<tr>
<td>YR</td>
<td>MEN</td>
<td>WOMEN</td>
<td>MEN</td>
<td>WOMEN</td>
<td>MEN</td>
</tr>
<tr>
<td>30-39</td>
<td>43.0±24.9</td>
<td>10.5±9.9</td>
<td>68.1±22.1</td>
<td>23.9±19.5</td>
<td>91.8±7.7</td>
</tr>
<tr>
<td>40-49</td>
<td>69.4±12.3</td>
<td>28.3±20.8</td>
<td>86.5±11.8</td>
<td>52.9±25.8</td>
<td>97.1±2.8</td>
</tr>
<tr>
<td>50-59</td>
<td>80.7±15.6</td>
<td>56.3±24.9</td>
<td>91.4±7.9</td>
<td>78.1±17.3</td>
<td>98.2±1.7</td>
</tr>
<tr>
<td>60-69</td>
<td>84.5±13.1</td>
<td>76.0±18.4</td>
<td>93.8±5.8</td>
<td>89.9±9.2</td>
<td>98.8±1.2</td>
</tr>
</tbody>
</table>

*From Diamond and Forrester, The New England Journal of Medicine, 1979, modified.*
REFERENCES TO SECTION 2


3. STRESS MODALITIES AND PROTOCOLS FOR MPI

Several stress modalities can be applied in nuclear cardiology, including: Exercise, vasodilators, exercise combined with vasodilators, and dobutamine. In all cases, the purpose of the stress test (from the imaging point of view) is to produce coronary vasodilation, so after the radiotracer is injected, its myocardial distribution will reflect flow heterogeneity if significant coronary stenosis is present [3.1]. It is clear that, for appropriate diagnosis using this modality, true ischemia is not necessarily induced, in contrast to other modalities such as stress echocardiography, where transient abnormal wall motion due to myocardial ischemia is the main factor for detecting CAD [3.2].

3.1. TYPES OF STRESS

3.1.1. Physical exercise

— Exercise is the most physiological test for myocardial ischemia. Due to catecholamine release and sympathetic stimulation, exercise increases determinants of myocardial oxygen consumption: Heart rate, blood pressure (BP) and myocardial contractility.

— Exercise also produces coronary vasodilation through biochemical mechanisms in order to increase blood flow to the myocardium in response to the elevated oxygen demand.

— Hemodynamically significant coronary lesions with potential of causing ischemia are identified on MPI as areas of decreased myocardial tracer uptake [3.3].

— Under normal conditions, myocardial blood flow (MBF) increases approximately 3 fold at peak exercise compared to baseline. The difference between basal and maximum achieved MBF is called ‘coronary reserve’.

3.1.2. Pharmacologic stimulation

— Dipyridamole inhibits the action of an enzyme called adenosine deaminase, responsible for the degradation of endogenously produced adenosine, and blocks the reuptake of adenosine by cells inducing an elevation of extracellular adenosine, which causes vasodilatation [3.4, 3.5]. The biological half-time/life of Dipyridamole is approximately 45 minutes. This and other vasodilators described below (adenosine and regadenoson) are generally safe but can occasionally produce ischemia (sometimes severe) if severe coronary stenosis with some collateral circulation is present, provoking the so-called ‘steal phenomenon’ which results in deviation of blood flow from under-perfused areas to normally perfused ones. Detailed description of this phenomenon is beyond the scope of this document.

— Adenosine promotes vasodilatation by direct activation of vascular A2 receptors when injected intravenously. In myocardium supplied by normal arteries MBF increases approximately 3-4 fold compared to baseline with dipyridamole and approximately 4-5 fold with adenosine, whereas MBF increases less in myocardium supplied by diseased arteries [3.6, 3.7]. Ischemic or potentially ischemic areas can be identified on MPI by heterogeneous tracer distribution, due to a differential capacity of vessels to dilate. Adenosine biological half-time/life is about 10 seconds or less.
Selective A2a receptor agonists are becoming available for utilization. Regadenoson has been approved by the Food and Drug Administration of the United States in 2008, since it has been shown to have similar accuracy to adenosine for the detection of myocardial ischemia, with fewer overall side effects [3.8, 3.9].

Dobutamine is a beta adrenergic agonist drug that increases heart rate and myocardial contractility, promoting coronary hyperaemia through mechanisms similar to exercise [3.10]. It is a fast acting drug with the effect starting approximately two minutes into infusion. Hemodynamic effects are dose-dependent; at low-doses of 5 to 10 mcg/kg/min it increases myocardial contractility without significant change in heart rate. Doses above 10 to 20 mcg/kg/min increases both heart rate and myocardial contractility.

### 3.1.3. Patient preparation

- Instructions regarding fasting vary, but in general, heavy meals should be avoided before testing (see Table 3.1).

- Interruption of medications will depend on the clinical question, if the reason for testing is diagnosis of ischemia in patients with no known CAD, then medications that could reduce ischemic burden should be withheld [3.11]; nevertheless, referring physicians may prefer to maintain medical therapy to be able to monitor the efficacy of the treatment instituted.

- It is preferable to give additional instructions to prepare for vasodilator stress as well (such as caffeine restriction), in case the patient cannot exercise to target heart rate and an alternative pharmacologic study should become necessary [3.12]. In the case that dobutamine stress is planned, beta-blockers should be discontinued for 2 days, similar to the preparation for exercise stress.

- All patients should be informed of the purpose of the test, procedure sequence, exam duration and potential risks. An informed consent form should be signed according to local regulations. Before initiating the procedure, specific information must be obtained regarding potential pregnancy in women at child bearing age, or those breast feeding and a pregnancy test should be performed if needed. It is to be emphasized at this point that the local customs and traditions in the respective countries need to be taken into consideration, and a reflective approach regarding the cultural aspect is imperative when dealing with younger women, particularly with regard to pregnancy issues.

- A secure intravenous line should be established for the administration of radiotracer and medications when needed during or after the stress, as well as for the pharmacologic stressors when these are to be used.

- All stress procedures must be supervised by a qualified health care professional. The physician in charge should be experienced in the selection of the appropriate stress test for the individual patient and the clinical question being asked. All involved personnel should also have the clinical skills to be able to recognise patients who might be at increased risk of complications (and thereby exclude them from stress testing) and respond to potential medical emergencies.
Life support instrumentation and emergency drugs must be available in the immediate vicinity of the stress laboratory; personnel trained in ACLS (Advanced Cardiac Life Support) or at the least BLS (Basic Life Support) should be available.

TABLE 3.1. GENERAL RECOMMENDATIONS FOR PATIENTS SCHEDULED FOR A STRESS TEST

<table>
<thead>
<tr>
<th>Medication*</th>
<th>Withhold (minimum)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrates</td>
<td>24 hours</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>2-5 days (gradually to prevent rebound)</td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>24-48 hours</td>
</tr>
<tr>
<td>Methyl xanthine compounds</td>
<td>72 hours</td>
</tr>
<tr>
<td>Pentoxyphylline</td>
<td>72 hours</td>
</tr>
<tr>
<td>Oral Dipyridamole/Persantine</td>
<td>48 hours</td>
</tr>
<tr>
<td>Phosphodiesterase inhibitors</td>
<td>12 hours</td>
</tr>
</tbody>
</table>

**Food, Beverages**
- Xanthine containing (coffee, tea, chocolate, soft drinks) - Withhold (minimum) 12 hours
- Fasting Avoid heavy meals; 2-4 h fasting recommended
- Comfortable clothing and shoes, no accessories and avoid clothing with metallic elements.
- Dressing Comfortable clothing and shoes, no accessories and avoid clothing with metallic elements.

3.2. SELECTION OF STRESS TEST

Physical exercise is the stress modality of choice for all patients able to exercise adequately, providing additional information (compared to pharmacological stress), such as: Total exercise duration, ST segment changes, development of symptoms (chest pain), hemodynamic changes (BP and heart rate) and arrhythmias. In addition, the quality of myocardial perfusion images is often better with exercise compared to pharmacological stress, and this is related to less sub-diaphragmatic uptake and less inferior wall artefacts. Details regarding the diagnostic criteria for the stress testing are included in specific guidelines [3.13, 3.14].

Accepted indications for vasodilator stress include:

1. Inability to exercise.

2. Failure to achieve 85% maximum predicted heart rate (MPHR, see below) in the absence of typical angina or ischemic ST segment depression.

3. Concurrent beta-blockade (or calcium antagonist) therapy (relative indication).

4. Presence of left bundle branch block (LBBB) or pacemaker. Dobutamine stress is mainly indicated in patients with reactive airway disease (severe COPD or asthma) who are unable to exercise adequately and in whom vasodilators are contraindicated (adenosine and – indirectly – dipyridamole have the potential to induce bronchospasm in susceptible patients).

* Medication withdrawal according to clinical questions and physician indications.
3.3. STRESS PROTOCOLS

3.3.1. Exercise

— The ECG, heart rate, and BP should be carefully monitored and recorded during each stage of exercise as well as during ST-segment abnormalities and chest pain. The patient should be continuously monitored for transient rhythm disturbances, ST-segment changes, and other electrocardiographic manifestations of myocardial ischemia.

— Since monitoring of a single ECG lead is not sufficient for the detection and recognition of arrhythmias or ischemic patterns, 12 leads are strongly recommended.

— The goal of exercise is to stress the patient to exhaustion and to the maximum predicted heart rate (MPHR) for his/her age (220 – age = maximum heart rate). If the patient is unable to reach MPHR, then 85% of the MPHR is an acceptable target.

— If the increase in heart rate does not reach at least 85% of MPHR, in the absence of typical angina or clearly positive ECG by ST segment criteria, then the patient should be switched to a pharmacological stress protocol since otherwise the sensitivity of the test would be compromised.

— The most popular methods to exercise patients are the treadmill test (TMT) or the cycle ergometer. Several protocols can be used; all staged with incremental physical effort to progressively increase oxygen consumption. Modified protocols can be used to evaluate patients with limited exercise capacity, such as elderly, or subjects with higher effort tolerance, such as athletes.

— Professionals performing the test should judge when the ideal moment to inject the tracer is achieved, being aware that the patient should continue exercising for an additional 1-2 minutes after injection.

3.3.2. Dipyridamole

— It is commonly used at a dose of 0.56 mg/kg over 4 minutes, but protocols using additional 0.28 mg/kg involving 2 additional minutes can also be applied, to a maximum total dose of 60 mg.

— Radiopharmaceutical should be injected between 3-5 minutes after termination of dipyridamole (7-9 minutes from start) [3.15].

— Patients receiving dipyridamole may experience symptoms after completion of the infusion when they have already left the laboratory. Administration of aminophylline prevents these occurrences in most patients; aminophylline is administered at slow IV push until symptoms resolve, or, in some laboratories, this is done routinely regardless of the occurrence of any effect of the drug. The usual dose is 125 mg, with a maximum total dose up to 250 mg.
3.3.3. **Adenosine**

— It is infused IV with a pump at a rate of 140 mcg/kg/min over 4–6 minutes. BP, heart rate and ECG must be monitored every minute.

— The radiopharmaceutical is administered IV two minutes into the adenosine infusion when the 4 minutes protocol is used, or at three minutes into the infusion when the 6 minutes protocol is used.

— Adenosine has a very short half-life of less than 10 seconds; this does not necessarily mean that all side effects occurring with adenosine will resolve after cessation of infusion. Once the adenosine receptors have been activated, a cascade of events is triggered, and therefore side effects may last much longer than may be suggested by the drug’s very short half-life.

3.3.4. **Selective A2a receptor agonists**

— Regadenoson is given as a 10-second bolus, at a fixed dose of 400 mcg, administered 30 seconds prior to tracer injection. Patient monitoring and other measures apply the same as for dipyridamole and adenosine, although fewer side effects are expected.¹

3.3.5. **Dobutamine**

— The protocol most commonly used starts with an infusion rate of 10 mcg/kg/min, increasing by an additional dose of 10 mcg/kg/min every 3 minutes, to a maximum dose of 40–50 mcg/kg/min.

— The radiopharmaceutical is injected once the target heart rate is achieved and the infusion of dobutamine is continued for another minute. ECG and BP are monitored at baseline and every 3 minutes thereafter.

— Atropine may be used to increase heart rate, starting at the second stage [3.16]. Boluses of 0.5 mg of atropine can be given, with an interval of at least 1 minute between boluses, to a maximum dose of 2 mg in order to increase heart rate. Atropine use is contraindicated in the presence of glaucoma, obstructive uropathy including prostatic hypertrophy, atrial fibrillation with uncontrolled heart rate, and prior adverse reaction to the drug. Patients should also be informed of possible difficulties while driving in the 2 hours following atropine administration due to reduced ocular accommodation.

— The overall complication rate using dobutamine is higher than that for other stressors: 1 severe adverse reaction every 335 tests has been reported in a meta-analysis of 26,438 patients. Moreover, significant supraventricular or ventricular arrhythmias occur in 8–10%.

---

¹ The antidote to vasodilators is aminophylline, which blocks adenosine cell membrane receptors. It is given as a slow IV bolus until symptoms resolve with a maximum dose of 250 mg. In view of the brief half-life of adenosine, termination of the infusion is often (but not always) adequate to manage adverse events. If possible, wait 2 - 3 minutes after radiopharmaceutical injection to terminate infusion and give aminophylline. In case of very severe ischemic symptoms or signs, administration of nitrates may be necessary, following aminophylline administration. Caution should be taken in patients who had recent use of phosphodiesterase inhibitors (e.g. sildenafil).
3.3.6. Combination of vasodilators with low workload physical exercise

— Vasodilators induce dilatation of the splanchnic vasculature resulting in a higher concentration of radiopharmaceuticals in the liver and intestinal tract. Protocols combining vasodilators (dipyridamole or adenosine) with exercise have been established in the past several years [3.17–3.19].

— Exercise promotes a redistribution of blood flow to the skeletal musculature and away from intra-abdominal organs such as the liver. These effects result in a higher heart-to-background activity ratio on images obtained after exercise compared with those obtained after vasodilator infusion alone. In addition, reduction of side effects with this strategy have been described. Besides resulting in better image quality, the images can also be acquired earlier after administration of the radiopharmaceutical in patients undergoing a combined exercise/vasodilator protocol compared to vasodilator alone.

— Indications for combining vasodilator and exercise stress include: (1) Inability to exercise to 85% maximum predicted heart rate, but able to at least walk, and (2) Concurrent use of medications that may limit heart rate increase.

— It is important to note that patients with LBBB or pacemaker should undergo vasodilator stress alone to reduce the false positive rate associated with exercise.

— Most patients for the combined protocol are exercised at low workload as per patient’s abilities, and the tracer is injected at the same time as described for adenosine or dipyridamole protocols.

3.4. CONTRAINDICATIONS

— Absolute and relative contraindications to stress tests and test interruption criteria are described in Tables 3.2 and 3.3 [3.13, 3.14].

3.5. OPTIMIZATION OF STRESS TESTS IN MPI

In summary, there are two main options available to suit the clinical condition of the patient and the available resources in terms of stress agents and radiopharmaceuticals. A schematic suggested workflow for the optimization of stress tests with the use of MPI is presented in figure 3.1.
Symptoms suggestive of CAD

ECG interpretable?

YES

Pharmacological Test

Able to exercise?

NO

Able to reach target HR? (e.g., no HR limiting tx)

YES

Exercise Test

NO

Contraindications to Vasodilators

Vasodilators

Consider rescheduling or alternative imaging

NO

Switch to Pharmacological Test

YES

Complete Test

---

**FIG. 3.1. Optimization of stress tests in MPI.**

* CAD = Coronary Artery Disease

* HR = Heart Rate
TABLE 3.2. CONTRAINDICATIONS FOR VARIOUS TYPES OF STRESS

| Contraindications for all types of stress | — High risk unstable angina. 
| | — Acute myocardial infarction (within 2 days).
| | — Uncontrolled symptomatic heart failure.
| | — Uncontrolled arrhythmias causing symptoms or hemodynamic compromise.
| | — Unwillingness or unable to give informed consent (legislation dependent).

| Contraindications for exercise testing |
| Absolute | — Symptomatic severe aortic stenosis.
| | — Acute pulmonary embolism or pulmonary infarction.
| | — Acute myocarditis or pericarditis.
| | — Acute aortic dissection.

| Relative | — Left main coronary stenosis (known by angiography).
| | — Moderate stenotic valvular heart disease.
| | — Electrolyte abnormalities.
| | — Severe arterial hypertension. 
| | — Tachyarrhythmias or bradyarrhythmias.
| | — Hypertrophic cardiomyopathy and other forms of outflow tract obstruction.
| | — Mental or physical impairment leading to inability to exercise adequately.
| | — High-degree atrioventricular block.

| Contraindications for vasodilators (dipyridamole and adenosine) | — Second or third degree A-V block or sick sinus syndrome.
| | — Bronchospastic disease (active wheezing/rhonchi, steroid dependency for asthma/COPD, depressed forced expiratory volume 1 (FEV1), hospitalization for respiratory failure).
| | — Hypotension (SBP <90mmHg).
| | — On-going transient ischemic attack (TIA) or recent cerebrovascular accident (<6 months).
| | — Caffeine/Theophylline (or similar) intake within the past 12 hours.

| Contraindications for dobutamine | — Cardiac arrhythmias, including atrial fibrillation and ventricular tachycardia.
| | — Severe aortic stenosis or hypertrophic obstructive cardiomyopathy.
| | — Hypotension (systolic BP, SBP <90mmHg) or uncontrolled hypertension (SBP >200 mmHg).
| | — Aortic abdominal aneurysm >5 cm diameter (relative contraindication).
| | — Presence of LV thrombus (relative contraindication).
| | — Presence of an implanted ventricular defibrillator.
| | — LVEF <25% (this represents a relative contraindication due to increased risk of ventricular arrhythmia; risk/benefit to be carefully evaluated).

---

2 ACC/AHA Guidelines for the management of patients with unstable angina/non-ST-segment elevation myocardial infarction.
4 No definitive evidence, committee suggests SBP >200 mmHg and/or DBP >100 mmHg.
### TABLE 3.3. CRITERIA FOR EARLY TERMINATION OF EXERCISE TESTING

<table>
<thead>
<tr>
<th>Absolute indications for interruption</th>
<th>Relative indications for interruption</th>
</tr>
</thead>
<tbody>
<tr>
<td>— Drop in SBP &gt;10 mmHg from baseline SBP despite an increase in workload, when accompanied by other evidence of ischemia.</td>
<td>— ST or QRS changes such as excessive ST segment depression (&gt;2mm of horizontal or downsloping ST-segment depression) or marked axis shift.</td>
</tr>
<tr>
<td>— Moderate to severe ischemia in ECG (ST depression &gt;3 mm).</td>
<td>— Arrhythmias other than sustained ventricular tachycardia, including multifocal PVCs, triplets of PVCs, supraventricular tachycardia, heart block, or bradyarrhythmias.</td>
</tr>
<tr>
<td>— Increasing nervous system symptoms (e.g., ataxia, dizziness, or near-syncope).</td>
<td>— Fatigue, shortness of breath, wheezing, leg cramps, or claudication.</td>
</tr>
<tr>
<td>— Signs of poor peripheral perfusion.</td>
<td>— Development of bundle branch block or IVCD that cannot be distinguished from ventricular tachycardia.</td>
</tr>
<tr>
<td>— Technical difficulties in monitoring ECG or SBP.</td>
<td>— Increasing chest pain.</td>
</tr>
<tr>
<td>— Patient’s request to stop.</td>
<td>— Hypertensive response (SBP &gt;250 mmHg and/or diastolic BP &gt;115 mmHg).</td>
</tr>
<tr>
<td>— Sustained ventricular tachycardia.</td>
<td>— Signs of poor peripheral perfusion.</td>
</tr>
<tr>
<td>— ST segment elevation (1 mm) in leads without diagnostic Q-waves (other than V1 or aVR).</td>
<td></td>
</tr>
</tbody>
</table>

### 3.6. RADIOPHARMACEUTICALS AND IMAGING PROTOCOLS

#### 3.6.1. 99mTc-MIBI and 99mTc-Tetrofosmin

— The perfusion imaging agents now most commonly used clinically are 99m Tc-MIBI (methoxyisobutylisonitrile) and 99mTc-tetrofosmin. The recommended administered activities are shown in figures 3.2–3.4 and expressed in mCi, with 10 mCi representing 370 MBq.

— Myocardial uptake of 99mTc-labeled tracers increases proportionately with myocardial blood flow up to 1.5–2 times above the resting state, and then myocardial uptake levels off, i.e. the extraction fraction is non-linear and is reduced at slightly lower perfusion levels than for 201-thallium.

— Unlike 201-TI, 99m-Tc MIBI and tetrofosmin have no significant redistribution, and separate injections are given to assess stress and resting perfusion. The six hour halflife of 99m-technetium means that the two studies should ideally be performed on separate days to allow for the decay of activity from the first injection.

---


3.6.2. Imaging protocols for 99mTc agents

- **Two-day protocol**: This is theoretically the most preferable one because it provides best quality images (Fig. 3.2). Studies are obtained using the same administered activity for each. This not only facilitates a comparison between both studies but it also keeps the total radiation burden to the patient (and to the staff) at a level lower than that of the single-day protocol.

![Fig. 3.2. Schematic representation of separate day protocol with 99mTc agents.](image)

- **Single-day protocol**: The order of studies on a single-day protocol depends to some extent on the indication for the investigation. If the indication is to detect viable myocardium and reversibility of a defect, in a patient with previous infarction, it may theoretically be preferable to perform the resting study first. Conversely, when the study is performed for the diagnosis of myocardial ischemia, the stress study should be performed first, in order to avoid reducing the contrast of a stress-induced defect by a previous normal resting study, and if the stress image is totally normal, resting imaging might not be required. Single- or same-day protocols may also be used for patients’ convenience (Fig. 3.3 and Fig. 3.4).

![Fig. 3.3. Schematic representation of same day rest-stress protocol with 99mTc agents.](image)
FIG. 3.4. Schematic representation of same day stress-rest protocol with 99mTc agents.

— Acquisition: Image acquisition using 99mTc agents should begin 30-40 minutes after exercise injection to allow for hepatobiliary clearance; longer delays are generally required both for resting images and for stress with vasodilators alone because of the higher sub-diaphragmatic tracer activity.

— Nitrates: If the patient is referred for viability evaluation or in a patient with a severe uptake defect on stress images, sublingual nitroglycerin, usually at a dose of 400-800μg (or isosorbide dinitrate 10 mg) can be administered at least 5 minutes before radiotracer injection in order to maximize resting perfusion and to increase the correspondence of the resting images with myocardial viability. Nitrates are ideally given with the patient in the supine position to avoid symptomatic hypotension. When SBP is ≤90 mmHg nitrates are not recommended.

— Fluid intake like plain water can be used in an attempt to clear intestinal activity. Fatty meals were initially recommended with 99mTc tracers in order to accelerate hepatobiliary clearance of activity, however today most laboratories try to avoid this since gallbladder contraction after a meal produces a large amount of activity to be excreted into the intestinal lumen, with unpredictable consequences on image quality.

— Medication such as beta-blockers can modify left ventricular function parameters (volumes and EF). Therefore, patients should be ideally kept under the same medication between the two sets of images or these differences should be taken into account during the study interpretation.

3.6.3. 201-Thallium

— After intravenous injection at stress, 201-Tl is distributed in the myocardium according to myocardial perfusion and viability. Myocardial uptake of 201-Tl increases proportionately with perfusion up to 2–2.5 times above the rest levels, and then a plateau is reached.

— 201-Tl subsequently redistributes from its initial distribution over several hours thus late images will reflect both rest perfusion and viability, to be acquired usually 3–4 hours after injection.

— Comparison between the stress and redistribution images distinguishes between the reversible defect of inducible hypo-perfusion and the fixed defect of myocardial necrosis.
— In some cases, redistribution may be incomplete at four hours; a second injection of 201-Tl can then be given and reinjection images acquired for a more accurate assessment of myocardial viability.

— Different imaging protocols can be followed, depending on clinical indication(s) and local practices: Stress-redistribution, stress-reinjection, stress-redistribution-reinjection, stress-reinjection-delayed 24 hour imaging, rest-redistribution.

3.6.4. Imaging protocols for 201-Tl

— Stress imaging should begin within 5–10 minutes of tracer injection and should be finished within 30 minutes of injection.

— Redistribution imaging should be performed after 3–4 hours delay.

— Late imaging can also be performed 24 hours after injection using a longer acquisition time for the assessment of myocardial viability.

— Reinjection: In patients with severe perfusion defects in the stress images or if redistribution is thought to be incomplete at the time of redistribution imaging, a resting injection can be given (ideally after sublingual nitrates) with imaging after a further 60 minutes of redistribution.

**FIG. 3.5.1. Stress-redistribution 201-Tl protocol**
Dual isotope protocols

— These protocols use both 201-Tl and 99mTc tracers and are not frequently used, with the exception of selected centres.

— Normally, 201-Tl injection at rest is given first and then stress imaging is performed, following a stress injection of the 99mTc agent (MIBI or tetrofosmin).

— Imaging can be performed simultaneously taking advantage of the different energy windows used for each isotope; however image quality can be compromised due to downscatter of 99mTc photons into the 201-Tl window.

### TABLE 3.4. COMMON DRAWBACKS ASSOCIATED WITH DIFFERENT IMAGING PROTOCOLS [3.20]

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Drawback</th>
</tr>
</thead>
<tbody>
<tr>
<td>99mTc-MIBI/Tetrofosmin stress/rest: general</td>
<td>— Tracer uptake often (rest and pharmacologic stress studies) high in subdiaphragmatic regions with extracardiac hot spots.</td>
</tr>
<tr>
<td>2-day protocol</td>
<td>— Logistics: Patient must come on 2 different days, if stress study is not normal.</td>
</tr>
<tr>
<td>1-day stress/rest protocol</td>
<td>— Reversibility may be underestimated because of interference from remaining myocardial activity from the stress study.</td>
</tr>
<tr>
<td>Protocol</td>
<td>Notes</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------------------------------------------------------------------</td>
</tr>
<tr>
<td>1-day rest/stress protocol</td>
<td>Two tracer injections necessary even if stress study is normal.</td>
</tr>
<tr>
<td></td>
<td>Stress defects may be less clearly visualized due to interference</td>
</tr>
<tr>
<td></td>
<td>from remaining myocardial activity from the resting study.</td>
</tr>
<tr>
<td>Dual isotope protocol</td>
<td>Comparison of $^{201}$TI and $^{99m}$Tc tracer uptake may be</td>
</tr>
<tr>
<td></td>
<td>influenced by differences in attenuation and spill-over from</td>
</tr>
<tr>
<td></td>
<td>extracardiac sources.</td>
</tr>
<tr>
<td></td>
<td>High radiation exposure.</td>
</tr>
<tr>
<td>201-thallium stress – redistribution</td>
<td>Attenuation artefacts may affect interpretation.</td>
</tr>
<tr>
<td></td>
<td>Evaluation of LV EF and wall motion is inferior compared to Tc-</td>
</tr>
<tr>
<td></td>
<td>labelled tracers.</td>
</tr>
<tr>
<td></td>
<td>Higher radiation exposure compared to Tc-labelled tracers.</td>
</tr>
</tbody>
</table>
REFERENCES TO SECTION 3


4. ACQUISITION AND PROCESSING OF MPI STUDIES

4.1. ACQUISITION

4.1.1. General recommendations

— The procedure should be explained to the patient before commencing.

— Implanted radiopaque objects (pacemakers, silicone implants, etc.) should be noted as potential attenuators.

— Patients should be frequently observed until the acquisition is completed.

— Female patients might be required to remove their brassiere.

— SPECT is currently the standard technique for MPI studies; planar acquisition is generally no longer accepted for this procedure.

— A list of acquisition parameters is presented in Table 4.1.

4.1.2. Patient positioning

— Patient arms must be positioned away from the field of view (at least the left arm) and the position must be the same in both acquisitions (stress-rest). If available, supporting devices appropriate for gamma cameras can be used for the patient’s comfort.

— The supine position is commonly used. The prone position is recommended when the patient demonstrates significant motion during supine acquisition and if there is an equivocal perfusion defect in the inferior wall. However, it should be noted that the prone position might also produce artefacts.

<table>
<thead>
<tr>
<th>TABLE 4.1. ACQUISITION PARAMETERS FOR MPI ACQUISITION [4.1, 4.2]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isotope</td>
</tr>
<tr>
<td>Energy window</td>
</tr>
<tr>
<td>20% symm, 167 KeV</td>
</tr>
<tr>
<td>Collimators</td>
</tr>
<tr>
<td>Rotation (1 or 2 head)</td>
</tr>
<tr>
<td>Acquisition type</td>
</tr>
<tr>
<td>Nº projections (pr), 180°</td>
</tr>
<tr>
<td>Time per projection</td>
</tr>
<tr>
<td>25 s (64 pr)</td>
</tr>
<tr>
<td>2nd (high dose): 20 s</td>
</tr>
</tbody>
</table>

* Symm = symmetric.
** LEGP = Low energy general purpose.
*** LEHR = Low energy high resolution.
4.1.3. **Field of view**

— It is imperative that the area of interest (i.e., the heart) is included in every projection image. If this is not the case, the resulting truncation of the images will produce artefacts in the final reconstructed images.

— Special caution should be taken when using magnification factor (zoom).

4.1.4. **Orbit**

— A 180º orbit (45º right anterior oblique, RAO to 45º left posterior oblique, LPO) is recommended for single and dual detector systems.

— For a 180º acquisition with dual head cameras, detectors should be in a 90º configuration. The majority of cameras allow an adaptation of the configuration (i.e. 75 %) depending on the contours of the patient. The main orbit options are circular and noncircular (elliptical or body-contoured).

— Noncircular orbits follow the contour of the patient, bringing the camera closer to the chest, thereby improving spatial resolution but may suffer from reconstruction artefacts due to changes in spatial resolution [4.3].

— Circular orbits maintain a fixed radius of rotation but - on average - result in the detector being further from the patient. In general, there is reduced (but more uniform) spatial resolution with circular orbits since the detector-to-source distance is greater (yet constant) with this technique.

— When available, the use of non-circular orbit with body auto-contouring is recommended.

4.1.5. **Acquisition type**

— The camera may move in a continuous motion during acquisition but typically it should remain stationary during the acquisition of each projection image before advancing to the next position in a ‘step and shoot’ mode of operation, in order to avoid degradation of resolution.

— An alternative can be the ‘continuous step and shoot’ mode which slightly improves the count statistics for a given scan time even though there is a slight loss in angular resolution [4.4, 4.5].

4.1.6. **Pixel and matrix size**

— Pixel size is typically 6.4±0.4 mm for a 64×64 image matrix.

— Zoom should be applied as necessary for cameras with a large field of view. This provides a good balance between image resolution and image noise. Zoom should be standard for all patients both in stress and rest for LV size evaluation, with the exception of particular situations where the heart is very small or large, in which case the routine magnification factor can be altered, but keeping in mind to use the same factor for both sets of studies for appropriate comparison.
Selection of the matrix relies on the pixel size and the system spatial resolution. The selected matrix should imply a pixel size less than 1/3 of the system spatial resolution in order to keep an adequate spatial resolution, as depicted in Table 4.2.

**TABLE 4.2. RELATIONSHIP BETWEEN SYSTEM RESOLUTION (FULL WIDTH AT HALF MAXIMUM, FWHM) MATRIX AND PIXEL SIZE**

<table>
<thead>
<tr>
<th>System spatial resolution</th>
<th>Matrix size (pixels)</th>
<th>Pixel size (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isotopes FWHM = 12 mm</td>
<td>128 x 128</td>
<td>3.2 ± 0.2</td>
</tr>
<tr>
<td>Isotopes FWHM = 20 mm</td>
<td>64 x 64</td>
<td>6.4 ± 0.4</td>
</tr>
</tbody>
</table>

4.1.7. **Acquisition time**

- The time per projection is always a compromise between improved count statistics and increasing the risk of patient movement.
- It is recommended that the overall acquisition time be kept below 20–30 min.
- With higher sensitivity detectors, scanning time may be shorter but particular attention must be paid to count density.
- Modified iterative reconstruction software and new cameras architecture offer the possibility of performing fast acquisition protocols in order to reduce the scanning time or the injected dose (refer to section about new scanners).

4.1.8. **Gated studies**

- Gated SPECT studies can be performed both with Tl-201 and 99m-Tc labelled tracers (sestamibi, tetrofosmin). However, the assessment of regional wall motion is more accurate with 99m-Tc-labelled tracers because of the higher count statistics [4.6].
- Special attention must be paid to adequate count density and in particular to lower activity acquisitions.
- Before starting the acquisition, a careful check for a correct ECG trigger signal must be performed (gating is recommended only if the patient has fairly regular heart rhythm). Functional information may not be reliable in patients with atrial fibrillation, sinus arrhythmia, frequent premature beats, intermittent or dual chamber pacing.
- There is no clear consensus on the tolerance (acceptance) window for the frame/bin length (the majority of guidelines suggest considering a 90-100% window) [4.2].
- A wide window is recommended in order to be able to analyse good quality perfusion images in case of arrhythmia or wide heart rate variability (otherwise, in some systems rejected beats will also not be contributing to the generation of ‘non-gated’ perfusion images).
Using 8 frames/cardiac cycle results in a slight underestimation of LVEF values, nevertheless 8 intervals might provide better assessment of regional wall motion and it is probably the most widely used value. Many institutions are now using 16 frames/cycle (especially with high sensitivity detectors) allowing a more accurate measure of LVEF (Table 4.3).

Whatever number of gated frames is used, consistency must be kept in order to establish normal values for own population and for intra- and inter- patient comparison. It is recommended that both stress and rest studies be gated.

TABLE 4.3. ACQUISITION PARAMETERS FOR GATED SPECT MPI STUDIES

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frames/cycle</td>
<td>8 (16 optional)</td>
<td>8 (16 optional)</td>
</tr>
<tr>
<td>R-to-R window</td>
<td>90-100%</td>
<td>90-100%</td>
</tr>
</tbody>
</table>

4.1.9. Quality Assurance

Quality control is crucial to all aspects of nuclear medicine practice, including the measurement of radioactivity, the preparation of radiopharmaceuticals, the use of instrumentation to obtain images, computations to calculate functional parameters, and the interpretation of the results by the physician. It plays an integral part in fulfilling the regulatory requirement for establishing a comprehensive quality assurance programme as described in the International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources. We strongly recommend and encourage readers to take a closer look at the literature regarding Quality Assurance for SPECT Systems in the IAEA Human Health Series No.6. [4.7].

4.2. PROCESSING

4.2.1. Motion correction

Quality control of cardiac studies implies primarily the evaluation of presence of motion during acquisition [4.8]. If present to a significant degree, it is suggested to repeat the acquisition; an alternative may be the use of motion correction software.

A number of motion correction packages are available from different manufacturers. It should be noted that these methods only correct relatively simple forms of motion such as motion in the longitudinal axis. More complex patterns of motion involving rotational motion cannot be adequately corrected using current methods.

It has been demonstrated that movement by 1 pixel does not produce significant artefacts in the reconstructed images [4.9, 4.10]. Correction of significant motion should be attempted by software but if this is not possible the entire acquisition should be repeated, also considering prone position.

Images must be reviewed immediately after acquisition to check for motion and extra-cardiac hot spots, before the patient is discharged from the department.
4.2.2. Image reconstruction

— Both filtered back-projection (FBP) and iterative methods are useful but the latter (like maximum likelihood expectation minimization, MLEM or ordered subset expectation maximization, OSEM) are preferred since they offer more accurate modelling of physical processes and reduce noise [4.11]. These are now generally available from all manufacturers and are included in the standard reconstruction software packages.

— Generally, if FBP is used, the type of filter, cut-off frequency and order factors may follow the recommendations of vendors if standard activity amounts of tracers and imaging techniques are applied. Butterworth or Hamming are the most widely used filter types for FBP. However, the mathematical way of implementing the filter functions are not always the same across manufacturers so the final results may vary slightly.

— The same reconstruction technique should be used consistently for all studies unless modifications are needed in specific cases to keep a comparable count density/image appearance in both sets of stress and rest images. In Table 4.4 a list of recommended reconstruction parameters is presented.

TABLE 4.4. SUMMARY OF RECOMMENDATIONS REGARDING THE MORE COMMON RECONSTRUCTION TECHNIQUES APPLIED IN MYOCARDIAL PERFUSION SPECT.

<table>
<thead>
<tr>
<th>FBP</th>
<th>Radioisotope</th>
<th>Activity(mCi)</th>
<th>Cut-off</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butterworth</td>
<td>201-Tl</td>
<td>2.5-4.0</td>
<td>0.3-0.4</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>99m-Tc</td>
<td>8-12</td>
<td>0.3-0.4</td>
<td>6</td>
</tr>
<tr>
<td>Hamming</td>
<td>201-Tl</td>
<td>2.5-4.0</td>
<td>0.25-0.40</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>99m-Tc</td>
<td>8-12</td>
<td>0.30-0.45</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24-36</td>
<td>0.45-0.60</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ITERATIVE</th>
<th>MLEM</th>
<th>Iterations: 10-15</th>
<th>No pre-filtering needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITERATIVE</td>
<td>OSEM</td>
<td>Iterations: 2-5 Subsets: 8</td>
<td>No pre-filtering needed</td>
</tr>
</tbody>
</table>

4.2.3. Reorientation

— A critical phase of myocardial processing is reorientation of tomographic data into the natural approximate symmetry axes of an individual patient’s heart. This is performed either manually or automatically.

— Automated methods of reorientation are available and have been shown to be at least as accurate as trained operators and may achieve greater reproducibility and results in sectioning the data into vertical long-axis, horizontal long-axis, and short-axis planes. [4.12, 4.13]

— Inappropriate plane selections can result in misaligned myocardial walls between rest and stress data sets, potentially resulting in artefacts and in incorrect interpretation.
— All axis choices must be available as QC screens in order to verify that axes were selected properly.

4.2.4. Image display

— Stress and rest images should be appropriately aligned and presented in a format that allows ready comparison.

— Each SPECT study should be displayed with the top of the colour scale at the maximum count/pixel within the myocardium for each set of images. It is recommended to use a linear colour scale or a grey scale.

— Displays with the top of the colour scale at the maximum of each individual tomogram and those that use the same maximum for stress and rest images should not be used [4.14].

— The bottom end of the colour scale should be set to zero and background subtraction should be avoided.

— Care should be taken if the pixel with maximum counts lies outside the myocardium, in which case manual adjustment or masking of extracardiac activity may be required. Removal of subdiaphragmatic activity should be attempted for final display.

— Three set of axis should be displayed: Short-axis slices (SA) from apex to base, vertical long-axis (VLA) from septal to lateral and horizontal long-axis slices (HLA) from inferior to anterior wall. Sequential images (stress and rest) should be aligned and adjacent to each other serially.

— Normalization: Each series stress, rest (and/or redistribution in case of Tl-201) should be normalized to the brightest pixel in the entire series separately.

4.2.5. Quantification

This is an extremely valuable tool in MPI, as it provides an objective assessment of the parameters under investigation, conveys the degree of severity of the parameter, and thus aids the physician in the interpretation of results and eventually allows taking further appropriate action based on these results. It is adequate for follow-up when the same software is used. There are several commercially available software packages, among them the most extensively used are: Cedars Sinai (QGS, QPS), Emory Cardiac Toolbox, and 4DM SPECT (Ann-Arbor, Michigan). These methods have been extensively validated, but their use is not fully interchangeable [4.15 – 4.17]. For further reference please see figures 5.8 and 5.9.

4.2.6. Perfusion defect size

A perfusion defect (stress & rest) is usually considered as significant when the perfusion intensity is less than 2.5 standard deviations below that of the normal database. Extent of defects can generally be calculated in one of two ways:

— Quantification by percentage size of LV (% terms, limits 0-100%):
  — Small (0-10%)
Quantification by number of segments in a 17 or 20 segment model [4.18]. In a 20 segment model, each segment would represent 5%; in the 17 segment model, each segment would represent 5.9%. The summed score for both stress & rest images are then calculated (integer) based on severity & size of defect. When available, the 17 segment model is recommended (Fig. 5.9).

4.2.7. Perfusion defect severity

The perfusion defect severity is also extremely important. It can be divided and scored into (Fig. 4.1):

— Absent uptake = 4
— Severely reduced uptake = 3
— Moderately reduced uptake = 2
— Mildly reduced uptake = 1
— Normal uptake = 0

4.2.8. Summed scores

The difference between the stress & rest defect size and severity is considered the size and severity of ischemia, which should be reported routinely as it has a significant prognostic value. It is important to highlight that though the scores serve as reference for the interpretation of the MPI studies, they should always be analysed in addition to the images. The value can best be expressed in terms of score numbers: Summed Scores = Severity score of each defect x Number of segments with defect. In this way, three scores are computed, either manually or automatically through the available software:
— Summed Stress Score (SSS). This represents the perfusion defect seen at stress but does not distinguish between ischemia and infarction.

— Summed Rest Score (SRS). This is considered equal to the magnitude of a fixed defect, and hence represents - in most cases - the size and severity of a myocardial infarction (although in some cases this may prove to be due to the presence of hibernating myocardium with viability).

— Summed Difference Score (SDS). This is the most important parameter in terms of prognosis, and expresses the magnitude of ischemia (reversibility).

— It is generally accepted to consider a Summed Score ≤3 consistent with a normal result; while 4-8 is a mild defect, 9-12 is a moderate defect and >12 is a severe defect. However, interpretation of Summed Scores should be consistent with the visual analysis of the images since there are several possible pitfalls in the score calculation, especially when it is derived from automated software.

4.2.9. Polar maps

The location of perfusion defects, based on the 17 or 20 segment model, must be registered as well. This is best achieved through the polar maps (Bull’s eye) which are 2-dimensional representations of the 3-dimensional distribution of activity in the myocardium. Stress, rest and ‘reversibility’ maps are widely used to represent the distribution of activity through the different walls of the myocardium and the location of defects, sometimes with correlation with the three main coronary territories.

4.2.10. Left Ventricular Ejection Fraction

Gated MPI using either 8 or 16 frames can be used to automatically calculate left ventricular ejection fraction (LVEF), derived from estimating the LV end-diastolic and end-systolic volumes (EDV & ESV). The measure is highly reproducible and adds significantly to the overall interpretation of the study and its clinical impact, especially in terms of prognosis. Post-stress and rest LVEF should be registered, as well as the difference between both values (so-called delta EF).

— Post-stress EF: Note that since post-stress EF is acquired when the stress test has already been terminated and the patient is at ‘rest’, LV function can either reflect the true ‘rest’ state or it can still be undergoing a recovery period if the stress has caused ischemia. Thus, it should not always be considered either a true ‘stress’ EF or a true ‘rest’ EF. It has been demonstrated that post-stress LVEF has a prognostic value by itself, regardless of the rest EF.

— Rest EF: When using a 2-day protocol, this can be considered a true ‘rest’ EF. However, when using a 1-day protocol and stress is performed first, the ‘rest’ EF can still be under the influence of ischemia developed during the stress test, and thus be lower than a true rest EF in the same patient. Nevertheless, this is infrequent and only expected to occur when ischemia is very severe.

— Difference between stress EF and rest EF (delta EF): When a significant difference between these two values is encountered, the presence of post-ischemic myocardial ‘stunning’ should be considered, especially if reversible perfusion defects exist [4.19]. Regardless of the absolute values, a stress EF value which is at least 10% lower than
the rest EF value is generally considered pathological and is associated with high risk of cardiac events. This parameter is of particular value for protocols using equal dose of radiotracer injection (two-day protocols).

— To ensure that the EF values are reliable, proper gating is required, with a stable regular heart rate during acquisition. LVEF estimation by gated MPI has certain limitations: Because of partial volume effect, the estimation of volumes in very small or very large hearts may be compromised, resulting in erroneously high or low EF respectively. In general, LVEF should be reported as >75% for all values beyond 75% and <15% for all values below 15%. In general, the normal lower limit of LVEF is 50% although values as low as 45% have been reported in normal patients.

4.2.11. Regional LV function

— Regional wall motion can be visually assessed as:
  — Normal wall motion = 0
  — Mild hypokinesis = 1
  — Moderate hypokinesis = 2
  — Severe hypokinesis = 3
  — Akinesis (infarct) = 4
  — Dyskinesis (infarct, aneurysm) = 5

— Software can now assess the amount of cardiac motion (from diastole to systole) in mm of motion in each of the 17/20 segments of the heart, in a fully quantitative manner. Again emphasis is made on the importance of careful analysis, which should always combine the visual analysis to the software data.

— Regional wall thickening can be assessed quantitatively (% wall thickening from diastole to systole) and expressed in scores and colour-scaled polar plots. Wall thickening can be evaluated using a semi-quantitative scale where:
  — Normal thickening = 0
  — Mild reduction in thickening = 1
  — Moderate to severe reduction in thickening = 2
  — No thickening = 3

— Phase analysis of gated MPI studies has been applied to investigate asynchronous myocardial contraction and is now available in certain software packages. The method has been proven useful in assessing the need for resynchronization therapy and to evaluate its results.

4.2.12. Left Ventricular volumes

— Left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) for both stress and rest images should be routinely registered as well (in ml or cc), as it has been shown that these numbers also have significant prognostic implications.

— The consistency when comparing stress and rest values must be checked, in order to detect significant differences between both, in cases of severe ischemia.
— Reference values for LVEDV and LVESV are variable according to the software employed. Volume estimation by MPI has certain limitations due to the partial volume effect and suboptimal spatial resolution. Because of partial volume effect, the estimation of volumes in very small and very large hearts can be compromised.

— There is also a limitation of the software when there is a large transmural infarction since accurate edge detection can be difficult to achieve in the infarcted wall with no radionuclide uptake.

4.2.13. Transient Ischemic Dilation

Assessment of transient ischemic dilation (TID) is suggested as part of the report; however there is no consensus on how to measure this parameter (ungated or gated images). Significant TID usually implies severe ischemia and can be explained by the presence of diffuse subendocardial ischemia resulting in an apparent enlargement of LV cavity during stress, or by true dilatation of the LV when regional or diffuse ischemia is severe [4.20, 4.21]. TID may be especially useful when there is suspicion of ‘balanced’ ischemia resulting in an ‘apparently normal’ perfusion scan. TID has a large prognostic significance. Normal upper limit of TID (stress LV volume or rest LV volume) is between 1.2 and 1.3.

4.2.14. Lung-to-Heart Ratio

Lung-to-Heart ratio (LHR) is considered another important parameter with significant prognostic value. Depending on the tracer used, LHR is considered abnormal when LHR is >0.44 (99m-Tc) or >0.50 (201-Tl). Raised LHR reflects poor LV function, resulting in an elevation of LV end-diastolic pressure and a delay in return of blood from the pulmonary vessels into the left heart, causing increased lung uptake of tracer. Studies with TI-201 are more sensitive for this parameter since post-stress images are obtained earlier than with 99m-Tc agents [4.22].

4.2.15. Right Ventricular uptake

This parameter is usually not quantifiable with available software, although some methods have been proposed. Normally, the right ventricular uptake (RV) shows faint uptake of the tracer mostly due by the fact that the RV wall thickness is about 1/3 of that of the LV. When the RV uptake is high compared to the LV uptake, it may represent severe LV ischemia or RV hypertrophy. This is an insensitive but specific marker of multi-vessel and/or left main CAD [4.23]. Acute or chronic LV dysfunction causes RV overload due to an increase in pulmonary BP.

4.2.16. Overall image quality

This can be semi-quantitatively assessed. The quality of the image should be reported and can be assessed as:

— Excellent.
— Good.
— Poor.
— Un-interpretable (need to repeat the scan).

This will give an indication of the confidence of the interpreter in reporting the images, as a poorly performed scan can result in many artefacts. Sometimes, the quality of the study cannot be improved significantly by repeated imaging the same day (e.g. large body habitus,
insufficient dose, persistent unavoidable patient movement, interposition of sub-diaphragmatic activity, etc.) and the patient should be re-scheduled.
REFERENCES TO SECTION 4


5. INTERPRETATION AND REPORTING OF MPI STUDIES

5.1. INTRODUCTION

A systematic review of the images and study details is important to ensure that the report is complete and comprehensive [5.1, 5.2]. Appropriate review of myocardial perfusion images includes the steps of quality control (QC), image display, artefact recognition, and image interpretation.

5.2. QUALITY CONTROL

5.2.1. Raw projection images

The raw projection images (Fig. 5.1) must be reviewed in cine mode to determine the presence of potential sources of image degradation and artefacts. The raw projection images are used to evaluate several important items:

— **Counting statistics**: Injection can be checked if extravasation is suspected.

— **Tracer bio-distribution**: Abnormal distribution of the tracer, for example in the stomach, or lack of visualization of the myocardium, represents poor labelling efficiency and the study should be repeated after quality control of the radiopharmaceutical.

— **Patient motion**: Since conventional SPECT images are obtained in a step and shoot mode, patient motion is evident on the rotating projection images as a step up or down.

— **Soft-tissue attenuation**: Photon attenuation from the soft tissues (breast in females, diaphragm in males) could cause false positive results.

— **Interposition of metallic objects**: These can rarely cause artefacts but should be identified.

— **Increased pulmonary uptake of radiotracer**.

— **Position of sub-diaphragmatic organs**: Excessive uptake in the liver, gall bladder and bowel, and hiatus hernia can cause imaging artefacts and should be recognised.

— **Extra-cardiac abnormal areas of focal increased or decreased uptake**: For example, focal uptake in the breast or lung could represent an unsuspected cancer and a focal decrease in uptake could be seen in liver or kidney cysts.

— **Missing projections**: This can eventually occur due to camera malfunction.

— **Acquisition zoom**: Should be the same for stress and rest. Similar image acquisition zoom will be important to adequately align both sets of images.

— **Arms position**: Should be the same for stress and rest. Usually, the left arm is raised above the shoulder and must be in a similar position during the rest and stress acquisition.
— *Truncation of the heart in some projections*: This is more common with large hearts and should be considered since it can result in incomplete evaluation of myocardial segments after reconstruction.

![Image of chest with SPECT MPI study](image)

*FIG. 5.1. Anterior view of the chest from a set of 64 projection images of a SPECT MPI study depicting normal biodistribution of 99m-Tc-sestamibi.*

5.3. **GATING PROCEDURE**

Gated studies are the standard in MPI and quality should be checked before quantitative results of ventricular function are considered reliable.

— The QC page of the gated images typically shows a beat histogram. It should present a narrow peak (less variable R-R cycle lengths); a widened peak or multiple peaks would indicate variable heart rate, frequent arrhythmias, or improper gating.

— A sinogram analysis is helpful in detecting EKG gating errors and should be used whenever in doubt. With significant gating error, beats may be rejected and the sinogram may show missing data.

5.3.1. **Reconstructed images**

Once the SPECT myocardial images have been reconstructed, several steps are to be performed before the information is considered ready to be interpreted. To ensure quality of data and to minimize the possibility of artefact production or to facilitate its recognition, the following verifications are necessary.

— *Alignment of slices*: Stress and rest set of slices should be correctly aligned- that is: Short axis (SA), vertical long axis (VLA) and horizontal long axis (HLA) tomograms should be displayed in a way that each stress slice corresponds anatomically with a matching rest slice for comparison (Fig. 5.2.). It is possible that ventricular size differs in respective situations (typically larger at stress if severe ischemia is present), so precise slice-matching may be difficult or even impossible. In any case, it is recommended that a stress mid-ventricular tomogram is selected and matched with the corresponding rest image, then the matching pair of slices positioned at the centre of the display, with corresponding number of slices at both sides.
Count density for stress and rest: Visual assessment of count density is important to ensure adequate comparison and avoidance of artefacts or wrong interpretation. Poor signal-to-noise ratio may be due to partial dose extravasation at injection, poor labelling of the radiopharmaceutical, biodegradation of the tracer with low myocardial uptake, or mismatch between patient body habitus (weight) and injected dose (i.e., using a standard dose for an obese patient instead of adjusting it by weight). Poor signal-to-noise ratio may lead to the false appearance of reversible defects. Reprocessing of data using different filter parameters to compensate for low count density or even a repeat study might be necessary.

Selection of LV long axis: Reorientation of the heart after SPECT reconstruction should be done by proper selection of the LV long axis in the stress and rest studies; otherwise the orthogonal planes depicted by the three sets of slices will not be perpendicular to each other and comparison can be misleading.

Masking: Masking is particularly important in order not to include extra-cardiac activity (Fig. 5.3.); if masking is not properly performed, any structure with activity higher than that of the myocardium can produce scaling artefacts with apparent lower cardiac counts in the corresponding images.
— Normalisation: Usually, image count normalisation is automatically performed by the software on display; if this is not the case the operator will need to do it taking as reference the maximum count density in any image of the pair of image sets. Caution must be taken not to normalise against a ‘hot’ extra-cardiac structure due to inadequate masking.

5.3.2. Polar maps

These are helpful tools for study interpretation but are subject to a number of errors.

— Generation of polar maps require that the basal and apical limits of the myocardium are properly selected; even if current software packages can perform the operation automatically, it is recommended that these limits are checked visually by the operator.

— A basal limit positioned away from the base will produce an external ring ‘defect’ in the polar maps, whereas a limit away from the apical tip will produce a central circular ‘defect’.

5.3.3. Gated images

Accurate calculation of LVEF is based on an edge-detection algorithm that permits the three-dimensional geometrical evaluation of ventricular volumes.

— Verification of the computer-generated contours, especially the endocardial contours, is essential for assessing the reliability of the software performance.

— This also includes checking the automatic selection of apical and basal (valvular plane) limits, as well as the LV long axis (Fig. 5.4.).

— If inaccuracy is detected, the operator is usually able to correct the contours or some reference limits affecting their positioning.

— Cine display (‘beating heart’) is essential to check for missing frames, ‘flickering’, and other gating artefacts.

FIG. 5.4. Computer-generated LV contours of gated images used for calculation of LV volumes and EF. Contours should only track myocardial activity and the valve plane.
5.3.4. Attenuation correction

Attenuation artefacts can limit the specificity of SPECT MPI [5.3].

- Due to energy considerations, TI-201 images are more prone to attenuation artefacts than 99m-Tc images.

- There are several ways to deal with attenuation artefacts; most commonly, gated images are used to differentiate attenuation artefacts from real defects. Fixed perfusion defects with normal wall motion and wall thickening on the gated images are typically assumed to represent attenuation artefacts.

- Soft-tissue attenuation can be measured using a transmission map and corrected. Transmission maps can be performed using a dedicated radionuclide line source (Ga-153 or Ge-68), or a low-dose CT scan of the chest. The transmission/attenuation maps are typically performed before or after the emission scan.

- The transmission maps need to be checked for count density and count uniformity. This is particularly important for radionuclide source attenuation maps. If the source activity is old (decayed), the attenuation map can be count-poor and will need to be acquired for a longer duration. This is not a problem with CT based AC, since the transmission maps are typically count rich.

- The other QC step in attenuation correction is to check for registration of the transmission and emission images. This is critical to avoid artefacts from mis-registration between transmission and emission images. Registration should be checked in the axial, sagittal and coronal projections, as well as the standard cardiac planes of short axis, horizontal and vertical long axis images.

- If the transmission and emission images are mis-registered, they need to be re-aligned appropriately using software and a new attenuation map needs to be generated. The emission images must then be corrected for attenuation using the new attenuation map.

5.4. IMAGE DISPLAY

5.4.1. Slice display

Interpretation of the myocardial perfusion scan findings is based primarily on assessment of the conventional SPECT slices.

- The standard cardiac tomographic image sets should be used: Short-axis oblique, vertical long axis and horizontal long axis.

- Summed gated images must be used for slice display.

- The LV should be well represented. All slices must be properly aligned and normalized.

- Proper adjustment of brightness and contrast might be necessary in the presence of hot spots.
— It is recommended that image interpretation be performed using the computer monitor whenever possible.

— Good quality colour hard copies may be used as an alternative only if these are consistent with the computer monitor images.

— If images are provided together with the report, they should reflect the findings and interpretation of the report.

5.4.2. **Polar map display**

— Polar maps should only be used for assisting interpretation of image slices, and not be interpreted on its own.

— The polar map display varies depending on the software used.

— The reference polar map used should take into account factors such as the radiotracer, gender, body habitus, and prior mastectomy.

— Interpreting physicians should recognise that the loaded polar maps may not conform to their patient population. Ideally, a local reference polar map should be used if available.

5.4.3. **Gated display**

The gated display format will be largely dependent on the software available.

— Representative slices of all the axes should be shown (at a minimum the apical, mid-ventricular and basal short-axis, central vertical long axis and central horizontal long axis).

— The left ventricular contours as outlined by the software should be checked to make sure that only myocardial activity is tracked (the study should be reprocessed as necessary).

— Gated slices are preferably read without the contours.

— The grey scale is recommended for wall motion assessment.

— Due to the ‘partial volume effect’, wall-thickening is more easily assessed using a colour scale.

— LVEF should be considered reliable if proper contouring is achieved and there is no significant arrhythmia. Software based gated scoring is typically not used for clinical interpretation.

— A good QC for gated images is to evaluate the LV volume curve and to check for the integrity and shape of all phases of the curve (Fig. 5.5.).
FIG. 5.5. Volume curve of the left ventricle (black curve) of a 16-frame gated SPECT study, showing a normal shape (systolic and diastolic phases). Checking the LV volume curve is a critical aspect of the study QC.

5.4.4. Three-dimensional images and quantitative analysis

Since artefacts can lead to quantification errors it is advisable to always use these software tools with caution, and compare them with slides and raw data.

— Three-dimensional volume-rendered static (perfusion) and gated (ventricular function) images (Fig. 5.6.) may assist in image evaluation but should not be used as the primary images for diagnostic interpretation.

— Similarly, automated semi-quantitative or fully quantitative scoring software should not be the sole basis for study interpretation, and should only be used for supplementary information or to double-check the visual findings.

FIG. 5.6. Left and right, respectively: Three-dimensional volume-rendered static perfusion image, and gated end-diastolic and end-systolic volumetric display depicting anterior-apical abnormalities in perfusion and wall motion. These types of images should be used only as an aid for study interpretation.
5.5. ARTEFACT RECOGNITION

5.5.1. Motion artefacts

Patient motion is one of the most frequent sources of artefacts in MPI [4.4, 4.5].

— Besides checking for patient motion by looking at the rotating raw data or the sinograms, once the images have been reconstructed motion artefacts can be recognized.

— Usually, motion artefacts produce a characteristic misalignment of myocardial walls in the horizontal long axis slices, more prominent at the apex.

— In the short axis images, motion is suggested when the so-called ‘hurricane sign’ appears, with a ‘tail’ of activity emerging from one of the myocardial walls.

5.5.2. Attenuation artefacts

Soft-tissue photon attenuation in the thorax leads to a non-uniform reduction of counts from myocardial activity, possibly producing imaging artefacts (Fig. 5.7.). The extent of these artefacts is based upon the distribution of the soft tissue, bone and lung, overall patient body size, and the depth of the heart in the thorax [5.4].

— Attenuation artefacts usually manifest as a persistent perfusion defect that may be incorrectly interpreted as a true perfusion defect, i.e. a myocardial scar. In addition, these ‘defects’ may demonstrate reversibility with changes in position and may be confused with myocardial ischemia.

— This may produce a decrease in diagnostic accuracy due predominantly to an increase in false positive studies, although sometimes this may also lead to an under-interpretation of true perfusion abnormalities, when the effects of soft tissue attenuation is overestimated by the observer.

— Diaphragmatic attenuation is most often seen in men and occurs in up to 25% of MPIs. It results in a variable decrease in counts detected from the inferior wall, which may be confused with an inferior wall scar. Although there is generally a relationship between diaphragmatic attenuation and body size, this is not always predictable. Prone imaging can overcome the problem in the majority of cases; however acquisition time is prolonged. Usually, acquiring only the stress study in the prone position will suffice to demonstrate the presence of inferior wall attenuation.

— Breast attenuation produces the effect of less photons emanating from the anterior regions of the heart and may occur in up to 40% of women; furthermore, these artefacts can occur in a variety of locations — anterior, anterolateral, anterosetal, and apical. Special concern for artefacts arises in women with breast implants or following mastectomy. Although quantitation software takes breast tissue into account by the development of normal female databases, these databases cannot account for all body types. Repeating the study with breast re-positioning might reveal that an anterior defect was due to an attenuation artefact.
Attenuation due to obesity can produce global or localized attenuation artefacts which are difficult to predict. In general, the use of 99m-Tc agents (with higher photon energy) rather than TI-201 and adjusting the injected dose by patient weight will help to minimize artefacts.

Analysis of gated images showing preserved wall motion and thickening is useful to characterize most fixed attenuation artefacts [5.5]. The generation of attenuation maps with external sources or CT may overcome the problem of soft tissue attenuation artefacts, although these methods are not widely available.

5.5.3. Extracardiac activity

Activity in various sub-diaphragmatic organs can interfere with evaluation of perfusion of inferior wall.

In patients with hiatus hernia and prominent gastric uptake there can be overlapping with lateral wall activity of the LV. Intense liver activity adjacent to the inferior wall may render impossible to tell if there is any defect; a repeat acquisition with longer delay may result in cleared liver activity.

5.5.4. Extravasation of tracer

Infiltrated injection results in low counts in the corresponding stress or rest images, making difficult to assess the presence of defects.

This may result either in overestimation or underestimation of defects and a repeat study might be necessary, depending on the degree of degradation.

5.5.5. Polar plots

Proper delineation of the apex and base segments of the polar plots is critical.

Raw patient polar plots at rest, stress and reversibility should be reviewed.

Gender and tracer specific polar plots are recommended to define the extent and severity of perfusion defects on the polar plots.
5.5.6. Gating errors

— Gating two waves per cycle (i.e. P and R waves) will result in two beats per cycle when reviewing the gated images in cine display. The volume curve will show two humps and valleys instead of a single one.

— High variability of R-R interval during gated acquisition will result in image ‘flickering’ due to loss of counts of the last images in the cardiac cycle. The volume curve will show a tail ‘drop off’.

5.5.7. Hot spots

— High activity areas (‘hot spots’) close to the heart may interfere with interpretation.

— If there are hot spots with ‘negative’ (cold) surrounding areas due to a FBP artefact, reconstruction with iterative methods should be attempted.

— Incidental findings, especially hot spots in the lungs should be confirmed both in the reconstructed and raw images, with appropriate localization in the SPECT tomograms (if necessary, a specific reconstruction should be performed) and the information included in the report.

5.6. IMAGE INTERPRETATION

5.6.1. Perfusion defects

The perfusion images should be interpreted without knowledge of the clinical and stress information (to avoid bias), as categories of normal, probably normal, equivocal, probably abnormal or abnormal. Once the images are interpreted, the clinical and stress data can be reviewed and the interpretation finalized as normal or abnormal and the terms of probably normal or probably abnormal must be avoided.

— Normally, there should be homogeneity of tracer uptake in the LV myocardial wall on both rest and stress images.

— Any segmental or diffuse decrease of uptake during stress would correspond to ischemia, if reversible on rest images.

— The finding could correspond to an infarct if the defect is fixed (similar on both phases). However, hibernating myocardium could produce the same result.

— Areas of mixed reversible and fixed defects can also be identified as infarct plus ischemia.

— All findings would be supported by semi-quantitative analysis with available software (Fig. 5.8.). The software could help in determining the severity and extent of defects.
FIG. 5.8. Semi-quantitative perfusion analysis with polar plots, 3-D LV display, summed scores and 17-segment model in a patient with anterior and apical ischemia.

— A 17-segment ASNC/AHA/ACC visual scoring method is recommended for visually scoring the myocardial perfusion defects. The suggested model is shown in Fig. 5.9.

FIG. 5.9. SPECT myocardial segmentation using a 17-segment model: 1 = basal anterior, 2 = basal anteroseptal, 3 = basal inferoseptal, 4 = basal inferior, 6 = basal anterolateral, 7 = mid anterior, 8 = mid anteroseptal, 9 = mid inferoseptal, 10 = mid inferior, 11 = mid inferolateral, 12 = mid anterolateral, 13 = apical anterior, 14 = apical septal, 15 = apical inferior, 16 = apical lateral, 17 = apex.

5.6.2. High risk scan features

The following features should be noted on the image interpretation as high risk scan features and, when present, preferably be communicated to the referring physician.
Findings in MPI studies associated with high risk of cardiac events:

- Transient dilation of the left ventricle.
- Transient increase in right ventricle uptake.
- Increased pulmonary uptake of radiotracer.
- Multiple and extensive perfusion defects.
- Transient wall motion abnormalities.
- Post-stress LVEF lower than rest LVEF.

5.6.3. 

**Transient ischemic dilatation of the LV**

Before segmental analysis of the perfusion images, it should be noted whether or not there is LV cavity enlargement at rest, post stress or both. Transient ischemic dilation is defined based on the endocardial borders of the LV cavity observed on the static/summed images (there is no consensus about using gated images). An increased stress:rest LV cavity ratio (Fig. 5.10.) has been described as a marker for high risk (severe and multi-vessel coronary disease). Although non-specific for ischemia, when not associated with segmental perfusion defects TID may represent either global sub-endocardial ischemia or balanced ischemia in the 3 coronary territories. TID is described qualitatively but may be quantified using software. Normal upper limit of TID (LV cavity ratio) is 1.2–1.3 but may vary based on the study protocol and radiotracer used. Apparent TID may be observed in dual isotope studies (rest Ti-201 and stress 99m-Tc), and hence the normal limits may be higher compared to single isotope protocols.

![Image](image.png)

**FIG. 5.10.** Transient ischemic dilation (TID) of the left ventricle. LV volume is greater at stress (upper row on each set of paired images) than at rest (bottom row). TID is an additional high-risk finding with independent prognostic value, although severe and extensive perfusion defects (like in this particular case) are frequently – but not always – present as well.
5.6.4. **Lung uptake**

The presence of increased lung uptake during rest or post stress TI-201 imaging has been described as an indicator of poor prognosis. This can also be observed with 99m-Tc radiopharmaceuticals with exercise or pharmacological stress imaging (Fig. 5.11.). Typically, it is estimated visually based on the review of the rotating projection images. Software may be used to draw regions of interest and compute lung/heart ratios (L/H). Ratios >0.45 for 99m-Tc and >0.55 for TI-201 are considered abnormal.

**FIG. 5.11.** Lung uptake of 99m-Tc-sestamibi at rest (anterior view of raw projections) in a patient with recent myocardial infarction and impaired ventricular function. Lung uptake can be assessed either qualitatively or quantitatively.

5.6.5. **Stunning**

Stunning is defined as a prolonged reduction in LV systolic function following a transient episode of severe ischemia that does not result in myocardial necrosis. Ischemia can produce a decrease in global LVEF associated or not with transient global or segmental hypokinesia. Stunning is typically observed on the gated images as regions of reduced regional wall motion and wall thickening corresponding to regions of severe myocardial ischemia. Presence of stunning in the context of reversible perfusion defects improves the specificity for identifying ischemia. Post-ischemic stunning and reversible regional wall motion abnormalities also improve the sensitivity to identify severe obstructive CAD. There is no consensus on what to consider significant difference between post-stress and rest LVEF, although a 10% difference is generally accepted.

5.6.6. **RV tracer uptake**

Right ventricular uptake may be qualitatively assessed on the raw projection data and on the reconstructed data (Fig. 5.12.). In general, the intensity of the RV is approximately 50% of maximum LV intensity. RV uptake increases in the presence of RV hypertrophy or overload, most typically because of pulmonary hypertension. The intensity of the RV may also appear relatively increased when LV uptake is globally reduced. Transient increase in RV tracer uptake (>20% higher RV uptake compared to LV uptake) is a specific sign of left main disease. The size of the RV should also be noted, as RV dilation can provide a clue to the presence of right heart volume overload due to conditions such as atrial-septal defect or severe tricuspid regurgitation.
5.6.7. Multiple and extensive perfusion defects

Several studies have demonstrated the prognostic value of myocardial perfusion images [5.6]. The number as well as the extent of perfusion defects are powerful predictors of future adverse cardiovascular events [5.7].

![Image of SPECT study](image)

**FIG. 5.12. Short-axis slices of a SPECT study. At stress (upper row) the right ventricle is clearly seen, associated with extensive LV perfusion defects which are mostly reversible at rest (bottom row) where RV uptake almost disappears.**

5.7. REPORTING AND ESSENTIAL ELEMENTS OF A COMPREHENSIVE REPORT

5.7.1. Introduction

Accurate reporting is one of the most critical steps in MPI. The report is the final product of a complex process, involving substantial human and material resources. Quality reports typically must be concise and include all the relevant information for the referring physician [5.1, 5.2]. Structured reporting will facilitate not only high quality patient care but also appropriate recognition and accreditation by the health system, insurance companies and academic institutions. Reports include separate sections on demographics, methods, interpretation and conclusions related to the stress test, static and gated myocardial perfusion images (including all of the critical elements listed in section 5.8). Calcium score and CT coronary angiogram studies are also reported when performed as a part of the MPI study with hybrid systems.

- **Demographics**: The patient age, gender, coronary risk factors, prior cardiac history, cardiac medications and rest ECG information should be listed in this section.

- **Clinical question or reason for referral**: This is a very important point and should be clearly stated.

- **Stress test**: The details of the stress test must be provided (Table). Whenever possible, the stress test report should be combined with the MPI report. If not, the relevant details of the stress test report must be also included in the MPI report.

- **Acquisition protocol**: The MPI report must include details about the technique and type and dose of radiotracer used. The imaging protocol including attenuation correction parameters (if performed) should be described.
— **General description**: A comment about image quality (un-interpretable, fair, good, excellent). The LV and RV size, relative cavity size between stress and rest (TID), and lung tracer uptake should be described first.

— **Perfusion defects**: The defect size, severity, location and reversibility must then be described following either vascular distributions or myocardial walls or segments. Reporting the summed scores is generally not routine, unless specifically requested by the referring physician or when a quantitative follow-up evaluation might be relevant.

— **LV function**: It should be reported including estimation of global LV systolic function (LVEF), regional wall motion and wall thickening whenever feasible. LVEF values greater than 75% should be reported as “>75%” and EF less than 15% as “<15%” without giving specific numbers (e.g., if EF = 90%, report should read “LVEF >75%; if EF = 11%, report should read “LVEF <15%”). If height and weight are available, LV volumes may be normalized to body surface area (it is recommended not to report EDV <60 ml). Any high risk scan features can be described.

— **Conclusions**: This section must include a definitive statement about the overall scan results taking into consideration the stress ECG and MPI findings.

  — The clinical question should be specifically addressed.

  — The report should clearly state whether the overall study is normal or abnormal. Terms of ‘probably’ or ‘equivocal’ should be avoided.

  — A list of possible causes for the imaging findings (e.g. attenuation vs. scar, vs. ischemia) should be avoided in this section.

  — The gated results must be summarized also as normal or abnormal.

  — High risk scan features should be highlighted.

  — Medium or low-risk classification should be reported optionally.

  — Comparison should be made to prior study images if available.

  — Essential components for the report are listed below.

**ESSENTIAL ELEMENTS OF A COMPREHENSIVE REPORT**

5.7.2. **General information**

*Information about the laboratory and study date.*

*Name of referring physician and contact information.*

*Patient demographics:*
  — Name.
  — Age and Gender.
  — ID number.
  — Institution.
  — Contact information (telephone number, address).
5.7.3. Clinical background

Clinical reason for test; common reasons (among others):

— Diagnosis of CAD.
— Risk stratification in chronic CAD.
— Risk stratification after myocardial infarction.
— Risk stratification before non-cardiac surgery.
— Evaluation of therapy.

Clinical history:

— Coronal risk factors.
— Past cardiac history.

Current cardiac medications (specify withdrawal).

Resting ECG interpretation.

5.7.4. Methods

MPI protocol:

— One day/ two day/rest-stress or stress-rest.
— Radiotracer type and dose used for rest and stress.
— Attenuation correction technique (if performed).
— Imaging position:
  — Supine
  — Prone
  — Supine followed by prone

Stress protocol:

— Protocol type.
— Exercise duration.
— Functional capacity (METS).
— Resting HR, systolic and diastolic BP.
— Maximal systolic and diastolic BP.
— Maximal HR and % of age predicted maximal heart rate achieved.

Stress ECG changes:

— Arrhythmias: Type of arrhythmia should be described.
— ST segment changes: ST depression or elevation (mm). Type of depression (horizontal/down/up-sloping). HR or workload at onset of ST changes. Time at which ST changes resolved.
— Symptoms: Type of symptoms (chest pain, dyspnoea). Type of pain (typical/atypical). HR or workload at onset of symptoms. Time at which symptoms resolved. Intervention required if any (nitrates, etc.).

Reason for termination of test:

— Exhaustion.
— Chest pain.
— ST changes.
— Arrhythmias.
— BP.
— Others.

5.7.5. Perfusion (rest and stress 99m-Tc perfusion imaging)

Overview:
Image quality (good or with technical limitations due to: Patient motion, dose extravasation, body habitus of the patient, attenuation artefacts, etc.).

— LV size (rest LV size and transient cavity dilation if present).
— LV hypertrophy.
— RV size and tracer uptake.
— Lung uptake.

Defect description:

— Size.
— Severity.
— Location.
— Reversibility.

5.7.6. Ventricular function:

— Segmental wall motion assessment (visual).
— Wall thickening (visual).
— RV function (visual).
— Post stress/Rest LVEF (recommended).
— Rest LVEF only (optional for one day protocol).
— LV volumes (optional).

5.7.7. Ancillary findings

Any abnormal increase or decrease in radiotracer distribution, focal uptake.

5.7.8. Conclusions

Myocardial perfusion:

— Normal.
— Abnormal: Describe the extent and magnitude of scar and/or ischemia. A statement about risk if high risk findings are seen

LV function:

— Normal or abnormal.
— Post stress stunning.

Comparison to prior studies (date and findings if changed or unchanged).

Final report should be sensitive to the needs of the local community and answer the primary question posed by the referring MD.

Date of report and signature.
REFERENCES TO SECTION 5


APPENDIX I.

PATIENT INFORMATION BROCHURE

The need for patient education before the scan must be emphasized. The patient is to be informed of the risks and benefits of the procedure, the technical details of the actual stress test and the imaging protocol, the need to avoid medications as instructed by the referring physician, the need to avoid caffeine for 24 hours before the test, etc. These are all important details that should be given to the patient as a brochure before the actual test, so that he or she can conform to the instructions. The brochure will serve to keep the patient informed, so as to avoid unexpected circumstances on the day of the test.

Note: This procedure serves as a guide to what a comprehensive Brochure should include, therefore if there should be information that does/does not apply with your internal procedures at the Institute, then make sure to accommodate these changes accordingly.

Information for the patient:

— Please bring your medications and any medical history information with you.
— If you are breast-feeding, pregnant or think you may be pregnant, please inform your doctor and staff about this, since other tests may be recommended and could be preferred in this case. You should discuss further procedures with your doctor who may advise you to postpone the test.
— Your doctor has ordered a Myocardial Perfusion Scan for assessment of your heart arteries. This test is actually a scan of the blood flow in the heart muscle, an indirect indicator of the status of the patency of your coronary arteries.
— To perform this test, your doctor would have informed you of certain medications that you should avoid for a period of time (usually some days) to make the test more accurate*. If not, please continue all regular medications. Do not take drugs for erectile dysfunction for 2 days prior to the studies.
— Please also avoid all caffeinated beverages (coffee, all forms of tea, chocolate drinks, chocolates, soft drinks (such as Coca Cola, Pepsi Cola, 7 Up, Sprite, Root Beer, etc.) for 24 hours before the test, as this may interfere with the efficacy of the stress testing.
— An intravenous device will first be inserted into a vein in your hand or elbow.
— The protocol may either start with a stress test or with a tracer injection for a rest scan. In certain circumstances, another injection of tracer may be given later the same day or after 24 hours for better diagnostic accuracy.
— Subsequent to completing this test, your referring physician may or may not ask you to continue to another form of medical imaging (e.g. CTA or calcium score) as required, depending on the result.
— To perform this test, you will be required to do some form of exercise (stress) on either a treadmill exercise machine (walking, jogging, running) or a bicycle ergometer (cycling).
— Please wear proper exercise attire and comfortable shoes for this test.
— If you think you are unable to exercise, or the doctor has directed you not to exercise, you will instead be given intravenous medication to ‘stress’ your heart. You may also be required to perform some slow walking or cycling if possible.
— Possible mild self-limiting side-effects of the medication given for the ‘stress’ state, may include nausea, vomiting, a hot feeling, abdominal discomfort, headache &
giddiness. These side-effects may last for approximately 5-10 minutes following the infusion in approximately 40-50% of patients given the medication. We do have an antidote to the medication which can be given if necessary.

— The test will also involve an injection of a radioactive tracer into you vein. The amount of radiation involved is very small and will disappear within hours.
— To promote more rapid removal of the tracer from the body, you are encouraged to drink liquids liberally to promote urinary excretion. However, because of the short lifespan of the tracer, most of the radioactive tracer would be automatically inactivated quickly.
— There are no significant side effects of this tracer, except perhaps a short-lasting metallic taste in the mouth.
— You will then be under the scanning machine (gamma-camera) 5 to 60 minutes after the stress test, depending on the tracer injected.
— This will require you to lie (on your back or chest/abdomen) on a couch while the camera taking pictures of your heart rotates around you.
— You will be asked to lie as still as possible for about 3-20 minutes, breathing in a regular manner, without taking deep breaths.
— The camera may come very close to your chest but will not touch or harm your body in any way.
— The interpreting physician will then look at the results of your heart scan. Usually, a second scan is required in the resting state so a second injection of tracer will be required, either on the same day or on another day.
— Before the rest scan injection, you may occasionally (depending on the clinical question to be addressed by the test) be given a tablet to be placed under the tongue and allowed to dissolve slowly.
— After the second tracer injection, you will be required to wait for about 20-60 minutes before your scan is performed. Upon completion of the scan, the technologist will inform you when you can go home.
— In total, you may have to spend up to 6-8 hours to complete the entire scan in a single day.
— As there is very little radiation involved using this technique, it is completely safe to resume all forms of daily activities once you have completed your scan. There is no danger of passing the radiation to others around you, and you should not isolate yourself unnecessarily. The only exception is that if there are young children (<10 years) in the household, they should be advised not to be in your close proximity for the first 6 hours after tracer injection, and women who are breast-feeding should avoid close contact to the baby post-scan.
— The interpreting physician will report on your scan, and then ask you to either pick-up your results or he/she will transmit the results to your referring physician (who will then arrange an interview with you for further advice.
— You should continue with all regular medications, including ones you were told to stop specifically for this test.
APPENDIX II.

CHECKLIST FOR MPI STUDIES

II.1. Scintillation camera quality control

— Scintillation camera quality control should be performed periodically, according to system requirements and to manufacturer’s specifications. They are usually measured according to the National Electrical Manufacturers Association (NEMA).

— Multiple head detectors performance must be matched. Images from the heads aligned.

— Collimators checked periodically. Clear messages to avoid damages during collimator change should be displayed.

— Daily quality control: symmetry of Energy window, position over the photo-peak, low count uniformity (Intrinsic ≤2%, Extrinsic ≤3%, Maximum difference in system sensitivity between heads <5%).

— Periodically (at least every 6 months, frequency depending on stability of systems): spatial resolution, linearity, centre of rotation (COR) offset (128°—128 matrix <0.5 pixel for 360°). Tilt of detector heads, measured by COR (128°—128 matrix), Variation <4mm/1pixel for 360°.

— Check for monitor linearity and uniformity by proper phantoms.

— For comprehensive instructions on scintillation camera quality control, we highly recommend all readers to refer to the IAEA Human Health Series No. 6 for further reading [II.1].

II.2. Radiopharmaceuticals

— Provide all radiopharmaceutical QC as specified by manufacturers.

— Define the range of activities you want to inject to get similar count statistics in all your patients according to patient weight, height and shape.

— Optimize injected activity in order to reach optimal count statistics according to acquisition system characteristics and to keep radiation doses as small as possible (see reconstruction algorithms).

— For further reading we refer readers to the IAEA document on Operational Guidance on Hospital Radiopharmacy, A Safe and Effective Approach [II.2].

II.3. Before acquisition

— Find the most comfortable position on SPECT bed.

— Inform him/her to avoid movements, to breathe normally and to avoid deep breaths.

— In case of problem during acquisition, ask the patient to inform the technologist without moving.
— Inform the patient of the expected acquisition time.

— Check for heart rhythm: Atrial fibrillation, sinus arrhythmia, frequent premature beats, intermittent and dual-chamber pacing etc. These patients should not be studied with ECG triggering or type of rhythm should be registered for the interpreting physician to consider.

II.4. During acquisition

— Ask frequently if everything is OK.

— Inform the patient of the residual time.

— Instruct him/her to avoid movements.

II.5. After acquisition

— Check immediately for lateral or vertical movements of the heart and for extra-cardiac ‘hot spots’ that can interfere with reconstruction and processing (e.g. lung, liver, gall-bladder, muscle) on the rotating cinematic review of the projection data.

— Consider whether repeat acquisition immediately (movements) or after a time interval (hotspots).

— Check for truncation of cardiac activity or severe truncation of body activity.

— Consider a second acquisition in supine/prone position in presence of suspected severe diaphragmatic/breast attenuation.

II.6. Image processing

— Verify the need of applying motion correction algorithms for the vertical movements (≥2 pixel motion, 4mm)

— Prefer iterative reconstruction. Since most of the automatic programs quantifying gated SPECT perfusion data are based on edge detection algorithms and are relatively insensitive to count statistics, it is always recommended to use the same filter parameters independent of the actual count density in a given patient.

— Wide beam reconstruction and resolution recovery with scatter corrections, allowing dose reduction are recommended according to availability.

— When defining contracts for new SPECT equipment acquisitions, consider the opportunity of including these hardware/software packages in the requested options.

— In case of attenuation correction by CT, verify alignment between SPECT and CT in a three dimensional display after motion correction. In presence of discrepancy realign studies manually.

— Always display corrected and uncorrected images.

— Verify perfect correspondence between apical and basal slices in short axis views.
— Verify long axes orientation in both vertical and horizontal long axes
— Realign studies even in presence of minimal differences.
— Set count windows and thresholds in order to have 1 pixel only with maximum count density in the entire myocardium. Do the same for stress and rest images.
— Standardize the use of both linear or colour graded scales. A linear scale should be considered for evaluating myocardial viability.
— The supervising physician is always responsible for the quality of processing
— Perfusion defects must be seen in all projections and in at least two consecutive slices
— Check the correlation between visual inspection of studies and, if available, quantitative evaluation. If needed correct manually the perfusion scores. Consider that discrepancies between visual interpretation and quantitative results can raise doubts about reliability of the study, especially if both results are included in the hard copy (CD). Quantitative analysis should not be used in isolation without qualitative review.
— In gated studies always verify the selection of endocardial, epicardial, valvular edges. If not correct, try to modify them. Sometimes, the LV function cannot be reported or only be reported qualitatively without an LVEF and absolute volume values. In small hearts consider the negative impact of the partial volume effect.
— Always check correlation between perfusion and RWM abnormalities.

II.7. Reporting

— A standardized institutional model should be considered for all physicians entitled to report MPI at that institution (see corresponding section and appendix in this document).
— Verify that in the report are included: reason for the MPI request, description of the stress test results, description of MPI and GSPECT results.
— Clinical conclusion especially focused on the request and with review of previous MPI and to other imaging modalities (if available).
— If possible, adopt a double check and systematic review of the final report.
REFERENCES TO APPENDIX II


APPENDIX III.

EXAMPLES OF MPI REPORTS

III.1. Sample 1

Exercise MPI report adapted with permission from Brigham and Women’s Hospital, Non-Invasive Cardiovascular Imaging Laboratory:

III.1.1. General information:

Referring physician: Dr __________________

Mr/Ms _______, a ____ year old _________male/female with a history of (hypertension, diabetes, dyslipidemia, diabetes, smoking) was referred to us for the evaluation of (typical angina/atypical angina/non-anginal chest pain, dyspnoea, etc.).

Past cardiac history includes (a prior coronary artery bypass surgery or percutaneous coronary intervention, myocardial infarction, etc.).

Medications include: β-Blockers, Antiplatelet drugs, Hypolipidemic drugs.

Resting electrocardiogram was (normal) or showed__________ (describe abnormality).

Study protocol was (Single-day/Two-day 99m-technetium sestamibi rest/stress myocardial perfusion).

The patient received ___mCi/MBq of 99m-technetium sestamibi/tetrofosmin/201-thallium intravenously and (stress) rest gated SPECT imaging was performed.

Attenuation correction was performed using a rotating line source-multidetector CT scan (10 mA, 120 KeV, gantry rotation time 500 msec).

For viability assessment, delayed images were obtained at___time (201-thallium) or nitrates given (Tc-99m tracers).

III.1.2. Exercise stress protocol:

Mr./Ms______ exercised on a ______________(standard Bruce/modified Bruce) protocol for ___minutes (___ METS).

The heart rate increased from ____ beats per minute at rest to _____ bpm at peak stress.

The SBP (increased/decreased/remained unchanged) from _______ mm Hg to______mm Hg during peak stress [(rate pressure product of XXXX (product of peak stress SBP and peak stress heart rate)].

His/her heart rate recovery was ____ (normal < 12 bpm).

The Duke treadmill score was __(≥+5 = low risk, + to -11 = intermediate risk, ≤-11 = high risk).
Exercise was terminated due to __________ (describe reasons for termination: chest pain, fatigue, dyspnea, arrhythmia, ST etc.).

The BP response was (normal/hypertensive/hypotensive).

There were (no symptoms, symptoms = describe) during stress.

There were (no ST segment changes, changes = describe mm, slope) during stress.

There were (no arrhythmias, yes = describe) during stress.

<table>
<thead>
<tr>
<th>Speed / grade</th>
<th>Time</th>
<th>Heart rate (bpm)</th>
<th>Blood pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>1.7 MPH, 10%</td>
<td>2 min</td>
<td></td>
</tr>
<tr>
<td>Stage II</td>
<td>2.5 MPH, 12%</td>
<td>5 min</td>
<td></td>
</tr>
<tr>
<td>Stage III</td>
<td>2.8 MPH, 14%</td>
<td>8 min</td>
<td></td>
</tr>
<tr>
<td>Stage IV</td>
<td>3.4 MPH, 14%</td>
<td>11 min</td>
<td></td>
</tr>
<tr>
<td>Stage V</td>
<td>4.2 MPH, 16%</td>
<td>14 min</td>
<td></td>
</tr>
<tr>
<td>Stage VI</td>
<td>5.0 MPH, 18%</td>
<td>17 min</td>
<td></td>
</tr>
<tr>
<td>Recovery</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

III.1.3. Vasodilator stress protocol:

The left ventricle was (normal/mildly dilated/moderately dilated/severely dilated) in size.

The right ventricle was (normal/mildly dilated/moderately dilated/severely dilated) in size.

The RV tracer uptake was (normal/increased/transiently increased).

The rest and stress myocardial perfusion images were normal (or the stress myocardial perfusion images demonstrated a _______(small/medium/large) perfusion defect of_____ (mild/moderate/severe) intensity in the ________(list segments in vascular distribution) that was ______________(fixed, reversible, mildly reversible, moderately reversible, completely reversible).

III.1.4. Gated myocardial perfusion images:

The left ventricle was (normal/abnormal in size with normal/abnormal wall motion and thickening).

The post stress/ rest LVEF was normal (abnormal) at______%.

The right ventricle was normal (abnormal) in size with normal (abnormal) wall motion and thickening.

III.1.5. Ancillary findings:

None, or (there was a focal abnormal increase in Tc-99m Sestamibi uptake in the region of_______; suggest clinical examination and further evaluation if clinically indicated).
III.1.6. **Conclusions:**

— The rest and stress myocardial perfusion imaging study was normal (or abnormal demonstrating a large/medium/small area of severe/moderate/mild ischemia in the anterior, anteroseptal and apical walls, or vascular distribution optional).

— The gated study was normal, or abnormal and demonstrated (wall motion abnormalities = describe).

— LVEF values were within (below) normal limits, and post-stress LVEF was similar (decreased with respect to) rest LVEF.

— A prior myocardial perfusion study was performed on _____(date). The current study demonstrates (no significant change / significant disease progression / significant improvement) when compared to the prior study in the anterior/lateral/inferior walls.

— Viability: Based on the imaging findings, the myocardial segments are (viable or non-viable).

Signed by: Dr. _______________________      Date_____________________________
III.2. Sample 2

Stress MPI Datasheet reproduced with permission from Cardiac PET and PET/CT, Eds. Di Carli and Lipton, Springer:

III.2.1. General information

Nuclear Cardiology/Stress Laboratory, XXX Hospital

NAME: ID:

DATE OF TEST: __/__/__   [ ] Outpatient   [ ] In-patient  Room #: 

Test Location - Nuclear Medicine / Cardiology

DEMOGRAPHICS:

DOB: Age: 

Sex: Male Female

Height (in):______(mts)_______ Weight: (lbs)______ (kg)_______ BSA:______

Address & Phone: _______________________________________________

Staff physician: ______________________________, MD, Phone No._____________

Referring physician: __________________________, MD, Phone No._____________

Fellow: Physiologist: Technologist:

Most recent stress test result:

Brief history:

<table>
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<tr>
<th>Cardiac risk factors</th>
<th>Yes</th>
<th>Prior cardiac history</th>
<th>Date</th>
<th>Chest pain history</th>
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<tbody>
<tr>
<td>Hypertension</td>
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<td>No Cardiac Hx</td>
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<td>Dyslipidemia</td>
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<td>Recent MI (&lt;1mo)</td>
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<td>Diabetes</td>
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<td>Prior MI (&gt;1 mo)</td>
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<td>No</td>
</tr>
<tr>
<td>Family Hx</td>
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<td>CABG</td>
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<td>Exertional</td>
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<td>Tobacco</td>
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<td>PTCA</td>
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<td>CHF</td>
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<td>Postmenop.</td>
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<td>relieved by</td>
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<td>Vascular Dz</td>
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<td>rest/NTG</td>
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### Reason for test

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### Medications

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<td>Digoxin</td>
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<tr>
<td>Betablockers</td>
<td>Diuretics</td>
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<td>Ca channel blockers</td>
<td>Other</td>
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<td>ACE inhibitors</td>
<td>ALLERGIES?</td>
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### Normal ECG

<table>
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<tr>
<th>Rhythm</th>
<th>A-V conduction</th>
<th>Infarct pattern (Q wave)</th>
<th>ST-T changes</th>
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</thead>
<tbody>
<tr>
<td>Normal sinus</td>
<td>1stº AVB</td>
<td>Inferior (2,3.AVF)</td>
<td>Non-spec ST abn</td>
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<tr>
<td>Sinus brady</td>
<td>2ndº AVB, Mob1</td>
<td>Post-lat (tall R V1-V2)</td>
<td>Non-spec T abn</td>
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<tr>
<td>Sinus tachy</td>
<td>2ndº AVB, Mob2</td>
<td>Ant-sep (V1-V2)</td>
<td>Non-spec ST/T abn</td>
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<tr>
<td>Atrial fibrillation</td>
<td>WPW</td>
<td>Anterior (V1-V4)</td>
<td>ST dep c/w ischemia</td>
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<tr>
<td>Atrial flutter</td>
<td>Cond abnorm</td>
<td>Lateral (V5-V6)</td>
<td>Early repolarization</td>
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<td>RBBB</td>
<td>Poor R wave progr</td>
<td>Long QT</td>
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<td>LBBB</td>
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<tr>
<td></td>
<td><strong>Hypertrophy</strong></td>
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<tr>
<td>APC’s</td>
<td>LAHB</td>
<td>LVH w/repolarization</td>
<td>L atrial enlargement</td>
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<tr>
<td>PVC’s</td>
<td>LPHB</td>
<td>LVH</td>
<td>R atrial enlargement</td>
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<tr>
<td>Other</td>
<td>IVCD (&gt;0.12 s)</td>
<td>RVH</td>
<td>Other</td>
</tr>
</tbody>
</table>

### III.2.2. Stress protocol:

- [ ] Bruce
- [ ] Modified Bruce
- [ ] Dobutamine
- [ ] Dipyridamole
- [ ] Adenosine
- [ ] Regadenoson

85% of APHR (age predicted heart rate): ____________
### III.2.3. Result of stress test:

**Exercise time (min):** ________

<table>
<thead>
<tr>
<th>Minutes</th>
<th>Stage/Dose</th>
<th>HR</th>
<th>BP (mmHg)</th>
<th>ECG</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>REST</td>
<td>Supine:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Standing:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STRESS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RECOVERY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Rest HR: _______ bpm  Peak HR: _______ bpm
Rest BP: _________ mmHg  Peak BP: _________ mmHg

% of APHR: _______  RPP: _______  METS achieved: _______

ST changes during the test: Y / N,  Chest pain during the test: Y / N
Dipyridamole: _______ mg
Adenosine: _______ mg
Amynophylline: ______ mg
Max Dobutamine: ______ mcg/kg/min  Atropine: ______ mg  Metoprolol: ______ mg
NTG: _______ mg

Rest  99mTc Dose: ______ mCi,  Stress 99mTc dose: ______ mCi
III.2.4. **Reason for termination:**

- [ ] Achieved target workload
- [ ] Completed infusion
- [ ] Leg fatigue
- [ ] Mod-severe chest pain
- [ ] Dyspnea
- [ ] Fatigue
- [ ] >10 mm Hg drop in BP
- [ ] Sustained VT (≥3 beat run)
- [ ] ST elevation (≥1.0 mm)
- [ ] ST depression (≥2 mm horizontal or downsloping)
- [ ] Hypertensive response (SBP>220 mm Hg and/or DBP>115 mm Hg)
- [ ] Other:

III.2.5. **Blood pressure response:**

- [ ] Normal
- [ ] Flat BP response
- [ ] Hypotensive response
- [ ] Hypertensive response
- [ ] Not applicable – Vasodilator stress
- [ ] Other:

III.2.6. **Arrhythmias:**

- [ ] None
- [ ] Atrial Fib/Flutter
- [ ] SVT
- [ ] PVCs: _______________
- [ ] PACs: _______________
- [ ] VT: _______________
- [ ] A-V block: _______________
- [ ] Other: _______________

III.2.7. **ST segment changes:**

- [ ] No ST changes
- [ ] ST segment depression:
  - [ ] Horizontal  [ ] Downsloping  [ ] Upsloping

Max ST depression in leads: _______________

Additional leads with ST depression: ______________________________

Began at ___ min into test, at a HR: ________, at a SBP: ____________

Resolved ___ min into recovery
[☐] ST segment elevation (in non-Q wave lead)

In leads: _______________________

Began at ____ min into test at a HR: _______

Resolved ____ min into recovery

[☐] Other:

III.2.8. Symptoms:

[☐] None

[☐] Typical chest pain: ____/10 during test/recovery

Began at ____ min into test at a HR: ________, at a SBP: _______

Resolved ____ min into recovery

[☐] Atypical chest pain

Began at ____ min into test at a HR: ________, at a SBP: _______

Resolved ____ min into recovery

[☐] Dyspnea

Began at ____ min into test at a HR: ________, at a SBP: _______

Resolved ____ min into recovery

[☐] Other:

III.2.9. Functional Capacity:

[☐] Excellent
[☐] Very good
[☐] Good
[☐] Reduced
[☐] Not measurable – Pharmacologic stress

III.2.10. Impression:

[☐] Negative test for myocardial ischemia
[☐] Positive test for myocardial ischemia
[☐] Positive test for ischemia but reduced specificity due to baseline ECG abnormalities
[☐] Borderline positive test
[☐] Non-diagnostic test due to baseline ECG abnormalities
[☐] Non-diagnostic test due to LBBB
[☐] Clinically significant rhythm disturbance
[☐] No ECG changes during infusion
[☐] ST segment depression during infusion
[☐] Other:

Staff Physician___________________________________________________________
Physiologist/Nurse/Technologist____________________________________________
APPENDIX IV.

STRATEGIES TO REDUCE RADIATION DOSE IN MPI

Myocardial perfusion imaging (MPI) is a radiation intensive technique. According to UNSCEAR 2008 data, 26% of the radiation dose given to a population for medical imaging is attributable to MPI. There are now many alternative strategies to myocardial perfusion imaging that can possibly provide similar information to MPI (e.g. stress ECHO, CT/MR perfusion). There is a trend towards lowering the radiation burden, given the increasing recognition of the lifetime risks of radiation. Modern technology has reduced the dose of cardiac CTA four-fold (20 mSv to 4-5 mSv). Furthermore, MR and ECHO confer no radiation risk when used. Similarly, the nuclear community would also have to develop strategies to reduce the amount of radiation dose needed without sacrificing sensitivity or specificity for the test [IV.1].

Strategies include:

Stress imaging only or stress-rest protocol. For the sake of reducing the amount of tracer and radiation exposure, theoretically if the stress image is completely normal then the rest image is not required [IV.2]. Avoiding an unnecessary rest scan can reduce the amount of radiation exposure by more than a half, depending on the protocol utilized. However, for this to be a reliable protocol, it is suited best for patients at low risk for CAD, and the interpretation of the study should be made by an experienced physician.

Development of solid state (e.g. CZT) gamma-cameras with high photon sensitivity/efficiency. This has resulted in the reduced need for the amount of dose required to obtain a diagnostic image. In general, the new generation cameras have led to the reduction in administered dose of about 40%, without sacrifice in diagnostic accuracy [IV.3, IV.4].

New software algorithms such as Wide Beam Reconstruction (WBR) technology is now incorporated into all major vendor cardiac imaging software. When WBR is combined with resolution recovery and iterative reconstruction, the dose required for a diagnostic image can be reduced by as much as half, even when conventional camera technology is used [IV.5]. This should be validated on the camera-type to be used.

Tc-99m based tracers are associated with a lower radiation load, even when 2 injections are required for a stress & rest scan. The use of TI-201 is associated with an increased radiation dose, especially so if the imaging protocol is combined with a reinjection protocol. The move away from TI-201 is a good way of reducing radiation load for the patient, especially when viability is not an issue. The use of the dual-isotope (TI+Tc) protocol should also be discouraged.

Separate-day protocol. The imaging protocol used for imaging can also influence the radiation dose received by the patient. Subject to patient convenience and scheduling, reduced doses and separate day protocols can be selected, resulting in reduced radiation exposure [IV.6, IV.7].

Tailored dose. The injected dose should be tailored to the size & shape of the patient, and not be provided in a “one size fits all” standard dose. The weight, chest circumference, breast size, etc. should all be taken into consideration when preparing the individual doses.
Cardiac PET. The use of certain PET perfusion tracers can also lead to a reduced radiation load.

The previously mentioned measures will, when used appropriately, reduce the amount of radiation the patient will receive for MPI. The best measure to reduce radiation risk would be to perform MPI in patients who will most benefit from the test. The appropriateness use criteria (AUC) and following national and international guidelines for MPI use should be adhered to, so that MPI is not done inappropriately. The test performed should be a decision between the referring physician and the MPI team.
REFERENCES TO APPENDIX IV


NUCLEAR CARDIOLOGY FOR THE REFERRING PHYSICIAN

The role of myocardial perfusion imaging (MPI) as a gatekeeper for patients with and without documented CAD in the diagnostic algorithm is well established. Choosing the right test for the right patient is in the domain of the referring doctor. While certain patients may be suitable for other non-invasive tests (stress ECG, MRI, echocardiography, or cardiac CT), other patients, particularly with unstable coronary syndromes are more suited to invasive coronary angiography. The team supervising the MPI will be aware of keeping radiation doses to a minimum; doses used must be within accepted guidelines. Pregnant patients should be avoided if possible. Patients who may benefit from MPI are listed below.

V.1. Clinical indications for MPI

Evaluation of patients with chest pain or ischemic equivalent:

— Those with intermediate (>20%) or high (>50%) likelihood of coronary artery disease (CAD)*.

— Those with low likelihood of CAD (<20%), with un-interpretable resting ECG or unable to exercise.

— Possible acute coronary syndrome/new or recent onset chest pain.

Clinical situations or symptoms other than ischemic equivalent:

— Cardiac enzyme elevation in conjunction with chest pain and/or ECG abnormalities.

— Patients with abnormal, equivocal or discordant stress testing by ECG or other imaging modality in which the diagnosis of CAD remains a concern.

— Evaluating coronary stenosis of uncertain significance observed on invasive or non-invasive coronary angiography.

— Evaluation of new onset or newly diagnosed heart failure.

— Evaluation of ventricular tachycardia.

— Syncope in patients with an intermediate (>10%) or high (>20%) absolute 10-year risk of a cardiac event based on pre-test CAD risk factors**.

* Algorithms are available to estimate the likelihood of CAD. However, as the prevalence and age of onset of CAD varies from country to country, these algorithms are most applicable to the population on which they were based and not to all populations.

** Algorithms are available to estimate the absolute 10-year risk of a cardiac event (references for the various score, Framingham, PROCAM etc.). Analogous to the likelihood evaluation described above, differences in the prevalence and age of onset of CAD vary from country to country making these algorithms most applicable to the population on which they were based.
Risk stratification and prognosis assessment:

— Chest pain syndrome in a patient with high pre-test likelihood of CAD.

— Following myocardial infarction or acute coronary syndrome.

— Monitoring the effects of treatment of CAD, including revascularization and medical therapy.

— Patients with past abnormal coronary angiography or stress imaging study in whom MPI would be expected to alter clinical management.

— Viability assessment in patients with left ventricular (LV) systolic dysfunction in whom this assessment would be expected to alter clinical management.

— Patients undergoing non-cardiac major surgery and having an intermediate (>20%) or high (>50%) likelihood of CAD.

Possible indications for asymptomatic patients:

— Patients with an intermediate (>10%) or high (>20%) absolute 10-year risk of a cardiac event based on pre-test CAD risk factors.

— Diabetic patients with evidence of a diabetic complication, prolonged duration of diabetes or an additional CAD risk factor, or who are female.

— Patients with evidence of extra-cardiac atherosclerotic vascular disease.

— Patients with coronary calcium Agatston score of >400 or >100 in diabetics.

— Chronic kidney disease (GFR<30ml).

— Troponin elevation without evidence of acute coronary syndrome.

— Syncope with intermediate to high pre-test likelihood of CAD.

Patient preparation prior to testing will help achieve maximal accuracy in the study. Ideally, an information sheet should be given to the patient (see appendix I). Below is a list of important considerations for the referring doctor.

V.2. Patient preparation – key issues for referring clinicians

(1) Anti-anginal medication, especially beta-blockers, should ideally be ceased for up to 48 hours prior to testing. This is particularly important for an exercise or dobutamine protocol. In occasional prognostic evaluations, a study can be performed on medication.

(2) Patients should cease all caffeine (or similar) intake 24 hours prior to study. This will allow a dipyridamole or adenosine protocol to be performed, even unscheduled. Caffeine will block adenosine receptors and may result in a false negative study.
Asthma can be aggravated by dipyridamole and adenosine, which may be contra-indicated. Dobutamine can be used instead. Patients with COPD without bronchospasm may still be suitable for dipyridamole and adenosine testing.

The patient should always come prepared to exercise (which may even be combined with pharmacological studies to improve sensitivity and image quality).

The study may involve 2 sets of imaging, possibly even a 2-day protocol, so that ischemia can be evaluated by looking for a reversible defect.

If a LBBB or paced rhythm is present, a dipyridamole or adenosine protocol is often used. Higher heart rates (such as those with exercise or dobutamine) will increase the likelihood of a false positive reversible septal defect in these patients.

The MPI study will provide the clinician with a combination of clinical information, stress data and the perfusion image:

- The study may be normal (after the exclusion of artefacts), ischaemic (with the identification of a reversible defect) or indicative of a previous infarct (a fixed defect), or a combination of the latter.

- The MPI study will provide the clinician the ability to triage their patient accordingly. Additionally, this decision is often guided not simply by the presence of ischemia but by the amount of ischemia and the level of stress performed.

- In most patients, LV function can also be assessed by gating the study at stress and/or rest. This may allow further implementation of varying heart failure strategies.

- Increased lung uptake of tracer and transient ischaemic dilatation may also infer increased cardiac risk.

- Once the result is available, the clinician can incorporate the results into the management algorithm.

- If the study is normal, the patient’s risk of a cardiac event remains less than 1% per annum, slightly greater in diabetic patients, patients with prior CAD and patients undergoing pharmacological stress testing. The MPI remains a test of ischemia, not of atherosclerosis and hence the non-obstructive lesion will be missed. The option remains of combining the MPI with coronary CT angiography or calcium scoring to address this issue.

- Conversely, the presence of increasing ischemia is associated with an increasingly adverse prognosis. Studies have shown that if more than 12.5 % of the patient’s heart is ischaemic, they will do better with revascularisation (if possible) rather than medical therapy.

- However, this cannot be applied to all patients universally – any decision regarding management must incorporate the patient’s symptomatic status, clinical examination, other tests and any potential benefit of an intervention. If the MPI result and clinical data/stress ECG results are discordant, a more aggressive management plan may be necessary.
In conclusion, MPI remains a powerful and robust test which can become a vital part of the clinician’s armamentarium in the diagnosis and management of coronary disease. Discussion with the physician supervising the MPI should always be encouraged.
ROLE OF CARDIAC PET AND PET/CT IN DEVELOPING COUNTRIES

VI.1. General considerations

— Coronary artery disease (CAD) is a major health problem in developing countries. Non-invasive imaging has an important cost-effective role for diagnosis and to guide therapy in this group of patients. PET/CT is now more available in many of these countries; it is used mainly in oncology, but cardiac studies may increase in the future, especially with new 18F-labeled perfusion agents [VI.1, VI.2].

— Cardiac PET/CT, a hybrid imaging technique, allows an anatomic and functional evaluation of the heart. This method gives information about coronary artery calcium score (CCS), coronary anatomy through computed tomography angiography (CTA), myocardial perfusion and metabolism, and rest and stress EF. CCS has an important role to estimate coronary risk. CTA has a high negative predictive value to exclude CAD but its positive predictive value is still low.

— The goal of evaluating myocardial perfusion with PET imaging is to detect hemodynamically significant CAD. PET tracers have a short half-life and are more physiologic agents than those used in SPECT. The most commonly used agents for perfusion are N-13 ammonia, Rubidium-82 and O-15 water. PET tracers are valuable agents for measuring either absolute or relative myocardial blood flow; for absolute measure, dynamic acquisition from time of injection is required. Myocardial blood flow assessment is a promising technique and its clinical value is still under research.

— The major indication of a PET/CT study is to establish the diagnosis and prognosis of patients with known or suspected CAD through the evaluation of myocardial blood flow (perfusion agents) and viability (metabolic agents).

— For stress-rest PET perfusion studies, patient preparation is similar to that described for a myocardial SPECT study. Pharmacological stress is always preferred because patients need to be positioned under the camera during injection. If an F-18 fluorodeoxyglucose (FDG) (viability) study is to be performed, appropriate consideration of the patient’s glucose level should be made with utilization of glucose load and insulin clamps according to local protocols.

— The acquisition protocols are related to the duration of uptake and clearance of the different radiopharmaceuticals and their physical half-life. CT is used for rest and stress attenuation correction. The recommendations for display of PET perfusion rest-stress images are consistent with those for SPECT.

VI.2. Image analysis and interpretation

— Myocardial perfusion: The images should be interpreted initially without clinical information in order to minimize any bias in study interpretation.

— Lung uptake.

— Right ventricle uptake (rarely seen with Rubidium-82).
— Blood pool activity.

— Evaluation of perfusion defects at rest and during stress to detect necrosis and ischemia, perfusion defect location, perfusion defect severity and extent. Left ventricle and right ventricle size.

— Extra-cardiac findings.

— Metabolic images: These images are performed with 18F-FDG and are used for viability assessment.

— Metabolism images need to be compared with perfusion images to establish the mismatch or match pattern.

— A mismatch pattern (a perfusion defect with metabolic uptake of FDG) represents viability, while a matched pattern (perfusion defect with no FDG uptake) represents scarred tissue.

— After revascularization, patients with a mismatch pattern usually have improvement in heart failure symptoms, EF, and survival.

— Extra-cardiac findings can be related to the presence of malignant tumours and should be investigated.

VI.3. Clinical applications of PET/CT

— Myocardial perfusion: This is an important clinical application of PET for diagnosis and prognosis of patients with CAD with a sensitivity higher than 90%.

— Myocardial blood flow quantification: Quantitative assessment of myocardial blood flow (MBF) in absolute units (ml/min/g tissue) offers an objective interpretation that is inherently more reproducible than visual analysis. Absolute quantification may aid in assessing the physiological significance of a coronary stenosis, in describing changes between two studies in the same patient and may identify balanced impaired myocardial blood flow due to multi-vessel disease or diffuse, small-vessel disease. It requires the acquisition of images in dynamic mode (list mode). The added value in term of diagnosis and prognosis is still under research.

— Endothelial function: Endothelial dysfunction represents the first stage of coronary atherosclerotic disease. It appears in asymptomatic patients with coronary risk factors. The evaluation of PET myocardial blood flow can be done at rest and stress and, if required by the Cold Pressor Test (CPT). This can help to identify endothelial dysfunction, through the evaluation of coronary flow reserve (stress/rest MBF) and endothelial dependent vasodilation index (CPT/rest MBF).

— Combination of perfusion and coronary CTA: The accuracy of the study increases with the combination of anatomic and functional information. However, dual-modality studies are associated with higher radiation burden, and on the other hand the true clinical utility of combined information is currently under investigation.

— Myocardial viability: PET represents a helpful technique for diagnosis of myocardial viability, based on a mismatch pattern.
— Coronary plaque inflammation: High FDG uptake can be observed in atherosclerotic coronary plaques; this issue is still under investigation.
REFERENCES TO APPENDIX VI


APPENDIX VII.

GALLERY OF CASE STUDIES

VII.1. CASE 1- ARTIFACT

Left: Stress (upper row of each panel) and rest (bottom row of each panel) myocardial perfusion study with 99mTc-sestamibi. There are apparent perfusion defects at stress while the rest images are almost normal, indicating possible extensive ischemia. However, there is significant subdiaphragmatic activity (i.e. short axis slices numbers 24 & 25 at the top) which might be producing an artifact. After masking this activity (right), the distribution of the radiopharmaceutical in the stress images looks homogeneous and similar to the rest condition. Hence, this was a normalization artifact which occurs because the ‘hottest’ point in the image lies outside the heart so the myocardium occupies a lower range of the color scale.
VII.2. CASE 2- DIAGNOSIS: RCA ISCHEMIA

Myocardial perfusion study with 99mTc-sestamibi from a 67-year old male with atypical angina (abdominal discomfort at stress) and normal exercise ECG. Upper panel: Short axis; middle panel: Vertical long axis; bottom panel: Horizontal long axis. There is a perfusion defect at stress (upper row at each panel) involving the inferior and infero-lateral walls, which normalizes almost completely at rest (bottom row of each panel). This is a reversible defect representing ischemia in the territory of the right coronary artery (RCA). Some uptake deficit is still present at rest, probably due to diaphragmatic attenuation which is more common in men. Abdominal pain or discomfort is not infrequent in patients with inferior wall ischemia; furthermore, sensitivity of exercise ECG is limited especially in patients with one-vessel disease. Coronary angiography revealed a critical stenosis of RCA and PTCA was performed successfully; there were lesions with <50% luminal stenosis in the circumflex artery (Cx) and first diagonal branch. The patient remained asymptomatic at 6 months after the procedure.
VII.3.  CASE 3- DIAGNOSIS AND RISK STRATIFICATION

A 56-year old diabetic woman with a history of dyspnea and an equivocal exercise ECG. With dipyridamole (upper row at each panel), a perfusion defect is seen at the mid-portion of the anterior wall, which resolves completely at rest. This reversible defect is consistent with ischemia in the territory of a diagonal branch of the LAD artery. In addition, there is transient ischemic dilation (TID) of the left ventricle (compare the size of the LV cavity at stress and at rest). Coronary angiography demonstrated multiple lesions in the LAD artery and its main branches, Cx and distal RCA. TID is associated with high risk for cardiac events and is commonly seen in patients with multi-vessel disease. In this case, the perfusion defect is only evident in the distribution of the diagonal branch, however the presence of TID should raise the suspicion of more extensive disease.
VII.4. CASE 4- ISCHEMIA AFTER PTCA

Myocardial perfusion study with 99mTc-sestamibi at stress (exercise) and rest. The patient was a 54-year old man with previous PTCA to the LAD artery 2 years before who presented with shortness of breath and chest discomfort after walking 200 m. At the time of intervention, mild lesions (<50% stenosis) were noted in other vessels. A perfusion defect is seen at stress involving the apex and the inferior wall, which normalizes at rest. The finding is consistent with ischemia in the territory of the LAD and RCA. MPI is indicated in patients with previous PTCA in whom symptoms reappear in order to detect possible restenosis and/or progression of CAD involving different territories. In this case, coronary angiography demonstrated patency of LAD artery and a critical distal stenosis of the RCA, which was dominant, explaining both the inferior and apical perfusion defects. The lesion was dilated successfully.
VII.5. CASE 5- INTERMITTENT LBBB

Myocardial perfusion study with 99mTc-sestamibi at stress (exercise) and rest in a 56-year old woman. The patient had coronary risk factors but was asymptomatic, however an exercise test was non-diagnostic because of development of LBBB at maximum exercise, which disappears at rest. There is a perfusion deficit involving the anteroseptal and apical regions, which is totally reversible at rest. LBBB usually causes perfusion defects in the territory of the LAD artery, so this result is non-specific for ischemia; since in this case the conduction disorder is related to an increase in heart rate (it also worsens with exercise in patients with fixed LBBB), a dipyridamole test should have been indicated instead of exercise, because of its minimal chronotropic effect. The patient was further referred to coronary angiography, with no coronary lesions detected.
VII.6. CASE 6- HIGH RISK SCAN RESULT

Myocardial perfusion study with 99mTc-sestamibi at stress (dipyridamole) and rest in a 72-year old man with hypercholesterolemia and atypical chest pain. Exercise stress was not possible because of bilateral knee prostheses. The patient had previously undergone coronary CT angiography which was non-diagnostic because of a high calcium score of 800, precluding correct visualization of coronary lumen. In the nuclear scan there is a large perfusion defect on the anterospetal and apical regions, with almost complete recovery at rest. LVEF was 42% at stress and 66% at rest. The patient was urgently referred for coronary angiography and a critical proximal lesion of the LAD artery was found, followed by PTCA. This is a high risk scan due to the extent and location of the ischemic territory, and a significant drop in LVEF at post-stress as compared to rest (myocardial stunning).
VII.7. CASE 7- PRE-OPERATIVE ASSESSMENT

Myocardial perfusion study with 99mTc-sestamibi at stress (dipyridamole) and rest in a 68-year old man with high likelihood of CAD scheduled for carotid endarterectomy. An extensive perfusion deficit, mostly reversible, is seen affecting the lateral and inferior walls. In addition, there is TID of the left ventricle. Even if asymptomatic from the cardiac point of view, patients undergoing non-cardiac major surgery and with an intermediate (>20%) or high (>50%) likelihood of CAD are candidates for myocardial perfusion studies, since coronary revascularization might be indicated first in order to minimize the chance of peri-operative ischemic events. Although not contraindicated, dipyridamole stress should be used with caution in patients with cerebrovascular disease.
VII.8. CASE 8- TRANSIENT ISCHEMIC DILATATION WITH NEAR-NORMAL PERFUSION

Myocardial perfusion study with 99mTc-sestamibi at stress (dipyridamole) and rest in a 45-year old diabetic woman with a syncopal episode and no previous cardiac history. At admission, periods of self-limited ventricular tachycardia were registered but with no ischemic ECG changes and normal troponin serum levels. Although only few equivocal perfusion defects are observed in the nuclear scan (apex, inferior wall), there is very significant TID of the left ventricle. Since the nuclear result was not conclusive and the patient was now stable and asymptomatic, as a second non-invasive test she was referred to CT angiography where multiple coronary lesions were detected. Cardiac catheterization was performed, followed by CABG with by-pass grafts to the three main coronary arteries. In the absence of definite perfusion defects, TID suggests triple-vessel disease with balanced ischemia. Diabetes can also be associated with small-vessel disease, adding to the diffuse nature of ischemic episodes.
VII.9. CASE 9- POST MYOCARDIAL INFARCTION

Myocardial perfusion study with 99mTc-sestamibi at stress (dipyridamole) and rest (after nitrates) in a 54-year old man with previous MI and severe heart failure. There is LV dilatation with a large perfusion defect at the anterior, anteroseptal, and apical walls, with no significant change between stress and rest. LVEF was 27% and 25%, respectively. Diverging walls towards the apex suggests a ventricular aneurysm, which was confirmed by the presence of apical dyskinesis. The result indicates a large transmural infarction with LV remodeling and no significant associated ischemia nor evidence of viability in the infarct area. The patient was not sent for catheterization and maximum medical therapy was installed, with cardiac transplantation to be eventually considered after a follow-up period.
VII.10. CASE 10- VIABILITY EVALUATION

Myocardial perfusion study with 99mTc-sestamibi at rest (upper row) and after nitrates (bottom row) in a 78-year old man with previous MI and heart failure. The rest images show extensive perfusion defects at the postero-lateral and inferior walls, showing significant improvement after nitrates (although latero-basal regions have little change). There is also a small anteroseptal area with the same findings. The result is consistent with the presence of viable myocardium in most parts of the affected areas, thus with potential of recovery after revascularization. Myocardial viability studies are important in patients with heart failure and coronary heart disease in order to identify patients in whom revascularization (either CABG or PTCA) could result in functional improvement.
APPENDIX VIII.
FORMULAS

Bayes’ Theorem:

\[
P(D^+ | T^+) = \frac{P(D^+) \times P(T^+ | D^+)}{P(D^+) \times P(T^+ | D^+) + (1 - P(D^+)) \times (1 - P(T^+ | D^-))} \tag{1}
\]

Pretest likelihood:

\[
P(D^+) = \frac{\text{number of patients with disease in the test population}}{\text{total number of patients in the test population}}
\]

Sensitivity:

\[
P(T^+ | D^+) = \frac{\text{number of patients with disease showing a given test result}}{\text{total number of tested patients with disease}}
\]

Specificity:

\[
P(T^- | D^-) = \frac{\text{number of disease-free patients not showing the test result}}{\text{total number of disease-free patients tested}}
\]

Post-test likelihood:

\[
P(D^+ | T^+) = \frac{\text{number of patients with disease showing a given test result}}{\text{total number of patients showing the test result}}
\]
CONTRIBUTORS TO DRAFTING AND REVIEW

Drafting

Alexanderson, E.  Universidad Nacional Autónoma de México, PET/CT Cyclotron Department, Mexico
Better, N.  Department of Nuclear Medicine, Royal Melbourne Hospital, Australia
Bouyoucef, S-E.  Centre Hospitalier Universitaire de Bab El-Qued, Algeria
Dondi, M.  International Atomic Energy Agency
Dorbala, S.  Brigham and Women's Hospital, RAD/NUC, USA
Giubbini, R.  Spedali Civili di Brescia, Medicina Nucleare, Italy
Keng, F.  National Heart Centre Mistri Wing, Singapore
Kumar, A.  Fortis Escorts Heart Institute and Research Centre, India
Marcassa, C.  Cardiology Division Fondazione Salvatore Maugeri IRCCS, Italy
Massardo, T.  Universidad de Chile, Hospital Clínico "José Joaquín Aguirre", Chile
Milan, E.  Ospedale Civili U.O., Medicina Nucleare - Centro PET, Italy
Mut, F.  Nuclear Medicine Service, Asociación Española, Uruguay
Obaldo, J.  Philippine Heart Center For Asia, Nuclear Medicine Department, Philippines
Paez, D.  International Atomic Energy Agency
Peix, A.  Instituto de Cardiología y Cirugía Cardiovascular, Cuba
Thomas, G.  Mission Internal Medical Group, USA
Vitola, J.  Quanta Diagnostico Nuclear, Brazil
Vorster, M.  Pretoria Academic Hospital, South Africa

Review

El-Haj, N.  International Atomic Energy Agency
Mut, F.  Nuclear Medicine Service, Asociación Española, Uruguay
Paez, D.  International Atomic Energy Agency

Consultants meeting

Vienna, Austria: 21–25 February 2011