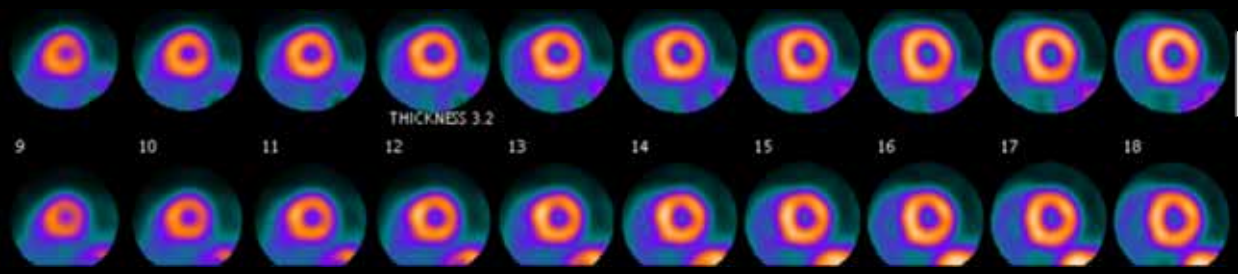
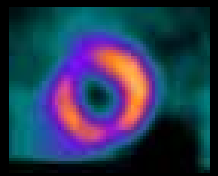
Myocardial Perfusion PET with Myocardial Blood Flow & Flow Reserve in Clinical Practice

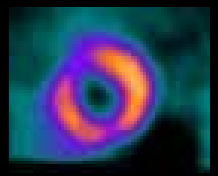
Shana Elman, MD
Assistant Professor, Department of Radiology
University of New Mexico Health Sciences
SNMMI – SWC Annual Meeting, 3/22/2019





Disclosures

- I have no financials disclosures.



Objectives

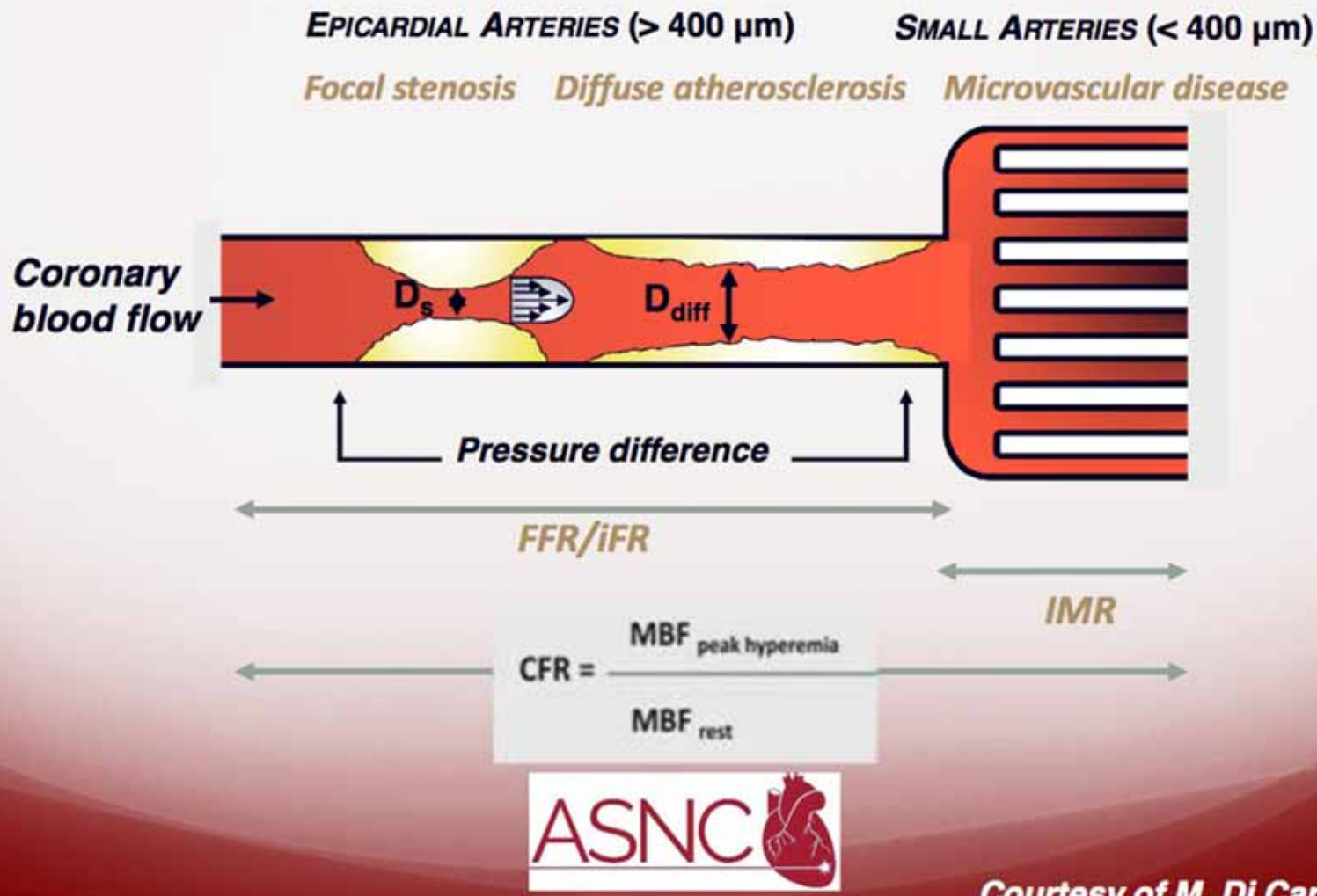
- Understand benefits of PET over SPECT for myocardial perfusion imaging
- Discuss how to add value to myocardial perfusion imaging with myocardial blood flow (MBF) and myocardial flow reserve (MFR)
- Identify patient populations that will benefit from myocardial perfusion PET
- Discuss challenges of incorporating cardiac PET into clinical practice

Changing epidemiology of CV disease

- CV disease remains the number one cause of death and disability, but clinical presentations are changing
  - ↓ *incidence of atherothrombotic plaque rupture causing ST-segment elevation MI*
  - ↑ *rates of hospitalizations with a secondary MI diagnosis and heart failure with preserved ejection fraction (HFpEF)*
- These observations follow the epidemiologic shifts in the prevalence of CVD risk factors in the population, including the growth of obesity, glucose intolerance and older age

1.Sources: Heart disease and stroke statistics: Circulation. 2018; N Engl J Med 2010;362:2155-65; Am Heart J 2015;170:1211-9; N Engl J Med 2006;355:251-9

Factors affecting the pathophysiology of myocardial ischemia and injury in stable IHD



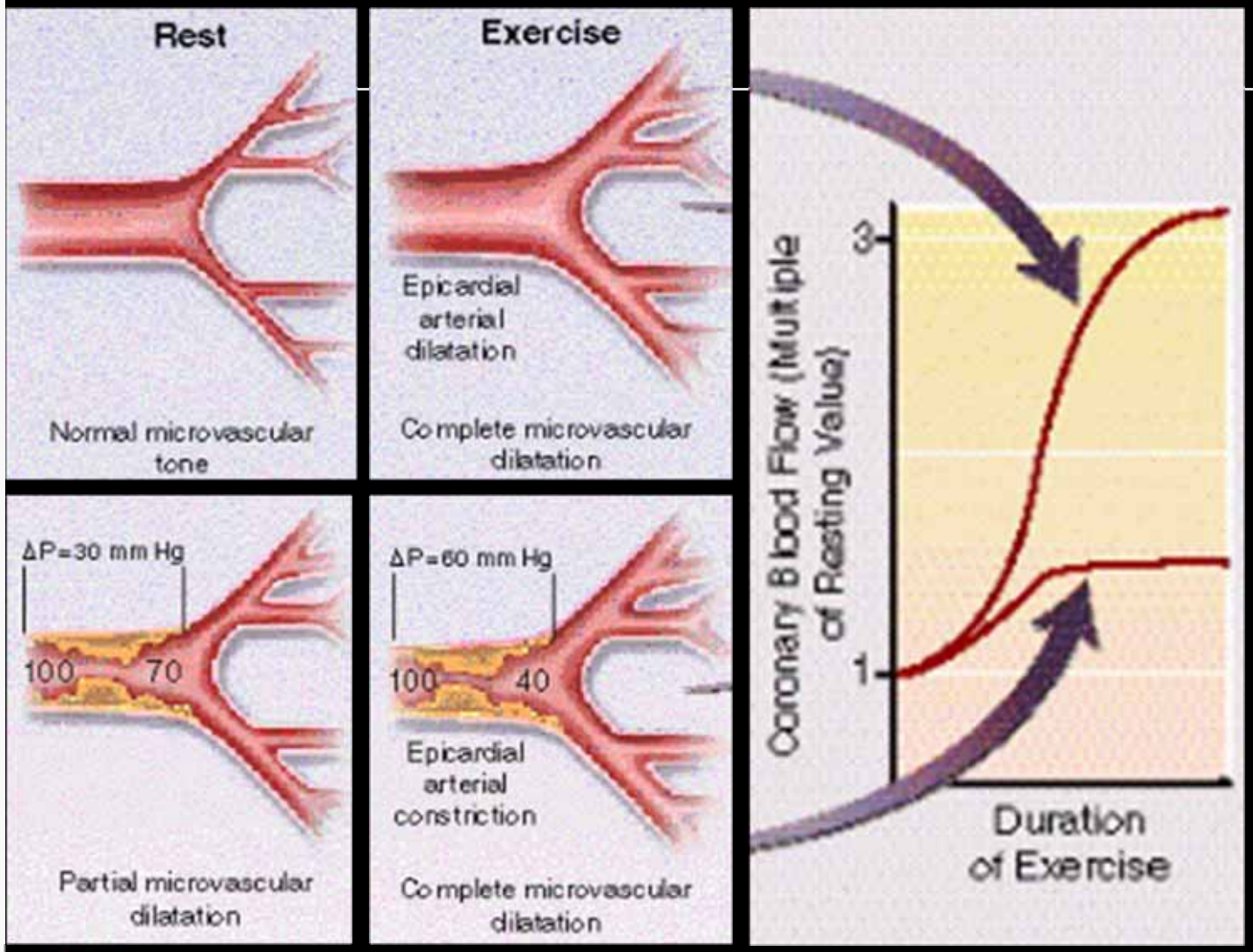
ASNC

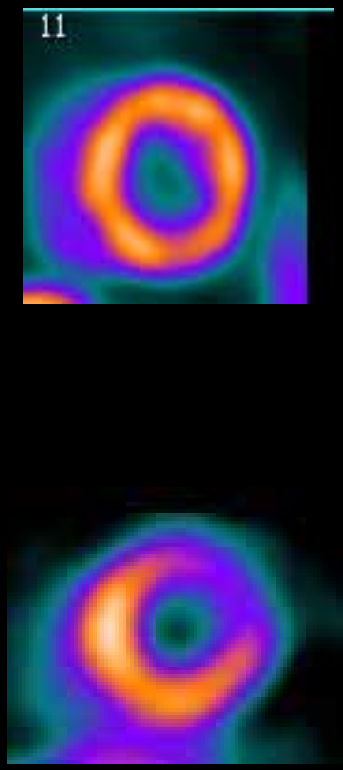
Courtesy of M. Di Carli 2018

Physiology

Normal Artery

Atherosclerotic Artery





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Wilson R. N Engl J Med 1996; 334:1735-1737

Benefits of PET over SPECT

- Low radiation exposure (1-5 mSv)
- Short acquisition protocols (< 1 hr w/ Rb-82)
- High-quality images (particularly helpful to minimize artifacts from tissue attenuation and scatter)
- High diagnostic accuracy
- Ability to identify non-response to stress
- Strong prognostic power

Bateman et al. J Nucl Cardiol 2016

Radiopharmaceuticals

	Rb-82	^{13}N-Ammonia	^{18}F-Flurpiridaz	^{15}O-Water
Half-Life	75 sec	~10 min	~2 hours	~2 min
Positron Range (mm)	5.9	1.5	0.6	2.5
Myocardial Extraction	Good	Very Good	Excellent	Excellent
FDA Status	Approved	Approved	Soon????	Not Approved
Stress Type	Pharm	Pharm (or Exercise)	Pharm or Exercise	Pharm
Per Dose Cost	$$$ $ (if you do enough)	$$	Unknown	$$

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Bateman et al. J Nucl Cardiol 2016

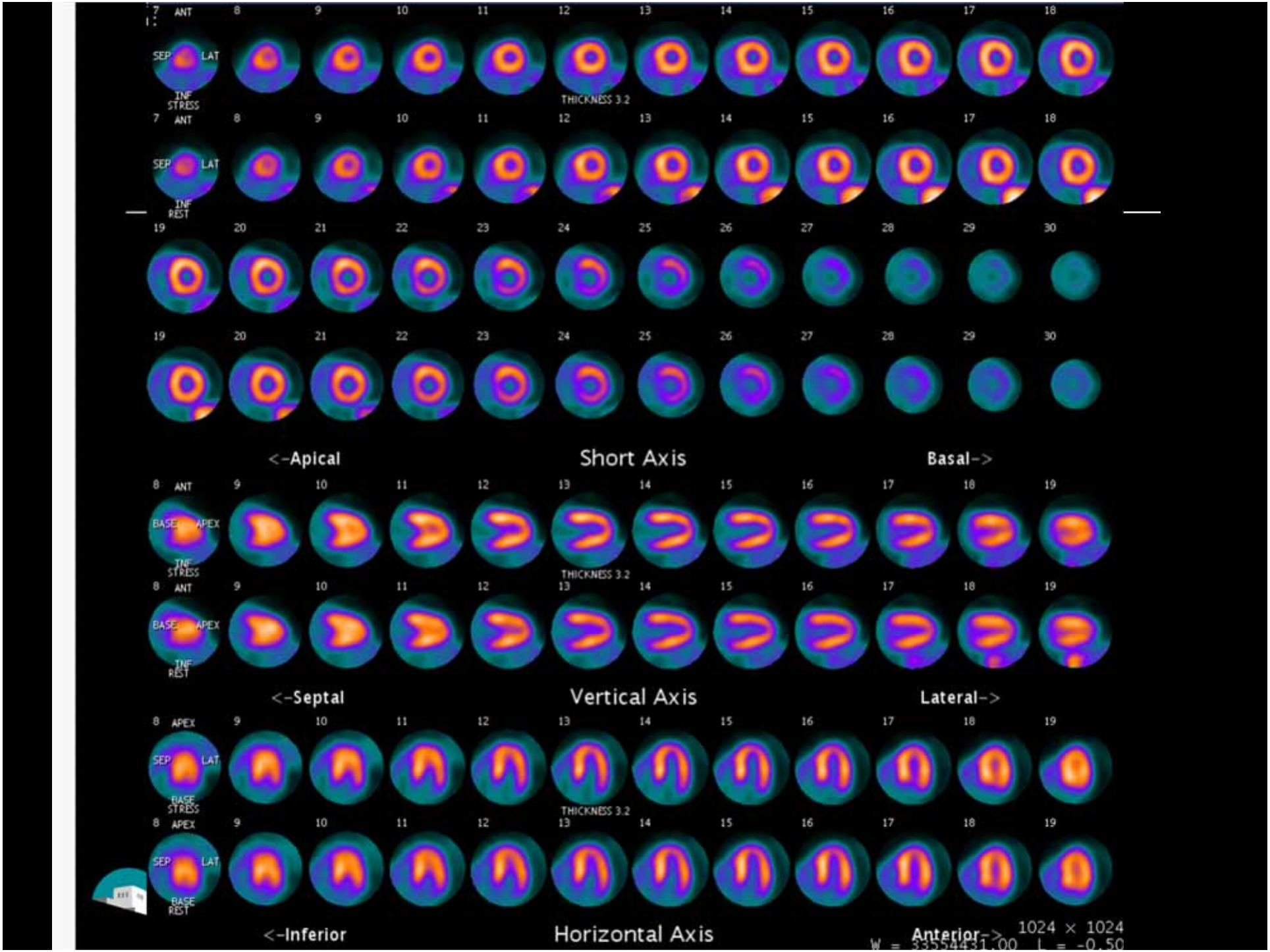
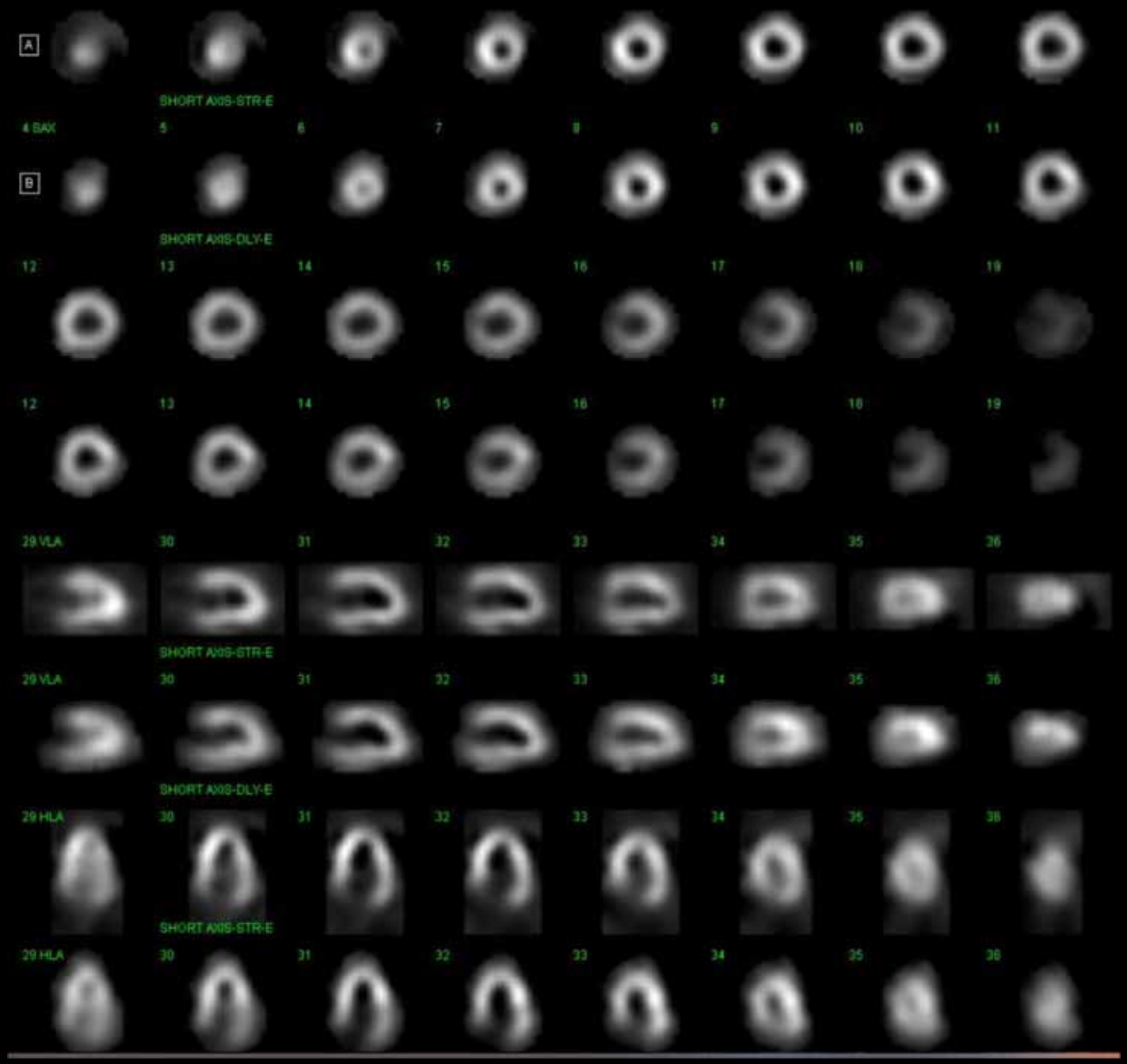
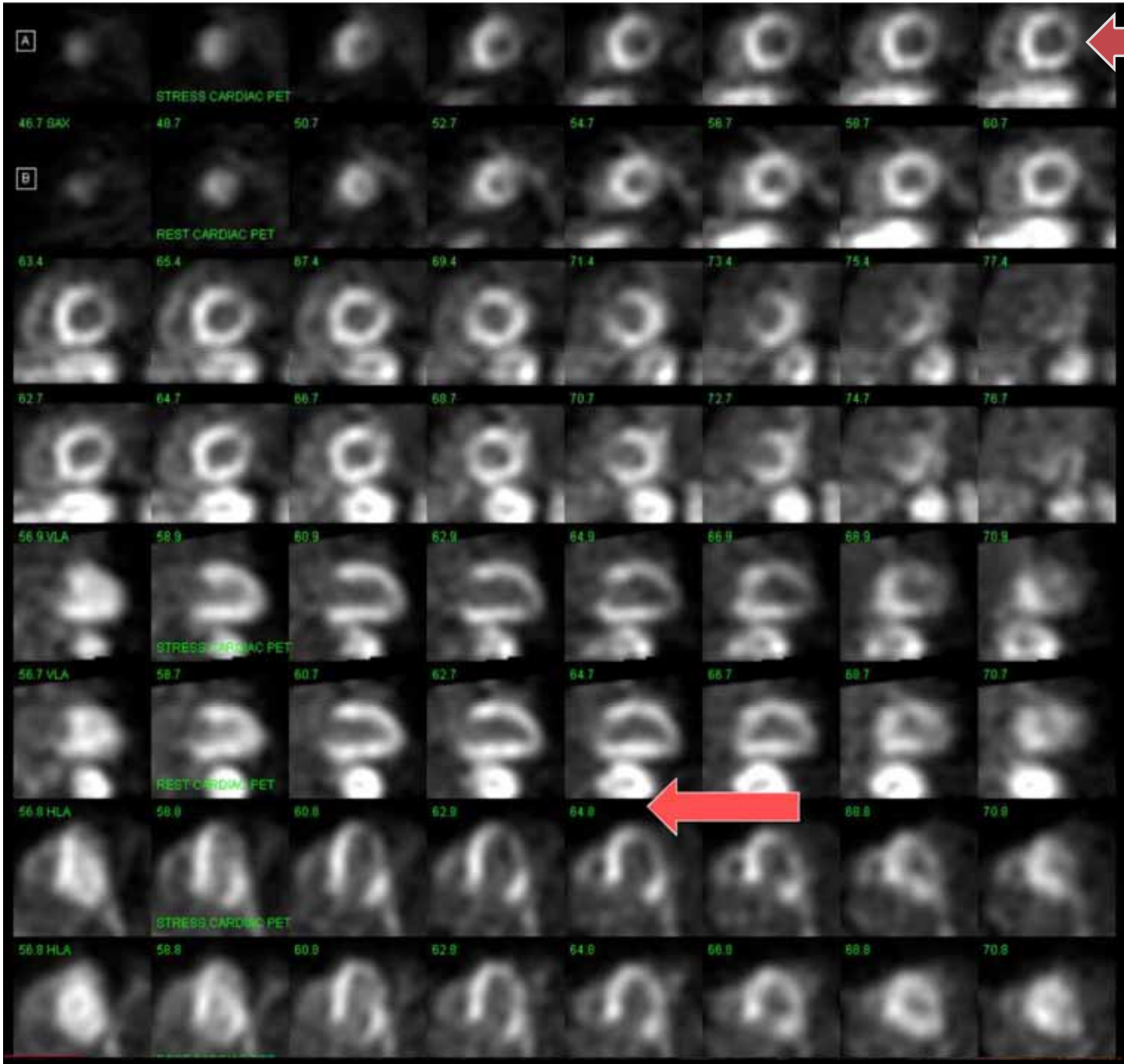

ANT
SEP
LAT
INF
STRESS
THICKNESS 3.2
INF
REST
<-Apical
Short Axis
Basal->
BASE
APEX
<-Septal
Vertical Axis
Lateral->
BASE
STRESS
BASE
REST
<-Inferior
Horizontal Axis
Anterior->
1024 × 1024
W = 33554431.00 L = -0.50

Image Quality of PET over SPECT

- Improved spatial resolution
- Improved attenuation correction
- Improved temporal resolution
- Improved myocardial extraction
- Leads to fewer false negatives and fewer false positives with increased diagnostic accuracy independent of gender or body habitus and improved identification of multivessel disease

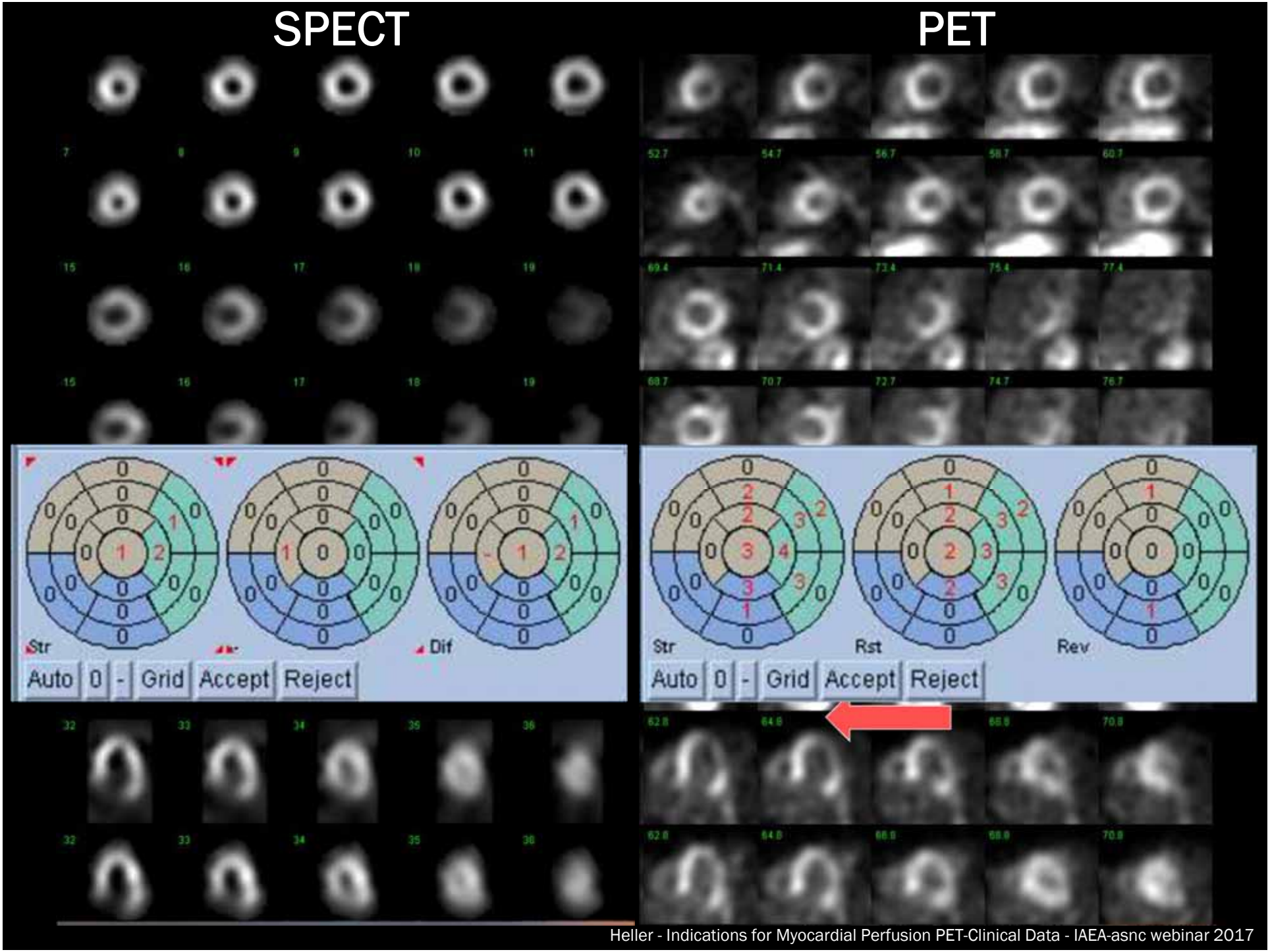


SPECT from 65-year-old man with anginal symptoms



PET from same

65-year-old man with anginal symptoms



Heller - Indications for Myocardial Perfusion PET-Clinical Data - IAEA-asnc webinar 2017

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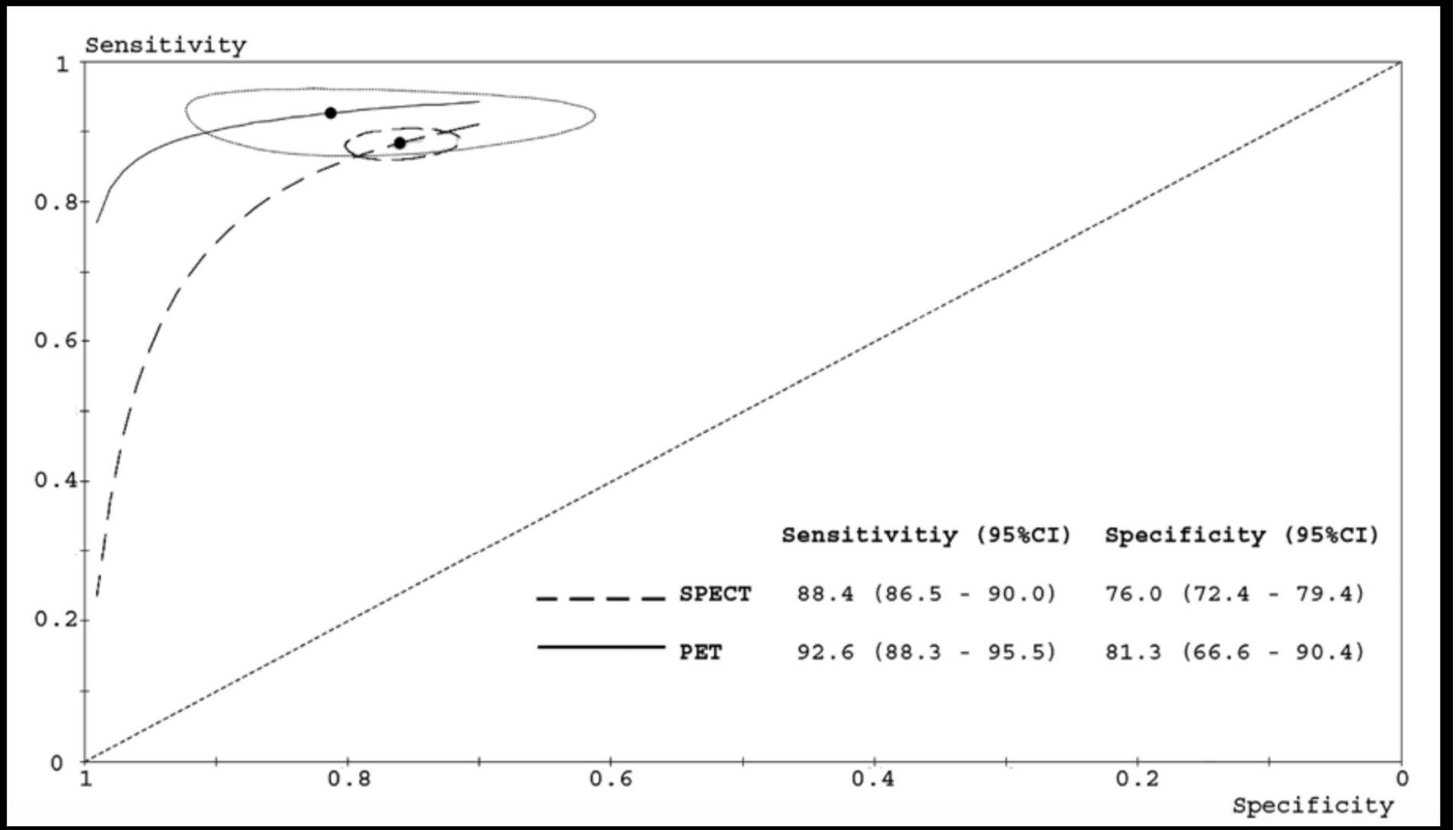
Bateman et al. J Nucl Cardiol 2016

Table 4. Summary of published literature on diagnostic accuracy of PET

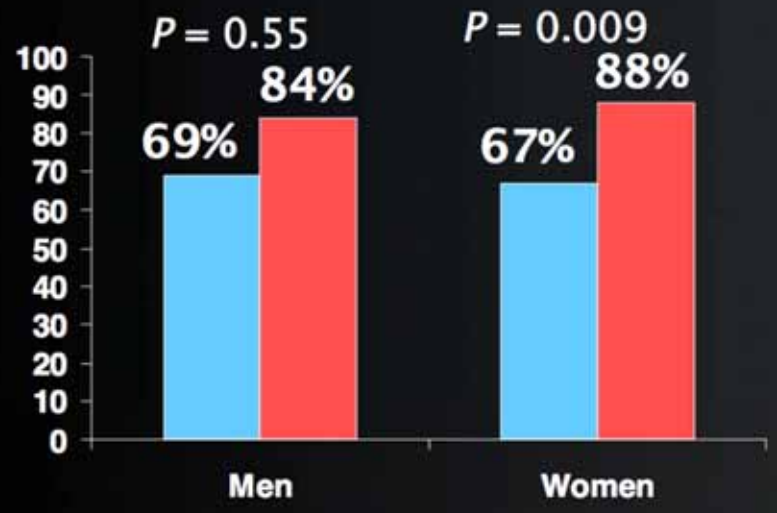
Author	Year	Number	Tracer	Sensitivity (%)	Specificity
Schelbert et al[7]	1982	45	$^{13}NH3$	97	100
Tamaki et al[8]	1985	25	$^{13}NH3$	95	100
Yonekura et al[9]	1987	50	$^{13}NH3$	97	100
Tamaki et al[10]	1988	51	$^{13}NH3$	98	100
Gould et al[11]	1986	50	$^{82}Rb/^{13}NH3$	-	-
Demer et al[12]	1989	193	$^{82}Rb/^{13}NH3$	83	95
Go et al[13]	1990	202	^{82}Rb	93	78
Stewart et al[14]	1991	81	^{82}Rb	83	86
Marwick et al[15]	1992	74	^{82}Rb	90	100
Grover-McKay et al[16]	1992	31	^{82}Rb	100	73
Laubenbacher et al[17]	1993	34	$^{13}NH3$	88	83
Wallhaus et al[18]	2001	45	^{64}Cu-PTSM	84	100
Bateman et al[19]	2006	112	^{82}Rb	86	100
Walsh et al[20]	1988	33	^{15}O-H_2O	92	-
Williams et al[21]	1994	287	^{82}Rb	87	88
Simone et al[22]	1992	225	^{82}Rb	83	91
Sampson et al[23]	2007	102	^{82}Rb	93	83
Husmann et al[24]	2007	70	$^{13}NH3$	96	-
Total weighted mean		1660		90	89

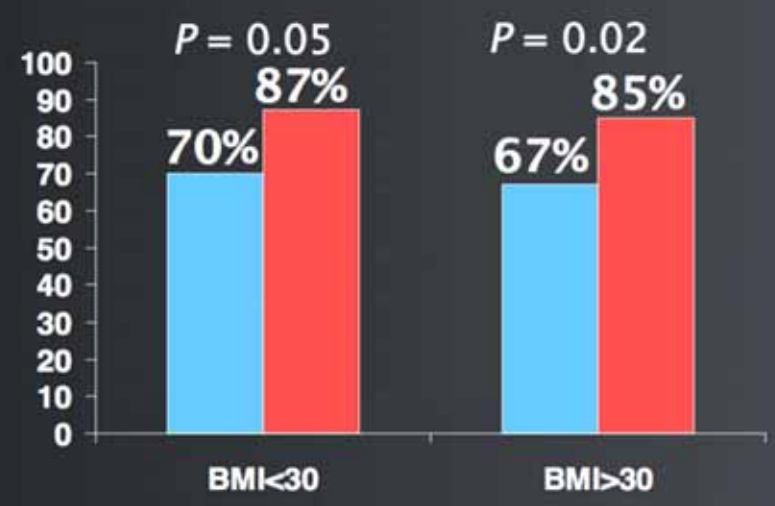
Adapted from Ziadi MC, et al. Diagnosis and prognosis in cardiac disease using cardiac PET perfusion imaging. In: Zaret BL, Beller GA, editors. Clinical nuclear cardiology: State of the art and future directions, 4th edn (in press) (with permission).

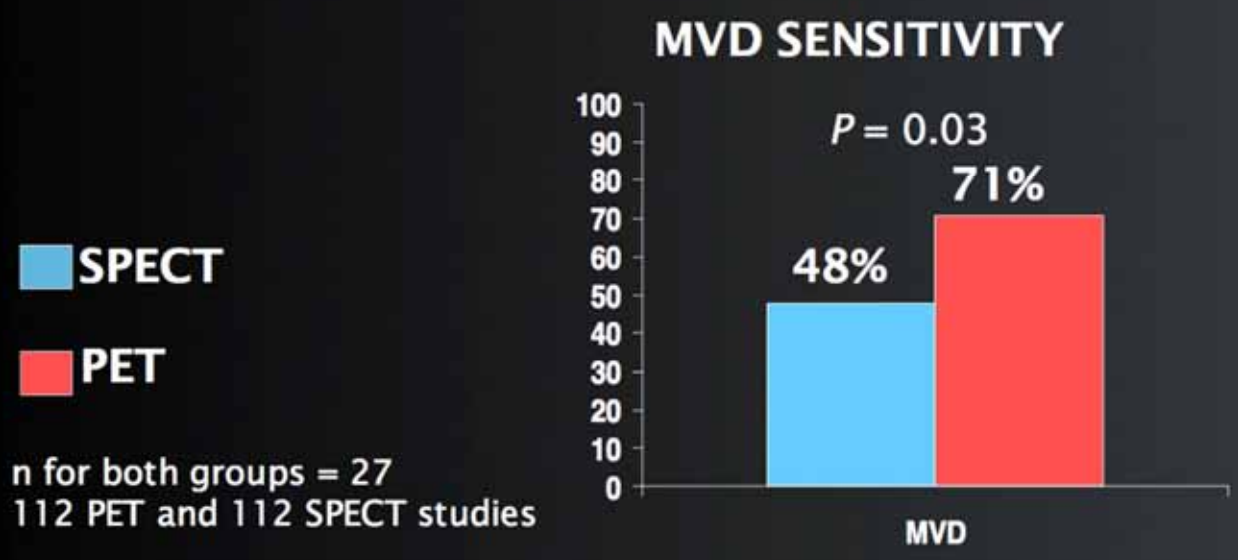
Beanlands and Youssef JNC 2010;17:683



Parker et al. *Circ Cardiovasc Imaging* 2012;5:700–707



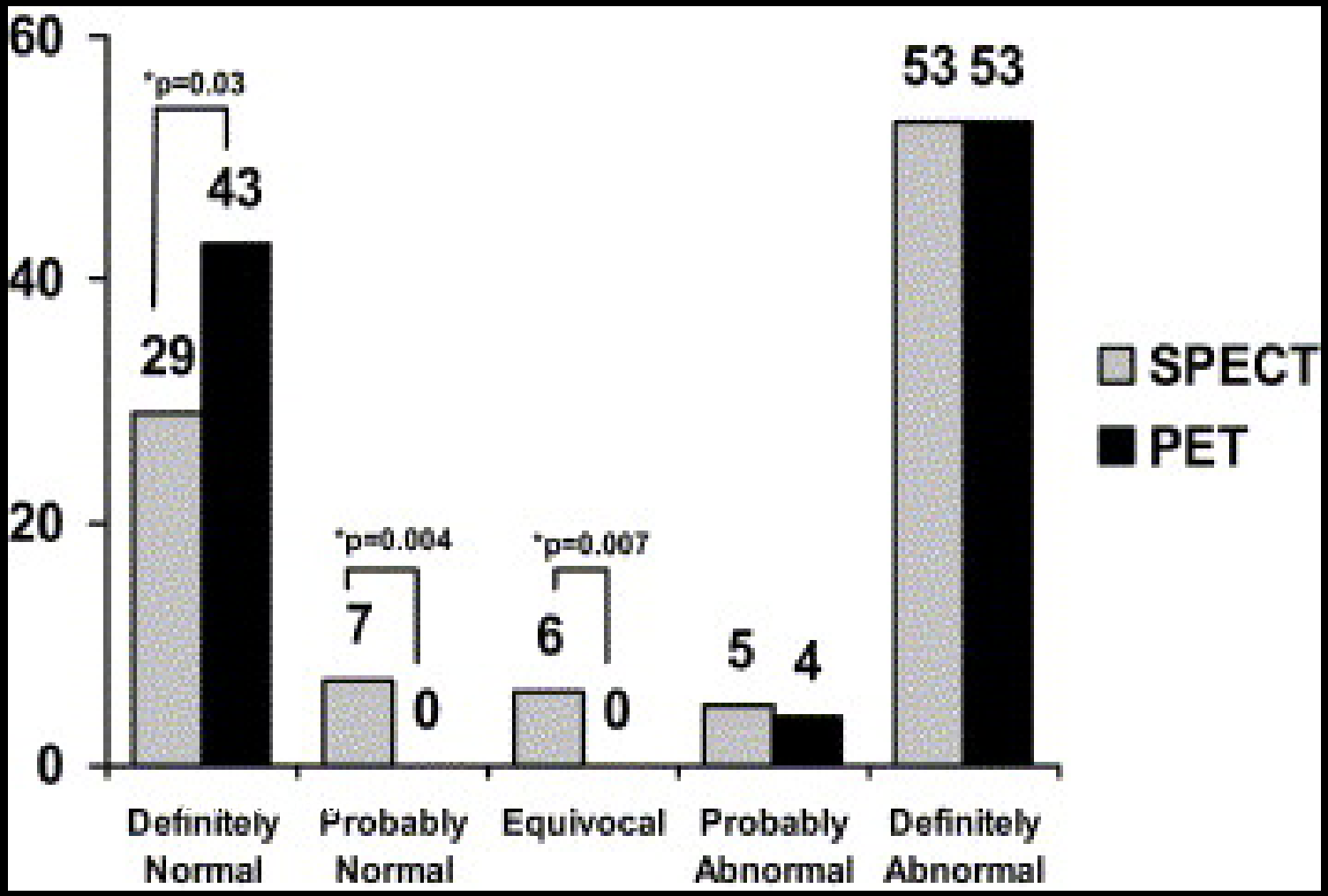




Bateman et al. J Nucl Cardiol. 2006; 13:24-33

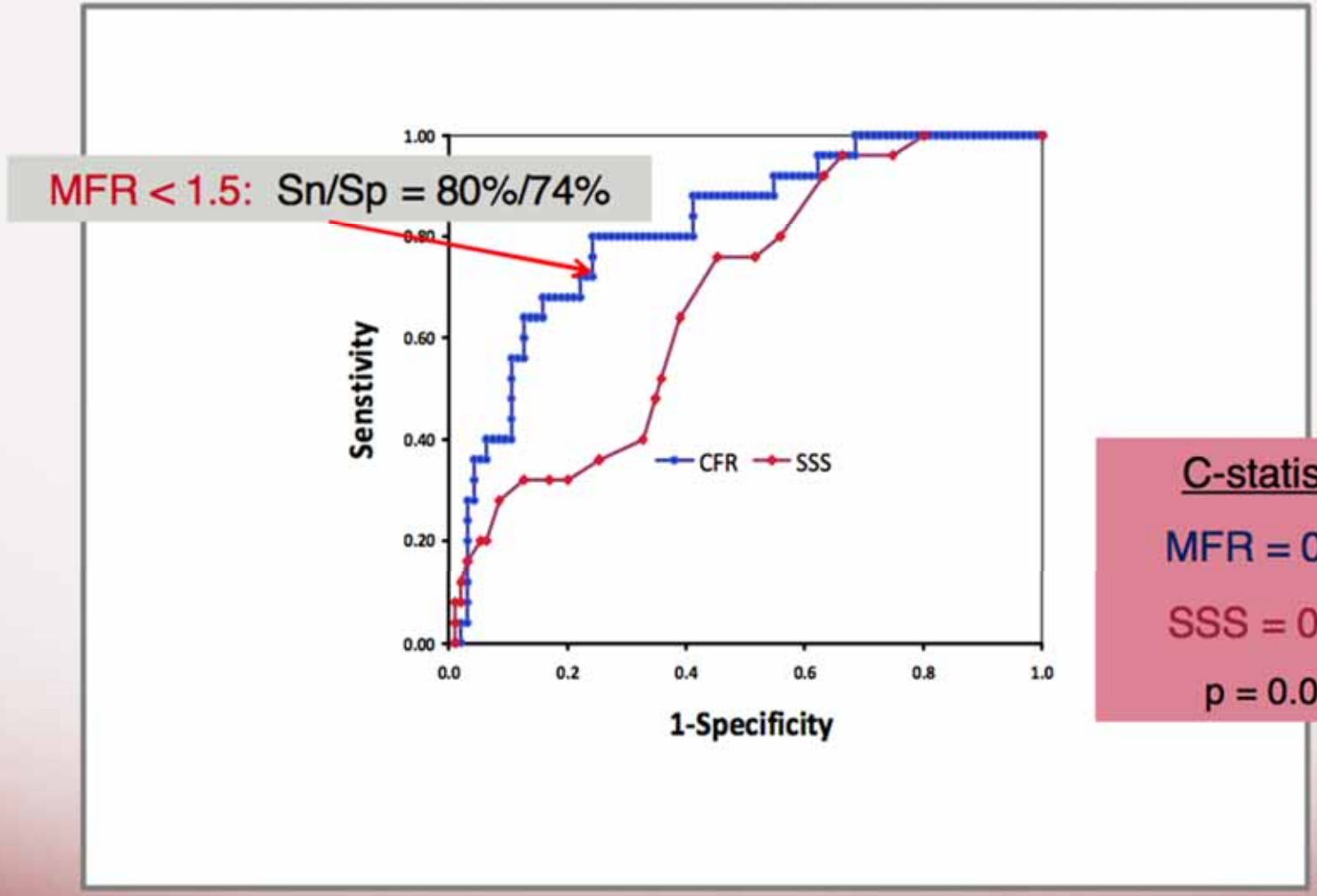
↓ Diagnostic Uncertainty

Interpretive Certainty



Bateman et al (2006). J Nucl Cardiol **13**: 24.

^{82}Rb PET Global MFR in 3-vessel disease detection



C-statistics

MFR = 0.817

SSS = 0.679

p = 0.018

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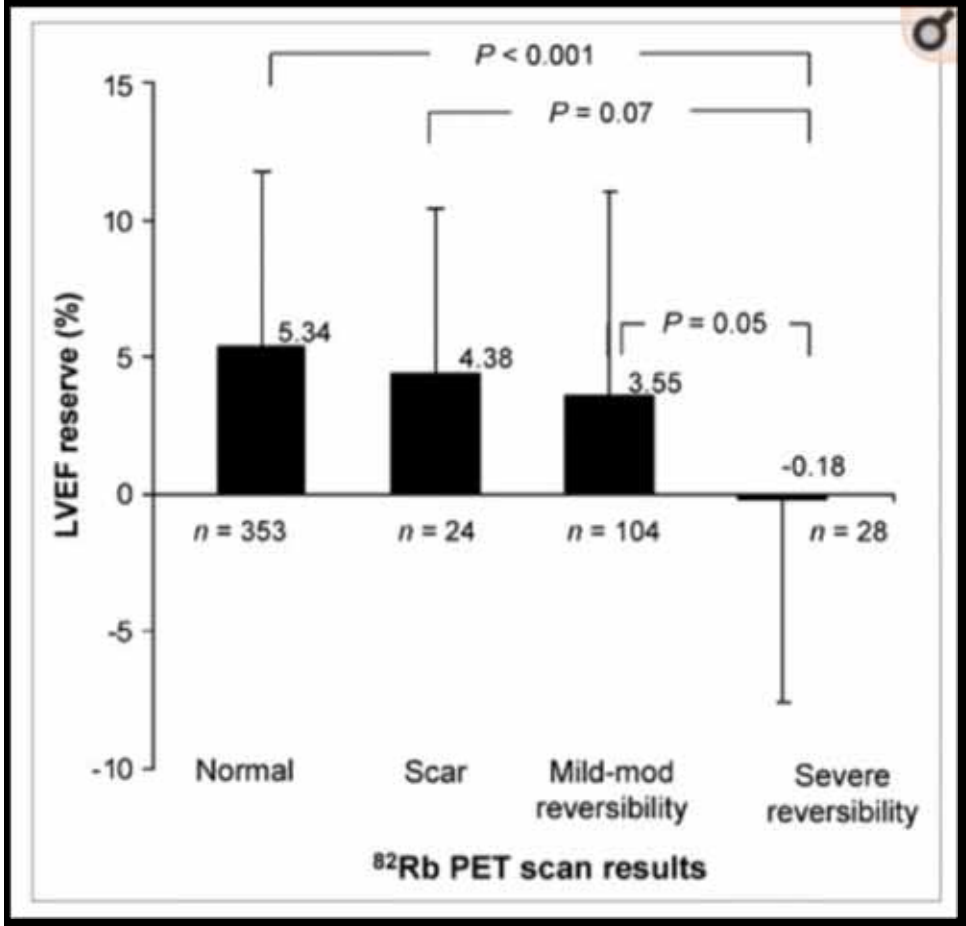
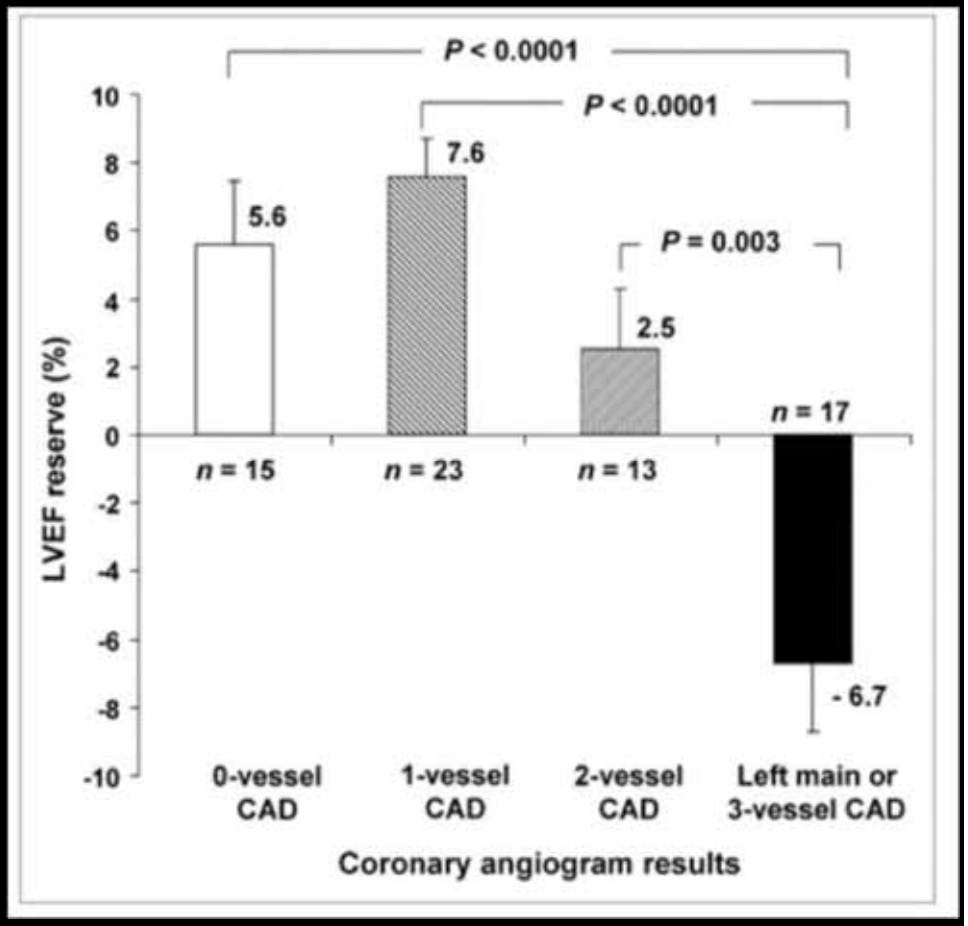
Ziadi et al. J Nucl Cardiol 2012





Dorbala et al.. J Nucl Med. 2007;48:349–58.

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Bateman et al. J Nucl Cardiol 2016

Non-responsiveness to pharmacological stress

- Patient does not demonstrate features expected with severe multivessel CAD.
- Global and regional flows are at or near 1.0, with homogeneous rather than heterogeneous MFR
- Uptake similar to rest and no new defects
- Little or no hemodynamic changes
- No high-risk response features (e.g., ECG changes, stress-induced perfusion defects, wall motion abnormalities, TID, RV uptake)

High Risk Scan Features on PET MPI

ECG	>1 mm ST elevation >2 mm ST depression
Heart rate reserve[59]	< 4 beats
Imaging variables	
Stress defect size and severity[5, 25]	≥ 10%
Rest defect size and severity[5, 25]	≥ 10%
Reversibility size and severity[8, 48]	≥ 10%
Transient cavity dilation[19]	>1.13
Increased lung uptake	Visual estimate
Rest LVEF[25, 33]	<40%
Stress LVEF[2, 25]	<40%
LVEF reserve[1]	<+5%
Increased RV tracer uptake	Visual estimate
Transient increase in RV tracer uptake[60]	≥ 10% increase in RV/LV uptake ratio with stress or ≥ 10% increase in the RV/LV ratio at stress compared to rest
Calcium score[43]	> 400
CT coronary angiography	Severe CAD
Quantitative blood flow assessment (CFR)[34]	< 1.5

Dorbala et al. Semin Nucl Med. 2014 Sep; 44(5): 344–357.

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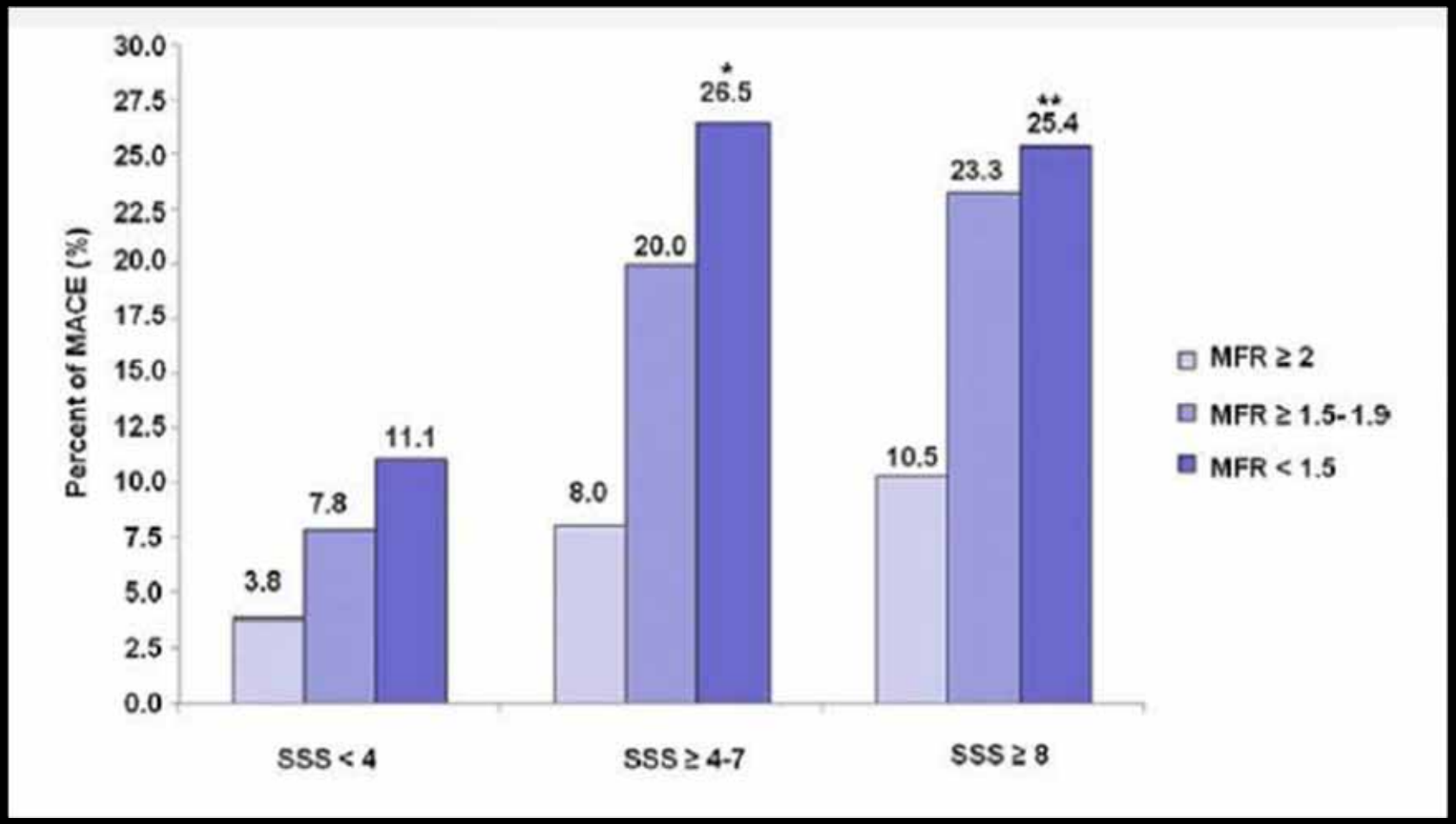
Bateman et al. J Nucl Cardiol 2016

Myocardial Flow Reserve and Prognosis



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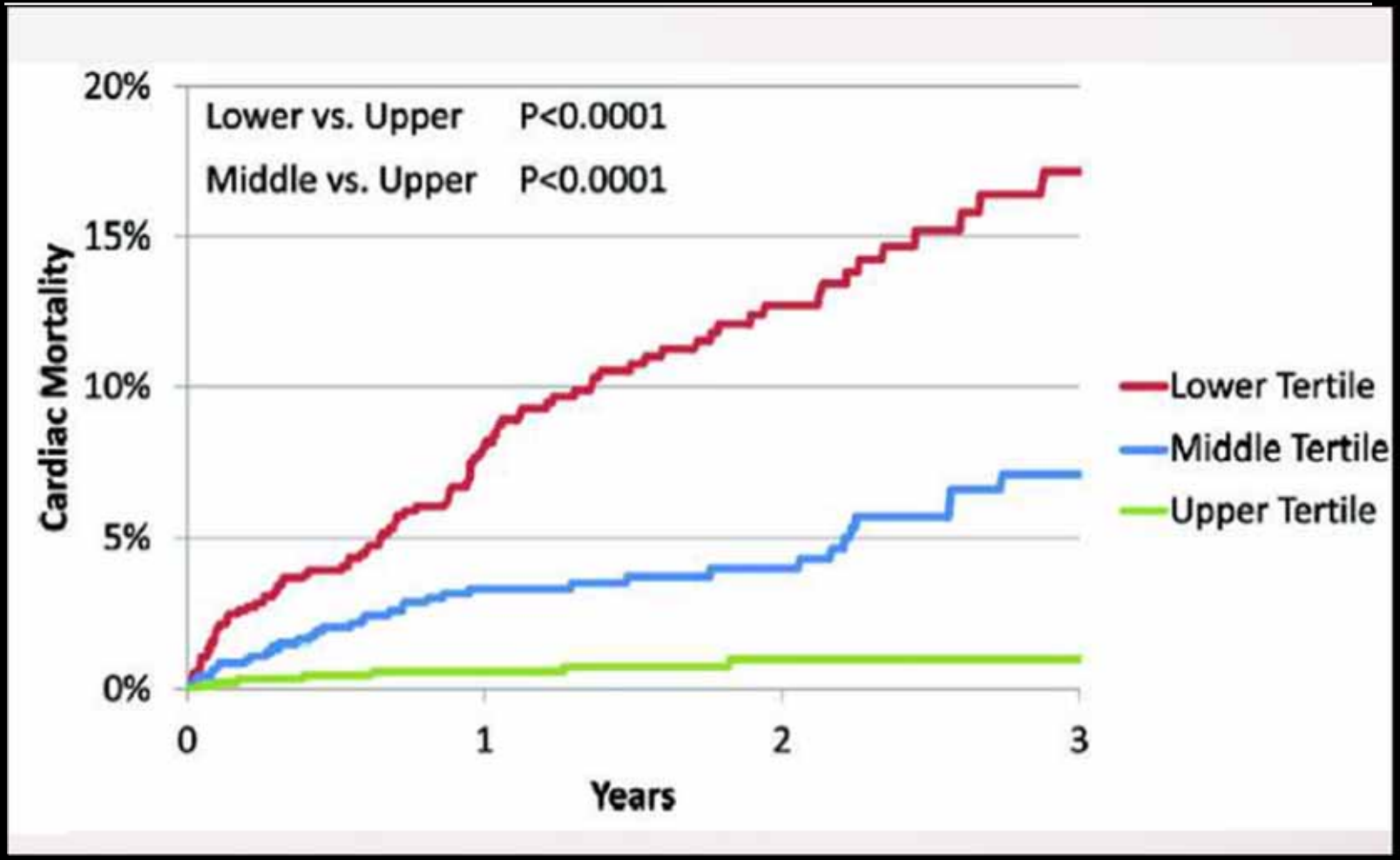
Ziadi et al. J Nucl Cardiol 2012

Myocardial Flow Reserve and Prognosis



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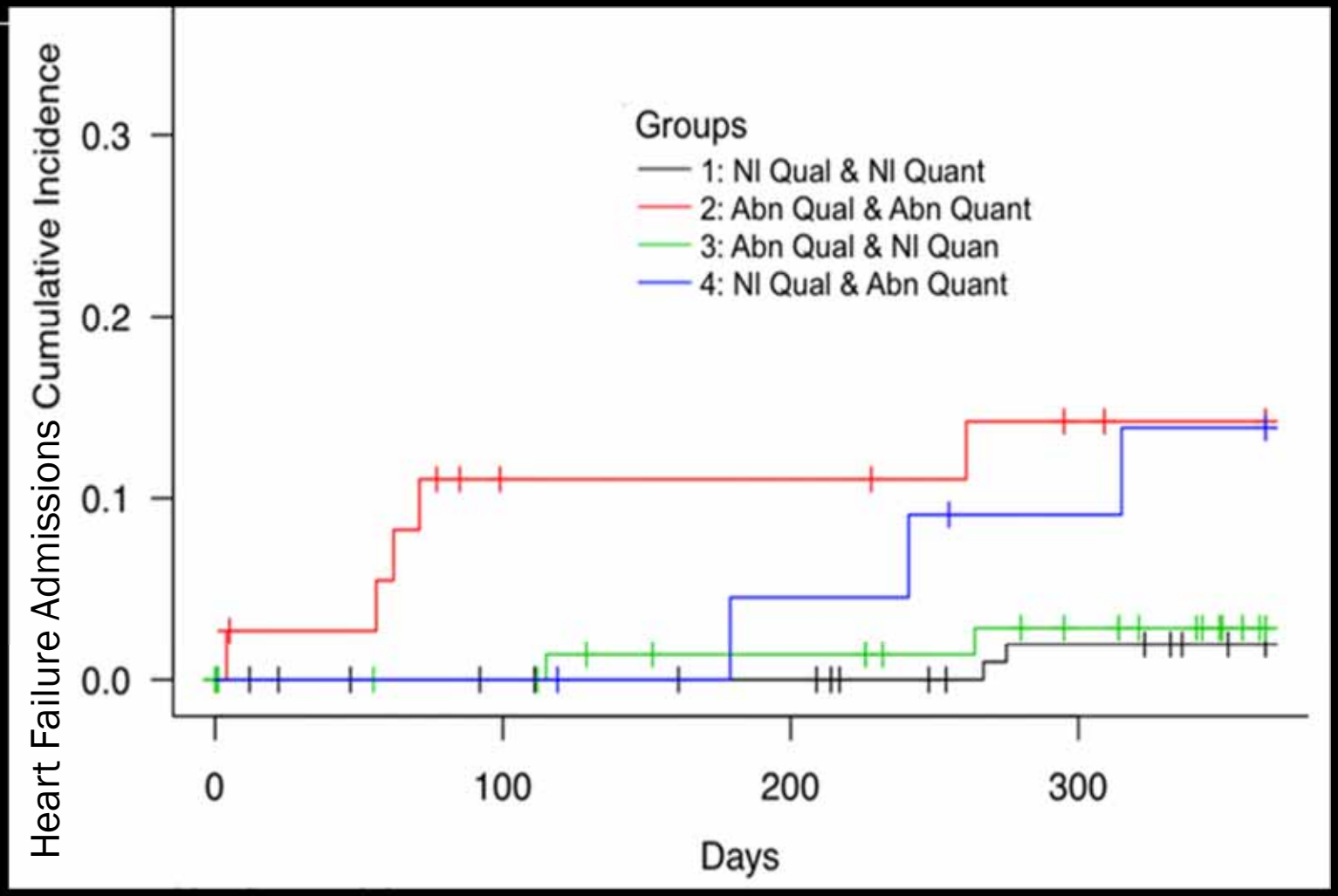
Murthy et al. Circulation 2011

Myocardial Flow Reserve and Prognosis



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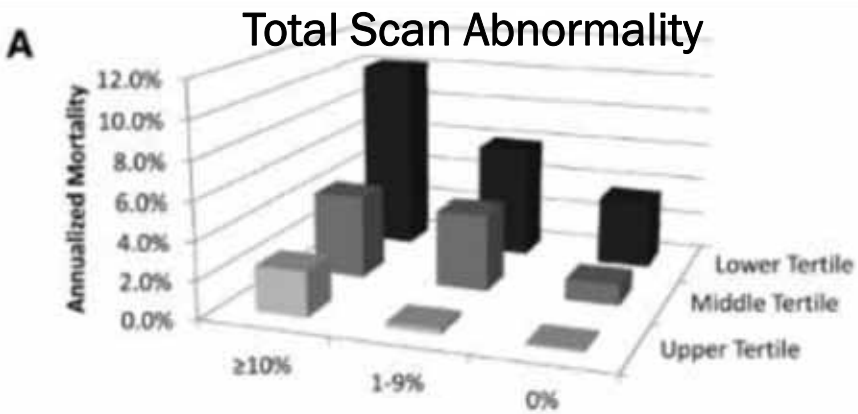
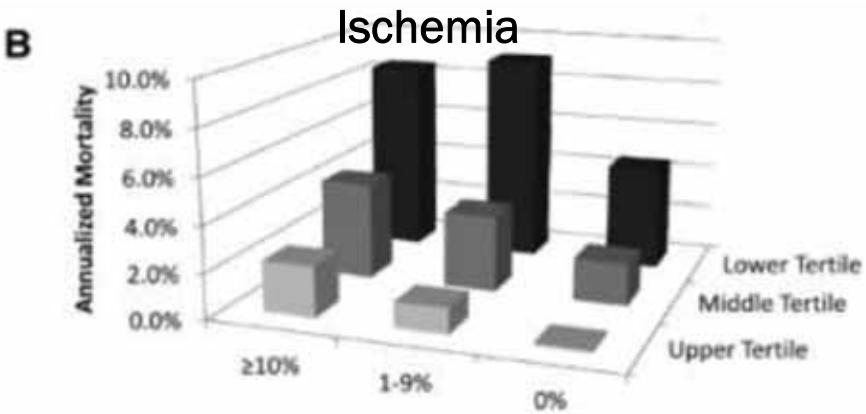
Elman et al. ASNC 2018



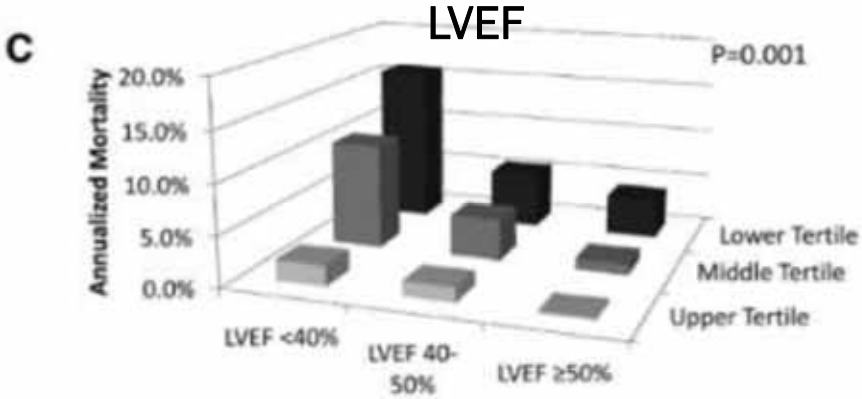


CFR

	≥10%	(n)	1-9%	(n)	0%	(n)
Upper Tertile	2.4%	(119)	0.3%	(195)	0.1%	(614)
Middle Tertile	4.4%	(217)	4.0%	(202)	1.1%	(509)
Lower Tertile	10.2%	(416)	6.0%	(190)	3.6%	(321)

CFR

	≥10%	(n)	1-9%	(n)	0%	(n)
Upper Tertile	2.2%	(50)	1.1%	(197)	0.1%	(681)
Middle Tertile	4.2%	(119)	3.3%	(234)	1.8%	(575)
Lower Tertile	8.5%	(232)	9.1%	(298)	4.5%	(397)



CFR

	LVEF <40%	(n)	LVEF 40-50%	(n)	LVEF ≥50%	(n)
Upper Tertile	2.0%	(65)	1.4%	(89)	0.2%	(774)
Middle Tertile	10.5%	(116)	4.1%	(120)	1.1%	(692)
Lower Tertile	15.9%	(230)	5.6%	(144)	4.0%	(553)

Murthy VL et al. Circulation. 2011;124:2215–24

EDITORIAL

Reporting myocardial flow reserve with PET. Ready or not, here it is! But walk before you fly!

Daniel Juneau, MD,[a] Robert A. deKemp, PhD,[b] and Rob S. B. Beanlands, MD[b]

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J Nucl Cardiol 2018;25:164–8.

Challenges of Incorporating PET into Practice

- Cost
  - *Rb-82 generator is expensive (cost per patient decreases the more patients you do)*
    - How do you get a lot of pts referred for a test you aren't even offering yet?
  - *PET scanner*
    - Need a new scanner?
    - Use the scanner you already have
      - *How incorporate cardiac PET into your oncologic PET schedule*
    - Avoiding detector saturation
      - *Dose must be adjusted to avoid detector saturation during the blood pool phase (particularly challenging with ^{82}Rb).*
    - Reimbursement
      - *Patient selection*
- Understanding how to integrate additional info into report
- Educating referring clinicians

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Decision Analysis

Occasional Imaging	*and*	On-site cyclotron	N-13 ammonia
Daily Imaging	*and*	PET/CT capacity	Rb-82 chloride

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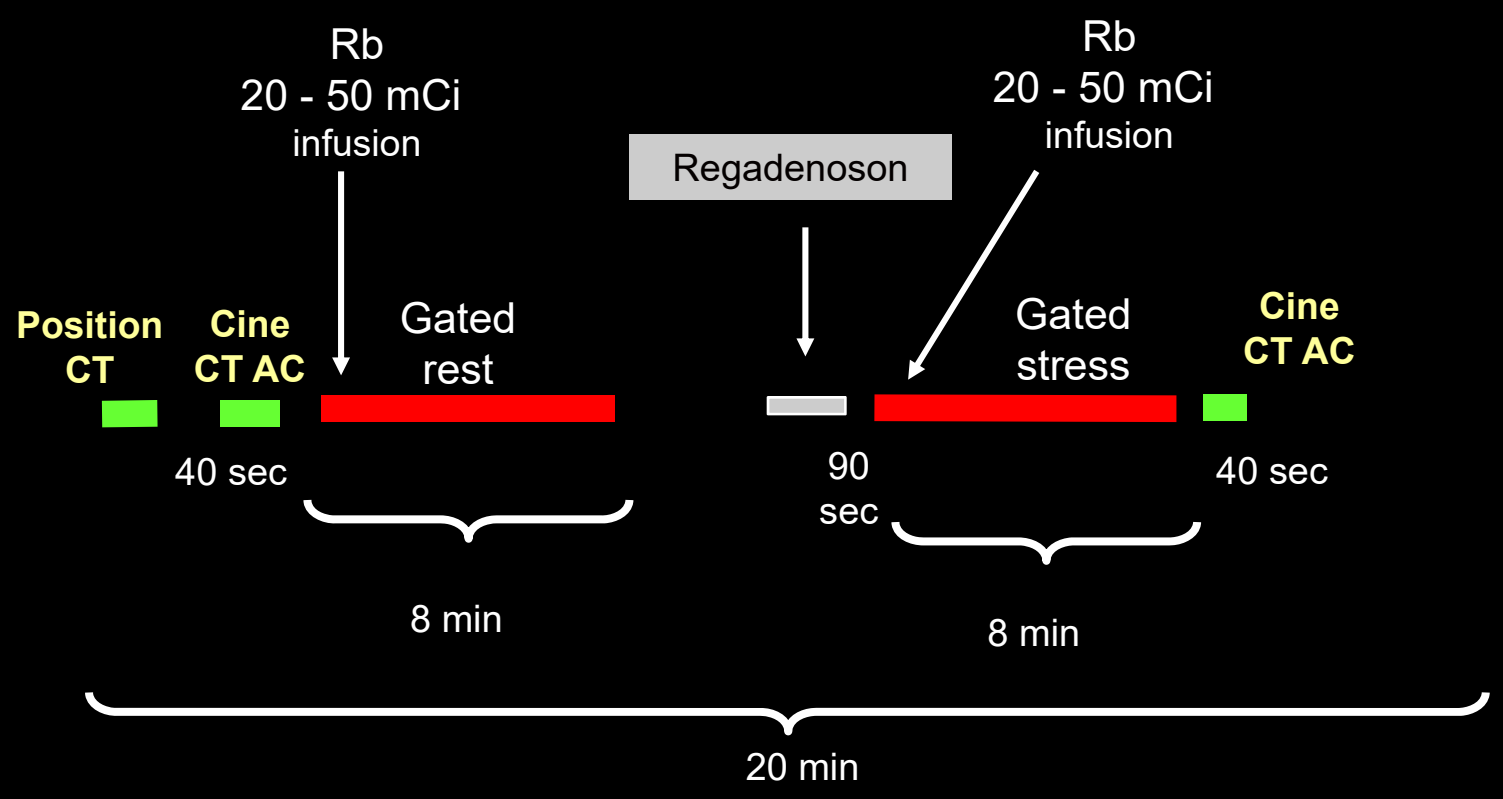
Myocardial Perfusion PET/CT Protocol



Cine CT Acquisition (120 kVp, 20mA, 2.5mm slice, 0.8 sec rot, ~4.8 sec cine duration)

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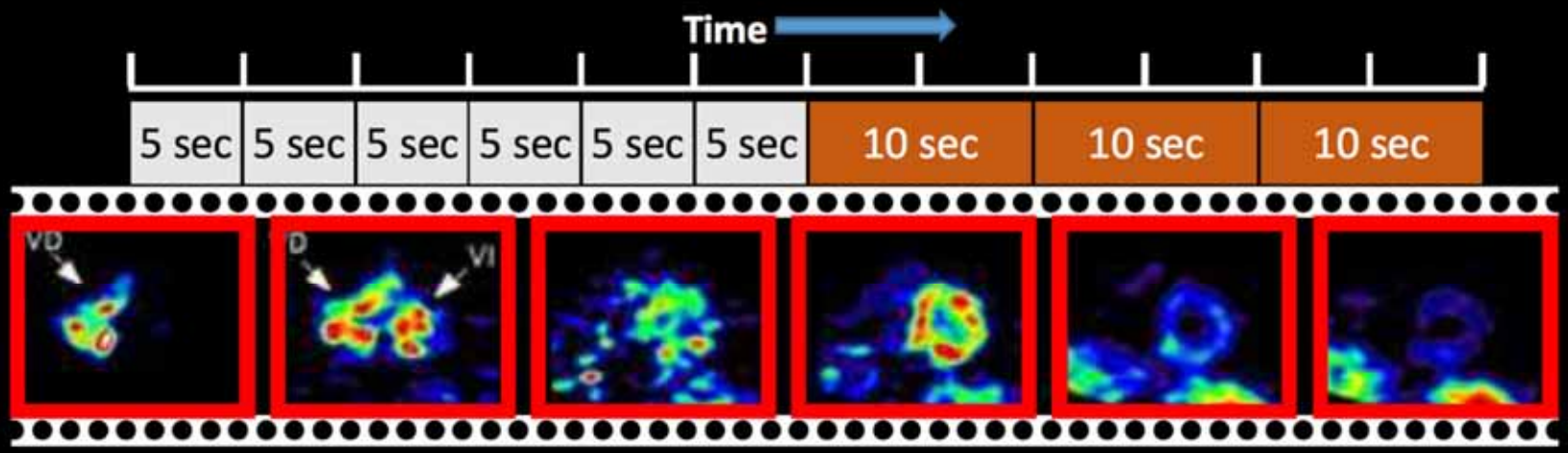
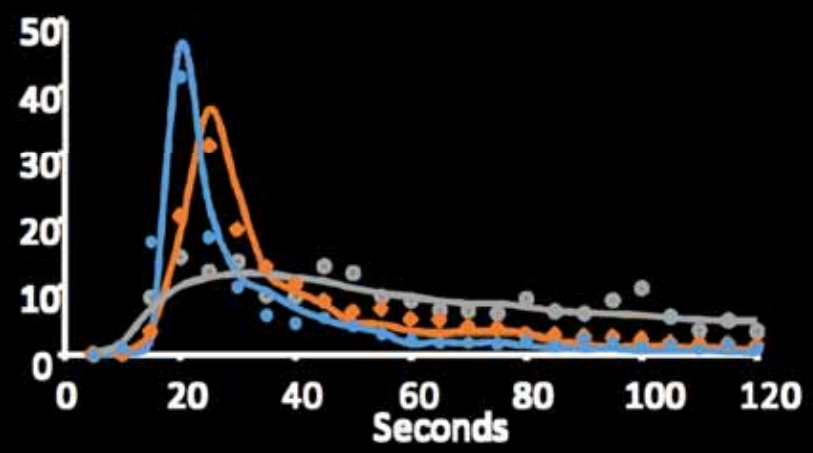
Courtesy of Laurie Soine, ARNP

Dynamic Acquisition



Number of Frames	Frame Duration
14	5 seconds
6	10 seconds
3	20 seconds
3	30 seconds
1	150 seconds



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Murthy. Nuts & Bolts of Cardiac PET Perfusion Imaging ASNC Webinar: Clinical Quantification of Myocardial Blood Flow Using PET: Joint Position Paper of the SNMMI Cardiovascular Council and the ASNC

Clinical Appropriateness Guidelines: Advanced Imaging

Appropriate Use Criteria: Imaging of the Heart

Effective Date: January 1, 2018

Proprietary

Date of Origin: 03/30/2005
Last revised: 11/14/2017
Last reviewed: 11/14/2017

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Patient Selection

- When non-invasive imaging is required in morbidly obese patients (BMI > or = 40 kg/m2), with suspected or established CAD, perfusion PET imaging may be considered as the initial test (because of a higher likelihood of technically suboptimal image quality on nuclear stress testing and stress echocardiography in this patient subgroup).
- PET perfusion imaging may also be a preferable initial noninvasive test for other patients in whom conventional nuclear perfusion imaging is likely to be suboptimal including those with breast implants, previous mastectomy, pleural or pericardial effusion, chest wall deformity and those with suboptimal prior nuclear imaging due to attenuation artifact.
- Perfusion PET myocardial imaging is not appropriate for screening for coronary artery disease in asymptomatic low-risk patients regardless of age or body habitus. Whenever possible and clinically appropriate, exercise stress testing should be used in preference to pharmacological testing. However, for patients who are unable to exercise or who have baseline EKG abnormalities which make pharmacological testing preferable, PET imaging is preferable to conventional nuclear perfusion imaging or stress echocardiography.

ASNC

ASNC/SNMMI POSITION STATEMENT

AMERICAN SOCIETY OF NUCLEAR CARDIOLOGY AND SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING JOINT POSITION STATEMENT ON THE CLINICAL INDICATIONS FOR MYOCARDIAL PERFUSION PET

Writing Group:

Timothy M. Bateman MD (Co-Chair), Vasken Dilsizian MD (Co-Chair), Rob S. Beanlands MD, E. Gordon DePuey MD, Gary V. Heller MD, PhD, David A. Wolinsky MD

provided by a noninvasive cardiac imaging test. Cardiac imaging tests can provide information regarding the presence, extent, and severity of CAD, estimate risk for early and late major adverse cardiac events, and assist in determining the most appropriate treatment, including medical therapy and/or coronary revascularization. Valuable information can also be provided from a normal scan result that can obviate the need for further cardiac tests, reduce unnecessary medication expenses, lead to expeditious referrals for assessment of other causes of symptoms, and relieve anxiety over potential life-threatening etiologies for symptoms.

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Bateman et al. J Nucl Cardiol 2016

Clinical Indications

- Prior stress imaging study that was of poor quality, equivocal or inconclusive, affected by attenuation artifact, or discordant with clinical impressions or other diagnostic test results including findings at coronary angiography.
- Body characteristics that commonly affect image quality [large breasts, breast implants, obesity (BMI greater than 30), protuberant abdomen, chest wall deformities, pleural effusions, and inability for proper body positioning such as inability to position arms outside of a SPECT scanner's field of view].

Bateman et al. J Nucl Cardiol 2016

Clinical Indications

- High-risk patients in whom diagnostic errors carry even greater clinical implications.
  - *Chronic kidney disease stage 3, 4 or 5*
  - *Diabetes mellitus*
  - *Known or suspected potentially high-risk CAD such as left main, multivessel, or proximal LAD disease*
  - *Known extensive coronary disease following CABG or PCI*
  - *Suspected transplant coronary vasculopathy*
  - *When ischemia is suspected in patients with LV dysfunction*
  - *Patients for whom revascularization carries increased morbidity and mortality risk.*

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Bateman et al. J Nucl Cardiol 2016

Clinical Indications

- Young patients with established CAD who are anticipated to need repeated exposures to radiation-associated cardiac imaging procedures, in order to minimize accumulated life-time exposure.
- Patients in whom myocardial blood flow quantification is identified by clinicians to be a needed adjunct to the image findings, to better identify or exclude multivessel CAD, for improved risk stratification, and when assessment of microcirculatory function is needed for clinical decision making.
- NO clinical scenarios where PET should not be considered a preferred test for patients who meet appropriate criteria for a stress imaging test and who require pharmacologic stress.

Bateman et al. J Nucl Cardiol 2016

CATEGORY III CODES

MSN HEALTHCARE SOLUTIONS

New

- **+0482T** Absolute quantitation of myocardial blood flow, positron emission tomography (PET), rest and stress (List separately in addition to code for primary procedure)

  (Use 0482T in conjunction with 78491, 78492)

  (For myocardial imaging metabolic evaluation, use 78459)

  (For positron emission tomography [PET] myocardial perfusion study, see 78491, 78492)

AMA Announces New CPT Category III Code for PET Absolute Quantification of Myocardial Blood Flow

By: admin **On**: 07/31/2017 13:43:30 **In**: Advocacy

As ASNC announced earlier this year, the **American Medical Association**'s Current Procedural Terminology (CPT®) Editorial Panel has approved a category III billing code for PET absolute quantitation of myocardial blood flow, effective **Jan. 1, 2018**.

This is an important early step in accurate billing and reimbursement for this service. Much advocacy work remains to be done, however.

Unlike permanent category I CPT codes, category III CPT codes (also called "temporary" codes or "tracking" codes) are used for emerging technologies and procedures to allow tracking as these new services become better established. In fact, it is not proper to use a different code, such as an unlisted code, if the category III code applies.

The new CPT code language is provided below:

This is an add-on code, which means that it must be reported in conjunction with the codes for PET myocardial perfusion, 78491 or 78492. Code +0482T would be expected to be reported on the same day as codes 78491 / 78492.The establishment of this category III code is an important step.The requirement for a category I CPT code with subsequent relative values in the Medicare physician fee schedules will require widespread use of the service and more advocacy by the ASNC community.

Effective Jan. 1, 2018

+0482T Absolute quantitation of myocardial blood flow, positron emission tomography (PET), rest and stress (list separately in addition to code for primary procedure)

Use 0482T in conjunction with 78491, 78492.
For myocardial imaging metabolic evaluation, use 78459.
For positron emission tomography (PET) myocardial perfusion study, see 78491, 78492.

eviCore Adds Coverage for Thyroid Imaging, Cites SNMMI Guideline

April 25, 2018

eviCore, one of the leading medical benefits management companies in the U.S., has updated its coverage guidelines for whole-body thyroid imaging. eviCore cites SNMMI's practice guideline as the reasoning/evidence to support the change to add thyroid imaging coverage. Specifically, eviCore added "whole-body thyroid nuclear scan post-thyroidectomy" and "whole-body thyroid nuclear scan within two weeks of RAI therapy."

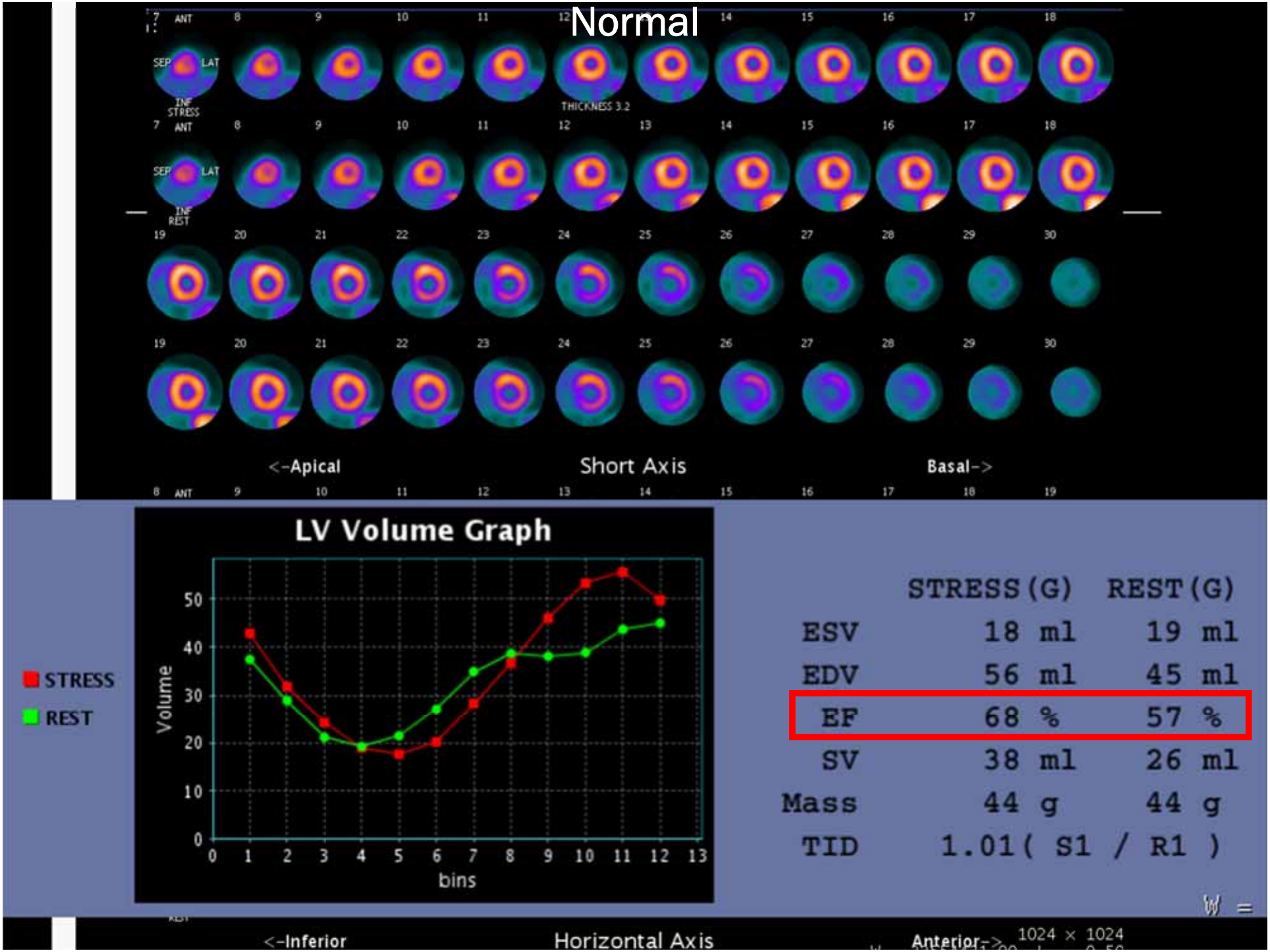
eviCore also added the new CPT Category III Code for cardiac PET, CPT +0482T absolute quantitation of myocardial blood flow, positron emission tomography (PET), rest and stress.

View the full list of eviCore Cardiology & Radiology Imaging Guideline Revisions, effective May 1, 2018 »

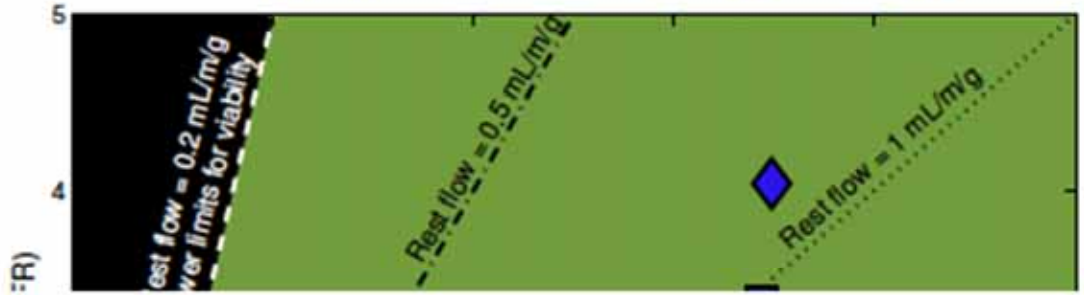
CPT Codes

- 78459: Myocardial imaging, (PET), metabolic evaluation
- 78491: Myocardial imaging, positron emission tomography, (PET), perfusion; single study at rest or stress
- 78492: Myocardial imaging, positron emission tomography, (PET), perfusion; multiple studies at rest and/or stress
- 0482T: Absolute quantitation of myocardial blood flow, positron emission tomography (PET), rest and stress (List separately in addition to code for primary procedure) (effective 1/1/2018)
- Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.
- CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Normal


ANT
SEP
LAT
INF
STRESS
THICKNESS 3.2
REST
<-Apical
Short Axis
Basal->
LV Volume Graph
STRESS
REST
Volume
bins
STRESS(G) REST(G)
ESV 18 ml 19 ml
EDV 56 ml 45 ml
EF 68 % 57 %
SV 38 ml 26 ml
Mass 44 g 44 g
TID 1.01(S1 / R1)
<-Inferior
Horizontal Axis
Anterior->
1024 × 1024

Interaction between Resting MBF, Stress MBF, and CFR



Myocardial Blood Flow (mL/min/g) & CFR (Stress/Rest) from Base to Apex

	LAD			RCA			Circumflex		
	Base	Mid	Apex	Base	Mid	Apex	Base	Mid	Apex
Rest	1.28	1.24	1.02	0.94	1.02	0.86	0.93	1.15	0.97
Stress	3.43	3.59	2.69	2.84	3.43	3.49	2.09	2.78	2.79
CFR	2.68	2.89	2.63	3.02	3.36	4.04	2.25	2.42	2.89
Interpret	*7	*7	*7	*7	*7	*7	*6	*7	*7

*Table 1: Interpretation based on [3]: *6: No ischemia, minimally reduced flow capacity; *7: Normal flow;*

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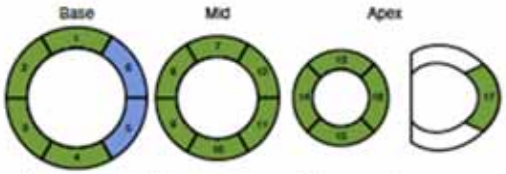
*Table 1: Interpretation based on [3]: *6: No ischemia, minimally reduced flow capacity; *7: Normal flow;*



Patient specific mapping of flow estimates to relationship plotted above.

History

- **69 year-old female admitted to hospital after a cerebrovascular accident; found to be in atrial fibrillation; small increase in troponin i.**
- **PMH: Hypertension; Type II diabetes**

Rest/dipyridamole stress Rubidium-82 myocardial perfusion PET study

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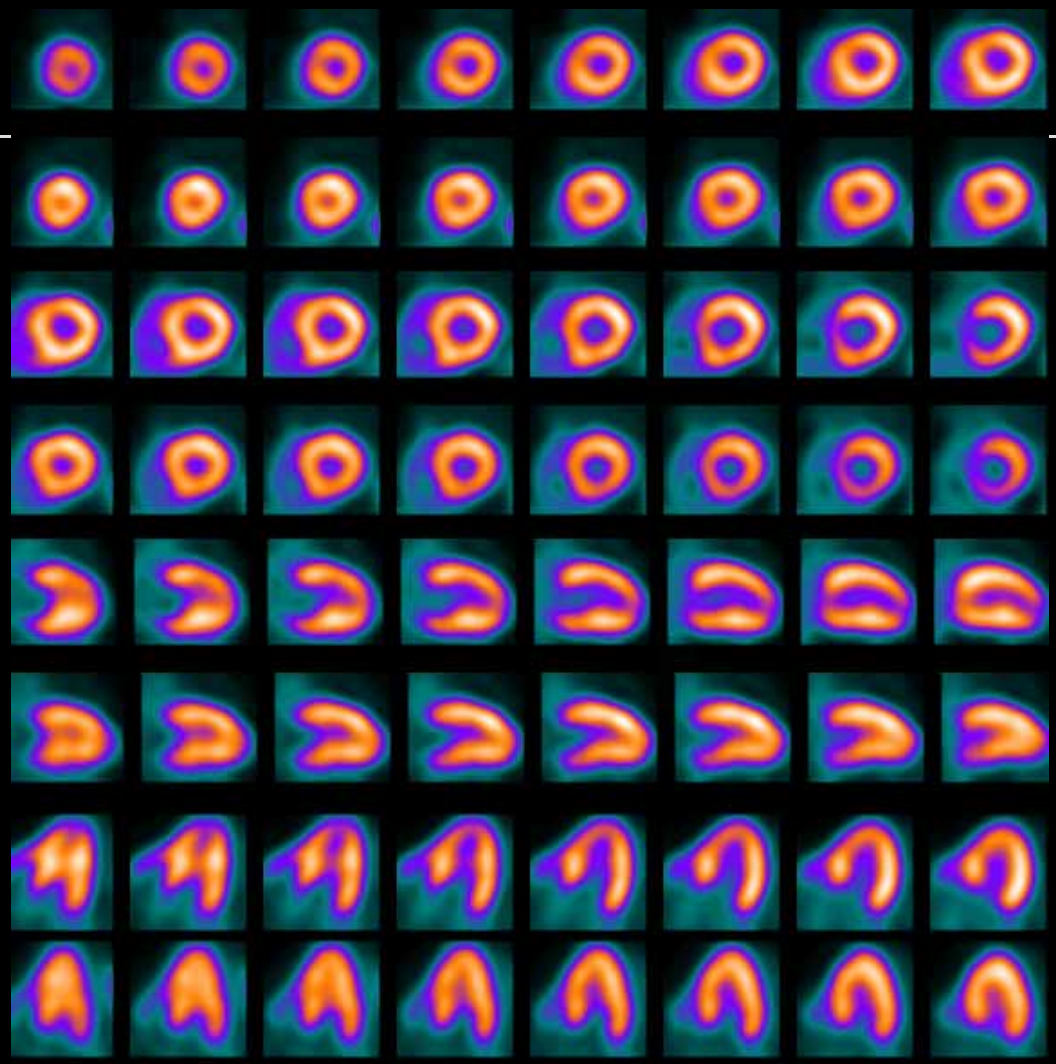
Case courtesy of Tim Bateman, MD, Cardiovascular Consultants, Kansas City, MO

^{82}Rb PET Images

Near Balanced Flow Reduction



STRESS

REST

TID Ratio 1.63

Case courtesy of Tim Bateman, MD, Cardiovascular Consultants, Kansas City, MO

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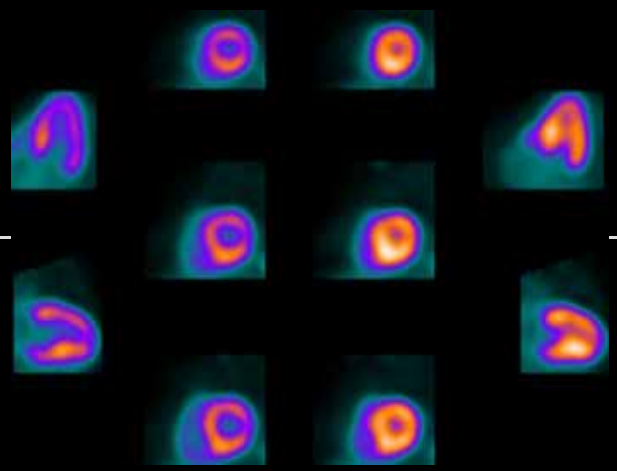
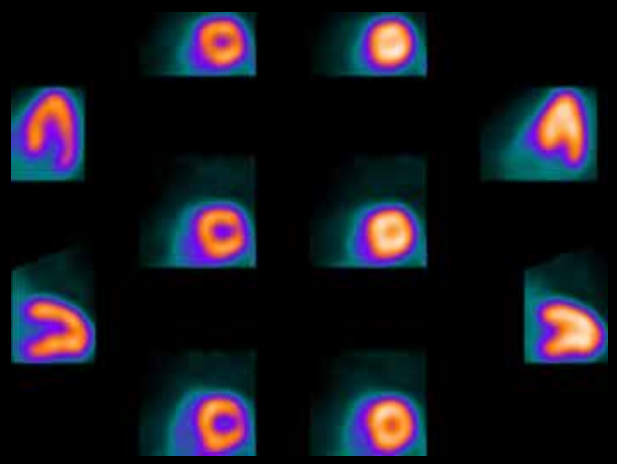
^{82}Rb PET Functional Images



PEAK STRESS

LVEF 50%



REST

LVEF 61%

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Case courtesy of Tim Bateman, MD, Cardiovascular Consultants, Kansas City, MO

PET Report

The combined test findings indicate the following:

1. Virtually diagnostic for the presence of CAD.
2. Apical ischemia probably in the distribution of the left anterior descending coronary artery.
3. Severe transient ventricular dilation, suggesting possible near-balanced flow reduction in multiple coronary territories.
4. Normal left ventricular function at rest (LVEF 61%).
5. Significant drop in LVEF in response to pharmacologic stress.
6. Prognostically concerning scan, with numerous markers of high-risk for major adverse coronary events.

Case courtesy of Tim Bateman, MD, Cardiovascular Consultants, Kansas City, MO

Cath Correlation

- Coronary angiography showed a 75% left main stenosis, a 90% stenosis of the mid LAD, and a 70% right coronary artery stenosis.
- CABG surgery was performed after recovery from the CVA.

Case courtesy of Tim Bateman, MD, Cardiovascular Consultants, Kansas City, MO

Quantitative Coronary Flow Capacity for Risk Stratification and Clinical Decision Making: Is It Ready for Prime Time?

Marcelo F. Di Carli[1–3] and Rory Hachamovitch[4]

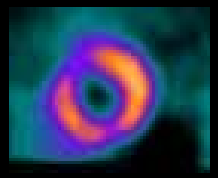
[1]Cardiovascular Imaging Program, Departments of Medicine and Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [2]Division of Nuclear Medicine and Molecular Imaging, Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [3]Division of Cardiovascular Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; and [4]Cardiovascular Imaging Section, Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Cleveland, Ohio

See the associated article on page 410.

Semiquantitative evaluation of regional myocardial perfusion has been standard practice in nuclear cardiology for more than 3 decades. This approach has proven to be accurate and reproducible. Most importantly, semiquantitative measures of total perfusion deficit and myocardial ischemia are powerful markers of clinical risk and have served as clinically relevant guides to patient

the underestimation of the extent of ischemia and obstructive atherosclerosis in the setting of multivessel CAD and the inability to identify patients with clinically important nonobstructive atherosclerosis. Indeed, a growing body of data have demonstrated that quantitative MBF and MFR are unique phenotyping tools to assess vascular health and preclinical atherosclerosis, which, in higher risk patients, can reveal flow-limiting coronary artery stenoses, thereby improving the accuracy of myocardial perfusion imaging in the diagnostic evaluation of known or suspected CAD (*7–10*). More recent data support the notion that coronary vascular dysfunction, as quantified by reduced MFR, is highly prevalent among patients with known or suspected CAD (*11,12*), increases the se-

Take Home Points – Myocardial Perfusion PET



- Low radiation exposure (1-5 mSv)
- Short acquisition protocols (< 1 hr w/ Rb-82)
- High-quality images (particularly helpful to minimize artifacts from tissue attenuation and scatter)
- High diagnostic accuracy
- Ability to calculate LVEF Reserve
- Ability to identify non-response to stress
- Strong prognostic power

Questions?
shaelman@salud.unm.edu
Thank you!

Which of the following is an advantage of SPECT over PET for myocardial perfusion imaging?

A. *Ability to obtain LVEF reserve*
B. *Shorter acquisition times*
C. *Lower radiation dose*
D. *Ability to perform treadmill stress*

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A. *Ability to obtain LVEF reserve*
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D. *Ability to perform treadmill stress*

D is correct, exercise stress remains the preferred stress modality for optimal risk assessment. However, patients referred for PET MPI all undergo pharmacologic stress since the currently FDA-approved positron-emitting tracers (Rb-82 & N-13 Ammonia) have very short half-lives, thereby precluding upright exercise testing with its inherent delay in moving patients post-exercise for imaging in the PET camera. If/when F-18 Flupiridaz is approved, the longer half-life associated with this tracer will allow for treadmill stress.

Ability to obtain LVEF reserve, shorter acquisition times, and lower radiation dose are all benefits of PET myocardial perfusion imaging over SPECT.

References:

Gonzalez and Beller. Choosing exercise or pharmacologic stress imaging. J Nucl Cardiol 2017; 24(2): 555–557.

Dorbala et al. Incremental Prognostic Value of Gated Rb-82 Positron Emission Tomography Myocardial Perfusion Imaging Over Clinical Variables and Rest LVEF. JACC Cardiovasc Imaging. 2009; 2(7): 846–854.

Myocardial flow reserve (MFR) is:

A. *The ratio of resting MBF to MBF during maximal coronary vasodilation*
B. *The ratio of MBF during maximal coronary vasodilation to resting MBF*
C. *Resting MBF + MBF during maximal coronary vasodilation/resting MBF*
D. *Resting MBF + MBF during maximal coronary vasodilation/ MBF during maximal coronary vasodilation*

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D. *Resting MBF + MBF during maximal coronary vasodilation/ MBF during maximal coronary vasodilation*

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