MAYO CLINIC

12th Houston Methodist Annual Multimodality Cardiovascular Imaging for the Clinician

PET/CT IN CORONARY ARTERY DISEASE

SHOULD IT REPLACE SPECT?

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Professor of Medicine
Education Chair
Director of Nuclear Cardiology

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DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INDUSTRY

- Consulting: Clario, GE Healthcare
- Royalties: UpToDate
- Speakers' honorarium: Ionetix

DISCLOSURE OF NON-FINANCIAL RELATIONSHIP(S)

- American Society of Nuclear Cardiology Board of Directors and Executive Council

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- F-18 Flurpiridaz
- O-15 Water

𝕏@PanithayaC

LEARNING OBJECTIVES

- Review characteristics of PET and SPECT MPI
- Discuss pragmatic issues affecting utilization of PET MPI

SHOULD PET/CT REPLACE SPECT MPI

- Diagnostic accuracy
- Prognostic value
- Guides management

SHOULD PET/CT REPLACE SPECT MPI

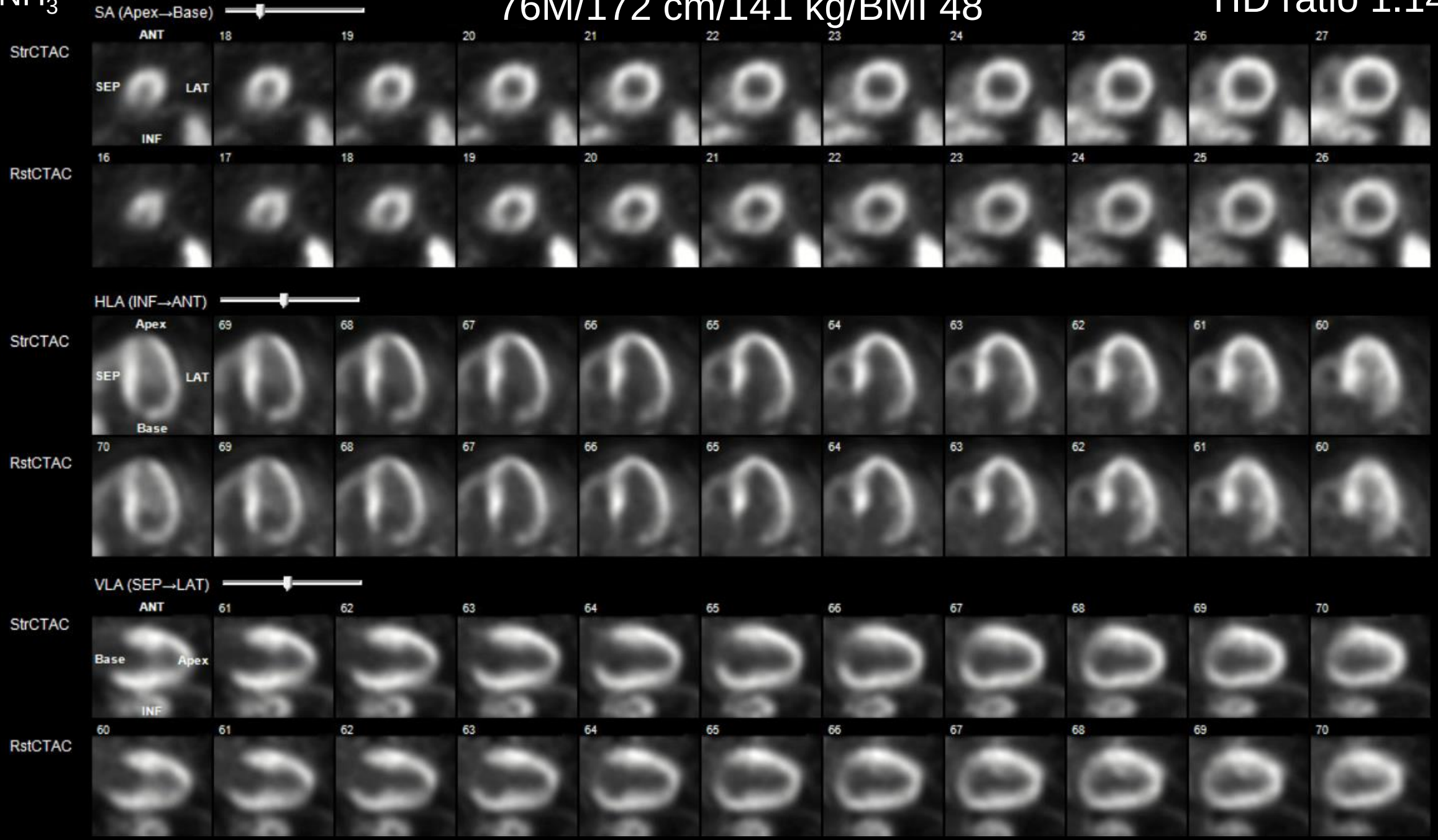
- Diagnostic accuracy
- Prognostic value
- Guides management
- Image quality and interpretive certainty
- Ancillary data from hybrid systems
- Radiation exposure
- Protocol efficiency
- Availability of PET perfusion tracers
- Ability to perform exercise or pharmacologic stress
- Availability of camera systems
- Cost and reimbursement
- Guideline recommendation

DIAGNOSTIC ACCURACY

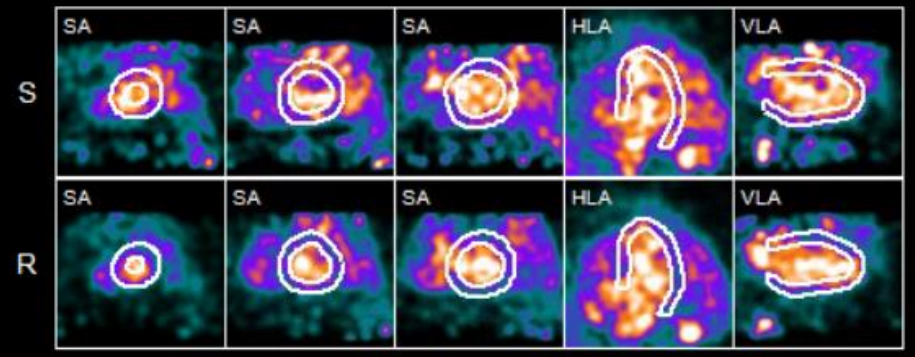
$^{13}NH_3$

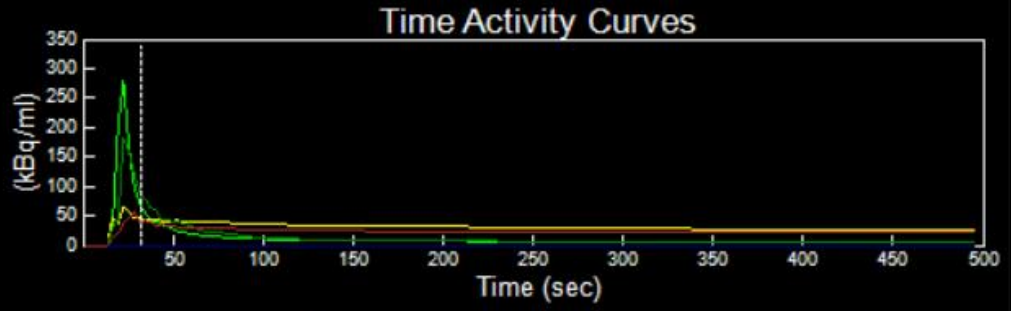
76M/172 cm/141 kg/BMI 48

TID ratio 1.14



$^{13}NH_3$

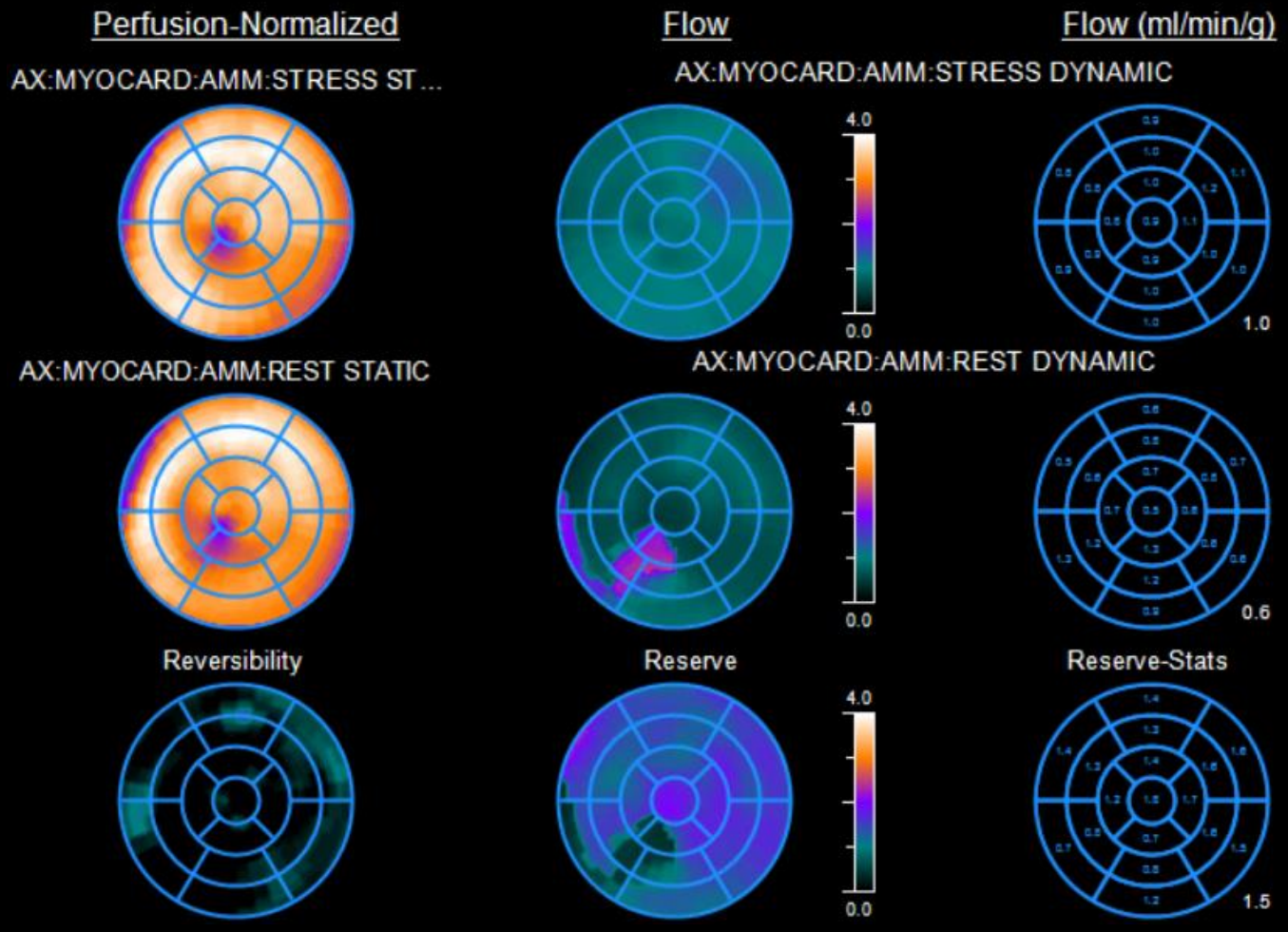


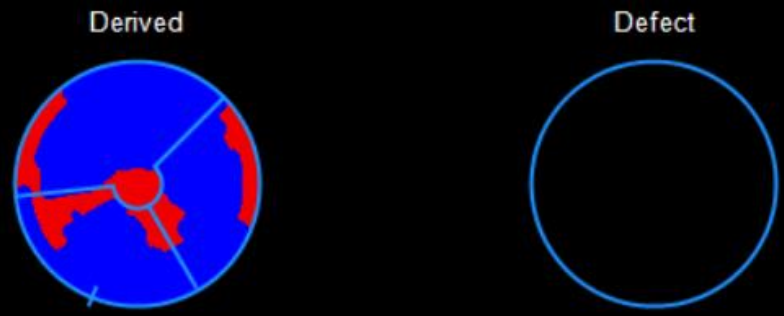


Algorithm (MC Str): INVIA N-13 ROI 1:1
Algorithm (MC Rst): INVIA N-13 ROI 1:1

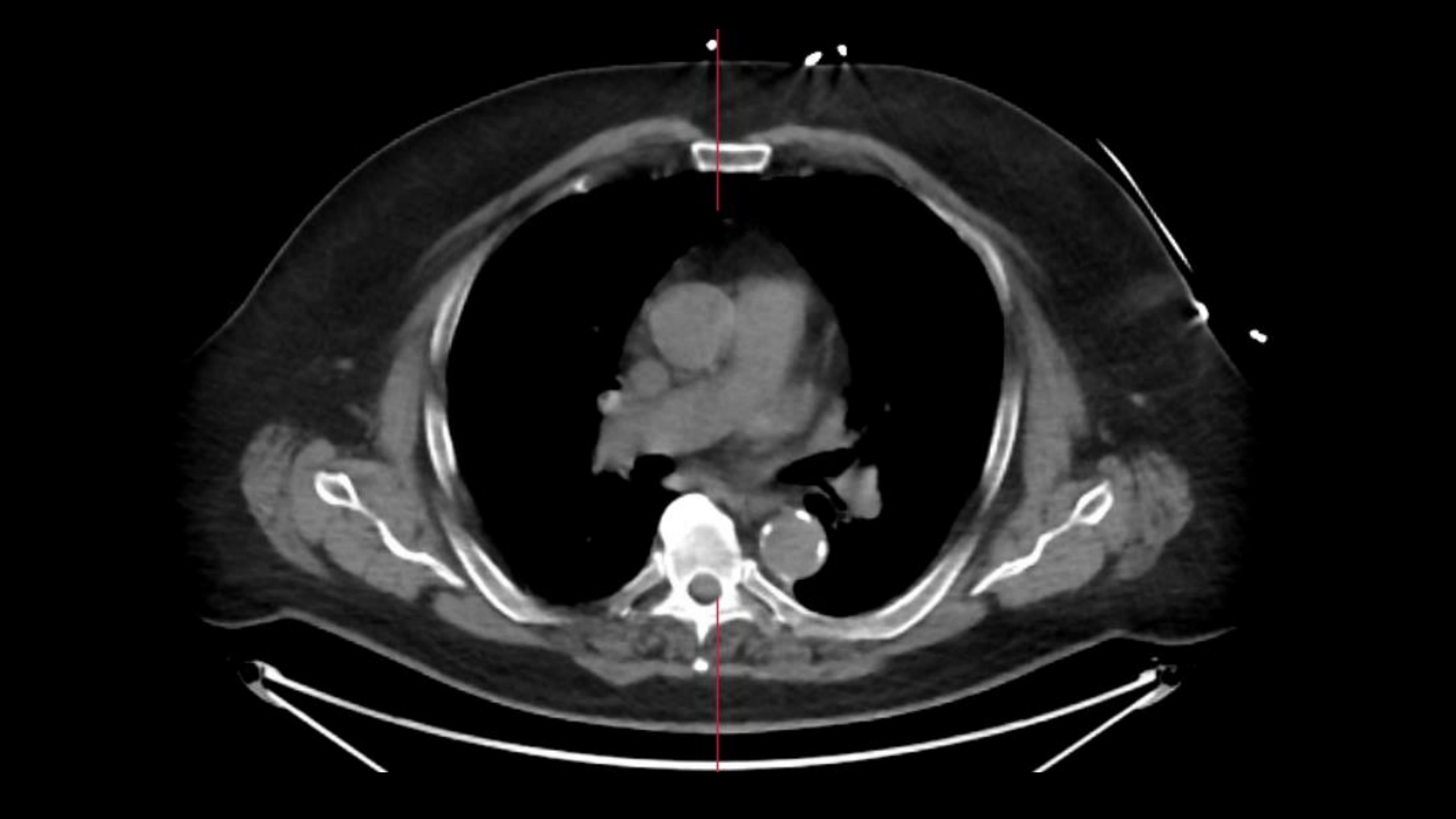
Global Results

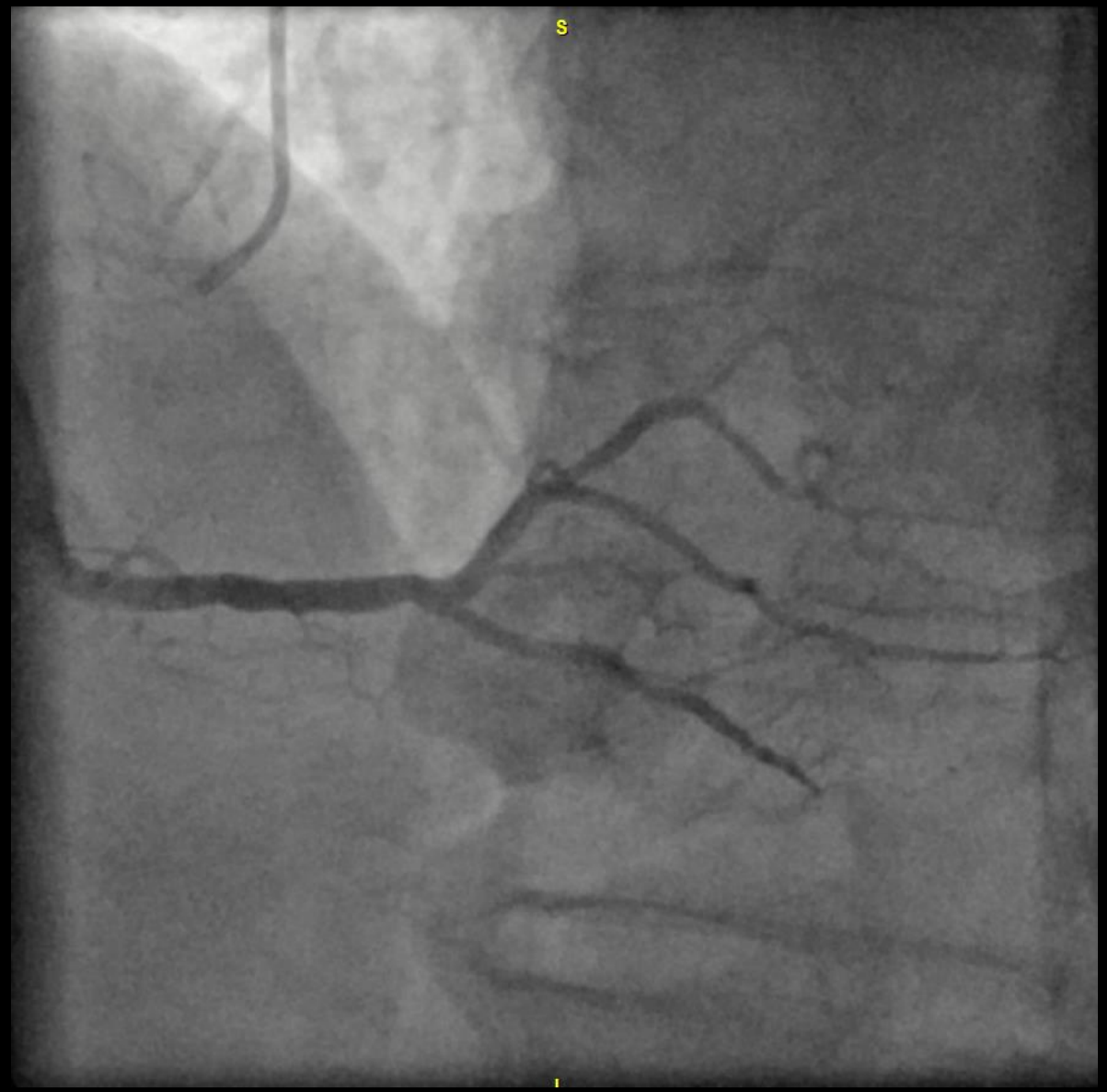
Region	Mean Flow (ml/min/g) MC Str	MC Rst	MC Str	MC Rst	Reserve
LAD	86%	85%	0.91	0.65	1.39
LCX	83%	82%	1.06	0.66	1.60
RCA	81%	76%	1.20	0.73	1.64
TOT	84%	81%	0.96	0.65	1.48





Region	Normal	N Perf/ A Flow	A Perf/ N Flow
LAD	18 % (1.73)	82 % (1.39)	0 % (--)
LCX	23 % (1.65)	77 % (1.60)	0 % (--)
RCA	27 % (1.54)	73 % (0.85)	0 % (--)
TOT	22 % (1.64)	78 % (1.30)	0 % (--)



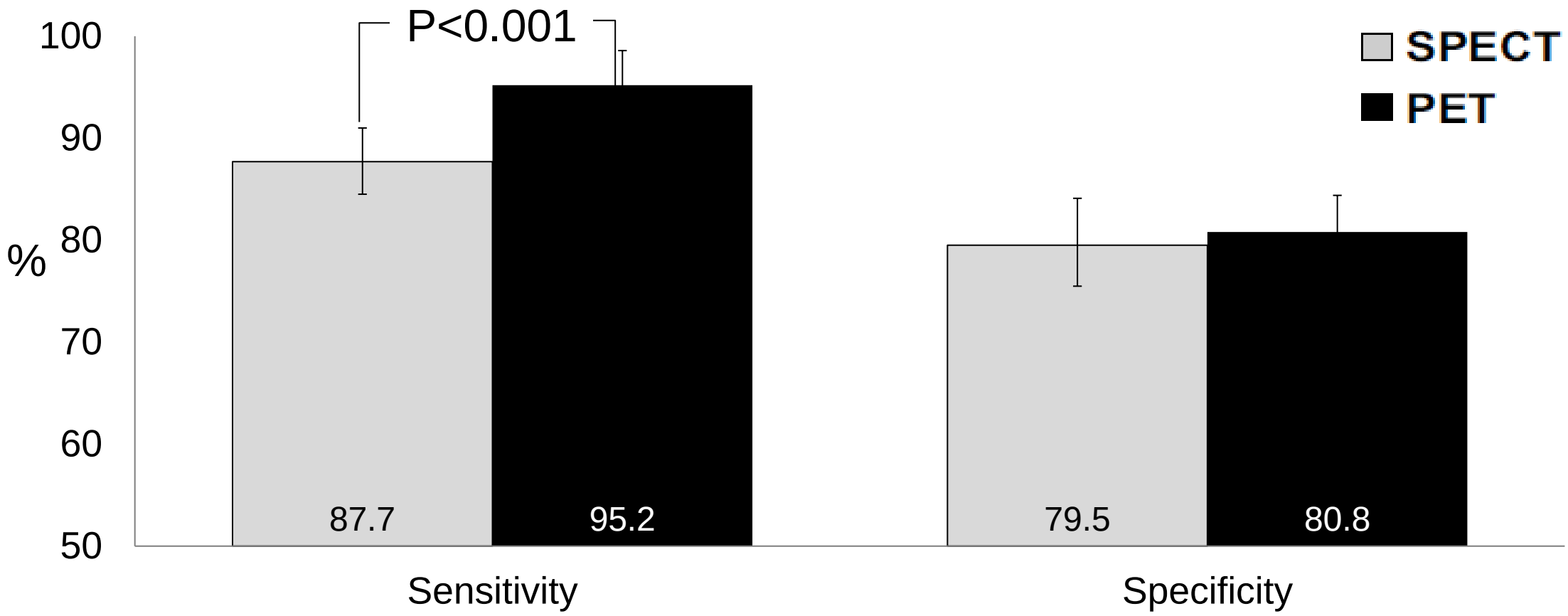


80% LM with post-stenotic dilation into origin of LAD and LCx
Ramus 70%, ostial RCA 70%

DIAGNOSTIC ACCURACY

META-ANALYSIS OF 11,862 PATIENTS

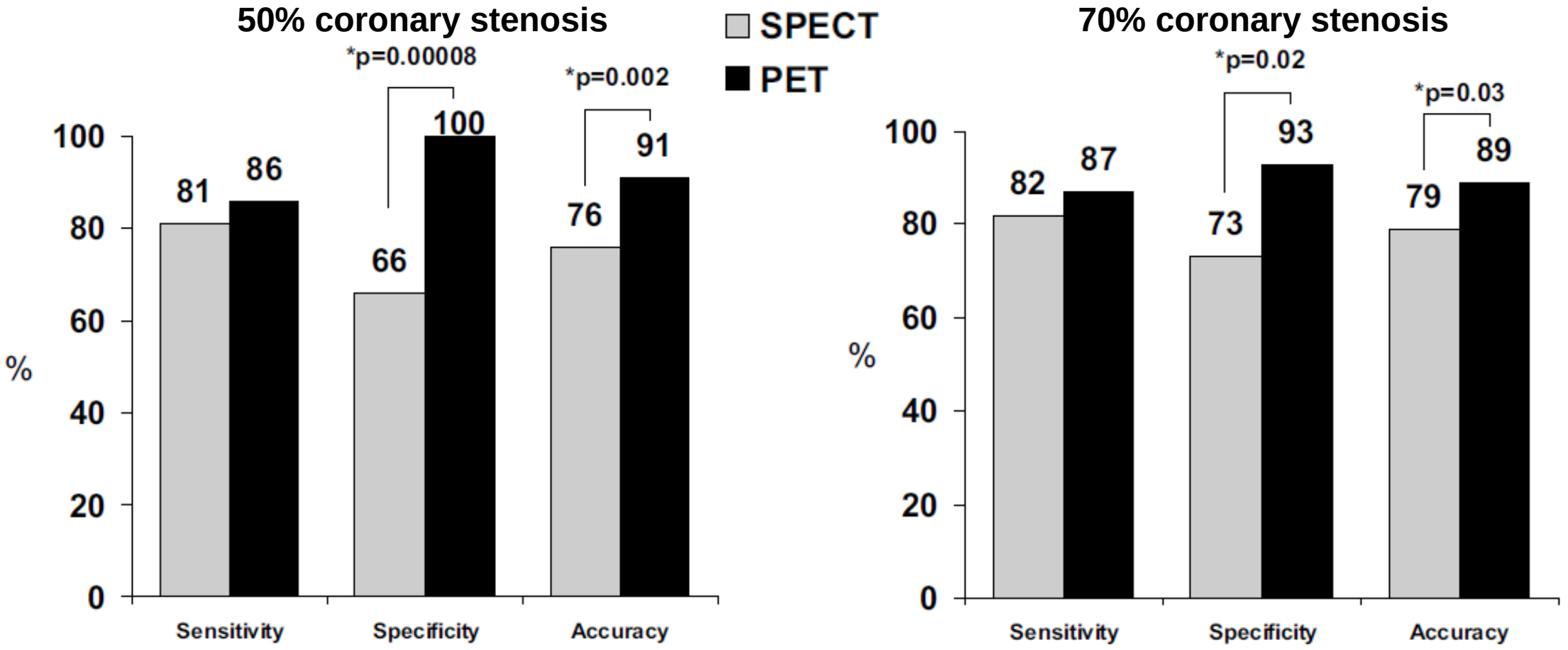
PET MPI HAS SIGNIFICANTLY HIGHER SENSITIVITY



Parker MW et al. Circ Cardiovasc Imaging 2012;5:700-707

DIAGNOSTIC ACCURACY

^{82}RUBIDIUM PET VS SPECT MPI IN 112 PATIENTS MATCHED BY GENDER, BMI, AND CAD EXTENT



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

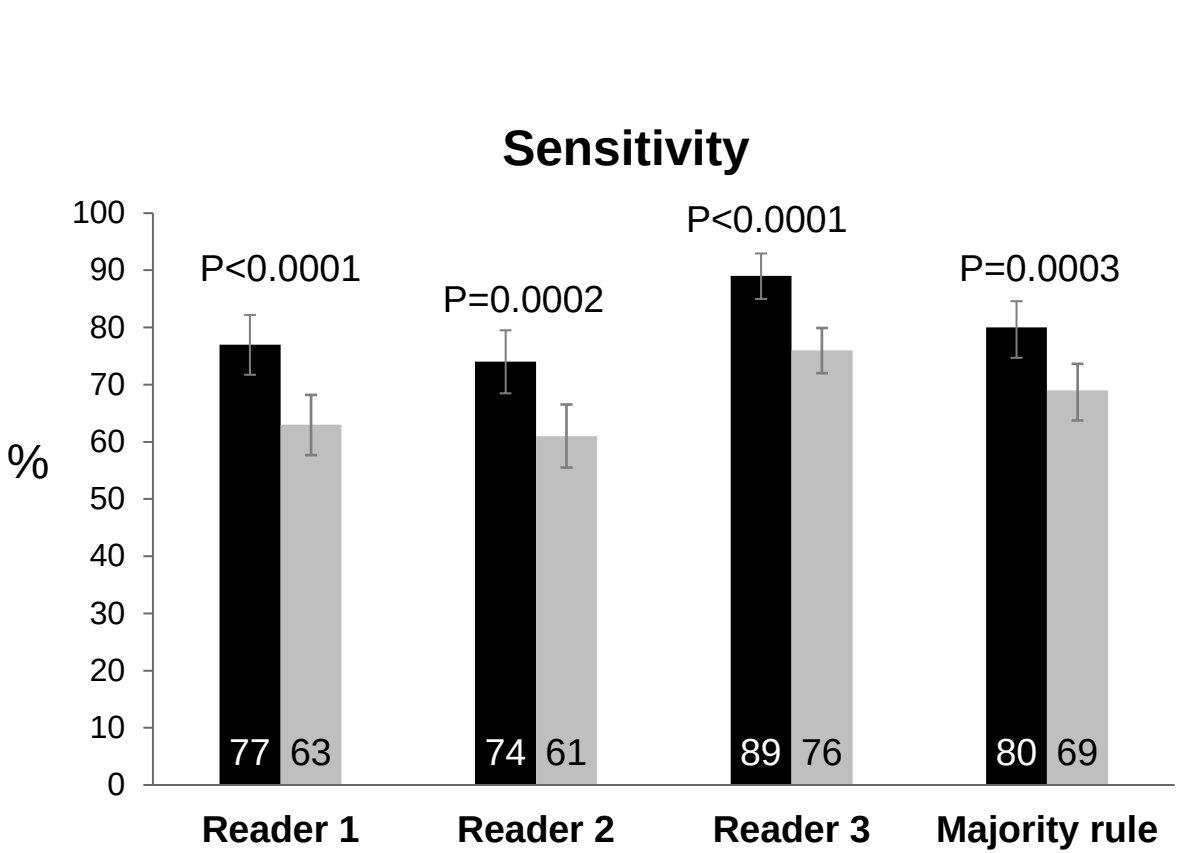
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 82, NO. 16, 2023

Flurpiridaz F-18 PET Myocardial Perfusion Imaging in Patients With Suspected Coronary Artery Disease

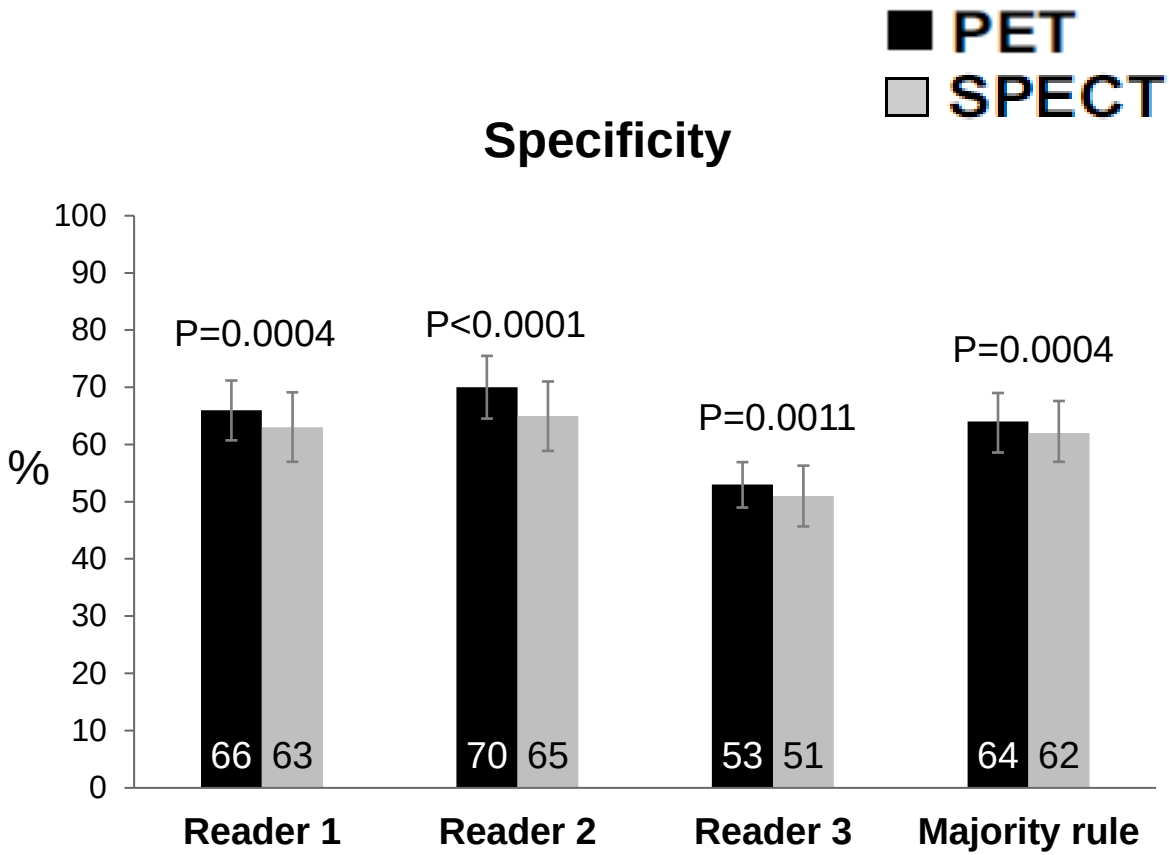
Jamshid Maddahi, MD,[a,b] Denis Agostini, MD, PhD,[c] Timothy M. Bateman, MD,[d] Jeroen J. Bax, MD,[e] Rob S.B. Beanlands, MD,[f] Daniel S. Berman, MD,[g] Sharmila Dorbala, MBBS,[h] Ernest V. Garcia, PhD,[i] James Feldman, MD,[j] Gary V. Heller, MD, PhD,[k] Juhani M. Knuuti, MD,[l] Pedro Martinez-Clark, MD,[m] Matthieu Pelletier-Galarneau, MD,[n] Benjamin Shepple, MD,[o] Nagara Tamaki, MD,[p] Francois Tranquart, MD, PhD,[q] James E. Udelson, MD[r]

^{18}F FLURPIRIDAZ DIAGNOSTIC ACCURACY

OVERALL CAD DETECTION (≥50% QCA)



n=249 patients

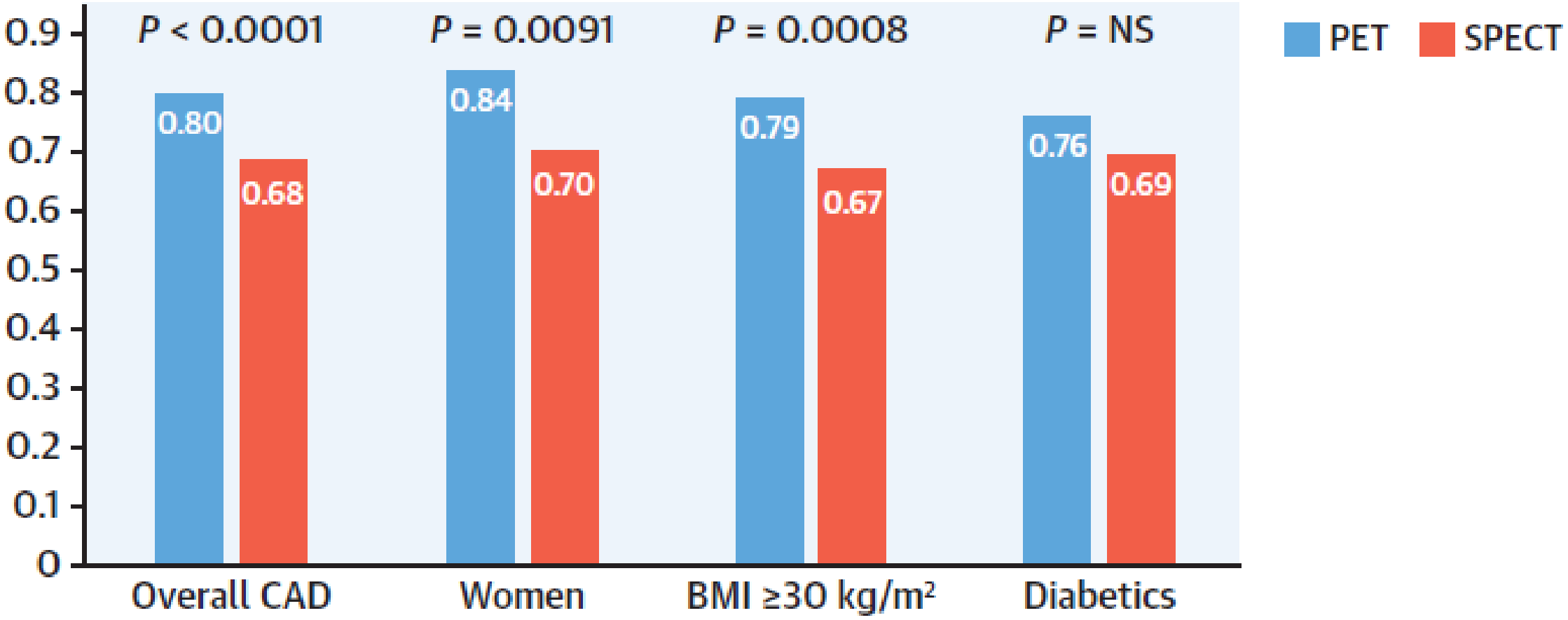


n=329 patients

Maddahi J et al. J Am Coll Cardiol 2023;82:1598-1610

^{18}F FLURPIRIDAZ DIAGNOSTIC ACCURACY

CLINICALLY IMPORTANT PATIENT SUBSETS



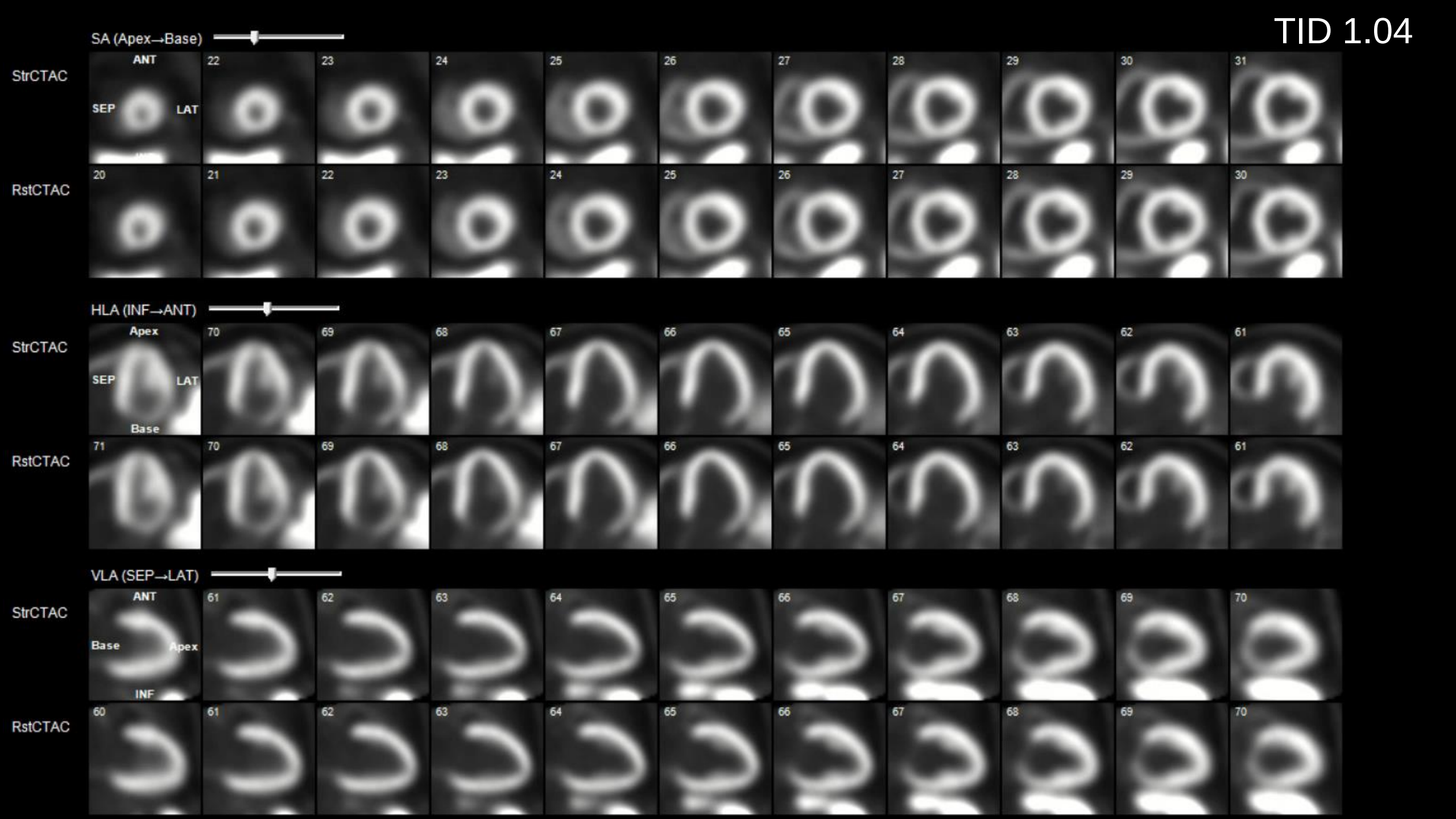
Maddahi J et al. J Am Coll Cardiol 2023;82:1598-1610

ADDED VALUE OF MYOCARDIAL BLOOD FLOW

MOST COMMON SCENARIOS WHEN FLOW REPORTING CAN BE HELPFUL CLINICALLY

- Confirmatory of perfusion assessment
- Discrepant with perfusion assessment
- To increase likelihood of MVD
- To reduce likelihood of MVD
- To be confident that vasodilator was effective
- To convey concern for microvascular disease
- Heart transplant patients for serial studies

Bateman TM et al. J Nucl Cardiol 2021; 28:768–787.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SA (Apex→Base)
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HLA (INF→ANT)
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Apex
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LAT
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VLA (SEP→LAT)
StrCTAC
ANT
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Apex
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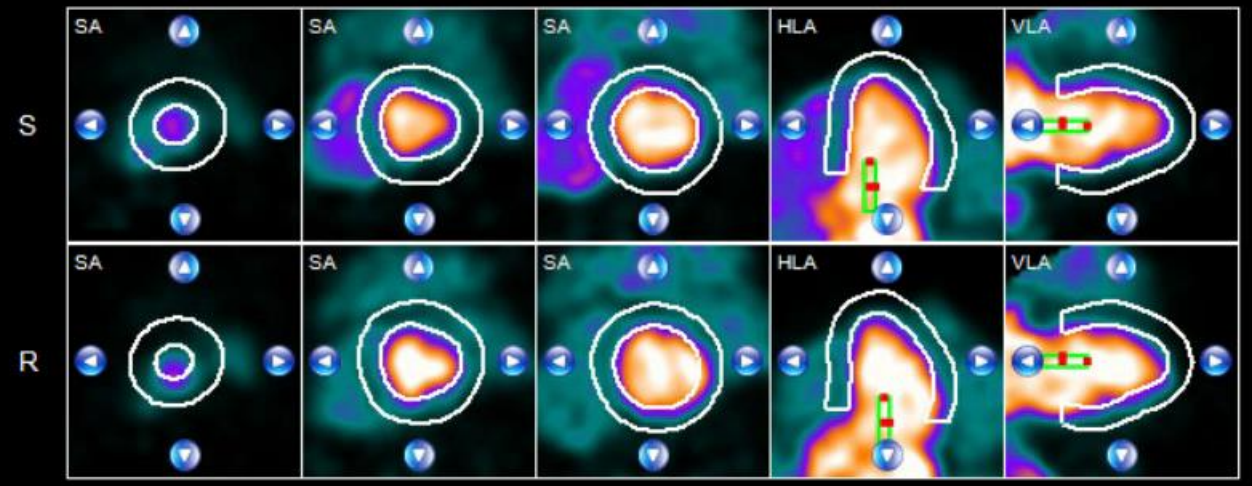
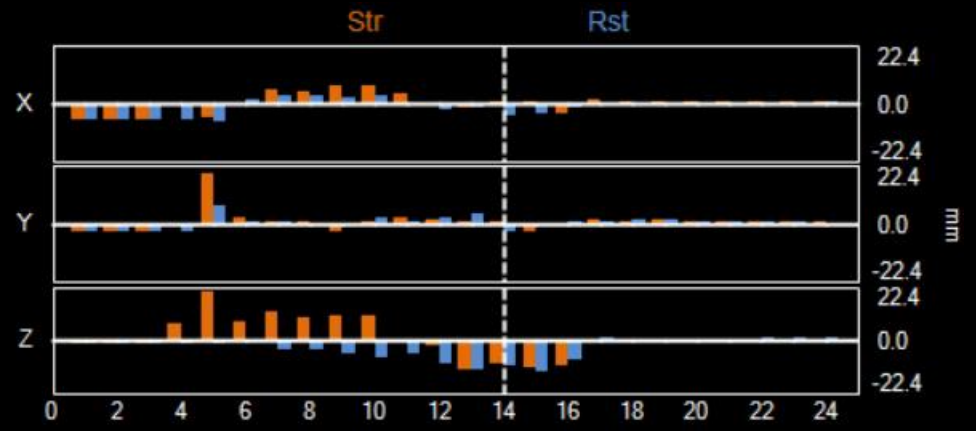
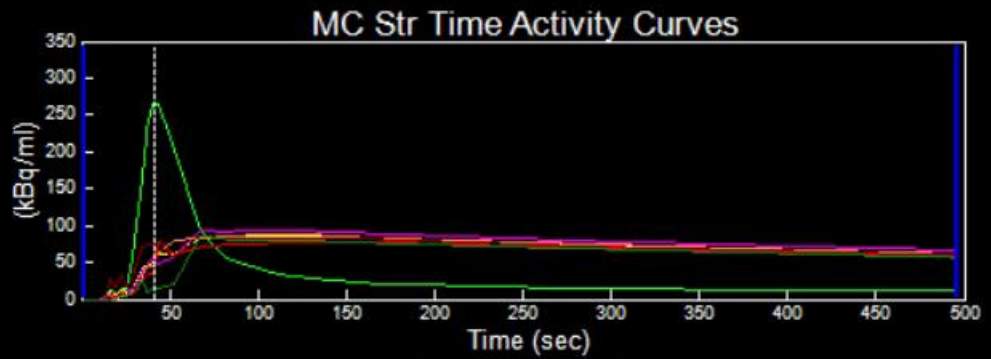
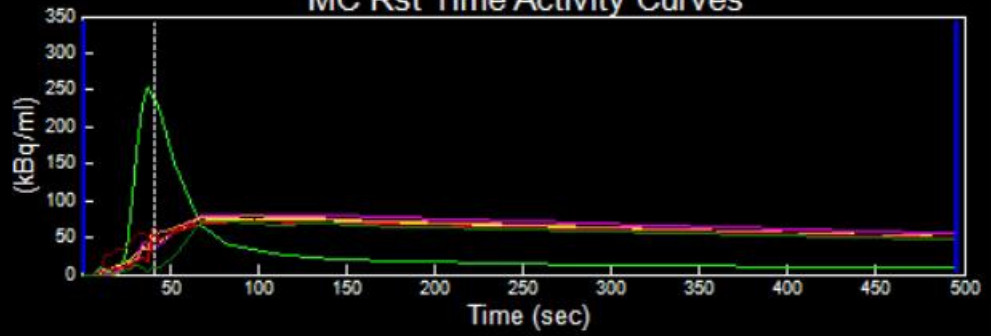




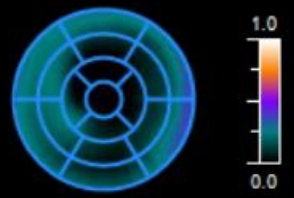
Algorithm (MC Str): INVIA N-13 ROI 1:1

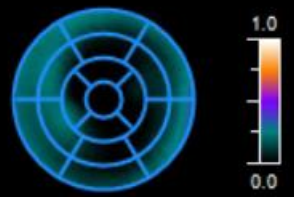
Algorithm (MC Rst): INVIA N-13 ROI 1:1





LV Spillover

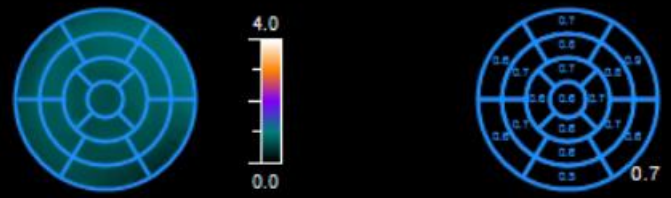




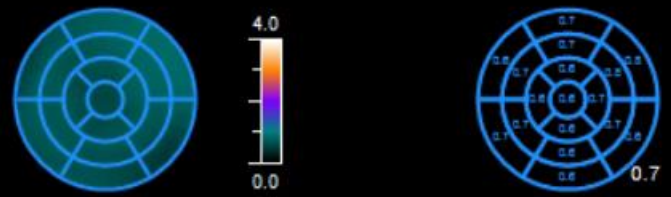
Flow

Flow (ml/min/g)

AX:MYOCARD:AMM:STRESS DYNAMIC

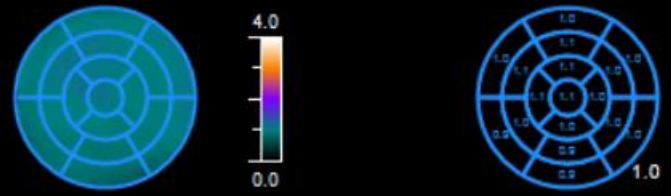


AX:MYOCARD:AMM:REST DYNAMIC



Reserve

Reserve-Stats

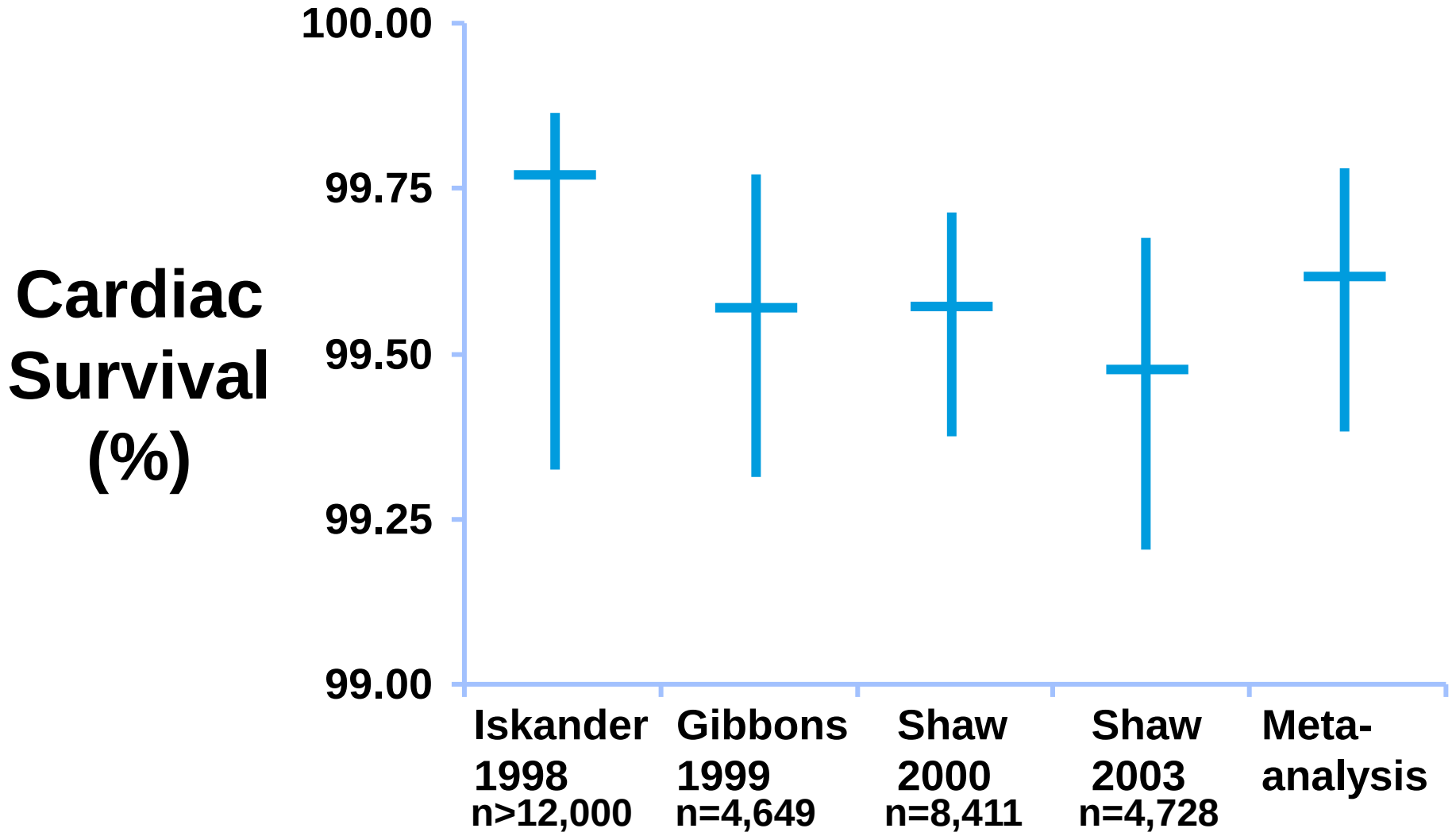


☑ LV ☑ Global ☑ LAT ☑ SEP

☐ RV ☑ ANT ☑ INF ☑ APX

INCREMENTAL PROGNOSTIC VALUE

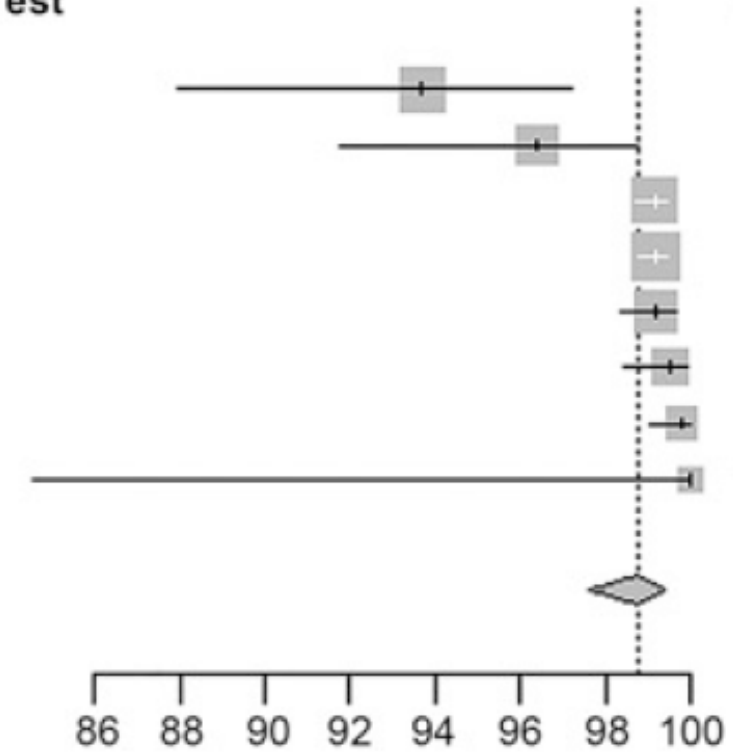
NORMAL SPECT → RATE OF CARDIAC DEATH/MI = 0.7% PER YEAR



NORMAL PET → RATE OF CARDIAC DEATH/MI = 0.4% PER YR

Study ID	Nr. of patients	Nr. of Negative Test	Nr. of True Negative Test	NPV(%)	95% CI
Herzog et al[36] 2009	229	127	119	93.70	[87.97; 97.24]
Marwick et al[32] 1997	657	138	133	96.38	[91.75; 98.81]
Chow et al[33] 2014	6037	2521	2500	99.17	[98.73; 99.48]
Dorbala et al[28] 2013	7061	3109	3084	99.20	[98.81; 99.48]
Murthy et al[35] 2011	2783	875	868	99.20	[98.36; 99.68]
Van Tosh et al[29] 2010	452	452	450	99.56	[98.41; 99.95]
Murthy et al[26] 2014	1218	577	576	99.83	[99.04; 100.00]
Schindler et al[31] 2005	72	22	22	100.00	[84.56; 100.00]
Pooled Estimates				**98.80**	**[97.64; 99.39]**

Heterogeneity: $I^2 = 83.2\%$, tau-squared = 0.6775, $p < 0.0001$

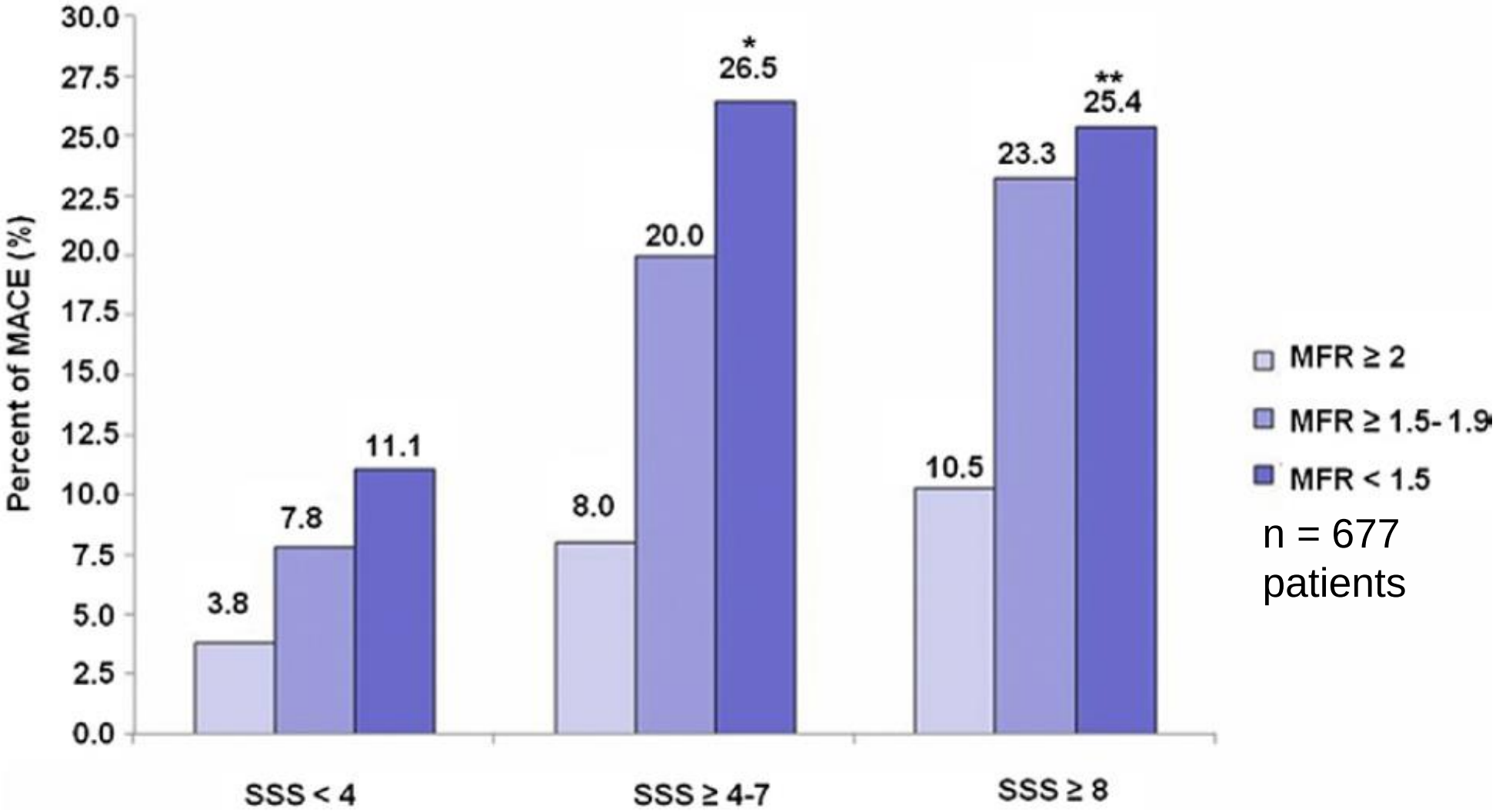


Chen A et al. Br J Radiol 2017; 90: 20160702

MFR > 2 CORRELATES WITH LOW RISK FOR MACE

- Unselected populations
- Men and women
- No known CAD
- Known CAD
- Diabetics
- CKD
- Microvascular disease
- With or without perfusion defects

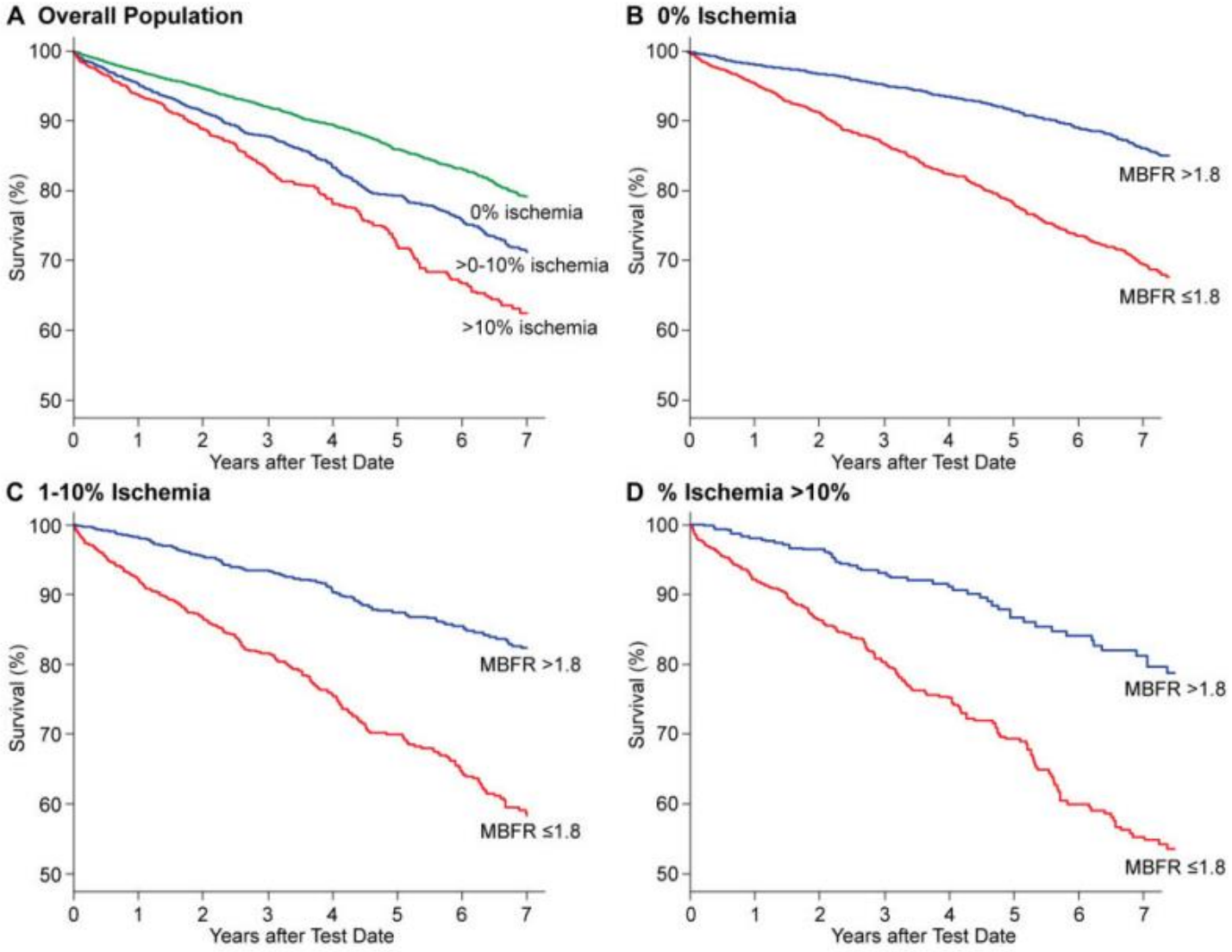
ADDED PROGNOSTIC VALUE OF ^{82}RUBIDIUM PET MFR



n = 677 patients

Ziadi MC et al. J Am Coll Cardiol 2011;58:740–8

KAPLAN–MEIER UNADJUSTED SURVIVAL ESTIMATES AS A FUNCTION OF PERCENT ISCHEMIC MYOCARDIUM

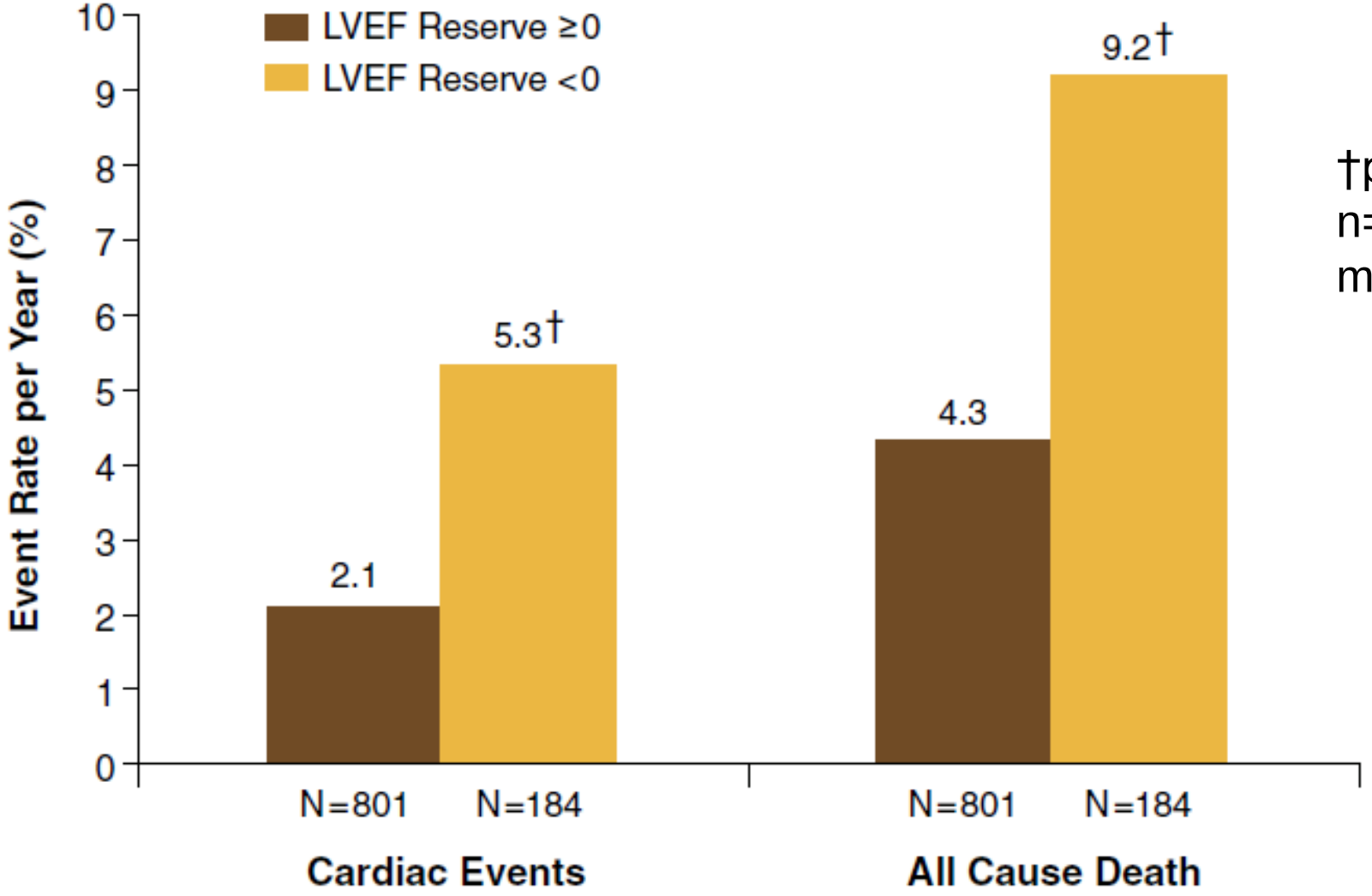


Every 0.1 unit decrease in MFR was associated with a 9% greater hazard of death

n = 12,549 patients
Median FU 3.2 yrs

Patel KK et al. European Heart Journal 2020; 41:759-68.

PROGNOSTIC VALUE OF ^{82}RUBIDIUM PET LVEF RESERVE



†p < 0.001
n= 985 patients
mean FU 1.7 ± 0.7 yrs

Dorbala S et al. J Am Coll Cardiol Img 2009;2:846 –54

PATIENT SELECTION FOR REVASCULARIZATION

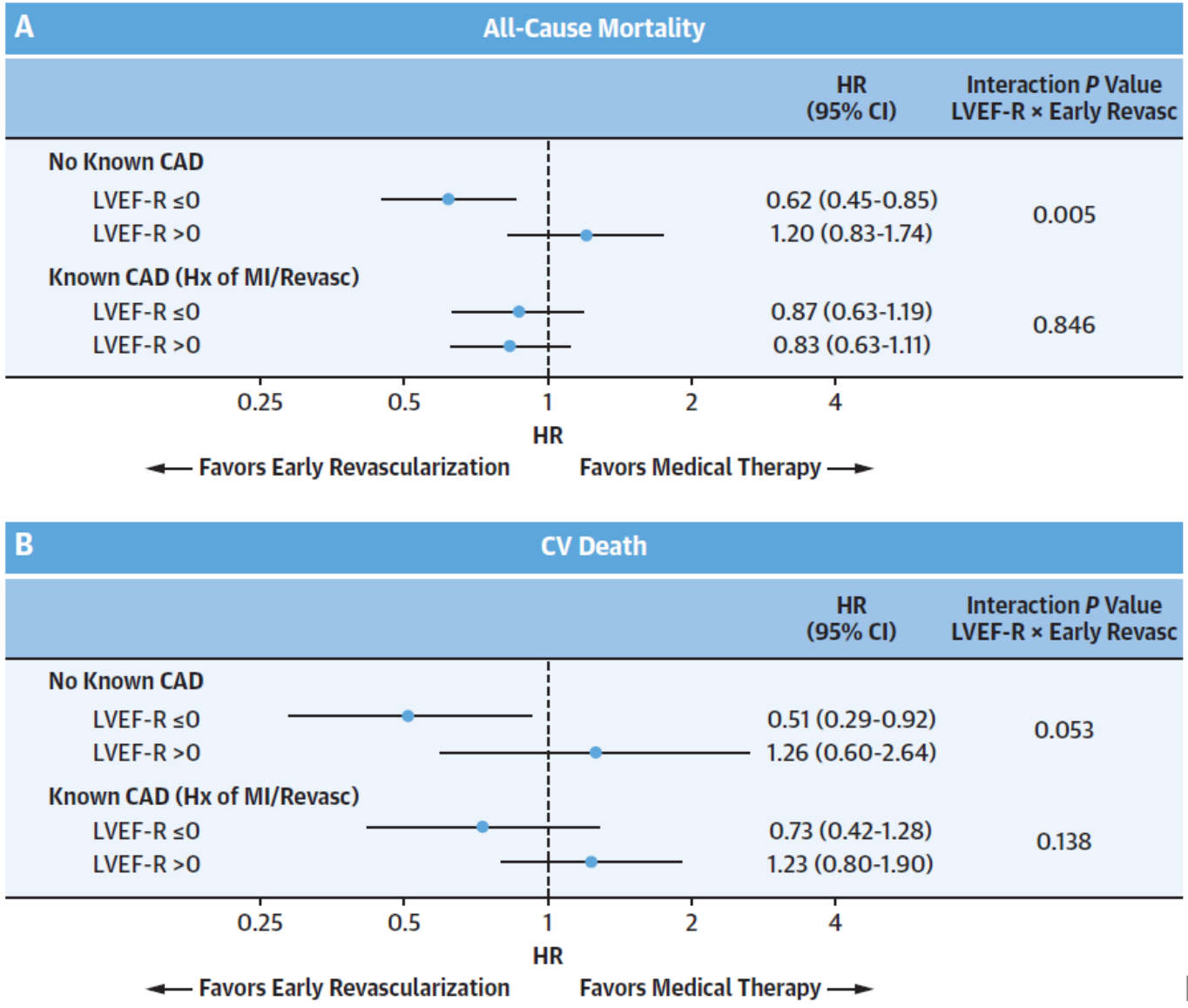
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 82, NO. 17, 2023

PUBLISHED BY ELSEVIER

Impact of Positron Emission Tomographic Myocardial Perfusion Imaging on Patient Selection for Revascularization

Krishna K. Patel, MD, MSc,[a,b] A. Iain McGhie, MD,[b] Kevin F. Kennedy, MS,[b] Randall C. Thompson, MD,[b] John A. Spertus, MD,[b] Brett W. Sperry, MD,[b] Leslee J. Shaw, PhD,[a] Timothy M. Bateman, MD[b]

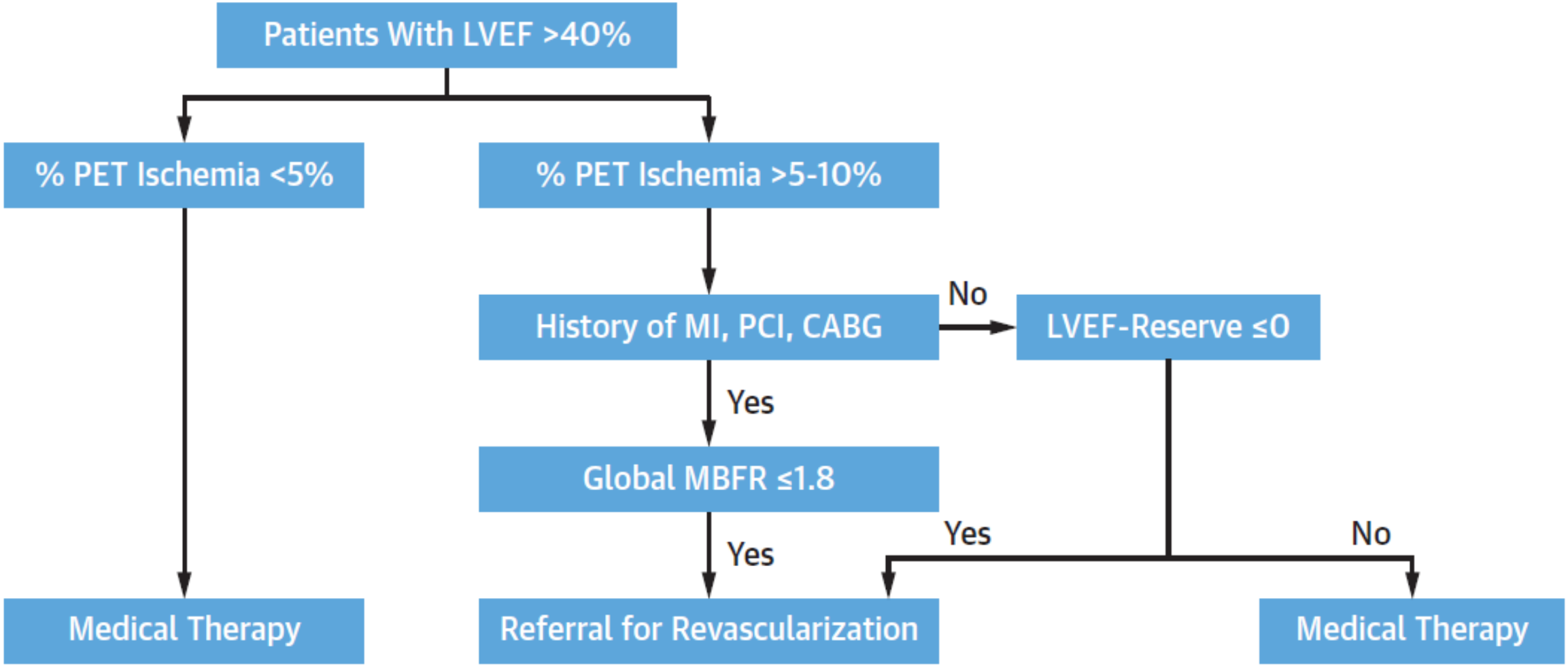
^{82}RUBIDIUM PET LVEF RESERVE IDENTIFIES PATIENTS WITH BETTER SURVIVAL WITH REVASCULARIZATION



n= 14,649 patients
mean FU 3.4 yrs

Patel K et al. J Am Coll Cardiol 2023;82:1662–1672

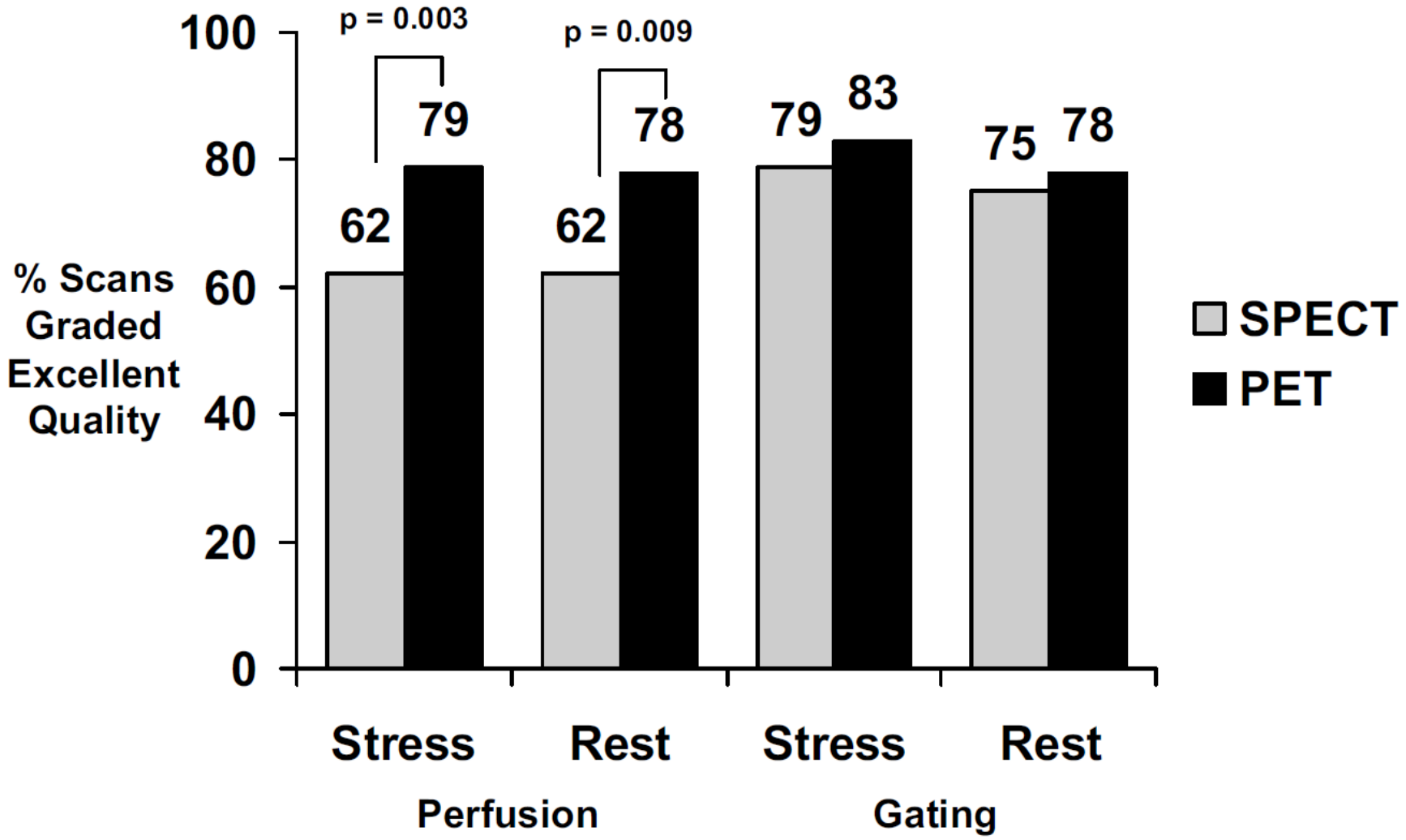
PROPOSED MULTIPARAMETRIC ALGORITHM FOR PET-BASED OPTIMAL CANDIDATE SELECTION FOR REVASCULARIZATION



Patel K et al. J Am Coll Cardiol 2023;82:1662–1672

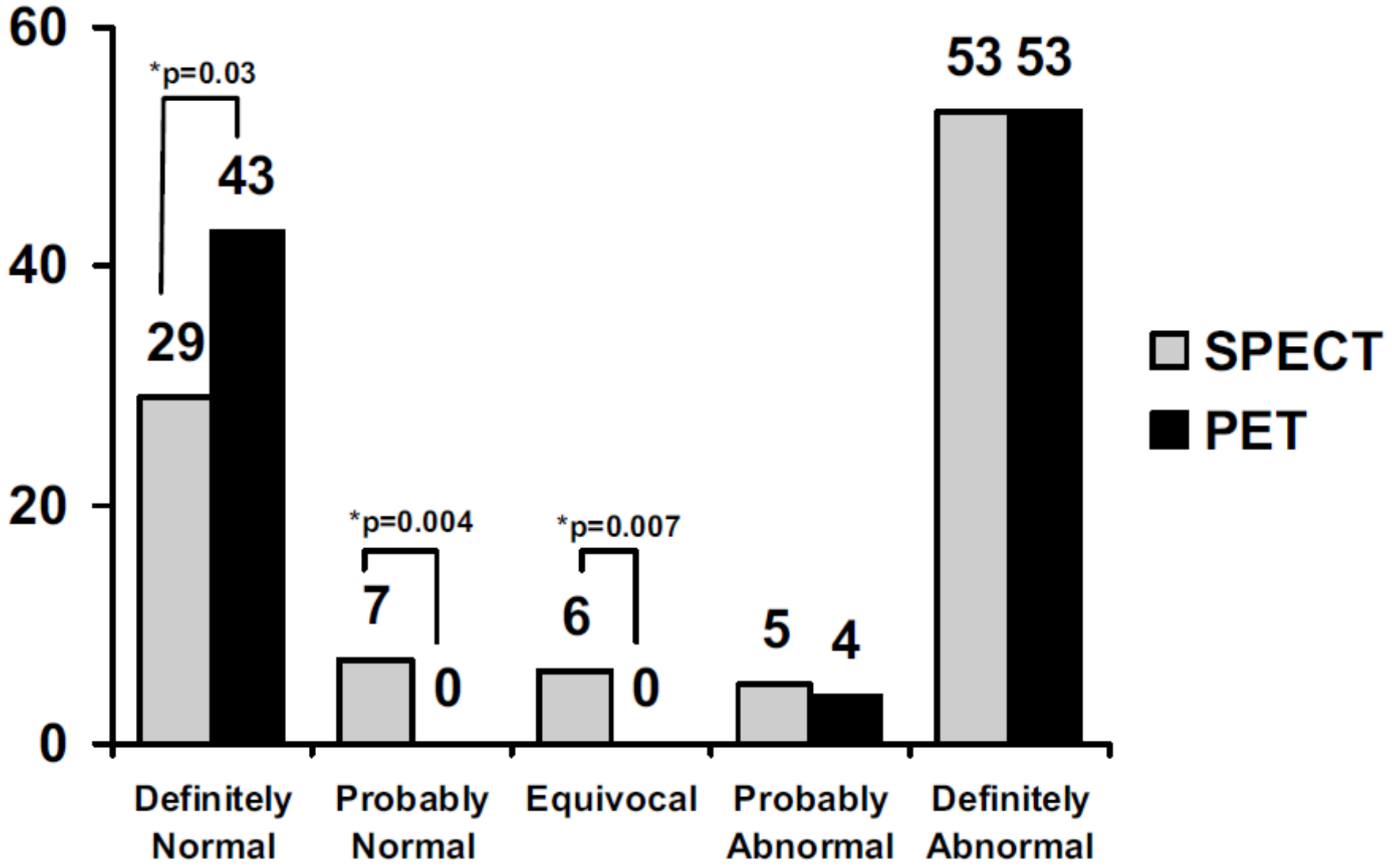
IMAGE QUALITY AND INTERPRETIVE CERTAINTY

BETTER IMAGE QUALITY WITH ^{82}RB PET COMPARED TO SPECT MPI



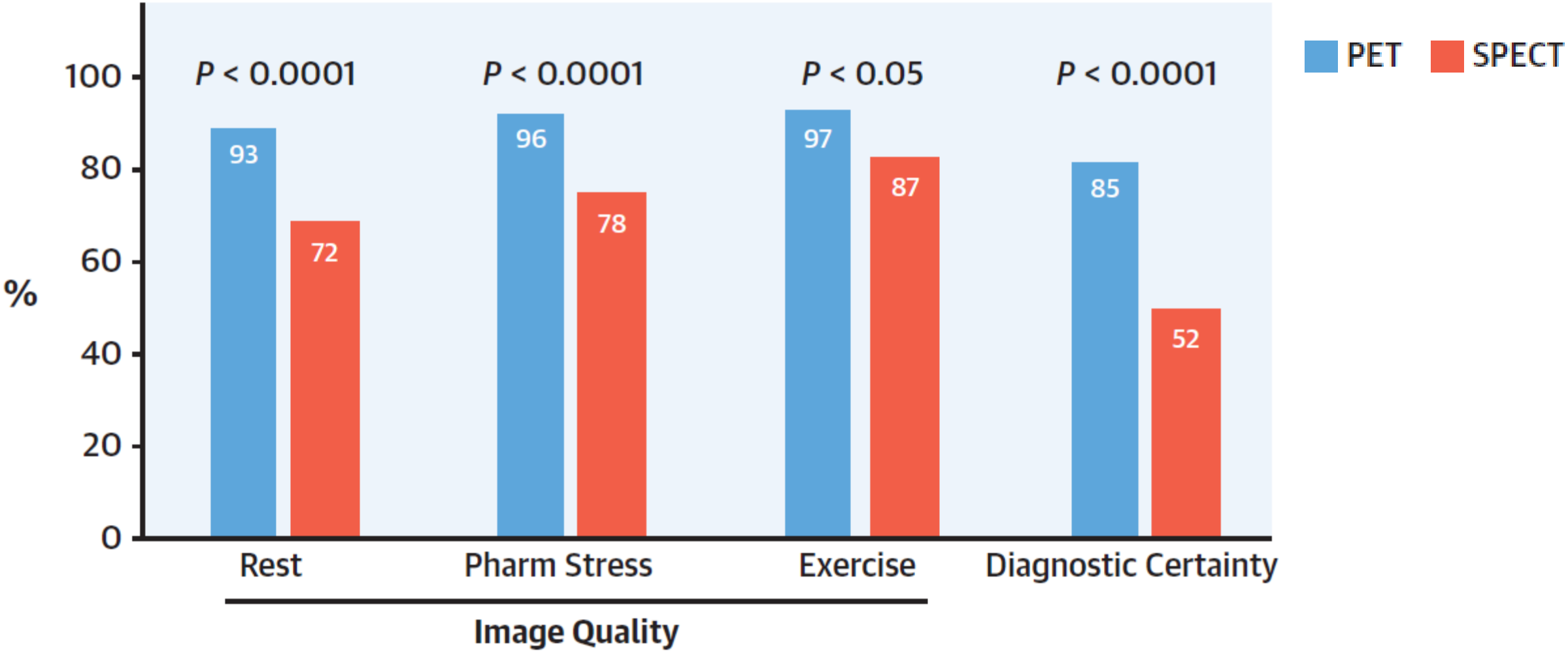
Bateman TMM et al. J Nucl Cardiol 2006;13:24-33

HIGHER INTERPRETIVE CERTAINTY WITH ^{82}RB PET COMPARED TO SPECT MPI



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

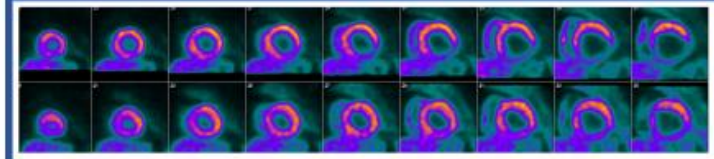
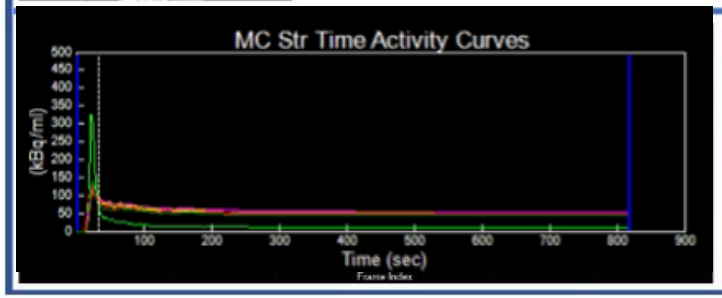
BETTER IMAGE QUALITY AND HIGHER DIAGNOSTIC CERTAINTY WITH ^{18}F FLURPIRIDAZ PET COMPARED TO SPECT MPI



Maddahi J et al. J Am Coll Cardiol 2023;82:1598-1610

ANCILLARY DATA FROM HYBRID SYSTEMS PROVIDE COMPREHENSIVE ASSESSMENT

PET/CT PROVIDES COMPREHENSIVE CARDIAC AND THORACIC ASSESSMENT

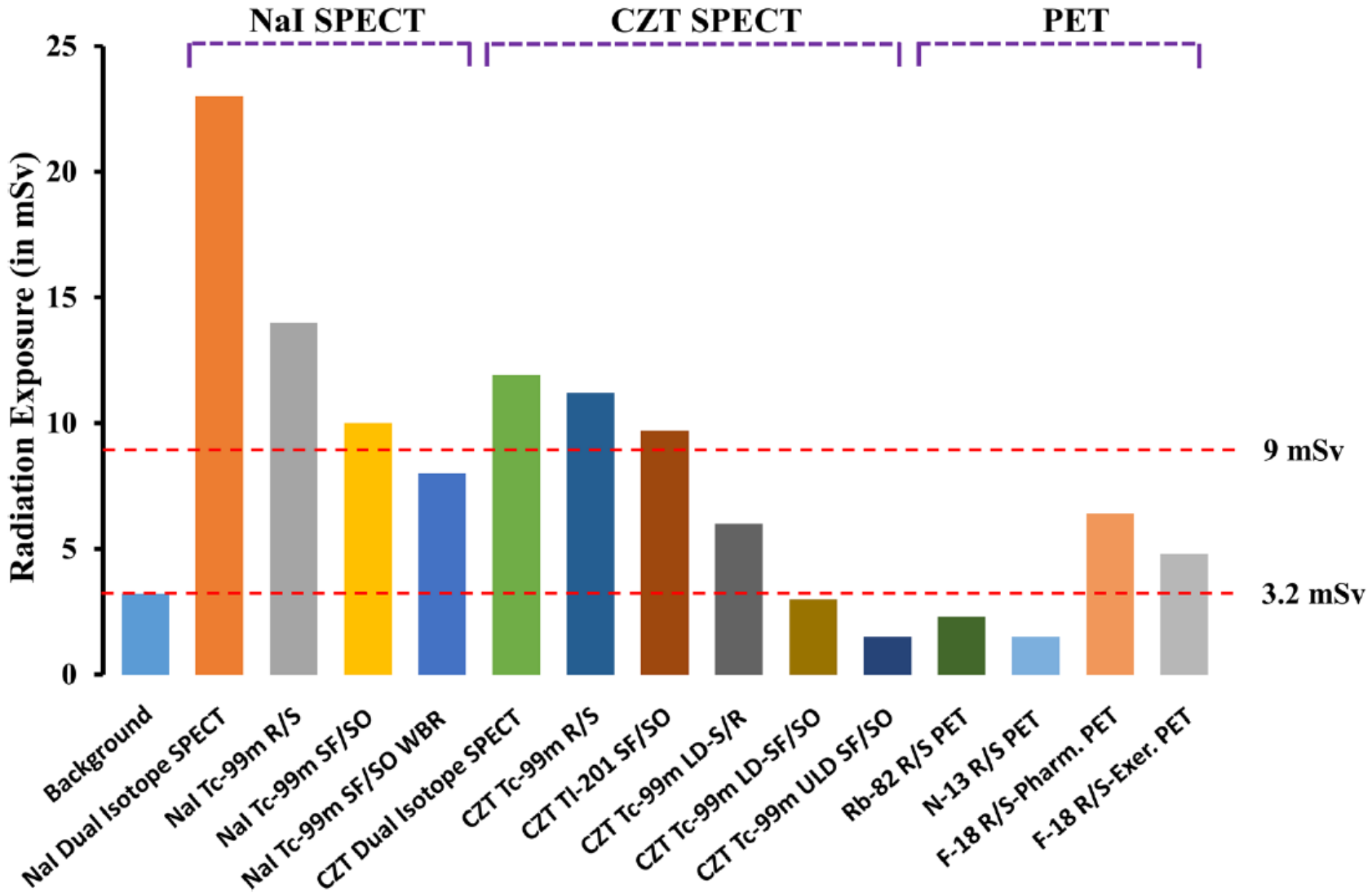
Comprehensive PET/CT imaging	Quantitative marker	Pathophysiologic process
	Perfusion defect extent and severity	Focal disease
	LV volumes and ejection fraction	LV function
	Calcified coronary plaque burden	Atherosclerosis burden
	Quantitative myocardial blood flow and flow reserve	Diffuse disease and microvascular function

+incidental findings

Adapted from DiCarl MF. Semin Nucl Med 50:227-237

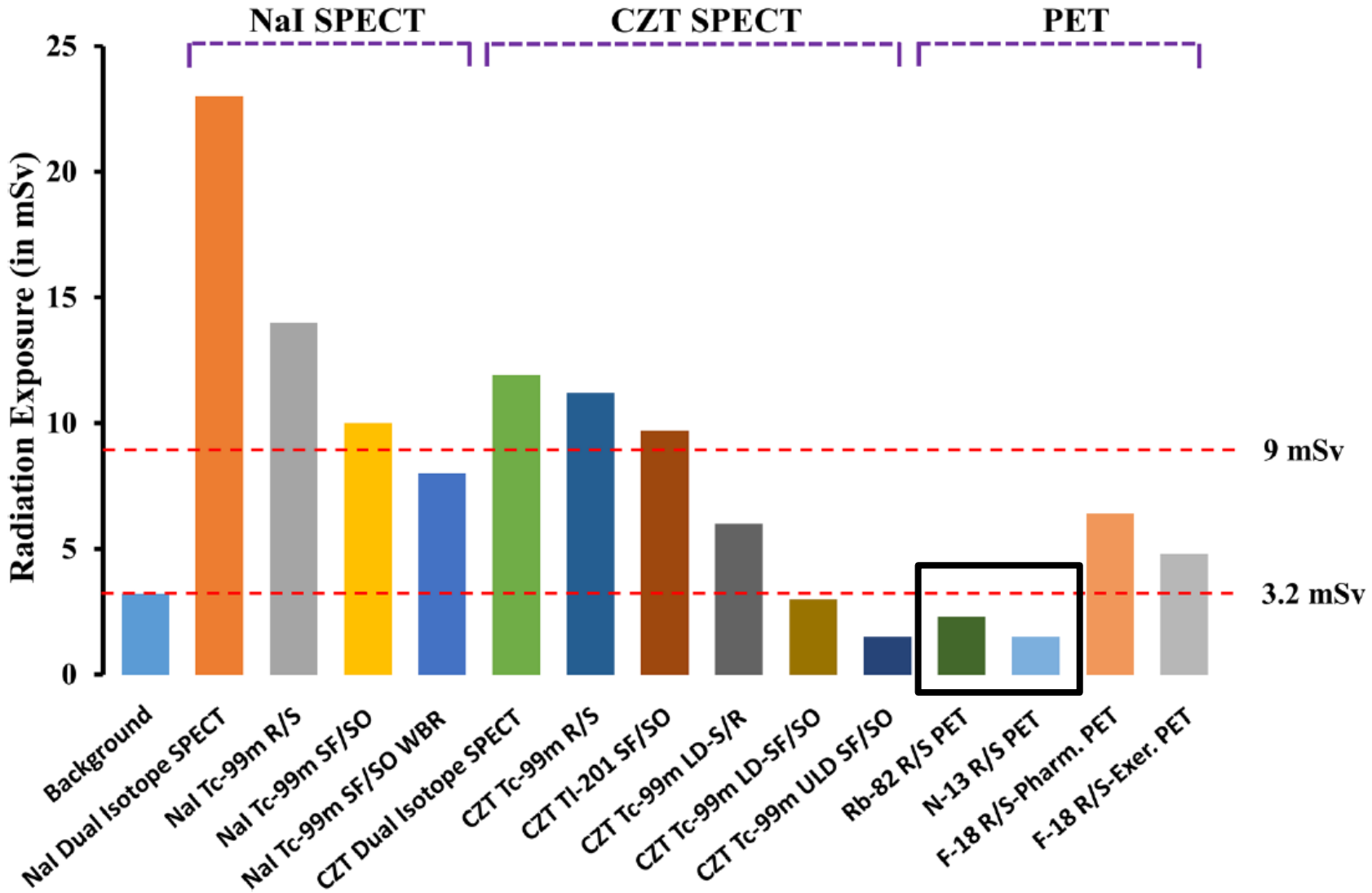
RADIATION EXPOSURE

PET MPI HAS LOWER RADIATION EFFECTIVE DOSES THAN SPECT MPI



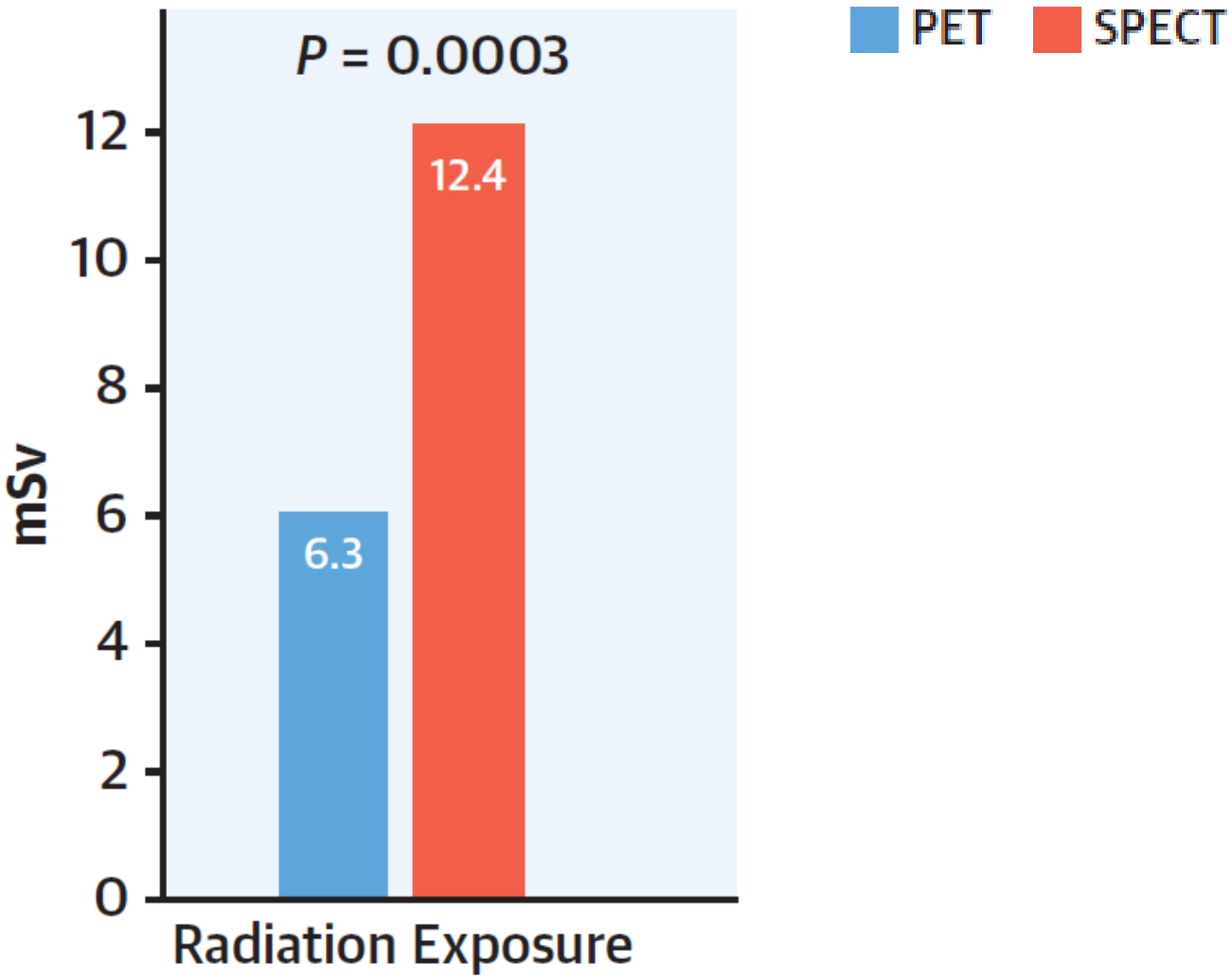
Malhotra S et al. J Nucl Cardiol 2019;26:1280–3.

PET MPI HAS LOWER RADIATION EFFECTIVE DOSES THAN SPECT MPI



Malhotra S et al. J Nucl Cardiol 2019;26:1280–3.

^{18}F FLURPIRIDAZ PET HAS LOWER RADIATION EFFECTIVE DOSES THAN SPECT MPI

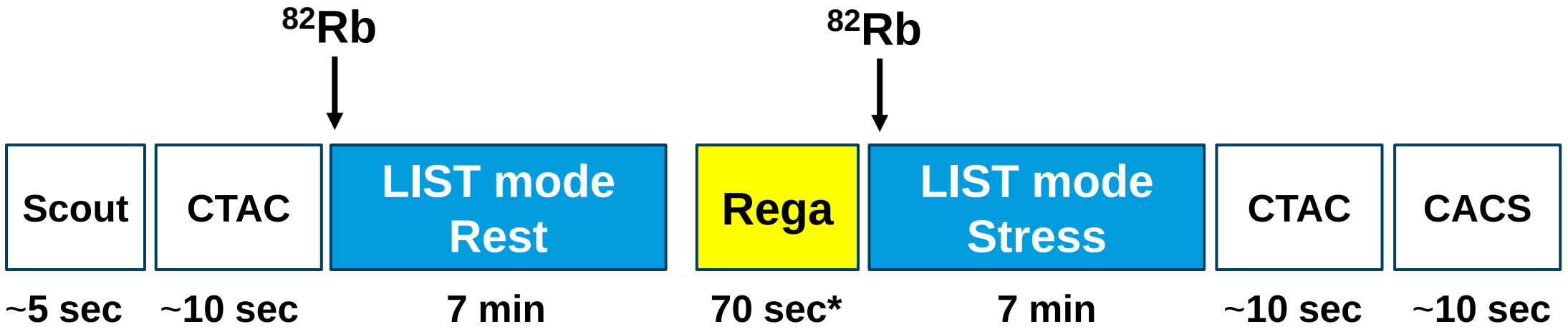


Maddahi J et al. J Am Coll Cardiol 2023;82:1598-1610

PROTOCOL EFFICIENCY

REST-STRESS PET MPI + MBF + CAC SCORE

PET/CT WITH ^{82}RUBIDIUM AND REGADENOSON



~ 25 minutes

*activate ^{82}Rb generator 55 sec after the start of regadenoson bolus

*Johnson NP and Gould LK. J Am Coll Cardiol Img 2015;8:438–47

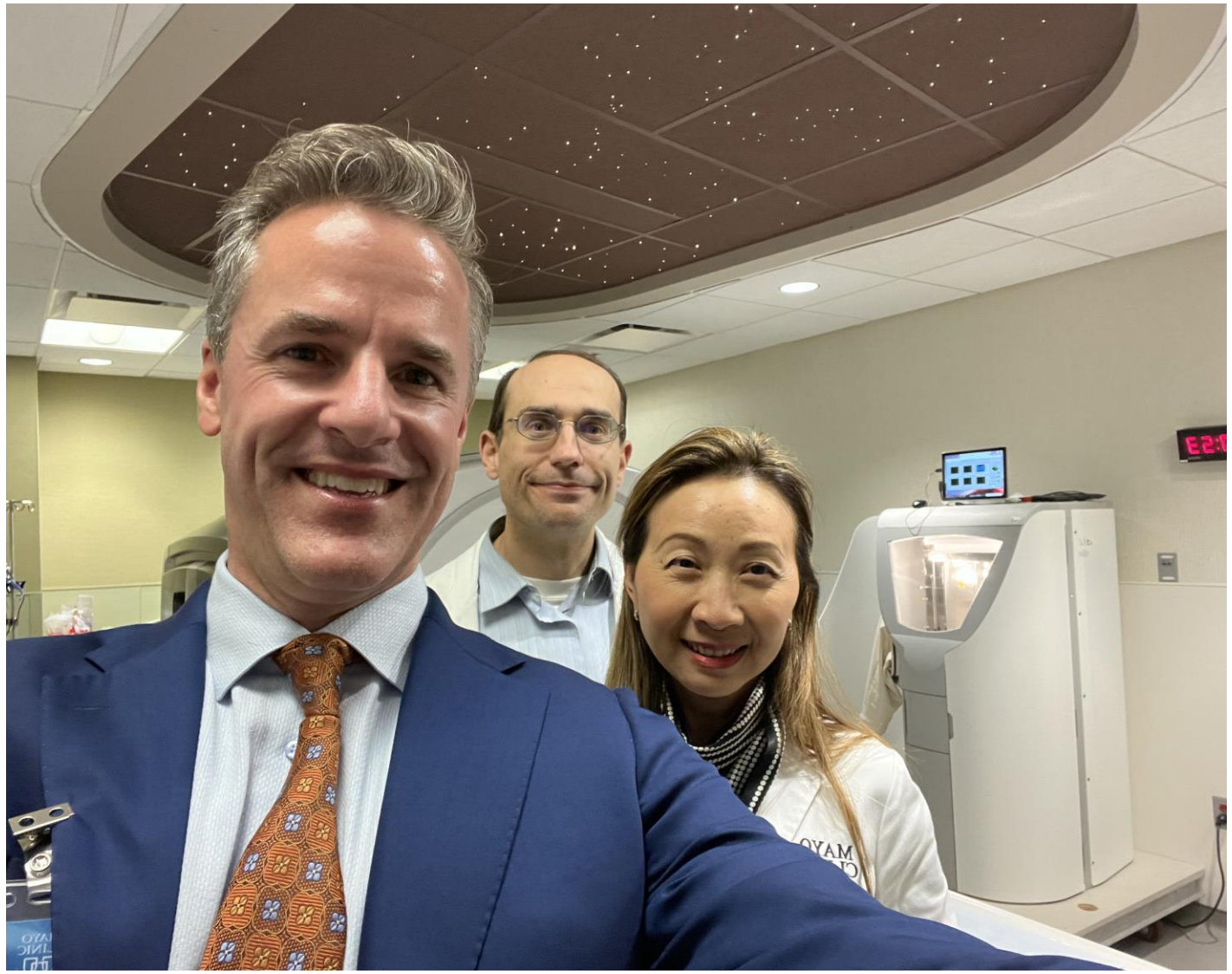
AVAILABILITY OF PET PERFUSION TRACERS

RUBIDIUM-82

- Now supplied by two vendors
- Requires delivery system (lease ~$2,000/mo)
- Generator replaced every 42 or 60 days (~$40,000)
- On-demand option now available

CURRENT CYCLOTRON OPTIONS

1ST US PATIENT IN THE RAPID-WATER-FLOW TRIAL W/ MEDTRACE O-15 WATER DELIVERY SYSTEM



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Flurpiridaz F-18 PET Myocardial Perfusion Imaging in Patients With Suspected Coronary Artery Disease

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^{18}F FLURPIRIDAZ PHASE III PART 2 PROTOCOLS

	Rest	Pharmacologic stress	Exercise stress
F-18 Flurpiridaz	2.5-3.0 mCi	6.0-6.5 mCi	9.0-9.5 mCi

- Injection of rest and stress doses of ^{18}F Flurpiridaz will occur at least 30 minutes apart
- Exercise stress PET images will be acquired as a single 10-minute list-mode static acquisition with cardiac gating that will start 15-25 minutes postinjection

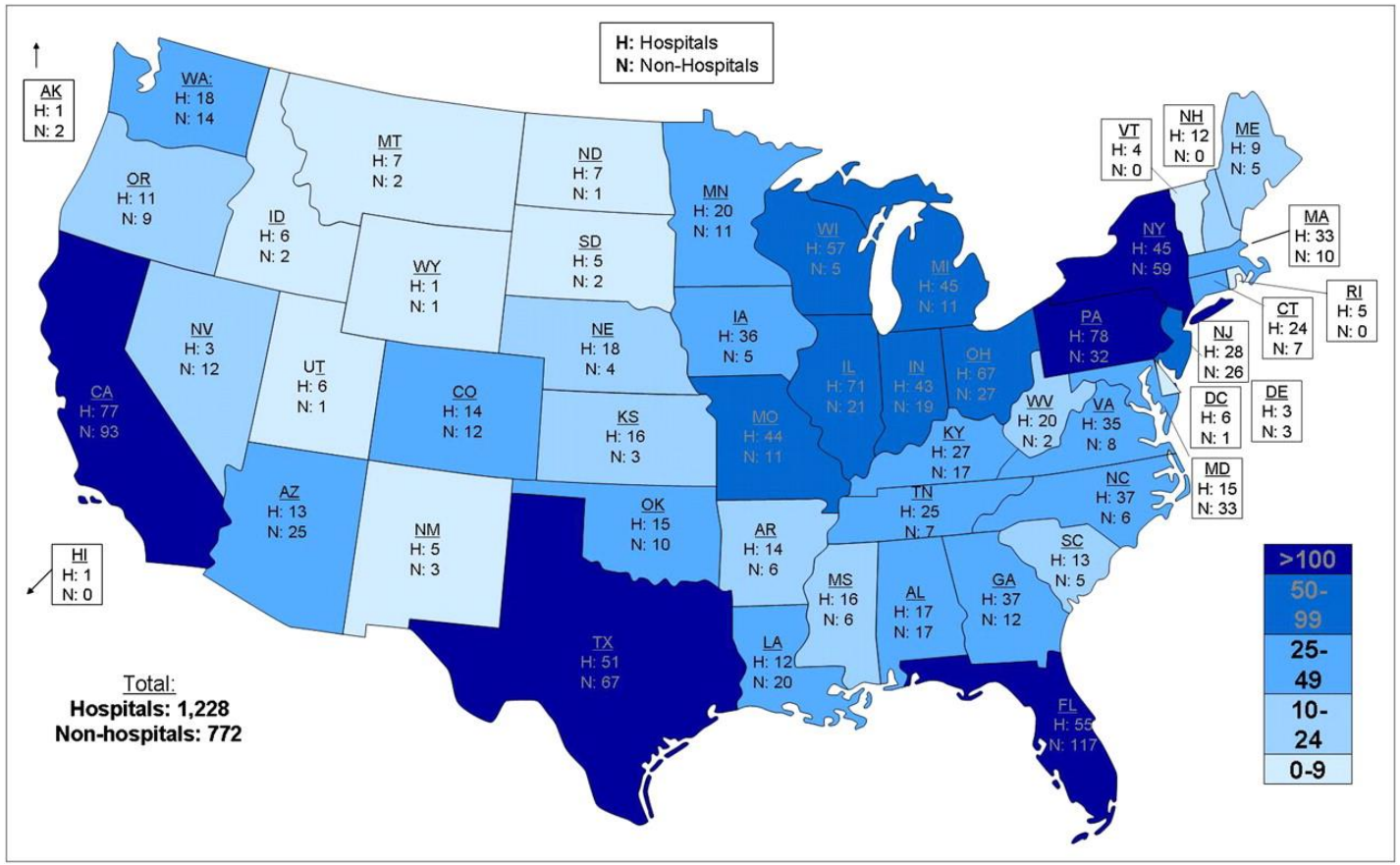
Redrawn from: Bourque JM et al: J Nucl Cardiol 2021;28:1105-16

AVAILABILITY OF PET CAMERA SYSTEMS

PET Install Base in USA

HOUSTON Methodist DEBAKEY HEART & VASCULAR CENTER

In 2009, approximately 2,000 PET/CT scanners were installed in the United States and approximately 350 were installed in Europe.



Journal of Nuclear Medicine Technology March 2010, 38 (1) 6-17

Slide courtesy of Dr. Al-Mallah

COST AND REIMBURSEMENT

PET MPI AND MBF

- 78431 PET/CT MPI with ECG gating, rest and stress
- 78492 PET MPI with ECG gating, rest and stress
- 78434 AQMBF
- As of January 1, 2020, PET flow quantification is a Category 1 code
  - Under HOPPS → bundled and anticipated to be performed and reported in most studies when appropriate
  - Under the Physician Fee Schedule → add-on code
  - Payable by CMS

GUIDELINES

2021 AHA/ACC/ASE/CHEST/SAEM/ SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain

2a	B-R

3. For intermediate-high risk patients with stable chest pain and no known CAD for whom rest/stress nuclear MPI is selected, PET is reasonable in preference to SPECT, if available to improve diagnostic accuracy and decrease the rate of nondiagnostic test results (36-39).

2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease

2a	B-NR

5. In patients with CCD undergoing stress PET MPI or stress CMR imaging, the addition of myocardial blood flow reserve (MBFR) can be useful to improve diagnostic accuracy and enhance risk stratification.[18-23]

Gulati M et al. J Am Coll Cardiol. 2021;78(22):e187-e285
Virani SS et al. J Am Coll Cardiol. 2023;82 (9) 833–955

PET/CT *SHOULD* REPLACE SPECT MPI

- Higher diagnostic accuracy
- High prognostic value
- Guides management
- Better image quality and higher interpretive certainty
- Comprehensive assessment with PET/CT systems
- Lower patient radiation exposure
- More efficient protocols and greater throughput
- Increasing availability and options for PET perfusion tracers
- Ability to perform exercise or pharmacologic stress
- Availability of camera systems
- Cost offset by reimbursement
- Recommended by Guidelines

QUESTIONS & ANSWERS