NUCLEAR CARDIOLOGY

Nuclear cardiology is a scan of the heart using a radioactive isotope imaged with a gamma camera to assess:

- Myocardial perfusion (with SPECT or PET)
- Myocardial viability (with SPECT or PET)
- Ventricular function (planar imaging with MUGA or with gated SPECT/PET)

RADIATION & RADIOPHARMACEUTICALS

- **Radioactivity** is a natural process in which ionising radiation is emitted from unstable atoms known as radioisotopes. The activity will gradually decay away and the time taken for the activity to halve is known as the half-life. For most applications a half-life of a few hours is convenient for imaging without leaving activity in the patient for an unnecessary length of time.

- **Radioactive decay** is the process in which unstable atomic nuclei release radiation to become more stable.

- **There are three main types of radiation that can be emitted in radioactive decay:**
  1. **Alpha particles**: composed of two protons and two neutrons (helium nucleus), has the greatest mass and the least penetrating power; can be stopped by a thick sheet of paper or even a layer of clothes; not used in nuclear medicine
  2. **Beta particles**: high-energy electrons or positrons, can only penetrate through a few millimetres of tissue, so their radiation will all be absorbed in the local organ. This makes beta emitters useful for therapy, but beta particles cannot be used for imaging because they can't escape from the patient
  3. **Gamma-rays**: are not particles but a high energy electromagnetic radiation (like x-rays except more powerful). They have no mass or charge. They are considered to have the least ionizing power and the greatest penetration power. Therefore more rays exit the body (most will exit the body as long as their energy > 100 kilo electron volts, keV) and are available for detection by a gamma camera.

- **X ray vs Gamma Ray:** X-rays are a type of electromagnetic radiation with higher energy and shorter wavelengths than visible light, produced by the collision of high-speed electrons with matter in metal form. Gamma rays are the highest-energy form of electromagnetic radiation produced by the decay of atomic nuclei. X-rays have a lower energy and longer wavelength than Gamma-rays. Dense materials like bones absorb X-rays, while Gamma-rays can penetrate through thick layers of matter. X-rays are commonly used for medical imaging, while Gamma-rays are used for radiation therapy and nuclear imaging

- **Radioactivity or the strength of a radioactive source is measured in units of Becquerel (Bq)**. One Bq = 1 event of radiation emission or disintegration per second. One Becquerel is an extremely small amount of radioactivity. Commonly used multiple of the Bq unit is MBq (mega-becquerel). An old and still popular unit of measuring radioactivity is the curie (Ci). One Ci = 37000 MBq. One curie is a large amount of radioactivity. Commonly used subunits are mCi (milli-curie).

- **The energy of ionizing radiation is measured in electronvolts (eV).** One eV is an extremely small amount of energy. Commonly used multiple unit is kilo electronvolt (keV). One joule = 6,200 billion MeV

- **X-ray and gamma-ray exposure is often expressed in units of roentgen (R).** The roentgen (R) unit refers to the amount of ionization present in the air. One roentgen of gamma- or x-ray exposure produces approximately 1 rad (0.01 Gy) tissue dose.

- **The absorbed dose is the amount of energy absorbed per unit weight of the organ or tissue and is expressed in units of gray (Gy).** One gray dose is equivalent to one joule of radiation energy absorbed per kilogram of organ or tissue weight. Rad is the old and still used unit of absorbed dose. One gray is equivalent to 100 rads. Another unit of measuring gamma ray intensity in the air is "air dose or absorbed dose rate in the air" in grays per hour (Gy/h) units.

- **Risks of Radiation**: People are exposed to natural background ionising radiation every day and the average dose across the UK from this is approximately 2 mSv per year. Ionising radiation is so called because it has sufficient energy to remove electrons from atoms in tissue; this can lead to damaged cells in tissues and organs with a consequent risk that this can eventually lead to cancer developing. The risk increases with the dose that is absorbed. Typical doses from nuclear medicine imaging procedures in the range of 1 to 15 mSv. Studies on radiation risk estimate that the probability of a fatal cancer developing from an exposure to 1 mSv of ionising radiation is approximately 50 in a million.

- **A radiopharmaceutical** is a radioisotope chemically bound to a pharmaceutical. For a nuclear medicine procedure the patient is injected with a small amount of an appropriate radiopharmaceutical. The pharmaceutical is designed to concentrate in a particular organ or biological process, and the radioisotope which is attached to it allows the distribution of the pharmaceutical to be detected. This can therefore produce a map of where the pharmaceutical has concentrated. For example, if the pharmaceutical concentrates in the myocardium, its distribution will reflect myocardial blood flow. In nuclear cardiology the most commonly used radiopharmaceuticals that are labelled with 99mTc are tetrofosmin (marketed as Myoview) and sestamibi (Cardiolite)**.** ^{99}mTc emits gamma-rays with an energy of 140 keV and has a half-life of 6 hours.

- **Tracers for perfusion imaging**

Tracer	Type of tracer	Production	Half -life	Positron range (mm)	Scan duration (rest and stress)	Intravenously administered activity (MBq)	Effective dose (mSv/MBq)	Approval year		
								FDA	Europe	Japan
SPECT										
^{201}Thalium (^{201}Tl)	Metal cation	Cyclotron	73 h	–	4-h	74–148	0.23	1977	1980	1991
^{99m}Tc-sestamibi	Metal complex	Generator	6 h	–	4-h or 2-days	740–1480	0.0085	1990	1987	1993
^{99m}Tc-tetrofosmin	Metal complex	Generator	6 h	–	4-h or 2 days	740–1480	0.0067	1996	1993	1996
^{99m}Tc-teboroxime		Generator	6 h	–				1990	–	–
PET										
^{82}Rubidium ($^{82}Rb^{+}$)	Metal cation	Generator	76 s	8.6	30-min	370–740	0.0048	1989	–	–
^{13}N-ammonia ($^{13}NH_3$)	Inorganic compound	Cyclotron	9.96 min	2.53	1.5-h	370–740	0.0022	2007	–	2012
^{15}O-water ($H_2{}^{15}O$)	Inorganic compound	Cyclotron	2.04 min	4.14	30-min	370–740	0.0011	–	–	–
^{18}F-flurpiridaz	Organic compound	Cyclotron	109.8 min	1.03	1.5-h or 2 days	222–370	0.019	–		

- **Tracers for metabolic imaging**

Tracer	Characteristics	Approval year		
		FDA	Europe	Japan
^{123}I-BMIPP	Long-chain fatty acid analogue	–	–	1993
^{123}I *p*-IPPA	Long-chain fatty acid analogue	–	–	–
^{123}I *o*-IPPA	Long-chain fatty acid analogue	–	–	–
^{123}I-9-MPA	Long-chain fatty acid analogue	–	–	–
^{18}F-FDG	Glucose analogue	1997	1994	2002
^{18}F-FTHA	Long-chain fatty acid analogue	–	–	–
^{11}C-palmitatic acid	Long-chain fatty acid analogue	–	–	–
^{11}C-acetic acid	^{11}C labelled acetic acid, oxidative metabolism	–	–	–

- **Ideal Radiotracer**

Of critical importance, the ideal quantitative MPI agent should have a quantifiable concentration that increases linearly with coronary flow over a large range of flow values. Ideally, the tracer should have a high first-pass extraction without significant recirculation. Of note, for most clinically used radiotracers with increasing coronary flow levels, a competitive back diffusion into blood can be observed after the myocardial tracer uptake or the uptake mechanism of tracer becomes saturated. These mechanisms can result in a progressive decline in myocardial extraction and retention at higher flow rates (roll-off phenomenon; Figure). The ideal tracer should show minimal roll-off phenomenon at higher stress-induced flows. The tracer kinetics ideally are not affected by changes in metabolism or type of pharmacological stress, and the agent should demonstrate rapid clearance from the blood pool. The ideal tracer has low extra-cardiac uptake (especially liver and lung uptake, given their relative proximity to the heart). Last but not the least, the ideal perfusion agent should be safe without significant side effects, stable, and easy to produce at low cost.

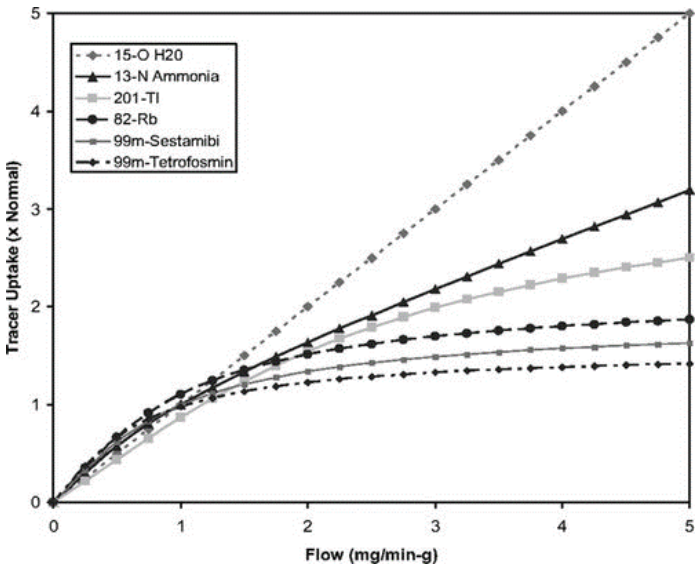
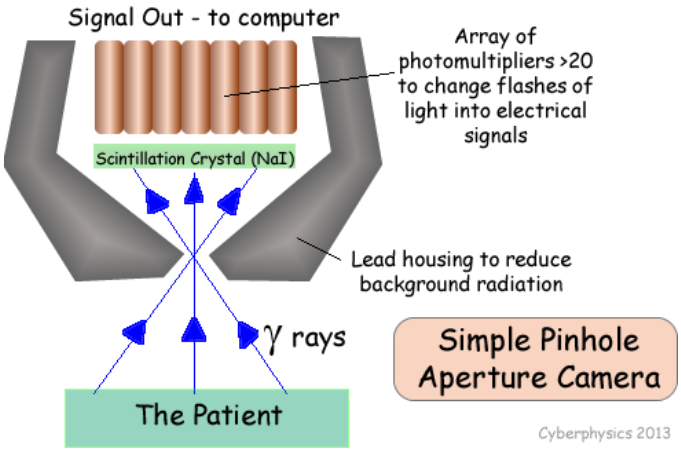


Figure. *Relationship between myocardial blood flow and tracer uptake for common SPECT and PET radiotracers demonstrates a roll-off phenomenon at high flow rates because uptake of some radiotracers becomes diffusion limited at higher flows. This results in reduced accuracy in the quantification of hyperemic coronary flow and coronary flow reserve (CFR).*

THE GAMMA CAMERA



The gamma camera is a specialised device that is used to detect and produce images from the gamma-rays emitted from a patient who received unstable atoms (Radioisotopes). The device is based on the photoelectric effect.

Unstable atoms (Radioisotopes) are introduced into the patient → emits ionising radiation (gamma-rays) → pass through holes in a **lead collimator** that is used to direct rays from a point on the patient towards a single point on a sodium iodide crystal (the **scintillation crystal**) where their energy is converted to a small flash of light → The light is detected by an array of **photomultiplier tubes** → create measurable electrical pulses → This enables a computer to build up an image showing the distribution of radioisotope within a patient.

Gamma cameras only acquire one, or sometimes two, planar images at one time, but by rotating the camera around the patient and acquiring a series of images from many directions, it is possible to generate a 3-dimensional tomographic image. This technique, called Single Photon Emission Tomography (SPECT), is commonly used in nuclear cardiology to produce cross sectional images of perfusion to the myocardium.

Three types of gamma camera exist.

1. **Single-crystal camera** consists of one large sodium iodide crystal. Other essential elements of this camera include the collimator, a lead device that screens out background or scattered photons, and the photomultiplier, an electronic processor that translates photon interactions with the crystal into electric energy.
   - Electric signals from the photomultiplier are processed by the pulse height analyser before reaching a final form. Only signals in a specified energy range are incorporated into the interpreted images. The range recognized by the pulse height analyser is adjustable and is established on the basis of the radiopharmaceutical used.
   - Digitalization of the single-crystal camera has greatly enhanced its performance.
2. **Multicrystal camera** works with an array of crystals with increased count detection capability. Because of the availability of an individual crystal to detect scintillation at any given time, this type of camera can be used to detect many more counts than can a single-crystal camera.
3. **Positron camera** (PET) is a gamma camera used to detect the photon products of positron annihilation. Interaction between a positron and an electron causes annihilation, with the generation of two high-energy photons (511 keV) that travel in opposite directions.
   - An array of multiple concentric rings of crystals constitute a positron camera. Each crystal is linked optically to multiple photomultipliers. The crystals are oriented in diametric pairs in such a way that each pair of crystals must be struck simultaneously by annihilation photons to record activity. Background interference and stray photon energy are automatically accounted for, and artifact is limited.
   - Most positron cameras contain bismuth germanate for annihilation photon detection.

PLANAR AND SPECT IMAGING

Basic perfusion imaging can be performed by means of planar and tomographic techniques. The tomographic, or SPECT, method is the most commonly used today.

Planar Imaging

Gamma cameras have one, or sometimes two, detectors allowing them to produce images of radiopharmaceutical distribution viewed from just one, or two, particular directions. These are called planar images.
Planar images are acquired in three views: (1) anterior, (2) left anterior oblique (LAO), and (3) steep LAO or left lateral (LLAT) orientation. The patient is supine for anterior and LAO views but is placed in the lateral decubitus position for LLAT image acquisition. Although it allows examination of specific myocardial segments, planar imaging superimposes vascular distributions and therefore can compromise the ability to implicate a specific vascular supply when a defect is present. For example, normally perfused myocardial segments may overlap perfusion defects in a separate distribution.
Planar images may be static (showing a fixed distribution of radiopharmaceutical), dynamic (showing how the distribution changes with time) or ECG gated (showing how the distribution changes during each heart beat). In nuclear cardiology rapid dynamic images can be used to observe the passage of a bolus of radiopharmaceutical through the heart in a first pass study. Gated images of a pharmaceutical that remains in the blood can be used to measure cardiac ejection fraction.

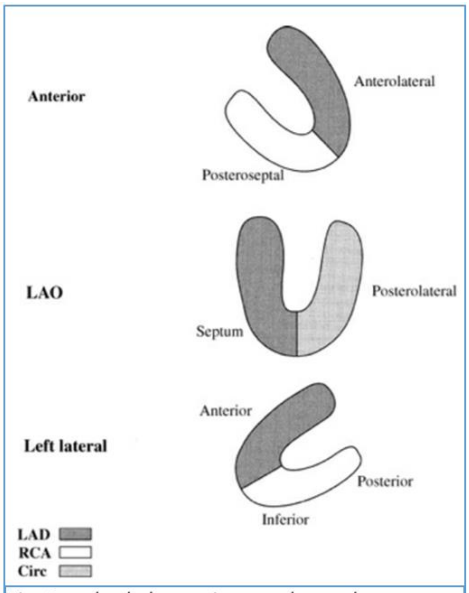


Fig. Standard planar views and vascular territories. Circ: circumflex artery; LAO, left anterior oblique; LAD: left anterior descending artery; RCA: right coronary artery.

SPECT Imaging

The gamma camera can be used to assess myocardial perfusion by imaging the distribution of a radiopharmaceutical such as tetrofosmin or sestamibi that is fixed in the heart muscle in proportion to local blood flow. However, planar images are difficult to interpret because of overlap between anterior and inferior walls of the heart. By rotating the camera around the patient and acquiring a series of planar images are usually obtained over a 180° arc, a computer can be used to reconstruct a 3-dimensional tomographic image of the myocardium. This technique is called Single Photon Emission Tomography (SPECT) and it makes it much easier to detect areas of reduced perfusion without interference from the other wall. The arc typically extends from the 45° right anterior oblique plane to the 45° left posterior oblique plane, with the patient in the supine position.

1) Three orientations are analysed in the final representation: short axis, vertical long axis, and horizontal long axis.

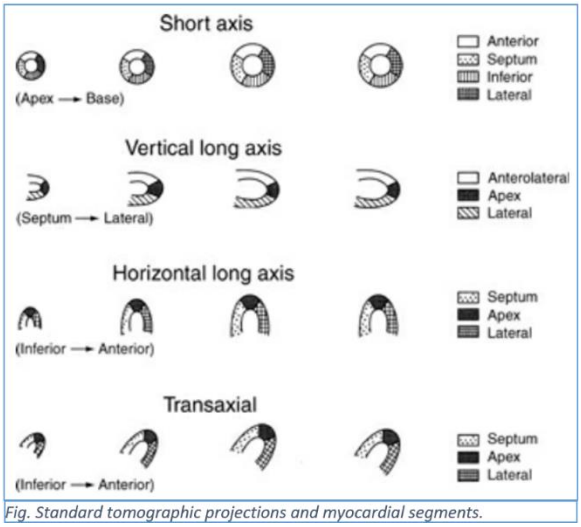
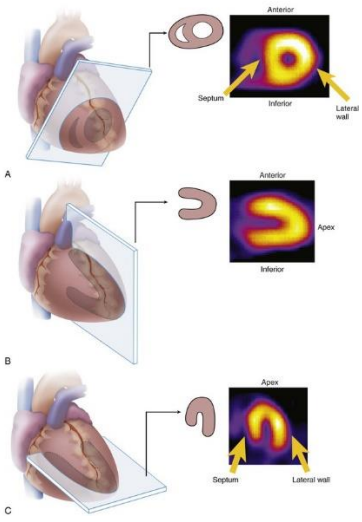
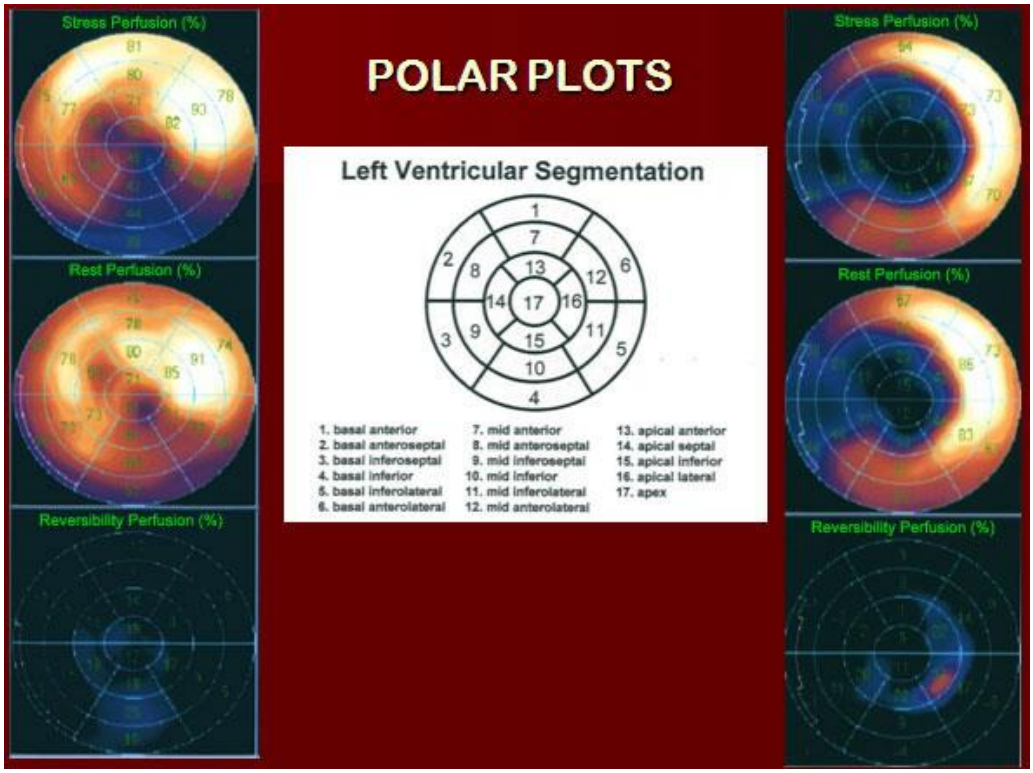


Fig. Standard tomographic projections and myocardial segments.



2) A computer-generated display, the polar map, is also analysed as a quantifiable representation of count density. Unlike planar imaging, SPECT can be used to separate vascular territories (detect areas of reduced perfusion without interference from the other wall) and improve image interpretation.



3) If ECG gating is also used, then gated SPECT images can show how the heart wall moves during the cardiac cycle and also be used to calculate left ventricular ejection fraction. SPECT, however, also increases the time needed for image acquisition and requires close attention to quality control issues.

RNV (ERNV vs. FPRNV)

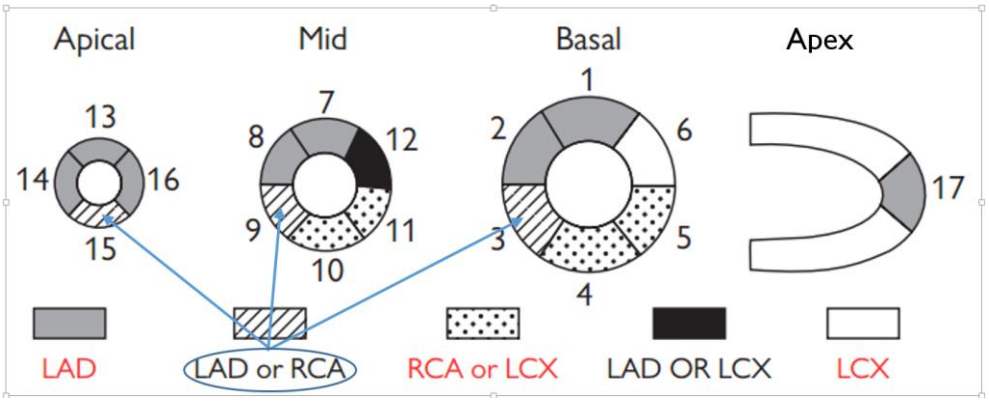
Radionuclide Ventriculography (RNV) is a nuclear cardiology imaging technique used to assess the heart's ventricular function and ejection fraction. In RNV, a radiotracer, typically technetium-99m (Tc-99m) labelled red blood cells, is injected intravenously. Images are acquired using a gamma camera to track the distribution of the radiotracer within the heart's chambers.

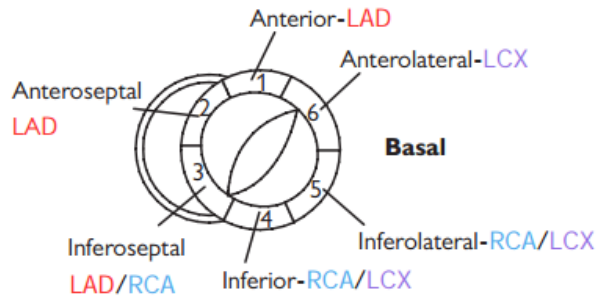
1. **Equilibrium Radionuclide Ventriculography (ERNV)** refers to the technique where the radiotracer reaches equilibrium within the ventricle before imaging. ERNV provides information about the heart's ejection fraction and ventricular function under resting conditions.
1. **First-Pass Radionuclide Ventriculography (FPRNV)**, on the other hand, is a technique used to assess cardiac output and haemodynamics. It involves the intravenous injection of a radiotracer, often technetium-99m (Tc-99m) labelled albumin or macro-aggregated albumin. The radiotracer is injected as a bolus, and a gamma camera is positioned over the heart to capture the first-pass transit of the radiotracer through the heart's chambers. FPRNV provides information about cardiac output, stroke volume, and hemodynamic parameters by tracking the radiotracer's passage through the heart during its first circulation. It is used to assess resting cardiac function and can be valuable in diagnosing conditions like valvular heart disease or congenital heart defects.

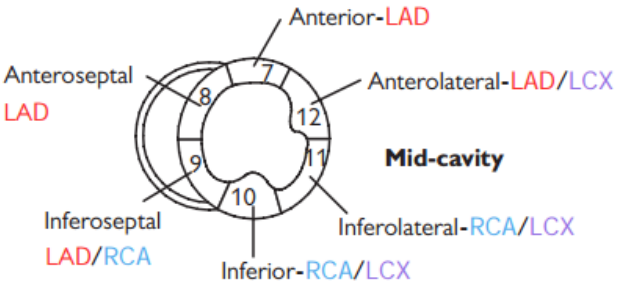
In summary, the key difference lies in the focus and purpose of these techniques. ERNV assesses ventricular function and ejection fraction under resting conditions, while FPRNV is used to evaluate cardiac output and haemodynamics by tracking the first-pass transit of a radiotracer through the heart. Both techniques play distinct roles in assessing different aspects of cardiac function.

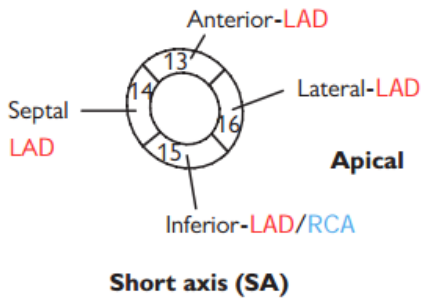
CORONARY TERRITORIES

	Anterior	Anteroseptal	Septal	Inferoseptal	Inferior	Inferolateral	Lateral	Anterolateral
Basal	LAD	LAD		LAD/RCA	Dominant (RCA/LCX)	Dominant (RCA/LCX)		LCX
Mid	LAD	LAD		LAD/RCA	Dominant (RCA/LCX)	Dominant (RCA/LCX)		LAD/LCX
Apical	LAD		LAD		LAD/RCA		LAD	
Apex	LAD							

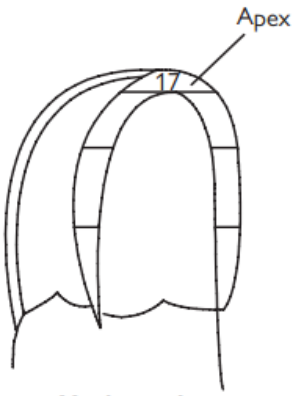




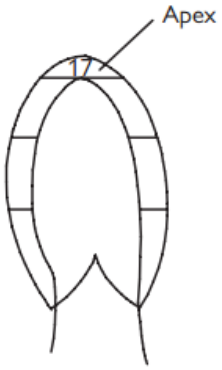




Short axis (SA)



Horizontal long axis (HLA) (4 Chamber)



Vertical long axis (VLA) (2 Chamber)

STRESS TESTING

Dynamic

Dynamic exercise is the modality of choice in myocardial perfusion imaging as image quality is usually superior and addition information is acquired about the patient general fitness. The two common forms of exercise are treadmill and bicycle. Patients are advised to stop medication that may interfere with heart rate response during exercise e.g. beta blockers. Treadmill exercise is usually performed using the Bruce protocol where speed and elevation of the treadmill are increased at 3 minute intervals. Bicycle exercise is an alternative. A typical protocol will involve the patient pedalling at a constant 50rpm with the workload increasing in steps of 25W every 3 minutes.
Blood pressure and 12 ECG are monitored during the stress test and in the recovery phase. The aim is to achieve at least 85% of the MAPHR (220 minus patient's age). Although the test may be terminated earlier if there are symptoms or changes in blood pressure / ECG. The possibility to detect exercise induced myocardial ischemia decreases dramatically if the exercise is sub-maximal. The 85% of maximal predicted heart rate level has been established as the lower acceptable limit for a maximal exercise test. The radioisotope is injected at peak stress and exercise is carried on for at least another 1 minute post tracer injection. Dynamic exercise should not be performed in patients who cannot achieve an adequate haemodynamic response because of non-cardiac limitations including lung diseases, peripheral vascular disease, musculoskeletal diseases, neurological diseases or poor motivation. These patients should undergo pharmacological stress perfusion testing.

Vasodilator

When the patient is unable to perform dynamic exercise, vasodilators are the pharmacological agent of choice. It causes flow heterogeneity between areas with normal blood supply and that of stenosis. Rarely, it may induce ischaemia due to steal phenomena. Vasodilator stress is also preferred in patients with un-interpretable ECG e.g. left bundle branch block or cardiac pacemaker. Patients need to be caffeine-free for at least 24 hours prior to vasodilator stress.
The vasodilators commonly used are regadenoson, adenosine and dipyridamole, all of which are administered intravenously.

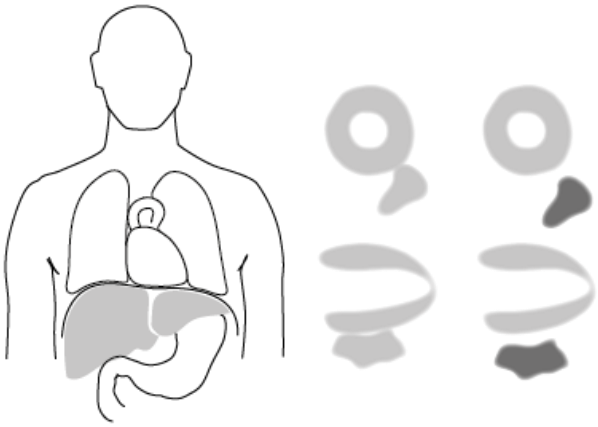
- **Regadenoson** is given as a single IV injection of 400 micrograms in 5mL over at least 10 seconds. This is followed by a 10mL saline flush and injection of the tracer 20 to 30 seconds later. Regadenoson injection can be combined with low-level exercise. This can help improve test tolerability and scan quality. Regadenoson is also commonly used to "rescue" dynamic exercise tests, which would otherwise be suboptimal. Common side effects of regadenoson are breathlessness, abdominal discomfort and headache. They are short-lasting although abdominal symptoms and headache may time up to 30 minutes to resolve completely.
- **Adenosine** is usually given as an infusion over 6 minutes although an abbreviated 5-minute protocol has been found to be equally effective. The tracer is injected between the third and fourth minute, and the infusion is continued for at least a further 2 minutes post-tracer injection. Low level dynamic exercise can be used in conjunction with the adenosine infusion. Common side effects of adenosine are breathlessness, chest discomfort and flushing. These resolve within a few minutes after discontinuation of the infusion, and therefore aminophylline is seldom used to treat adenosine-induced symptoms.
- **Dipyridamole** is given as an infusion over 4 minutes. Three to four minutes after the end of the infusion the radioisotope is given. Low-level exercise can also be used following dipyridamole.
  Dipyridamole side effects are similar to those of adenosine. Side effects are less frequent but tend to last longer and therefore aminophylline is commonly administered after tracer injection to alleviate symptoms.

Inotropic

When the patient is unable to undergo dynamic exercise testing and has a contraindication to vasodilator stress, inotropic stress may be considered. Dobutamine is used as the stress agent the dose is calculated from the patient's weight. Dobutamine is given as an infusion with the infusion rate increasing at 3 minute intervals until target heart rate is achieved. Sometimes atropine is given to augment the effects of the dobutamine. The radioisotope is given when target heart rate is reached. Common side effects of dobutamine are nausea and hypotension.

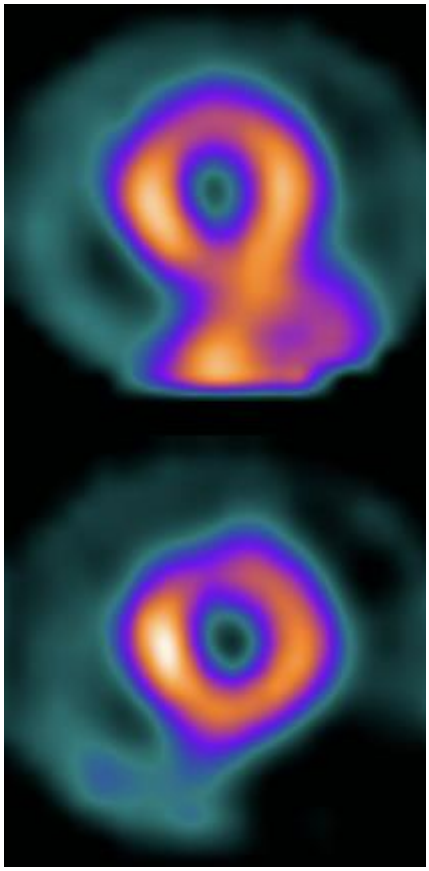
IMAGE QUALITY

Image quality- Extra cardiac uptake



The $99^{m}TC$ - labelled tracers used for myocardial perfusion imaging are cleared by the liver and excreted by the biliary system. Activity in the sub diaphragmatic organs can cause artefacts in the images, both simulating perfusion defects and concealing true defects. The artefacts due to high extra cardiac activity are patient dependent and their impact on the image interpretation is difficult to predict. A repeat acquisition is useful when:

1. The intensity of the extra cardiac uptake is equal to or higher than the cardiac uptake when there is no separation between the extra cardiac uptake and the inferior cardiac wall (left images).
2. When the intensity of the extra cardiac uptake is higher than the cardiac uptake when there is a separation between the extra cardiac uptake and the inferior wall of less than one cardiac wall (right images).



The upper slice shows extra-cardiac activity and the lower slice was obtained after a repeat acquisition.

Image quality- patient motion

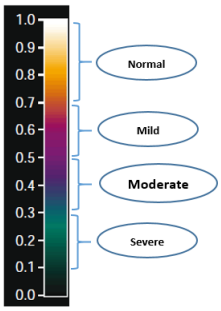
Patient motion during the acquisition may cause clinically significant artefacts in the slice images. Abrupt patient motion in the axial direction increases the risk of artefact compared to gradual motion and movement in the lateral direction. Motion correction software can be used, but at least in case of large amount of motion, a repeat acquisition is preferred. Raw images should be reviewed in cine mode to assess for patient motion directly after acquisition. No patient motion or patient movement less than one pixel rarely causes a clinically significant artefact.

INTERPRETATION OF REGIONAL MYOCARDIAL PERFUSION

All images should be interpreted from the workstation view screen with careful inspection of the raw data to assess quality before reviewing the reconstructed slices. Planar acquisition has mostly been taken over by SPECT, which allows left ventricular myocardial perfusion to be viewed as sets of orthogonal slices. SPECT provides information about relative myocardial perfusion. A 9, 17 or 20 segment grid is superimposed on a polar plot (reconstructed from short axis slices summarizing the SPECT acquisition data). If ECG gating is also used, then gated SPECT images can show how the heart wall moves during the cardiac cycle and also be used to calculate left ventricular ejection fraction. Myocardial perfusion abnormalities should be assessed in terms of the extent, severity, and reversibility (by comparing stress and rest images), incorporating data from gated images when available.

Semi-quantitative scoring of defect **severity** (BNCS website)

Score	Category	Tracer uptake (count density)
0	Normal	≥70% Yellow
1	Mild Reduction	50–69% Red
2	Moderate Reduction	30–49% Blue
3	Severe Reduction	10–29% Green
4	Absent count	<10% Black



Semi-quantitation of defect **extent**, expressed as percentage of the overall left ventricular myocardium (BNCS website)

Extent	% of Myocardium	Segments affected (of 17)	
Small	5-10%	1-2	The extent of a perfusion abnormality should not only be classified as small, intermediate or large. Quantitative data should be added. In 2014 ESC/EACTS Guidelines on myocardial revascularization, a large area of ischaemia (>10% LV) in patients with stable angina or silent ischaemia is an indication for revascularization.
Medium	10-20%	2-3	
Large	15-20%	2-3	

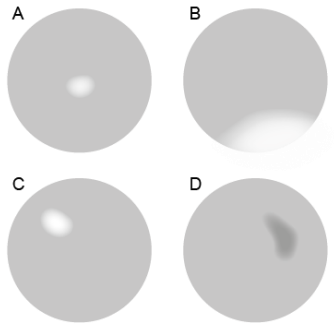
Reversibility: fixed / partial reversibility / complete reversibility

- Fixed defects (minimal counts at stress and rest) suggest scar
- Reversible defects show improvement in counts at rest, suggest inducible ischaemia and therefore significant coronary stenosis

For quantitative analysis, data can be compared to a database with a low pre-test-probability of coronary disease

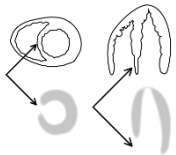
Normal myocardial perfusion

- Normal myocardial perfusion appears as a homogeneous or close to homogeneous uptake of the left ventricle, in both stress and rest images.
- The septal wall is shorter due to the membranous part of basal septum.
- Lower activity can also be seen in the apical part (A) Known as apical thinning.
- A decreased activity due to attenuation can be seen in the inferior wall (B) and in the anterior wall (C) due to breast attenuation in women.
- The lateral wall shows the highest activity (D) at least partly because of the insertion of the papillary muscle.
- If a stress study is performed first and the images show a normal myocardial perfusion, the rest study is not needed to differentiate between ischemia and infarction and can therefore be avoided.

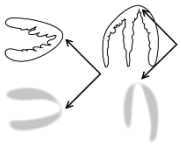


Perfusion- Septum membranaceum

The septal wall of the left ventricle appears shorter than the anterior, lateral and interior walls in myocardial perfusion image. Is this normal finding is caused by the membranous part of basal septum.



Perfusion- Apical thinning



Low counts in the apical region is known as “apical thinning”. The appearance is caused by reduced myocardial thickness at the apex of the left ventricle and the relation between myocardial count and thickness due to the partial volume effect. This normal finding is more common in attenuation corrected images.

Perfusion- Apical stress defect

An area with reduced uptake in apex in the stress images. Apical thinning should also be considered as an explanation for the finding, especially if the reduction is mild. A comparison with the rest images is necessary for the differentiation between ischemia and infarction. The extent of the stress defect should be described in the report in a quantitative way or as small (<10%), medium sized (10-20%) or large (>20%). A stress defect in the apical region is in the majority of cases due to stenosis of the left anterior descending artery especially if the defect also includes parts of the antero-apical wall.

Perfusion- Apical fix defect

An area with reduced uptake in both the stress and rest images in apex. Small differences in the extent or severity can be explained by normal variability in the imaging procedure, but no distinct part of the defect should show clear improvement between stress and rest. The extent of the fixed area should be described in the report in a quantitative way or as small (<10%), medium sized (10-20%) or large (>20%). A fixed defect in the apical region is likely due to a myocardial infarction in the territory of the left anterior descending artery, especially if the defect also includes parts of the antero-apical wall. Figure shows stress images above corresponding rest images.

Perfusion- Apical reversible defect

An area with reduced uptake in the stress images combined with normal or nearly normal uptake in the rest images in apex. The extent of the reversible area should be described in the report in a quantitative way or as small (<10%), medium sized (10 - 20%) or large (>20%). A reversible defect in the apical region is likely due to stenosis of the left anterior descending artery, especially if the defect also includes parts of the antero-apical wall. Figure shows stress images above corresponding rest images.

Perfusion- Inferior fixed defect

An area with reduced uptake in both the stress and rest images in the inferior wall. Small differences in the extent or severity can be explained by normal variability in the imaging procedure, but no distinct part of the defect should show clear improvement between stress and rest. The extent of the fixed area should be described in the report and quantitative way or as small (<10%), medium sized (10 - 20%) or large (>20%). A fixed defect in the inferior wall is likely due to a myocardial infarction in the territory of the right coronary artery. Figure shows stress images above corresponding rest images.

Perfusion- Inferior reversible defect

An area with reduced uptake in the stress images combined with normal or nearly normal uptake in the rest images in the inferior wall. The extent of the reversible area should be described in the report in a quantitative way or as small (<10%), medium sized (10-20%) or large (>20%). A reversible defect in the inferior wall is likely due to stenosis of the right coronary artery. Figure shows stress images above corresponding rest images.

Perfusion- Anterior fixed defect

An area with reduced uptake in both the stress and rest images in the anterior wall. Small differences in the extent or severity can be explained by normal variability in the imaging procedure, but no distinct part of the defect should show clear improvement between stress and rest. The extent of the fixed area should be described in the report in a quantitative way or as small (<10%), medium sized (10-20%) or large (>20%). A fixed defect in the anterior or antero-apical region is likely due to a myocardial infarction in the territory of the left anterior descending artery. Figure shows stress images above corresponding rest images.

Perfusion- Anterior reversible defect

An area with reduced uptake in the stress images combined with normal or nearly normal uptake in the rest images in the anterior wall. The extent of the reversible area should be described in the report in a quantitative way or as small (<10%), medium sized (10-20%) or large (>20%). A reversible defect in the anterior or antero-apical region is likely due to stenosis of the left anterior descending artery. Figure shows stress images above corresponding rest images.

Perfusion- Lateral fixed defect

An area with reduced uptake in both the stress and rest images in the lateral wall. Small differences in the extent or severity can be explained by normal variability in the imaging procedure, but no distinct part of the defect should show clear improvement between stress and rest. The extent of the fixed area should be described in the report in a quantitative way or as small (<10%), medium sized (10-20%) or large (>20%). A fixed defect in the lateral wall is likely due to a myocardial infarction in the territory of the left circumflex artery. Figure shows stress images above corresponding rest images.

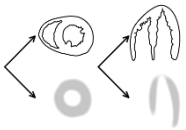
Perfusion- Lateral reversible defect

An area with reduced uptake in the stress images combined with normal or nearly normal uptake in the rest images in the lateral wall. The extent of the reversible area should be described in the report in a quantitative way or as small (<10%), medium sized (10-20%) or large (>20%). A reversible defect in the lateral wall is likely due to stenosis of the left circumflex artery. Figure shows stress images above corresponding rest images.

Perfusion- Septal reversible defect

An area with reduced uptake in the stress images combined with normal or nearly normal uptake in the rest images in the septal wall. The extent of the reversible area should be described in the report in a quantitative way or as small (<10%), medium sized (10-20%) or large (>20%). A reversible defect in the septal wall is in the majority of cases due to stenosis of the left anterior descending artery. Figure shows stress images above corresponding rest images.

Perfusion- Right Ventricle



The right ventricular wall is thinner than the left ventricular wall and it is therefore difficult to visualize. In patients with right ventricular hypertrophy, the right ventricle appears more prominent.

Artefacts

Types of artifacts

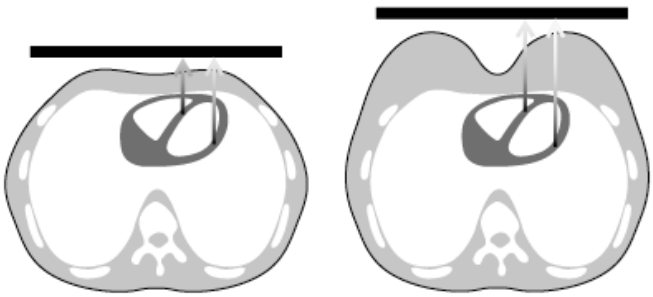
- Patient related artefacts
  - Movement during image acquisition
  - Anterior attenuation due to breast tissue (mostly women)
  - Inferior attenuation due to elevated diaphragm in obese patients in horizontal position (mostly men)
  - Attenuation by non-anatomical structures (breast implants, pacemaker/ICD)
  - Cardiac variants (short septum, apical thinning)
- ECG-related artefacts
  - Significant variation in RR-interval (frequent ectopy, atrial fibrillation)
  - LBBB/RV pacing: septal relaxation becomes increasingly dyssynchronous as the heart rate increases which in turn reduces septal perfusion relative to other walls.
- Artefacts in DCM
  - Often present with LBBB
  - Due to LV dilation there is increased inferior attenuation
  - Patchy myocardial fibrosis with fixed defects

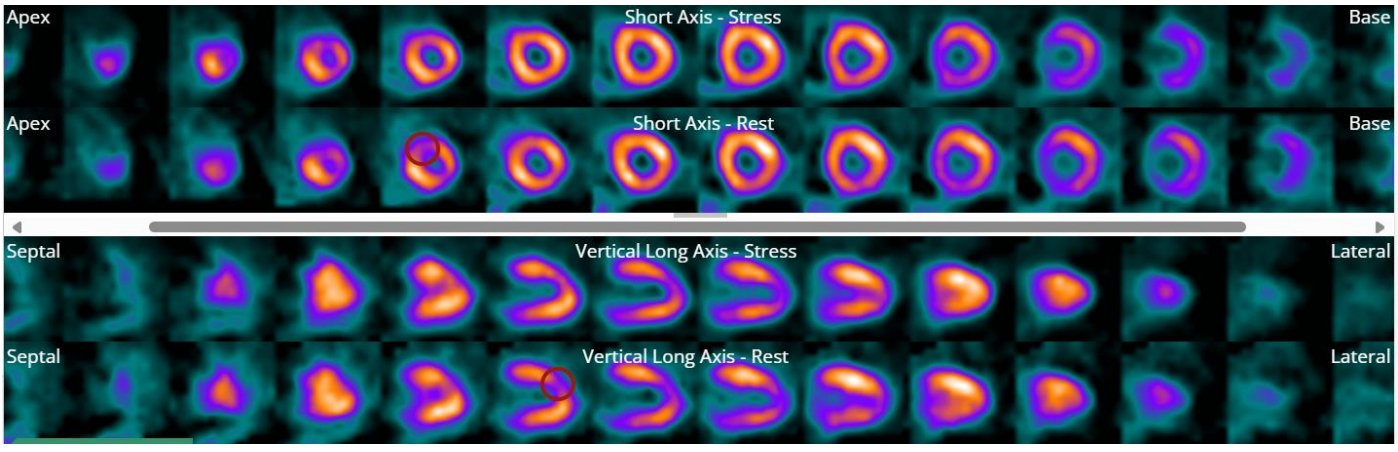
Attenuation Artifact

Apical thinning and short septal wall due to septum membranaceum appear in both the rest and stress images. Another finding that may be confused with true perfusion abnormalities is attenuation artifacts. Photons are attenuated in tissues and fluids (blood) between the myocardium and the detector, resulting in lower activity in the SPECT images. The distance from the inferior wall to the detector is longer than the corresponding distance from the anterior wall. Therefore the inferior wall may falsely appear as having reduced perfusion compared to the anterior wall. Dense breasts can cause attenuation artifacts in the anterior wall. Attenuation artefacts can appear very differently in different patients, but is not influenced by type of study or stress method. Therefore attenuation artefacts makes the interpretation of infarction more difficult, but less so for the assessment of ischemia.

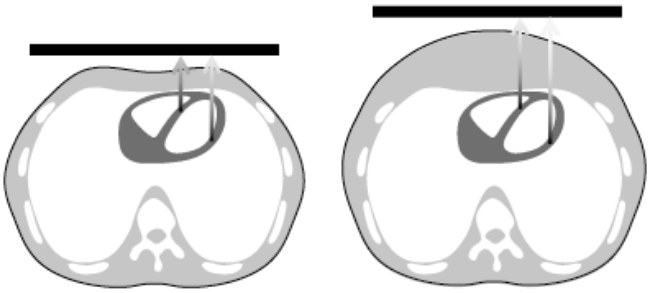
Attenuation artifact breast:

Attenuation of photons in tissues between the myocardium and the detector may cause artefacts that may be confused with true perfusion abnormalities. In women, the left breast may cause an artefact appearing as reduced profusion in the anterior wall in both stress and rest images. The artifact is dependent on the size, position and density of the breast. If gated images show normal wall motion and wall thickening in the same area, attenuation artifact rather than myocardial scaring is most likely.





Attenuation artifact inferior:



Attenuation of photons in tissue and fluids (blood) between the myocardium and the detector may be confused with true perfusion abnormalities. The artifact is dependent on the depth of the myocardium, related to the overall size of the patient and the densities of the tissues, and therefore it varies from patient to patient. The distance from the Antero-septal wall to the detector (left arrows) is shorter than the corresponding distance from the inferior wall (right arrows). Therefore, an artifact can appear as reduced profusion in the inferior wall in both stress and rest images. If gated images show normal wall motion and wall thickening in the same area, attenuation artifact rather than myocardial scaring is most likely.

Conditions associated with pitfalls in interpretation

- LV hypertrophy, HCM, congenital heart disease
- Balanced multi-vessel disease (seen in diabetics, elderly, previously documented severe three-vessel-disease)
    - MPS assesses relative myocardial perfusion, count density is colour-coded and areas of low count density (abnormal) are compared to areas with high density (normal)
    - In significant stenoses of all coronary arteries, valid determination of regional ischaemia becomes difficult
    - Potentially significant stenoses might therefore be underestimated
    - TID is a prognostic discriminator and sometimes can be the only sign of balanced multi-vessel ischaemia

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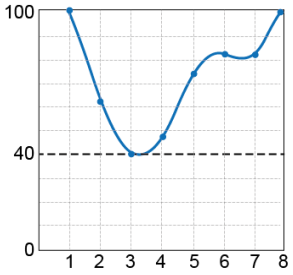
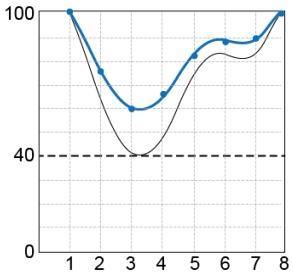
LV FUNCTION

Function - Normal global systolic function.



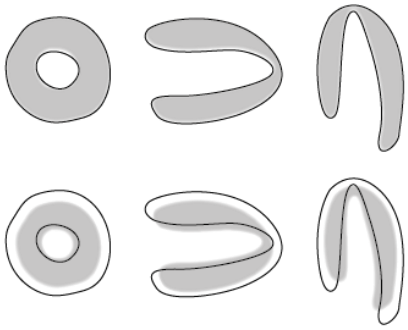
A quantitative analysis of the global left ventricular function showing normal ejection fraction (EF> 60% for women and > 55% for men) and normal end diastolic volume (EDV< 135 ml for women and < 180 ml for men). Note that an abnormal regional function (reduced wall motion an thickening) can be found despite normal EF & EDV. Note that separate criteria for abnormal EF & EDV need to be used depending on the software package used. Figure shows a normal left ventricular volume/ time (frame) curve.

Function- Reduced global systolic function



A quantitative analysis of the global left ventricular function showing reduced ejection fraction (EF<60% for women and <55% for men) or increased end-diastolic volume (EDV>135 ml for women and >180 ml for men). Figure shows a normal left ventricular volume/time (frame) curve in black and the corresponding curve from a patient with reduced systolic function in blue.

Function- Normal wall motion

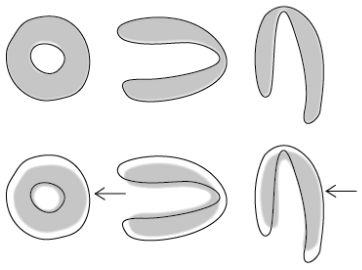


Regional function is evaluated as wall motion and wall thickening either by visually reviewing the cine-mode of gated images or by quantitative analysis using a software package.

Wall motion is measured as the distance between a given endocardial point at end-diastole and end-systole, perpendicular to the myocardial surface. A linear colour scale without computer-derived edges is the best display for evaluation of regional function. There is a normal variation between ventricular walls with less motion in the septal region compared to the lateral region, but no significant difference between basal and apical regions. Figure shows end-diastolic images above corresponding end-systolic images. The end-diastolic outline is superimposed on the end systolic images.

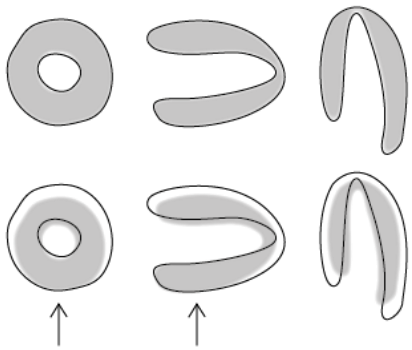
Wall thickening is measured as the increase in counts per pixel between diastole and systole and is best visualised in a linear color scale without computer-derived edges. There is a normal variation between ventricular walls with a substantial apex to base decrease in wall thickening, but no significant difference between septal, lateral, anterior or inferior regions. Normal wall thickening and motion in an area with a fixed defect should most likely be interpreted as an attenuation artifact and not a myocardial infarction. Figure shows end-diastolic images above corresponding end-systolic images.

Function - hypokinetic wall



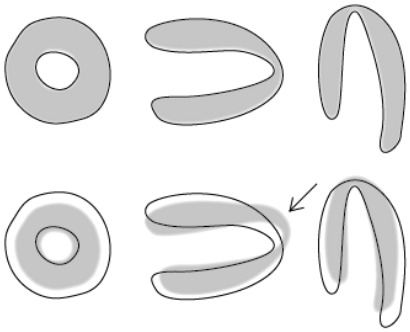
Reduced wall motion indicates regional dysfunction as a result of myocardial infarction or severe myocardial ischaemia caused by coronary artery disease. Wall motion is assessed either by visually reviewing the cine- mode of gated images or by quantitative analysis using a software package. Wall motion is measured as the distance between a given endocardial point at end-diastole and end-systole, perpendicular to the myocardial service. A linear colour scale without computer- derived edges is the best display for evaluation of regional function. Abnormal wall motion in apparently fixed perfusion defects may help in the discrimination of infarction from attenuation artefact. Figure shows end-diastolic images above corresponding end-systolic images. The end-diastolic outline is superimposed on the end-systolic images. The lateral wall in the figure is hypokinetic (arrows).

Function- Akinetic wall



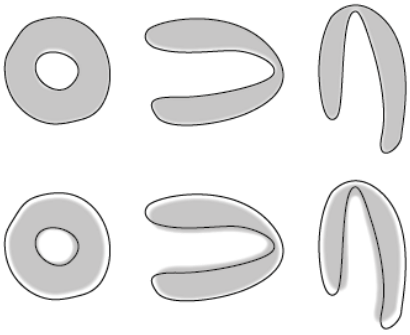
Absent wall motion indicate regional dysfunction as a result of myocardial infarction or severe myocardial ischemia caused by coronary artery disease. Wall motion is assessed either by visually reviewing the cine-mode of gated images or by quantitative analysis using a software package. Wall motion is measured as the distance between a given endocardial point at end-diastole and end-systole, perpendicular to the myocardial surface. A linear colour scale without computer-derived edges is the best display for evaluation of regional function. Abnormal wall motion in apparently fixed perfusion defects may help in the discrimination of infarction from attenuation artefact. Figure shows end-diastolic images above corresponding end-systolic images. The end-diastolic outline is superimposed on the end systolic images. The inferior wall in the figure is akinetic (arrows).

Function- Dyskinetic wall



Dyskinetic or paradoxical wall motion indicate regional dysfunction as a result of myocardial infarction or severe coronary artery disease. Wall motion is assessed either by visually reviewing the cine-mode of gated images or by quantitative analysis using a software package. Wall motion is measured as the distance between a given endocardial point at end-diastole and end-systole, perpendicular to the myocardial surface. A linear colour scale without computer-derived edges is the best display for evaluation of regional function. Figure shows end-diastolic images above corresponding end-systolic images. The end-diastolic outline is superimposed on the end systolic images. The antero-apical wall in the figure is dyskinetic (arrows).

Function- Transient ischemic dilation



Transient ischemic dilation (TID) of the left ventricle is present if the left ventricle appears larger in the stress image than in the rest image. The ratio between the left ventricular volume at stress and rest is normally close to 1.0. A TID value greater than approximately 1.2 indicates a dilation due to ischemia during the stress procedure. TID is a marker for severe and extensive coronary artery disease. The exact cut off value varies with different protocols. Abnormal TID is a more specific marker when using exercise stress protocol compared to pharmacological stress. Figure shows stress images above corresponding rest images. The outline of the left ventricle at stress is superimposed on the rest images to show the size difference.

Indirect Markers of Severe CAD

- Exercise-induced increase in Tl-201 uptake in the lungs due to chronically increased left atrial pressure following left ventricular dysfunction
- Transient ischaemic dilatation (TID), i.e. larger left ventricle on stress compared to rest (possible explanations include stunning, following vasodilator stress without true ischaemia, diffuse subendocardial ischaemia with false appearance of chamber dilatation). In the presence of perfusion defects TID predicts severe CAD and a high risk of cardiac events
- Reversible LV impairment after stress with a decrease in EF of more than 5 % may indicate severe CAD

REPORTING

Summary of recommendations for reporting

1. Patient details: Name, age, gender, hospital identification number and date(s) of study
2. Indication(s) for study: Relevant data from medical history
3. Stress technique:
    - Stress protocol: exercise type and maximal load and/or pharmacological stress agent and infused amount
    - Response to stress: heart rate, systolic blood pressure, ECG changes, symptoms and adverse events (duration and intervention done)
4. Tracer and imaging protocol: Imaging protocol, including radiopharmaceutical and injected activities
5. Findings:
    - Suboptimal image quality, significant artefact is present, if relevant
    - Myocardial perfusion: presence, extent and depth of stress and rest defect(s), incl. information from gated images.
    - LV function: global and regional function, possible stress-induced abnormalities
    - Pathology outside left ventricle: right ventricular visualisation, lung uptake, extracardiac focal accumulation
6. Conclusions
    - LV perfusion: inducible ischaemia (reversible perfusion defect); myocardial infarction (irreversible or permanent perfusion defect)
    - LV function: global and regional function, possible stress-induced abnormalities
    - Inconclusive study—may occasionally be the correct conclusion
    - Correlation with and deviations from clinical information and other data if available. If clinically relevant: myocardial viability (hibernation, stunning), prognosis/risk assessment

CLINICAL APPLICATIONS OF NUCLEAR CARDIOLOGY

Myocardial perfusion scanning (MPS)

- Myocardial perfusion scanning (MPS) is a commonly used test to assess myocardial ischaemia and viability
- Stress testing in MPS can be performed either physically (i.e. treadmill/bicycle) or pharmacologically (Adenosine, Dipyridamole or Dobutamine)

A normal myocardial perfusion scintigram does not exclude coronary artery disease, but indicates a low likelihood of symptomatic or prognostically significant coronary artery disease. Furthermore patients with a normal scintigram have showed a rate of cardiac death or myocardial infarction of 0.7% per year, a rate similar to that of an asymptomatic population. Because of its prognostic power, myocardial perfusion scintigraphy is used as a gatekeeper to coronary angiography. A reversible perfusion abnormality on the other hand indicates impaired perfusion, which in turn corresponds to coronary artery disease.

Assessment in suspected CAD

- Perfusion defects can be attributed to specific myocardial territories
- The sensitivities to detect single and multi-vessel disease are high
- In patients with low risk clinical features the absence of inducible ischaemia predicts a low risk - <1% annual cardiac event rate; by comparison ETT is a poor discriminator
- Higher risk patients unable to exercise undergoing pharmacological stress still have a low cardiac event rate if the MPS is normal

Assessment of acute chest pain

- Perfusion defects are detectable until several hours following the resolution of CP
- Imaging can be delayed without redistribution (using Tc-99m tracers)
- Patients with normal resting MPS can be safely discharged (negative predictive value for ACS >99%)
- Resting SPECT has similar sensitivity to serial Troponin testing, but is superior to initial Troponin alone
- Patients with abnormal resting MPS need further invasive investigation
- Patients with normal MPS have a rate < 1% of developing MI within the next 30 days
- Patients with an abnormal MPS have a rate of 10% of developing MI within 30 days

Assessment in known CAD

- MPS is more precise in localising a significant stenosis in coronary arteries than the pattern of ST-depression in ETT
- Perfusion defects can help make a decision given any number of angiographic stenoses to target for revascularization
- A normal MPS in patients with known CAD is associated with a low risk for adverse cardiac events
- MPS is of prognostic significance in terms of revascularization if inducible ischaemia of more than 10% of the left ventricular myocardium is present
- Inducible ischaemia of less than 10% of the left ventricular myocardium should be treated medically, as this management is associated with a lower cardiac event rate

Prognostic value in patients with chest pain

- MPS delivers additional information towards risk stratification in patients with known or suspected CAD
- The major cardiac event rate in patients with chest pain and normal MPS is less than 1% per year (comparable to asymptomatic population)
- The major cardiac event rate in patients with chest pain and abnormal MPS is about 7.4% per year

Pre-Operative Risk Assessment

- Aging population are undergoing even more complex surgery
- Non-cardiac surgery: absence of inducible ischaemia predicts low risk of postoperative cardiac death or non-fatal myocardial infarction
- NPV of a normal study is very good, however the PPV of an abnormal study is <10%
- Current guidelines essentially only recommend MPS for high risk aortic and vascular surgery patients

MPS in Patients Before/After Revascularization

- High sensitivity and specificity to detect significant coronary stenosis after revascularization
- Identification of hibernating myocardium which is dysfunctional but retains the potential to recover following revascularization
- Assessment of functional significance of anatomical stenosis and need for revascularisation also after angiography
- Perfusion defects due to microvascular dysfunction after successful PCI are common but do not represent inducible ischaemia; therefore assessment for ischaemia early after PCI (2 months) should not be done via MPS

MPS in patients with diabetes

- MPS is a good alternative to ETT in diabetic patients who are frequently impaired in their exercise capacity due to raised BMI, polyneuropathy and claudication
- The major adverse cardiac event rate in diabetic patients with normal MPS is <3%, and 27% with abnormal MPS
- MPS delivers additional information for risk stratification over clinical data
- Any given perfusion deficit in a diabetic is associated with a higher risk compared to the non-diabetic population
- Any given perfusion deficit in a type I diabetic is associated with a higher risk compared to a type II diabetic

MPS in elderly patients

- Pharmacological MPS has been shown to be safe and feasible in elderly patients (>65 years) whose exercise capacity is often reduced
- A combination of pharmacological & dynamic stress often helps to improve image quality and overall diagnostic accuracy

MPS in women

- High proportion of false positive ETT
    - often atypical symptoms
    - lower pre-test-probability of IHD
    - lower exercise capacity
    - less specific ST-changes
- Prognostic value and cost effectiveness of MPS in women as good as in men
- Gated SPECT in particular very useful at distinguishing artefacts from genuine defects. In general, normal wall thickening and motion in an area with a fixed defect should most likely be interpreted as an attenuation artifact and not a myocardial infarction.

VIABILITY/HIBERNATION

Definition:
"Assessment of myocardial viability is defined as relatively preserved perfusion ≥50% of normal tracer uptake, or reversible inducible ischaemia in a **dysfunctional segment**"

Viability assessment in patients with severely impaired LV systolic function and CAD helps planning for revascularisation.

Role of MPS in the interpretation of LV dysfunction:

- Intact micro-circulation and myocardial cells take up tracer
- Allows for exclusion of significant CAD as underlying cause of LV dysfunction if no perfusion defects
- Assessment of hibernating myocardium (dysfunctional at rest but with tracer uptake and relatively reduced tracer uptake during stress) and the likely value of revascularization in patients with known CAD
- Functional improvement occurred in 80% of those segments after revascularization compared to 30% of segments with viability and dysfunction but without reversibility
- Myocardial segments whose count density is at least 50% of maximal counts are considered to contain sufficient viable myocardium to justify revascularization
- Segments with count density of 30 – 50% are likely to contain a mixture of viable myocardium and scar but functional recovery is unlikely
- A left ventricle, in which 25% or more of the myocardium remains viable, is likely to improve with revascularization.

CARDIAC PET

Cardiac positron emission tomography (Cardiac PET)

- requires intravenous administration of a radionuclide on its own or tagged to a chemical
- the radionuclide used for PET ultimately emit pairs of high energy gamma photons which move in opposite directions which can be imaged using a special equipment (PET camera)
- PET tracers are produced either in a cyclotron or locally with a generator. Cyclotrons are very expensive (both capital and maintenance costs) and hence not every centre with a PET camera can afford it. Longer lived radionuclide like F-18 can be remotely produced and transported to other centres

Cardiac PET has a number of clinical uses including

- identification of coronary artery disease and risk stratification
- in patients who have an equivocal SPECT scan
- currently in clinical practice it is mostly utilised for stress-rest myocardial perfusion imaging using Rubidium-82
- or hibernation imaging using a combination of both 18F-FDG for metabolic viability and Rubidium-82 for perfusion

Rubidium-82 is the most commonly used cardiac PET perfusion tracer

- It decays with a half-life of 75 seconds making stress imaging possible only with pharmacological agents
- Its short half-life means lower radiation (typically 3 mSv) compared to conventional SPECT (range 7 -15 mSv)
- It is delivered via a generator making it available locally and it replenishes activity every 10 minutes to be delivered to the patient
- It requires delivery every 4 weeks and the generator is expensive requiring a reasonably high throughput to justify generator cost

N-13 Ammonia is another perfusion tracer which is cyclotron produced

- It has better tracer kinetics than Rubidium but an on-site cyclotron is necessary, due to its short half-life (10 minutes), hence limiting its use

Another commonly used metabolic imaging tracer is 18F-fluorodeoxyglucose (18F-FDG)

- this analogue combines glucose with the radioisotope Fluorine-18
- it is used principally for myocardial viability imaging
- Optimal uptake of 18F-FDG requires euglycaemia and the presence of insulin, which may require an oral glucose load to be given to the patient to stimulate native insulin production prior to imaging
- Cardiac PET with 18F-FDG is the most sensitive means by which to identify hibernating myocardium. This is myocardium that has the potential for functional recovery if revascularised and is therefore important to distinguish from scar tissue.
  The use of Cardiac PET has been increasing in recent years, particularly in the US and in some selected centres in Europe. There are both advantages and disadvantages of Cardiac PET compared to SPECT.

Advantages of Cardiac PET over SPECT

- higher spatial and contrast resolution
- higher diagnostic accuracy
- lower radiation dose with Rubidium
- exact attenuation and excellent scatter correction
- ability to quantify absolute myocardial blood flow in ml/gm/min
- procedure time of 30-40 minutes with Rubidium 82 tracer
- peak stress wall motion and function assessment
- can be combined with CT imaging to get structural information e.g. coronary calcium scoring
- better in patients who have more soft tissue attenuation; e.g. obese patients

Disadvantages of Cardiac PET

- perfusion imaging almost exclusively with pharmacological stress
- requires expensive equipment (PET camera, generator and cyclotron access)- limited availability