

# Myocardial Perfusion Scintigraphy

CDL Bavelaar-Croon, Ziekenhuis Gelderse Vallei, Ede  
S van Eeckhoudt, Bravis ziekenhuis, Roosendaal

## 1. Introduction

Myocardial perfusion scintigraphy (MPS) produces images of regional tracer uptake in the myocardium, reflecting myocardial blood flow. Patients with a coronary stenosis develop hypo-perfusion during stress. On a SPECT MPS this hypo-perfusion is displayed as diminished regional tracer uptake in stress; the rest study then shows higher tracer uptake. Myocardial cell loss after a myocardial infarction will lead to diminished or absent tracer uptake on the stress and the rest images. In the last decade of the previous century, software programs were developed which can calculate and display LV volumes and function if the study is acquired in an ECG-triggered or "gated" mode.

Different stress modalities are available: physical exercise e.g. bicycle ergometry or pharmacological stress e.g. Adenosine, Dipyridamol, Regadenoson or Dobutamine. For myocardial perfusion scintigraphy, several radiopharmaceuticals can be used. The most widely used gamma tracers are  $^{99m}\text{Tc}$  Tetrofosmin and  $^{99m}\text{Tc}$  Sestamibi. These radiopharmaceuticals have a stable myocardial retention after injection. In contrast, as plasma concentration diminishes  $^{201}\text{Tl}$  diffuses back to the bloodpool after uptake in myocardial cells. This makes  $^{201}\text{Tl}$  less suitable for delayed and long acquisition protocols.

## 2. Methodology

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

## 3. Indications

- a. Patients in whom coronary artery disease(CAD) is suspected:
  - Pre-test probability of CAD 15-65% with LVEF >50% and stress ECG not possible due to physical limitations or an inconclusive stress ECG or in patients with ECG characteristics such as LBBB which lead to non-interpretable stress ECG.
  - Pre-test probability 66-85% for CAD or LVEF <50% without typical angina.
- b. Patients with known CAD diagnosed by an anatomical imaging modality in whom the functional significance of the stenosis should be determined.
- c. To exclude ischemia as a trigger for rhythm disorders.
- d. Patients with persistent symptoms after revascularization procedures.
- e. Patients with >3 risk factors who will undergo high risk surgery.
- f. To assess viability of dysfunctional myocardium, sometimes followed by viability testing with FDG.
- g. Patients with an agatston calcium score >400 and any risk.

#### 4. Contra indications for reliable MPS

- Unstable AP
- Recent myocardial infarction (<4 days).
- Recent revascularization procedure (<3 month).

#### 5. Relations to other diagnostic procedures

- Stress echocardiography: exercise stress echo and pharmacological stress echo have a comparable sensitivity to MPS and a slightly higher specificity. However the reliability of this test is dependent on the operator's skills and it is not feasible in patients with poor ultrasound window.
- PET: vasodilator stress PET with  $^{82}\text{Rb}$  or  $^{13}\text{N}$ -Ammonia has a higher sensitivity and specificity as compared to vasodilator SPECT. Another advantage is the possibility of flow quantification. However, limited access and higher costs prevents this imaging modality being used as a routine clinical imaging modality.
- Cardiac Magnetic Resonance Imaging (CMR): Vasodilator CMR and vasodilator SPECT have comparable sensitivity and specificity in detecting coronary artery disease. An advantage of CMR is the high soft tissue contrast with precise imaging of scar tissue and reliable viability assessment. Disadvantages include the high cost, contra indications (e.g. claustrophobia, pacemaker) and limited availability.
- Coronary CT: this is an anatomical imaging modality with a high negative predicted value (NPV) in patients with low - intermediate pre-test probability (15-50%). However, there is a low NPV in patients with high pre-test probability. There is no clear relationship between the percentage of stenosis and functional ischemia. Moreover, assessment is limited in patients with extensive coronary calcification or previous stent implantation. In addition, the image quality is limited by arrhythmias or high heart rates that cannot be reduced to 60-65/min.

#### 6. Medical information necessary for planning

- Relevant patient history and risk factors.
- Clear description of the indication.
- Symptoms.
- Physical capacity.
- Previous stress and/or rest ECG.
- Past medical history and permission from referring physician to temporarily stop calcium antagonists, nitrates, beta blockers, dipyridamol and xanthine derivatives which influence the sensitivity of the MPS.

#### 7. Radiopharmaceutical

Dose: It is not possible to make precise recommendations on the administered dose. This depends on the camera and acquisition protocol. The dosages advised below is based on a dual head camera system with a gated acquisition:

$^{99m}\text{Tc}$ -sestamibi or  $^{99m}\text{Tc}$ -tetrofosmin, intravenous injection:

- 2-day protocol: same dose for both rest and stress study; for a patient of normal weight (BMI <25) 600 MBq; increase the dose according to weight, up to 900MBq for a patient with a BMI >35.

- 1-day protocol: the activity injected should be divided into a third for the first study and two-thirds for the second study. 250-400 MBq for the first injection.

*<sup>201</sup>Tl-chloride, intravenous injection:*

74-111 MBq. An additional 37 MBq can be given at rest for reinjection.

## 8. Radiation safety

The dose received by patients' relatives is negligible.

In table 1 the radiation dose for an adult is displayed for the stress and rest study.

In table 2 the radiation dose is displayed for a foetus when a pregnant woman undergoes a SPECT myocardial perfusion scintigraphy.

Table 1:

	Stress	Rest
<sup>99m</sup> Tc-tetrofosmin	0,0069 mSv/MBq	0,008 mSv/MBq
<sup>99m</sup> Tc-sestamibi	0,0079 mSv/MBq	0,0090 mSv/MBq
<sup>201</sup> Tl-chloride	0,14 mSv/MBq	0,14 mSv/MBq

Table 2:

	Stress	Rest
<sup>99m</sup> Tc-tetrofosmin	0,0076 mGy/MBq	0,0072 mGy/MBq
<sup>99m</sup> Tc-sestamibi	0,0072 mGy/MBq	0,0078 mGy/MBq
<sup>201</sup> Tl-chloride	0,051 mGy/MBq	0,051 mGy/MBq

*Breastfeeding:*

Breast feeding should be interrupted for 48 h when using <sup>201</sup>Tl according to ICRP 106. According to ICRP 106 there is no need to interrupt breastfeeding using <sup>99m</sup>Tc labelled radionuclides, but due to possible free <sup>99m</sup>Tc pertechnetate it is advisable to interrupt the feeding for 4 h.

## 9. Patient preparation

1. Written information with a confirmation of the appointment should be sent to the patient at least 3 days before the investigation. This information should include:
  - A brief description of the procedure and possible side effects.
  - The duration of the examination.
  - Details on the medication which should be withheld before the stress test.
2. Medication: beta-blockers, calcium antagonist and nitrates should be stopped 48 h before the stress test. However, short acting nitrates can be withheld for as little as 3 h before the stress test.
 

Persantin /Dipyridamol should be stopped at least 72 h before the stress test if the patient is scheduled for a pharmacological vasodilator stress test. \*

Xanthine derivatives such as Theophylline should be stopped at least 48 h before the

- stress test if the patient is scheduled for an pharmacological vasodilator stress test. \*
3. Patients scheduled for a pharmacological vasodilator stress test\* should avoid caffeine containing beverages and medication for at least 12 h but preferably 24 h prior to the stress testing as there is a large variation of  $T_{1/2}$  of caffeine between individuals.
  4. Patients should avoid heavy food en beverages 6 h before the rest and stress study. A light meal is permitted up to 4 h before the stress and rest test. A fasting state is recommended for a minimum of 4 h prior to the injection of the radiopharmaceutical. Diabetics may consume a light meal within 4 h before the test and should lower their insulin dose.

\*However, it is advisable to also give these instructions to patients who are scheduled for a physical stress test. If the patient does not reach an adequate heart rate the test be converted to a pharmacological vasodilator stress test.

## 10. Study protocols

### <sup>99m</sup>Tc labelled radiopharmaceuticals:

- One day protocol:

In a one day protocol the first study should be the study with the lowest injected dose. The second study can be initiated 3-4 h later. Several factors (medical or logistical) may influence which of the studies should be performed first. If the stress study is performed first and it is normal then the rest study may not be required. However, the stress study is the most important in terms of disease detection and low dose image statistics are relatively poor meaning perfusion defects may be missed.

- Two-day protocol:

The stress and rest study are done on two separate days with at least 24 h in between. The stress and rest study are done with a similar dose between 600-900 MBq. (based on a dual head camera system with a gated acquisition).

Acquisition should begin 30-60 min after injection of the radiopharmaceutical, to allow for hepatobiliary clearance. In order to accelerate hepatobiliary clearance a fatty meal can be consumed. However this may be counterproductive if the tracer reaches the transvers colon which can lead to artefacts of the inferior wall. Consumption of fluids just before acquisition may also reduce gastrointestinal interference in the inferior wall. If the stress study is done on the first day and the myocardial perfusion as well as the LV function assessed with Gated-SPECT are normal then the rest study may be cancelled.

### <sup>201</sup>Tl-chloride:

There are several protocols which can be followed:

- Stress-4h-redistribution.
- Stress-4h-redistribution-reinjection.
- Stress-reinjection.

The reinjection protocols allow for better discrimination between reversible and persistent perfusion defects. The stress study is always preformed first. The stress study can be physical or pharmacological. Imaging should begin as soon as possible after the <sup>201</sup>Tl-chloride is injected. The reinjection and imaging can be planned on the same day or on a subsequent day.

- Rest-4h-redistribution: this protocol is used to assess viability of hypo functional myocardium only.

Dual isotope  $^{99m}\text{Tc}$  labelled radiopharmaceutical and  $^{201}\text{Tl}$ -chloride:

First the rest study is done using 74 MBq of  $^{201}\text{Tl}$ -chloride, the acquisition can begin as soon as 15 min after injection.

After completion of the rest study, a stress study is performed using a  $^{99m}\text{Tc}$  labelled agent.

When comparison of the two studies shows a fixed defect, the patient can be asked to return the next morning for a delayed  $^{201}\text{Tl}$ -chloride study. An alternative is to inject the patient with  $^{201}\text{Tl}$ -chloride the afternoon before the study and perform the redistribution acquisition the morning after the injection. This is immediately followed by the stress study with a  $^{99m}\text{Tc}$  labelled agent.

## 11. Stress modalities

Physical stress:

Dynamic exercise is preferred wherever possible. Physical exercise capacity gives extra information regarding heart performance.

Different dynamic exercise modalities are available e.g. bicycle ergometry, treadmill exercise.

Exercise may be stopped if typical symptoms occur with patients achieving >85% of their predicted target heart rate for optimal diagnostic accuracy.

Contraindications (absolute) to maximal dynamic exercise:

- Recent acute coronary syndrome. Patient must be stable for at least 4 days.
- Acute pulmonary embolism.
- Uncontrolled severe hypertension (>200/110 mmHg)
- Acute aortic dissection.
- Aortic aneurysm.
- Symptomatic aortic stenosis.
- Hypertrophic obstructive cardiomyopathy (HOCM).
- Uncontrolled cardiac arrhythmias causing symptoms or haemodynamic instability.

Contraindications (relative) to maximal dynamic exercise:

- LBBB or ventricular paced rhythm.
- Deep vein thrombophlebitis or deep vein thrombosis.
- Endocarditis, myocarditis, pericarditis.

Stress study performance:

- An intravenous cannula should be inserted for the radiopharmaceutical injection.
- A 12-lead ECG should be monitored continuously during the exercise test and for at least 3-5 min of recovery.
- The blood pressure should be checked at least every 2 min during exercise.
- The level of exercise is adequate if typical symptoms of fatigue occurs with patients achieving >85% of their age-predicted maximum heart rate. The radiopharmaceutical should be injected at peak stress. The patient is subsequently asked to continue the exercise for at least 1 min after injection. If the patient has symptoms and/or signs

typical of ischemia without achieving the 85% heart rate the radiopharmaceutical may be injected.

- If the patient does not achieve >85% of the maximum heart rate and does not have symptoms of ischemia the radiopharmaceutical should not be injected. The stress test should be continued using pharmacological stress (see below).

Pharmacological stress:

Patients who are unable to exercise or who are in a poor physical condition and therefore unlikely to achieve >85% of heart rate may undergo a pharmacological stress test. In addition patients with a contraindication for physical exercise stress test should also be stressed pharmacologically.

There are 2 groups of pharmacological stress modalities:

- Vasodilators (adenosine, dipyridamol and regadenoson) that cause coronary hyperaemia. In stenotic vessels the vasodilation will be less as compared to non-stenotic vessels.
- Beta stimulator (dobutamine) which increases myocardial oxygen demand.

Adenosine:

Adenosine is a naturally occurring purine which causes direct vasodilatation by binding to the A<sub>2</sub> receptor and increasing intracellular cyclic AMP. It has a short half life of 2-10 sec. It leads to a modest increase in heart rate and a modest decrease in blood pressure.

Contra indications: unstable angina pectoris, bronchospasm, severe COPD (GOLD III-IV), asthma with ongoing wheeze, 2nd or 3d degree AV block, severe sinus bradycardia (<40/min), systolic blood pressure <90 mmHg, bilateral stenosis of the carotid artery, severe mitral valve insufficiency, use of dipyridamol, known hypersensitivity to adenosine.

Protocol:

- An intravenous cannula should be inserted for the infusion of Adenosine and the radiopharmaceutical injection.
- A 12-lead ECG should be monitored continuously during the test and for at least 3-5 min of recovery.
- The blood pressure should be checked at least every 2 min during the test.
- Dose: 0,84 mg/kg with 0,9% NaCl in a 50 ml syringe. This should be given intravenously as 0,14 mg/kg/min during 6 min. The radiopharmaceutical is injected 3 min after the start of the infusion. In patients with mild COPD a salbutamol inhaler may be given before starting the adenosine infusion to prevent bronchoconstriction.

Side effects: chest pain, headache, flushes, dizziness, ECG changes, dyspnoea, high degree AV block, SA block. Due to the short half-life of Adenosine most side effects will resolve rapidly after discontinuation of the infusion.

Dipyridamol:

Dipyridamol is an indirect coronary vasodilator; it increases the tissue levels of adenosine. It has a half-life of 30 min. It leads to a modest increase in heart rate and a modest decrease of blood pressure.

Contra indications are similar to those of Adenosine.

*Protocol:*

- An intravenous cannula should be inserted for the infusion of Dipyridamol and the radiopharmaceutical injection.
- A 12-lead ECG should be monitored continuously during the test and for at least until least 3-5 min of recovery.
- The blood pressure should be checked at least every 2 min during the test.
- Dose: 0,56 mg/kg with 0,9% NaCl in a 50 ml syringe. It should be given intravenously in a dose of 0,14mg/kg/min during 4 min. 7 min after the start of the infusion the radiopharmaceutical is injected. If possible the patient should perform low level exercise from minute 4 to minute 8 after the start of the infusion. This should reduce side effects and improve image quality. Patients with mild COPD may be given a salbutamol inhaler before starting the Dipyridamol infusion to prevent bronchoconstriction.

Side effects: chest pain, headache, flushes, dizziness, ischemic ECG changes, dyspnoea, high degree AV block, SA block. The frequency of side effects is less than that seen with adenosine but they last longer due to the longer half-life. In order to resolve side effects, Aminophylline (125-250 mg) may be given intravenously 3 min after tracer injection.

*Regadenoson:*

Regadenoson is a low affinity A<sub>2a</sub> adenosine receptor agonist which leads to coronary artery dilatation and an increase in blood flow with at least a 10 fold lower affinity for the A<sub>1</sub> adenosine receptor and a weak affinity for the A<sub>2b</sub> and A<sub>3</sub> receptors. The selectivity of regadenoson towards the A<sub>2a</sub> receptor reduces side effects such as AV block and bronchospasm which are mediated by the other 3 known adenosine receptors. Patients with asthma or COPD tend to show less dyspnoea with regadenoson as compared to adenosine or dipyridamol. Maximum plasma concentration is achieved within 1-4 min after injection. The half-life of the initial phase is 2-4 min. An intermediate phase follows with a half-life of 30 min. The terminal phase half-life is 2 h.

Contra indications: unstable angina pectoris, 2nd or 3rd degree AV block, severe sinus bradycardia (<40/min), systolic blood pressure <90 mmHg, bilateral stenosis of the carotid artery, severe mitral valve insufficiency, use of dipyridamol, known hypersensitivity to regadenoson. Severe COPD is not a contra indication but dyspnoea may occur.

*Protocol:*

- An intravenous cannula should be inserted for the injection of Regadenoson and injection of the radiopharmaceutical.
- A 12-lead ECG should be monitored continuously during the test and for at least 3-5 min of recovery.
- The blood pressure should be checked at least every 2 min during the test.
- Fixed dose of 0,4 mg in a 10 ml syringe with 0,9% NaCl. It is administered intravenous as a bolus in 10 sec and immediately followed by a 10 ml saline flush over 10 sec. The radiotracer is administered 10-20 sec after the saline flush.

Side effects: headache, flushing, chest discomfort, dizziness, chest pain, nausea, conduction or rhythm abnormalities. Aminophylline may be given in a dose of 50-250 mg by slow intravenous injection (100 mg over 60 sec) to attenuate severe and/or persistent side effects.

Dobutamine:

Dobutamine is a synthetic catecholamine. It increases oxygen demand in a dose-related manner due to an increase in heart rate, blood pressure and myocardial contractility. These effects lead to vasodilatation. The half-life is 2 min. This stressor is used in patients who cannot undergo physical exercise and have contra indications to vasodilators. If the heart rate response is suboptimal then Atropine may be used.

Contra indications: similar to the contraindications for physical exercise.

Contra indication for Atropine: glaucoma, obstructive uropathy, atrial fibrillation with uncontrolled heart rate, obstructive gastro intestinal disease, paralytic ileus. Inform the patient of possible difficulties of ocular accommodation for 2 hours following atropine administration.

Protocol:

- An intravenous cannula should be inserted for dobutamine infusion and radiopharmaceutical injection.
- A 12-lead ECG should be monitored continuously during the test and for at least 3-5 min of recovery.
- The blood pressure should be checked at least every 2 min during the test.
- Dose: 0,315 mg/kg in a 50 ml syringe with 0,9% NaCl. The infusion starts at 10 microgr/kg/min and the dobutamine dose should be increased by 10 microgr/kg/min at 3 minute-intervals with a maximum dose of 40 microgr/kg/min. If 85% of the age-predicted maximal heart rate is reached the radiotracer is injected. The dobutamine infusion should be continued for 1 min. If the heart rate response is suboptimal at 40 microgr/kg/min then Atropine 0,25 mg could be given 1-3 times with 30 sec time interval.

Side effects: palpitations, chest pain, headache, flushing, dyspnoea, supra ventricular or ventricular arrhythmias, hypotension. Severe side effects can be attenuated by an intravenous beta blocker such as esmolol, sotalol or propranolol.

**12. Acquisition and processing**Acquisition

In earlier years images were recorded using several planar views. Compared to SPECT imaging these tests have a significantly lower sensitivity and specificity. Gamma cameras with SPECT capability are now widely available thus planar imaging of myocardial perfusion should not be used.

The acquisition of the SPECT study can be performed with a conventional gamma camera. In recent years significant advances have been made both in hardware technology (hybrid camera systems with integrated CT, specialized collimators and solid state detectors) and in software features (iterative reconstruction with collimator modelling, resolution recovery, attenuation correction and scatter correction). These advances facilitate improvement of image quality, reduction of scan time and/or reduction of the injected dose. Some of these new techniques can be applied to or can be retrofitted on existing conventional camera systems to provide a high impact, low cost improvement. As most of these new techniques utilize vendor specific hardware and/or software features, this chapter will focus on generally applicable techniques.

Images are acquired using a gamma camera equipped with a low energy collimators.

A matrix size of 64x64 is advised.

Energy windows are isotope dependant: 20% at 72 keV and 20% at 167 keV for  $^{201}\text{Tl}$  studies, 15% at 140 keV for  $^{99\text{m}}\text{Tc}$  studies.

Dual or triple head camera systems are preferred to single head systems. For dual head systems a 180° rotation is used, ranging from 45° right anterior oblique to 45° left posterior oblique. The camera heads are positioned in a 90° configuration. For triple head systems a 360° rotation is used.

A non-circular, body contoured orbit is preferred in order to maintain minimal distance between the patient and the camera. Both step and shoot and continuous modes are suitable. For  $^{201}\text{Tl}$  images 32 or 64 projections can be used in a 180° acquisition, for  $^{99\text{m}}\text{Tc}$  images 64 projections are sufficient in a 180° acquisition, 128 projections are common in a 360° acquisition. The optimal time per view is a trade-off between count statistics and risk of patient movement. Total acquisition time should be kept below 20-30 min.

Supine positioning is most commonly used, the patient should have both arms above the head, if possible. The use of a pillow, arm rests and knee support reduces the likelihood of patient motion and artefacts. Prone positioning may reduce inferior attenuation artefacts or infra-diafragmatic scatter typical for supine images, however this might induce antero-septal artefacts. Prone positioning has been reported to cause less patient motion. Both positions are equally suitable, however it is paramount that both stress and rest images are acquired in the same position (either supine or prone, either arms raised or beside the body). Female patients should be imaged without a bra. A chest band can be used to minimize breast attenuation or to ensure reproducible positioning during stress and rest acquisitions.

Studies should be acquired in an ECG triggered gated mode whenever possible. Gated images allow for the evaluation of left ventricular function (ejection fraction, volume, wall motion). Gating also improves diagnostic accuracy of irreversible perfusion defects that might be caused by attenuation artefacts, preventing the misinterpretation of an artefact as a scar when function is maintained.

Correct ECG triggering requires a fairly regular rhythm and distinguishable R waves as a trigger. Highly variable sinus arrhythmia or atrial fibrillation, frequent premature beats, paroxysmal arrhythmias and pacemaker spikes can cause difficulties in correct triggering and, depending on software settings, might lead to longer acquisition times and unreliable ejection fraction calculation. There is no consensus on the optimal R-R interval tolerance window, classically cardiac cycles that fall within 20% of the average cycle length (= R-R interval) are accepted.

The cardiac cycle is usually divided into 8 frames which is a good compromise between sufficient count statistics and correct representation of the cardiac cycle and thus accuracy of function and wall motion assessment.

In gated SPECT each projection can be set to a fixed time, similar to non-gated SPECT, or to a fixed number of accepted beats (cardiac cycles). Using a fixed time setting, caution should be applied regarding cycles that do not fall within the R-R interval tolerance window. These unaccepted cycles are not used to construct the gated images, however they should be stored to process the non-gated, perfusion images. A highly variable distribution of accepted and unaccepted cycles over the entire acquisition can result in

insufficient quality for the correct assessment of left ventricular function. The use of a fixed number of accepted beats can address these issues while risking a significant and unwanted prolongation of the acquisition.

$^{99m}\text{Tc}$  tracers are more suitable for gated acquisition than  $^{201}\text{Tl}$  due to higher count statistics.

### Processing

Processing of the acquired data requires several steps including filtering, reconstructing, correcting and reorienting.

Prior to processing the raw cine data and sonograms should be reviewed to evaluate overall quality, count statistics, ECG triggering and possible motion or other artefacts. It is possible to correct minor and simple forms of motion such as an upward creep (commonly due to a decrease in respiratory rate). Slight up and down movements by 1 pixel have been demonstrated not to cause significant artefacts and should not be corrected. Patients should remain in the department until the acquired data is accepted for further processing allowing for repeat imaging when necessary.

Filtering is used to reduce noise. Typically a low pass filter is used, to allow low frequencies to pass while attenuating the higher, noisier frequencies. Software packages typically use predefined, camera dependent filter settings. Unless the physician is thoroughly familiar with the effects of filter adjustments, it is not advisable to change these settings. Many software features depend on edge detection, changing filter settings may have a significant impact on the resulting images and calculations.

Reconstruction traditionally used the filtered back projection technique which is relatively straightforward and fast but lacks correction methods and is prone to noise. Nowadays all vendors provide iterative reconstruction algorithms. These algorithms consist of cycles of projecting an image derived from an initial guess, comparing it to the measured data, applying a correction and updating the initial guess after back projection of the corrected image. Due to the ever increasing computing power this technique is equally fast and applicable to routine clinical use. These algorithms also allow the addition of several correction methods such as resolution recovery (a compensation for the loss of resolution due to the collimator and the detector), scatter correction and attenuation correction (using either a transmission scan or a CT scan).

The different options and user changeable settings are highly vendor dependent thus it is advisable to consult your vendor to assist in changing or choosing optimal reconstruction settings.

The final reconstruction step consists of the reorientation of the image data. The tomographic data can be manually or automatically reoriented into the three standard cardiac planes (short axis, horizontal long axis and vertical long axis). Inappropriate plane definition can lead to artefacts and interpretation errors. Caution is advised using automated reorientation in cases of large myocardial infarction defects or (congenital) orientation abnormalities. It is crucial that stress and rest images are reoriented in a uniform fashion.

## **13. Interpretation**

### Perfusion:

For the interpretation of the perfusion images the visual interpretation is the most reliable.

There are several software programmes available for the interpretation of the myocardial perfusion images. However, the assessment of myocardial perfusion with software

programmes should be used as a supplement. The visual interpretation should not be abolished.

- Review raw data for quality control. (patient movement, count statistics, attenuation, adjacent gastro intestinal activity)
- The display should consist of 3 image planes (short axis, vertical long axis and horizontal long axis) for both rest and stress study. The stress and rest study should be displayed simultaneously. A continuous colour scale should be used.
- If attenuation/ scatter compensation has been applied, the images without compensation should also be evaluated.
- Describe the localisation, severity and extent of the areas with diminished uptake of the radiopharmaceutical. Normal variation in count rates should always be kept in mind; e.g. lower activity in the septal wall as compared to the lateral wall, attenuation in the antero-lateral wall due to large breasts.

The visual rating of perfusion can be described as followed:

Normal, mildly reduced, moderately reduced, severely reduced and absent perfusion.

- If a perfusion abnormality is seen in the stress study but not in the rest study this can be judged as ischaemia. If a perfusion abnormality is seen in stress and rest this can be due to an attenuation artefact or a myocardial infarction.

#### Quantitative analysis:

Quantitative analysis of myocardial SPECT data is another approach to verifying perfusion abnormalities, however, quantitative analysis should never be used without visual review of the images.

There are several quantitative software programmes available.

The myocardium is displayed in a polar map with the apex in the centre and the base on the periphery. This is the so called Bull's-eye. This Bull's-eye is made for the rest and the stress study. The difference in counts between stress and rest circle is displayed in a third polar map. It is important that the rest and stress polar maps are based on identical delineation and orientation of the left ventricle.

In addition, this circle representing the left ventricle in segments, preferably using the American Heart Association 17 segment model. These segments are scored using a 5-point model of a reference population ranging from 0 (normal) to 4 (uptake absent). The total score of the left ventricle is referred to as the summed stress score (SSS), summed rest score (SRS) and summed difference score (SDS). If these scores are reliable, taking into account possible artefacts, they may be reported. The reference database consists of men and women with a low probability of coronary artery disease or proven normal coronary arteries. It should be highlighted that the reference database may not be a good reference population for your patients. Many parameters influence how the counts are distributed throughout the myocardium e.g. sex, body habitus, tracer, acquisition and processing protocols, patient position etc.

#### Left ventricular volume and function:

Gated SPECT and routine SPECT acquisitions can occur simultaneously for any myocardial perfusion study.

However, as  $^{201}\text{Tl}$  has lower count statistics as compared to  $^{99\text{m}}\text{Tc}$  labelled tracers the inter

observer variability for wall motion and wall thickening is higher in  $^{201}\text{Tl}$  studies.

If available, functional information should always be reported as it is known to be an independent prognostic marker for cardiac events and cardiac death.

Several software programmes are available to quantify LV volumes and ejection fraction and to display the wall motion and wall thickening.

Although good correlations are found between different software programmes and imaging modalities normal values for EDV (end diastolic volume) and ESV (end systolic volume) and EF (ejection fraction) depend on acquisition and processing protocols and vary between different software programmes and imaging modalities.

In addition normal values for LV volumes and ejection fraction differ between men and women.

Taking into account all these variables one should rely on the department's own experience of whether LV volumes and ejection fraction values are normal or pathological.

Routinely review the end diastolic and end systolic edges in which errors may occur.

Large perfusion defects, small left ventricles, extra cardiac activity and LV hypertrophy cause less reliable functional parameters.

Regional wall motion and thickening should be assessed visually and reported as normal, mildly affected, severely affected, absent or dyskinetic. Wall motion and wall thickening can be different therefore both parameters should be assessed; e.g. patients with an LBBB may have normal wall thickening but paradoxical septal wall motion.

Most gated SPECT software programmes divide the LV in 17 segments and these segments are scored for wall motion and wall thickening on a 5 point scale. (0=normal wall motion/thickening to 4 =dyskinesia). These scores may be reported if they seem reliable at visual inspection.

It should be emphasized that the gated SPECT study of the stress study using  $^{99\text{m}}\text{Tc}$  labelled agents is acquired in LV resting conditions approximately 30-60 min after stress. However, in patients with coronary artery disease a worsened LV ejection fraction and/or LV dilatation in stress may persist for >60 min after stress. This post stress myocardial stunning or dilatation is an additional sign of stress induced ischaemia. Post stress LV dysfunction has an independent prognostic value.

#### Integration of perfusion and function:

On images with mild-moderate perfusion defects in the rest study one may differentiate between an infarction and attenuation artefact by assessing the regional wall thickening. In patients with an artefact the regional wall thickening should be normal whereas patients with an infarction will show pathological regional wall thickening.

If there is normal perfusion but diminished LV ejection fraction and/or a LV dilatation the patient may have a non-ischaemic cardiomyopathy.

## **14. Report**

Reports should contain:

- Patient's name, age, sex and date of study.
- Relevant medical history.
- Relevant medication list and information on which medication has been temporarily

withdrawn.

- Stress imaging modality; physiological response on the stress modality, symptoms, description of stress ECG.
- Name and dose of the radiopharmaceutical.
- Pathological findings outside the LV on the raw images and possible artefacts.
- Scintigraphic LV perfusion pattern with the stress and rest regional perfusion abnormalities and if available and reliable quantitative perfusion information.
- Information on LV function and volumes from the gated SPECT study.
- If available comparison with a previous cardiac imaging study.
- Conclusion : the conclusion should answer the clinical question.
- Relevant stress findings: e.g. stress induced ischaemia.
- LV perfusion: normal, ischaemia (mild, moderate, severe), infarction, artefacts.
- LV function: LV volumes (dilatation, normal) and global and or regional functional findings.
- If relevant, recommendation on further investigations or patient management.
- If relevant, shortcomings of the investigation such as suboptimal quality due to low count statistics or irregular heart rate.

## 15. Literature

- Al JW, Iskandrian AE. Regadenoson: a new myocardial stress agent. *J Am Coll Cardiol.* 2009;54(13):1123-30.
- Carlsson M, Jogi J, Bloch KM et al. Submaximal adenosine-induced coronary hyperaemia with 12 h caffeine abstinence: implications for clinical adenosine perfusion imaging tests. *Clin Physiol Funct Imaging.* 2014.
- DePuey EG, Parmett S, Ghesani M, Rozanski A, Nichols K, Salensky H. Comparison of Tc-99m sestamibi and Tl-201 gated perfusion SPECT. *J Nucl Cardiol.* 1999;6(3):278-85.
- Dorbala S, Di Carli MF, Delbeke D et al. SNMMI/ASNC/SCCT guideline for cardiac SPECT/CT and PET/CT 1.0. *J Nucl Med.* 2013;54(8):1485-507.
- Flotats A, Knuuti J, Gutberlet M et al. Hybrid cardiac imaging: SPECT/CT and PET/CT. A joint position statement by the European Association of Nuclear Medicine (EANM), the European Society of Cardiac Radiology (ESCR) and the European Council of Nuclear Cardiology (ECNC). *Eur J Nucl Med Mol Imaging.* 2011;38(1):201-12.
- Garcia EV, Faber TL, Esteves FP. Cardiac dedicated ultrafast SPECT cameras: new designs and clinical implications. *J Nucl Med.* 2011;52(2):210-7.
- Hacker M, Becker C. The incremental value of coronary artery calcium scores to myocardial single photon emission computer tomography in risk assessment. *J Nucl Cardiol.* 2011;18(4):700-11.
- Hesse B, Tagil K, Cuocolo A et al. EANM/ESC procedural guidelines for myocardial perfusion imaging in nuclear cardiology. *Eur J Nucl Med Mol Imaging.* 2005;32(7):855-97.
- Holly TA, Abbott BG, Al-Mallah M et al. Single photon-emission computed tomography. *J Nucl Cardiol.* 2010;17(5):941-73.
- Kubo S, Tadamura E, Toyoda H et al. Effect of caffeine intake on myocardial hyperemic flow induced by adenosine triphosphate and dipyridamole. *J Nucl Med.* 2004;45(5):730-8.
- Montalescot G, Sechtem U, Achenbach S et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J.* 2013;34(38):2949-3003.
- Nakajima K, Kusuoka H, Nishimura S, Yamashina A, Nishimura T. Normal limits of ejection fraction and

volumes determined by gated SPECT in clinically normal patients without cardiac events: a study based on the J-ACCESS database. *Eur J Nucl Med Mol Imaging*. 2007;34(7):1088-96.

- Schaefer WM, Lipke CS, Standke D et al. Quantification of left ventricular volumes and ejection fraction from gated  $^{99m}\text{Tc}$ -MIBI SPECT: MRI validation and comparison of the Emory Cardiac Tool Box with QGS and 4D-MSPECT. *J Nucl Med*. 2005;46(8):1256-63.
- Slomka PJ, Dey D, Duvall WL, Henzlova MJ, Berman DS, Germano G. Advances in nuclear cardiac instrumentation with a view towards reduced radiation exposure. *Curr Cardiol Rep*. 2012;14(2):208-16.
- van Dongen AJ, van Rijk PP. Minimizing liver, bowel, and gastric activity in myocardial perfusion SPECT. *J Nucl Med*. 2000;41(8):1315-7.
- Radioation protection 100. Guidance fo protection of unborn children and infants irradiated due to parental medical exposures. European Commission on-line publication catalogue 1998.