Versatility of Stress PET

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Introduction:- CAD

- Coronary artery disease (CAD) is complex with multifactorial etiology.

- CAD is the leading cause of mortality and morbidity worldwide.

- Although coronary angiography remains the "gold standard" for the detection and assessment of severity of CAD, various noninvasive imaging studies offer high sensitivity and specificity for CAD diagnosis and risk stratification and provide guidance for revascularization.

Introduction:- PET

- During the last few decades, PET has significantly contributed to improve our understanding of the heart physiology and pathophysiology.

- Initially, it emerged as a powerful investigative tool that allowed in vivo quantification of physiologic processes, including myocardial perfusion and metabolism, neuronal and receptor function, and molecularly targeted oncologic imaging.

Introduction:- PET

- Yet, similar to oncologic and neurology application of PET, Cardiac PET struggled to gain acceptance and widespread application due to its increased cost and slow reimbursement.

- Fortunately, we are now in a much better era, with the exponential growth in the number of PET/CT systems and the FDA approval if PET radiopharmaceutical for cardiac imaging.

Introduction:- Cardiac PET

- PET has proven to be a powerful and efficient noninvasive imaging modality to evaluate regional myocardial perfusion in patients with known or suspected CAD.

- Several technical advantages account for the improved diagnostic advantage of PET.

- Also, the use of radiopharmaceuticals with short half life allows fast, sequential same-day assessment of regional myocardial perfusion
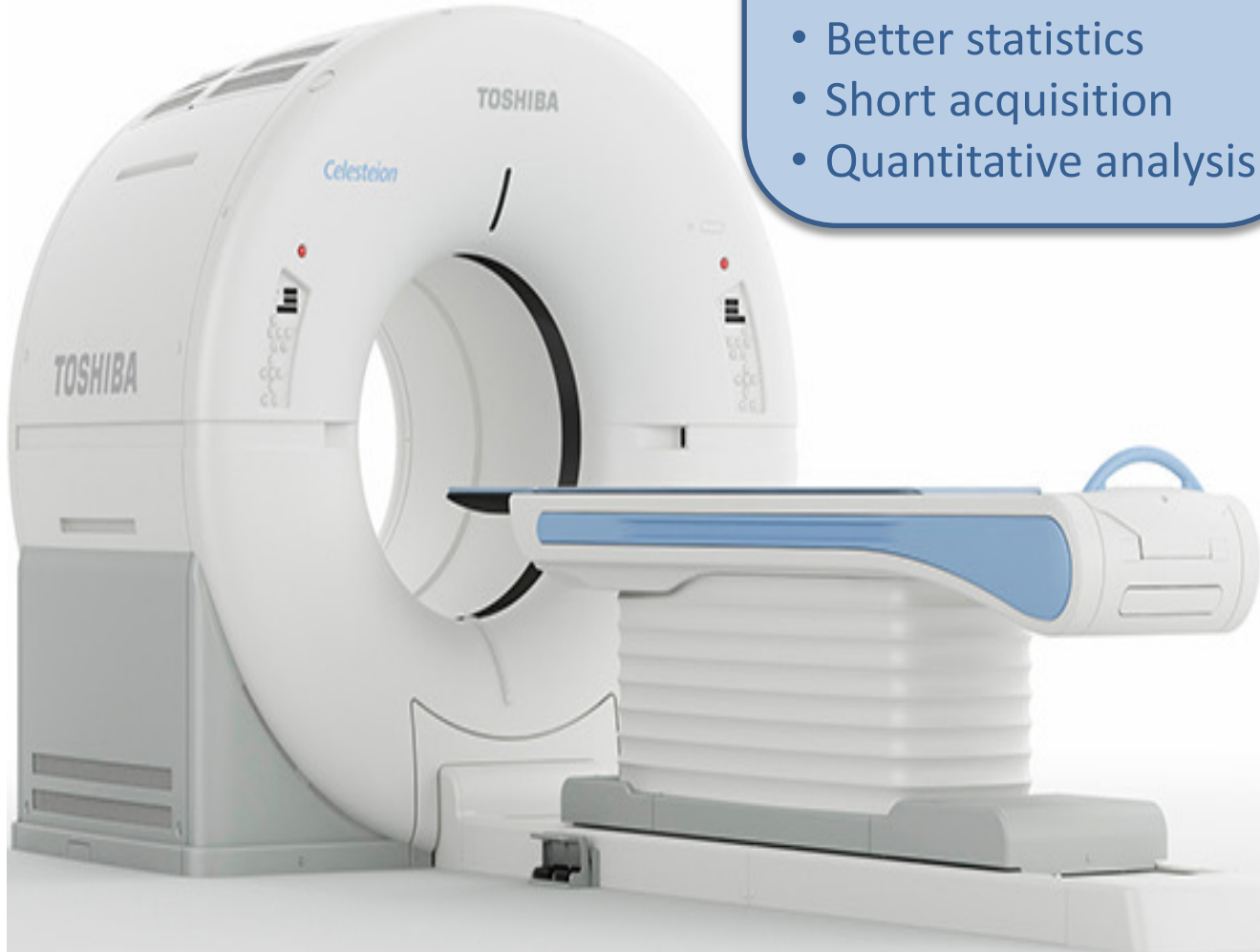
Introduction:- Myocardial Perfusion Imaging

- Myocardial perfusion imaging reflects relative differences in the distribution of blood flow in the myocardium at rest and during stress, which may be produced by exercise or by pharmacological means.

- At rest, myocardial arterioles distal to a significant epicardial coronary stenosis are dilated by autoregulation to maintain myocardial blood flow.

- At Stress, there is significant vasodilation of normal vascular beds and little additional dilation in vascular beds distal to significant coronary stenoses, leading to differences in perfusion, appearing as "defects" in myocardial perfusion images.
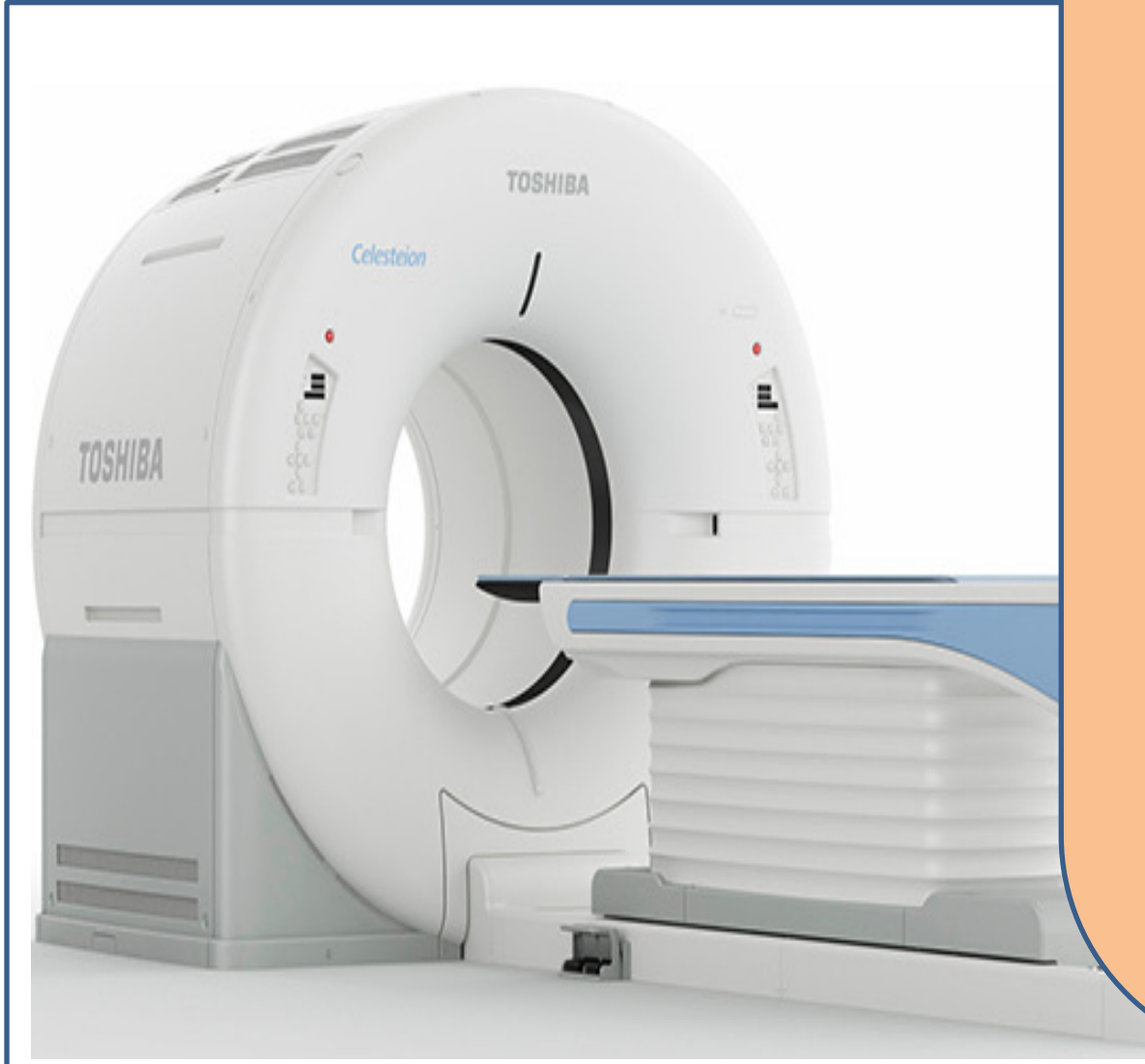
PET/CT

SPECT/CT

- Full detectors ring
- Better crystals
- Inherent electronic collimation
- Better resolution
- Better statistics
- Short acquisition
- Quantitative analysis

PET/CT

Advantages of PET and PET/CT Myocardial Perfusion Imaging

- **High diagnostic accuracy**: high sensitivity and specificity for multivessel CAD that outperforms other noninvasive techniques.
- **Radiation Exposure**: lower than most other radiation –based cardiac studies.
- **High quality images**: statistically robust images with high spatial and contrast resolution with reliable attenuation and scatter correction.
- **Short acquisition protocol**: Rest and stress studies can be completed in less than an hour (Rb-82), adding logistic and convenience advantage
- **Myocardial blood flow quantification** at rest and stress allows measurement in mL/min per gram of myocardial flow reserve and improves accuracy, risk stratification, and selection of patients for interventions
- Strong **prognostic** power for **risk stratification** in multiple patient populations (e.g., obese, renal dysfunction), especially when absolute myocardial perfusion quantification is included
- Allows detection of **coronary artery calcification** without additional imaging

J Nucl Med . **2016;57:1654-1656.**

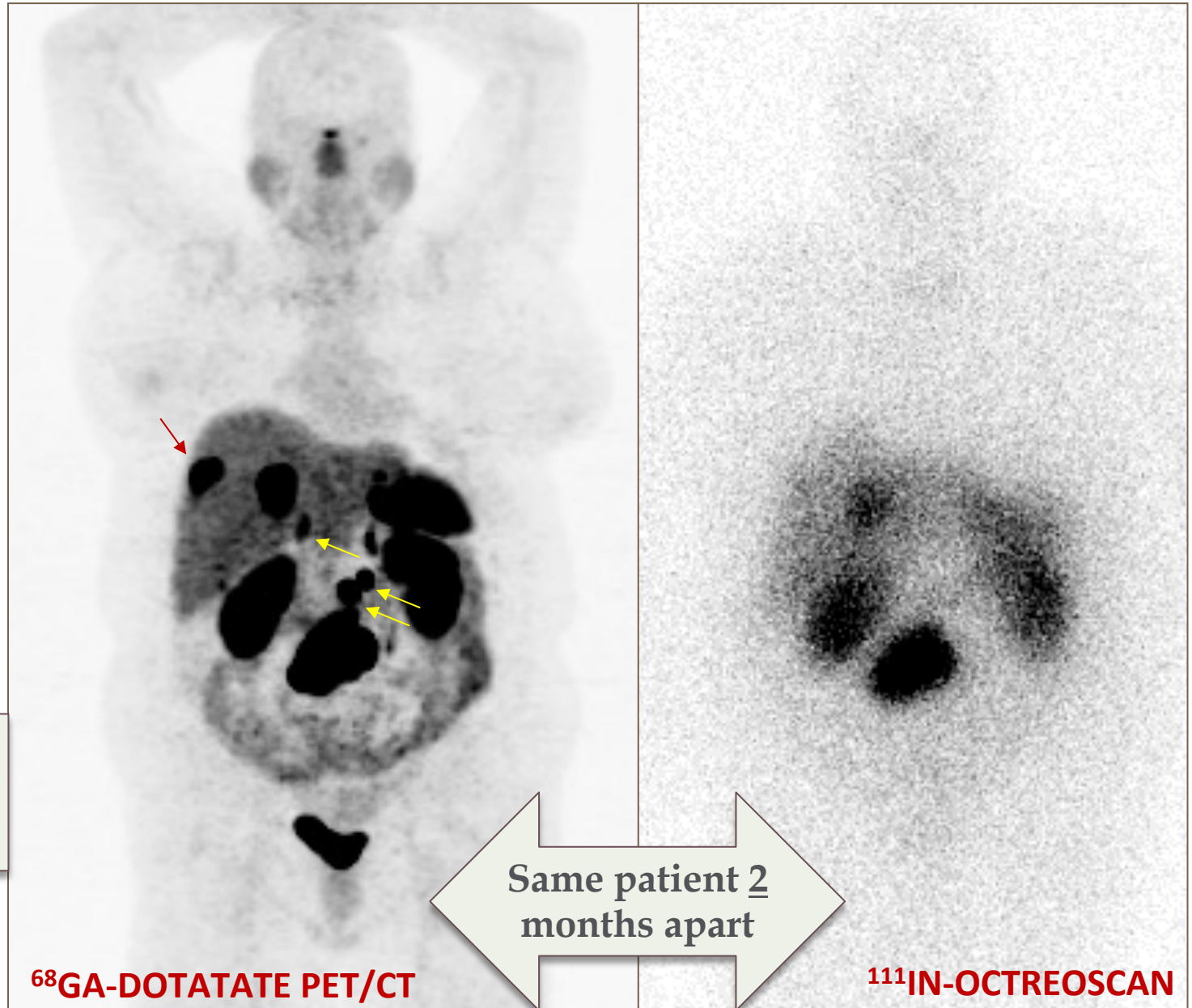# ^{68}Ga-DOTATATE versus ^{111}In-Octreoscan

^{68}Ga-DOTATATE PET/CT:

Better image quality

Better detectability

Better accuracy

Arrows indicate lesions seen in DOTATATE and not appreciated in Octreoscan

Same patient 2 months apart

^{68}GA-DOTATATE PET/CT

^{111}IN-OCTREOSCAN

Radiopharmaceuticals

	N-13 ammonia	Rb-82 Chloride
Advantage	Preferred PET MPI radiotracer due to superior imaging characteristics	Widely available due to the availability of the onsite generator system
Half life	10 minutes	76 seconds
Production	Cyclotron	Strontium-82/Rb-82 generator system
extraction rates	70-80%	60%
Myocardial uptake mechanism	Diffusion across cell membrane → converted to N-13 glutamine by glutamine synthetase → incorporated into amino acids and trapped within tissues.	It is a potassium analogue monovalent cation and true analog of potassium, taken up into the myocardium by active transport through the Na+/K ATPase pump

Radiation Dose

N-13 Ammonia rest (20-25 mCi) ➔ 1.35-1.85 mSv

N13 Ammonia stress(20-35 mCi➔ 1.35-2.59

Total effective dose 2.7-4.48 mSv

Rb-82 rest or stress scan 60 mCi=2.66 mSv

Total effective dose =5.24

Tc-99m Sestamibi rest 8 mCi ➔ 2.4 mSv

Tc-99m Sestamibi stress 22 mCi ➔ 6.6 mSv

Total effective Dose (Tc-99m)➔ 9.0 mSv,

PET/CT versus SPECT/CT

- Many studies have proved superior diagnostic accuracy of PET/CT over SPECT/CT in assessment of CAD.

	Number of Patients	SPECT Sensitivity	PET sensitivity	SPECT specificity	PET specificity
Go, et al.*	202	76	93	80	78
Stewart et al.**	81	84	86	53	83
Bateman et al***		62	79	17	44

*J Nucl Med. 1990;31:1899–1905
**Am J Cardiol. 1991;67:1303–1310
- ***J Nucl Cardiol. 2006;13:24–33

PET/CT versus SPECT/CT

- A meta-analysis included **15** PET and **8** SPECT (**1344** and **1755** patients)
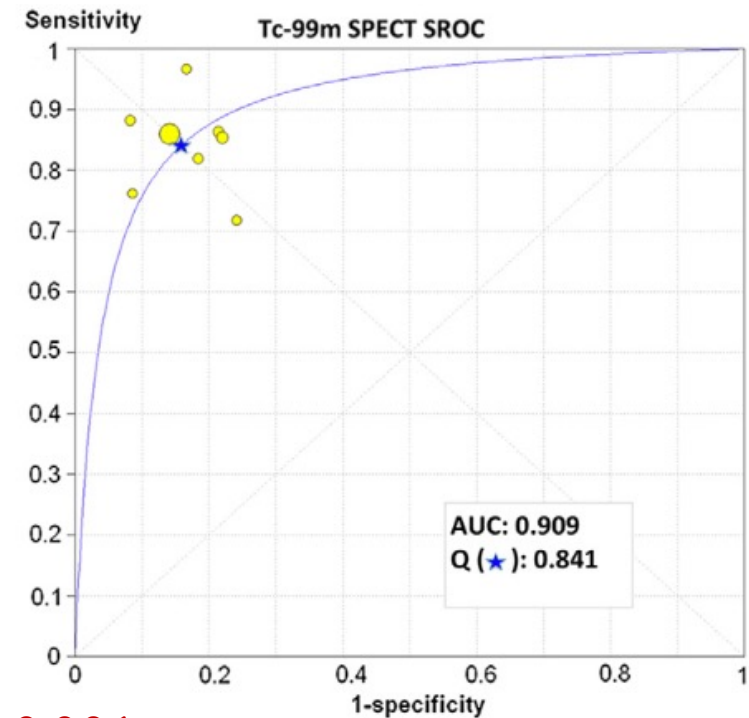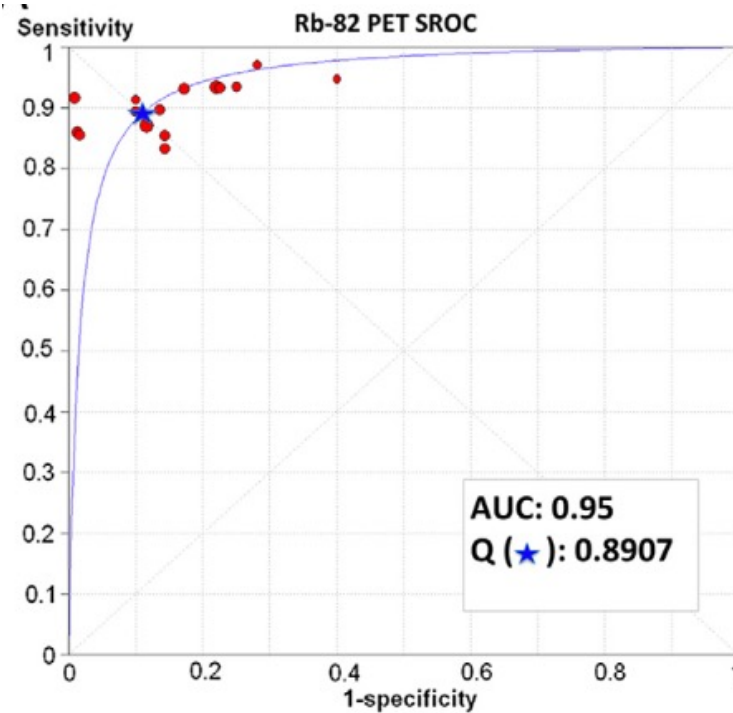
P-value < 0.001

Indications of PET Myocardial perfusion Imaging

Preferred Indication: *("First-Line Test")*

- Patients meeting the criteria for cardiac stress imaging who are unable to complete a diagnostic-level exercise stress imaging study.

Recommended Indications: *(Patients who meet appropriate criteria for a stress imaging test who also meet one of the conditions below)*

- Inconclusive, poor quality, or discordant prior stress imaging studies

- Patient body characteristic preventing conclusive stress imaging by other techniques

- High-risk patients in whom diagnostic accuracy has greater clinical implications

- Young patients with anticipated repeat examinations adding to lifetime radiation exposure

- Patients in whom absolute myocardial blood flow measurements are clinically important

Patient Preparation

- No Caffeine (12-24 hours prior to exam)

- No theophylline (48 hours prior to exam)

- NPO (6 hours prior to exam)
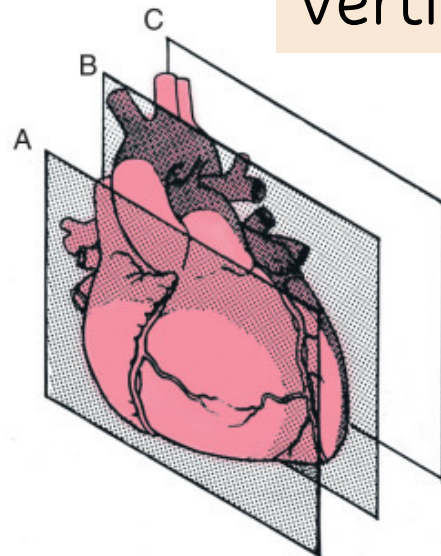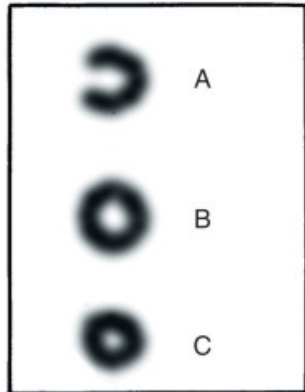
- 20-22 gauge IV (preferably in forearm

Technique

CT → DELAY → Rest Perfusion → STRESS → DELAY → Stress Perfusion → CT → Ca++ Score

Regadenoson*

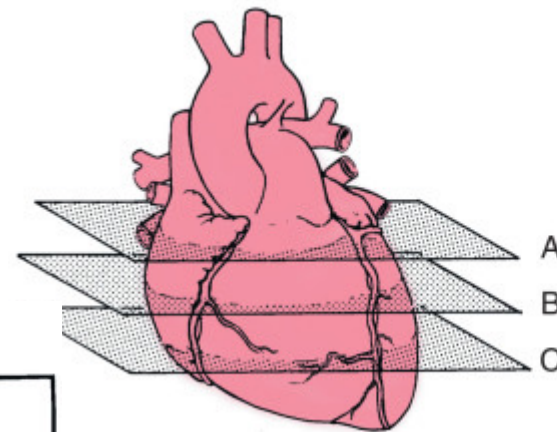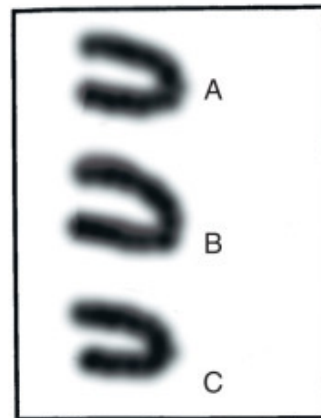90-120s after ⁸²Rb-

3-5 m after ¹³N-Ammonia
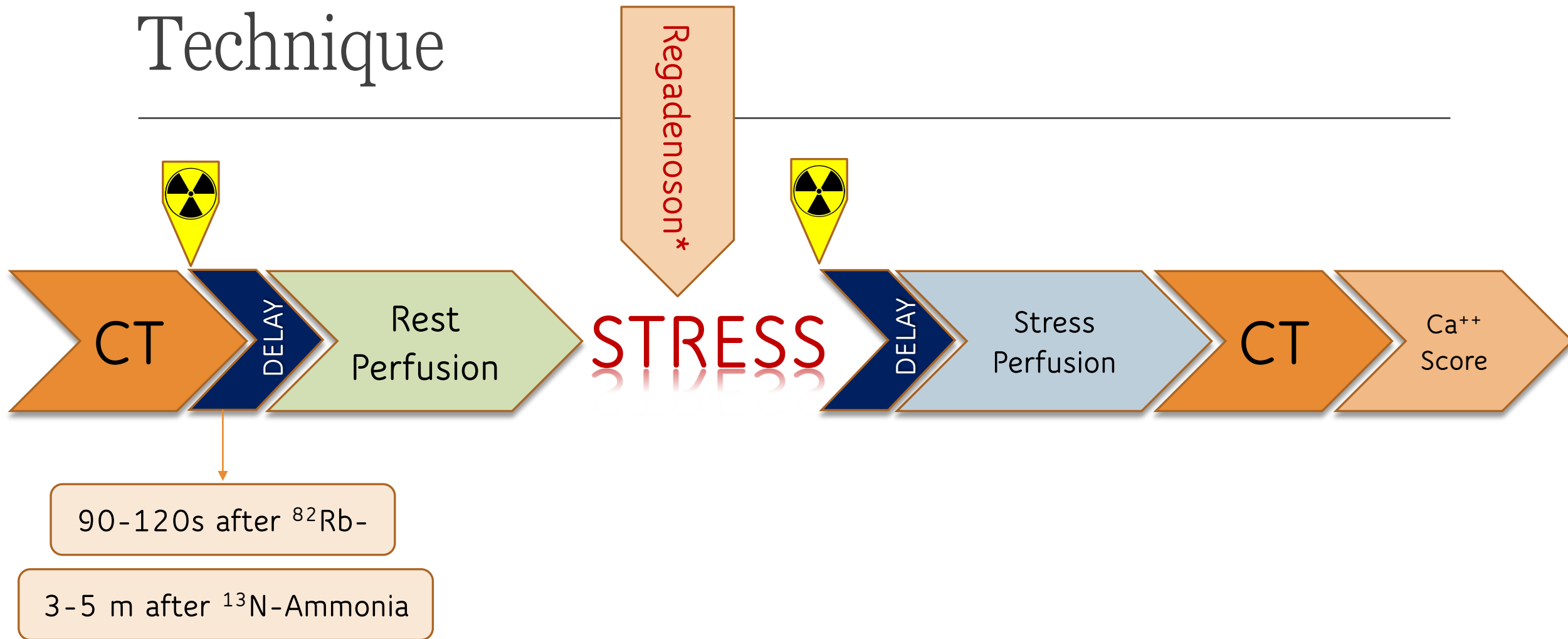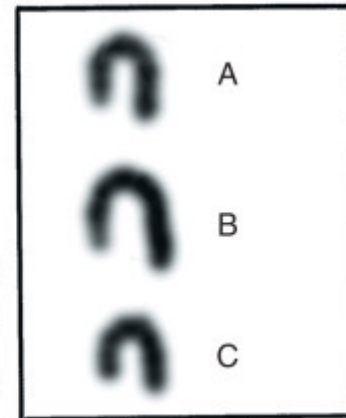
*Can be reversed with 125 mg Aminophylline

Standard Display
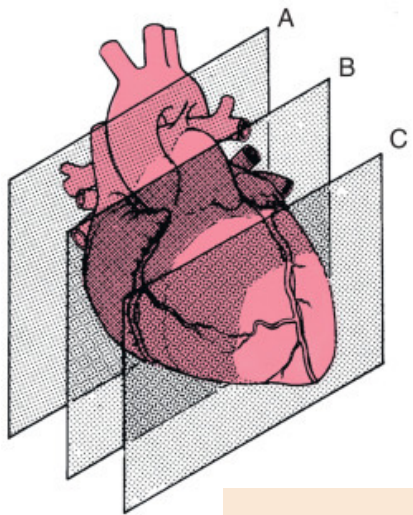
Short Axis

Vertical

Horizontal

Polar Map (Bull's Eye)

- The heart is viewed from its apex and opened up like an umbrella.

- Semiquantitative methods are applied to the polar map of the perfusion data and compare the radiopharmaceutical distribution of patient to a gender-matched normal database.

- Regional activity less than that expected in a normal population identifies a perfusion deficit and is displayed as such on the polar map.
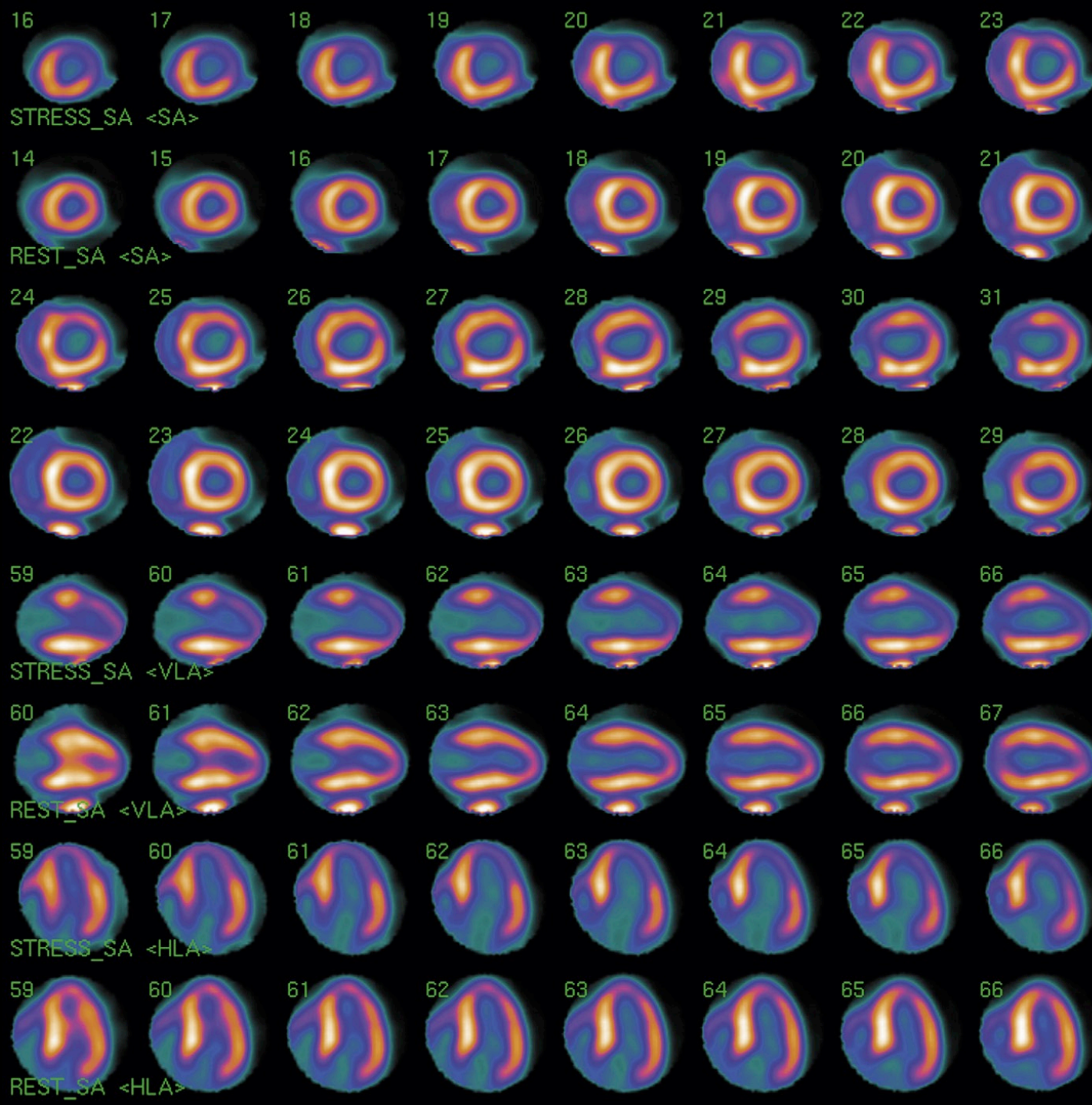
Polar Map (Bull's Eye)
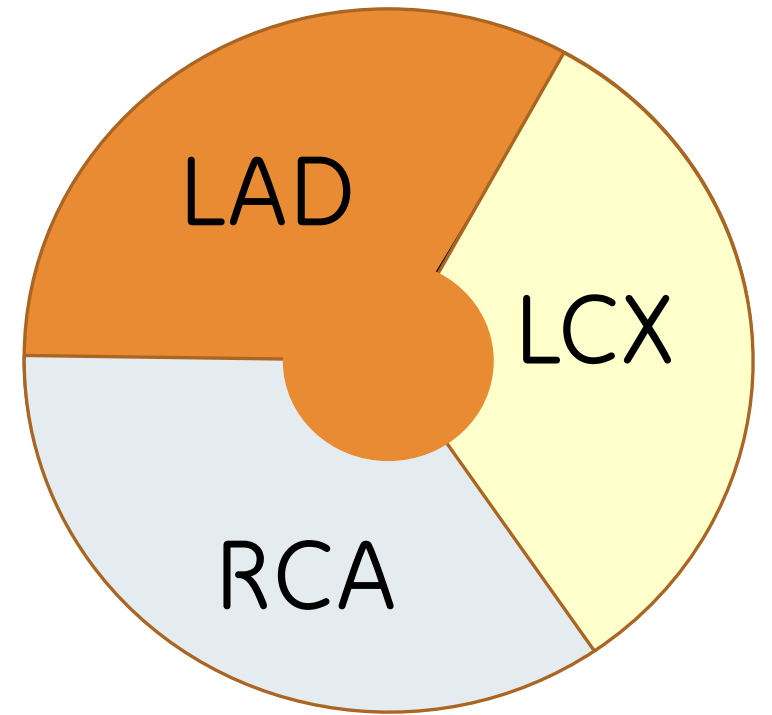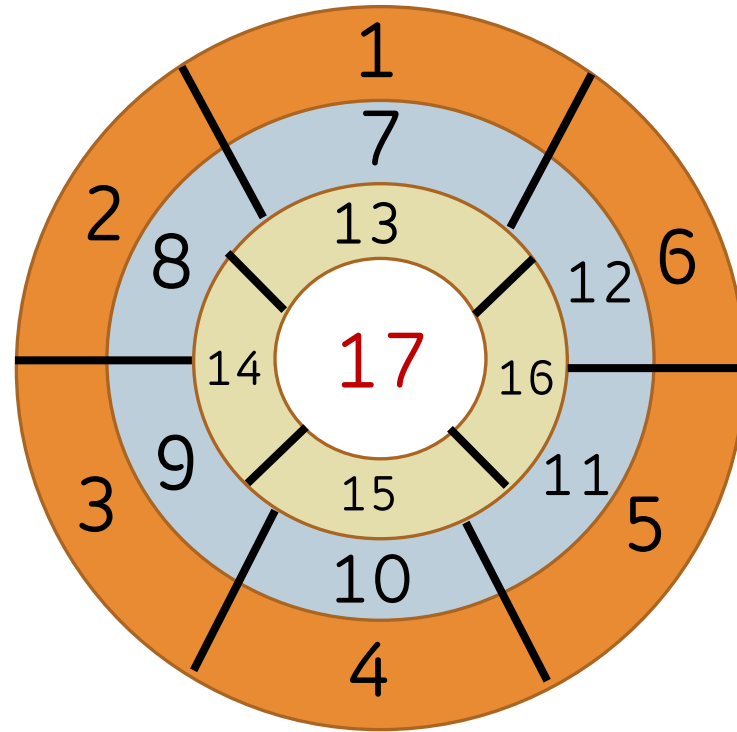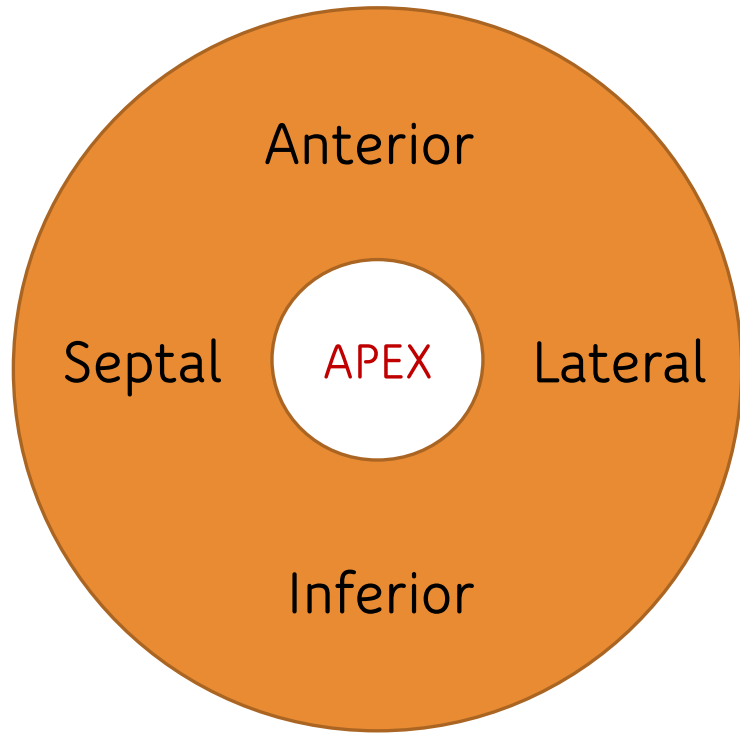
Rb-82
stress MPI

Reversible defect (ISCHEMIA) anterolateral wall and apical wall

Multi-vessel Disease

- Qualitative assessment of SPECT and often times PET images results in identification of myocardial territory supplied by the most severe stenosis.

- This is based on the fact that visual assessment is based on identifying differential heterogenous uptake and limit the ability to delineate the presence of multivessel CAD where balanced reductions in myocardial blood flow present.
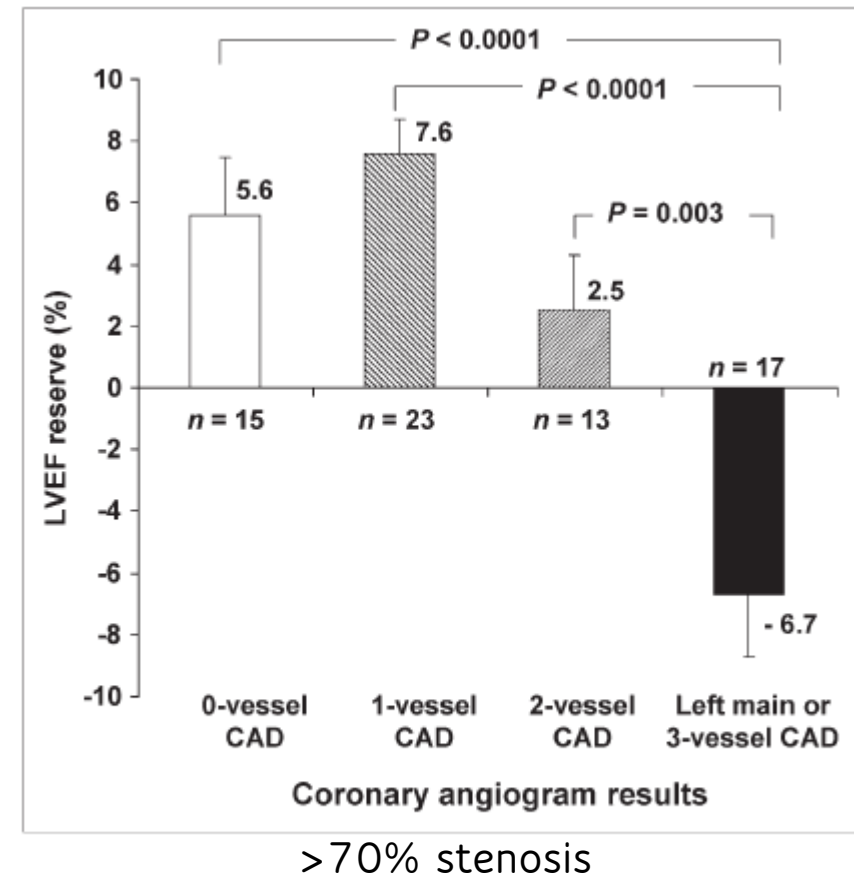
Multi-vessel Disease

- An advantage of ECG-gated PET is its unique ability to assess LV function at rest and during peak stress (versus post-stress assessment with gated SPECT).

- Patients without significant CAD or with 1-vessel disease show a normal increase in LVEF.
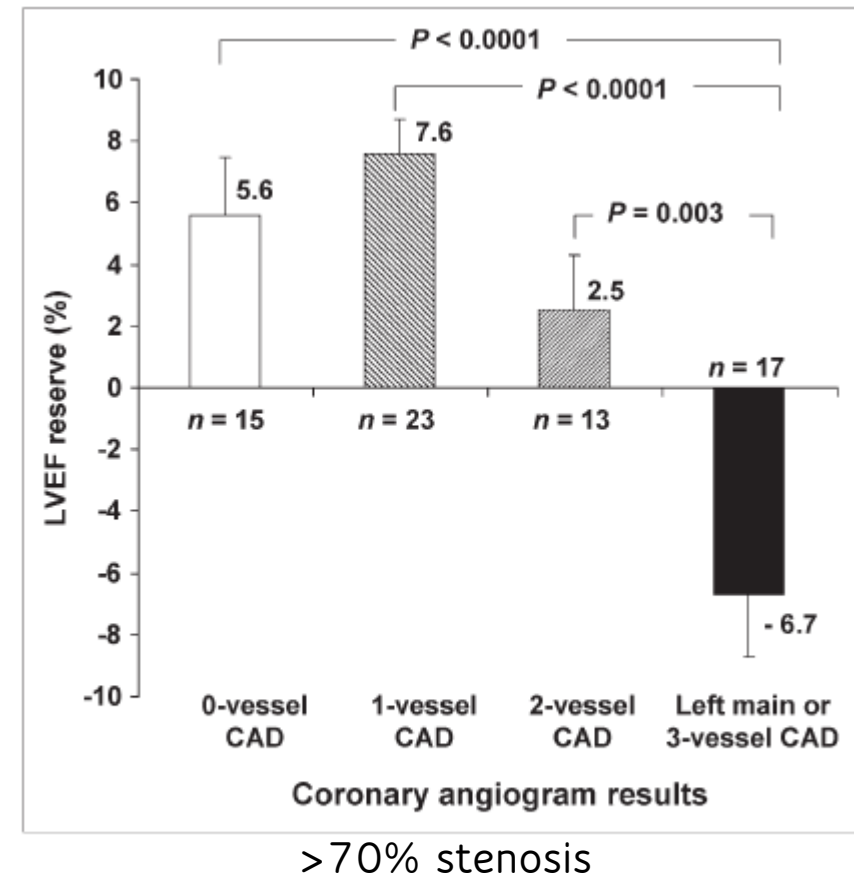
Multi-vessel Disease

- In patients with 3-vessel CAD or left main CAD, LVEF during peak stress decreases even in the absence of apparent perfusion abnormalities.

>70% stenosis

Multi-vessel Disease

- NPV of a delta increase in LVEF (from rest to peak stress) of 5% to exclude the presence 3-vessel or left main CAD is 97% .
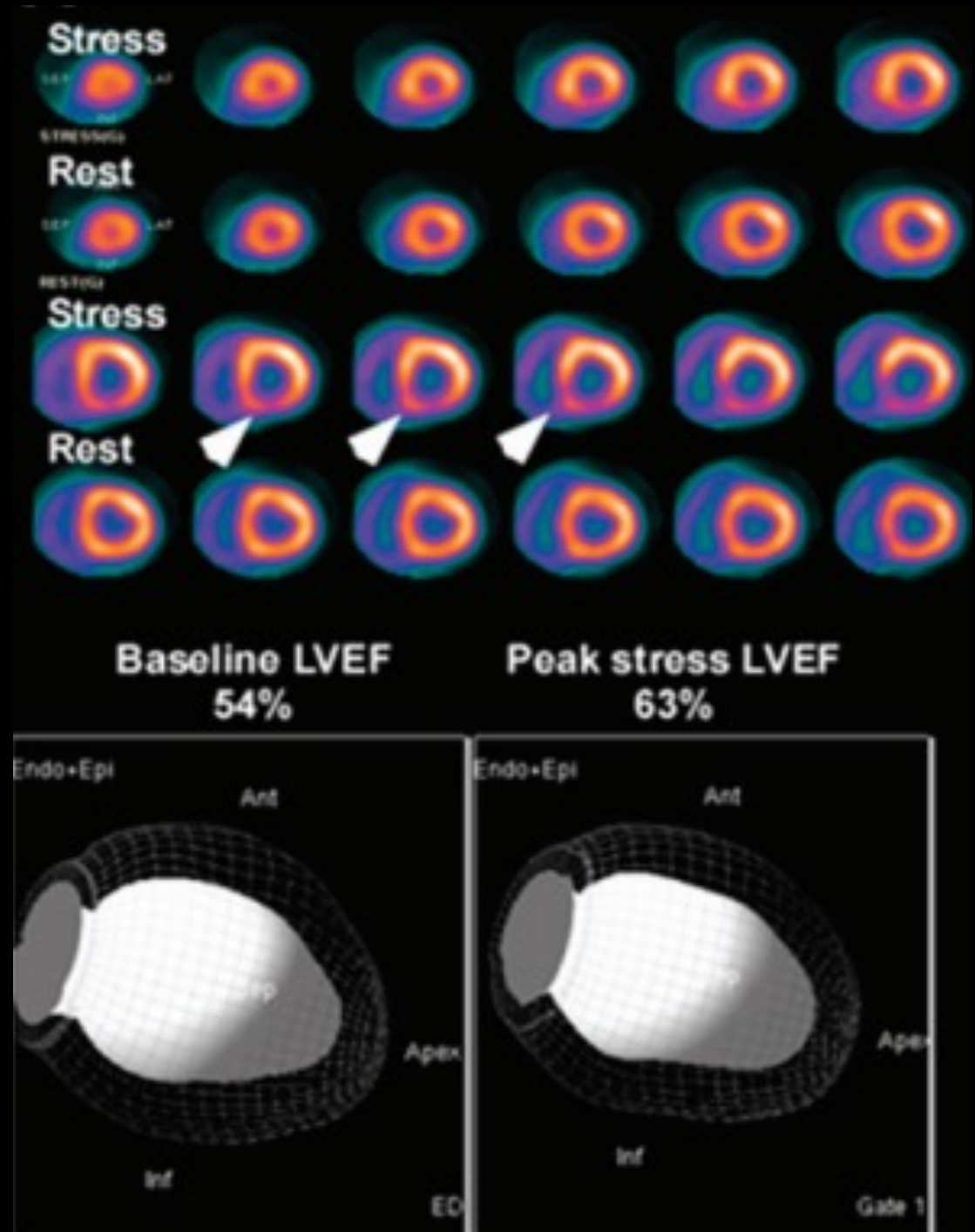

>70% stenosis

82Rb Myocardial Perfusion PET

Reversible defect at the inferior wall (RCA territory), Arrowhead.
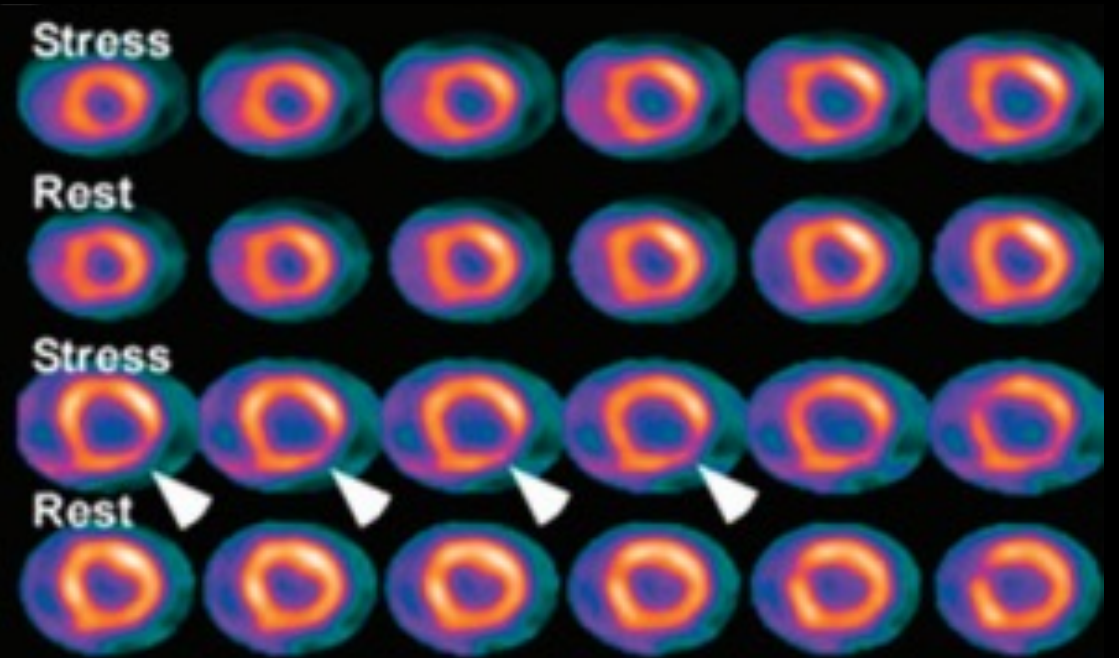
There was 9% increase in EF during peak stress

82Rb Myocardial Perfusion PET

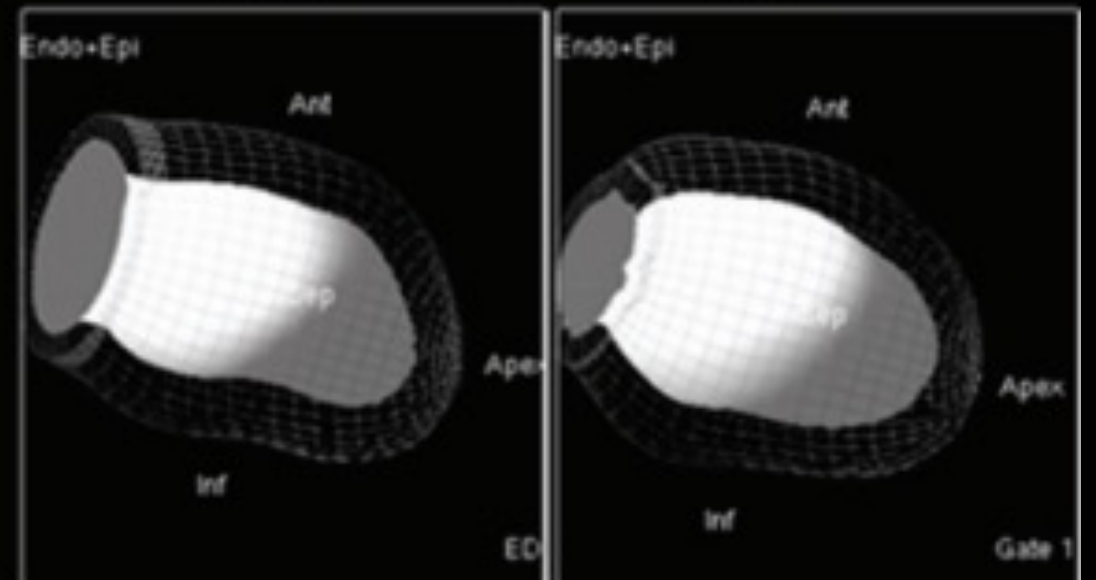Reversible defect at the inferolateral wall (LCX territory), Arrowhead.

There was 11% reduction in EF during peak stress

Angiography confirmed Multivessel CAD

Multi-vessel Disease: CFR

- Another unique advantage of cardiac PET is the ability to perform Quantitative analysis of PET myocardial perfusion data to calculate the **Myocardial Blood Flow (MBF)** (in mL/min/g) and **Coronary Flow Reserve (CFR).**

CFR: Peak Stress MBF/ Rest MBF

Multi-vessel Disease: CFR

- **MBF** and **CFR** help overcome the limitations of relative perfusion assessments with PET to detect multivessel CAD.

- Physiologic reference ranges for rest and stress MBF and MFR vary by tracer and may be slightly higher for ^{82}Rb than for ^{13}N-ammonia.

Multi-vessel Disease: CFR

	^{13}N-Ammonia	^{82}Rb
Rest MBF	0.71 (0.61-1.1)	0.74 (0.69-1.15)
Stress MBF	2.58 (1.86-4.33)	2.86 (2.5-3.82)
MFR	3.54 (3.16-4.8)	4.07 (3.88-4.47)

Weighted mean based on 23 studies including 363 healthy subjects for ^{13}N-ammonia and 8 studies including 382 healthy subjects using ^{82}RB

PET

Unadjusted predicted probability (red line) of 3 vessel CAD at different and MFR

When MFR is low, the likelihood of 3-vessel CAD increases

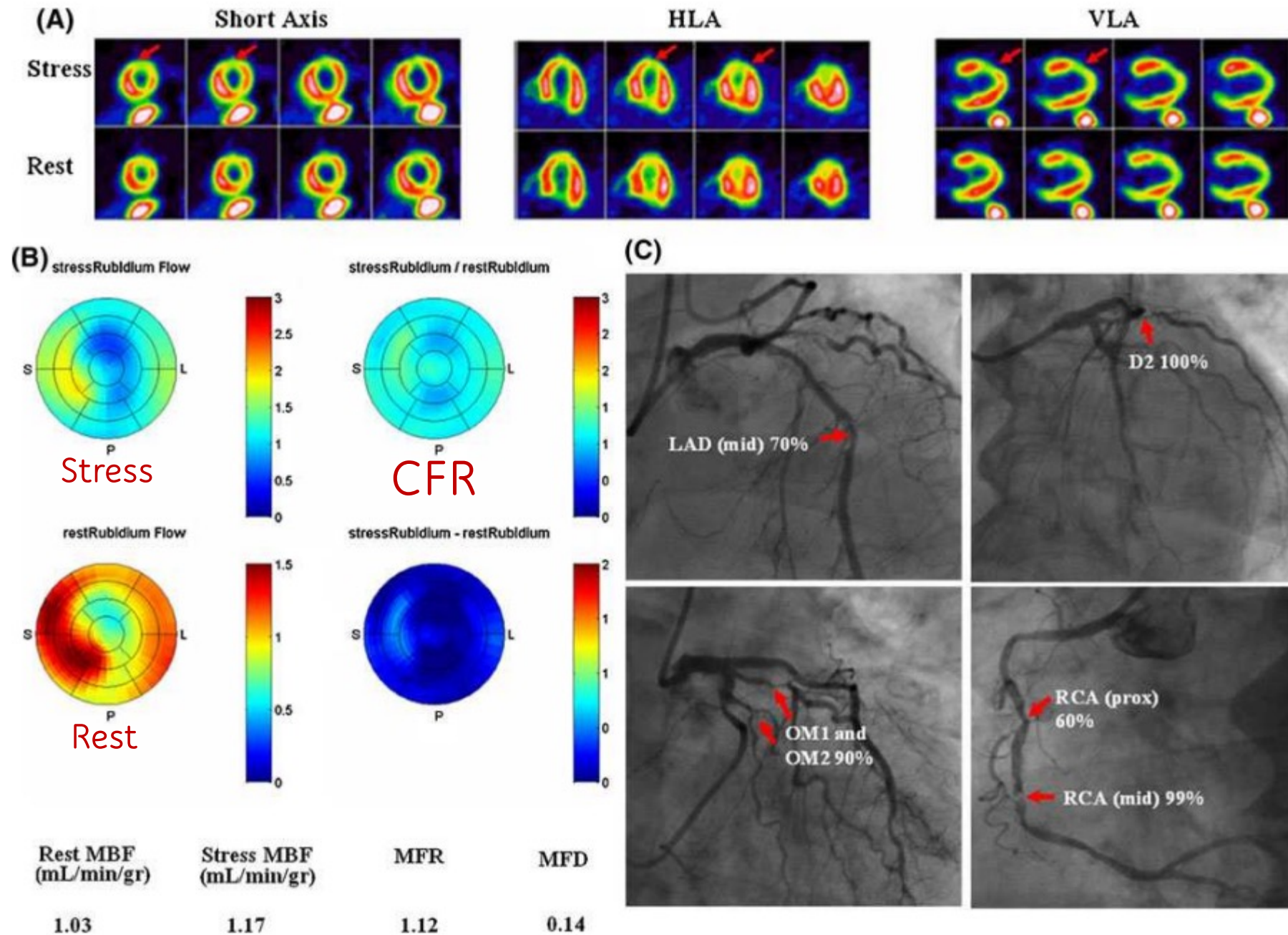Ziadi MC et al. J Nucl Cardiol 2012; 19: 670-680
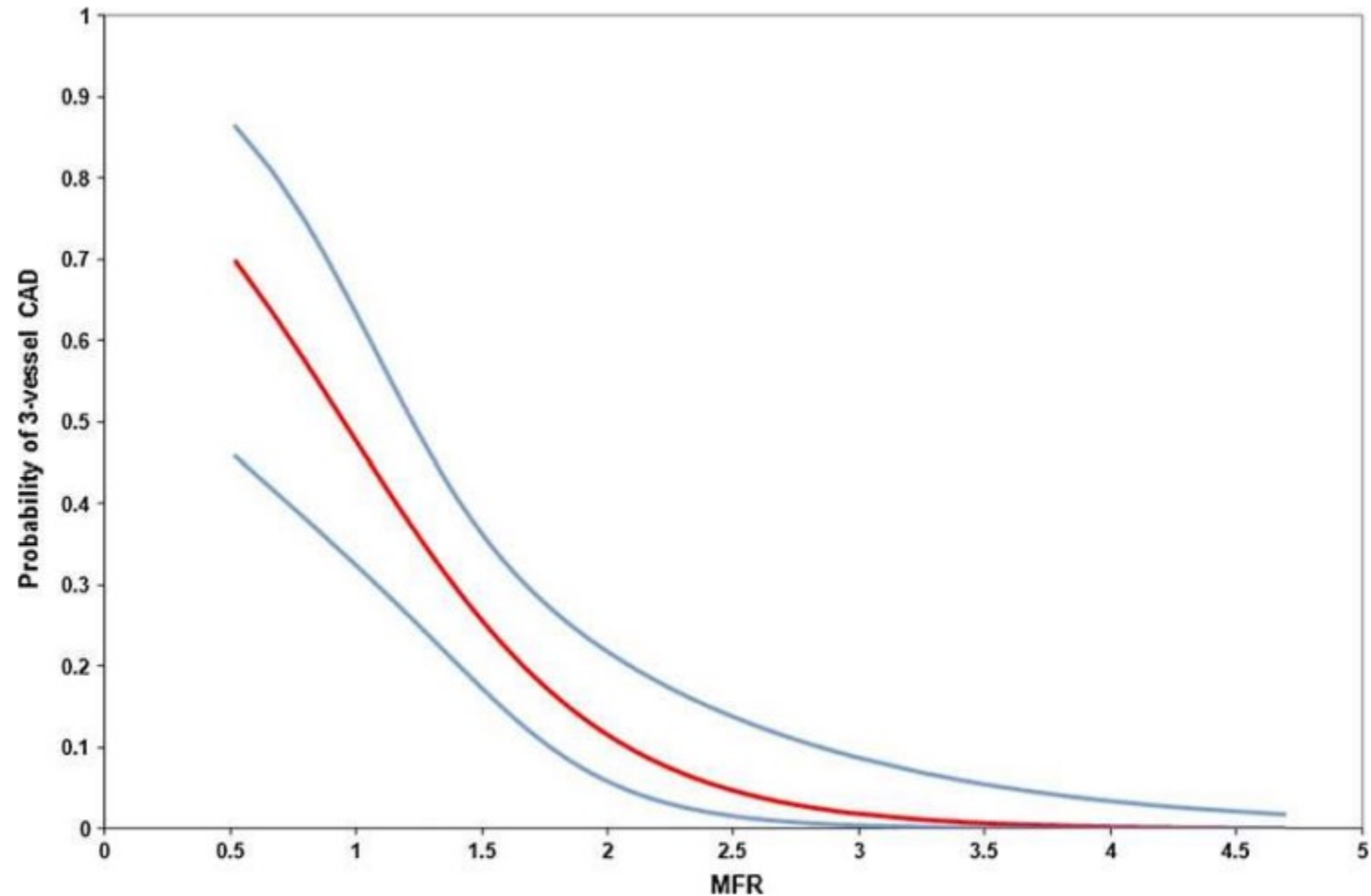
- 70 year-old female with multiple CAD risk factors presented with dyspnea with exertion.

- A. Small reversible defect in LAD territory

- B. 17 segment polar maps

- C. Coronary Angiograms

(A) Short Axis / HLA / VLA — Stress, Rest

(B) stressRubidium Flow (Stress) / stressRubidium / restRubidium (CFR) / restRubidium Flow (Rest) / stressRubidium - restRubidium

Rest MBF (mL/min/gr)	Stress MBF (mL/min/gr)	MFR	MFD
1.03	1.17	1.12	0.14

(C) LAD (mid) 70%; D2 100%; OM1 and OM2 90%; RCA (prox) 60%; RCA (mid) 99%

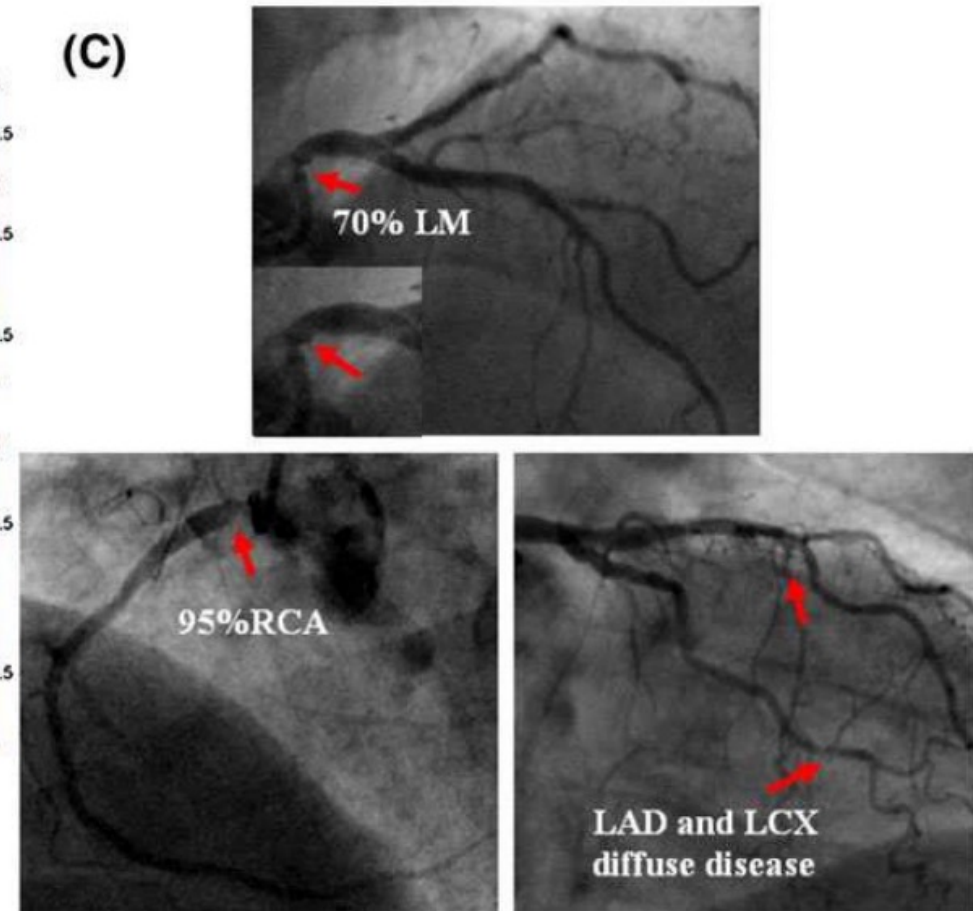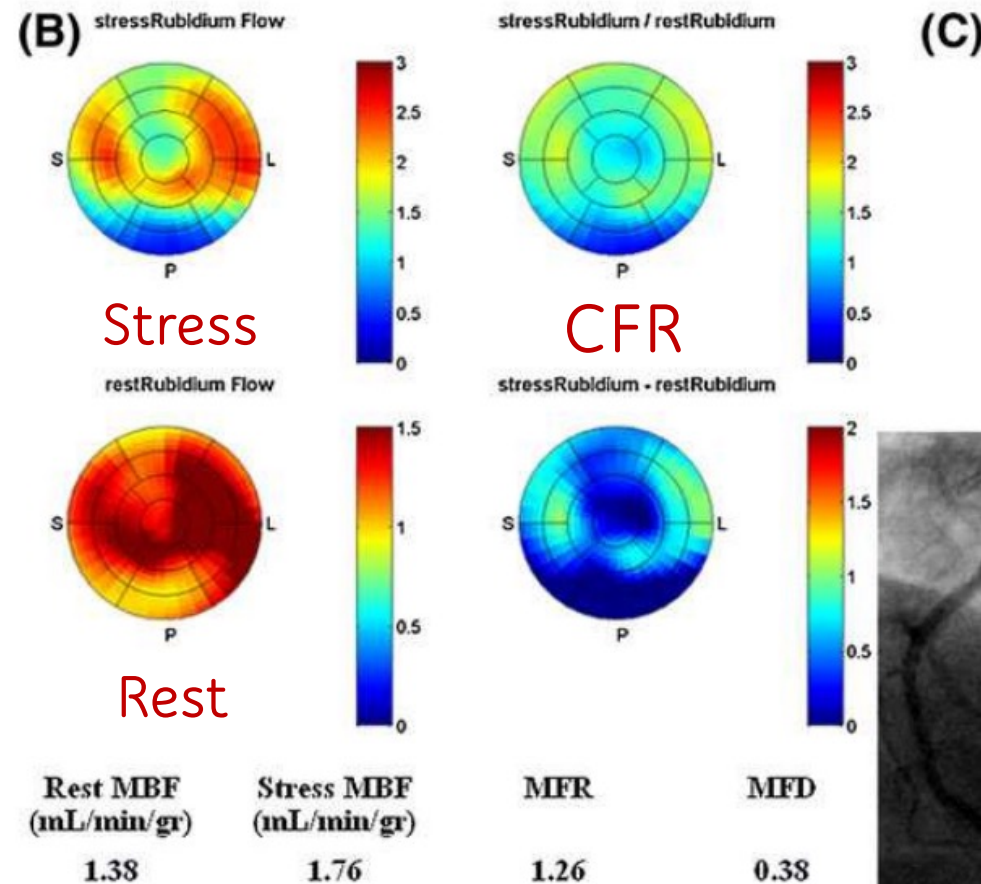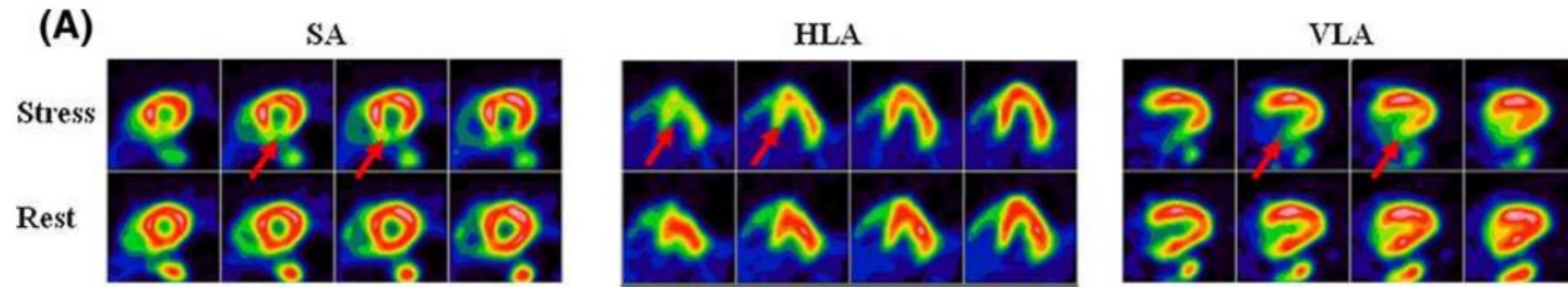Ziadi MC et al. J Nucl Cardiol 2012; 19: 670-680

- 70 year-old male with hypertension, renal insufficiency and worsening angina on exertion.

- A. moderate reversible defect in RCA territory

- B. 17 segment polar maps

- C. Coronary Angiograms

(A) SA | HLA | VLA

(B) stressRubidium Flow | stressRubidium / restRubidium

Stress | CFR

restRubidium Flow | stressRubidium - restRubidium

Rest

Rest MBF (mL/min/gr) 1.38 | Stress MBF (mL/min/gr) 1.76 | MFR 1.26 | MFD 0.38

(C) 70% LM

95%RCA

LAD and LCX diffuse disease

82Rb Myocardial Perfusion PET

Large severe fixed defect of the inferior and inferolateral walls.

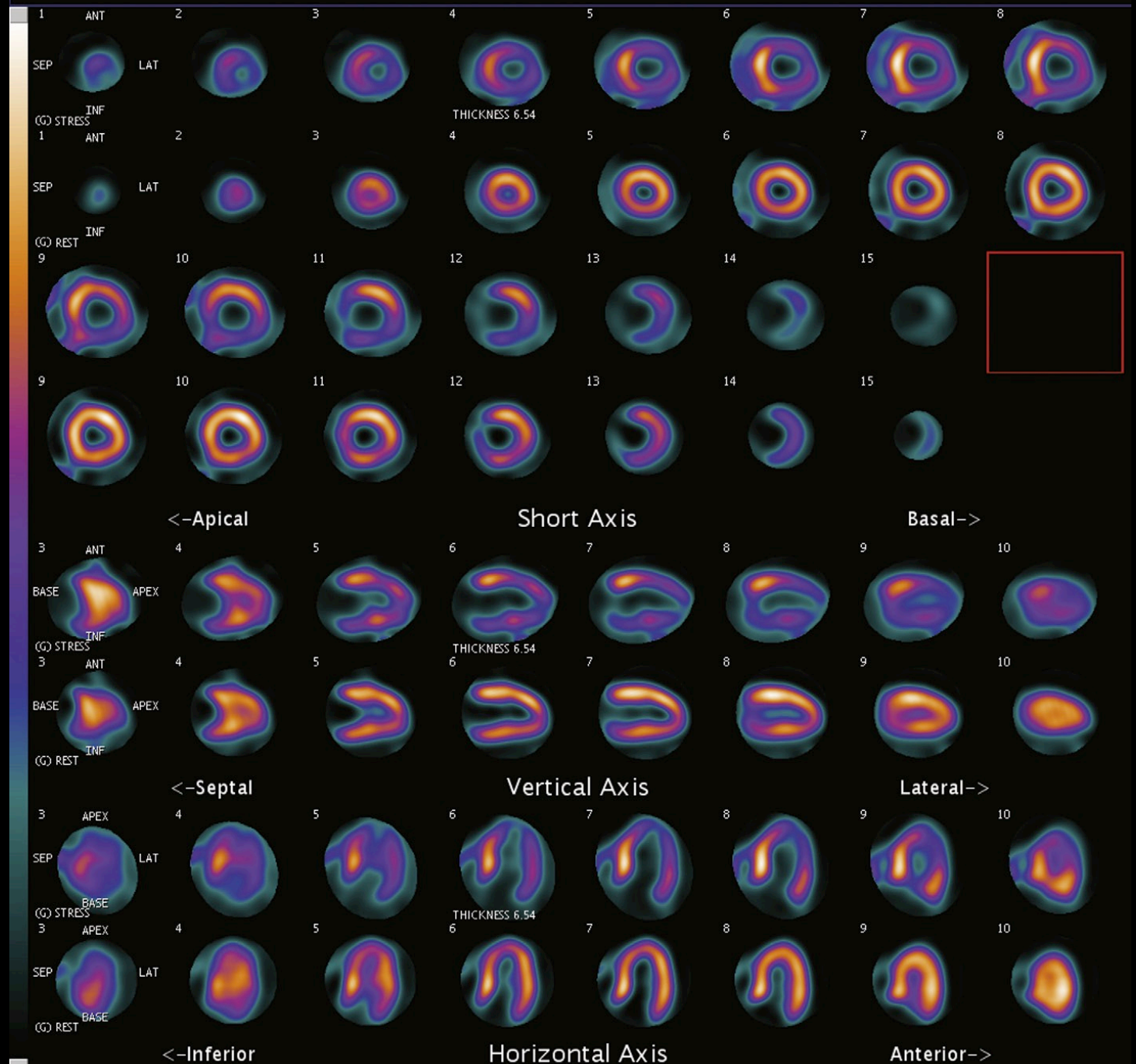Quantitative assessment of myocardial blood flow shows markedly reduced coronary flow reserve
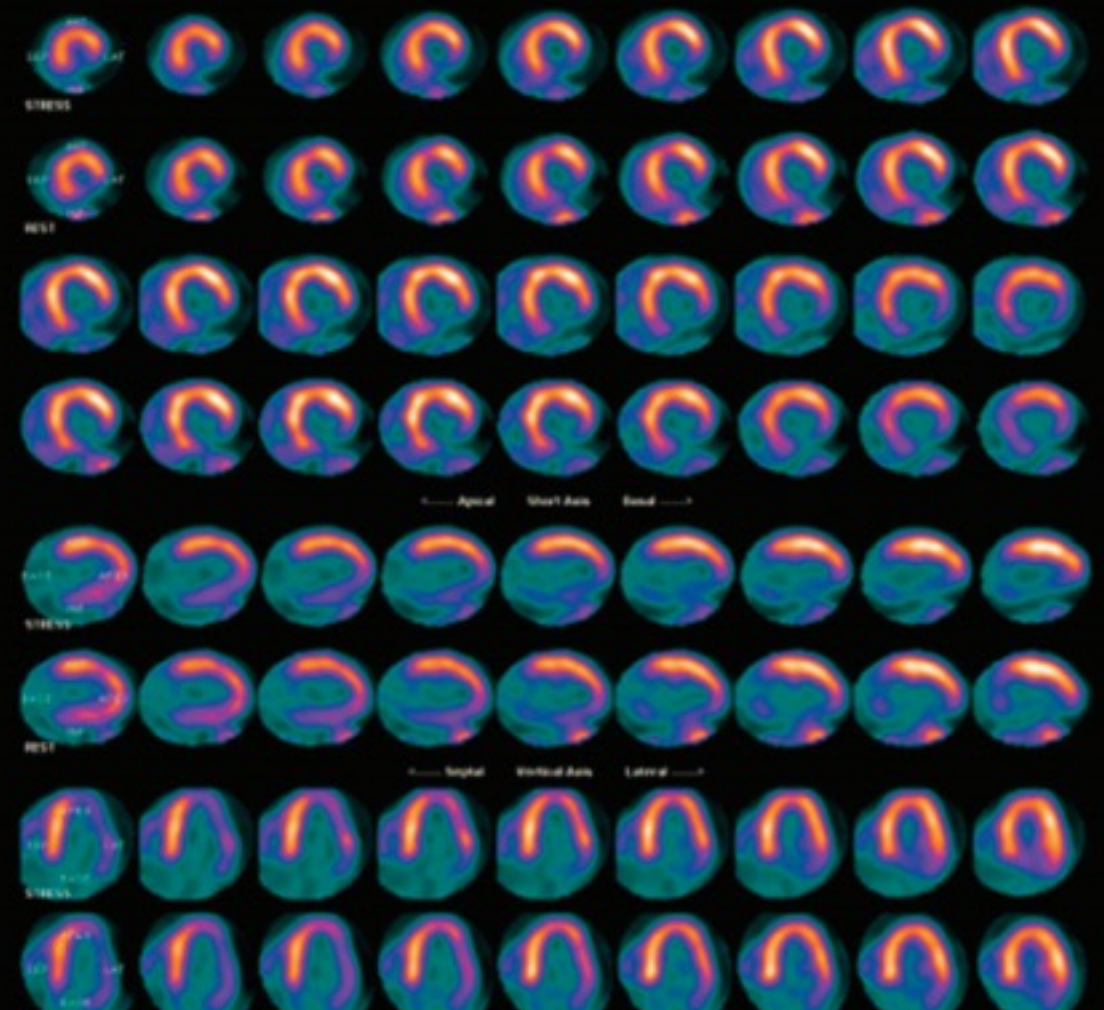
Coronary territory	Rest MBF (mL/min/g)	Stress MBF (mL/min/g)	CFR (stress/rest)
LAD	0.86	0.89	1.07
LCX	0.64	0.66	1.03
RCA	0.86	1.00	1.16

N-13 ammonia stress MPI

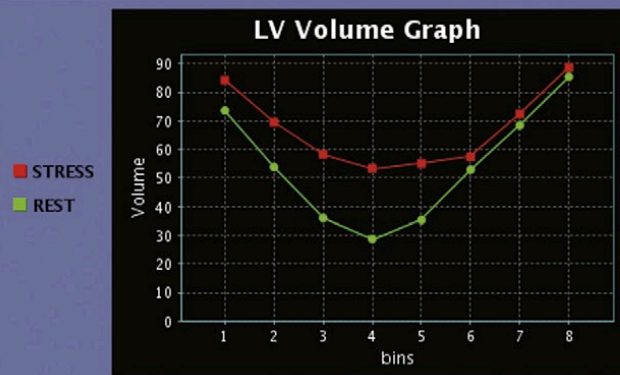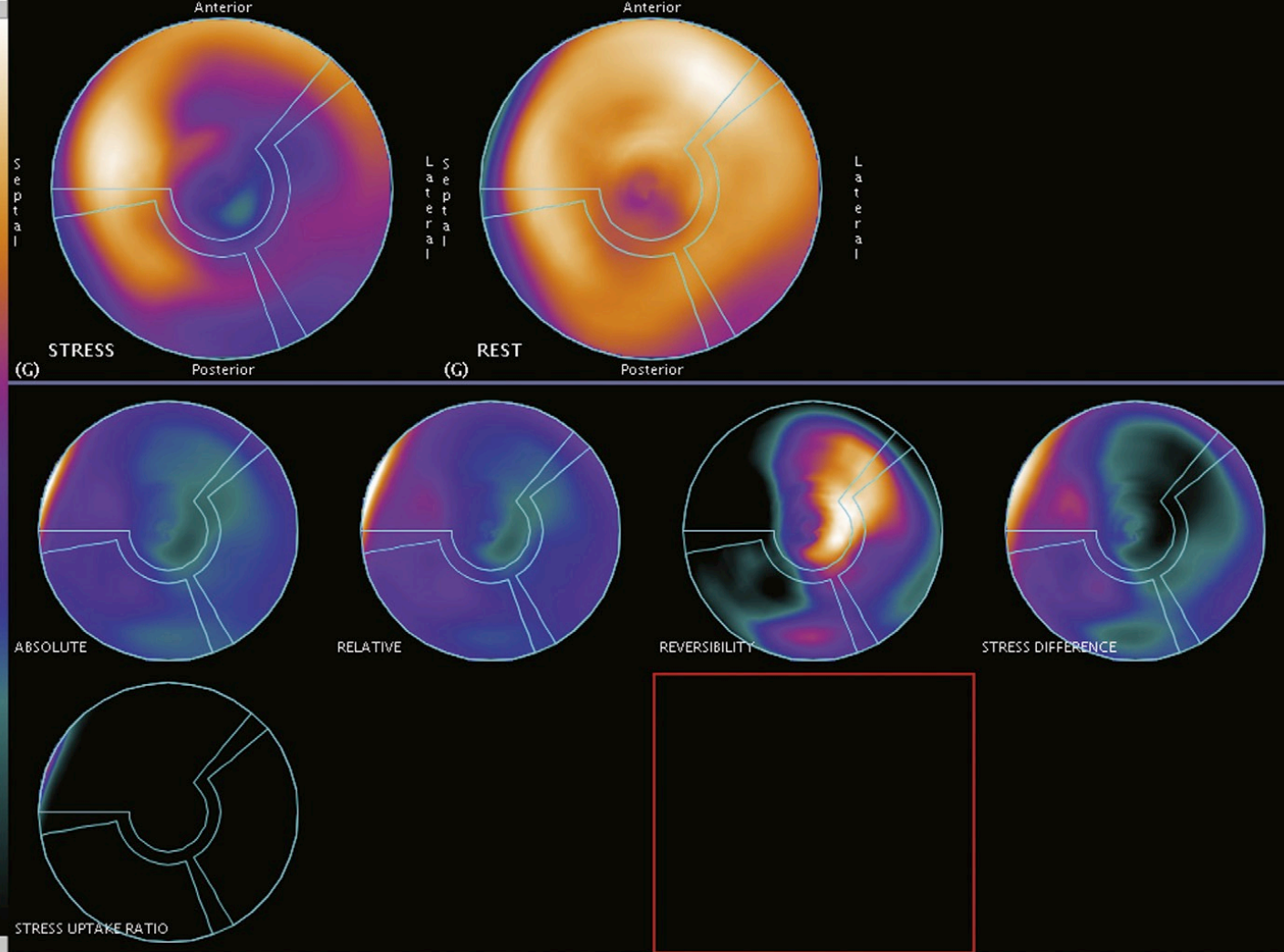Large reversible defect (ISCHEMIA) anterolateral, lateral, inferolateral, and inferior wall.

Multivessel Disease

N-13 ammonia stress MPI

Transient Ischemic Dilatation

Multivessel Disease

Risk stratification

- Many studies have shown incremental prognostic value of PET stress myocardial perfusion imaging.

- A stress ^{82}Rb PET/CT study by Yoshinaga and colleague*s included 367 patients and followed them up for 3.1 6 $\pm$ 0.9 y.
  - increasing extent and severity of perfusion defects with stress PET was associated with increasing frequency of adverse events.
  - Importantly, the hard event rate (i.e., myocardial infarction or cardiac death) in patients with normal stress PET was 0.4%/y

Risk stratification

- Another study by Dorbala and colleagues included 1,602 consecutive patients undergoing rest–stress ^{82}Rb myocardial perfusion PET/CT also suggest that it provides incremental value to clinical variables in predicting overall survival.

- An increases in the extent and severity of stress perfusion defects showed proportional increases in predicted mortality.

Relationship between MFR and risk of cardiac death

Venkatesh et al., J Nucl Cardiol 2018;25:269–97
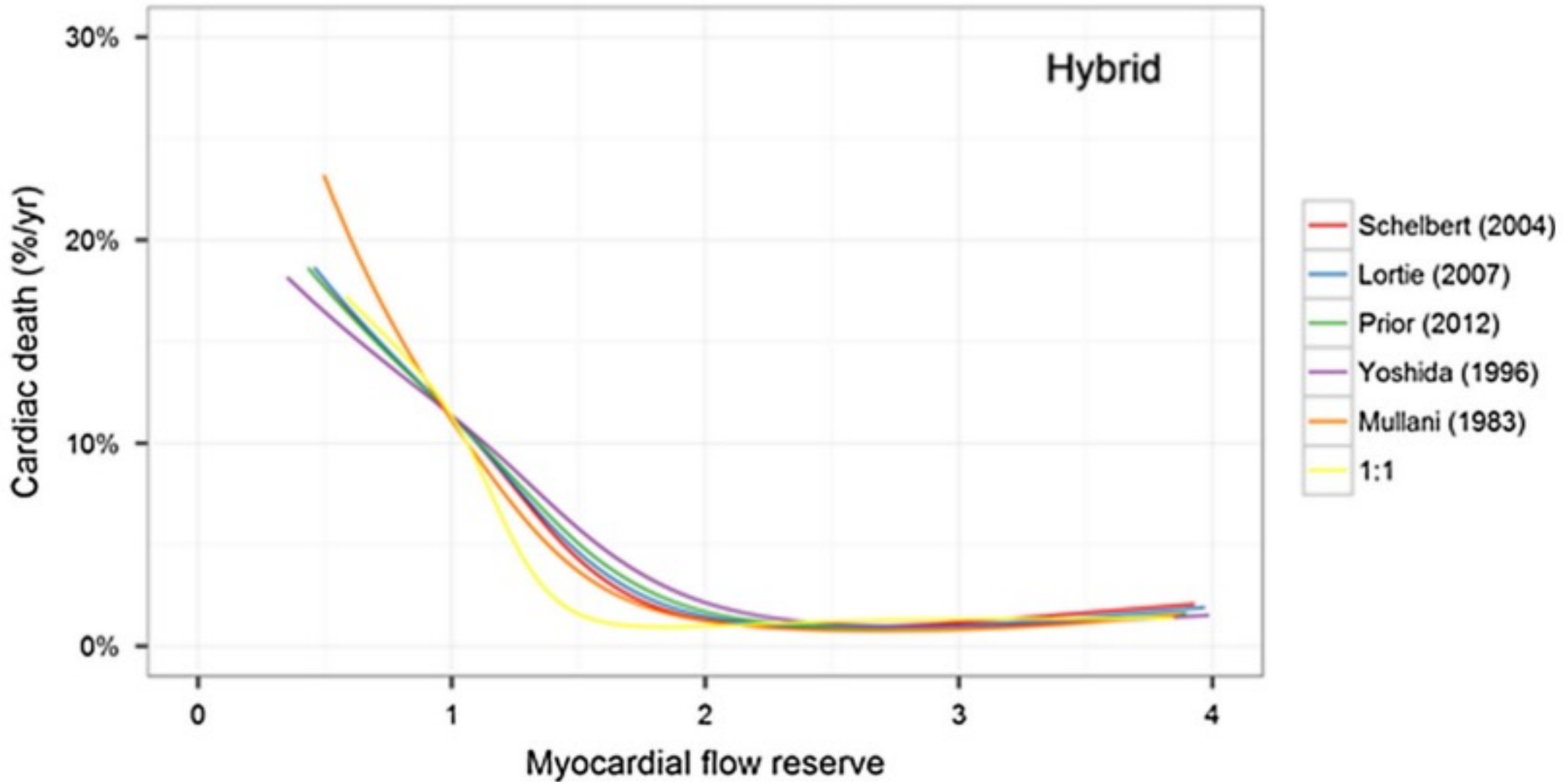
81 year-old male, smoker, with known medical history of CAD, SP CABG, presenting with severe dyspnea on exertion

Lateral wall reversible defect (Ischemia)
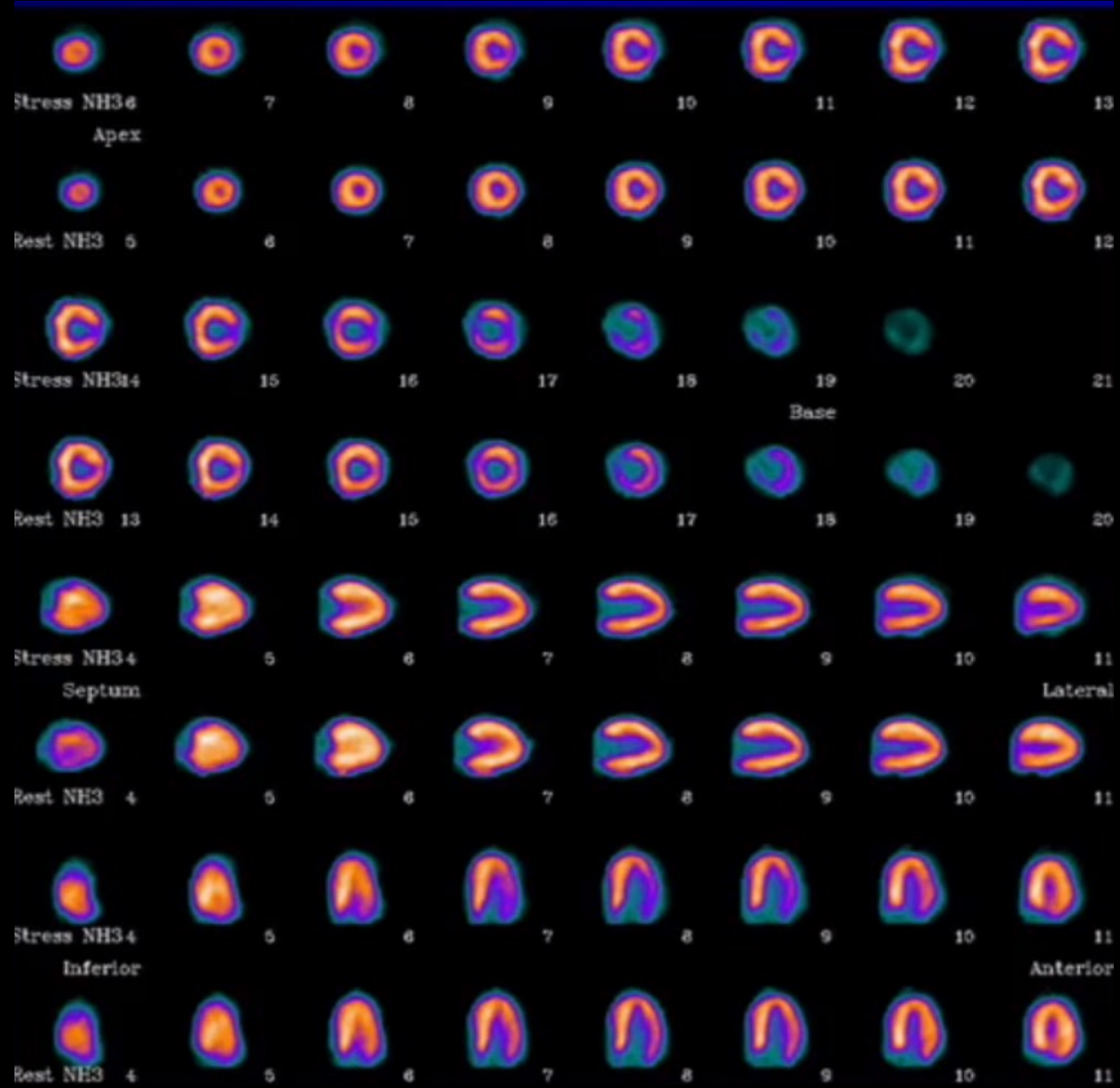
Take Home Points

- Preserved stress **MBF** of more than **2 mL/minute/g** and **MFR** of more than **2** reliably exclude the presence of high-risk angiographic disease (negative predictive value [95%) and are reasonable to report when used in clinical interpretation.

Take Home Points

- A severely decreased global **MFR (<1.5 mL/minute/ g)** should be reported as a high-risk feature for adverse cardiac events but is not always due to multivessel obstructive disease.

Take Home Points

- Regional decreases in stress **MBF (\1.5 mL/minute/ g) and MFR (\1.5)** in a vascular territory may indicate regional flow-limiting disease.

Summary

- Cardiac PET/CT offers many potential advantages over SPECT/CT in the assessment of myocardial perfusion.
  - Accuracy
  - Fast patient throughput
  - Less radiation doe and background contamination
  - Quantitative analysis

Summary

- Quantitative analysis of the cardiac PET provides absolute myocardial perfusion data including coronary flow reserve (CFR) improve our ability to detect multivessel CAD.

- It has prognostic value and hep risk stratification and guide treatment.

"By the way, your insurance doesn't cover these tests...JUST KIDDING! That was the stress test."