REVIEW ARTICLE

SPECT- Myocardial Perfusion Scintigrapy

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Nuclear imaging of the heart is fast emerging as a valuable and widely used non-invasive procedure, that reveals vital information about cardiac structure, physiology, perfusion and metabolism. Commonly performed nuclear imaging techniques in cardiology are radionuclide ventriculography (RNV) done by labelling autologous red blood cells with Technetium-99m (Tc-99m) and myocardial perfusion imaging with isotopes like Thallium-201 (Tl-201) and Technetium-99m labelled isonitriles or diphosphine compounds (1). Lately studies with positron emitting radio-isotopes like Nitrogen-13 labelled Ammonia ($^{13}NH_3$) and Fluorine-18labelled fluorodeoxyglucose (^{18}FDG) are fast emerging as the gold standard for assessment of myocardial viability and for other metabolic studies. The images are acquired on a computerized gamma camera or more commonly on a single photon emission computerized tomography (SPECT) system. Positron emission tomography (PET) has a greater sensitivity and specificity and is performed for perfusion, metabolic and viability imaging (2). The basic procedure is similar in all the studies. A radiopharmaceutical agent is created by chelation of a radioactive isotope to a pharmaceutical agent. This radiopharmaceutical agent or radio-isotope in the case of Thallium-201 is injected intravenously, and the emitted gamma rays are detected by a gamma camera, SPECT or PET imaging device. Images are acquired as per a pre-defined software programme protocol. The signals are than digitized and stored in a computer and reproduced as an image or functional data. The principal advantages of nuclear imaging of the heart are its non-invasiveness and its ability to assess quantitatively or semi-quantitatively myocardial flow and ventricular function. Its main disadvantages are its relative cost, the special equipment and the expertise required for accurate interpretation of the study.

In 1995, 3.3 million cardiac perfusion studies were performed in the United States of America. Sixty percent studies were performed with Tc-99m labelled agents and forty percent with Thallium-201. Most of the major medical centres in India are currently performing Thallium-201 or Tc-99m myocardial perfusion scintigraphy, using the state of the art imaging equipment, and computerized analysis (3). A dedicated PET system will soon be made operational at Radiation Medicine Centre, Mumbai.

Radiopharmaceuticals and radio-isotopes commonly used in myocardial perfusion imaging

A. Thallium-201

Thallium is a group-IIIA, cyclotron produced metallic element with biokinetic properties similar to potassium. The initial distribution of thallium is based on blood flow and cellular extraction by viable myocardium. The delayed phase of localization is based on redistribution or equilibrium in the myocardium based on continued extraction of thallium from blood and ongoing washout from previously localized thallium from myocardial cells.

B. Technetium-99m labelled compounds

i. Isonitriles (Tc-99m Sestamibi)
ii. Diphosphines (Tc-99m Tetrofosmin)
iii. Q-class agent (Tc-99m Furifosmin)

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TABLE - 1

Radio-Pharma-ceutical	Usual Dose	Route of Adminis-tration	Physical Half-life (h)	Time of Imaging	Absorbed Dose Estimate (rad/mci)* whole body	Gonads	Other	Remarks
^{99m}TC pyrophos-phate	10-20 mCi (370-740MBq)	IV	6	24 h	0.01	0.01-0.03	Bone, 0.02-0.07; bladder, 0.1-0.2**; marow, 0.01	Forcing fluids and frequent voiding reduce bladder close
^{99m}TC red cells (in-vivo labelling)	15-30 mCi (555 MBq - 1.11 GBq)	IV	6	0.32 h	0.015-0.057		Heart, 0.06-0.08; lungs, 0.03-0.13; spleen, 0.03-0.23	
^{99m}TC sestamibi	15-30 mCi (555 MBq-1116 GBq)	IV	6	30-90 min	0.02	Testes, 0.01; ovary, 0.05	Colon, 0.15**; heart, 0.02; kidneys 0.06	
^{201}TI chloride	1-3 mCi (37-111 MBq)	IV	73	Immediate (to 4 h)	0.06-0.3	Testes, 0.2-1.4; ovary, 0.3	Kidneys, 0.4-0.9**; heart, 0.2; colon, 0.6-0.8; thyroid, 0.43-0.93	

* To obtain absorbed dose in mGy/MBq, divide values by 3.7

** Critical organ

Technetium labelled compounds (Table-1) have advantages of higher energy (140 Kev) giving better image resolution and lesser artifacts due to breast and diaphragmatic attenuation. Larger dose's can be administered, because of its smaller physical half life (6 hours) which results in better image quality due to improved radioactive counting statistics. Tc-99m labelled compounds have comparatively longer myocardial retention on account of their fixation to cytoplasmic mitochondria. Unlike thallium, there is minimal redistribution in the myocardium. Due to prolonged fixed distribution in the myocardium there is convenience of delaying imaging when necessary without loss of sensitivity and introduction of artifacts. In case of equipment malfunction, power failure, positioning error or patient motion a re-imaging can be done.

Lack of redistribution makes it mandatory to give two separate injections for stress and rest conditions. This is unlike thallium-201 which receives only one injection during stress.

Indications of myocardial perfusion scintigraphy

1. Diagnosis of coronary artery disease (CAD)

Not all patients with suspected coronary artery disease need to be subjected to invasive and expensive coronary artery angiography. The approach and algorithm for selecting an ideal investigation in suspected CAD is based on the pre-test probability of CAD in a patient, which in turn depends on prevelance of CAD in the population to which the patient belongs. Patient can be classified as having a low, intermediate or high pretest probability of CAD. Placing a patient in one of these categories depends greatly on the clinical judgement of the physician who must take into consideration the population prevalence of CAD, patient's gender, age, coronary risk factors and characteristics of symptoms (4). The commonly followed algorithm for patients with chest pain is that a low pretest probability (less than 40%) is investigated in a non-aggressive manner with exercise stress electrocardiography on a treadmill following the

standard Bruce protocol. Coronary angiography is the initial evaluation in patients with high (grater than 70%) pre-test probability. Myocrdial perfusion scintigraphy has a discriminative role in patients of **intermediate (40-70%) pre-test probability** of ischaemia.

The following categories of patients have an **intermediate pre-test probability of CAD** and are ideal candidates for non-invasive myocardial perfusion scintigraphy.

i) **Symptomatic patients (chest pain),** those with high suspicion of CAD but with normal ECG.

ii) **Asymptomatic patients** with significant coronary risk factors, an abnormal resting ECG, or a positive exercise ECG.

iii) **Non-diagnostic ECG** patients with underlying ECG abnormalities like left bundle branch block (LBBB), pacemakers, left ventricular hypertrophy (LVH) and baseline ST changes that render exercise stress ECG on treadmill non-diagnostic, are also candidates for myocardial perfusion scintigraphy.

2. **Haemodynamic significance of angiographically demonstrated coronary stenosis.**

3. **Functional significance of collateral coronary vessels.**

4. **Follow-up after myocardial revascularization procedures**

Chest pain after a revascularization procedure may be cardiac or non-cardiac in origin. The chest pain of cardiac origin can be due to restenosis of a coronary artery bypass graft or that of percutaneous transluminal angioplasty (PTCA). Stress myocardial scintigraphy is superior to clinical findings and exercise ECG in predicting graft potency. The probability of graft restenosis increases significantly with worsening of defects seen before surgery or with the appearance of new perfusion defects.

5. **Risk stratification in coronary artery disease.**

6. **Risk stratification after myocardial infarction.**

7. **Myocardial viability assessment**

A study demonstrating a fixed perfusion defect that is visible on both the stress and rest image's, can be due to :

(i) Scar tissue after a myocardial infarction.

(ii) Hibernating myocardium, as a result of severe coronary stenosis.

(iii) Artifacts, due to tissue attenuation (Table-2).

Table 2. Stress Myocardial Perfusion Scintigrapy

SOURCES OF FALSE-POSITIVE EXAMINATIONS
True Defects
Coronary anomaly
Coronary spasm (variant angina)
Noncoronary disease
Mitral valve prosthesis
Cardiomyopathies
Aortic stenosis
Myocardial bridge
Idiopathic hypertrophic subaortic stenosis
Conduction defects (left bundle-branch block)
Miscellaneous
Long-distance runners
Young females
Ischemia of non-coronary origin
Apparent Defects
Artifacts
Chest wall artifacts
Breast tissue or pectoral muscles
Breast prosthesis
Electrocardiogram leads
Braces
Items in pockets, pendant, etc.
Obesity
High left hemidiphragm
Excess patient motion (deep respiration)
Misinterpretation of Normal Variants
Over-or underappreciation or inferoapical defects
Variant activity of cardiac base, proximal septal area, and posterolateral walls
Papillary muscle attachments
Small ventricular cavity.
SOURCES OF FALSE-NEGATIVE EXAMINATIONS
Early or delayed redistribution
Submaximal exercise
Noncritical stenosis (30%-40%)
Isolated right coronary lesion
Coronary collaterals
Multivessel disease (balanced)
Overestimation of stenosis on angiogram
Interfering medication

The most widely used protocols to demonstrate a viable myocardium involve the use of delayed thallium image (12 to 24 hours), or a reinjection of thallium at 4 hours or a combination of two as adjuncts to traditional stress and 4 hours redistribution study (5). Such protocols maximize the conditions under which redistribution can occur in viable but poorly perfused myocardium by providing additional thallium and/or time for redistribution and possible reversal of the perfusion defect. Almost 50% of fixed defects prove to be reversible after these protocols and reflect a hibernating myocardium amenable to revascularization procedures and not the non-salvageable myocardial scar. A PET scan is now considered as a "gold standard" for myocardial viability by demonstrating presence or absence of F-18, FDG metabolism in cardiac myocytes. Attenuation correction using Gadolinium-153 transmission scan or CT based systems can significantly reduce the possibility of artifacts. Gated SPECT by demonstrating wall motion also rules out an artifact with reasonable certainty.

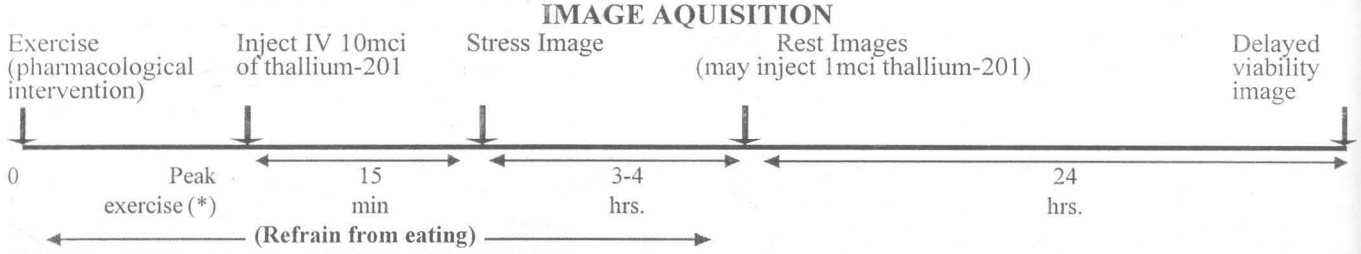
8) Evaluation of Acute Chest Pain.

In acute chest pain ECG and clinical features have a low sensitivity and specificity. About 10% of patients discharged from emergency develop myocardial infarction in 28 hours. Moreover, only 30% of patients admitted to the Coronary Care Unit have acute myocadial infarction. For these reasons, it has proved cost effective in some acute care facilities to use resting myocardial perfusion imaging for the detection of defects associated with myocardial ischemia or infarct (6).

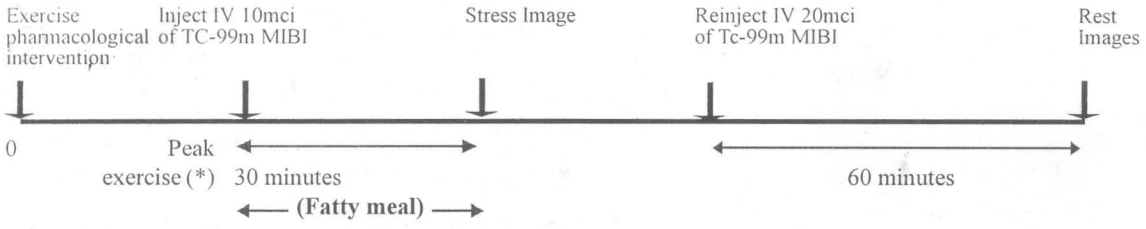
(9) Pre-operative risk assessement.

Image acquisition

Patient is fitted with chest electrodes for ECG monitoring and than asked to perform multistage treadmill exercise based on a Bruce or modified Bruce protocol with simultaneous monitoring of BP, pulse and ECG. Stress is considered as maximal or at peak when the heart rate reaches 85% of the predicted maximum heart rate, which is defined as 220 minus the patients age in years (220 - Age in years), or when the heart rate and blood pressure product (Double product) exceeds a value of 25,000. Other parameters indicating adequate stress are chest pain or significant ECG changes. At peak stress the patient is injected about 2 milli curies (mci) of Tl-201 or 10-15 mci of Tc-99m-sestamibi. In case of Tl-201 studies the stress imaging is done within 10 to 15 minutes after exercise (Fig. 1).



A) Thallium-201 Exercise (stress) Rest 1 day Imaging (Fig 1)



B) Tc-99m Sestamibi/Tetrofosmin Exercise(Stress)-Rest 1 day Imaging (Fig. 1)

(*) = Pharmacological end post (maximum predicted heart rate)

Indications for termination of exercise

Absolute

1. Drop in systolic blood pressure more than 10mmHg from base line; 2. Moderate to severe angina (grade 3-4); 3. Ataxia dizziness or syncope; 4. Cyanosis/Pallor; 5. Serious arrythmia (IVT etc's); 6. Inability to monitor BP or ECG.

Relative

1. ST depressed > 3mm horizontal or down slopped; 2. Increasing Chest pain; 3. Fatigue, shortness of breath, wheezing or cough; 4. Less serious arrythmis.

A delay of 15 minutes also allows for respiration to slow down so that the artifacts due to diphragmatic movements are minimized. In case of Tc-99m sestamibi or tetrofosmin imaging (Fig. 2), the stress images can be taken after 30-40 minutes of isotope injection since there is no redistribution as these agents are fixed to the myocardium.

Imaging is done on a standard SPECT camera with patient supine and left arm over the head. Using a single-detector SPECT camera, a rotational arc of 180 degrees is commonly used, frequently beginning at -45 degree right anterior oblique (RAO) and ending at 45 degrees left posterior oblique (LPO) position. Using 64x64 computer matrix, 64 images are obtained over 180 degree arc for a total study recording time of about 30 minutes. All patients are imaged twice, once for stress and second time at rest. Rest images or redistribution images of thallium-201 are obtained 3-4 hours later. To ensure that adequate ambient thallium is available for redistribution the administration of an additional dose of 1 mci of thallium-201 before the second set of images is helpful (7). In most of the centre's a delayed 24 hour's image is also obtained to see reversibility of a defect in a possible hibernating myocardium, and demonstrate myocardial viability (8).

Unlike thallium, in case of Tc-99m sestamibi there is no redistribution, so after initial exercise images, a second injection of 20-30 mci is given and 60 minutes later resting myocardial perfusion images, are acquired. To develop a differential gradient between post-exercise and rest images, the second injection (Rest) is nearly twice the first injection. The exercise and rest images can be acquired in a single day or a two day protocol may be followed.

Pharmacological stress/intervention

Indications for pharmacological stress/intervention

i. Patients who can not perform or tolerate adequate exercise.

ii. In patients with heart rate response limited by calcium channel and beta blockers.

iii. Patients with LBBB which may produce spurious exercise and tachycardia induced septal perfusion defects.

Commonly used intravenous agents for pharmacological stress/intervention

i) Dobutamine (beta-agonist, 10-40 micrograms/Kg of body weight).

ii) Dipyridamol (Coronary vasodilator, 0.5mg/Kg of body weight).

iii) Adenosine (Coronary vasodilator, 140 micrograms/Kg/of body weight).

Image processing

After acquisition, the exercise (stress) and rest (redistribution) images are reconstructed. The image reconstruction is done on a computer. Reconstruction of the cardiac tomograms is performed in three planes that are perpendicular or parallel to the long axis of the heart and oblique to the long axis at the body (Fig. 2). Three types of images are reconstructed.

i) Short axis (SA)

ii) Vertical long axis (VLA)

iii) Horizontal long axis (HLA)

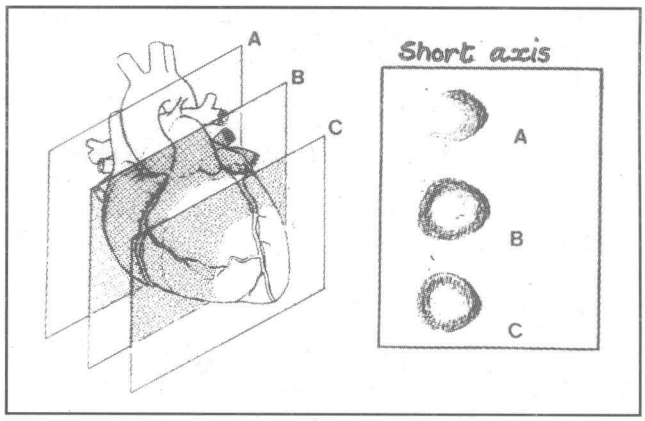


Fig 2. Short Axis (SA) images reconstruction slices.

Comparable sections are displayed for both the exercise (stress) and rest (redistribution) images (Fig. 3). In addition to the conventional display of tomographic slices, the entire three dimensional perfusion distribution of a set of exercise (stress) or redistribution (rest) images may be condensed into one two-dimensional display by using so-called polar or bull's eye map (Fig. 4).

This display may be thought of as the heart viewed from its apex and opened up like an umbrella. Perfusion defects are displayed as areas of low activity determined by gray or colour scale employed (Fig. 5).

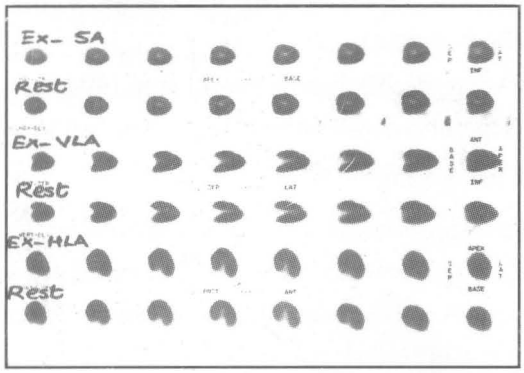


Fig 3. Comparable sections (SA, VLA, HLA) of exercise & rest.

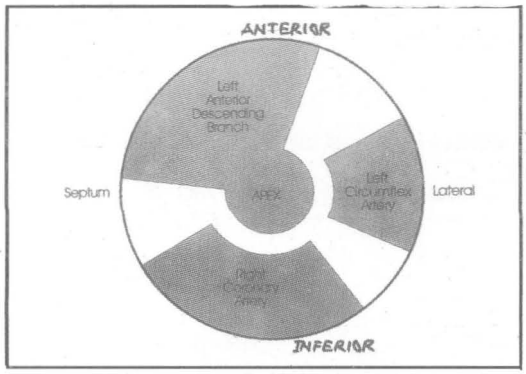


Fig 4. Bull's eye or Polar Map.

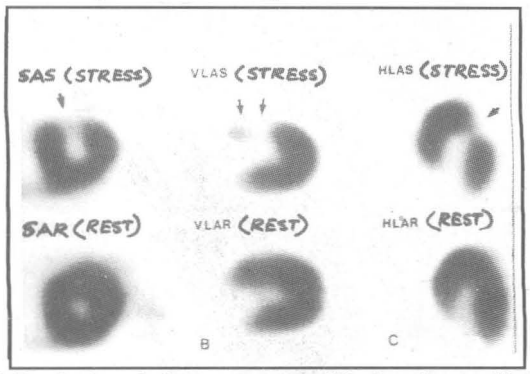


Fig 5. Perfusion defects at stress (S) showing redistribution at Rest (R) in SA, VLA & HLA images .

Image interpretation

In a particular plane (SA, VLA or HLA), the corresponding sections of exercise and rest images are compared for any perfusion defects seen on a gray scale as an area of relatively less blackening or increased whitening. The scan features to be ascertained are:

1. What is the extent of perfusion defect on a stress or exercise image? (small, medium or large).
2. How many vascular territories (Fig. 6) have the perfusion defect? (single, double or triple).

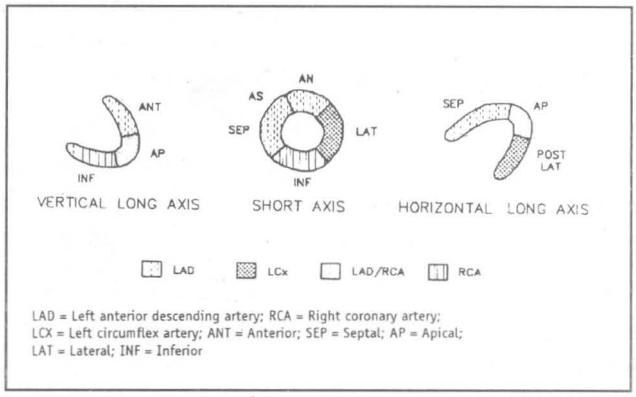


Fig 6. Vascular territories on SA, VLA, HLA slices.

3. Does the perfusion defect in a stress or exercise image become normal or improved in rest image? (Radistribution, suggesting ischaemia).
4. Does the perfusion defect persist in the delayed or rest image? (Fixed defects, suggesting infraction or hibernating myocardium).
5. Does a fixed defect improve on a delayed (24 hrs) Tl-201 image (Fig.7)? (Hibernating myocardium, suggesting myocardial viability, and amenability to revascularization procedures).

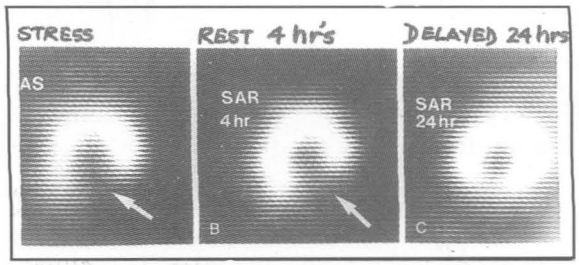


Fig 7. Improvement of fixed defect on a delayed (24 hrs) TL-201 image suggesting Hibernating myocardium.

6. Is there a possibility of a perfusion defect being a normal variant or an artifact (Table-2).

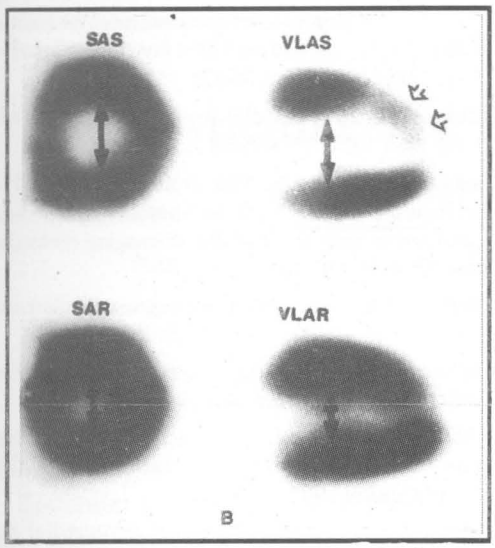


Fig 8. Transient stress or exercise related left ventricular cavity enlargement suggesting multivessel involvement with negative prognostic implications.

7. Could a non-coronary disease cause the perfusion defect (False +, Table-2).
8. Could a normal perfusion at stress be due to any of the reasons of a false negative study? (Table-2).
9. Is there transient (Fig. 8), stress or exercise related left ventricular cavity enlargement? (Multivessel involvement with negative prognostic implications).
10. Is there abnormal uptake of thallium-201 in lungs? (Multivessel involvement with high risk disease).
11. Has the stress been adequate? (Inadequate stress commonest cause of false -ve study).
12. Is the perfusion defect visible in at least two of the three standard sets (SA, VLA, HLA) of reconstructed slices.
13. Do the findings correlate with ancillary patient history, clinical findings, coronary angiography, revascularization procedures, and previous myocardial perfusion studies.
14. Does the study need to be repeated after taking measures to correct possible artifacts (Table-3).

Table 3. Single Photon Emission computed Tomography image artifacts and variants

CAUSE	RESULT	RECOGNITION/CORRECTION
Acquisition		
Soft tissue attenuation Breast or obesity	Anterior or lateral wall defect	Bind or elevate breast; view rotating planar image
Elevated left hemidiaphragm	Inferior wall defect	View rotating planar image
Abdominal visceral activity (liver or spleen)	Relative increased inferior wall activity Myocardial defect (dependent on	
Patient motion	type and direction of motion).	View rotating planar images or image sinogram; use computer motion correction algorithm.
Postexercise respiratory motion	Reversible inferior wall defect	Delay immeiate post-exercise images 10-15 min.
Processing Oblique axis Reconstruction; incorrect selection of left ventricular long axis	Myocardial defects, frequently basal	Review long axis selection
Instrumentation		
Center of rotation (COR) errors Rightward (+)	Posteroapical defect	Misaligned anteroposterior walls in horizontal axis view
Leftward (-)	Anteroapical defect	Strict quality and COR correction
Marked flood-field nonuniformity	Ring artifacts	Strict quality control and field uniformity correction.
Normal Variant		
Variable septal and apical thinning	Myocardial defects	Typical location
Papillary muscles	Focal myocardial hot spots. images).	Typical location (2-o' clock & 7-o' clock positions in transverse
Cardiac rotation	Fixed relative lateral wall defect	History of congenital heart disease; hyperexpanded lungs; marked right or left selective chamber enlargement
Levorotation	Fixed relative septal defect	Inspect electrocardiogram (ECG) and transaxial slices.
Noncoronary Disease		
Left bundle-branch block	Reversible septal defect	Review ECG
Myocardial hypertrophy	Fixed relative lateral wall defect (lower lateral-to-septal count ratio)	Review ECG; history of hypertension or valvular heart disease.

A systematic approach in analysing the processed images will answer all the aforementioned queries and help in image interpretation with higher degree of sensitivity, specificity and overall accuracy. SPECT myocardial scintigraphy is a very useful non-invasive technique provided, it is used with utmost precision and in a proper clinical context. The diagnosis of coronary artery disease in patients **with intermediate pretest probability,** is accurate with this modality and more often than not a negative test obviates the need for coronary angiography in this sub-set of patients. All the cardiac centres in the country need to have qualified, adequately trained manpower and state of the art SPECT systems to make optimal use of this non-invasive technology for evaluating patients of suspected coronary artery disease.

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