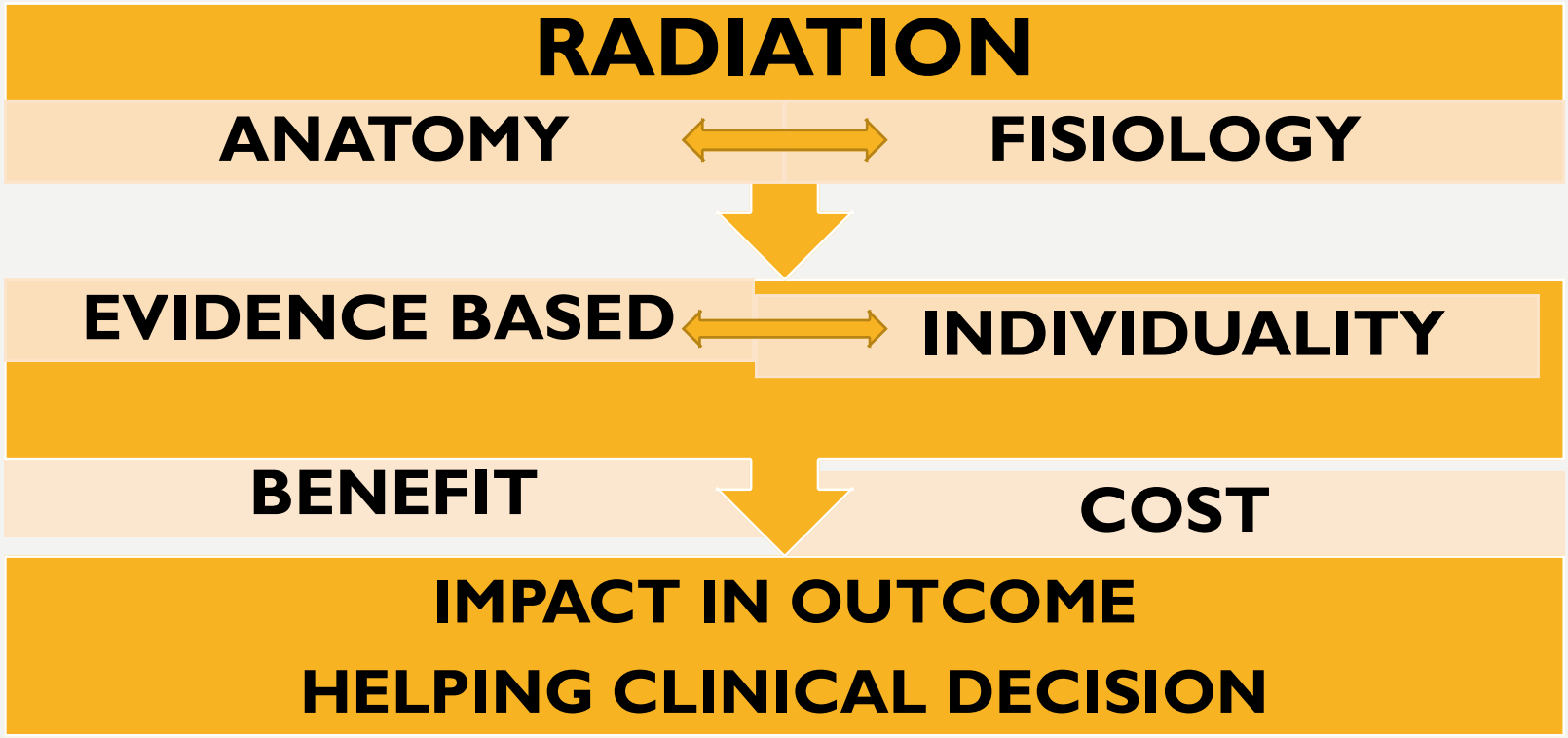
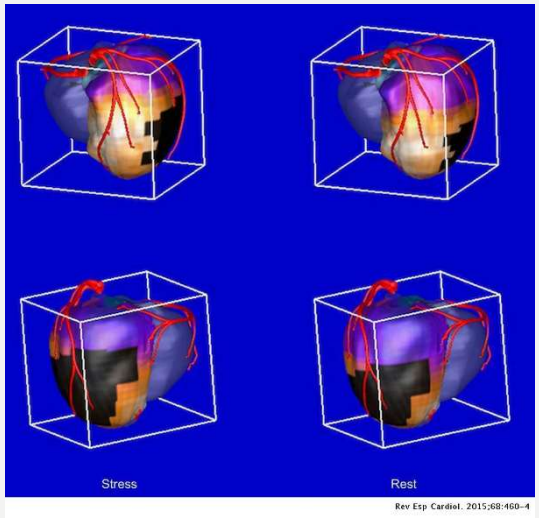
RADIONUCLIDE TECHNIQUES IN CARDIOVASCULAR IMAGING

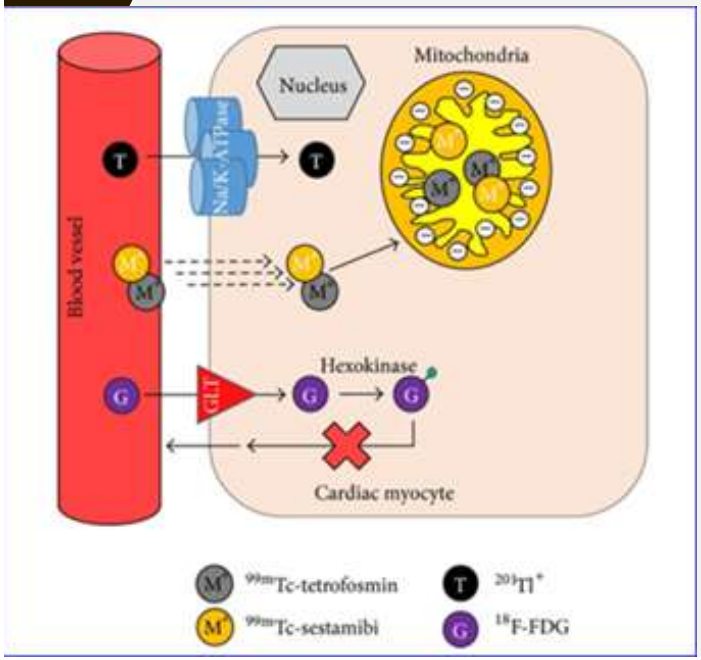
NUCLEAR CARDIOLOGY

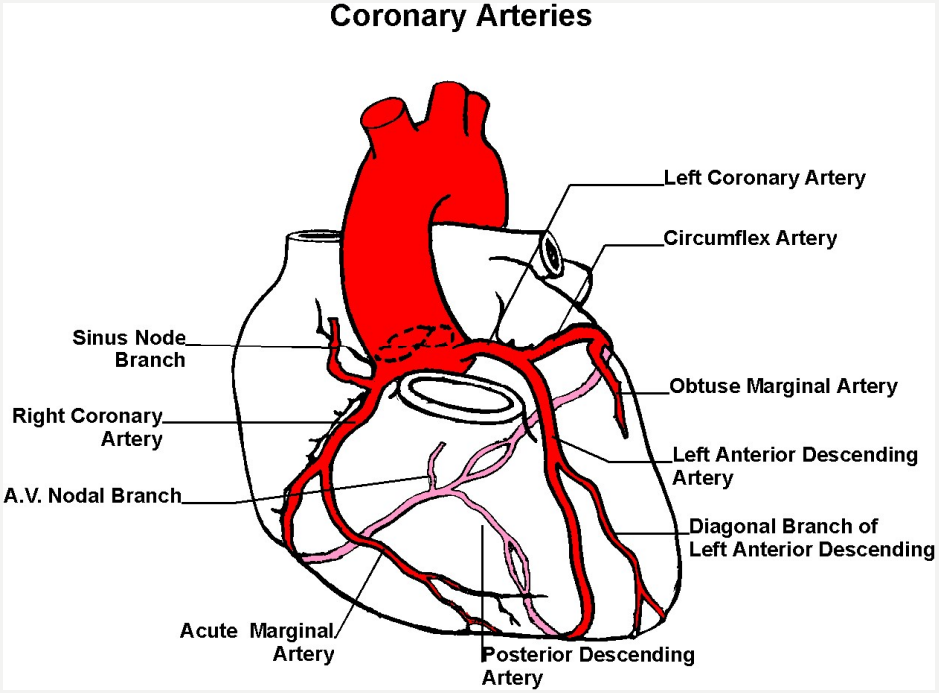
MULTIMODALITY CARDIAC IMAGING



Anatomical Considerations







- Radionuclide techniques provide both accurate and noninvasive means of evaluating cardiac function. Their role and clinical utility over the past 20 years are well established in the initial diagnosis of patients with suspected heart disease as well as in monitoring and deciding on prognosis in patients with known heart disease.
- Although most ventricular function studies are performed with the patient at rest, exercise functional studies can be also done to assess regional and global myocardial contraction changes with stress
- Clinical manifestations of coronary artery disease include angina pectoris, myocardial infarction, congestive heart failure, and sudden death.

MYOCARDIAL PERFUSION IMAGING (MPI)

- 75% of cardiac imaging in nuclear medicine
- Detection of CAD is based on the heterogeneity in blood flow between a normal coronary vessel and one with an anatomic stenosis or abnormal physiological function. Following exercise or pharmacologic stress, blood flow increases in normal coronary arteries. In vessels with a luminal stenosis, variously defined as 50–80% luminal cross sectional narrowing, three things may occur: there is no increase in flow, the increase is less than in a normal vessel or occasionally there may even be a constrictive effect and a decrease in coronary artery blood flow
- Areas of myocardium supplied by normal coronary arteries have a high and uniform uptake on both the stress and redistribution images.
- Areas of infarction have fixed defects with very low or absent uptake on both images.
- Areas of ischemia and infarction look identical on the post stress images.
- However, with ischemia the redistribution images show improvement in the ischemic areas and this allows the differentiation to be made between infarct and ischemic myocardium.

RADIOPHARMACEUTICALS: 201-THALLIUM

- acts as a potassium analogue in the body and is taken up into the myocardial tissue both actively by Na/K sodium/potassium cellular pump
- 90% first-pass extraction, uptake is linearly proportional to flow
- **washout or redistribution:** Following the rapid high initial uptake, Tl-201 re-equilibrates
- The patient must be imaged within 10–15 min of completion of stress to avoid early redistribution and a resulting decrease in sensitivity. This is followed 2.5–4 h later by a redistribution set of images (rest).
- Thallium has the disadvantages, delivering a relatively high radiation dose, so the administered activity is limited to 80 MBq (2 mCi), but also of emitting low-energy gamma rays which are subject to more attenuation than those of higher energy.

RADIOPHARMACEUTICALS: 201-THALLIUM

- One of the major advantages of using Tl-201 is that it is also an excellent marker of myocardial viability. The high and nearly linear initial myocardial uptake following stress makes Tl-201 a better marker of myocardial blood flow than the Tc-99m tracers, which have a low extraction fraction.
- Tl-201 uptake and redistribution over time is a marker of the K+ blood pool and of viable myocardium. In areas where blood flow is severely reduced following stress, there may be very low uptake of Tl-201 initially despite the presence of living myocytes. Even the 3–4 h redistribution images may still be abnormal. However, over 18–24 h or following re-injection of an additional dose to boast blood levels, if there are viable myocytes with an intact Na/K ATPase system, Tl-201 is eventually taken up and these areas will be clearly identified as hibernating myocardium and not infarction.

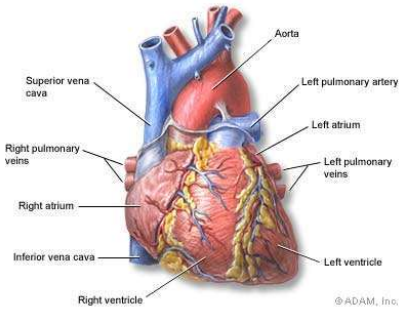
RADIOPHARMACEUTICALS:99mTc-TRACERS

- Two 99mTc tracers are currently commercially available; 2-methoxy-isobutyl-isonitrile (sestamibi or MIBI) and tetrofosmin. These tracers are highly lipophilic agent readily crosses myocardial cellular membranes
- the advantages over 201-Tl of fewer attenuation artifacts owing to the higher energy gammas, and better dosimetry allowing greater activity to be given (20-30 mCi).
- The minimal redistribution of Tc-99m tracers allows greater flexibility as to when acquisition can be performed; as soon as 10min or as far out as 4 h following stress. This allows the tracers to be administered to patients presenting with chest pain in the emergency room, a normal scan facilitating early discharge.
- first-pass ex traction is less than with thallium
- High subdiaphragmatic uptake in the liver or intestines occasionally interferes with evaluation of cardiac perfusion

RADIOPHARMACEUTICALS: ^{201}TI VS. ^{99m}Tc

	Thallium-201	Technetium-99m tracers
Radiotracer dose	3–4 mCi Additional 1 mCi for reinjection protocol	30 mCi if resting 10 + 20 mCi if both rest and stress imaging is performed
Radiation exposure	12–16 mSv	10 mSv
Study duration	4–5 h (rest and redistribution) 24 h if additional imaging is performed	≈1–2
Functional information	No	Yes
Tracer properties	Redistribution Needs repeat imaging to assess viability	No redistribution – Perfusion is fixed at the time of injection
Image quality	Inferior Low energy photons, lower photon count (noise)	Superior Higher energy photons, higher photon count (less noise)
Extracardiac activity	Frequent lung uptake may reduce image quality	Frequent liver and bowel uptake may delay acquisition or cause artifacts

Clinical Indications

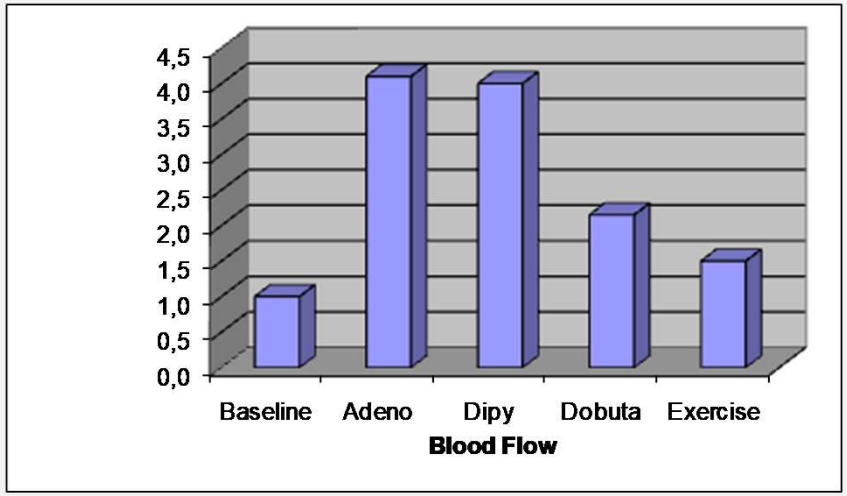


- Diagnosis of CAD
- in asymptomatic patients with multiple risk factors, SPECT can detect the presence of disease and give prognostic information
- Patients with diabetes mellitus (DM) are at a very high risk for having critical coronary stenosis and cardiovascular events
- Chest Pain in the Emergency Department-Patients presenting to an emergency department (ED) within several hours of chest pain and a nondiagnostic ECG can be risk stratified based on acute injection of a Tc-99m perfusion tracer.
- Myocardial Perfusion Imaging Before and After Revascularization
- Radionuclide Imaging Before Noncardiac Surgery

- Radionuclide Imaging After Percutaneous Coronary Intervention: In asymptomatic patients routine SPECT is not indicated at any time in the first 2 years following a procedure
- Radionuclide Imaging after CABG: Even with the altered anatomy following CABG, SPECT retains diagnostic and prognostic accuracy early and late for detection of stenosis in grafts as well as in the native vesse

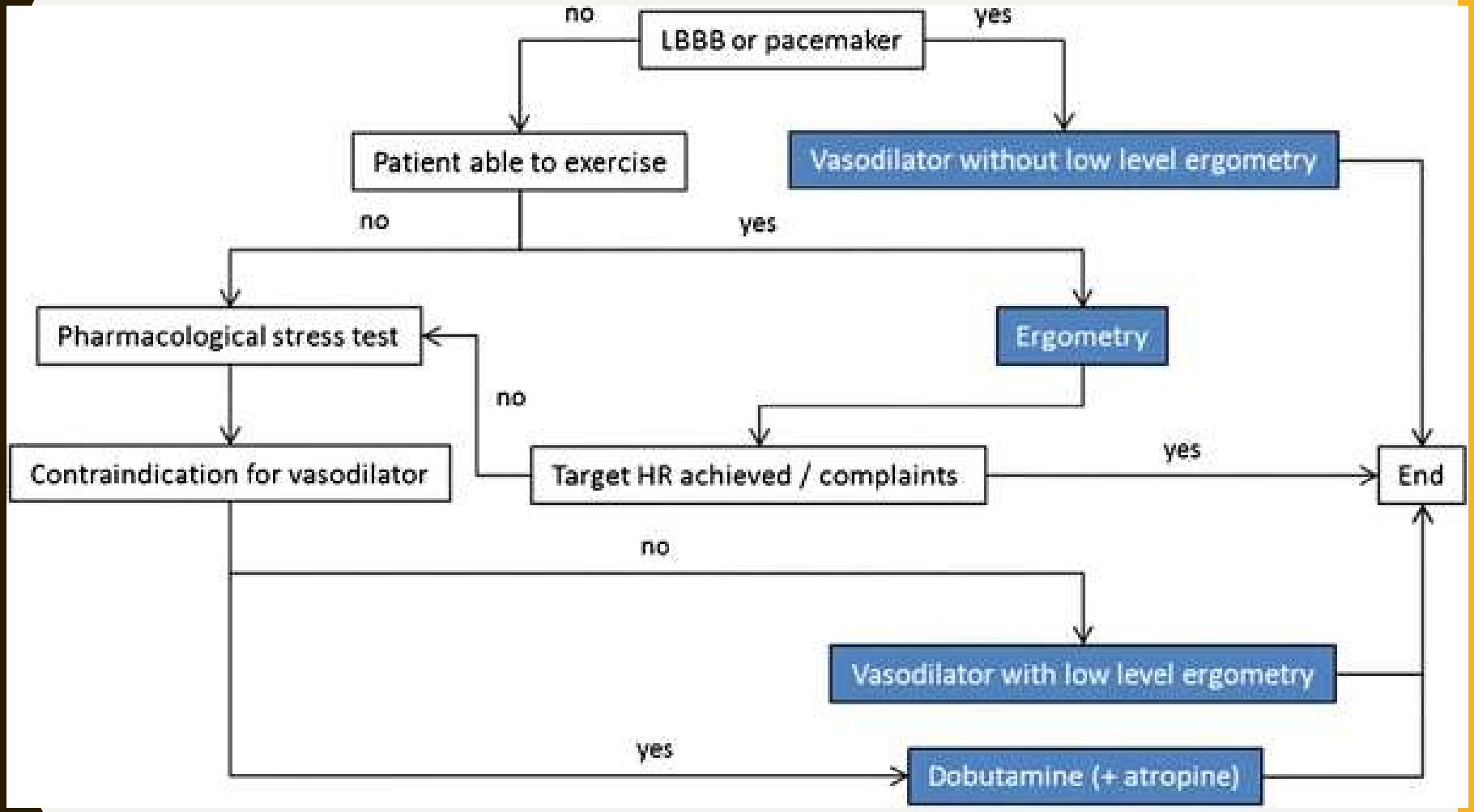
EXERCISE TREADMILL STRESS TESTING (ETT)

- In patients with suspected or known coronary artery disease (CAD) dynamic exercise is the first test ofchoice.
- patients must be able to exercise to a workload of at least 85% of age-adjusted maximal predicted heart rate (220-age)
- When combined with myocardial perfusion imaging, sensitivity is 85%–90%.
- treadmill exercise or bicycle is used.
- All monitored parameters (i.e., ECG, blood pressure, patient's appearance, and symptoms) are valuable not only for diagnosis, but also for prognosis.



PREPARATION FOR TEST

- Avoid all caffeine products for 24 hours (Coffee including decaffeinated and caffeine-free, tea, energy /soft drinks, chocolate, cocoa, strawberries, etc)
- Medications with caffeine
- Theophylline medications should be stopped 48 hours prior to the test.
- Several cardiac medications that also affect the heart rate -interruption recommended 3-5 half-lives (beta blockers, Calcium antagonists) .
- Do not eat or drink anything for 4 hours before the procedure.
- Notify the staff of all medications (prescription and over-the-counter) and herbal supplements that you are taking.
- Notify the staff if you have a pacemaker or defibrillator
- Please wear comfortable clothing, as well as a pair of comfortable walking shoes or sneakers.

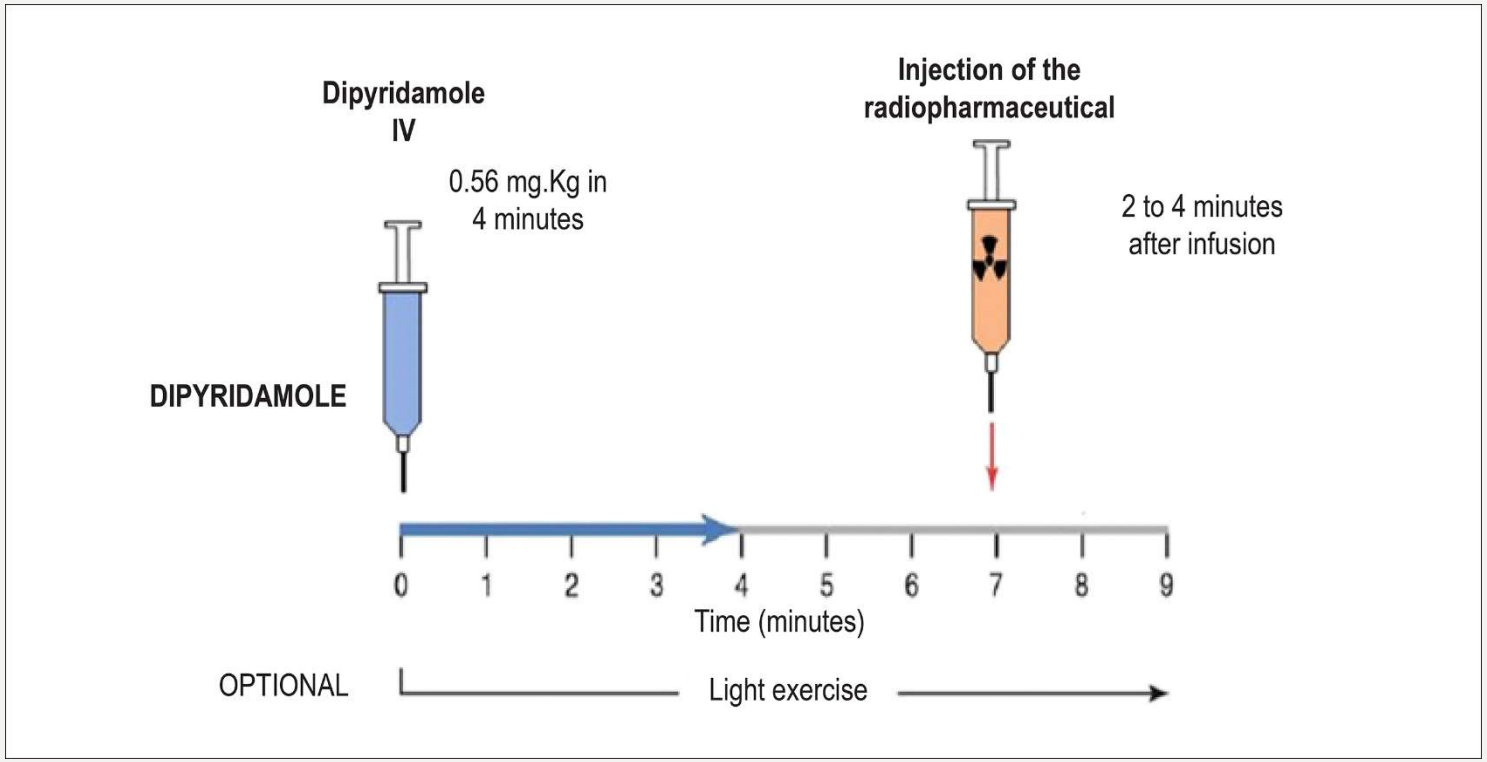

LBBB or pacemaker
no
yes
Patient able to exercise
Vasodilator without low level ergometry
no
yes
Pharmacological stress test
Ergometry
no
Contraindication for vasodilator
Target HR achieved / complaints
yes
End
no
Vasodilator with low level ergometry
yes
Dobutamine (+ atropine)

PHARMACOLOGIC STRESS AGENTS AND PROTOCOLS

- All myocardial perfusion imaging studies should be done using dynamic exercise stress whenever possible to obtain exercise duration.
- Pharmacologic stress is reserved for patients who are unable to exercise or are unable to achieve at least 85% of the maximal age-adjusted heart rate or reach an ischemic endpoint on the basis of symptoms or ECG changes.
- The pharmacologic agents in common use are vasodilators (adenosine and dipyridamole) and the adrenergic stimulant dobutamine. The vasodilators produce maximal coronary hyperemia, creating flow heterogeneity by causing a greater increase in blood flow in normal coronary arteries than in arteries with flow limiting stenosis.
- Dobutamine increases not only blood flow, but heart rate and blood pressure, and may create true ischemia.

DIPYRIDAMOLE STRESS TEST

Dipyridamole has a longer half-life than adenosine and does not affect A-V conduction. Dipyridamole is usually infused for 4 min. The perfusion tracer is injected at 7 min. An effective antidote is i.v. aminophylline.

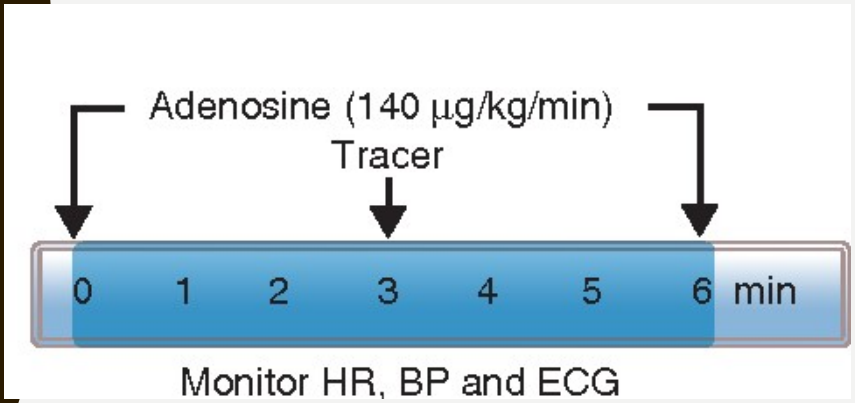


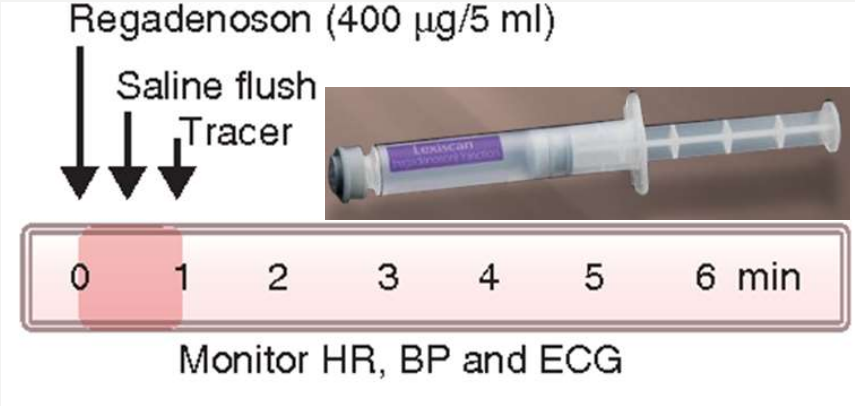
ADENOSINE AND REGADENOSON

Adenosine affects two kinds of receptors:

- A1 (slows A-V conduction) and A2 (coronary vasodilatation). The half-life of adenosine is extremely short (seconds only). Perfusion tracers are therefore injected during continuous adenosine infusion (140 μg/kg/min for 6 min).

- REGADENOSON is a selective A2a receptor agonist with a safer and better tolerability profile.
- REGADENOSON is administered as a single bolus, weight-unadjusted dose, unlike the weight-adjusted infusion dose of adenosine and dipyridamole





DOBUTAMINE

- is used infrequently for myocardial perfusion imaging. The protocol requires 3-min stepwise infusion stages of increasing doses of dobutamine and takes longer than vasodilator stress. Patients with hypertension, abdominal aortic aneurysms, poorly controlled supraventricular arrhythmias or ventricular arrhythmias should not be studied.
- Is used predominately in patients with severe and poorly controlled lung disease and in patients who have ingested caffeine on the day of testing and vasodilators cannot be used.

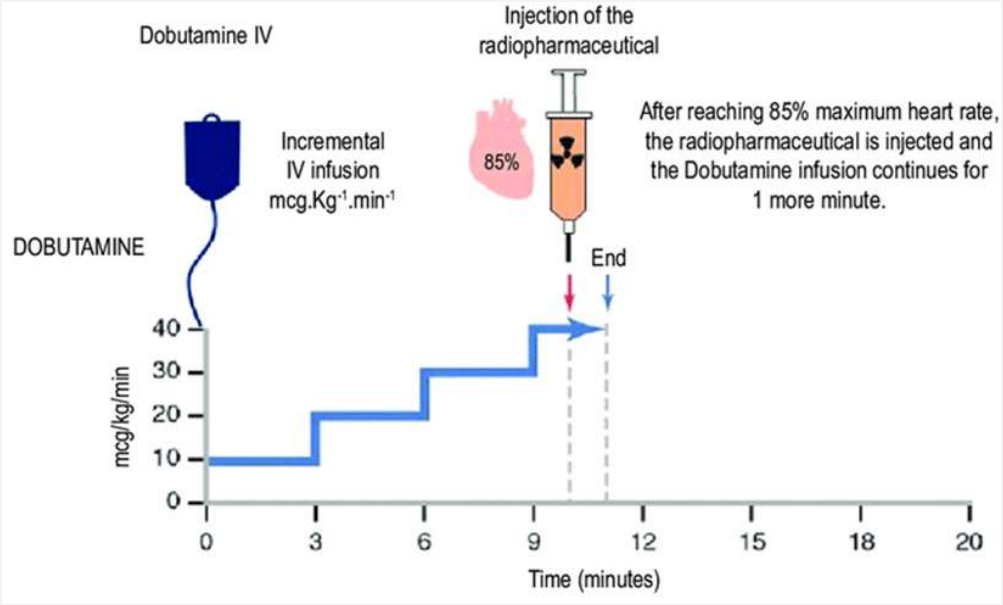


Table 4.7. Side effects (%) attributable to different pharmacologic stressors

	Adenosine	Dipyridamole	Dobutamine
Chest pain	45*	20	39
Flushing	35	3	<1
Dyspnea	33	3	6
Dizziness	9	3	4
Gastrointestinal discomfort	15	10	1
Headache	30	12	7
Hypotension	2	5	15
Arrhythmia	3	5	45
High-degree AV block	7	2	0
STΔ	6†	8	30
Bronchospasm	0.1	0.15	0
Fatal AMI/cardiac death	0	0.05	0
Nonfatal ACS	0.01	0.05	0.3
Any adverse effect	80	50	75

From References 2, 16, 33, 40.
AMI, acute myocardial infarction; AV, atrioventricular.
* Chest pain is nonspecific and not necessarily indicative of the presence of CAD.
† ST segment depression (1 mm) is indicative of significant CAD.

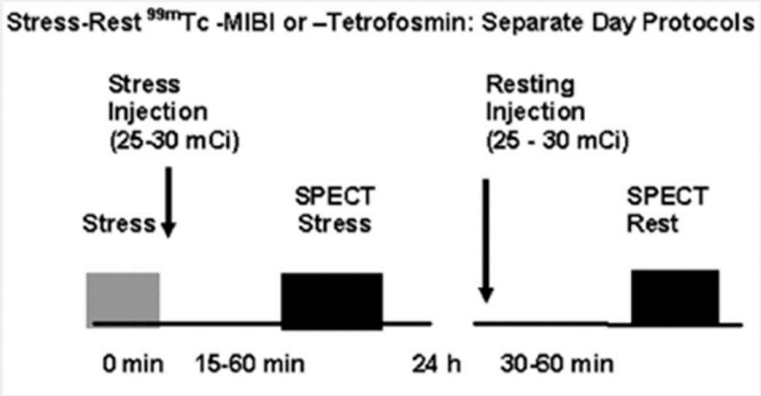
TWO DAY PROTOCOL

- The stress study should be done first and if normal the resting study is not needed. Stress first provides results sooner and has a lower radiation exposure.
- 20–30 mCi of Tc-99m-MIBI, is used and provides high counts and better image quality.
- This protocol is mandatory in obese patients and allows a rest ejection fraction (EF) to be calculated as well as a post stress measurement, which provides additional value.
- In obese patients with soft tissue attenuation and low counts, gating and attenuation correction improves specificity and decreases the number of patients needing to return for a rest study

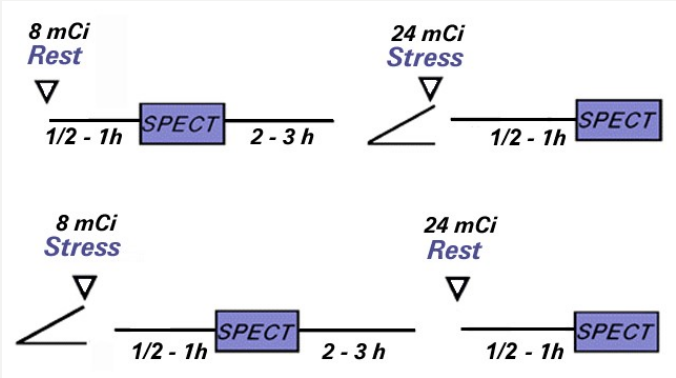
ONE DAY PROTOCOL

- For logistical reasons, stress and rest studies are usually performed using a 1-day protocol
- This requires administration of a low dose, one-third of the total dose or 8–12 mCi, for the "stress" study and a larger dose, (two -thirds of the total dose) or 20–30 mCi, for the second "rest" study and waiting between studies, usually 1.5–2.5 h, to allow for physical decay of Tc- 99m.
- If the stress study is normal, the rest study is not needed.

TWO DAY PROTOCOL

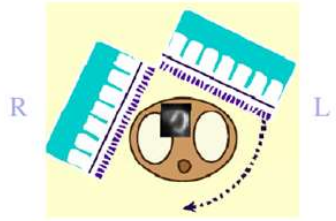


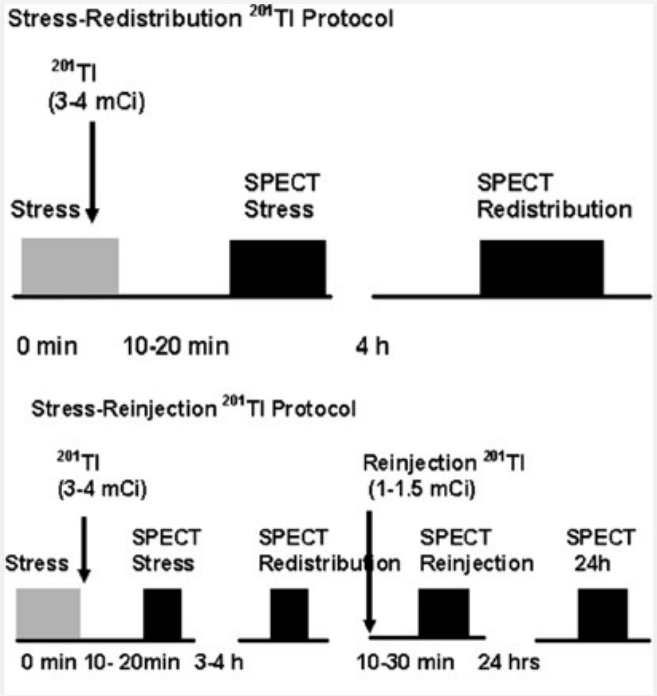
ONE DAY PROTOCOL



201-TI PROTOCOL

180° arc for cardiac studies (RAO to LPO)



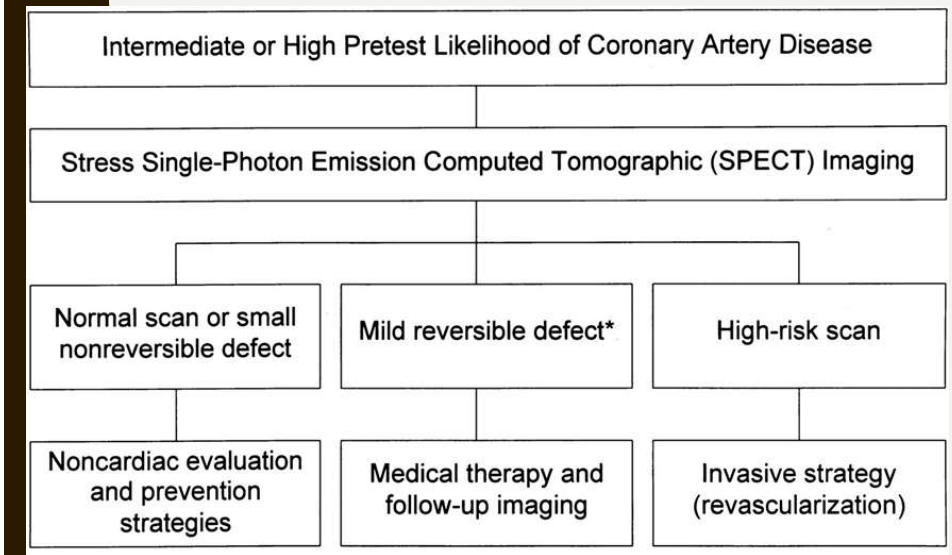


ECG GATING OF THE SPECT MYOCARDIAL PERFUSION

- provides, independently from the perfusion information, important information on global LV and RV function, the LV ejection fraction, and regional wall motion and thickening
- However, due to the higher count rates achieved with Tc-99m perfusion tracers, these are the preferred agents for ECG gated SPECT. Gated SPECT studies are acquired using 8 or 16 time frames in the heart cycle
- Quantitative analysis of myocardial perfusion images compares the patient's distribution at rest and during stress
- Since gated Tc-99m studies are acquired a minimum of 15 min following peak exercise stress, regional wall motion in most patients with ischemia usually returns to normal by the time of imaging.
- If there is profound ischemia, areas of myocardium may continue to have persistent wall motion abnormalities that are detected during gated acquisition. One of the most important benefits of gated SPECT acquisition is helping to differentiate attenuation due to the diaphragm or breast from areas of old myocardial infarction or scar.

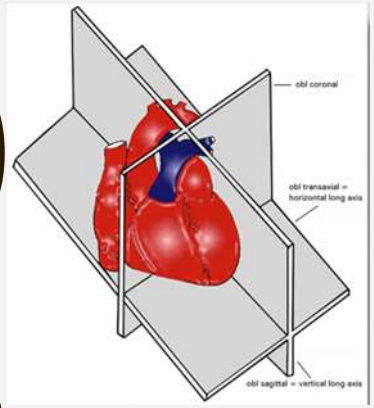
CLINICAL UTILITY OF MYOCARDIAL PERFUSION IMAGING

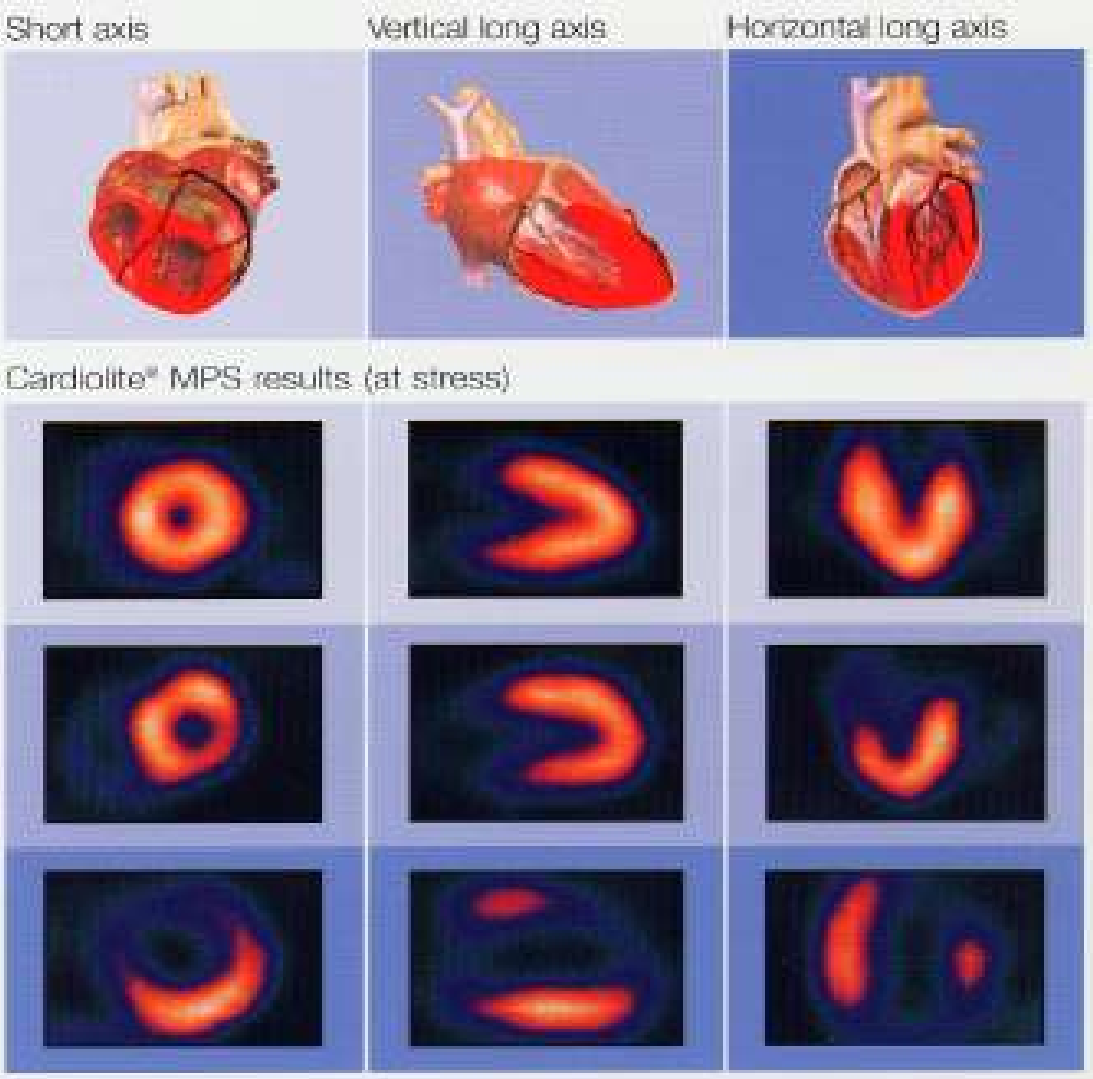
- SPECT is used to assess the relationship between coronary lesion severity and coronary flow reserve. Even in the presence of flow limiting stenosis, if exercise or pharmacologic stress perfusion is normal, patients are at low risk for cardiac events.
- Using SPECT as a gatekeeper for referral to coronary angiography has been shown to be cost effective,
- It also has a role in determining the sequence and number of grafted vessels in high risk coronary artery bypass graft (CABG) patients and for identification of the culprit lesion at the time of percutaneous coronary intervention (PCI).



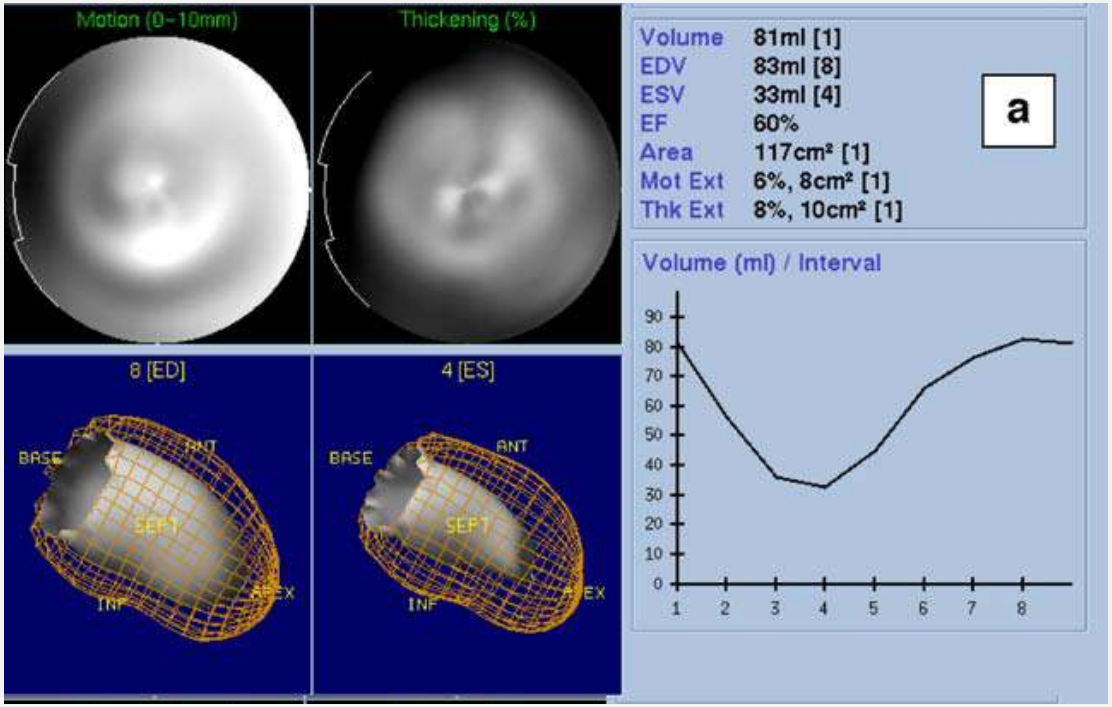
Scan Result	Annualized risk of cardiac events	Treatment implications (majority of patients)
Normal	<1% risk of both cardiac death and MI	Risk factor modification (RFM) in addition to current regimen
Mildly abnormal	Low risk of cardiac death; Intermediate risk of MI	Aggressive RFM/ medical treatment
Moderately to severely abnormal	Intermediate-to-high risk of ***both*** cardiac death and MI	Catheterization (possible revascularization)/RFM

Myocardial Perfusion Imaging



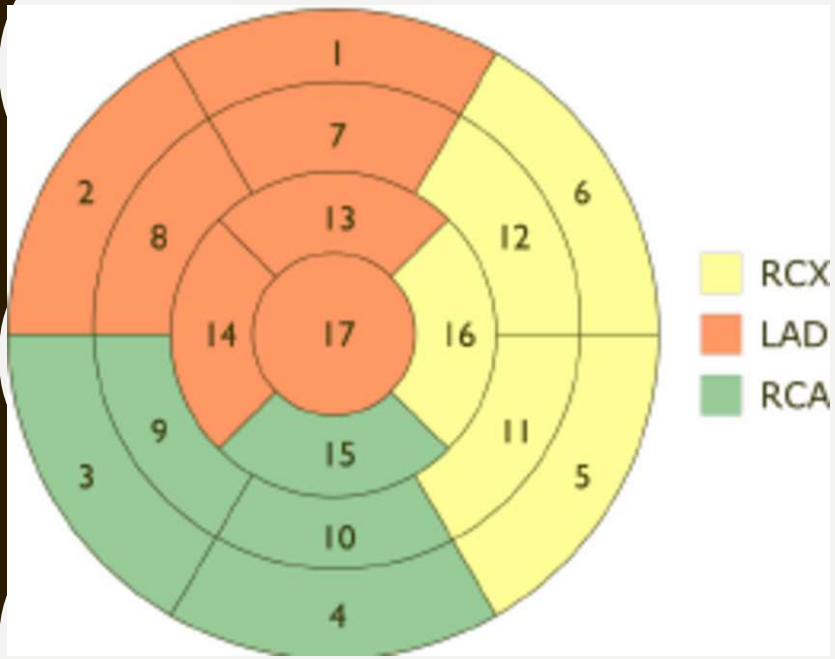


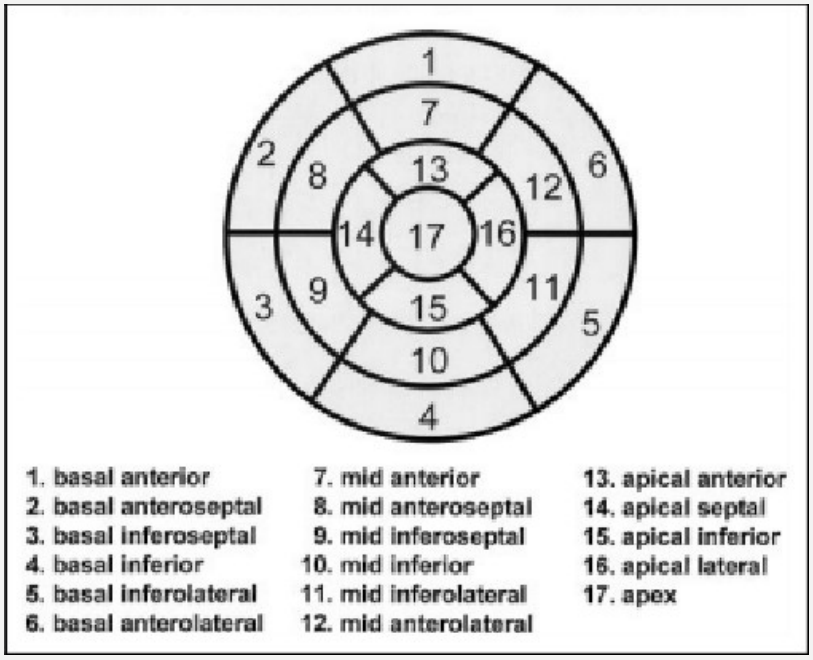
Gated-SPECT Three-dimensional display

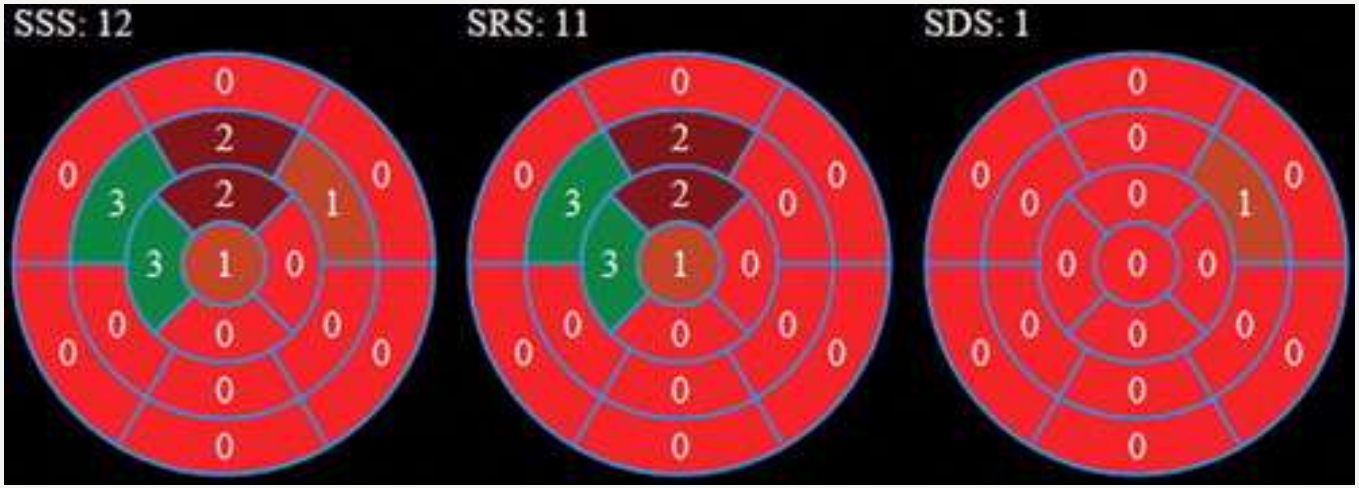


- Three-dimensional display.-This display may also facilitate the assessment of the presence, extent and location of LV perfusion abnormalities. LV size and configuration can be displayed.

POLAR MAPS (BULL'S EYE) DISPLAY







MYOCARDIAL STUNNING

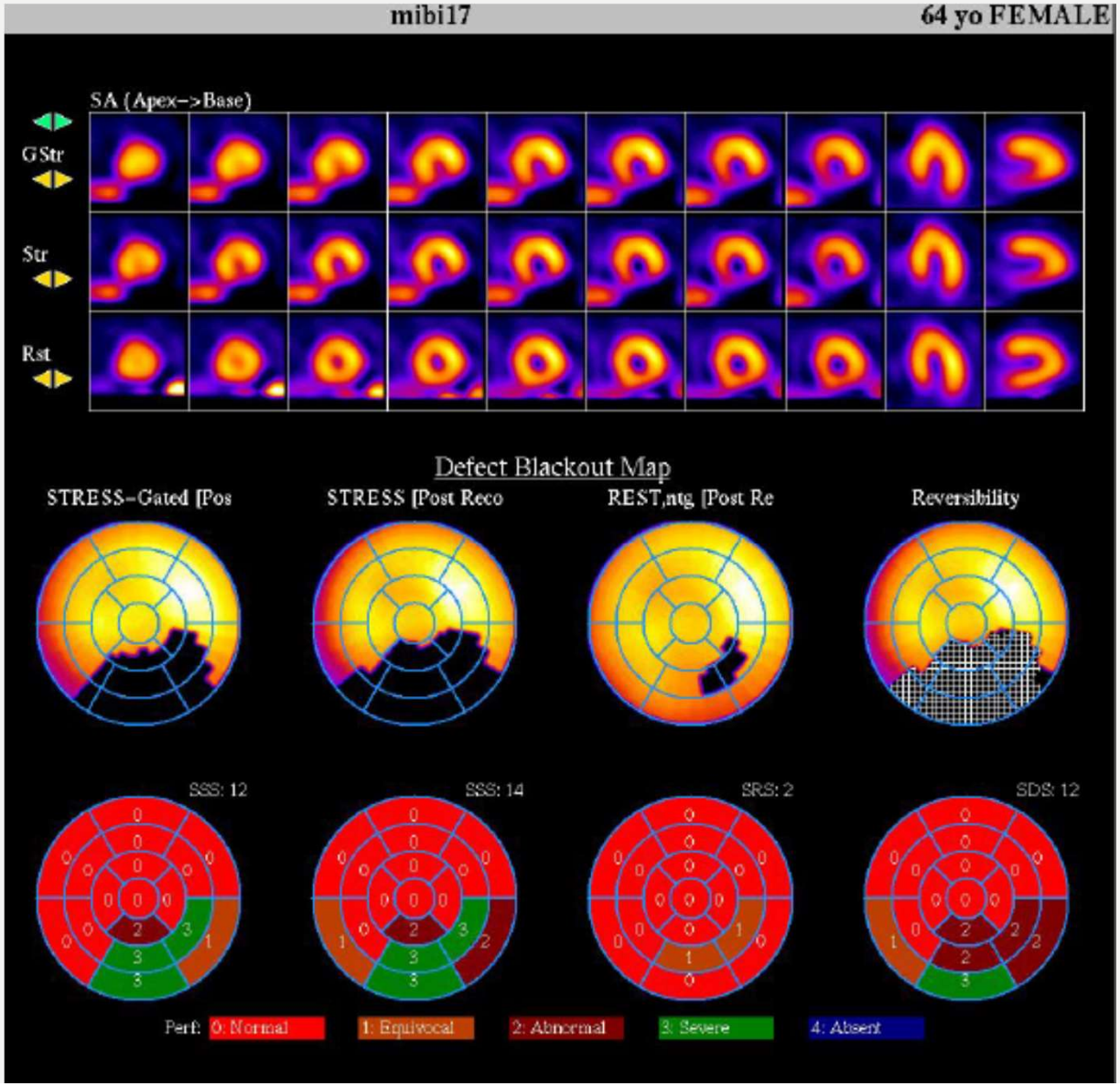
- Previously, myocardial stunning was considered as a regional contractile dysfunction that occurred after a brief episode of myocardial ischemia.
- recurrent episodes of ischemia in the same coronary territory may occur in patients with CAD, resulting in chronic contractile dysfunction which is known as "repetitive stunning"

MYOCARDIAL HIBERNATION

- "hibernating" myocardium is a persistently impaired myocardial function in the setting of reduced coronary blood flow.
- from a clinical standpoint, the "true mechanisms" of chronic poor LV dysfunction (i.e., hibernation or stunning) are not that relevant.
- a wide overlap of hibernation and stunning may occur

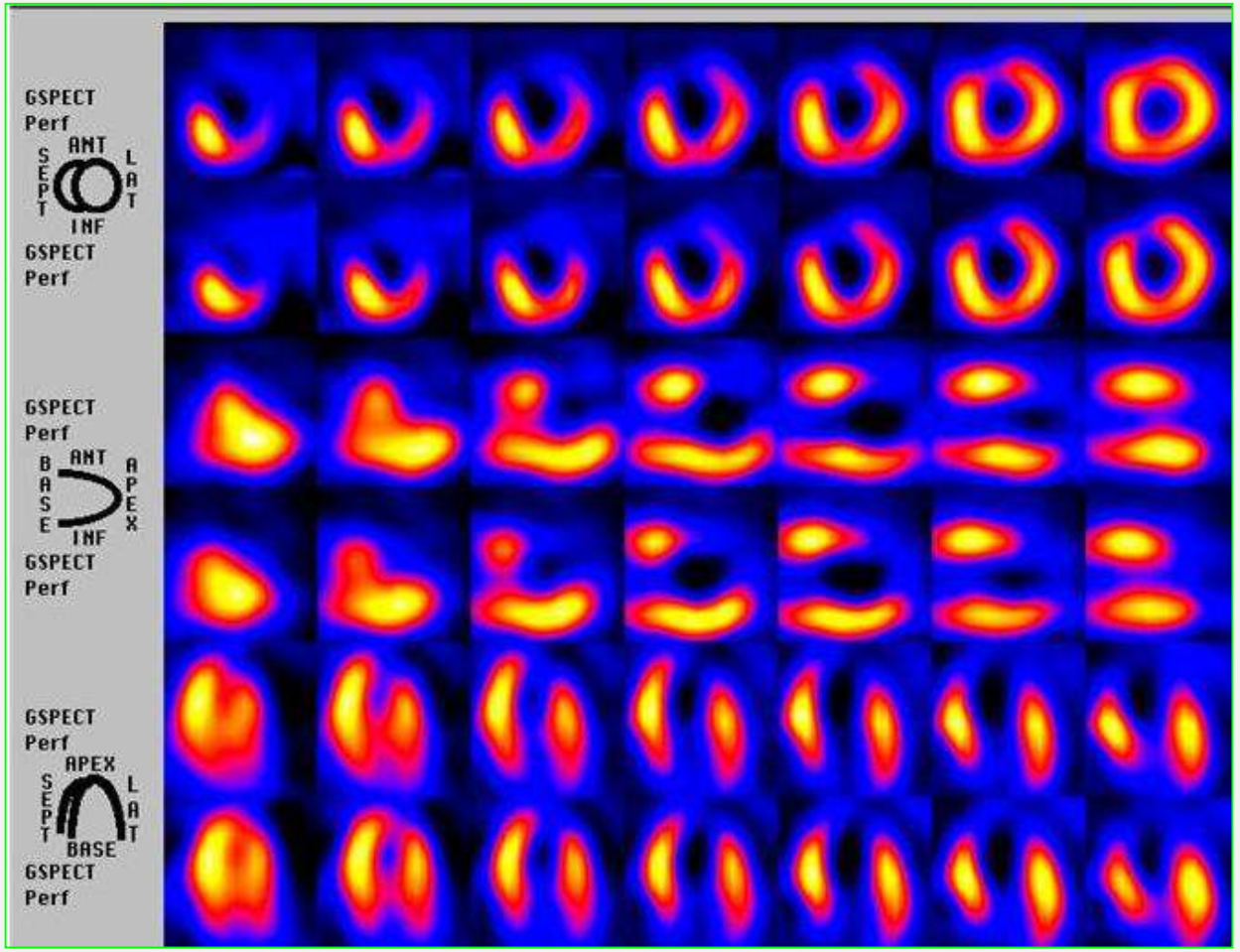
Regardless of the mechanism(s) involved, the identification of dysfunctional myocardium in patients with chronic poor LV function that will improve after coronary revascularization is important.

REVERSIBLE ISCHEMIA



SSS= 14
SRS= 2
SDS= 12

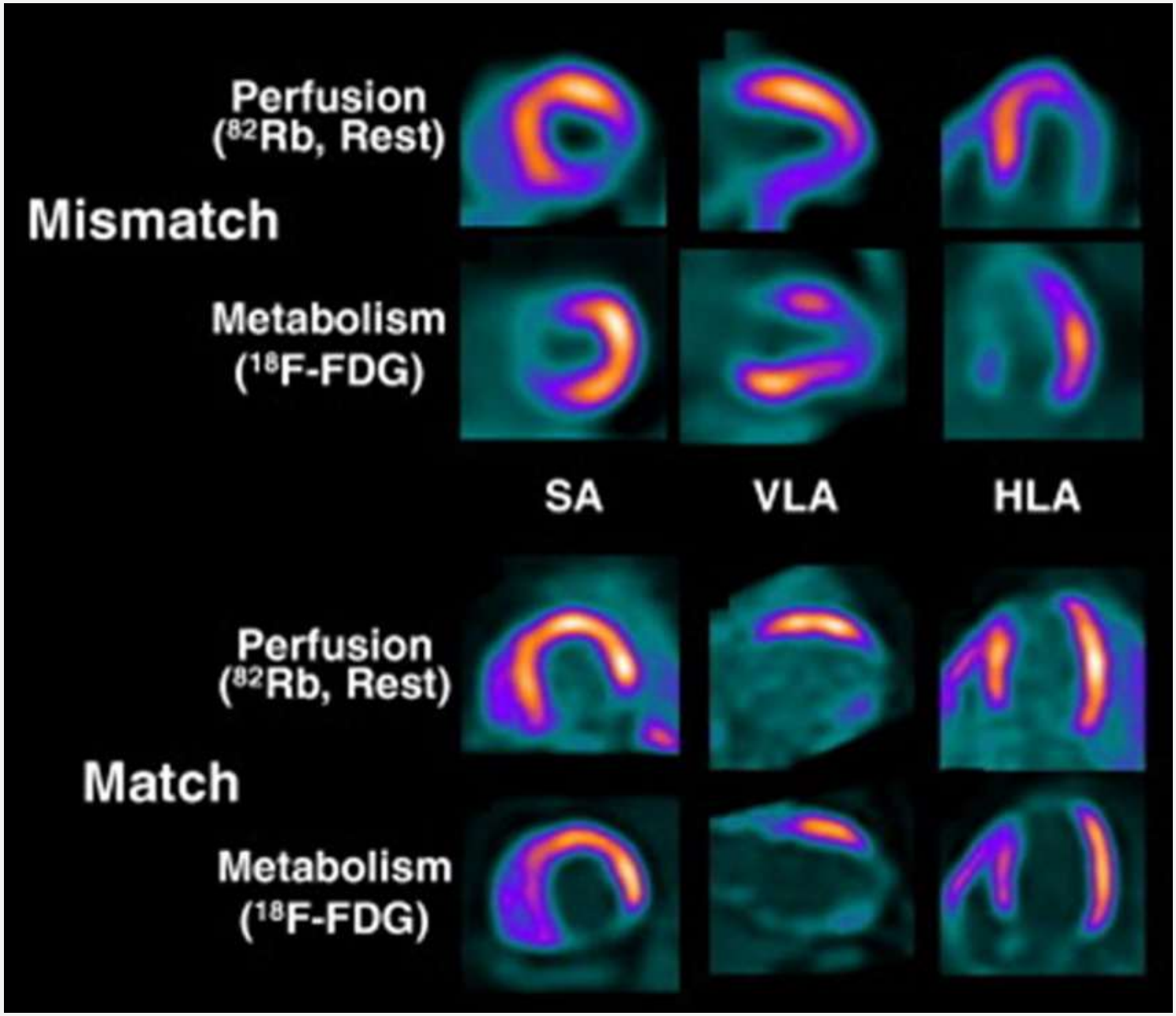
IREVERSIBLE ISCHEMIA INFARCTUS MYOCARDII



PERFUSION AND METABOLISM BY PET

- For the evaluation and quantitation of regional myocardial blood flow with PET, several tracers are available. Only rubidium-82 and N-13 ammonia are approved for clinical user. The initial distribution of these flow tracers in myocardium parallels the distribution of myocardial blood flow. Studies indicate that the most up-to-date PET imaging achieves both higher sensitivity and specificity for detection of coronary artery disease compared to gated Tc-99m-sestamibi SPECT imaging
- 18F-deoxyglucose (FDG) is an analog of glucose and is considered a marker of external glucose utilization. This tracer is transported into the myocyte by the same carrier as glucose and is phosphorylated to FDG-6-phosphate by the enzyme hexokinase

- For the detection of viable myocardium the most widespread approach is the evaluation of myocardial blood flow in conjunction with myocardial glucose uptake. With this protocol, three patterns are observed:
- normal blood flow with normal FDG uptake,
- reduced blood flow with normal or increased FDG uptake (flow metabolism mismatch)
- reduced blood flow with reduced FDG uptake (flow metabolism match).
- The pattern of mismatch between flow and metabolism detects reversibly dysfunctional myocardium (viable tissue), whereas the match pattern represents irreversibly dysfunctional myocardium (non-viable tissue).

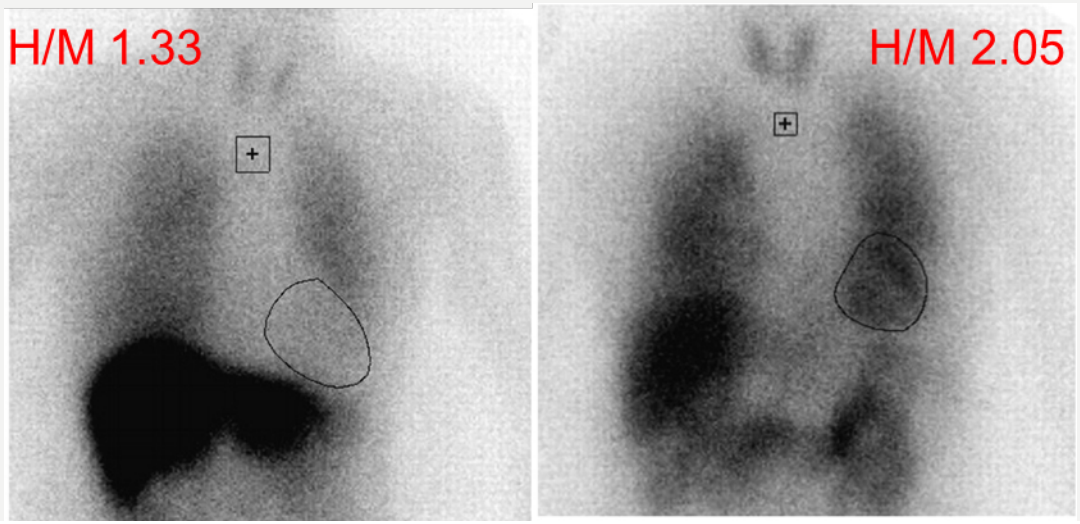

Perfusion
(82Rb, Rest)
Mismatch
Metabolism
(18F-FDG)
SA
VLA
HLA
Perfusion
(82Rb, Rest)
Match
Metabolism
(18F-FDG)

NEUROCARDIAC IMAGING

- Meta-iodo-benzylguanidine (MIBG) is a norepinephrine (noradrenaline) analogue and is taken up into vesicles within the presympathetic sympathetic nerve endings. It can be labeled with a variety of radionuclides, but for diagnostic purposes 1231 is usually used. Its main use is in diagnosing pheochromocytomas.
- However, it is also taken up by the left ventricle in proportion to the sympathetic nervous supply provided an insight into how beta-adrenergic blockers and heart failure affect the heart
- C-11-hydroxyephedrine with PET imaging (Presynaptic uptake-1 and storage of noradrenaline)

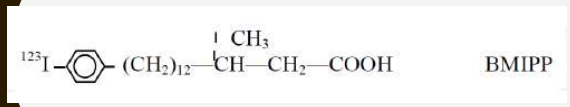
NEUROCARDIAC IMAGING

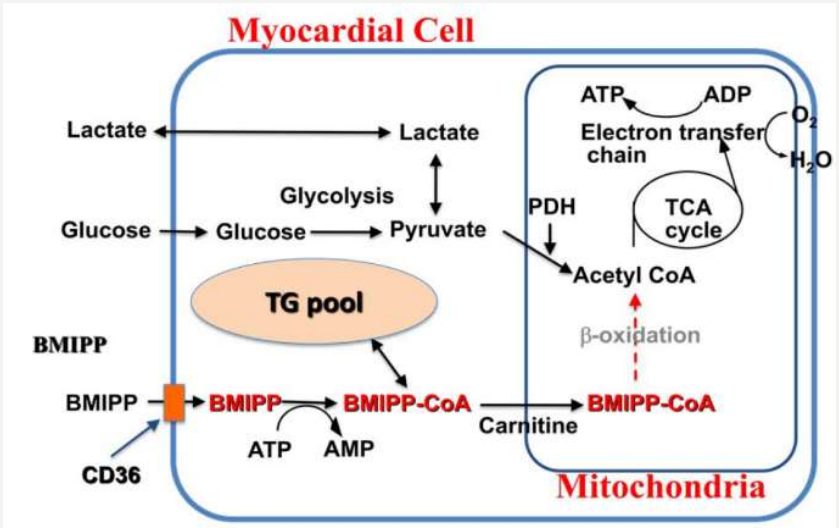
- I-123 MIBG for imaging of cardiac innervation could be extremely useful for the management of heart failure patients with regards to medical management as well as with the selection for expensive interventions such as implantable cardioverter-defibrillator (ICD) placement
- Uptake of MIBG in the heart, measured by the heart to-mediastinum activity ratio (H/M)



MYOCARDIAL METABOLISM WITH RADIOLABELED FATTY ACID ANALOGS

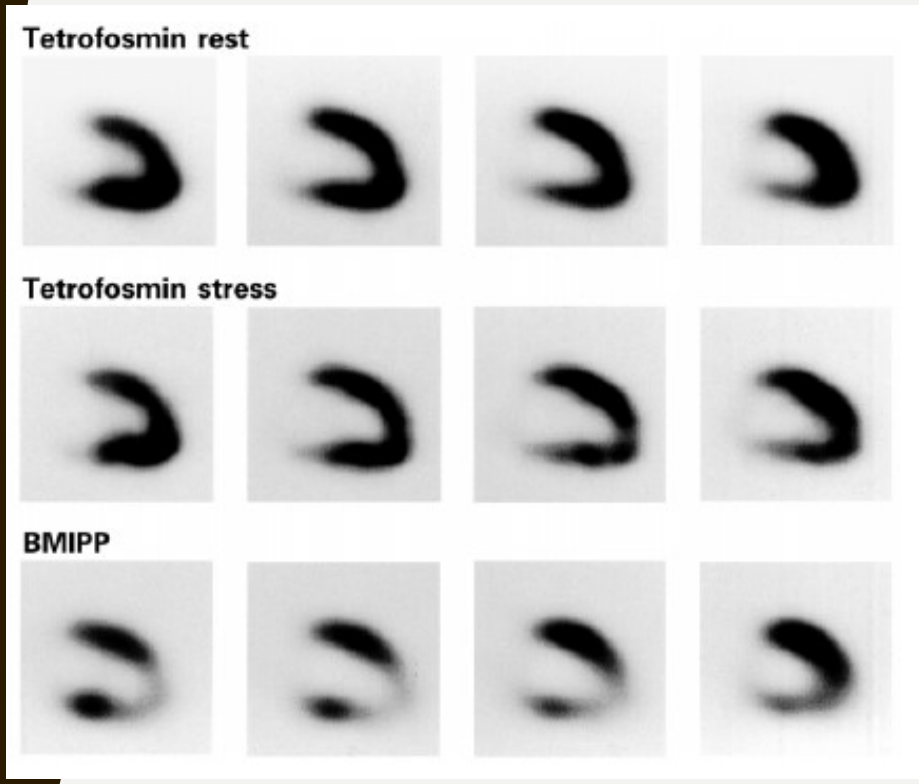
- Because fatty acids are the primary energy source in the myocardium, and a change in fatty acid oxidation is considered to be a sensitive indicator of myocardial ischemia
- single or multiple episodes of myocardial ischemia resulted in increased glucose uptake
- ^{123}I –fatty acid
- ^{11}C-palmitate





Myocardial Metabolism with Radiolabeled Fatty Acid Analogs

"**mismatch"** BMIPP and ^{99m}Tc-tetrofosmin



It may have a particular use in acute chest pain imaging as it seems to retain a "memory" for an ischemic event when conventional perfusion tracers may be normal.

Hence an ischemic event precipitated by coronary artery spasm will have an abnormal BMIPP image but a normal perfusion image both following stress and at rest.

INFARCT-AVID IMAGING AGENS

- **Tc-99m-pyrophosphate** is a bone-imaging agent. It is imaged at 4 h after intravenous injection. This tracer binds to microscopic calcium deposits in dead or dying cells and in severely ischemic cells. Consequently, it tends to overestimate infarct size .
- Its peak sensitivity is at 48 h after the infarction, with a useful range of 12 h to 8 days after infarction
- **In-111-labeled antimyosin Fab antibody imaging**-myocytes with disruption of cellular and sarcolemmal membranes expose the insoluble intracellular myosin to the antibodies, which are normally limited to the extracellular and intravascular space .
- The antimyosin antibodies can be administered any time after the the inferior wall, but a delay of 12–24 h is needed in order to image the resulting distribution, due to required blood pool clearance
- 96% sensitivity and a very high specificity. The time delay required for imaging has prevented this agent from becoming routinely used in clinical decision-making in the ER.

FIRST-PASS RADIONUCLIDE ANGIOGRAPHY

- Examination of the initial transit of a radionuclide bolus through the different major vascular compartments can provide information about the function of each chamber
- A bolus of radioactivity is injected into the venous system and multiple serial images are acquired that allows the radioactivity to be tracked from when it enters the RV to when it exits from the LV.
- measurements of global and regional RV and LV function can be performed. If there are atrial or ventricular shunts present, these may sometimes be detected and measured

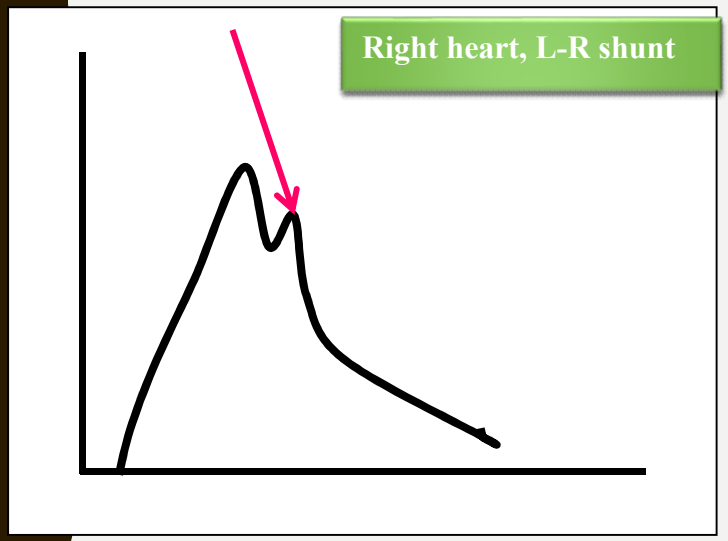
FIRST-PASS IMAGING

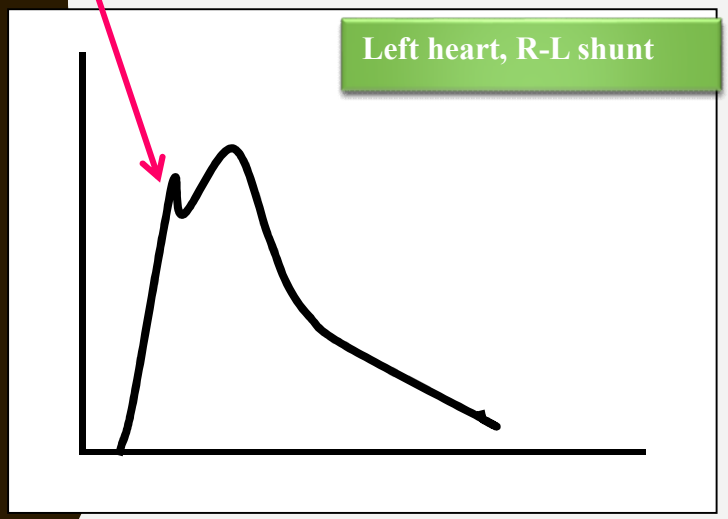
- Radiopharmaceutical: 10–25 mCi at rest and exercise of Tc-99m diethylaminetriaminepentaacetic acid (DTPA) or Tc-99m sestamibi or tetrofosmin
- The injection site should be in a large vein to allow rapid, compact bolus administration.
- Immediately following the bolus injection, 25– 100 frames/s are acquired in the ANT or 30° RAO position.

FIRST-PASS IMAGING

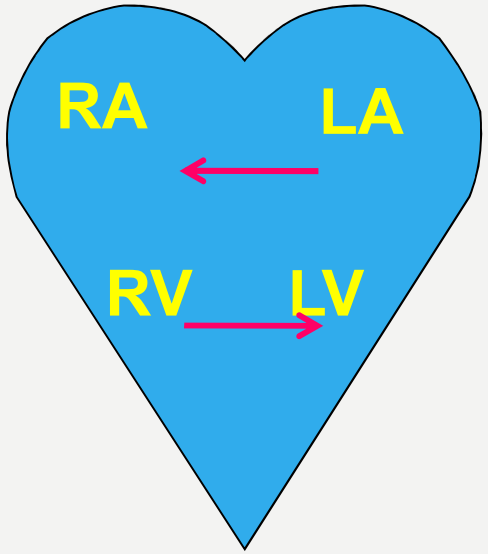
- Time–activity curves can be constructed for each chamber and, with background correction, ejection fractions obtained.
- It is also possible to measure "recirculation" through an interatrial or interventricular defect and calculate the size of the shunt.
- However, despite this method's attractions, it needs either a gamma camera with very high count rate capability or a multicrystal camera to be successful.
- As echocardiography and cardiac magnetic resonance (CMR) are now without question the modalities of choice for investigation of these problems, first-pass imaging has consequently become a technique carried out in only a few centers worldwide.

CARDIAC SHUNT EVALUATION





- in the presence of a right-to-left shunt, the pulmonary capillary system is bypassed and the particles enter the systemic circulation, where they are trapped in end organs such as the brain and the kidneys.



RADIONUCLIDE VENTRICULOGRAPHY (RNVG), EQUILIBRIUM RADIONUCLIDE VENTRICULOGRAPHY (ERNVG), MULTIGATED ACQUISITION (MUGA)

- echocardiography is the usual method of choice for assessing left ventricular function, RNVG studies remain very useful for a number of reasons.
- Information obtained by radionuclide evaluation of ventricular function

1. Global right and left ventricular EF
2. Regional right and left ventricular function
3. Absolute ventricular volumes
4. Systolic emptying and diastolic filling rates
5. Detection and quantitation of cardiac shunts

- LVEF is the amount of blood ejected per heart beat as a ratio of end-diastolic volume (EDV).

CLINICAL APPLICATIONS

- Monitoring Drug Therapy and Exposure to Cardiotoxins
- Assessment and Prognosis of Congestive Heart Failure
- Diagnosis of Coronary Artery Disease
- Assessment and Prognosis of Myocardial Infarction
- Preoperative Cardiac Risk Assessment
- Cardiac Transplant Evaluation
- Monitoring Valvular Heart Disease
- Myocardial Hypertrophy Evaluation
- Cardiac Shunt Evaluation

RADIOPHARMACEUTICALS

- the use of an intravascular tracer that equilibrates within the blood pool. The ease with which 99mTc-pertechnetate can be attached to the patient's own red blood cells (RBCs) makes labeled RBCs the preferred technique over labeled pooled human serum albumin. The usual adult dose is about 20-30 mCi.
- Three methods of labeling the RBCs are commonly used: in vivo, modified in vitro, and in vitro. All methods allow the 99mTc to bind irreversibly to the hemoglobin and remain in the intravascular space, allowing serial studies to be performed for up to 6 –8 h following labeling of the RBCs

IN VIVO TECHNIQUE

- The patient first receives stannous pyrophosphate intravenously. The stannous ion (tin) enters the RBCs and creates the optimal oxidation-reduction environment for reduction and binding of the 99mTc-pertechnetate, which is injected intravenously 15 –20 min later. Once the 99mTc-pertechnetate is in the RBCs, it is trapped inside by strong binding to the beta chain of the hemoglobin. Approximately 70% –80% of the 99mTc is attached to RBCs,

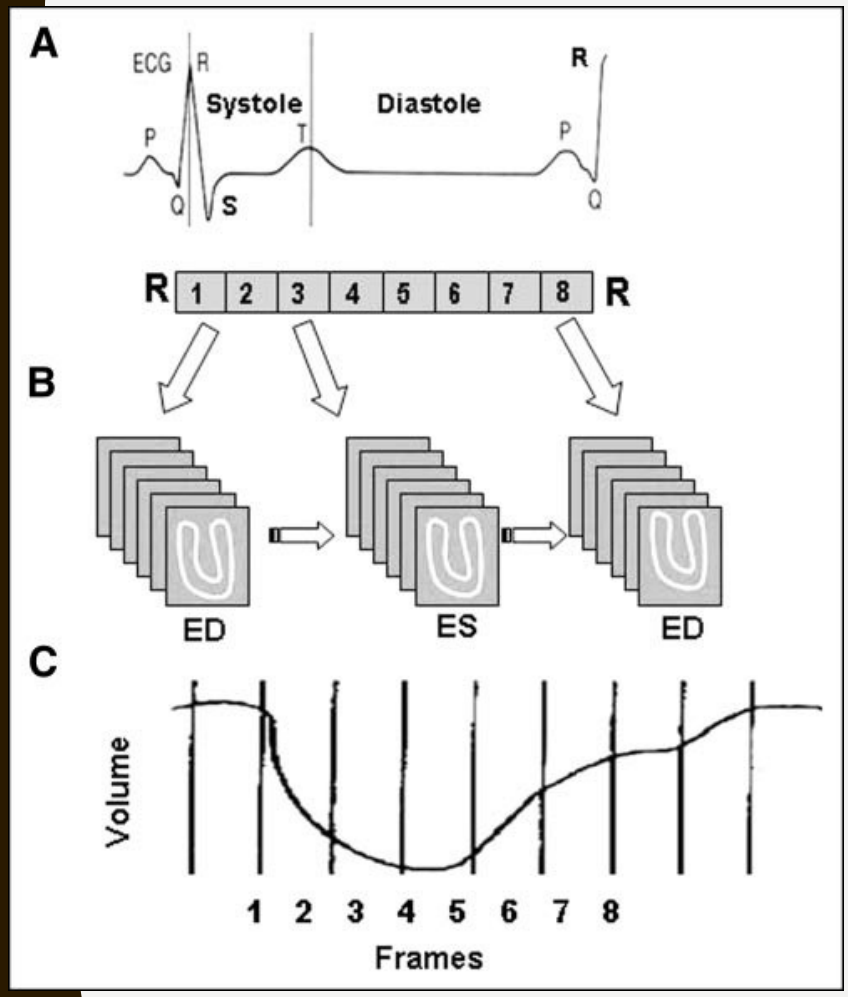
IN VITRO TECHNIQUE

- The labeling efficiency of this method approaches 100%. Patient blood is drawn and the RBCs are separated, washed with saline, and incubated first with stannous pyrophosphate and then with 99mTc-pertechnetate. The cells are washed with normal saline before and after each step to eliminate unbound material. Finally, the labeled cells are reinjected into the patient with very little or no free 99mTc-pertechnetate.

MODIFIED IN VITRO TECHNIQUE

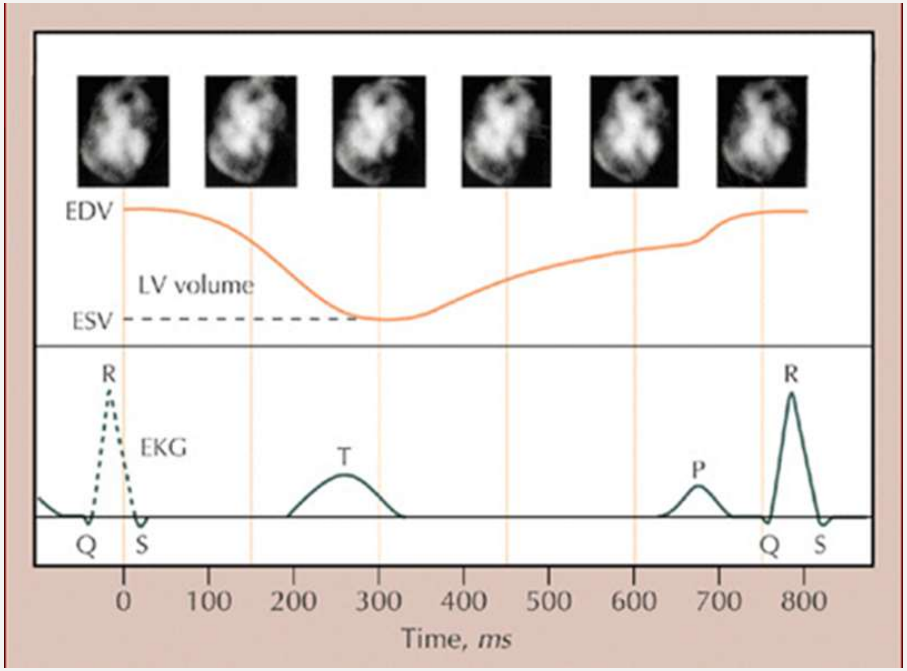
- This technique is used by many laboratories because it is easier to perform than the in vitro technique and results in a higher labeling efficiency than the in vivo method. As in the previous method, stannous pyrophosphate is first injected intravenously. Blood is then drawn from the patient into an anticoagulant treated, lead-shielded syringe containing 99mTc-pertechnetate.
- the syringe is placed in a mechanical rocker or rotated slowly by the technician for 10 –15 min, and the RBCs are then reinjected into the patient. Labeling efficiency is usually greater than 90%.

IMAGE ACQUISITION



- Assessing ejection fraction and regional wall motion requires measurement of volume changes and wall motion at different intervals throughout the cardiac cycle. The gamma camera is positioned in the "best septal" projection and imaging performed.
- The cardiac cycle is gated by simultaneously recording the ECG.
- Acquisition will then be triggered by each R-wave.
- The best septal views are left anterior oblique (LAO), anterior (ANT), which is 45° to the right from LAO, and left lateral (LLT), which is 45° to the left of LAO.

- By drawing a region of interest around, say, the left ventricle a time–activity curve can be obtained. After correcting for background activity, the LVEF can be obtained by measuring the total counts in a region of interest drawn around the left ventricle
- LVEF = (counts at end diastole− counts at end systole)/counts at end diastole.



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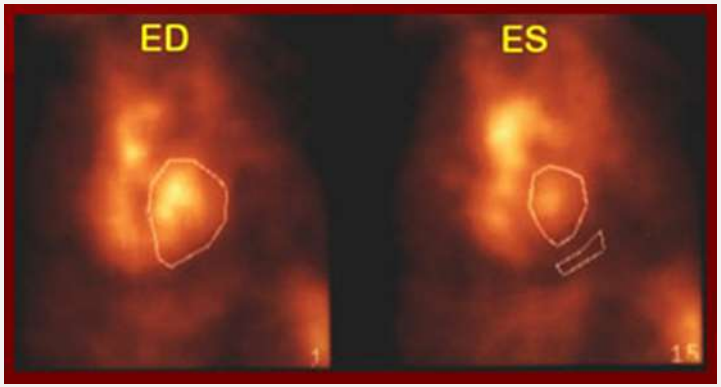
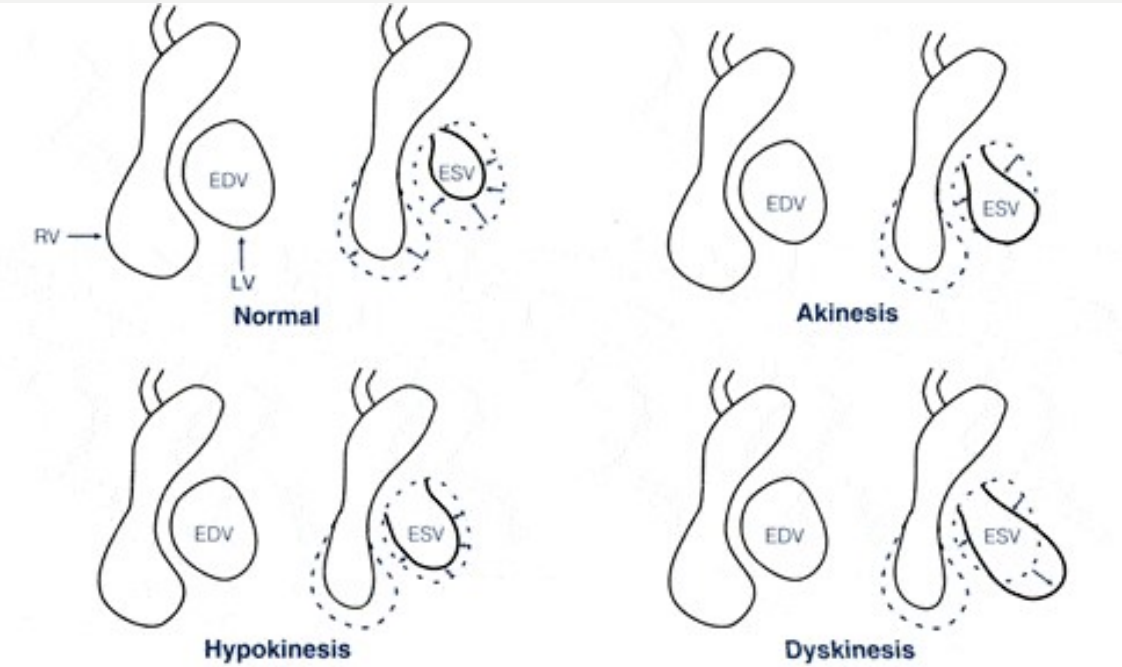


- Exercise radionuclide angiography is performed during supine or upright bicycle exercise.
- The patient is prepared for blood pressure and continuous ECG monitoring. Two or three ERNA are acquired in the resting state. Exercise is started at a workload of 25 W(150 kpm/min) and increased by 25 Wat the end of each 3- or 4-min exercise stage.

QUALITATIVE ASSESSMENT

- patients with normal LV contractility will have normal chamber size and volumes. In patients, with cardiac enlargement the apex may become hypokinetic in the absence of muscle damage, due to altered contractility and volume loading. Abnormal wall
- motion can be linked to a disease in the blood-supplying coronary artery. Patients with prior cardiac surgery, bundle branch block, or RV dilatation may have paradoxical septal motion in the absence of reduced coronary blood flow



EVALUATION OF ATTR CARDIAC AMYLOIDOSIS

- Systemic amyloidosis is disease caused by accumulation of amyloid fibrils sufficient to disrupt the inherent structure and function of the affected organ. Amyloid deposition can occur in almost any organ of the body; cardiac amyloid (CA) deposition inevitably results in a restrictive and/or infiltrative cardiomyopathy.
- Two precursor proteins are responsible for the majority of cases of CA, namely monoclonal immunoglobulin light chains in AL amyloidosis and transthyretin in ATTR amyloidosis.
- The use of 99mTc-labeled-pyrophosphate (Tc-PYP) for bone scintigraphy and myocardial uptake in patients with proven CA was first demonstrated 1983

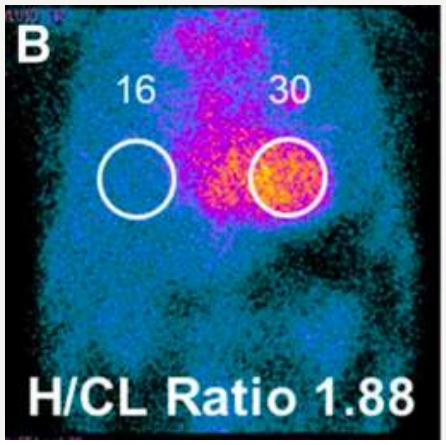
RADIOPHARMACEUTICALS

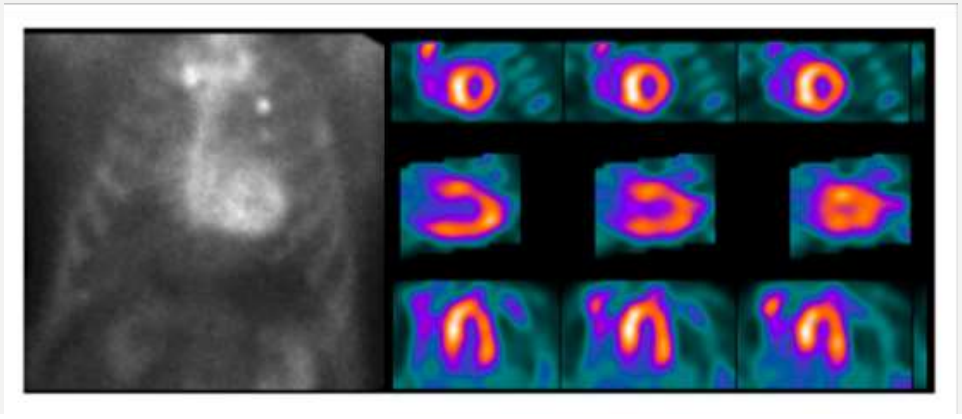
Radionuclide Tracers for Imaging of Amyloidosis

Tracer	Molecular target	Disease target
SPECT tracers		
Bone-seeking radiotracers	Phosphate binders	ATTR
^{99m}Tc-pyrophosphate		
^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid		
^{99m}Tc-hydroxymethylene diphosphonate		
Other radiotracers		
^{123}I-serum amyloid protein	Serum amyloid P	All amyloidoses
^{123}I-aprotinin	Serum protease inhibitor, amyloid binder	All amyloidoses
PET tracers		
Thioflavin-T derivatives	All amyloid fibrils (β-structure and side chains)	AL and ATTR
^{18}F-florbetapir		
^{18}F-florbetaben		
^{18}F-flutemetamol		
^{11}C-Pittsburgh compound B		
^{18}F-sodium fluoride	Microcalcification	ATTR
^{124}I-m11-1F4 monoclonal antibody	Immunoglobulin ALs	AL

CARDIAC SCINTIGRAPHY

- had a 100% specificity and positive predictive value for ATTR cardiac amyloidosis if there are combined findings of grade 2 or 3 myocardial radiotracer uptake on cardiac scintigraphy and the absence of monoclonal protein in serum or urine
- **Perugini score:** The Perugini grading scale is a semi-quantitative method of scoring cardiac uptake following injection of 99mTc-DPD, 99mTc-Pyrophosphate or 99mTc-HMDP scintigraphy in the investigation of cardiac amyloidosis (particularly ATTR amyloidosis). The grading scale visually compares tracer uptake in the myocardium and ribs





EVALUATION OF ATTR CARDIAC AMYLOIDOSIS