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No. 23 (Rev. 1)

Nuclear Cardiology: Guidance on the Implementation of SPECT Myocardial Perfusion Imaging



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NUCLEAR CARDIOLOGY:
GUIDANCE ON THE
IMPLEMENTATION OF
SPECT MYOCARDIAL
PERFUSION IMAGING

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INTERNATIONAL ATOMIC ENERGY AGENCY
VIENNA, 2016

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FOREWORD

According to the Global Action Plan 2013–2020 of the World Health Organization, non-communicable diseases — mainly cardiovascular diseases, cancers, chronic respiratory diseases and diabetes — are the world's biggest killers. In 2012, cardiovascular diseases were the leading cause of death worldwide, with low and middle income countries already bearing most of the burden of these premature deaths, resulting in huge cumulative economic losses and millions of people trapped in poverty.

Nuclear cardiology is one of the most widely used non-invasive techniques for the assessment of coronary artery disease and other cardiovascular conditions. It has proved to be a cost effective tool for the evaluation and management of cardiac patients and usually has a decisive role in diagnosis, prognosis and risk stratification, as well as in guidance of therapy. Clinical scenarios in which nuclear cardiology can be helpful are continually expanding, with special subgroups of patients being identified as potential beneficiaries of these methods and with technological developments in instrumentation and software which tend to enhance the cost–benefit ratio and the reliability of results. In particular, radionuclide myocardial perfusion imaging (MPI) is used extensively worldwide for the evaluation of known or suspected coronary artery disease, with an estimated 15–20 million procedures performed annually. The IAEA has long played a central role in the dissemination and promotion of nuclear cardiology through education and training targeted at Member States. Nevertheless, nuclear cardiology is still underutilized in many developing countries.

Many developing countries have successfully introduced nuclear cardiology, and its use is increasing in light of the epidemic 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 underlying the rapidly growing incidence of this life threatening condition. Today, cardiovascular diseases are the most common cause of death in adults in most countries. Thus, important measures including disease prevention, appropriate management and proper utilization of technological advances such as nuclear cardiology are essential to effectively combat coronary artery disease.

The practice of nuclear cardiology, however, is not homogeneous worldwide owing to differences in technological capabilities, availability of radiopharmaceuticals, education and training of professionals, and access to evidence based medicine, among other factors. With the aim of preparing a practical guide to single photon emission computed tomography (SPECT) MPI, particularly in light of the findings of the worldwide IAEA Nuclear Cardiology Cross-Sectional Protocols Study (INCAPS), published in July 2015, and to

incorporate more content on radiation dose optimization and appropriate use, the IAEA organized a consultants meeting. This meeting, on Improving Nuclear Cardiology Best Practices and Enhancing Educational Materials, was held in Vienna, 26–28 August 2015. Experts in the field from different countries participated in the discussions and contributed to the drafting of this publication.

The IAEA technical officers responsible for this publication were M. Dondi, T. Pascual and D. Paez of the Division of Human Health.

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This publication does not address questions of responsibility, legal or otherwise, for acts or omissions on the part of any person.

Guidance provided here, describing good practices, represents expert opinion but does not constitute recommendations made on the basis of a consensus of Member States.

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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 world and increasingly so in low and middle income countries. In the United States of America, it accounts for more than 500 000 deaths each year, and predictions foresee an annual toll of more than 23 million deaths worldwide by 2030.¹ Early diagnosis and treatment can mean the difference between life and death for many. Since the 1990s, advancements in the field of cardiology have made use of nuclear techniques to help with the diagnosis and treatment of heart diseases. One such development is 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 nuclear cardiology technique, in a variety of clinical conditions.

Owing to differences in technological capabilities, availability of radiopharmaceuticals, education and training of professionals, and access to evidence based medicine, the practice of nuclear cardiology is not homogeneous, as found from the worldwide IAEA Nuclear Cardiology Cross-Sectional Protocols Study (INCAPS) [1.1].

1.2. OBJECTIVE

This publication provides a detailed analysis of all the steps involved in the delivery of nuclear cardiology services, from referrals to reporting, and is intended to serve as guidance on the implementation, homogenization and enhancement of MPI practice in those Member States where the technique is under development. The aim is also to help to 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. Clinical scenarios where patients are most likely to benefit from single photon emission computed tomography (SPECT) or positron emission tomography (PET) MPI are clearly identified in Section 3. The list is not exhaustive, since based on clinical judgment, others can benefit from MPI as well.

¹ See http://www.who.int/cardiovascular_diseases/about_cvd/en/

This publication is an updated and revised version of Human Health Series No. 23, Nuclear Cardiology: Guidance and Recommendations for Implementation in Developing Countries [1.2], and it is also devoted to MPI. This publication should be considered as complementary to IAEA Human Health Series No. 18, Nuclear Cardiology: Its Role in Cost Effective Care [1.3], in which the role of other non-invasive imaging modalities is also discussed, along with MPI.

Although this publication closely follows the content of Ref. [1.2], there are some substantial changes. Given increased concern regarding radiation safety in medical imaging, content regarding approaches to optimizing radiation has been expanded and elevated from an appendix (appendix IV of Ref. [1.2]) to a full section (see Section 2). Similarly, content regarding appropriateness has been expanded and elevated from an appendix (appendix V of Ref. [1.2]) to a full section (see Section 3). The focus of this publication has also been expanded from the developing world to the entire world, and thus appendix VI of Ref. [1.2], pertaining to the developing world, has been eliminated. Appendix VII of Ref. [1.2], offering clinical cases, has been removed, since the IAEA now offers numerous clinical cases in nuclear cardiology on the on-line Human Health Campus.² Finally, an appendix with basic statistical formulas has been removed.

Guidance provided here, describing good practices, represents expert opinion but does not constitute recommendations made on the basis of a consensus of Member States.

1.3. SCOPE

The current publication is aimed mainly at nuclear medicine physicians, cardiologists and cardiac surgeons, but also at all other clinical specialists involved in managing and treating CAD.

1.4. STRUCTURE

Beginning with clinical indications, this publication covers the main aspects of this modality, including: comprehensive instructions for reducing patients' radiation exposure; indications for appropriate use; selection of stress tests; and acquisition procedures. The reader is also provided with guidelines on

² See <https://humanhealth.iaea.org/HHW/NuclearMedicine/index.html>

interpretation of studies and their reporting. A gallery of clinical cases has been added to the IAEA Human Health web site.³

REFERENCES TO SECTION 1

- [1.1] EINSTEIN, A.J., et al., Current worldwide nuclear cardiology practices and radiation exposure: Results from the 65 country IAEA Nuclear Cardiology Protocols Cross-Sectional Study (INCAPS), *Eur. Heart J.* **36** (2015) 1689–1696.
- [1.2] INTERNATIONAL ATOMIC ENERGY AGENCY, Nuclear Cardiology: Guidance and Recommendations for Implementation in Developing Countries, IAEA Human Health Series No. 23, IAEA, Vienna (2012).
- [1.3] INTERNATIONAL ATOMIC ENERGY AGENCY, Nuclear Cardiology: Its Role in Cost Effective Care, IAEA Human Health Series No. 18, IAEA, Vienna (2012).

³ See <https://humanhealth.iaea.org>

2. STRATEGIES TO REDUCE RADIATION DOSE IN MYOCARDIAL PERFUSION IMAGING

Since the 1980s, there has been a steady rise worldwide in radiation exposure of patients from medical imaging. While there is considerable heterogeneity in this growth, it is illustrated particularly saliently by published data from the United States of America, in which, according to the National Council on Radiation Protection and Measurements, cumulative medical radiation effective dose has increased sixfold since the early 1980s [2.1, 2.2]. In a large study of nearly one million individuals in five regions of the United States of America, 22% of the total effective dose from medical imaging was attributable to myocardial perfusion imaging (MPI) [2.3].

2.1. PRINCIPLES OF MEDICAL RADIATION PROTECTION

The growing radiation doses underscore the importance of minimizing radiation to patients by implementing the two fundamental principles of medical radiation protection: justification and optimization.

2.1.1. Justification

Justification refers to performing the right test for the right patient at the right time, and entails balancing the benefits of testing related to diagnosis, prognosis and guidance of management, against risks which include radiation exposure.

Justification is a shared responsibility of the referring physician and the imaging physician [2.4], and can be ensured by applying the ‘three As’ of awareness, appropriateness and audit [2.5], elaborated upon in Section 3.

2.1.2. Optimization

Optimization refers to performing the test in the right way and is often equated with the as low as reasonably achievable (ALARA) principle, keeping radiation as low as possible while ensuring diagnostically acceptable image quality.

A variety of strategies exist for the optimization of radiation protection and safety. The IAEA conducted a cross-sectional study of nuclear cardiology practice in 65 countries during a single week in March–April 2013, referred to as the IAEA Nuclear Cardiology Cross-Sectional Protocols Study (INCAPS) [2.6].

It found wide variation in radiation effective doses, which were in the range of 0.8–35.6 mSv (median 10.0 mSv) among the 7911 patients undergoing MPI (including fluorodeoxyglucose positron emission tomography (PET) scans). Median average laboratory effective dose was in the range of 2.2–24.4 mSv, and only 91 of 308 laboratories (~30%) achieved the median dose of 9 mSv or less, as suggested in American Society of Nuclear Cardiology recommendations [2.7]. As part of INCAPS, a committee of international experts convened by the IAEA, including physicians and medical physicists, identified eight best practices for nuclear cardiology laboratories aimed at optimization, and demonstrated a statistically significant association between a laboratory's use of these best practices and lower radiation doses to patients undergoing MPI in the laboratory.

2.1.3. Best practices

The eight best practices are [2.6]:

- (1) Avoid thallium stress testing;
- (2) Avoid dual isotope testing;
- (3) Avoid too much technetium;
- (4) Avoid too much thallium;
- (5) Perform stress-only imaging;
- (6) Use camera based dose reduction strategies;
- (7) Use weight based dosing for technetium;
- (8) Avoid inappropriate dosing that can lead to shine through artefacts.

2.1.3.1. Avoid thallium stress testing

The three widely available radiopharmaceuticals used for single photon emission computed tomography (SPECT) MPI are thallous chloride ($^{201}\text{TlCl}$), $^{99\text{m}}\text{Tc}$ -sestamibi and $^{99\text{m}}\text{Tc}$ -tetrofosmin. Thallium-201 has a much longer physical half-life (73 h) than $^{99\text{m}}\text{Tc}$ (6 h), and therefore stays in the body longer, exposing a patient to ionizing radiation for a long time after its utility for diagnostic imaging has passed. Thus, SPECT MPI performed with ^{201}Tl is associated with a considerably higher radiation dose to patients than when it is performed with $^{99\text{m}}\text{Tc}$, even when two injections of $^{99\text{m}}\text{Tc}$ are required for stress and rest scans [2.6]. This is particularly true when the imaging protocol incorporates thallium reinjection. Increased radiation dose is a bigger concern in younger patients, for whom radiation risk is greater. Moreover, spatial resolution for any given camera is better with $^{99\text{m}}\text{Tc}$ than with ^{201}Tl .

Thallium may be preferred to ^{99m}Tc when the purpose of the study is to assess viability rather than the typical SPECT MPI study obtained to assess ischaemia, or when a patient has documentation of a previous SPECT MPI study in which extracardiac uptake of ^{99m}Tc (e.g. subdiaphragmatic or due to a hiatal hernia) significantly interferes with cardiac images. Nevertheless, for the vast majority of patients undergoing SPECT MPI, a ^{99m}Tc based radiopharmaceutical should be the perfusion imaging agent of choice.

2.1.3.2. Avoid dual isotope testing

Dual isotope studies incorporate thallium rest imaging followed by ^{99m}Tc stress imaging. They are associated with the highest radiation doses of all SPECT MPI studies, and by using different tracers for rest and stress, image interpretation entails comparing two very different types of image. Unless viability imaging is required, dual isotope imaging should be avoided in patients for whom radiation risk is of concern. Even when viability imaging is clinically indicated, a thallium-only protocol offers stress, rest and 24 hour redistribution imaging at a lower cost in terms of patient radiation exposure.

2.1.3.3. Avoid too much technetium

Even for morbidly obese patients, 1332 MBq should be more than adequate to obtain sufficient count statistics to enable high quality imaging using a dual headed camera, and as such this is the maximum activity of ^{99m}Tc recommended by the committee of international experts convened by the IAEA (see Section 4) [2.6]. Activities above this level are not warranted. In addition, the effective dose should average less than 15 mSv for all studies in a laboratory using only technetium injections; for most patients, a considerably lower dose should be possible [2.6]. Using the most recent dosimetry coefficients, the effective dose of ^{99m}Tc -sestamibi is 6.55×10^{-3} mSv/MBq at stress and 7.03×10^{-3} mSv/MBq at rest; for ^{99m}Tc -tetrofosmin, these values are 5.76×10^{-3} mSv/MBq at stress and 6.29×10^{-3} mSv/MBq at rest [2.8].

2.1.3.4. Avoid too much thallium

While for non-obese patients, 93–110 MBq is generally adequate activity for diagnostic quality MPI images, the committee of international experts maintained that no more than 130 MBq of ^{201}Tl should be injected for stress testing or rest/redistribution imaging (see Table 4.4, in Section 4) [2.6]. An additional dose may be used if reinjection imaging is performed for viability assessment, although 24 hour redistribution imaging is an alternative approach for viability

assessment which does not entail any additional ionizing radiation. PET scanning with ^{18}F -fluorodeoxyglucose, where available, is a more sensitive test.

2.1.3.5. *Perform stress-only imaging*

In a stress-only $^{99\text{m}}\text{Tc}$ imaging protocol, stress imaging is performed first (stress first), and images are reviewed by a physician prior to performing a rest injection. If the stress images are interpreted as being completely normal (i.e. normal perfusion, normal function, normal left ventricular size, no regional wall motion abnormalities and no increased right ventricular tracer uptake), then the rest injection is omitted and no rest imaging is performed. In INCAPS, stress-only imaging was found to reduce radiation dose by 64% [2.9]. Prognostic data from over 20 000 patients suggest that stress-only imaging achieves this radiation reduction without compromising patient outcomes (see Fig. 2.1) [2.10–2.12].

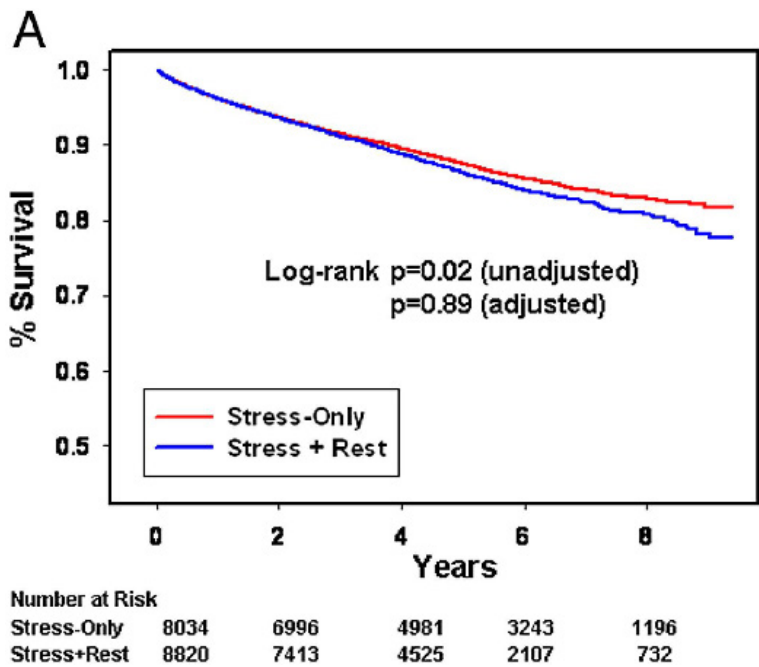


FIG. 2.1. Survival among patients undergoing stress-only versus stress and rest imaging, among 16 854 consecutive patients at Houston Methodist Debakey Heart and Vascular Center (reproduced from Ref. [2.12] with permission courtesy of Elsevier).

For patients for whom there is at least a reasonable chance of a normal study, stress-first imaging is a good option that can lower radiation dose. Even patients with a past history of coronary artery disease can be considered for stress-only imaging. For example, if a patient has single vessel obstructive coronary disease that is revascularized, and re-presents for stress testing, in many cases repeat testing will be normal and thus the patient is a candidate for stress-only imaging. Attenuation correction can increase the normalcy rate of stress imaging, by correcting for minor attenuation related defects caused by the breast or diaphragm [2.10], and thus the use of attenuation correction facilitates stress-only imaging. The same holds for multiple position imaging (e.g. imaging patients in both the supine and prone positions) [2.13].

2.1.3.6. Use camera based dose reduction strategies

A variety of camera based strategies should be considered to lower radiation dose. Attenuation correction and multiple position imaging, as mentioned above, facilitate stress-only imaging. Advanced image reconstruction software is available from several vendors that enables reduction of administered activity while maintaining image quality. Many of these packages incorporate iterative reconstruction, resolution recovery and noise reduction algorithms [2.14]. PET MPI is associated with considerably lower radiation doses than is SPECT imaging owing to the short half-life of the tracers used. Moreover, the diagnostic sensitivity of PET exceeds that of SPECT [2.15]. Multiple vendors now offer advanced SPECT hardware, including cardiac focused collimators and high efficiency cameras incorporating many cadmium zinc telluride (CZT) solid state detectors [2.16], which can also be used to reduce administered activity. This can reduce radiation effective dose from a SPECT study to as little as 1 mSv [2.17].

2.1.3.7. Use weight based dosing for technetium

Technetium activity should reflect patient weight and habitus. Larger patients generally need more technetium to achieve good image quality, and thus should receive more activity (MBq) than smaller patients. Table 4.4, in Section 4, provides a range of activities for each protocol. For a particular patient, selecting the administered activity within this range of activities for a given radiopharmaceutical is not an exact science. The same administered activity can yield strikingly different count statistics and thus image quality in different patients, owing to between patient differences in pharmacokinetics. Nevertheless, there should be an effort to tailor administered activity to the patient's habitus and the imaging equipment used. For example, thin patients without excessive breast tissue should receive activities at the low end of the recommended range,

while many patients weighing more than 120 kg benefit from the increased count statistics of a two day protocol with 660–1100 MBq administered each day.

There are a number of weight based strategies that can be used. No evidence supports one particular weight based dosing scheme over another. As one weight based strategy to consider, many laboratories may find it appropriate in one day studies to perform the first injection with:

- 300 MBq of ^{99m}Tc for patients with a body mass index (BMI) less than 25 kg/m²;
- 340 MBq of ^{99m}Tc for patients with a BMI of 25–30 kg/m²;
- 380 MBq of ^{99m}Tc for patients with a BMI of 30–35 kg/m²;
- 440 MBq of ^{99m}Tc for patients with a BMI greater than 35 kg/m² or a large chest, with three times this activity used for the second dose of the day.

In obese patients undergoing two day protocols, the radiation dose can be optimized by performing a two day protocol with stress imaging on the first day, and only performing rest imaging if these images are abnormal. For laboratories with advanced software and hardware, as in dose reduction strategy 6 above, reduced-dose protocols should be considered, as proposed in the bottom section of Table 4.4, in Section 4. One way to determine that weight based dosing is being performed within a laboratory is to ensure that there is a significant correlation between patient weight and technetium activity.

2.1.3.8. Avoid inappropriate dosing that can lead to shine through artefacts

This best practice, while directly impacting radiation dose, does not reduce radiation dose but may in fact increase it, so as to avoid significant shine through artefacts. According to Ref. [2.6]:

“Shine through occurs in two injection, single-day technetium studies when residual radioactivity from the first injection interferes with interpretation of images for the second injection. To avoid shine through, it is recommended in guidelines that the activity (mCi or MBq) imaged for the second injection be at least three to four times that of the first injection”.

The ratio of injected activity required to ensure this will vary depending on the time delay between the two injections. For example, if there is a six hour delay between the injections, no more than half of the activity from the first set of images will remain and shine through into the second set of images, and therefore a 1:2 ratio of injected activity should be adequate to avoid significant shine through artefacts. In most clinical workflows, however, the delay between

injections is much shorter and a higher ratio of injected activities should be used. In general, using a 1:4 ratio of injected activities in a one day stress/rest or rest/stress study (e.g. 300 MBq first injection and 1200 MBq second injection) will always ensure an adequate count ratio to minimize the risk of significant shine through artefacts.

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3. INDICATIONS FOR AND APPROPRIATE USE OF MYOCARDIAL PERFUSION IMAGING

Non-invasive cardiac imaging techniques, and in particular stress myocardial perfusion imaging (MPI), have a central role in the diagnostic workup [3.1] and risk assessment [3.2–3.4] of patients with known or suspected coronary artery disease (CAD), lowering the cost of managing these patients [3.5, 3.6].

Symptom evaluation is an important component of the decision making involved in the referral for MPI. For the purpose of this publication, an ischaemic equivalent is defined as a chest pain syndrome or atypical symptoms suggesting an anginal equivalent consistent with ischaemia. The use of MPI is appropriate for the following clinical conditions.

3.1. PATIENTS WITH CHEST PAIN OR ISCHAEMIC EQUIVALENT

Patients included are:

- Those with an intermediate (10–90%) or high (>90%) likelihood of CAD⁴;
- Those with a low likelihood of CAD (<10%), with an uninterpretable resting electrocardiogram (ECG) or unable to exercise;
- Those with a possible acute coronary syndrome, or new or recent onset chest pain.

3.2. PATIENTS WITH SYMPTOMS OTHER THAN ISCHAEMIC EQUIVALENT

The symptoms include:

- Cardiac enzyme elevation in conjunction with chest pain and/or ECG abnormalities;
- Abnormal, equivocal or discordant stress testing by ECG or other imaging modality in which the diagnosis of myocardial ischaemia remains a concern;
- Coronary stenosis of uncertain significance observed on invasive or non-invasive coronary angiography;

⁴ Algorithms are available to estimate the likelihood of CAD (see table 9 of Ref. [3.1]). However, as the prevalence and age of onset of CAD vary from country to country, these algorithms are most applicable to the population on which they were based and not to all populations.

- New onset or newly diagnosed heart failure;
- Arrhythmias (e.g. ventricular tachycardia or atrial fibrillation);
- Syncope in patients with an intermediate (10–20%) or high (>20%) absolute ten year risk of a cardiac event, based on pre-test CAD risk factors⁵.

3.3. RISK STRATIFICATION AND PROGNOSIS ASSESSMENT

Risk stratification and prognosis assessment are indicated in the case of:

- Chest pain syndrome in a patient with a high pre-test likelihood of CAD;
- Patients with a history of myocardial infarction or acute coronary syndrome, once the patient is stable for the procedure;
- A need to monitor 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 systolic dysfunction in whom this assessment would be expected to alter clinical management;
- Patients undergoing non-cardiac major surgery with an intermediate (10–90%) or high ($\geq 90\%$) likelihood of CAD;
- Patients undergoing evaluation prior to non-cardiac organ transplantation.

3.4. ASYMPTOMATIC PATIENTS

Asymptomatic patients include:

- Patients with an intermediate (10–20%) or high (>20%) absolute ten 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 female diabetic patients;
- Patients with evidence of extracardiac atherosclerotic vascular disease;

⁵ Algorithms are available to estimate the absolute ten year risk of a cardiac event (e.g. the Framingham Coronary Heart Risk Score and the PROCAM risk score). Analogous to the likelihood evaluation described above, differences in the prevalence and age of the onset of CAD vary from country to country, making these algorithms most applicable to the population on which they were based.

- Patients with a coronary calcium Agatston score of greater than 400, or greater than 100 in patients with diabetes;
- Patients with chronic kidney disease (glomerular filtration rate < 30), particularly in assessment of potential renal transplantation;
- Patients with elevated troponin levels without evidence of acute coronary syndrome.

Table 3.1 lists pre-test likelihoods of CAD according to age, sex and symptoms [3.1].

TABLE 3.1. PRE-TEST LIKELIHOOD OF CORONARY ARTERY DISEASE BY AGE, SEX AND SYMPTOMS

Age (y)	Sex	Typical/definite angina pectoris	Atypical/probable angina pectoris	Non-anginal chest pain	Asymptomatic
30–39	Male	Intermediate	Intermediate	Low	Very low
	Female	Intermediate	Very low	Very low	Very low
40–49	Male	High	Intermediate	Intermediate	Low
	Female	Intermediate	Low	Very low	Very low
50–59	Male	High	Intermediate	Intermediate	Low
	Female	Intermediate	Intermediate	Low	Very low
60–69	Male	High	Intermediate	Intermediate	Low
	Female	High	Intermediate	Intermediate	Low

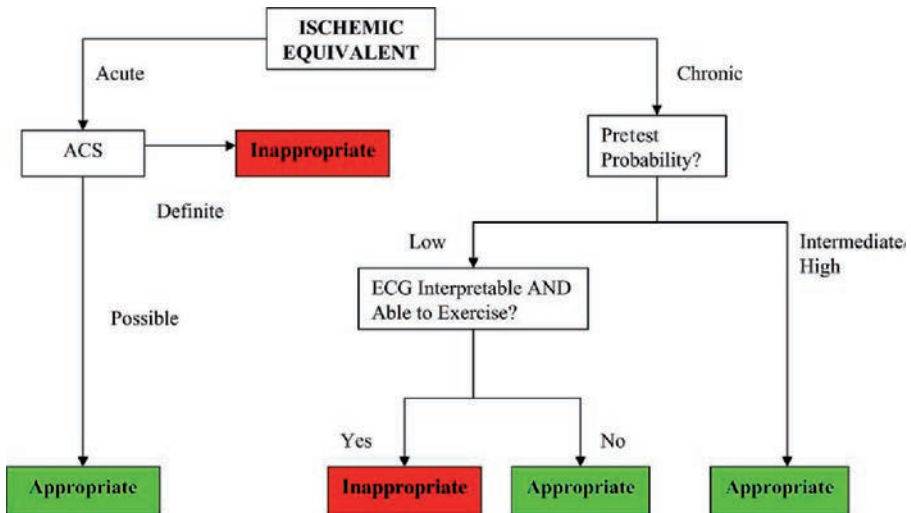
Note: High indicates >90%; intermediate 10–90%; low <10%; and very low <5%. No data exist for patients <30 or >69 years, but it can be assumed that prevalence of CAD increases with age. In a few cases, patients at the extremes of the ages listed may have likelihoods slightly outside the high or low range.

3.5. APPROPRIATE USE CRITERIA

In the environment of cost containment and radiation protection, the appropriate selection of patients is critical. Appropriate use criteria are well established and regularly revised to rate varying indications as either

“appropriate”, “may be appropriate” (formerly “uncertain”) or “rarely appropriate” (formerly “inappropriate”) [3.7]. These appropriate use criteria have been developed for radionuclide imaging and for various other cardiac imaging and interventional modalities and related sets of clinical conditions [3.8]. For this to remain beneficial for patients, these criteria need to be reviewed and discussed not just by the team performing the study, but also by, and with, the referring clinician. The American Society of Nuclear Cardiology has implemented the Choosing Wisely campaign and highlights certain subgroups where testing should be avoided if possible.⁶

The IAEA Consultation on Justification of Diagnostic Medical Exposures produced a report presenting the consensus of the group of experts who were invited to take part, which highlights the value of appropriateness in a three point strategy (the three As: awareness, appropriateness and audit) to increase the correct utilization of radiation for medical imaging [3.9]. Each clinical scenario dictates individual consideration, and algorithms exist in most circumstances to help to decide whether the study is appropriate. One such example highlights a patient presenting with an ischaemic equivalent, such as shortness of breath (see Fig. 3.1). By knowing the acute or chronic nature of the presentation, the



Note: ACS — acute coronary syndrome; ECG — electrocardiogram.

FIG. 3.1. Appropriateness of MPI in the evaluation of ischaemic equivalent (reproduced from Ref. [3.7] with permission courtesy of Elsevier).

⁶ See <http://www.choosingwisely.org>

pre-test probability, the interpretability of the ECG and the patient's ability to exercise, the team can decide on the appropriateness of the MPI study.

3.6. UNDERUTILIZATION OF MYOCARDIAL PERFUSION IMAGING

There is wide variation in the utilization of single photon emission computed tomography (SPECT) MPI worldwide. While the utilization in some countries may be excessive, in many other countries it is very low or non-existent. There is no easy way to define what adequate utilization in a country is. Nevertheless, publications on appropriate use criteria help to define, on an individual level, which patient is most likely to benefit from SPECT MPI [3.10, 3.11]. Unfortunately, most of the countries where utilization is low or non-existent are those potentially facing major increases in cardiovascular disease mortality. There are several possible reasons for low utilization of the technology, varying from economic potential and investments in health care in that country to a lack of appropriate education and knowledge with regard to the cost effective use of tools to manage ischaemic heart disease. The IAEA has been playing an important role in attempts to reduce the gaps in knowledge between developed and developing countries, bringing awareness of the potential role of nuclear cardiology to the forefront through several educational activities in the field [3.12].

One very important use of nuclear cardiology techniques, especially considering the economic challenges in developing countries, is to better select patients that will benefit from invasive, usually more costly, procedures. Furthermore, the invasive approaches may lead to an unnecessary risk that ranges from minor bleeding and infection to more complex and significant complications, including a risk of death estimated at 1 in 1000 [3.13].

Using MPI as a "gatekeeper" to angiography offers an excellent opportunity to better select patients with stable angina who may benefit from a non-invasive approach to diagnosis and management of CAD [3.14]. A normal MPI study is associated with a low cardiac event rate (<1% events per year); therefore, an invasive coronary angiogram can be safely avoided in these patients [3.15]. Similarly, patients with mild ischaemia can be managed non-invasively subject to symptom control. On the other hand, patients with significant ischaemia on MPI or high risk scan findings such as transient ischaemic dilatation [3.16], post-ischaemic stunning [3.17], increased right ventricular tracer uptake on stress imaging [3.18] and increased radiotracer uptake in the lungs [3.19] may be guided to an invasive approach [3.20].

Studies have found that patients with a positive result on MPI were significantly more likely to have obstructive disease than those who did not undergo non-invasive testing [3.21]. In patients recovering from myocardial infarction who are clinically stable, a vasodilator MPI can be considered as a gatekeeper to angiography [3.22, 3.23].

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4. STRESS MODALITIES AND PROTOCOLS FOR MYOCARDIAL PERFUSION IMAGING

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 that after the radiotracer is injected, its myocardial distribution will reflect flow heterogeneity if significant coronary stenosis is present [4.1]. It is clear that, for appropriate diagnosis using this modality, true ischaemia is not necessarily induced, in contrast to other modalities such as stress echocardiography, where transient abnormal wall motion due to myocardial ischaemia is the main factor for detecting coronary artery disease (CAD) [4.2].

4.1. TYPES OF STRESS

4.1.1. Physical exercise

Exercise is the most physiological test for myocardial ischaemia. Owing to catecholamine release and sympathetic stimulation, exercise increases determinants of myocardial oxygen consumption: heart rate, blood pressure 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.

Haemodynamically significant coronary lesions with the potential to cause ischaemia are identified on myocardial perfusion imaging (MPI) as areas of decreased myocardial tracer uptake [4.3]. Under normal conditions, myocardial blood flow (MBF) increases approximately threefold at peak exercise compared with the baseline. The difference between basal and maximum achieved MBF is called the coronary reserve.

4.1.2. 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 [4.4, 4.5]. The biological half-time/life of dipyridamole is approximately 45 min. This and other vasodilators described below (adenosine and regadenoson) are generally safe but can occasionally

produce ischaemia (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 underperfused areas to normally perfused ones. A detailed description of this phenomenon is beyond the scope of this publication.

Adenosine, a non-selective adenosine receptor agonist, promotes vasodilatation by direct activation of vascular A₂ receptors when injected intravenously. In myocardium supplied by normal arteries, the MBF increases approximately three- to fourfold compared with the baseline with dipyridamole and approximately four- to fivefold with adenosine, whereas the MBF increases less in myocardium supplied by diseased arteries [4.6, 4.7]. Ischaemic or potentially ischaemic areas can be identified on MPI by heterogeneous tracer distribution, owing to a differential capacity of vessels to dilate. Adenosine biological half-life is about 10 s or less.

Regadenoson, a selective adenosine A₂ receptor agonist, is now available for utilization in some countries. It has been shown to have similar accuracy to adenosine for the detection of myocardial ischaemia, with fewer overall side effects [4.8, 4.9].

Dobutamine is a beta adrenergic agonist drug that increases the heart rate and myocardial contractility, promoting coronary hyperaemia through mechanisms similar to exercise [4.10]. It is a fast acting drug, with the effect starting approximately 2 min into infusion. Haemodynamic effects are dose dependent: at low doses of 5–10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, it increases myocardial contractility without significant change in the heart rate. Doses above 10–20 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ increase both the heart rate and myocardial contractility. In most countries, this is a less frequently used stress modality when vasodilator alternatives are available.

4.1.3. Patient preparation

When preparing the patient, instructions on fasting vary, but in general, heavy meals should be avoided before testing (see Table 4.1).

The interruption of medications will depend on the clinical question. If the reason for testing is a diagnosis of ischaemia in patients with no known CAD, then medications that could reduce ischaemic burden should be withheld [4.11]. Nevertheless, referring physicians may prefer to maintain medical therapy to be able to monitor the efficacy of the treatment administered.

It is preferable to give additional instructions to prepare for vasodilator stress as well (such as caffeine restriction) for all patients, in case the patient cannot exercise to the target heart rate and an alternative pharmacologic study should become necessary [4.12]. In the case that dobutamine stress is planned,

TABLE 4.1. WITHHOLDING TIMES FOR PATIENTS SCHEDULED FOR A STRESS TEST

Item to be considered	Minimum withholding time and comments
Medication	
Nitrates	24 h
Beta blockers	2–5 d (gradually to prevent rebound)
Calcium channel blockers	24–48 h
Methylxanthine compounds	72 h
Pentoxifylline	72 h
Oral dipyridamole/persantine	48 h
Phosphodiesterase inhibitors	48 h
Food and beverages	
Xanthine containing drinks and foods (coffee, tea, soft drinks and chocolate)	12 h
Fasting	Avoid heavy meals 2–4 h fasting
Clothing	Comfortable clothing and shoes, no accessories and avoid clothing with metallic elements

Note: Medication should be withdrawn if clinically indicated and in accordance with the attending physician’s indications.

beta blockers should be discontinued for two 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 in women of child bearing age, information is required on whether the patient is breast-feeding or may be pregnant; a pregnancy test should be performed if necessary. Local customs and traditions need to be taken into consideration, and a reflective

approach regarding cultural aspects is important when dealing with younger women, particularly with regard to pregnancy issues.

A secure intravenous line should be established for the administration of the 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 need to 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 patient and the clinical question being investigated. All involved personnel should also have the clinical skills to be able to recognize patients who might be at increased risk of complications (and thereby exclude them from stress testing) and to respond to potential medical emergencies.

Life support instrumentation and emergency drugs should be available in the immediate vicinity of the stress laboratory. Personnel trained in advanced cardiac life support or at the least basic life support should be available.

4.2. SELECTION OF STRESS TEST

Physical exercise is the stress modality of choice for all patients able to exercise adequately. It provides additional information (compared with pharmacological stress) such as: total exercise duration, stress test segment changes, development of symptoms (chest pain), haemodynamic changes (blood pressure and heart rate) and arrhythmias. In addition, the quality of MPI is often better with exercise compared with pharmacological stress, and this is related to less subdiaphragmatic uptake and hence fewer inferior wall artefacts. Details on the diagnostic criteria for the stress testing are included in specific guidelines [4.13, 4.14].

Accepted indications for vasodilator stress include:

- An inability to exercise.
- Failure to achieve 85% maximum predicted heart rate (MPHR, see Section 4.3.1) in the absence of typical angina or ischaemic stress test segment depression.
- Concurrent beta blockade (or calcium antagonist) therapy (relative indication).
- The presence of a left bundle branch block or pacemaker; dobutamine stress is mainly indicated in patients with reactive airway disease (severe chronic obstructive pulmonary disease 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).

4.3. STRESS PROTOCOLS

4.3.1. Exercise

According to the recommendations of Ref. [4.15]:

“The electrocardiogram [ECG], heart rate and blood pressure must be recorded during each stage of exercise. The patient should be continuously monitored for transient rhythm disturbances, ST segment changes, other electrocardiographic manifestations of heart diseases and symptoms. A single ECG lead during stress testing is not sufficient for the detection and recognition of arrhythmias or ischaemic patterns, but a twelve lead ECG is recommended.”

The goal of exercise is to stress the patient to exhaustion and to the MPHR for the age ($220 - \text{age} = \text{maximum heart rate}$). If the patient is unable to reach the MPHR, then 85% of the MPHR is an acceptable target. If the increase in heart rate does not reach at least 85% of the MPHR, in the absence of typical angina or a clearly positive ECG by stress test 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 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 individuals, 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 minute after injection.

4.3.2. Pharmacologic stress agents

The most widely available pharmacologic agents used for stress testing include dipyridamole, adenosine, selective adenosine A2 receptor agonists and dobutamine:

(a) Dipyridamole:

- Dipyridamole is commonly used at a dose of 0.56 mg/kg over 4 min, but protocols using an additional 0.28 mg/kg can also be applied, to a maximum total dose of 60 mg.

- The radiopharmaceutical is injected 3–5 min after termination of dipyridamole (7–9 min from the start) [4.16]. Cardiac monitoring should be performed during the test.
 - 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. It is administered by slow intravenous push (approximately 25 mg every 20 s) 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 of up to 250 mg.
 - Supplemental exercise (e.g. bicycle, treadmill or straight leg raising) can be used to improve image quality and possibly sensitivity (see Section 4.3.3).
- (b) Adenosine:
- Adenosine is infused intravenously with a pump at a rate of $140 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ over 4–6 min. Blood pressure, heart rate and ECG are monitored every 1 min.
 - The radiopharmaceutical is administered intravenously 2 min into the adenosine infusion when the 4 min protocol is used, or 3 min into the infusion when the 6 min protocol is used.
 - Adenosine has a very short half-life of less than 10 s. 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. Therefore, side effects may last much longer than may be suggested by the drug's very short half-life.
- (c) Selective adenosine A2 receptor agonists:
- Regadenoson is given as a 10 s bolus, at a fixed dose of 400 μg , administered 30 s prior to tracer injection. The same patient monitoring and other measures apply as for dipyridamole and adenosine, although fewer side effects are expected.
- (d) Dobutamine:
- The protocol most commonly used starts with an infusion rate of $10 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, increasing by an additional dose of $10 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ every 3 min, to a maximum dose of $40\text{--}50 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$.
 - The radiopharmaceutical is injected once the target heart rate is achieved, and the infusion of dobutamine is continued for another minute. ECG and blood pressure are monitored at baseline and every 3 min thereafter.

- Atropine may be used to increase the heart rate, starting at the second stage [4.17]. Boluses of 0.5 mg of atropine can be given, with an interval of at least a minute between boluses, to a maximum dose of 2 mg in order to increase the 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 driving in the two 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 is reported in a meta-analysis of 26 438 patients [4.18]. Moreover, significant supraventricular or ventricular arrhythmias occur not infrequently. For example, in one study of 312 consecutive dobutamine stress tests, atrial fibrillation was noted in 6 (1.9%) studies, paroxysmal supraventricular tachycardia in 15 (4.8%) and ventricular tachycardia in 29 (9.3%) [4.19].

4.3.3. 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 [4.20–4.22].

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, a reduction in side effects with this strategy has been described [4.21]. As well as 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 with a vasodilator alone.

The main indications for combining vasodilator and exercise stress include:

- (i) an inability to exercise to 85% MPHR but the ability to at least walk; and
- (ii) concurrent use of medications that may limit heart rate increase.

It is important to note that patients with a left bundle branch block 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 according to the patient's abilities, and the tracer is injected at the same time as described for the adenosine or dipyridamole protocols.

4.4. CONTRAINDICATIONS

Absolute and relative contraindications to stress tests and test interruption criteria are described in Tables 4.2 and 4.3.

TABLE 4.2. CONTRAINDICATIONS FOR VARIOUS TYPES OF STRESS

Contraindications	Reason
All types of stress	High risk unstable angina Acute myocardial infarction (within two days) Uncontrolled symptomatic heart failure Uncontrolled arrhythmias causing symptoms or haemodynamic compromise Unwillingness or inability to give informed consent (legislation dependent)
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 (determined 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

TABLE 4.2. CONTRAINDICATIONS FOR VARIOUS TYPES OF STRESS
(cont.)

Contraindications	Reason
Vasodilators (dipyridamole and adenosine)	Second or third degree atrioventricular block or sick sinus syndrome Bronchospastic disease (active wheezing/rhonchi, steroid dependency for asthma/chronic obstructive pulmonary disease, depressed forced expiratory volume 1, hospitalization for respiratory failure) Hypotension (SBP < 90 mmHg) Ongoing transient ischaemic attack or recent cerebrovascular accident (<6 months). Caffeine/theophylline (or similar) intake within the past 12 h
Dobutamine	Cardiac arrhythmias, including atrial fibrillation and ventricular tachycardia Severe aortic stenosis or hypertrophic obstructive cardiomyopathy. Hypotension (SBP < 90 mmHg) or uncontrolled hypertension (SBP > 200 mmHg) Aortic abdominal aneurysm > 5 cm diameter (relative contraindication) Presence of left ventricular thrombus (relative contraindication) Presence of an implanted ventricular defibrillator Left ventricular ejection fraction < 25% (this represents a relative contraindication due to increased risk of ventricular arrhythmia; risk/benefit to be carefully evaluated)

Source: See Refs [4.13, 4.14, 4.23].

Note: SBP — systolic blood pressure.

TABLE 4.3. CRITERIA FOR EARLY TERMINATION OF EXERCISE TESTING

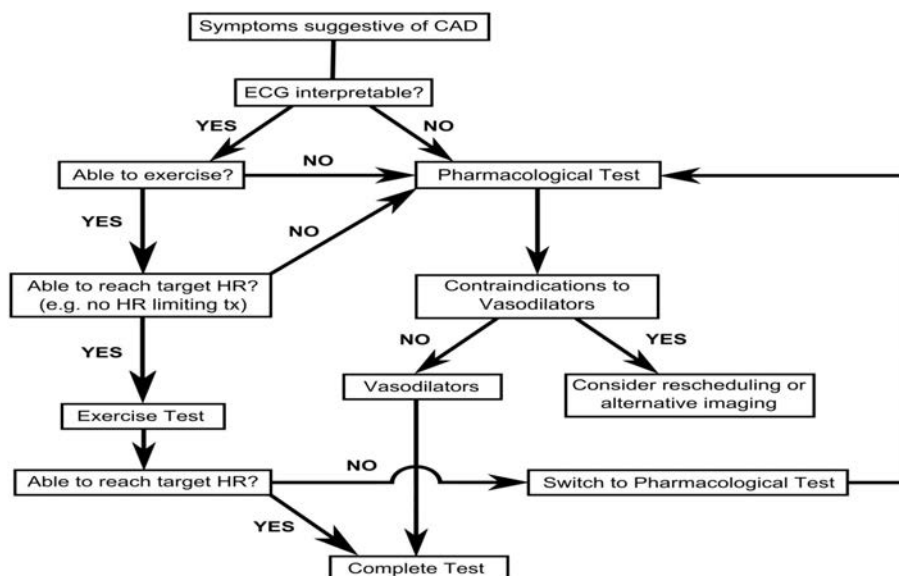
Indication	Reason
Absolute indications for interruption	Drop in SBP > 10 mmHg from baseline SBP despite an increase in workload, when accompanied by other evidence of ischaemia Moderate to severe ischaemia in ECG (ST depression > 3 mm) Increasing nervous system symptoms (e.g. ataxia, dizziness or near-syncope)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

Source: See Refs [4.13, 4.14, 4.23].

Note: ECG — electrocardiogram; DBP — diastolic blood pressure; PVC — premature ventricular contraction; SBP — systolic blood pressure.

4.5. OPTIMIZATION OF STRESS TESTS IN MYOCARDIAL PERFUSION IMAGING

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 Fig. 4.1.



Note: CAD — coronary artery disease; ECG — electrocardiogram; HR — heart rate.

FIG. 4.1. Optimization of stress tests in MPI.

4.6. RADIOPHARMACEUTICALS AND IMAGING PROTOCOLS

4.6.1. ^{99m}Tc -sestamibi and ^{99m}Tc -tetrofosmin

The perfusion imaging agents most commonly used clinically are ^{99m}Tc -sestamibi and ^{99m}Tc -tetrofosmin. The administered activities generally recommended, including by the International Commission on Radiological Protection, are shown in Table 4.4 [4.24].

Myocardial uptake of ^{99m}Tc labelled tracers increases proportionately with the MBF 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}Tl).

Unlike ^{201}Tl , sestamibi and tetrofosmin have no significant redistribution, and separate injections are given to assess stress and resting perfusion. The 6 h physical half-life of ^{99m}Tc means that stress and rest injections should ideally be performed on separate days to allow for the decay of activity from the first injection.

TABLE 4.4. SPECT MYOCARDIAL PERFUSION IMAGING PROTOCOLS: GENERALLY RECOMMENDED RADIOPHARMACEUTICAL ACTIVITIES AND THEIR CORRESPONDING RADIATION EFFECTIVE DOSES

Protocol	First injection			Second injection			Total effective dose if stress-only (mSv)
	Given at	Activity (MBq)	Effective dose (mSv)	Given at	Activity (MBq)	Effective dose (mSv)	
Tc-99m protocols							
Tc-99m one day stress first/stress-only	Stress	296–444	2.0–3.0	(Rest)	888–1332	7.0–10.5	9.0–13.5 2.0–3.0
Tc-99m one day rest/stress	Rest	296–444	2.3–3.5	Stress	888–1332	6.1–9.1	8.4–12.6 n.a.*
Tc-99m two day stress/rest	Stress	296–444	2.0–3.0	(Rest)	296–444	2.3–3.5	4.3–6.5 2.0–3.0
Tc-99m two day stress/rest (large patient)	Stress	666–1110	4.5–7.6	(Rest)	666–1110	5.2–8.7	9.8–16.3 4.5–7.6
Tc-99m two day rest/stress	Rest	296–444	2.3–3.5	Stress	296–444	2.0–3.0	4.3–6.5 n.a.*
Tc-99m two day rest/stress (large patient)	Rest	666–1110	5.2–8.7	Stress	666–1110	4.5–7.6	9.8–16.3 n.a.*
Tl-201 protocols							
Tl-201 stress/redistribution rest	Stress	93–130	10.9–15.3	n.a.*	n.a.*	n.a.*	10.9–15.3
Tl-201 stress/redistribution rest/reinjection	Stress	93–130	10.9–15.3	Rest	37–74	4.4–8.8	15.3–24.1 n.a.*
Tl-201 rest/redistribution	Rest	93–130	10.9–15.3	n.a.*	n.a.*	n.a.*	10.9–15.3 n.a.*
Dual isotope Tl-201 rest/Tc-99m stress	Rest	93–130	10.9–15.3	Stress	296–444	2.0–3.0	13.0–18.3 n.a.*
Dual isotope Tl-201 rest/Tc-99m stress (large patient)	Rest	111–130	13.1–15.3	Stress	666–1110	4.5–7.6	17.7–22.9 n.a.*

TABLE 4.4. SPECT MYOCARDIAL PERFUSION IMAGING PROTOCOLS: GENERALLY RECOMMENDED RADIOPHARMACEUTICAL ACTIVITIES AND THEIR CORRESPONDING RADIATION EFFECTIVE DOSES (cont.)

Protocol	First injection			Second injection			Total effective dose if stress-only (mSv)
	Given at	Activity (MBq)	Effective dose (mSv)	Given at	Activity (MBq)	Effective dose (mSv)	
Newer technology reduced-dose protocols							
Tc-99m one day stress first/stress only	Stress	148–222	1.0–1.5	(Rest)	444–666	3.5–5.2	1.0–1.5
Tc-99m one day rest/stress	Rest	148–222	1.2–1.7	Stress	444–666	3.0–4.5	n.a.*
Tc-99m two day stress/rest	Stress	148–222	1.0–1.5	(Rest)	148–222	1.2–1.7	1.0–1.5
Tc-99m two day stress/rest (large patient)	Stress	333–555	2.3–3.8	(Rest)	333–555	2.6–4.4	2.3–3.8
Tc-99m two day rest/stress	Rest	148–222	1.2–1.7	Stress	148–222	1.0–1.5	n.a.*
Tc-99m two day rest/stress (large patient)	Rest	333–555	2.6–4.4	Stress	333–555	2.3–3.8	n.a.*

* n.a.: not applicable.

Note: (Rest) denotes optional rest injection. Experts generally recommend that stress images be reviewed by a nuclear cardiology physician prior to rest injection, and that the rest injection only be performed where clinically warranted. Newer technology reduced-dose protocols have been studied for high efficiency cameras, and for image reconstruction with iterative reconstruction, depth dependent resolution recovery and noise modelling. Radiation effective dose values listed here are dose to a reference individual. Doses were determined using recent International Commission on Radiological Protection organ dose coefficients, and tissue weighing factors in Ref. [4.24]. Technetium-99m doses represent an average for ^{99m}Tc -sestamibi and ^{99m}Tc -tetrofosmin.

4.6.1.1. Two day protocol

A two day protocol is preferable to a single day protocol because it provides both images with virtually no shine through of counts from the first injection to the second injection and enables the radiation dose to be minimized (see Fig. 4.2). Doses to patients and staff are minimized because a two day protocol requires no more radioactivity for the second injection than for the first injection, in contrast to a single day protocol, in which the second injection should have at least three times as many counts as the first injection to minimize effects of shine through. Two day studies use the same administered activity each day, which also facilitates comparison between stress and rest images. Two day studies should generally be performed with stress imaging on the first day, which enables omitting the second day of the protocol if stress imaging is completely normal (e.g. normal perfusion, normal left ventricular volume and ejection fraction, and no increased right ventricular tracer uptake).

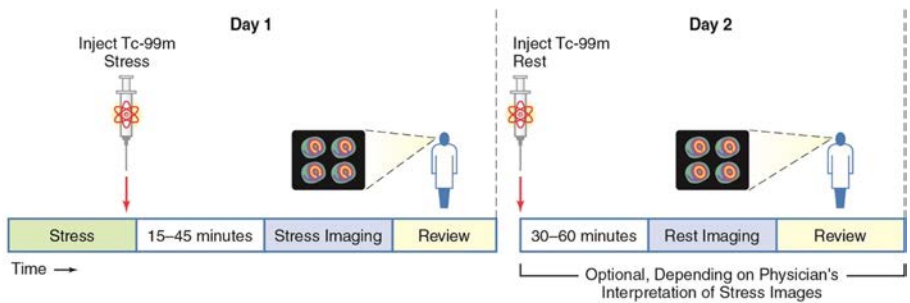


FIG. 4.2. Schematic representation of two day protocol with ^{99m}Tc agents (reproduced from Ref. [4.16] with permission courtesy of the American Society of Nuclear Cardiology).

4.6.1.2. Single day protocol

Single day protocols may be preferred in some settings for the patients' convenience, as they do not need to return to the nuclear laboratory on the second day if stress images demonstrate some abnormality (see Figs 4.3 and 4.4).

The order of stress and rest imaging in a single day protocol depends to some extent on the indication for the investigation. In any event, the second injection should provide at least 3–4 times as many scintigraphic counts as the first injection to minimize the problem of shine through. Unless there is a very

long delay between injections, this requires that the administered activity be at least three times greater for the second injection.

When the study is performed for the diagnosis of myocardial ischaemia, as is the case for most MPI studies, the stress study should be performed first to allow omission of rest imaging if stress imaging is completely normal (i.e. stress-only imaging) as well as to avoid shine through from the rest injection into the stress induced defect. In a patient with a known previous infarction, it may be preferable to perform the resting study first. A review of the rest images enables the next component of the study to be tailored as either stress imaging or viability assessment, as appropriate. Routine rest-first imaging (rest/stress) should not be performed, as it eliminates the possibility of performing stress-only imaging in patients with normal studies.

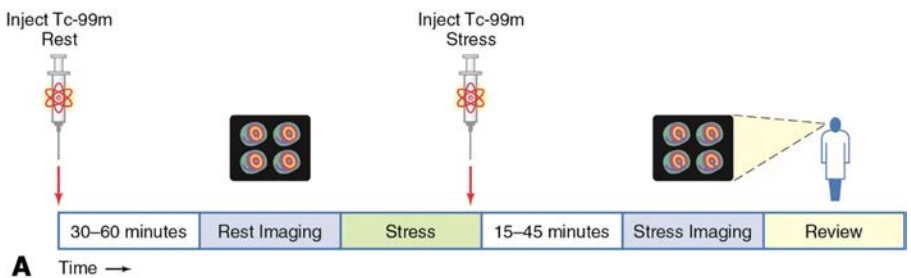


FIG. 4.3. Schematic representation of same day rest/stress protocol with ^{99m}Tc agents (reproduced from Ref. [4.16] with permission courtesy of the American Society of Nuclear Cardiology).

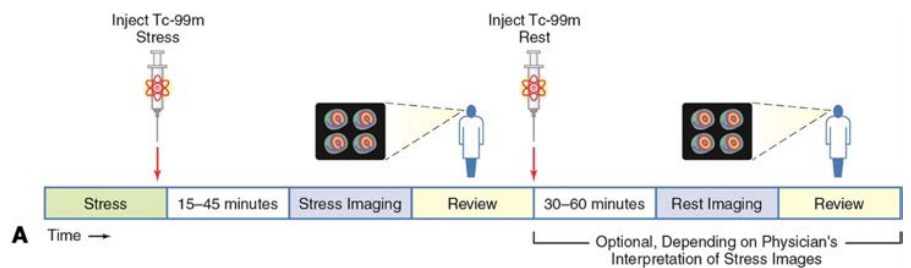


FIG. 4.4. Schematic representation of same day stress/rest protocol with ^{99m}Tc agents (reproduced from Ref. [4.16] with permission courtesy of the American Society of Nuclear Cardiology).

4.6.1.3. Acquisition

Image acquisition using ^{99m}Tc agents could begin as early as 10 min after exercise injection to allow for post-exercise stunning detection [4.25]. Longer delays are generally required for both resting images and stress with vasodilators alone because of the higher subdiaphragmatic ^{99m}Tc activity.

4.6.1.4. Nitrates

If the patient is referred for viability evaluation, or if the patient presents a severe perfusion defect on stress images, sublingual nitroglycerin, usually at a dose of 400–800 μg (or isosorbide dinitrate 10 mg) can be administered at least 5 min before radiotracer injection 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 the systolic blood pressure is less than or equal to 90 mmHg, experts generally do not recommend nitrates.

4.6.1.5. Fluids

The intake of fluid, such as plain water, can be used in an attempt to clear intestinal activity. Initially, experts generally recommended fatty meals with ^{99m}Tc tracers in order to accelerate hepatobiliary clearance of activity. However, most laboratories today try to avoid this, since gall bladder contraction after a meal produces a large amount of activity to be excreted into the intestinal lumen, with unpredictable consequences on image quality.

4.6.1.6. Medication

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

4.6.2. Thallium-201

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. Thallium-201 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 h after injection. When the clinical question is about viability, imaging at 24 h can be performed [4.26].

Comparison between the stress and redistribution images distinguishes between the reversible defect of inducible hypoperfusion and the fixed defect of myocardial necrosis. In some cases, redistribution may be incomplete at 4 h. A second injection of ^{201}Tl can then be given and reinjection images acquired for a more accurate assessment of myocardial viability [4.26].

Different imaging protocols can be followed, depending on the clinical indications and local practices (see Fig. 4.5):

- Stress/redistribution;
- Stress/reinjection;
- Stress/redistribution/reinjection;
- Stress/reinjection/delayed 24 h imaging;
- Rest/redistribution.

4.6.2.1. Imaging protocols for ^{201}Tl

Stress imaging should begin within 5–15 min of tracer injection and should be finished within 30 min of injection. Redistribution rest imaging should be performed after a 2.5–4 h delay. Late redistribution imaging can also be performed 24 h after injection using a longer acquisition time for the assessment of myocardial viability [4.26].

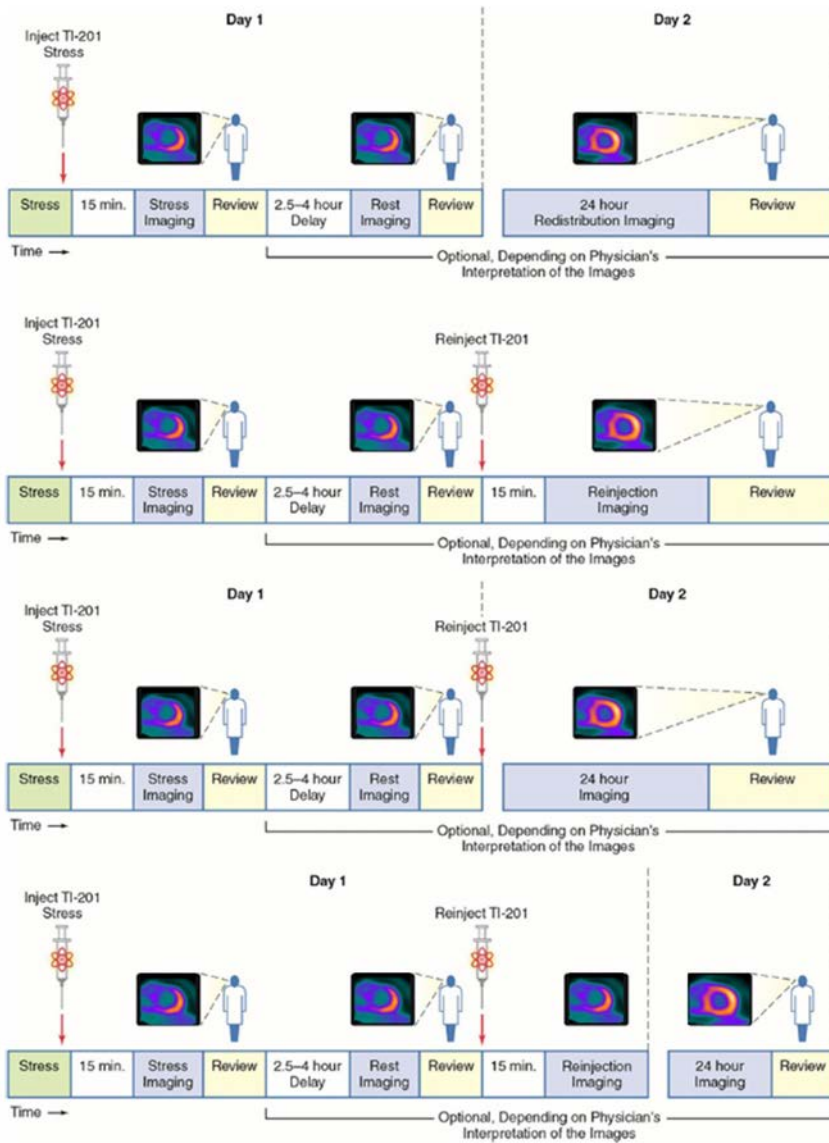
In patients with severe perfusion defects in the stress images or if redistribution is thought to be incomplete at the time of redistribution imaging, an additional ‘reinjection’ can be given (ideally after sublingual nitrates), with imaging after a further 60 min of redistribution [4.26].

For viability assessment, under certain clinical scenarios, the stress component can be omitted and only rest imaging performed.

4.6.3. Dual isotope protocols

Dual isotope protocols use both ^{201}Tl and $^{99\text{m}}\text{Tc}$ tracers and ideally should not be routinely used [4.27]. Not only do rest and stress images have a different appearance, owing to the different tracers used, but also the radiation effective dose is very high for this protocol.

Normally, the ^{201}Tl injection at rest is given first followed by the stress injection of the $^{99\text{m}}\text{Tc}$ agent ($^{99\text{m}}\text{Tc}$ -sestamibi or $^{99\text{m}}\text{Tc}$ -tetrofosmin). Common drawbacks associated with different imaging protocols are summarized in Table 4.5.



Note: Top row — Stress/redistribution rest/24 hour redistribution imaging. Second row — Stress/redistribution rest/reinjection/same day post-reinjection imaging. Third row — Stress/redistribution rest/reinjection/24 hour redistribution. Bottom row — Stress/redistribution rest/reinjection/same day post-reinjection imaging/24 hour redistribution imaging.

FIG. 4.5. Various imaging protocols for ^{201}Tl imaging (courtesy of the American Society of Nuclear Cardiology).

TABLE 4.5. COMMON DRAWBACKS ASSOCIATED WITH DIFFERENT IMAGING PROTOCOLS

Protocol	Drawback
^{99m} Tc-sestamibi/tetrofosmin stress/rest: general	Tracer uptake often (rest and pharmacologic stress studies) high in subdiaphragmatic regions with extracardiac hot spots
Two day protocol	Logistics: patient comes in on two different days if the stress study is not normal
One day stress/rest protocol	Reversibility may be underestimated because of shine through of remaining myocardial activity from the stress study
One day rest/stress protocol	Two tracer injections are necessary even if the stress study is normal Stress defects may be underestimated owing to interference from shine through myocardial activity from the resting study
Dual isotope protocol	Comparison of ²⁰¹ Tl and ^{99m} Tc tracer uptake may be influenced by differences in attenuation and spillover from extracardiac sources High radiation exposure
²⁰¹ Tl stress redistribution	Attenuation artefacts may affect interpretation Evaluation of left ventricular ejection fraction and wall motion is inferior compared with ^{99m} Tc labelled tracers Higher radiation exposure compared with ^{99m} Tc labelled tracers

Source: See Ref. [4.15].

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5. ACQUISITION AND PROCESSING OF MYOCARDIAL PERFUSION IMAGING STUDIES

5.1. ACQUISITION

5.1.1. General guidance

Experts generally recommend the following:

- The procedure should be explained to the patient before commencing.
- Implanted radiopaque objects (e.g. pacemakers and silicone implants) 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.
- Single photon emission computed tomography (SPECT) is currently the standard technique for myocardial perfusion imaging (MPI) studies. Planar acquisition is generally no longer accepted for this procedure.

5.1.2. Image acquisition

5.1.2.1. Patient positioning

The supine position is commonly used for conventional SPECT, with arms away from the field of view (at least the left arm folded behind head). The position needs to be the same in both acquisitions (stress/rest). If available, supporting devices appropriate for gamma cameras can be used for the patient's comfort.

Experts generally recommend the prone position 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.

Patient positioning for the new solid state SPECT scanners may vary (see Table 5.1).

5.1.2.2. Acquisition parameters

A list of acquisition parameters for conventional SPECT is presented in Table 5.2. The acquisition parameters for solid state SPECT scanners are typically manufacturer recommended.

TABLE 5.1. PATIENT POSITIONING FOR SPECT ACQUISITION

	Patient position		
	Supine	Upright	Prone
Conventional SPECT	Standard	n.a.	Suitable in setting of possible attenuation artefact
Solid state (CZT) SPECT with pinhole collimators	Standard	n.a.	Suitable in setting of possible attenuation artefact
CZT SPECT fanning detector SPECT	Optional Suitable (semi-recumbent) in setting of possible attenuation artefact	Standard	n.a.
Caesium iodide SPECT	n.a.	Standard	n.a.

Source: See Ref. [5.1].

Note: CZT — cadmium zinc telluride; n.a. — not applicable; SPECT — single photon emission computed tomography.

TABLE 5.2. CONVENTIONAL SPECT ACQUISITION PARAMETERS FOR ²⁰¹Tl AND ^{99m}Tc MYOCARDIAL PERFUSION IMAGING

Parameter	Isotope	
	²⁰¹ Tl	^{99m} Tc
Energy window	25–30% symm, 72–75 keV 20% symm, 167 keV	15–20% symm, 140 keV
Collimators	Low energy general purpose	Low energy high resolution
Rotation (1 or 2 head)	180° (optional 360° for triple head) (45° RAO to 45° LPO)	

TABLE 5.2. CONVENTIONAL SPECT ACQUISITION PARAMETERS FOR ²⁰¹Tl AND ^{99m}Tc MYOCARDIAL PERFUSION IMAGING (cont.)

Parameter	Isotope	
	²⁰¹ Tl	^{99m} Tc
Acquisition type	Step and shoot	
No. of prs, 180°	32 or 64	60 or 64
Time per pr	40 s (32 prs) 25 s (64 prs)	Two day protocol: 25 s One day protocol: 1st (low dose): 25 s 2nd (high dose): 20 s

Source: See Ref. [5.1].

Note: Solid state SPECT scanners acquire images in a continuous mode, with electronic collimators, in a 180° acquisition. LPO — left posterior oblique; pr — projection; RAO — right anterior oblique; symm — symmetric.

5.1.2.3. *Field of view*

It is important that the heart be included in every projection image. If this is not the case, the resulting truncation of the images may produce artefacts in the final reconstructed images.

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

Solid state SPECT scanners use cardifocal collimation, which makes it more important to position the heart at the centre of the field of view to avoid truncation artefacts. Positioning may be particularly important for scanners with converging pinhole collimators, as different z axis positioning for rest and stress may result in imaging artefacts.

5.1.3. **Orbit**

A 180° orbit (45° right anterior oblique to 45° left posterior oblique) is commonly used for both single and dual detector systems. For a 180° acquisition with dual head cameras, detectors should be in a 90° configuration. The majority of cameras (~75%) allow an adaptation of the configuration depending on the contours of the patient. The main orbit options are circular and non-circular (elliptical or body contoured). According to Ref. [5.1], “Noncircular orbits follow the contour of the patient, bringing the camera closer to the patient,

thereby improving spatial resolution”, but they may suffer from reconstruction artefacts due to changes in spatial resolution (see also Ref. [5.2]). Reference [5.1] continues:

“Circular orbits maintain a fixed radius of rotation and 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, a non-circular orbit with body autocontouring is generally used. The orbit for solid state SPECT scanners is predetermined by the type of scanner.

5.1.4. Acquisition type

According to Ref. [5.3]:

“The camera may move in a continuous motion during acquisition but typically remains 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 [5.4, 5.5].

Solid state SPECT scanners (pinhole collimator and fanning beam detector scanners) acquire images in a continuous mode without step and shoot. This may prove advantageous for tomographic dynamic image acquisition to quantify myocardial blood flow.

5.1.5. Pixel and matrix size

Pixel size is typically 6.4 ± 0.4 mm for a 64×64 image matrix. Zoom should be performed 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 in both stress and rest for left ventricular 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 remembering to use the same factor for both sets of studies for appropriate comparison.

The selection of the matrix relies on the pixel size and the system spatial resolution. The selected matrix should imply a pixel size less than one third of the system spatial resolution in order to keep an adequate spatial resolution (see Table 5.3).

Newer SPECT scanners use a 128×128 matrix size and pixelated detector arrays with a typical intrinsic spatial resolution of 2.4 mm [5.6].

TABLE 5.3. RELATIONSHIP BETWEEN SYSTEM RESOLUTION (FULL WIDTH AT HALF MAXIMUM) MATRIX AND PIXEL SIZE

System spatial resolution	Matrix size (pixels)	Pixel size (mm)
Isotopes FWHM = 12 mm	128×128	3.2 ± 0.2
Isotopes FWHM = 20 mm	64×64	6.4 ± 0.4

Note: FWHM — full width at half maximum.

5.1.6. Acquisition time

The time per projection is always a compromise between improved count statistics and increased risk of patient movement. Experts generally recommend that the overall acquisition time for each rest or stress scan be kept below 20 min.

Solid state SPECT detectors offer high count sensitivity. This property can be used to significantly reduce scanning time (as low as 2 min) or significantly reduce radiotracer activity to the patient (as low as 111 MBq of ^{99m}Tc) [5.7].

Modified iterative reconstruction software incorporating resolution recovery, and noise reduction methods both offer the possibility of performing fast acquisition protocols in order to reduce the scanning time or the injected dose [5.7].

5.1.7. Gated studies

Gated SPECT studies can be performed with both ^{201}Tl and ^{99m}Tc labelled tracers (^{99m}Tc -sestamibi and ^{99m}Tc -tetrofosmin). However, the assessment of regional wall motion is more accurate with ^{99m}Tc labelled tracers because of the higher count statistics [5.8]. Special attention needs to be paid to adequate count density and in particular to lower activity acquisitions.

Before starting the acquisition, a careful check for a correct electrocardiogram trigger signal is performed (experts generally recommend gating only if the patient has a fairly regular heart rhythm). Gated SPECT volumes and ejection fraction may not be reliable in patients with atrial fibrillation, sinus arrhythmia, frequent premature beats, or 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).

Experts generally recommend a wide window 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 is probably the most widely used method of gated SPECT MPI. This may result in a slight underestimation of left ventricular ejection fraction (LVEF) values when compared with 16 frames/cardiac cycle gating. Many institutions are now using 16 frames/cardiac cycle (especially with high sensitivity detectors) (see Table 5.4).

Whatever number of gated frames is used, consistency needs to be kept within a laboratory in order to establish normal values and to enable intra- and interpatient comparison. Experts generally recommend that both stress and rest studies be gated.

TABLE 5.4. ACQUISITION PARAMETERS FOR GATED SPECT ^{99m}Tc AND ²⁰¹Tl MYOCARDIAL PERFUSION IMAGING STUDIES

Parameter	Rest	Stress
Frames/cardiac cycle	8 (16 optional)	8 (16 optional)
R-to-R window	90–100%	90–100%

5.1.8. Quality assurance

Quality assurance 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

IAEA Safety Standards Series No. GSR Part 3, Radiation Protection and Safety of Radiation Sources: International Basic Safety Standards [5.9]. Readers are encouraged to take a closer look at the literature on quality assurance for SPECT systems in Ref. [5.10]. Experts generally recommend manufacturer recommended quality assurance practices for the newer solid state SPECT scanners.

5.2. PROCESSING

5.2.1. Motion correction

Images are to be reviewed immediately after acquisition to check for motion and extracardiac hot spots, before the patient is discharged from the department.

Quality control of cardiac studies implies primarily the evaluation of the rotating projection images for the presence of motion during acquisition. If significant motion is present, experts generally recommend a repeat image acquisition; a less desirable alternative may be the use of motion correction software. Nevertheless, for ^{201}Tl stress imaging, motion correction may be preferable. Repeat imaging more than 20 min after initial imaging will generally be associated with redistribution of radiotracers no longer reflecting stress imaging.

Each vendor may offer a specific motion correction package for each scanner. It should be noted that these methods only correct relatively simple forms of motion, such as motion in the vertical axis. More complex patterns of motion involving rotational motion cannot be adequately corrected using current methods.

It has been demonstrated that movement by one pixel does not produce significant artefacts in the reconstructed images [5.11, 5.12]. Correction of significant motion should be attempted by repeat image acquisition also considering prone position, or by using software if this is not possible.

Detection of motion, by a review of the rotating projection images, can be challenging with the solid state SPECT scanners owing to continuous image acquisition. The panogram or sinogram images may be reviewed to identify patient motion with the new solid state scanners.

5.2.2. Image reconstruction

Both filtered back projection (FBP) and iterative methods are useful but the latter (such as maximum likelihood expectation maximization or ordered subset expectation maximization) are preferred, since they offer more accurate modelling of physical processes and reduce noise [5.13]. These are now generally

available from all manufacturers and are included in standard reconstruction software packages.

Generally, if FBP is used, the type of filter, cut-off frequency and order factors might 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 is not always the same across manufacturers, so the final results may vary slightly.

The same reconstruction technique should be used consistently for the rest and stress portions of a patient’s study unless modifications are needed in specific cases to keep a comparable count density/image appearance in both stress and rest images. Table 5.5 presents a list of reconstruction parameters for conventional SPECT.

TABLE 5.5. COMMON RECONSTRUCTION TECHNIQUES APPLIED IN CONVENTIONAL SPECT MYOCARDIAL PERFUSION IMAGING

FBP				
	Radioisotope	Activity (MBq)	Cut-off frequency	Order factor
Butterworth	^{201}Tl	93–130	0.3–0.4	6
	$^{99\text{m}}\text{Tc}$	296–444	0.3–0.4	6
	$^{99\text{m}}\text{Tc}$ large patient	666–1110	0.4–0.5	6
Hamming	^{201}Tl	93–130	0.25–0.40	n.a.
	$^{99\text{m}}\text{Tc}$	296–444	0.30–0.45	n.a.
		666–1110	0.45–0.60	n.a.
Iterative				
MLEM	Iterations: 10–15		No prefiltering needed	
OSEM	Iterations: 2–5		No prefiltering needed	
	Subsets: 8			

Note: Novel solid state scanners typically use iterative reconstruction methods with resolution recovery and noise reduction algorithms included. FBP — filtered back projection; MLEM — maximum likelihood expectation maximization; n.a. — not applicable; OSEM — ordered subset expectation maximization.

5.2.3. Reorientation

According to Ref. [5.1]:

“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.... Inappropriate plane selections can result in misaligned myocardial walls between rest and stress data sets, potentially resulting in incorrect interpretation. It is crucial that all axis choices be available as QC [quality control] screens, and that these are reviewed by the technologist and the physician who reads each study to verify that axes were selected properly.”

Automated methods of reorientation are available and have been shown to be at least as accurate as trained operators and may achieve greater reproducibility. Automated methods result in the sectioning of the data into vertical long axis, horizontal long axis and short axis planes [5.14, 5.15].

5.2.4. Image display

Images should be displayed and interpreted using a dedicated workstation and commercial cardiac image display software. Experts generally do not recommend interpreting images using printed film, and rotating raw projection images should be reviewed in cine mode to check for the patient’s movements.

Stress and rest images should be displayed appropriately (stress on top and rest on the bottom) and appropriately aligned for ready comparison [5.16]. Each tomographic acquisition 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, using a linear colour scale, complemented in some cases with a grey scale or a step scale. Step scales can artificially increase or decrease the size and intensity of a perfusion defect depending on the relationship between voxel intensities and the thresholds built into the map [5.16].

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. 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 [5.16]. Removal of subdiaphragmatic activity should be attempted for final display.

Three sets of axis should be displayed: short axis slices from apex to base; vertical long axis slices from septal to lateral; and horizontal long axis slices from inferior to anterior wall. Sequential images (stress and rest) should be aligned and adjacent to each other serially.

Each series of stress/rest (and/or redistribution in the case of ^{201}Tl) should be normalized to the brightest pixel in the entire series separately.

5.2.5. Quantification

Quantification is an extremely valuable tool in MPI because 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 (Quantitative Gated SPECT, Quantitative Perfusion SPECT), Emory Cardiac Toolbox and 4DM SPECT. These methods have been extensively validated, but their use is not fully interchangeable [5.17–5.19]. Quantitation software should only be used as an addition to qualitative assessment and not in isolation.

5.2.6. Perfusion defect size

The perfusion defect size correlates with the extent of coronary artery disease (CAD). The size of perfusion defects can generally be calculated in one of two ways: using software or using visual scoring. A perfusion defect (stress or rest) is usually considered as significant when the perfusion intensity is less than 2.5 standard deviations below that of the normal database or visually reduced compared with the most normal segment.

Quantification by percentage size of the left ventricle (% terms, limits 0–100%):

- Small (0–10%);
- Medium (>10% to 20%);
- Large (>20%).

5.2.7. Perfusion defect severity

The perfusion defect severity correlates with the severity of CAD. The perfusion defect severity can be divided and scored as follows (see Fig. 5.1):

- Absent uptake = 4;
- Severely reduced uptake = 3;
- Moderately reduced uptake = 2;
- Mildly reduced uptake = 1;
- Normal uptake = 0.

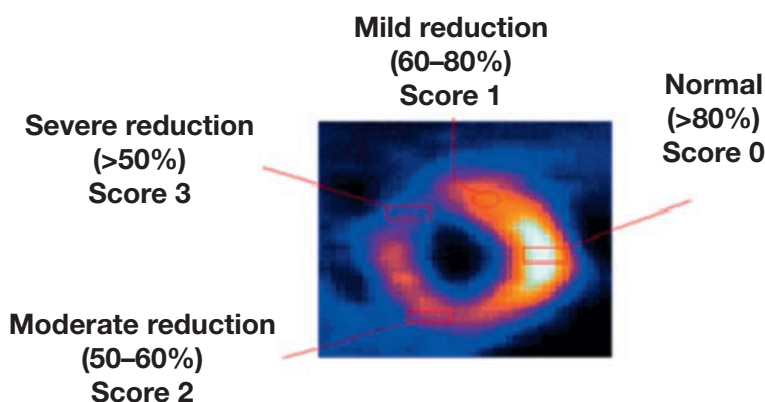
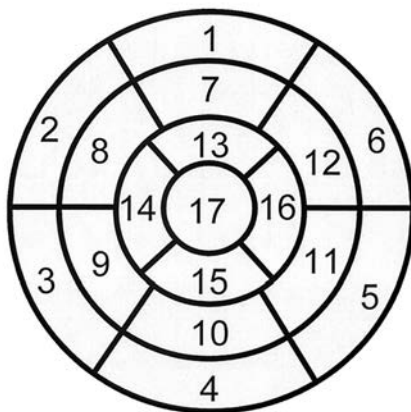


FIG. 5.1. Perfusion defect severity scoring of MPI (courtesy of R. Giubbini, University of Brescia, Italy).

5.2.8. Summed stress, rest and difference scores

The summed scores take into account the extent and severity of myocardial perfusion defects. The severity of perfusion defects in each of the 17 myocardial segments (see Fig. 5.2), as defined by the American Heart Association [5.20], is scored on a 0–4 scale as described above. The sum of the scores on the 17 left ventricular myocardial segments of the stress images is called the summed stress score. The difference between the stress and rest scores is the summed difference score. Software derived summed scores should be consistent with the

Left Ventricular Segmentation



- | | | |
|------------------------|-----------------------|---------------------|
| 1. basal anterior | 7. mid anterior | 13. apical anterior |
| 2. basal anteroseptal | 8. mid anteroseptal | 14. apical septal |
| 3. basal inferoseptal | 9. mid inferoseptal | 15. apical inferior |
| 4. basal inferior | 10. mid inferior | 16. apical lateral |
| 5. basal inferolateral | 11. mid inferolateral | 17. apex |
| 6. basal anterolateral | 12. mid anterolateral | |

FIG. 5.2. The 17 myocardial segments (reproduced from Ref. [5.20] with permission courtesy of the American Heart Association).

visual analysis of the images, since there are several possible pitfalls in the score calculation:

- Summed stress score: This represents the perfusion defect seen at stress and includes ischaemia and infarction. A summed stress score ≤ 3 is consistent with a normal result, while 4–8 is a mild defect, 9–12 is a moderate defect and >12 is a severe defect.
- Summed rest score: This is 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: This expresses the magnitude of defect reversibility or ischaemia. A summed difference score of 1–3 represents mild ischaemia, 4–7 moderate ischaemia and >7 severe ischaemia.
- The summed scores should be reported routinely, as they have a significant prognostic value, improve reproducibility of scan interpretation and minimize interreader variability in scan interpretation.

5.2.9. Polar maps

The polar maps (Bull's eye) are two dimensional representations of the three dimensional distribution of radiotracer 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.

5.2.10. Left ventricular ejection fraction

Gated MPI using either 8 or 16 frames can be used to calculate LVEF, derived from the left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volumes (LVESV). This measure is highly reproducible. It adds significantly to the overall interpretation of the study to differentiate scar from attenuation artefacts, to improve the specificity of perfusion defects and to stratify risk. Post-stress and rest LVEF should be reported, as well as the difference between both values (delta ejection fraction). In general, LVEF should be reported as greater than 70% for all values beyond 70% and less than 10% for all values below 10%. In general, the normal lower limit of LVEF is 50%, although values as low as 45% have been reported in men with a low likelihood of CAD:

- Post-stress ejection fraction: Note that since the post-stress ejection fraction is acquired when the stress test has already been terminated, for approximately 15–60 min, and the patient is at 'rest', left ventricular function either can reflect the true 'rest' state or it can still be undergoing a recovery period if the stress has caused significant myocardial ischaemia. Thus, LVEF on the stress images is reported as the post-stress ejection fraction. The post-stress LVEF has an independent prognostic value. Also, when using a one day protocol and stress is performed first, the 'rest' ejection fraction can still be under the influence of ischaemia developed during the stress test, and thus be lower than a true rest ejection fraction in the same patient. Nevertheless, this is infrequent and is only expected to occur when ischaemia is very severe.
- Rest ejection fraction: When using a two day protocol, this can be considered a true 'rest' or 'stress' ejection fraction.
- Difference between stress ejection fraction and rest ejection fraction (delta ejection fraction): When a significant decline in LVEF is encountered, the presence of post-ischaemic myocardial 'stunning' should be considered, especially if reversible perfusion defects exist [5.21]. Generally, a stress LVEF value of 5 absolute points or lower than the rest ejection fraction

value (e.g. LVEF 55% to $\leq 50\%$) is generally considered pathological and is associated with a high risk of cardiac events. Early post-stress image acquisition has a higher sensitivity to detect post-ischaemic stunning [5.21]. This parameter is of particular value for protocols using an equal dose of radiotracer injection (two day protocols).

To ensure that the ejection fraction 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 the partial volume effect, the estimation of volumes in very small hearts may be compromised, resulting in an erroneously high ejection fraction. Normal limits of LVEF may be higher in individuals with a low body mass index (e.g. women and certain ethnicities). Similarly, LVEF may be underestimated in individuals with large hearts and thinned myocardium owing to resolution limitations of the imaging system. Normal limits of LVEF may also vary based on the software used. LVEF may also be erroneous in patients with severe perfusion defects or absent uptake due to transmural infarction because of the difficulty in accurately tracking left ventricular myocardial walls with the help of software.

5.2.11. Regional left ventricular 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 a fully quantitative manner. Emphasis is again placed on the importance of careful analysis, which should always combine the visual analysis with the software data.

Regional wall thickening can be assessed quantitatively (percentage 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 [5.22].

5.2.12. Left ventricular volumes

LVEDV and LVESV for both stress and rest images should also be routinely registered (in millilitres) because it has been shown that the values also have significant prognostic implications. The consistency found when comparing stress and rest values needs to be checked in order to detect significant differences between both, in cases of severe ischaemia.

Reference values for LVEDV and LVESV vary according to the software used. Volume estimation by MPI has certain limitations owing to the partial volume effect and suboptimal spatial resolution. Because of the partial volume effect, the estimation of volumes in very small and very large hearts can be compromised.

As stated in Section 5.2.10, when there is a large transmural infarction, LVEF determination can be limited, as accurate edge detection can be difficult to achieve in the infarcted wall with no radionuclide uptake.

5.2.13. Transient ischaemic dilation

Transient ischaemic dilation (TID) is typically measured on the ungated images. The normal upper limit of TID (stress left ventricular volume or rest left ventricular volume) is between 1.2 and 1.3. Significant TID usually implies severe ischaemia. It can be explained by the presence of diffuse subendocardial ischaemia resulting in an apparent enlargement of the left ventricular cavity during stress, or by true dilatation of the left ventricle when regional or diffuse ischaemia is severe [5.23, 5.24]. TID may be especially useful when there is suspicion of 'balanced' ischaemia resulting in an 'apparently normal' perfusion scan. Although an invasive coronary angiogram is not warranted solely for evaluation of TID with normal perfusion, these patients may be further evaluated with a computed tomography based coronary angiogram, stress echocardiography or stress cardiac magnetic resonance imaging. TID has adverse prognostic implications.

5.2.14. Lung to heart ratio

Increased lung to heart ratio (LHR) with ^{99m}Tc or ^{201}Tl is an important parameter, with significant adverse prognostic implications. Depending on the tracer used, an LHR is considered abnormal when it is greater than 0.44 (^{99m}Tc) or greater than 0.50 (^{201}Tl). Raised LHR reflects poor left ventricular function, resulting in an elevation of left ventricular end-diastolic pressure (LVEDP) and a delay in return of blood from the pulmonary vessels into the left heart, causing increased lung uptake of tracer. Studies with ^{201}Tl are more sensitive for this parameter, since post-stress images are obtained earlier than with ^{99m}Tc agents [5.25]. Increased LHR at rest may indicate lung disease or high LVEDP from cardiomyopathy. Increased LHR only on the stress images may be seen in individuals with mitral stenosis, or increased LVEDP from significant left ventricular ischaemia.

5.2.15. Right ventricular uptake

This parameter is usually not quantifiable with available software, although some methods have been proposed. Normally, the right ventricular uptake shows faint uptake of the tracer mainly because the right ventricular wall thickness is about one third that of the left. When the right ventricular uptake is high compared with the left ventricular uptake, it may represent severe left ventricular ischaemia or right ventricular hypertrophy. When present, it should be considered a specific marker of multivessel or left main CAD [5.26]. Acute and chronic left ventricular dysfunction causes increased right ventricular tracer uptake owing to an increase in pulmonary arterial pressures.

5.2.16. 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 or uninterpretable (with a 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 and interposition of subdiaphragmatic activity) and the patient should be rescheduled.

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6. INTERPRETATION AND REPORTING OF MYOCARDIAL PERFUSION IMAGING STUDIES

A systematic review of the myocardial perfusion imaging (MPI) and stress testing details is important to ensure accurate and comprehensive scan interpretation and reporting [6.1]. Appropriate review of MPI includes the steps of quality control, image display, artefact recognition and image interpretation.

6.1. QUALITY CONTROL OF RAW PROJECTION IMAGES

The raw projection images (see Fig. 6.1) need to be reviewed in cine mode to determine the presence of potential sources of image degradation and artefacts. Several important items are evaluated:

- Counting statistics: Injection site (if in field of view) can be checked if extravasation is suspected.
- Tracer biodistribution: Abnormal distribution of the tracer, for example in the stomach, or lack of visualization of the myocardium may represent poor labelling efficiency, and the study should be repeated after a quality control of the radiopharmaceutical.
- Patient motion: Since conventional single photon emission computed tomography (SPECT) images are obtained in a step and shoot mode, patient motion is evident on the rotating raw projection images as a step up or down or as complex motion. However, detection of patient motion on

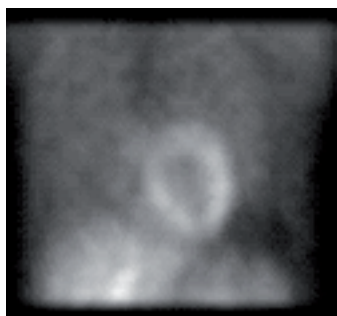


FIG. 6.1. Anterior view of the chest from a set of 64 projection images of a SPECT MPI study depicting normal biodistribution of ^{99m}Tc -sestamibi.

solid state SPECT scanners can be challenging owing to continuous image acquisition. A pannogram or linogram image is used to identify patient motion on a solid state scanner with continuous image acquisition.

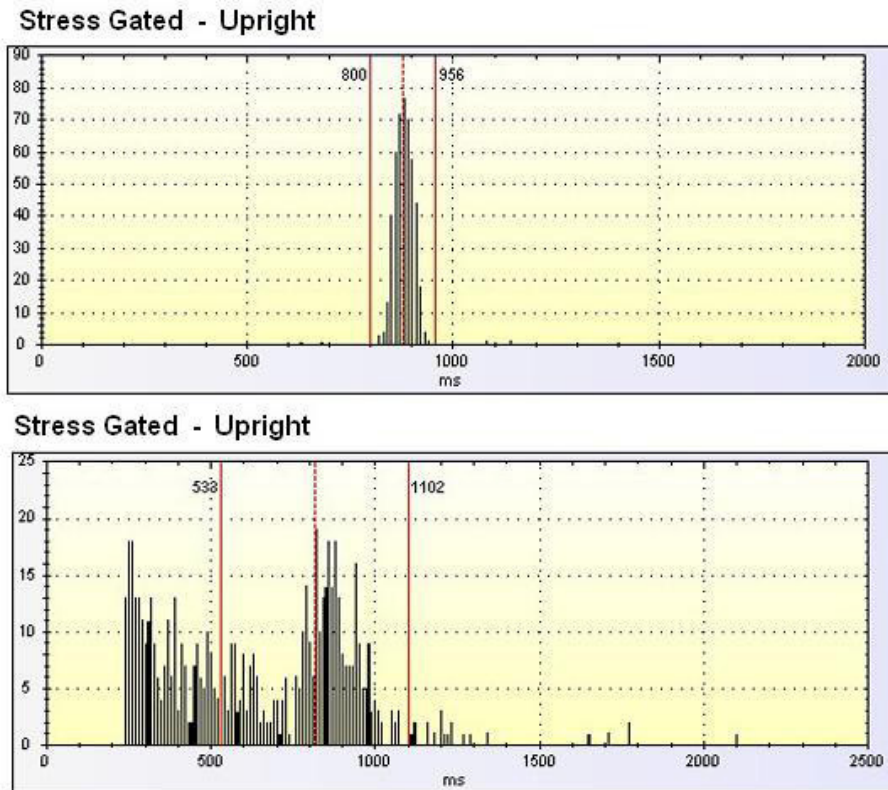
- Soft tissue attenuation: Photon attenuation from the soft tissues (breast in women, diaphragm in men) can be identified on the raw projection images. Attenuation can cause false positive results, which can be particularly challenging if variable attenuation is present.
- Interposition of metallic objects: These rarely cause artefacts but should be identified.
- Increased pulmonary uptake of the radiotracer: This can be identified on the raw projection images.
- Position of subdiaphragmatic organs: Excessive uptake in the liver, gall bladder and bowel, and hiatus hernia can cause imaging artefacts (ramp filter artefact from filtered back projection) and should be recognized. Iterative reconstruction methods may mitigate this artefact.
- Extracardiac abnormal areas of focal increased or decreased uptake: Focal uptake in the breast or lung, for example, could represent an unsuspected cancer; and a focal decrease in uptake may be seen in liver or kidney cysts.
- Missing projections: This can occur owing to camera malfunction.
- Acquisition zoom: This should be the same for stress and rest. Similar image acquisition zoom will be important to adequately align both sets of images.
- Position of the arms: This should be the same for stress and rest. Usually, the left arm is raised above the shoulder and needs to 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.

6.2. GATING PROCEDURE

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

- The quality control 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 (see Fig. 6.2).

- A sinogram analysis is helpful in detecting electrocardiogram gating errors and should be used whenever in doubt. With significant gating error, beats may be rejected and the sinogram may show missing data (see Fig. 6.3).



Note: The bottom panel exhibits a highly variable R-R cycle length. This may result in a rejection of counts and a poor image.

FIG. 6.2. A beat histogram with adequate gating (top panel) compared with one with a gating error (bottom panel).

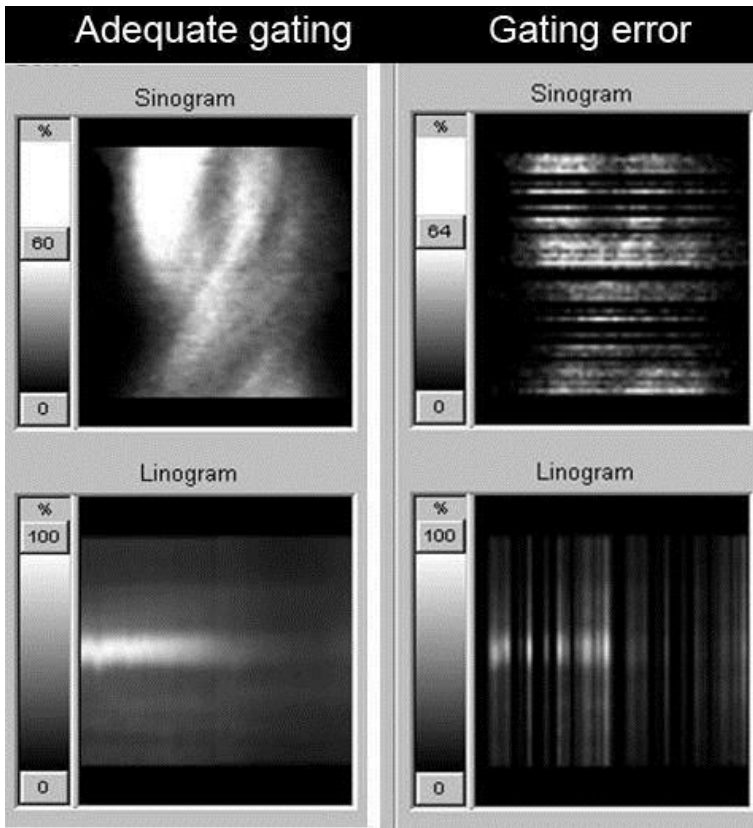


FIG. 6.3. A sinogram from a ^{99m}Tc MPI study with adequate gating (left panel) compared with one with a gating error (right panel).

6.2.1. 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.

6.2.1.1. Selection of left ventricular long axis

Reorientation of the heart after SPECT reconstruction should be performed by proper selection of the left ventricular 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.

6.2.1.2. Masking

Masking is particularly important in order not to include extracardiac activity (see Fig. 6.4). 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.

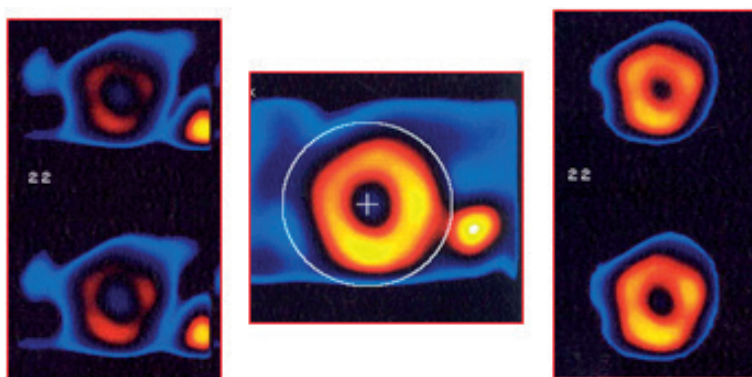


FIG. 6.4. Short axis slices with 'hot' extracardiac structure (left); mask definition to preserve activity within the region of interest only (centre); and original short slices after masking (right).

6.2.1.3. Alignment of slices

The stress and rest sets of slices should be correctly aligned; that is, short axis, vertical long axis and horizontal long axis tomograms should be displayed in such a manner that each stress slice corresponds anatomically with a matching rest slice for comparison (see Fig. 6.5). It is possible that ventricular size will differ in different situations (it is typically larger at stress if severe ischaemia is present), so precise slice matching may be difficult or even impossible. In any case, experts generally recommend that a stress midventricular tomogram be selected and matched with the corresponding rest image, then the matching pair of slices positioned at the centre of the display, with a corresponding number of slices at both sides.

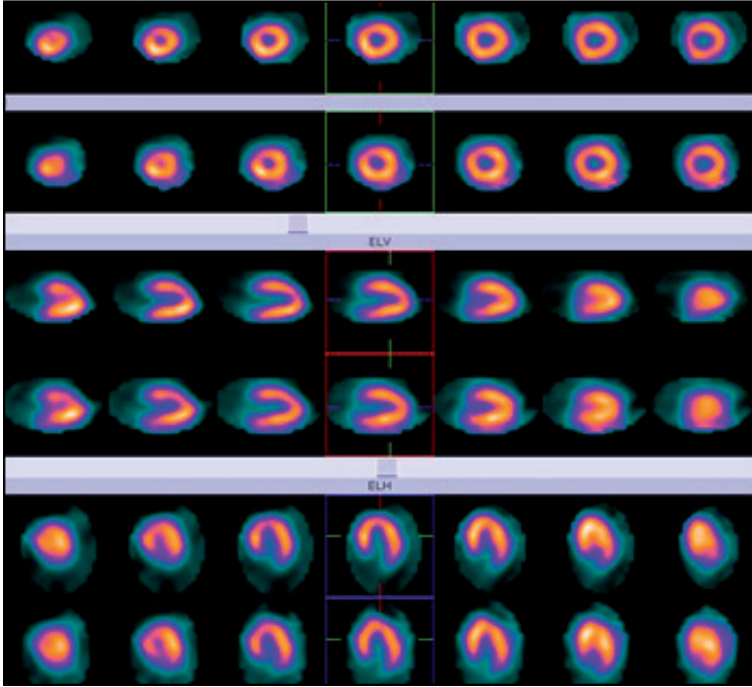


FIG. 6.5. Stress (upper row on each set of paired images) and rest (bottom row) ^{99m}Tc -sestamibi SPECT images.

6.2.1.4. Count density for stress and rest

Visual assessment of count density is important to ensure adequate comparison and avoidance of artefacts or wrong interpretation. A 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 the patient body habitus (weight) and injected dose (i.e. using a standard dose for an obese patient instead of adjusting it by weight). A 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.

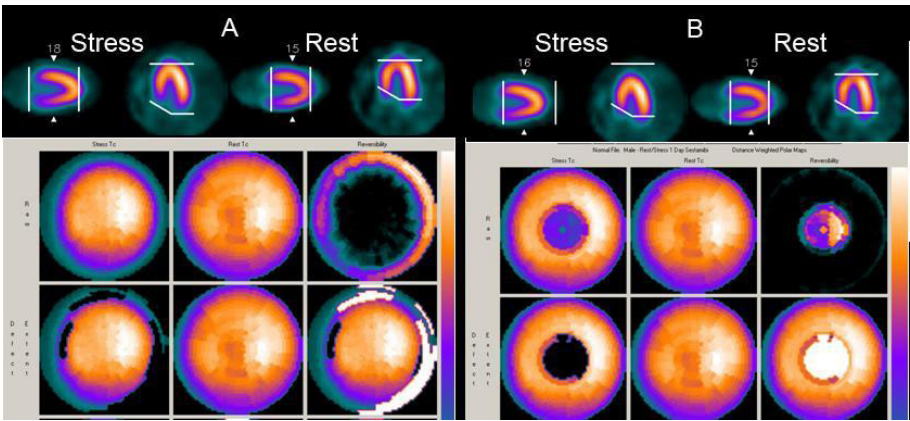
6.2.1.5. Normalization

Image count normalization is usually performed automatically by the software. If this is not the case, the operator may need to normalize the stress images and the rest images independently to the maximum in the series. Caution needs to be taken not to normalize against a ‘hot’ extracardiac structure due to inadequate masking.

6.2.2. Polar maps

There are helpful tools for study interpretation, but these are subject to a number of errors:

- The generation of polar maps requires that the basal and apical limits of the myocardium be properly selected. Even if current software packages can perform the operation automatically, experts generally recommend that these limits be 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’ (see Fig. 6.6).



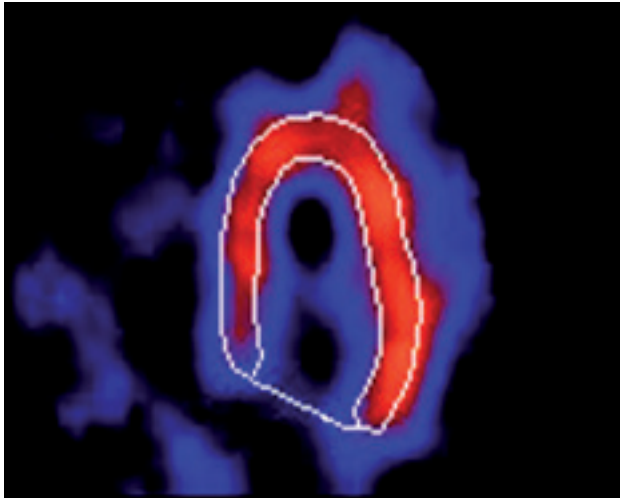
Note: The polar maps show improper basal slice selection (A) or improper apical slice selection (B) on the stress images with resulting basal or apical errors in the polar maps (left columns). Note normal slice selection at rest and corresponding polar maps without errors (middle columns).

FIG. 6.6. Polar maps.

6.2.3. Gated images

Accurate calculation of left ventricular ejection fraction (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 left ventricular long axis (see Fig. 6.7).
- 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.



Note: Contours should only track myocardial activity and the valve plane.

FIG. 6.7. Computer generated left ventricular contours of gated images used for calculation of left ventricular volumes and ejection fraction.

6.2.4. Attenuation correction

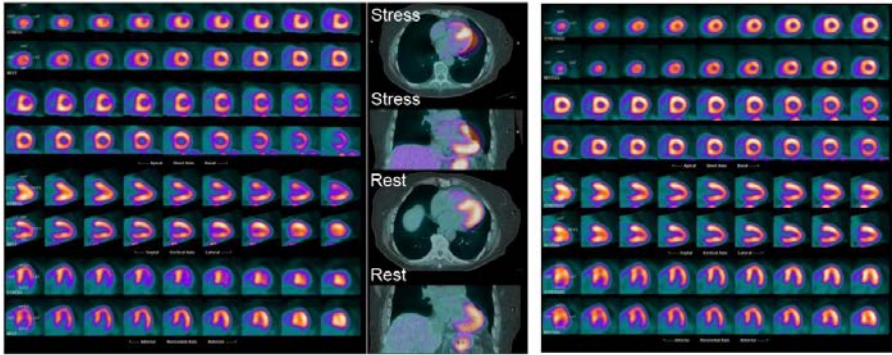
Attenuation artefacts can limit the specificity of SPECT MPI [6.2]. Owing to low energy photons, ^{201}Tl images are more prone to attenuation artefacts than are $^{99\text{m}}\text{Tc}$ images. There are several ways to deal with attenuation artefacts. Most commonly, gated images are used to differentiate 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, whereas fixed perfusion defects with reduced regional wall motion and wall thickening are typically assumed to represent scarring.

Soft tissue attenuation can be measured using a transmission map and corrected. Transmission maps can be performed using a dedicated radionuclide line source (^{153}Ga or ^{68}Ge) or a low dose computed tomography (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 attenuation correction, since the transmission maps are typically count rich.

The other quality control step in attenuation correction is to check for registration of the transmission and emission images. This is critical to avoid artefacts from misregistration between transmission and emission images. Registration should be checked at rest and stress and in the axial, sagittal and coronal projections, as well as the standard cardiac planes of short axis, horizontal long axis and vertical long axis images (see Fig. 6.8).

If the transmission and emission images are misregistered, they need to be realigned appropriately using software and a new attenuation map needs to be generated. The emission images then need to be corrected for attenuation using the new attenuation map.



Note: The panel on the left shows a reversible anterolateral perfusion defect due to misregistration of the stress emission and transmission images as seen in the fusion images (middle). Software was used to correctly register the images and to apply the new attenuation map with resolution of the anterolateral perfusion defect (right panel).

FIG. 6.8. An illustration of the impact of misregistration of emission and transmission images on MPI.

6.3. IMAGE DISPLAY

6.3.1. Slice display

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

- The standard cardiac tomographic image sets should be used: short axis, vertical long axis and horizontal long axis.
- Summed images are to be used for slice display.
- The left ventricle should be well represented. All slices need to be properly aligned and normalized.
- Proper adjustment of brightness and contrast might be necessary in the presence of hot spots. A linear colour scale or grey scale is a suggestion.
- Image interpretation should be performed using a computer monitor and a workstation.
- If images are provided together with the report, they should reflect the findings and interpretation of the report.

6.3.2. Polar map display

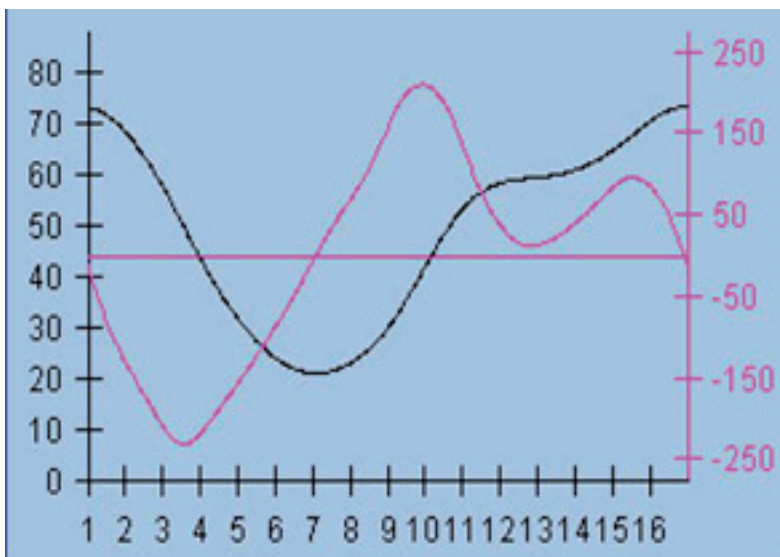
Polar maps should only be used for assisting interpretation of image slices and should not be interpreted on their own:

- The polar map display varies depending on the software used.
- The reference polar map used should take into account factors such as the radiotracer, patient's sex, body habitus and any prior mastectomy.
- Interpreting physicians should recognize that the loaded polar maps may not conform to their patient population. Ideally, a local reference polar map should be used if available.

6.3.3. Gated display

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

- Representative moving slices of all the axes should be shown (at a minimum, the apical, midventricular 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.
- Experts generally recommend the grey scale for wall motion assessment.
- Owing 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 not typically used for clinical interpretation.
- A good quality control for gated images is to evaluate the left ventricular volume curve and to check for the integrity and shape of all phases of the curve (see Fig. 6.9).



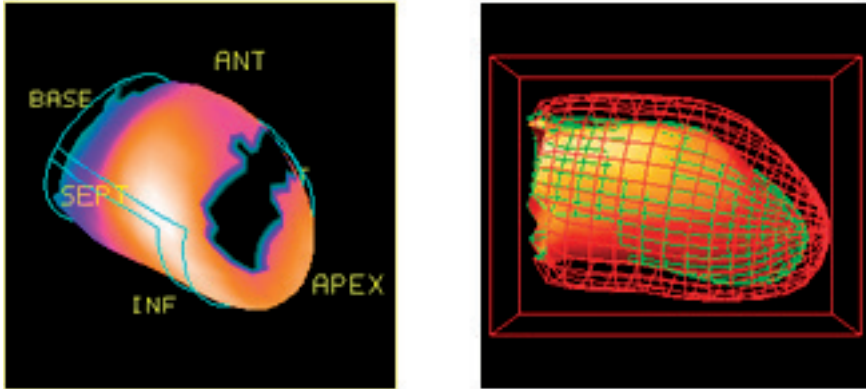
Note: Checking the left ventricular volume curve is a critical aspect of the study quality control.

FIG. 6.9. Volume curve of the left ventricle (black curve) of a 16 frame gated SPECT study, showing a normal shape (systolic and diastolic phases).

6.3.4. 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 to compare them with slides and raw data:

- Three dimensional, volume rendered, static (perfusion) and gated (ventricular function) images may assist in image evaluation but typically are not used as the primary images for diagnostic interpretation (see Fig. 6.10).
- 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.



Note: These types of image should be used only as an aid for study interpretation.

FIG. 6.10. Three dimensional, volume rendered, static perfusion image (left), and gated end-diastolic and end-systolic volumetric display (right) depicting anterior-apical abnormalities in perfusion and wall motion.

6.4. ARTEFACT RECOGNITION

6.4.1. Motion artefacts

Patient motion is one of the most frequent sources of artefacts in MPI [6.3, 6.4]:

- In addition to checking for patient motion by examining the rotating raw data or the sinograms, once the images have been reconstructed motion artefacts can be recognized.
- Motion artefacts usually produce a characteristic misalignment of the myocardial walls in the horizontal long axis slices, which is 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.

6.4.2. Attenuation artefacts

Soft tissue photon attenuation in the thorax leads to a non-uniform reduction of counts from myocardial activity, possibly producing imaging artefacts (see Fig. 6.11). 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 [6.3].



Note: Studies were performed with ^{99m}Tc -sestamibi. In both cases, no coronary lesions were found in the angiography.

FIG. 6.11. Anterior wall 'defect' due to breast attenuation in a woman (left) and inferior wall 'defect' due to diaphragmatic attenuation in a man (right).

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 ischaemia. This may produce a decrease in diagnostic accuracy owing predominantly to an increase in false positive studies, although sometimes this may also lead to an underinterpretation of true perfusion abnormalities when the effects of soft tissue attenuation are overestimated by the observer.

Diaphragmatic attenuation is most often seen in men and occurs in up to 25% of MPI. 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. Acquiring only the stress study in the prone position will usually suffice to demonstrate the presence of inferior wall attenuation.

Breast attenuation produces the effect of fewer 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, anteroapical and apical. Special concern for artefacts arises in women with breast implants or following a 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

repositioning 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 ^{201}Tl and adjusting the injected dose according to 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 [6.4]. 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.

6.4.3. Extracardiac activity

Activity in various subdiaphragmatic organs can interfere with evaluation of perfusion of the inferior wall.

In patients with hiatus hernia and prominent gastric uptake, there can be overlapping with lateral wall activity of the left ventricle. Intense liver activity adjacent to the inferior wall may make it impossible to tell whether there is any defect. A repeat acquisition with longer delay may result in cleared liver activity.

6.4.4. Extravasation of tracer

Infiltrated injection results in low counts in the corresponding stress or rest images. Importantly, in rest followed by stress imaging, infiltration of the stress radiotracer dose may be challenging for a single day. Apparent stress MPI may be obtained by reflecting rest counts. This may result in either overestimation or underestimation of defects, and a repeat study might be necessary, depending on the degree of degradation.

6.4.5. Polar plots

With regard to polar plots:

- The 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.
- Experts generally recommend sex specific and tracer specific polar plots to define the extent and severity of perfusion defects on the polar plots.

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

6.4.7. Hot spots

With regard to hot spots:

- Areas of high activity (hot spots) close to the heart may interfere with interpretation.
- If there are hot spots with 'negative' (cold) surrounding areas due to a filtered back projection 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.

6.5. IMAGE INTERPRETATION

6.5.1. 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. The terms of probably normal or probably abnormal are to be avoided:

- Normally, there should be homogeneity of tracer uptake in the left ventricular myocardial wall on both rest and stress images.
- Any segmental or diffuse decrease of uptake during stress would correspond to ischaemia if reversible on rest images.

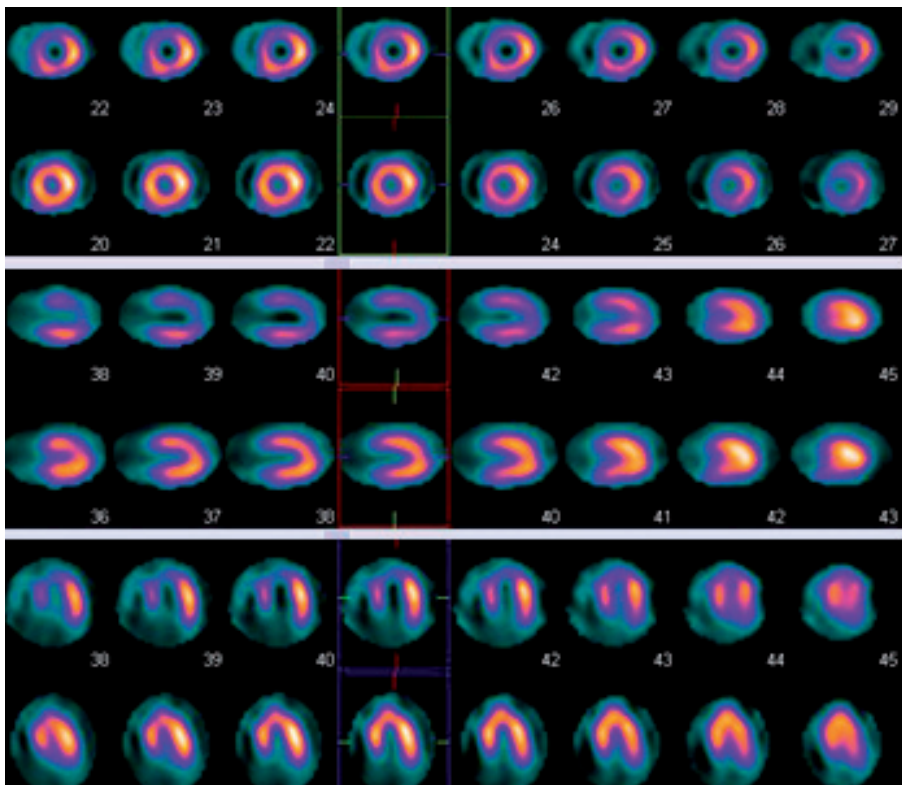
6.5.2. High risk scan features

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

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

6.5.3. Transient ischaemic dilatation of the left ventricle

Before segmental analysis of the perfusion images, it should be noted whether or not there is left ventricular cavity enlargement at rest, post-stress or both. Transient ischaemic dilation (TID) is defined based on the endocardial borders of the left ventricular cavity observed on the static/summed images. An increased stress to rest left ventricular cavity ratio has been described as a marker for high risk (severe and multivessel coronary disease) (see Fig. 6.13) [6.5]. Although non-specific for ischaemia, when not associated with segmental perfusion defects, TID may represent either global subendocardial ischaemia or balanced ischaemia in the three coronary regions. TID is described qualitatively but may be quantified using software. The normal upper limit of TID (left ventricular 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 ^{201}Tl and stress $^{99\text{m}}\text{Tc}$), and hence the normal limits may be higher compared with single isotope protocols.

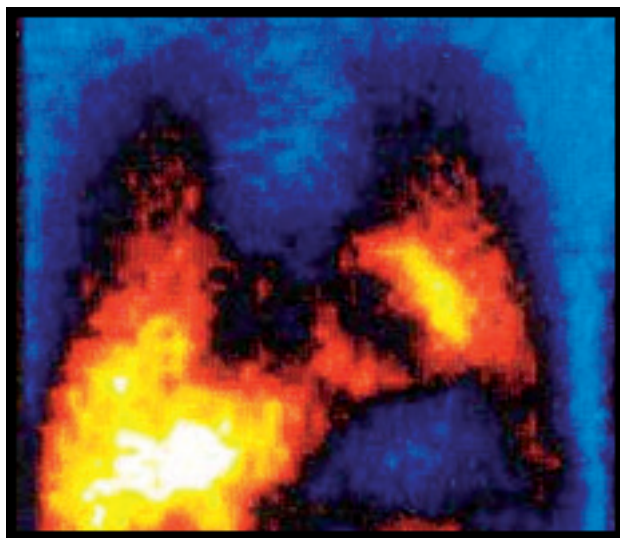


Note: Left ventricular volume is greater at stress (upper row on each set of paired images) than at rest (bottom row). Transient ischaemic dilation is an additional high risk finding with independent prognostic value, although severe and extensive perfusion defects (as in this particular case) are frequently — but not always — present as well.

FIG. 6.13. Transient ischaemic dilation of the left ventricle.

6.5.4. Lung uptake

The presence of increased lung uptake during rest or post-stress ^{201}Tl imaging has been described as an indicator of poor prognosis [6.6]. This can also be observed with $^{99\text{m}}\text{Tc}$ radiopharmaceuticals with exercise or pharmacological stress imaging (see Fig. 6.14). 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 to heart ratios. Ratios greater than 0.45 for $^{99\text{m}}\text{Tc}$ and greater than 0.55 for ^{201}Tl are considered abnormal.



Note: Lung uptake can be assessed either qualitatively or quantitatively.

FIG. 6.14. Lung uptake of ^{99m}Tc -sestamibi at rest (anterior view of raw projections) in a patient with recent myocardial infarction and impaired ventricular function.

6.5.5. Stunning

Stunning is defined as a prolonged reduction in left ventricular systolic function following a transient episode of severe ischaemia that does not result in myocardial necrosis. Ischaemia 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 ischaemia. The presence of stunning in the context of reversible perfusion defects improves the specificity for identifying ischaemia. Post-ischaemic stunning and reversible regional wall motion abnormalities also improve the sensitivity of identification of severe obstructive coronary artery disease. There is no consensus on what to consider as a significant difference between post-stress and rest LVEF, although a 10% difference is generally accepted.

6.5.6. Right ventricular tracer uptake

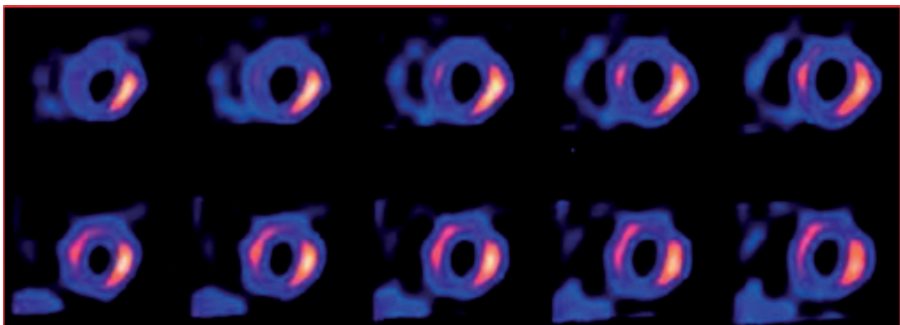
According to Ref. [6.6]:

“Right ventricular (RV) uptake may be qualitatively assessed on the raw projection data and on the reconstructed data. There are no established quantitative criteria for RV uptake, but in general, the intensity of the right ventricle is approximately 50% of peak LV [left ventricular] intensity. RV uptake increases in the presence of RV hypertrophy [or overload], most typically because of pulmonary hypertension. The intensity of the right ventricle may also appear relatively increased when LV uptake is globally reduced.”

Transient increase in right ventricular tracer uptake (>20% higher right ventricular uptake compared with left ventricular uptake) is a specific sign of left main disease. The size of the right ventricle should also be noted, as right ventricular 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.

6.5.7. Multiple and extensive perfusion defects

Several studies have demonstrated the prognostic value of MPI [6.7]. The number and extent of perfusion defects are powerful predictors of future adverse cardiovascular events [6.7]. Figure 6.15 illustrates myocardial perfusion with multiple, large perfusion defects.



Note: At stress (upper row), the right ventricle is clearly seen, associated with extensive left ventricular perfusion defects, which are mostly reversible at rest (bottom row) where right ventricular uptake almost disappears.

FIG. 6.15. Short axis slices of a SPECT study.

6.6. REPORTING AND ESSENTIAL ELEMENTS OF A COMPREHENSIVE REPORT

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 are typically concise and include all the relevant information for the referring physician [6.1]. 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 MPI (including all of the critical elements listed in Appendix III). The calcium score and CT coronary angiogram studies are also reported when performed as a part of the MPI study with hybrid systems.

The essential elements include:

- (a) Demographics: The patient's age, sex, coronary risk factors, prior cardiac history, cardiac medications and rest electrocardiogram (ECG) information should be listed in this section.
- (b) Clinical question or reason for referral: This is a very important point and should be clearly stated.
- (c) Stress test: The details of the stress test are to be provided. Whenever possible, the stress test report should be combined with the MPI report. If not, the relevant details of the stress test report also need to be included in the MPI report.
- (d) Acquisition protocol: The MPI report needs to include details about the technique, the type and dose of radiotracer, and the route of injection (intravenous) used. The imaging protocol including attenuation correction parameters (if performed) should be described.
- (e) General description: A comment should be included about the image quality (uninterpretable, fair, good or excellent). The left and right ventricle size, relative cavity size between stress and rest (TID) and lung tracer uptake should be described first.
- (f) Perfusion defects: The defect size, severity, location and reversibility are then described following either vascular distributions or myocardial walls or segments. Reporting the summed scores is not routine in some laboratories.
- (g) Left ventricular function: This should be reported and include an estimation of global LVEF, regional wall motion and wall thickening whenever feasible. LVEF values greater than 70% should be reported as >70% and an ejection fraction (EF) less than 15% as <15% without giving specific

numbers (e.g. if EF = 90%, the report should read LVEF >70%; if EF = 11%, the report should read LVEF <15%). If height and weight are available, left ventricular volumes may be normalized to body surface area (experts generally recommend not to report end-diastolic volume < 60 mL).

- (h) Any high risk scan features can be described.
- (i) Conclusions: This section includes 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 versus scar versus ischaemia) should be avoided in this section.
 - The gated results are to be summarized, also as normal or abnormal.
 - High risk scan features should be highlighted.
 - A statement about risk is optional.
 - A comparison should be made to prior study images if available.

In order to ensure that a report covers all necessary information, a structured thought process is imperative. See Appendix III for important points to consider for inclusion in a comprehensive report.

REFERENCES TO SECTION 6

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- [6.3] DePUEY, E.G., GARCIA, E.V., Optimal specificity of thallium-201 SPECT through recognition of imaging artifacts, *J. Nucl. Med.* **30** (1989) 441–449.
- [6.4] CHOI, J.Y., et al., Gating provides improved accuracy for differentiating artifacts from true lesions in equivocal fixed defects on technetium 99m tetrofosmin perfusion SPECT, *J. Nucl. Cardiol.* **5** (1998) 395–401.
- [6.5] ABIDOV, A., GERMANO, G., BERMAN, D.S., Transient ischemic dilation ratio: A universal high-risk diagnostic marker in myocardial perfusion imaging, *J. Nucl. Cardiol.* **14** (2007) 497–500.

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- [6.7] HACHAMOVITCH, R., et al., Impact of ischaemia and scar on the therapeutic benefit derived from myocardial revascularization vs. medical therapy among patients undergoing stress-rest myocardial perfusion scintigraphy, *Eur. Heart J.* **32** (2011) 1012–1024.

Appendix I

PATIENT INFORMATION BROCHURE

Before the scan, the elements which the patient is to be made aware of include: 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; and the need to avoid caffeine 24 h before the test, among other things. These are all important details that should be given to patients in a brochure before the actual test, so that they can follow the instructions. The brochure will serve to keep the patient informed in order to avoid unexpected circumstances on the day of the test.

This appendix serves as a guide to what a comprehensive brochure should include. Therefore, if there is information that does not apply to the internal procedures at the institute, it is important to make sure that the information in the brochure is changed accordingly.

I.1. INFORMATION FOR THE PATIENT

Information for the patient includes:

- Please bring your medications and any medical history information with you.
- If you are breast-feeding or pregnant, or think you may be pregnant, please inform your doctor and the staff, 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 heart scan for assessment of your heart arteries and muscle. The 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 the test, your doctor will have informed you of certain medications that you should avoid for a period of time (usually some days) to make the test more accurate.⁷ If not, please continue all regular medications. Do not take drugs for erectile dysfunction for two days prior to the studies.

⁷ A list of medications is to be given by the institution.

- Please avoid all caffeine-containing foods and beverages (coffee, all forms of tea, chocolate drinks, chocolates and soft drinks) for 24 h 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 h for better diagnostic accuracy.
- To perform the test, you will be required to do some form of exercise (stress) on either a treadmill exercise machine (walking, jogging or running) or a bicycle ergometer (cycling).
- Please wear proper exercise attire and comfortable shoes for the test.
- If you think you are unable to exercise, or the doctor has advised 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 side effects of the medication given for the ‘stress’ state may include nausea, vomiting, a hot feeling, abdominal discomfort, headache and giddiness. These side effects may last for approximately 5–10 min following the infusion in approximately 40–50% of patients given the medication. An antidote to the medication can be given if necessary.
- The test will also involve an injection of a radioactive tracer into your vein. The amount of radiation involved is very small and will disappear within hours.
- To promote more rapid removal of the tracer from your body, you are encouraged to drink liquids to help you pass water. However, because of the short lifespan of the tracer, most of the radioactive tracer will 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) 5–60 min 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 min, 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. A second scan is usually 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, depending on the clinical question to be addressed, you may 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 min 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 h 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 activity 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 (younger than 10 years old) in the household, they should be advised not to be in your close proximity for the first 6 h after tracer injection, and women who are breast-feeding should avoid close contact with the baby post-scan.
- The interpreting physician will report on your scan, and then will ask you to pick up your results or you may have them sent to your referring physician, who will then arrange an appointment with you for further advice.
- You should continue with all regular medications, including ones you were told to stop specifically for the test.
- After completing the test, your referring physician may ask you to continue to another form of medical imaging (e.g. computed tomography angiography or calcium score) as required, depending on the result.

Appendix II

CHECKLIST FOR MYOCARDIAL PERFUSION IMAGING STUDIES

II.1. SPECT CAMERA QUALITY CONTROL

Before sessions are planned, the equipment needs to be monitored with regard to its performance and as part of the laboratory quality system. Comprehensive instructions on scintillation camera quality control can be found in Ref. [II.1].

II.2. RADIOPHARMACEUTICALS

- Provide all radiopharmaceutical quality controls as specified by manufacturers.
- Define the range of activities to inject to achieve similar count statistics according to patient weight, height and shape.
- Optimize injected activity in order to reach optimal count statistics according to the acquisition system characteristics and to keep radiation doses as small as possible (see Ref. [II.2] for further information).

II.3. PLAN A PERSONALIZED PROTOCOL FOR EACH PATIENT

- Review requests: Each request should be reviewed by a qualified physician.
- Radiotracer should not be administered until a doctor signs off on the form with a protocol.
- Assess test appropriateness for the clinical question, considering the following factors:
 - Patient's age;
 - Sex;
 - Body habitus;
 - Pre-test probability of disease;
 - Other imaging options.
- Decide on imaging protocol:
 - Stress first;
 - Rest followed by stress;
 - Two day study;

- Technetium should be default but in specific instances, if viability is a question, thallium may be considered (positron emission tomography if available);
- High efficiency scanner (if available, for low dose imaging).
- Decide on what stress protocol to use:
 - Exercise should be default.
 - If patient cannot exercise, look for vasodilator contraindications.
 - If no contraindications and vasodilator available, use a vasodilator.
 - If vasodilator is contraindicated, consider dobutamine. If that is contraindicated, consider other modalities, such as computed tomography angiography.

II.4. BEFORE ACQUISITION

- Find the most comfortable position on single photon emission computed tomography (SPECT) bed.
- Ask the patient to avoid movements, to breathe normally and to avoid deep breaths.
- In case of a problem during acquisition, ask the patient to inform the technologist without moving.
- Inform the patient of the expected acquisition time.
- Check for heart rhythm, such as atrial fibrillation, sinus arrhythmia, frequent premature beats, intermittent and dual chamber pacing. These patients should not be studied with electrocardiogram triggering, or the type of rhythm should be registered for the interpreting physician to consider.

II.5. DURING ACQUISITION

- Ask frequently if everything is okay.
- Inform the patient of the residual time.
- Instruct the patient to avoid movements.

II.6. AFTER ACQUISITION

- Check immediately for lateral or vertical movements of the heart and for extracardiac hot spots (e.g. lung, liver, gall bladder and muscle), which can interfere with reconstruction and processing on the rotating cine mode review of the projection data.

- Consider whether to repeat acquisition immediately (movements) or after a time interval (hot spots).
- Check for truncation of cardiac activity or severe truncation of body activity.
- Consider a second acquisition in a supine/prone position in the presence of suspected severe diaphragmatic/breast attenuation.

II.7. IMAGE PROCESSING

- Verify the need to apply motion correction algorithms for the vertical movements (≥ 2 pixel motion, 4 mm).
- 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, experts generally recommend using the same filter parameters independent of the actual count density in a given patient.
- Experts generally recommend wide beam reconstruction and resolution recovery with scatter corrections, allowing dose reduction, 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 computed tomography (CT), verify alignment between SPECT and CT in a three dimensional display after motion correction. If there is a discrepancy, realign studies manually.
- Always display corrected and uncorrected images.
- Verify perfect correspondence between apical and basal slices in short axis views.
- Verify the orientation of the long axes in both vertical and horizontal long axes.
- Realign studies even in the presence of minimal differences.
- Set the count windows and thresholds in order to have one 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 need to be seen in all projections and in at least two consecutive slices.

- Check the correlation between the visual inspection of studies and, if available, quantitative evaluation. If necessary, correct the perfusion scores manually. Consider that discrepancies between visual interpretation and quantitative results can raise doubts about the reliability of the study, especially if both results are included in the hard copy. Quantitative analysis should not be used in isolation without qualitative review.
- In gated studies, always verify the selection of endocardial, epicardial and valvular edges. If they are not correct, try to modify them. Sometimes, the left ventricular function cannot be reported or can only be reported qualitatively without a left ventricular ejection fraction (LVEF) and absolute volume values. In small hearts, consider the negative impact of the partial volume effect.
- Always check the correlation between perfusion and regional wall motion abnormalities.

II.8. REPORTING

- A standardized institutional model should be considered for all physicians entitled to report myocardial perfusion imaging (MPI) at that institution.
- Verify that the report includes the following: the reason for the MPI request; a description of the stress test results; and a description of the MPI and gated SPECT results.
- The clinical conclusion should be especially focused on the request and with review of a 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

- [II.1] INTERNATIONAL ATOMIC ENERGY AGENCY, Quality Assurance for SPECT Systems, IAEA Human Health Series No. 6, IAEA, Vienna (2009).
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Appendix III

EXAMPLE OF A MYOCARDIAL PERFUSION IMAGING REPORT

In order to ensure that the report covers all necessary information, a structured thought process is essential. This sample provides the most important points to be considered and included in a comprehensive report.

III.1. EXAMPLE OF A MYOCARDIAL PERFUSION IMAGING REPORT

III.1.1. General information

Referring physician: Dr. _____

Mr./Ms. _____, a _____ year old male/female with a history of:

- ☐ Hypertension;
- ☐ Diabetes;
- ☐ Dyslipidemia;
- ☐ Smoking;
- ☐ Family history of premature coronary artery disease;

was referred to us for the evaluation of:

- ☐ Typical angina;
- ☐ Atypical angina;
- ☐ Non-anginal chest pain;
- ☐ Dyspnoea;
- ☐ Other: _____.

Past cardiac history includes:

- ☐ Percutaneous coronary intervention;
- ☐ Myocardial infarction;
- ☐ Prior coronary artery bypass surgery;
- ☐ Other: _____.

Medications include:

- ☐ Beta blockers;
- ☐ Calcium blockers;
- ☐ Hypolipidemic drugs;
- ☐ Other:_____.

The stress study was performed:

- ☐ Off medication;
- ☐ On medication.

The resting electrocardiogram:

- ☐ Was normal;
- ☐ Showed _____ (describe abnormality).

The SPECT study protocol was:

- ☐ ^{201}Tl stress/redistribution;
- ☐ $^{99\text{m}}\text{Tc}$ -sestamibi/tetrofosmin stress-only;
- ☐ Single day $^{99\text{m}}\text{Tc}$ -sestamibi/tetrofosmin rest/stress myocardial perfusion;
- ☐ Two day $^{99\text{m}}\text{Tc}$ -sestamibi/tetrofosmin rest/stress myocardial perfusion.

The patient received ____ MBq of:

- ☐ $^{99\text{m}}\text{Tc}$ -sestamibi/tetrofosmin;
- ☐ ^{201}Tl intravenously;
- ☐ (Stress) rest gated SPECT imaging was performed.

Attenuation correction was performed using:

- ☐ A rotating line source;
- ☐ A multidetector computed tomography scan (10 mA, 120 keV and gantry rotation time ____ ms).

For viability assessment, delayed images were obtained at ____ time (for ^{201}Tl) or nitrates given (for $^{99\text{m}}\text{Tc}$ tracers).

III.1.2. Exercise stress protocol

Mr./Ms. _____ exercised on a _____ (standard Bruce/modified Bruce) protocol for ____ min (____ METS).

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

The systolic blood pressure (SBP) (increased/decreased/remained unchanged) from _____ mmHg to _____ mmHg during peak stress [rate pressure product of _____ (product of peak stress SBP and peak stress heart rate)].

The heart rate recovery was ____ (peak stress heart rate minus heart rate at 1 min after termination of exercise, abnormal < 12 bpm).

The Duke treadmill score was ____ ($\geq +5$ = low risk, $+5$ to -11 = intermediate risk, ≤ -11 = high risk).

Exercise was terminated owing to _____:

- ☐ Chest pain;
- ☐ Fatigue;
- ☐ Dyspnoea;
- ☐ Arrhythmia;
- ☐ Stress test segment changes;
- ☐ Other (describe):_____.

The blood pressure response was:

- ☐ Normal;
- ☐ Hypertensive;
- ☐ Hypotensive.

During stress, there were:

- ☐ No symptoms;
- ☐ Symptoms (describe):_____;
- ☐ No stress test segment changes;
- ☐ Stress test segment changes (describe):_____.

(e.g. maximal stress test depression (or elevation), heart rate at onset of stress test changes, time of onset of stress test changes (minutes of exercise or recovery), leads with stress test changes, and time of resolution of stress test changes).

There were:

- ☐ No arrhythmias during the study;
- ☐ Arrhythmias (describe): _____

(e.g. transient self-terminating heart block was noted during adenosine infusion, frequent premature ventricular contractions, frequent premature atrial contractions, and non-sustained ventricular tachycardia).

III.2. EXAMPLE OF A REPORT OF A VASODILATOR STRESS PROTOCOL WITH ADENOSINE

For protocols using different agents, refer to Sections 4.3.2, 4.3.4 and 4.3.5:

- Vasodilator stress was achieved with a standard infusion of adenosine for 4 min for a total dose of 72.7 mg.
- The heart rate increased from 78 bpm at rest to a heart rate of 86 bpm, and the blood pressure increased from 89/52 mmHg at rest to 122/77 mmHg during vasodilator stress (rate pressure product: 10 492).
- Vasodilator stress was terminated owing to the completion of the vasodilator protocol. The symptomatic response to vasodilator stress was non-ischaemic.
- The blood pressure response was not applicable owing to vasodilator stress. The electrocardiogram response to vasodilator stress indicated no significant ST-T changes. During vasodilator induced stress, atrial fibrillation and multifocal, ventricular couplets, trip quadruplets premature ventricular contractions were observed.

The left ventricle was:

- ☐ Normal;
- ☐ Mildly dilated;
- ☐ Moderately dilated;
- ☐ Severely dilated.

The right ventricle was:

- ☐ Normal;
- ☐ Mildly dilated;
- ☐ Moderately dilated;
- ☐ Severely dilated.

The right ventricular tracer uptake was:

- ☐ Normal;
- ☐ Increased.

The rest and stress myocardial perfusion imaging was:

- ☐ Normal;

or demonstrated perfusion defects which were:

- ☐ Small:
 - ☐ Of mild intensity;
 - ☐ Of moderate intensity;
 - ☐ Of severe intensity;
- ☐ Medium:
 - ☐ Of mild intensity;
 - ☐ Of moderate intensity;
 - ☐ Of severe intensity;
- ☐ Large:
 - ☐ Of mild intensity;
 - ☐ Of moderate intensity;
 - ☐ Of severe intensity;

in the _____(list segments in vascular distribution) that was:

- ☐ Fixed;
- ☐ Mildly reversible;
- ☐ Moderately reversible;
- ☐ Completely reversible.

III.2.1. Myocardial perfusion imaging

The left ventricle was:

- ☐ Normal;
- ☐ Mildly dilated;
- ☐ Moderately dilated;
- ☐ Severely dilated.

The right ventricle was:

- ☐ Normal;
- ☐ Mildly dilated;
- ☐ Moderately dilated;
- ☐ Severely dilated.

The right ventricular tracer uptake was:

- ☐ Normal;
- ☐ Increased.

The rest and stress myocardial perfusion imaging was:

- ☐ Normal;

or demonstrated perfusion defects which were:

- ☐ Small:
 - ☐ Of mild intensity;
 - ☐ Of moderate intensity;
 - ☐ Of severe intensity;
- ☐ Medium:
 - ☐ Of mild intensity;
 - ☐ Of moderate intensity;
 - ☐ Of severe intensity;
- ☐ Large:
 - ☐ Of mild intensity;
 - ☐ Of moderate intensity;
 - ☐ Of severe intensity;

in the _____ (list segments in vascular distribution) that was:

- ☐ Fixed;
- ☐ Mildly reversible;
- ☐ Moderately reversible;
- ☐ Completely reversible.

III.2.2. Gated myocardial perfusion imaging

The left ventricle was:

- ☐ Normal;
- ☐ Abnormal;

in size with:

- ☐ Normal wall motion and wall thickening;
- ☐ Abnormal wall motion and wall thickening, involving the following myocardial segment(s): _____ (describe).

The post-stress/rest LVEF was:

- ☐ Normal at _____ %;
- ☐ Abnormal at _____ %.

The right ventricle size was:

- ☐ Normal;
- ☐ Abnormal.

Wall motion and thickening were:

- ☐ Normal;
- ☐ Abnormal.

III.2.3. Ancillary findings

None. If abnormal, describe (e.g. there was a focal abnormal increase in ^{99m}Tc -sestamibi uptake in left breast; suggest clinical examination and further evaluation if clinically indicated).

III.2.4. Conclusions

- The rest and stress MPI study was normal (or abnormal, demonstrating a large/medium/small area of severe/moderate/mild ischaemia in the anterior, anteroseptal and apical walls, or left anterior descending, left circumflex, right coronary artery (vascular distribution optional)).
- The gated study was normal. If abnormal, describe wall motion abnormalities.
- LVEF was normal. If abnormal, describe mild moderate or severely abnormal.
- A prior myocardial perfusion study was performed on _____ (date). The current study demonstrates (no significant change/significant disease progression/significant improvement) when compared with 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 _____

ABBREVIATIONS

CAD	coronary artery disease
ECG	electrocardiogram
INCAPS	IAEA Nuclear Cardiology Cross-Sectional Protocols Study
LVEDV	left ventricular end-diastolic volume
LVEF	left ventricular ejection fraction
LVESV	left ventricular end-systolic volume
MBF	myocardial blood flow
METS	metabolic equivalents of task
MPHR	maximum predicted heart rate
MPI	myocardial perfusion imaging
PET	positron emission tomography
SPECT	single photon emission computed tomography
TID	transient ischaemic dilation

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