

MR Impact:

(**M**agnetic **R**esonance **I**maging for **M**ycocardial **P**erfusion **A**ssessment
in **C**oronary Artery Disease **T**rial)

Comparison of MR Myocardial Perfusion Imaging with Single Photon Emission Computed Tomography in Known or Suspected Coronary Artery Disease: A Multicenter Multivendor Dose Finding Study

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Disclosure: ^{1.5.6.8.} GE Healthcare, ^{6.} Philips MS, Siemens MS, ^{7.} GE Healthcare Employee
MR Impact Sponsor: GE Healthcare

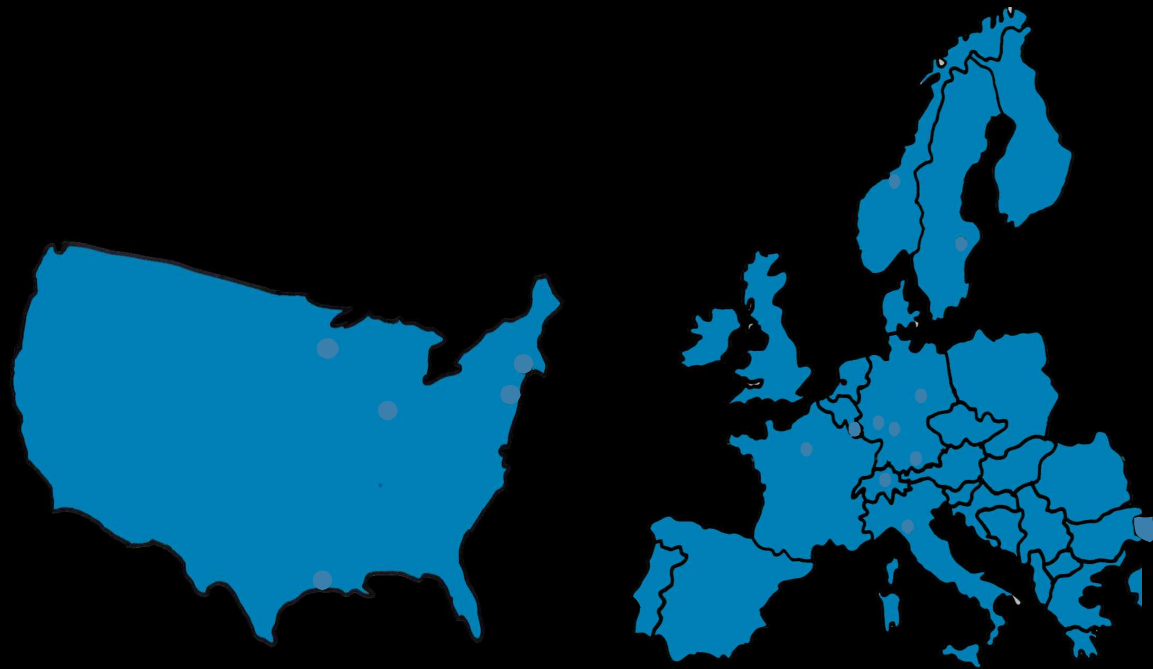
Background: Prevalence of Disease and Current Work-Up of CAD

Prevalence of CAD:

USA: 13.2 Mio*

Studies/Year:

QCA: 2.2 Mio SPECT: 6.0 Mio.



* 2001: Statistics AHA

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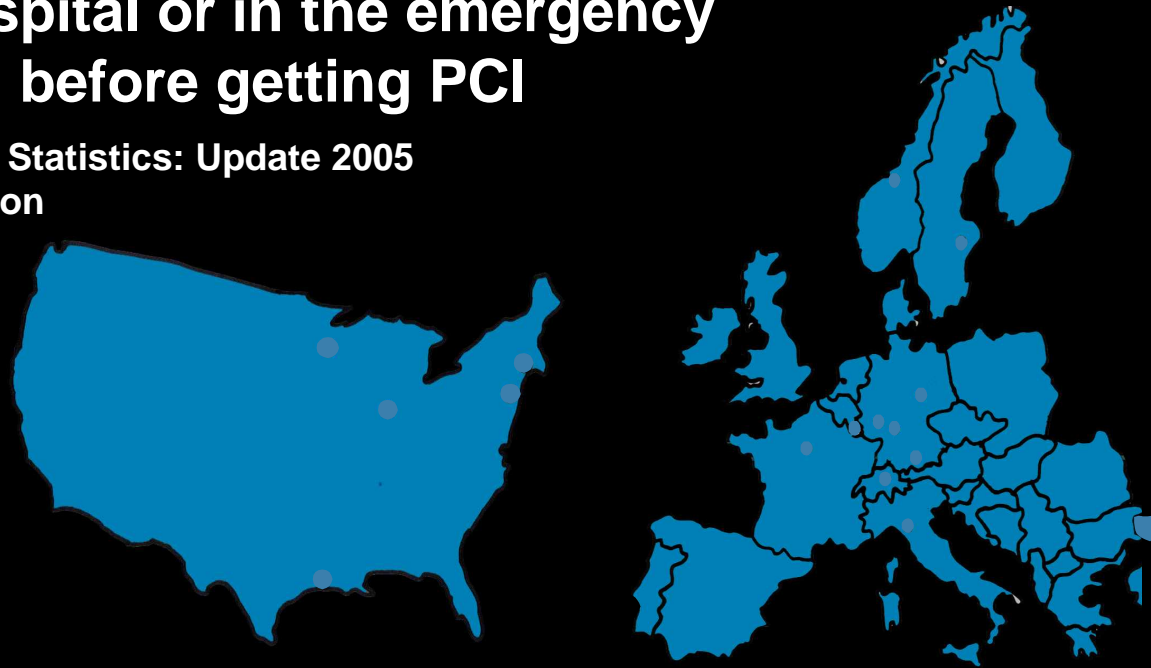
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**USA 2004: 60% of cardiac deaths occur before
reaching the hospital or in the emergency
department - i.e. before getting PCI**

Heart Disease and Stroke Statistics: Update 2005
American Heart Association



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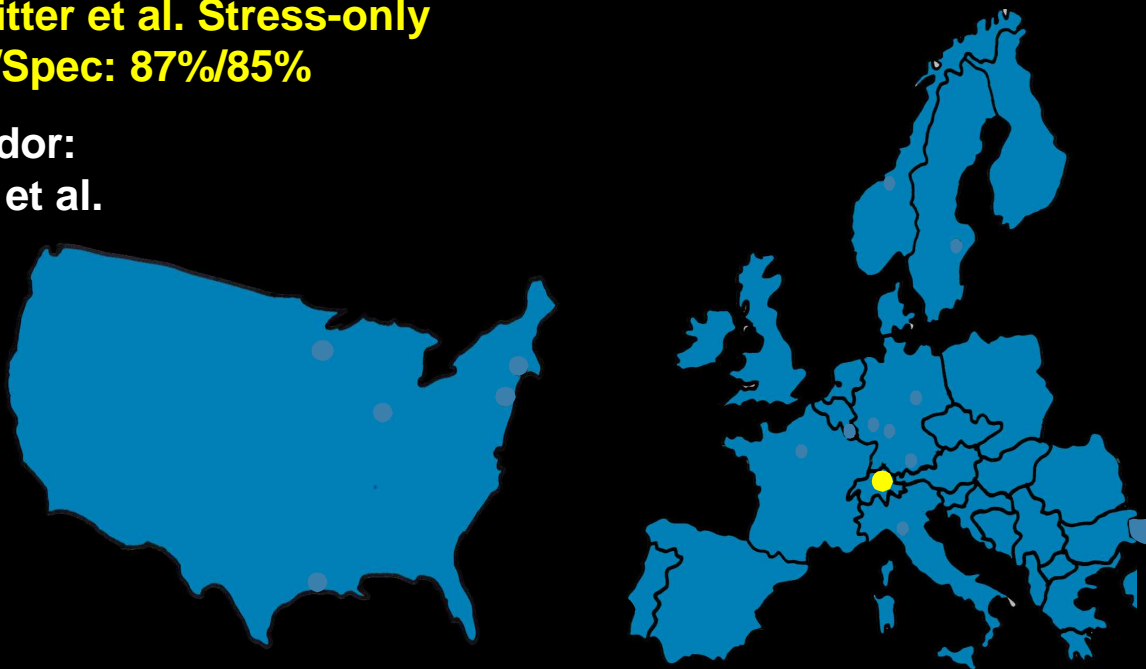
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Alternative: Perfusion MR detects CAD

**Single Center: J. Schwitter et al. Stress-only
Circulation 2001, Sens/Spec: 87%/85%**

**3 Centers – Single Vendor:
S. Wolff, J. Schwitter et al.
Circulation 2004
Stress/Rest,
Sens/Spec: 86%/90%**

**H. Giang et al.
Eur. Heart J. 2004
Stress-only,
Sens/Spec: 93%/75%**



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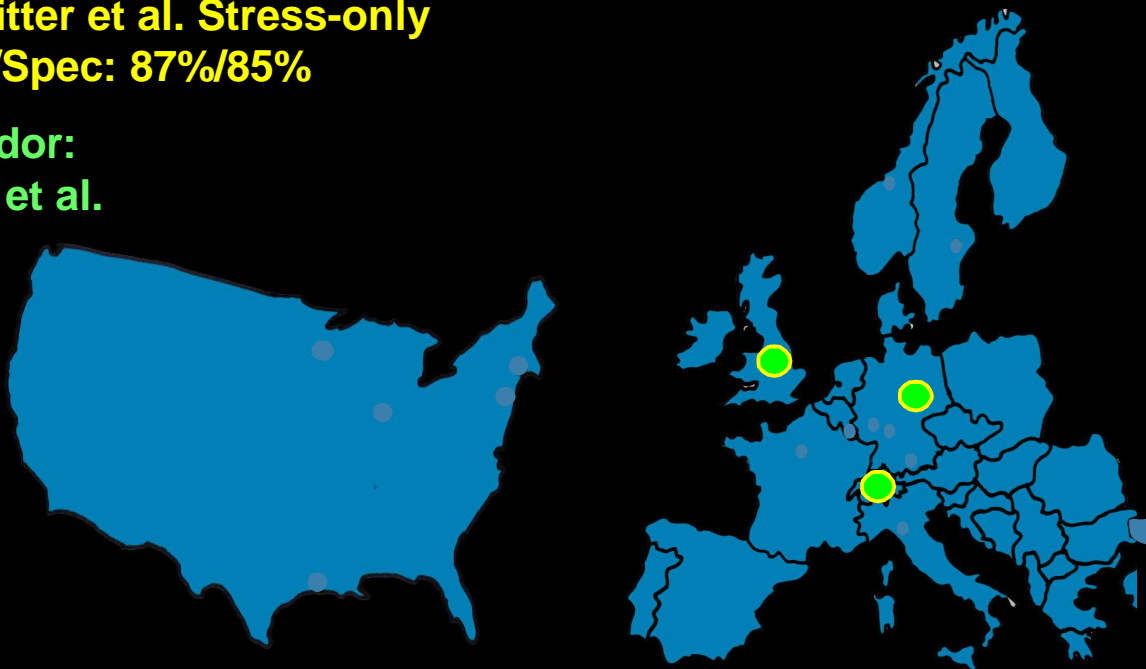
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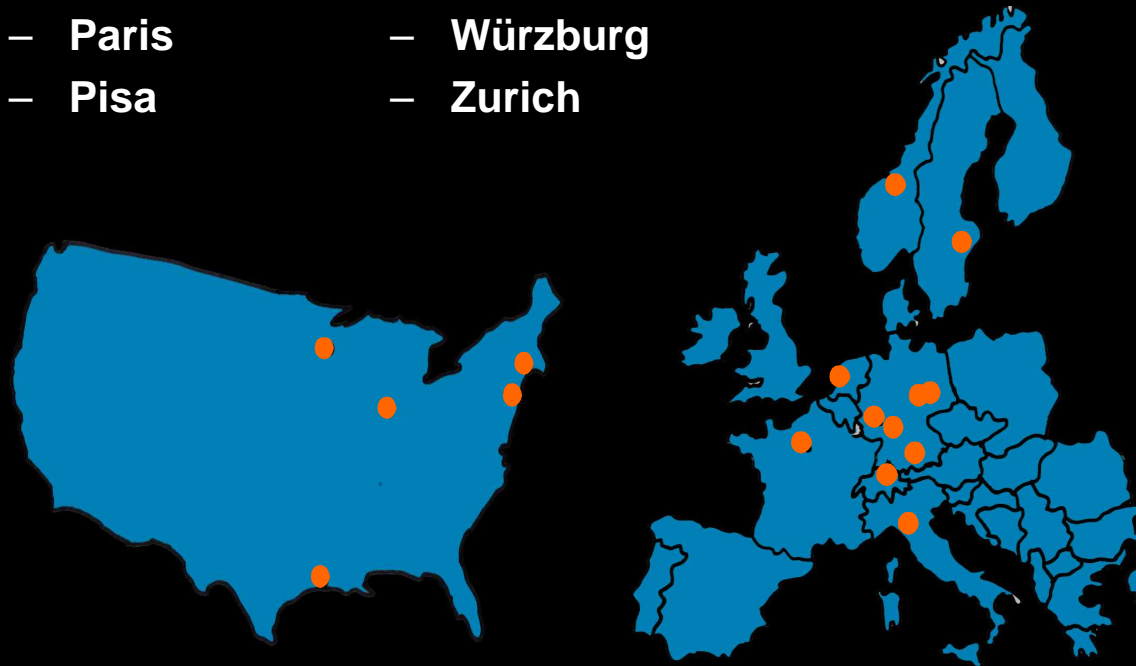
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MR Perfusion Imaging for Detection CAD

A Multicenter Dose Finding Study in Comparison With QCA and SPECT

18 Study Centers – Multi-Vendor:

- Amsterdam
- Bad Nauheim
- Berlin (3)
- Dresden
- Houston
- Minneapolis
- München
- New Haven
- New York
- Paris
- Pisa
- St. Louis
- Trondheim
- Uppsala
- Würzburg
- Zurich



Methods: Multicenter - Multivendor Design

Primary Endpoint

Determine the accuracies of MR diagnoses per subject relative to QCA achieved with 5 doses of Gd-DTPA-BMA (Omniscan™, GE Healthcare) ranging from 0.01 – 0.1mmol/kg

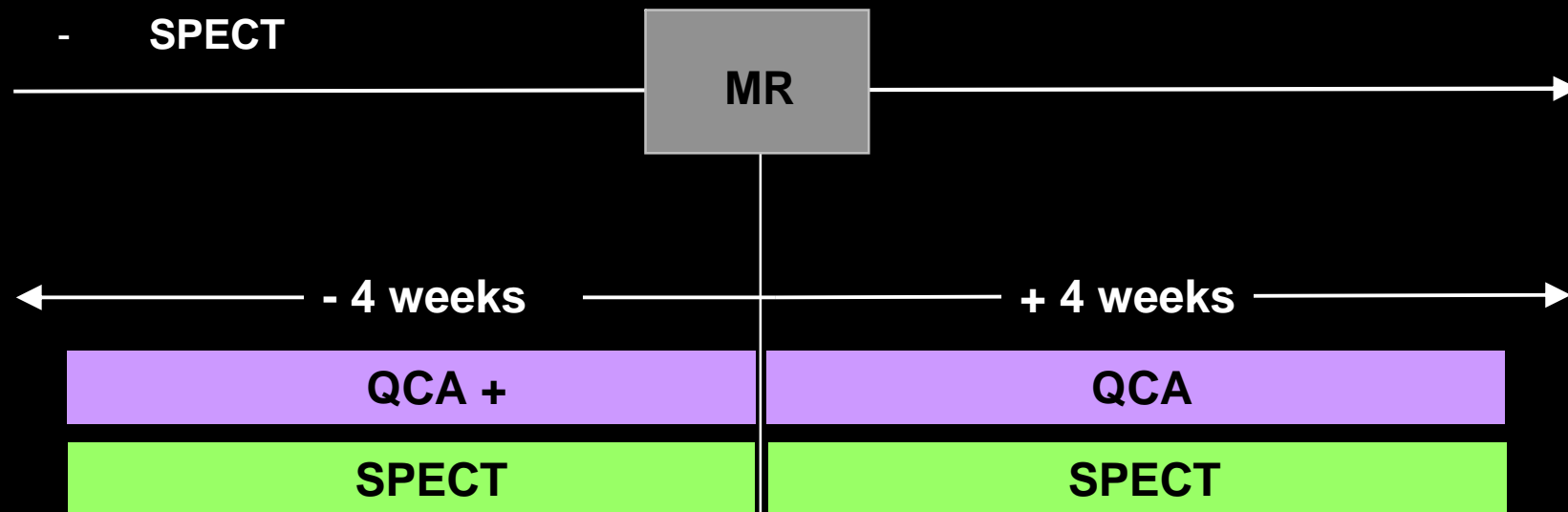
Secondary Endpoint

Comparison MR–SPECT results vs QCA (=standard of truth)

Methods

Inclusion Criteria:

- >18 years of age
- Non-pregnant or postmenopausal women
- Written informed consent
- QCA
- SPECT



Methods

Exclusion Criteria

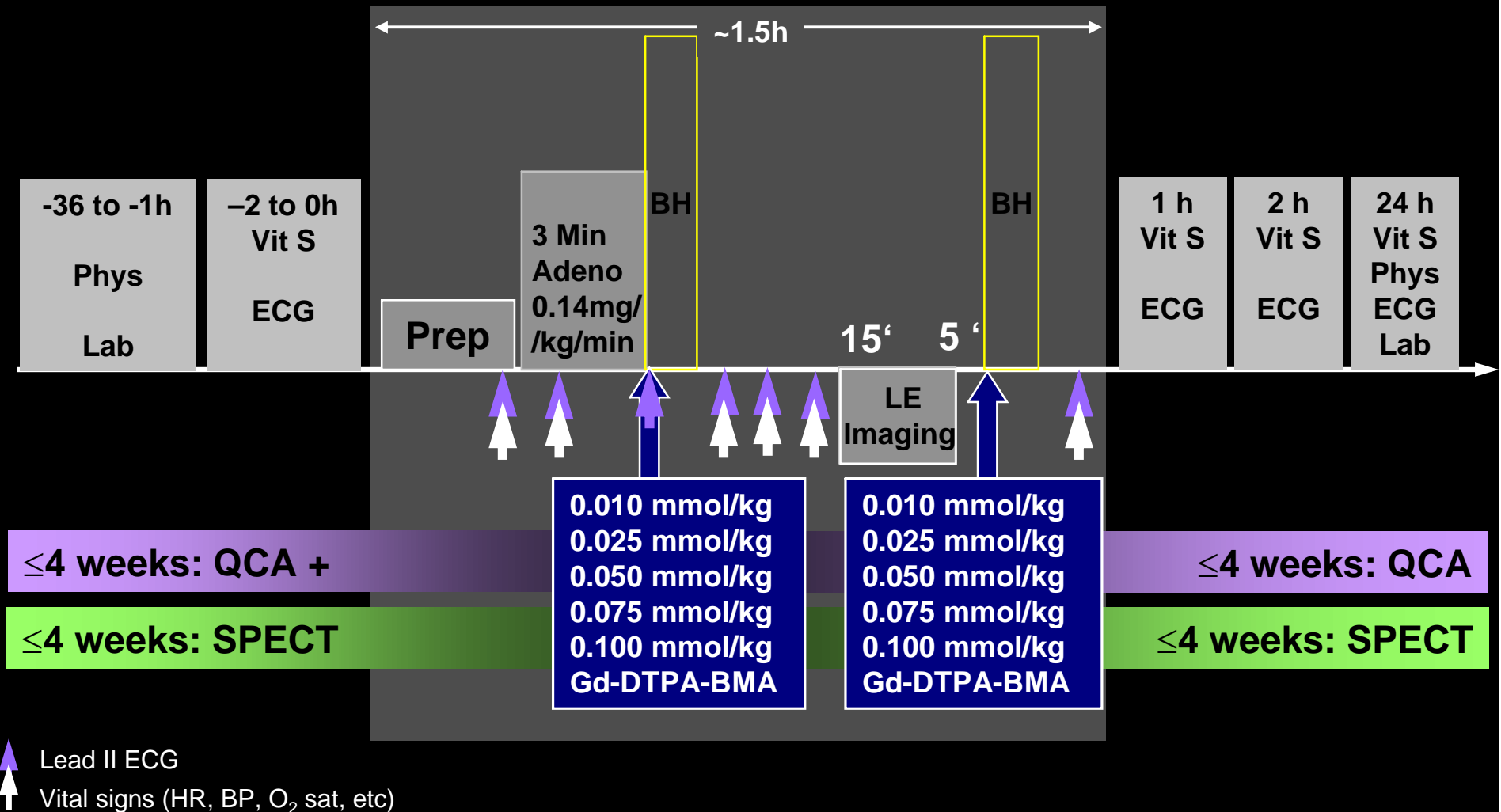
- Acute MI (within 1 week prior to MR)
- History of CABG
- Decompensated congestive heart failure
- unstable AP

- CI for vasodilator
(2^o/3^o-AV-Block, reactive airways disease ...)
- CI for MR (PM, frequent arrhythmias)

- caffeine within 24 hours prior to MR or SPECT

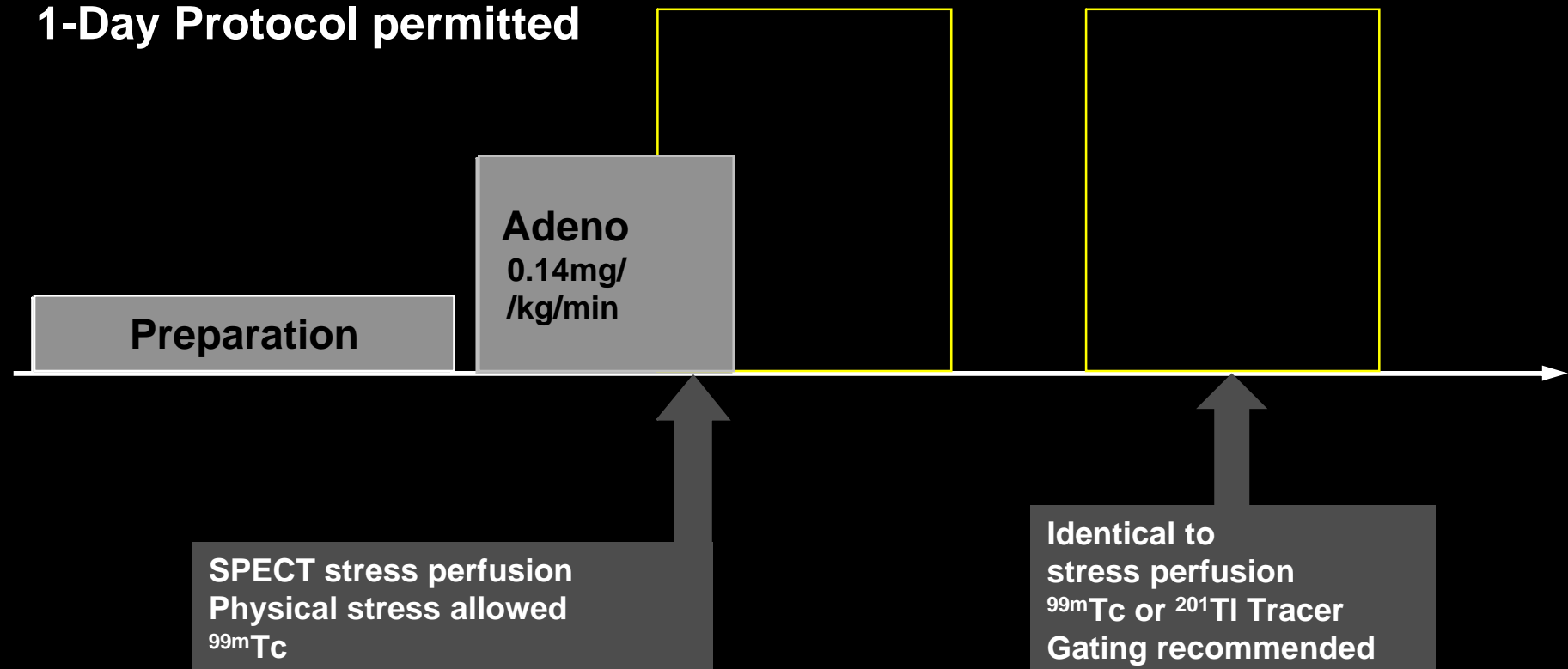
Methods

MR Study and Monitoring: Pats were randomly assigned to 1 of 5 CM doses



Methods

**SPECT Study:
Multi-Vendor
1-Day Protocol permitted**



Methods

QCA and SPECT: Protocol and Reading

QCA:

- QCA: 1 blinded reader
- Diameter stenosis $\geq 50\%$ in ≥ 1 vessel = CAD
- Vessels with ≥ 2 mm lumen diameter included only

MR:

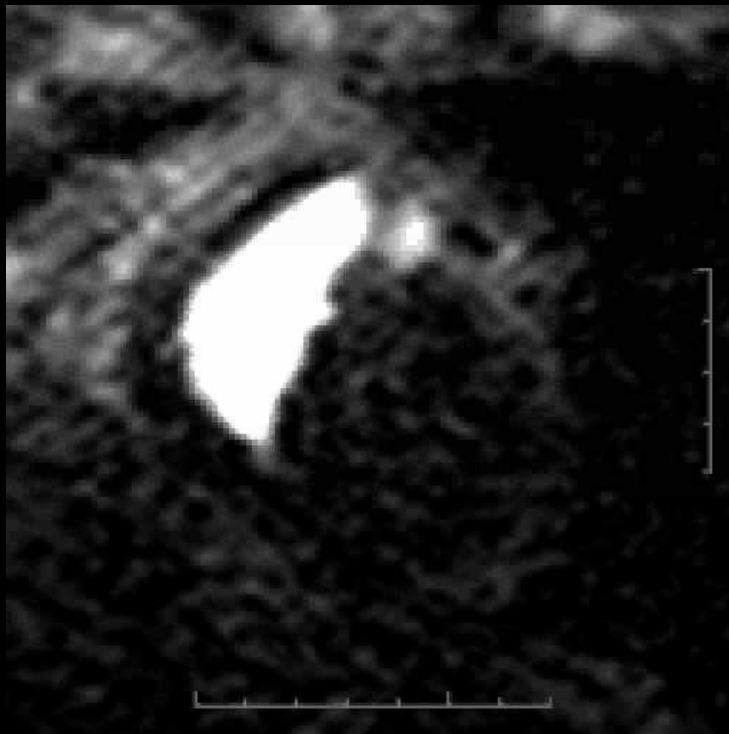
- Stress/rest data: 3 blinded readers

SPECT:

- Rest and stress data: 3 blinded readers

MR Evaluation:

Example: 5 months after LAD-Stenting, atypical chest pain
Scheduled for QCA and SPECT



MR Evaluation: 16 Segment Model



Score:

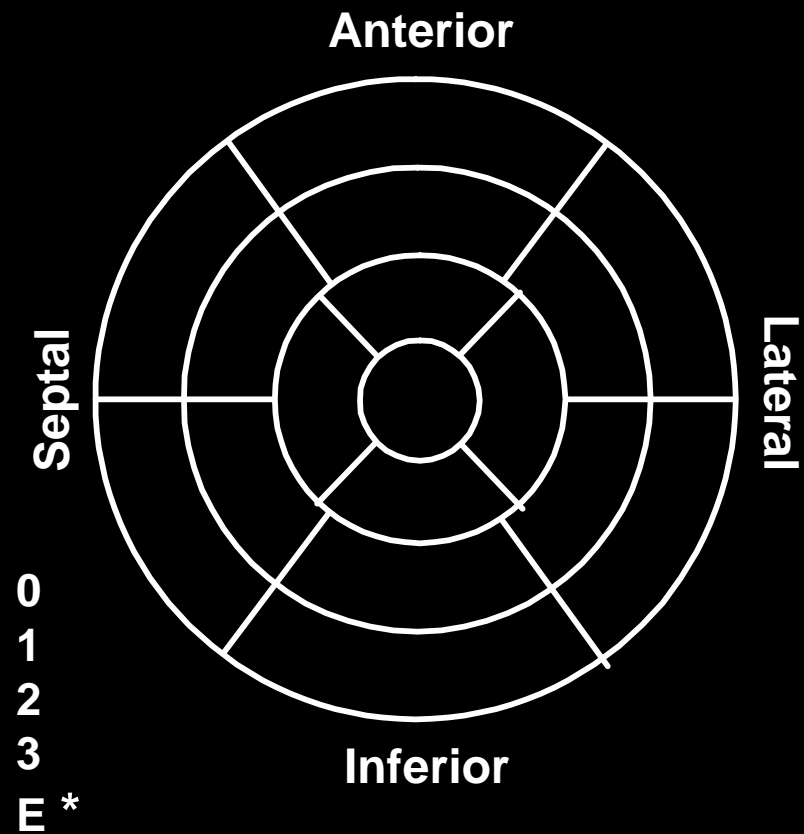
Normal – high likelihood

Normal – low likelihood

Abnormal – low likelihood

Abnormal – high likelihood

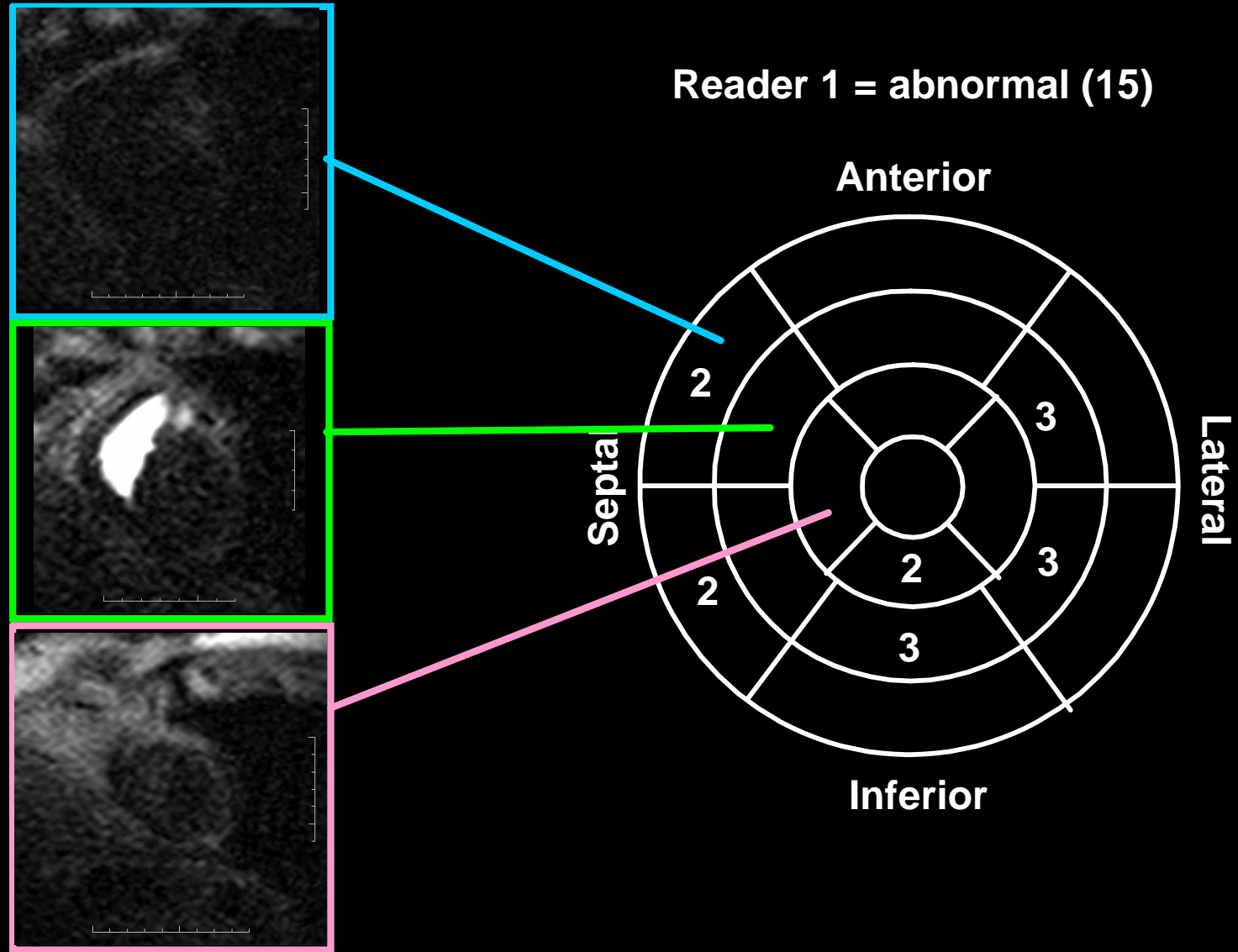
Artefact – diagnosis impossible



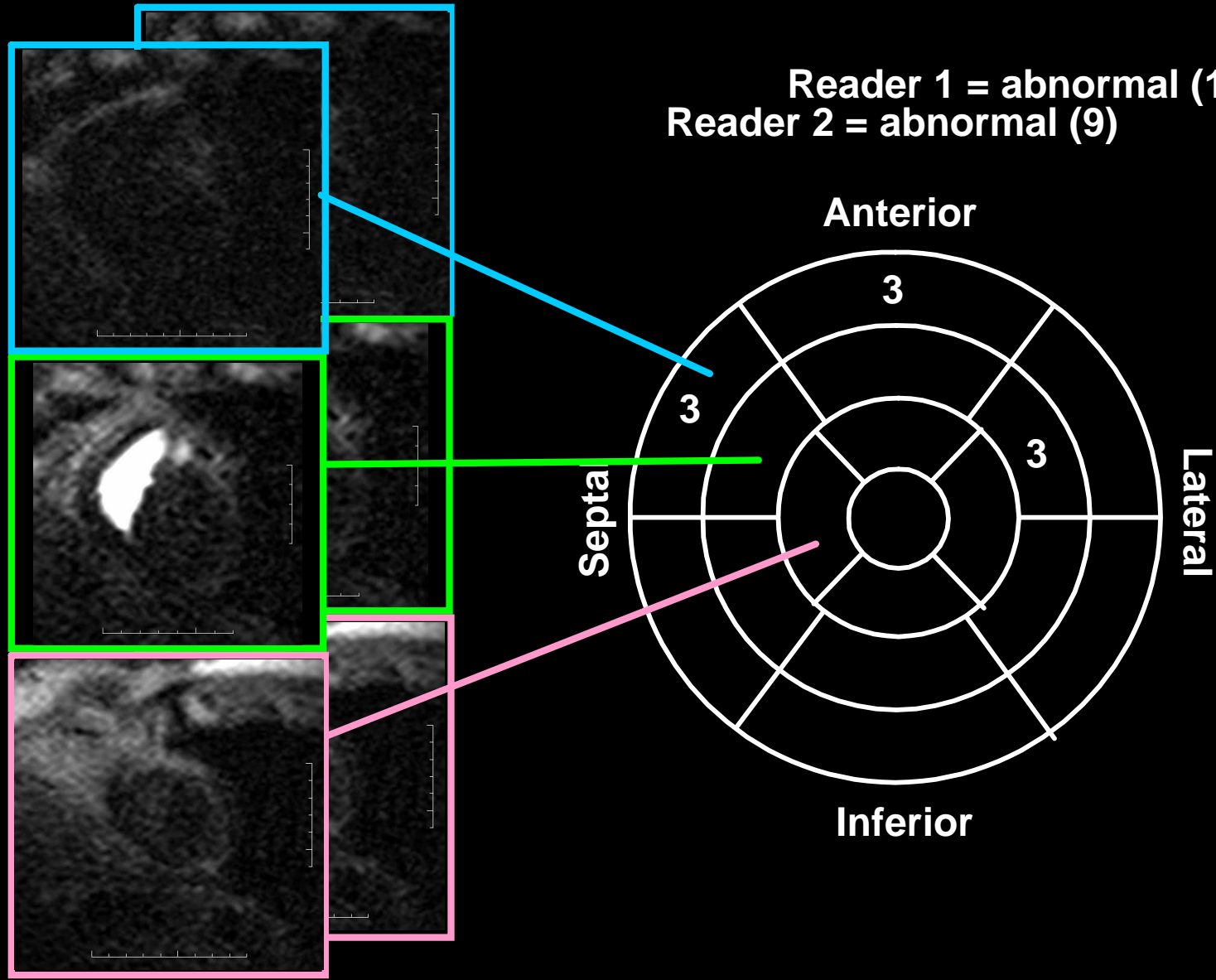
* 4.8% (see Results)

MR Evaluation:

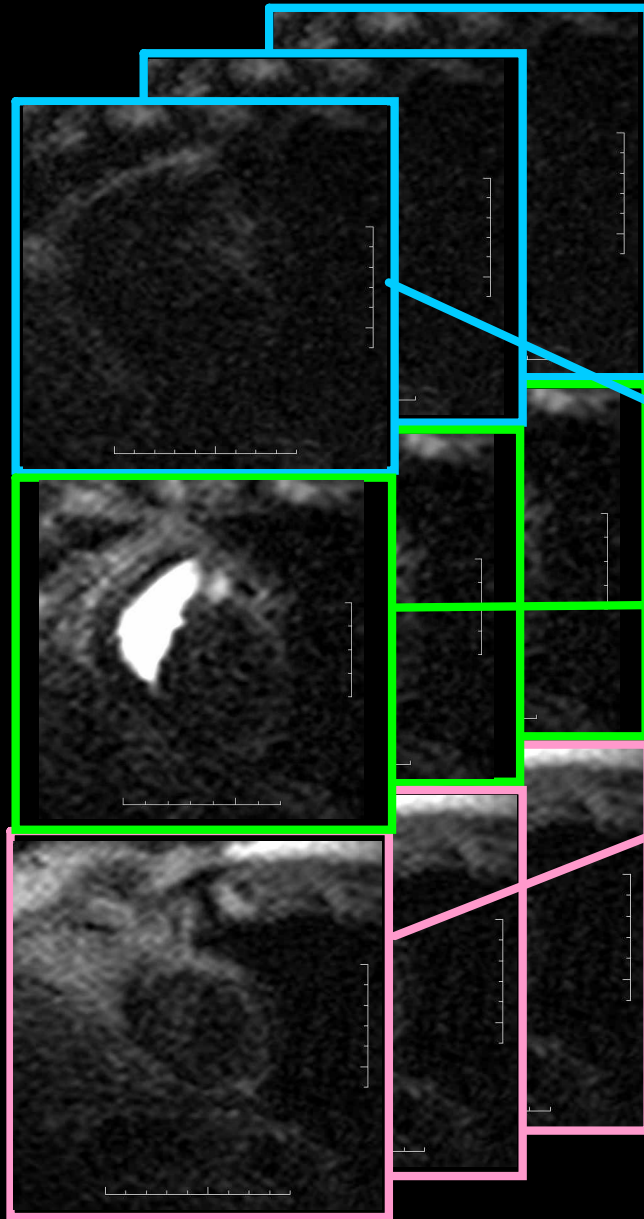
Reader 1 = abnormal (15)



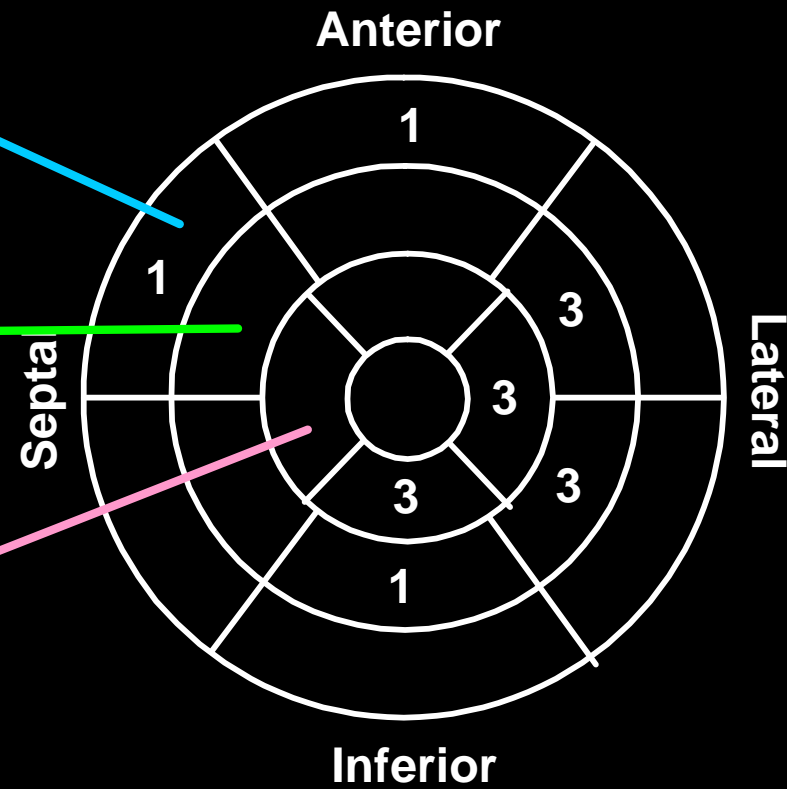
Reader 1 = abnormal (15)
Reader 2 = abnormal (9)



MR Evaluation:



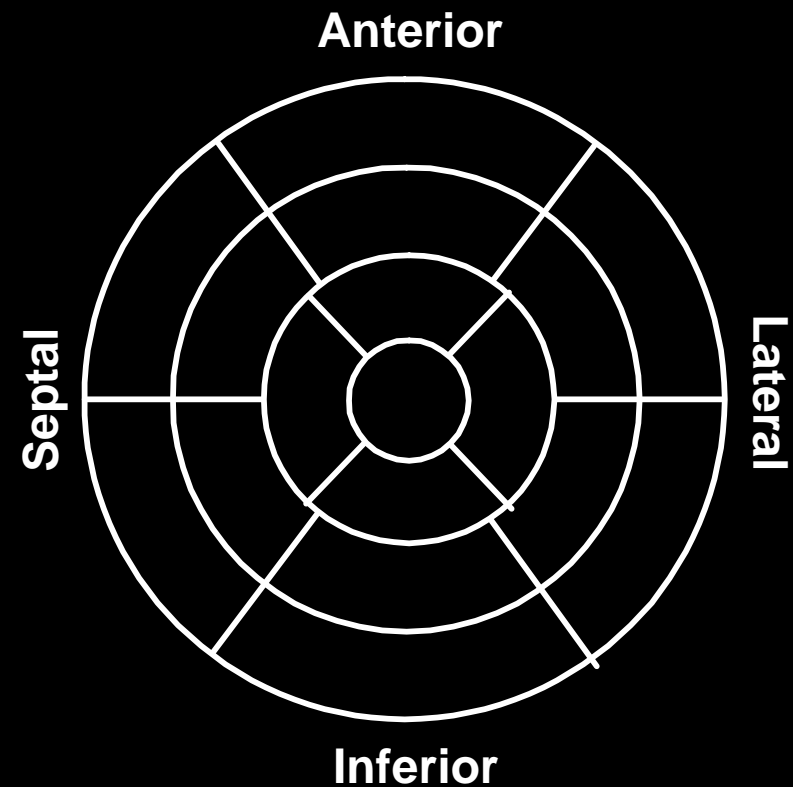
Reader 1 = abnormal (15)
Reader 2 = abnormal (9)
Reader 3 = abnormal (15)
Mean Score
39/3=13



SPECT Evaluation:

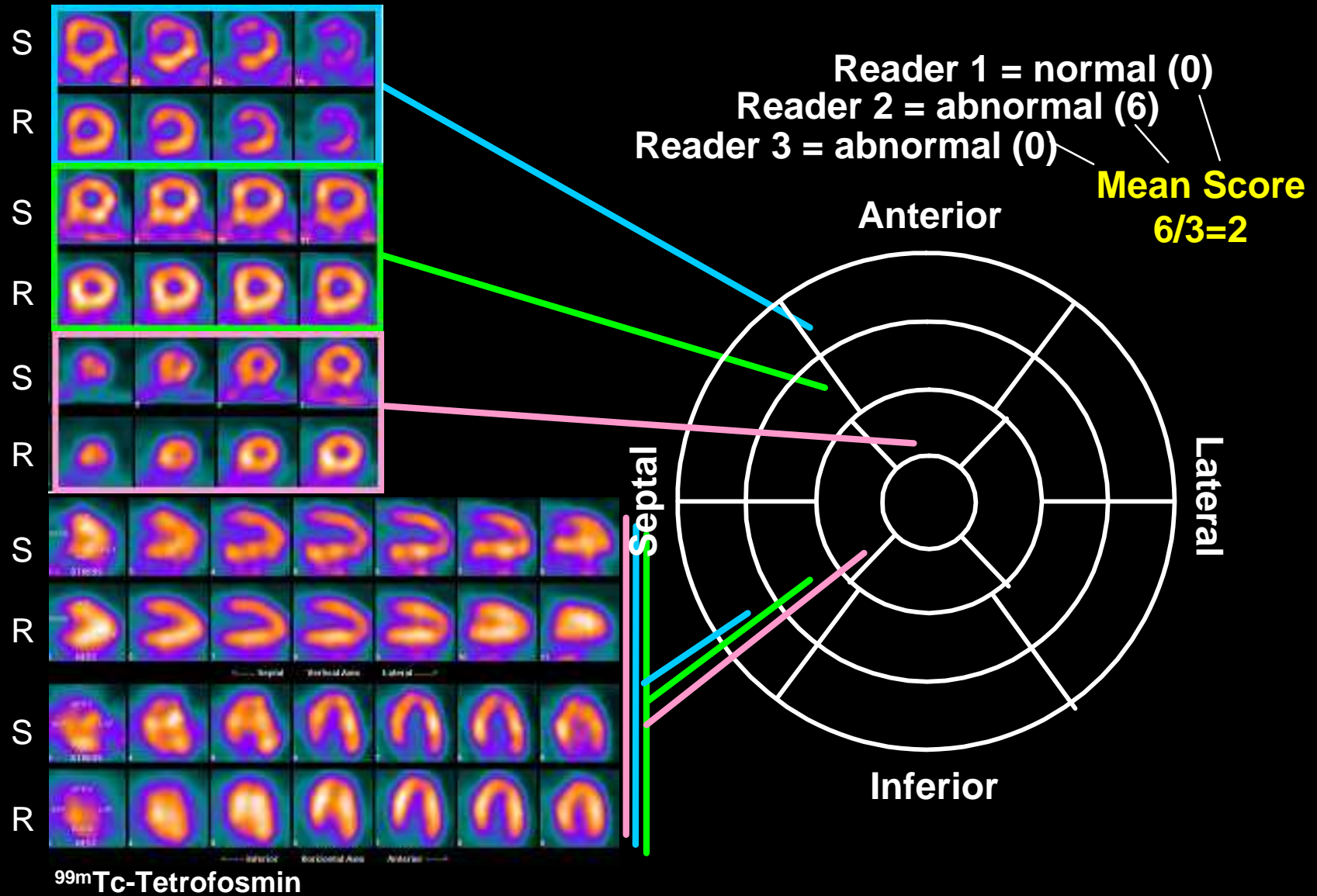
Score:

Normal	0
Fixed defect	1
Partially reversible	2
Fully reversible	3
Artefact – diagnosis impossible	E *



* 5.3% (see Results)

SPECT Evaluation:



Primary Endpoint - Accuracy: MR vs QCA

Accuracy for each Reader

Reader 1 = abnormal, i.e. true positive

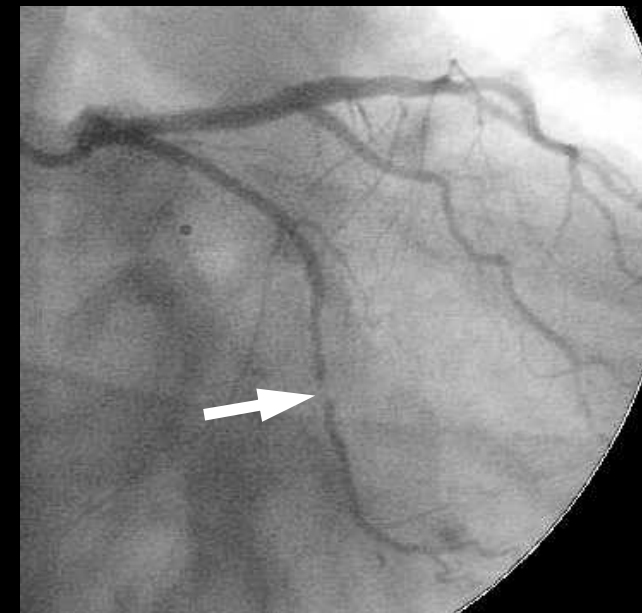
Reader 2 = abnormal, i.e. true positive

Reader 3 = abnormal, i.e. true positive

Reference - QCA:

52% Diameter Stenosis
distal LCX

Stress-only



Secondary Endpoint – CMR vs SPECT

ROC: Sens/Spec-Pairs at various thresholds

MR

Reader 1 = 15

Reader 2 = 9

Reader 3 = 15

Mean Score: $39/3 = 13$

SPECT

Reader 1 = 0

Reader 2 = 6

Reader 3 = 0

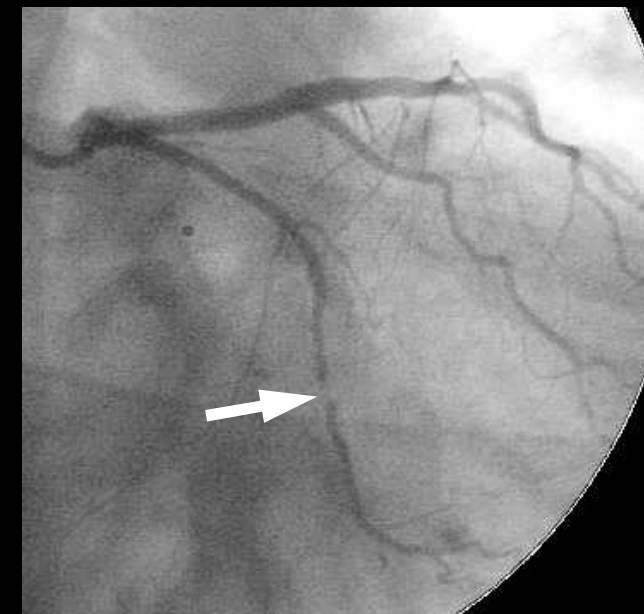
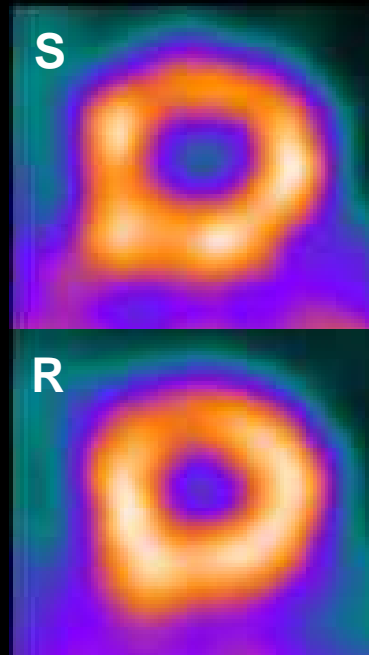
Mean Score: $6/3 = 2$

Reference - QCA:

52% Diameter Stenosis
distal LCX

ROC-Analysis for paired sens/spec analysis = $\Delta AUC_{MR-SPECT}$

Stress-only



Results

Demographics

	Dose 1 (N=45)	Dose 2 (N=50)	Dose 3 (N=48)	Dose 4 (N=45)	Dose 5 (N=45)
Male sex – no (%)	32 (71.1)	40 (80.0)	33 (68.8)	33 (73.3)	32 (71.1)
Age – yr					
Mean±SD	61.3±9.4	60.6±10.1	59.7±10.3	61.3±10.8	60.5±10.6
Range	43.8-79.6	38.6-82.3	36.1-79.9	41.1-81.0	39.7-78.2
BMI – kg/m ²					
Mean±SD	27.6±3.6	26.7±4.2	27.5±4.4	27.6±4.3	27.4±3.9
Range	21.0-36.0	19.0-39.0	19.0-38.0	16.0-42.0	20.0-38.0
Angina pect. – n (%)	38 (84)	38 (76)	38 (79)	37 (82)	36 (80)
Hypertension – n (%)	35 (78)	35 (70)	32 (67)	31 (69)	28 (62)
MI – n (%)	19 (42)	24 (48)	14 (29)	17 (38)	16 (36)
PCI – n (%)	12 (27)	20 (40)	14 (29)	16 (36)	10 (22)
Heart Failure – n (%)	6 (13)	4 (8)	6 (13)	7 (16)	8 (18)
CAD – n (%)	34 (76)	41 (84)	35 (74)	34 (77)	33 (73)
MVD – n (%)	20 (44)	32 (65)	22 (47)	22 (50)	21 (47)
LM – n (%)	1 (2)	2 (4)	1 (2)	2 (5)	2 (4)
LAD – n (%)*	22 (49)	35 (71)	18 (38)	26 (59)	26 (58)
LCX – n (%)	17 (38)	24 (49)	20 (43)	20 (45)	14 (31)
RCA – n (%)	23 (51)	31 (63)	23 (49)	18 (41)	20 (44)
MR – not evaluable (%)	13.3	2.0	4.3	2.4	2.2
SPECT – not evaluable (%)	8.9	4.1	6.4	0	6.7

* Overall p<0.02

Results: Accuracy MR vs QCA

QCA: Abnormal: 177 (77.6%), Normal: 51 (22.4%)

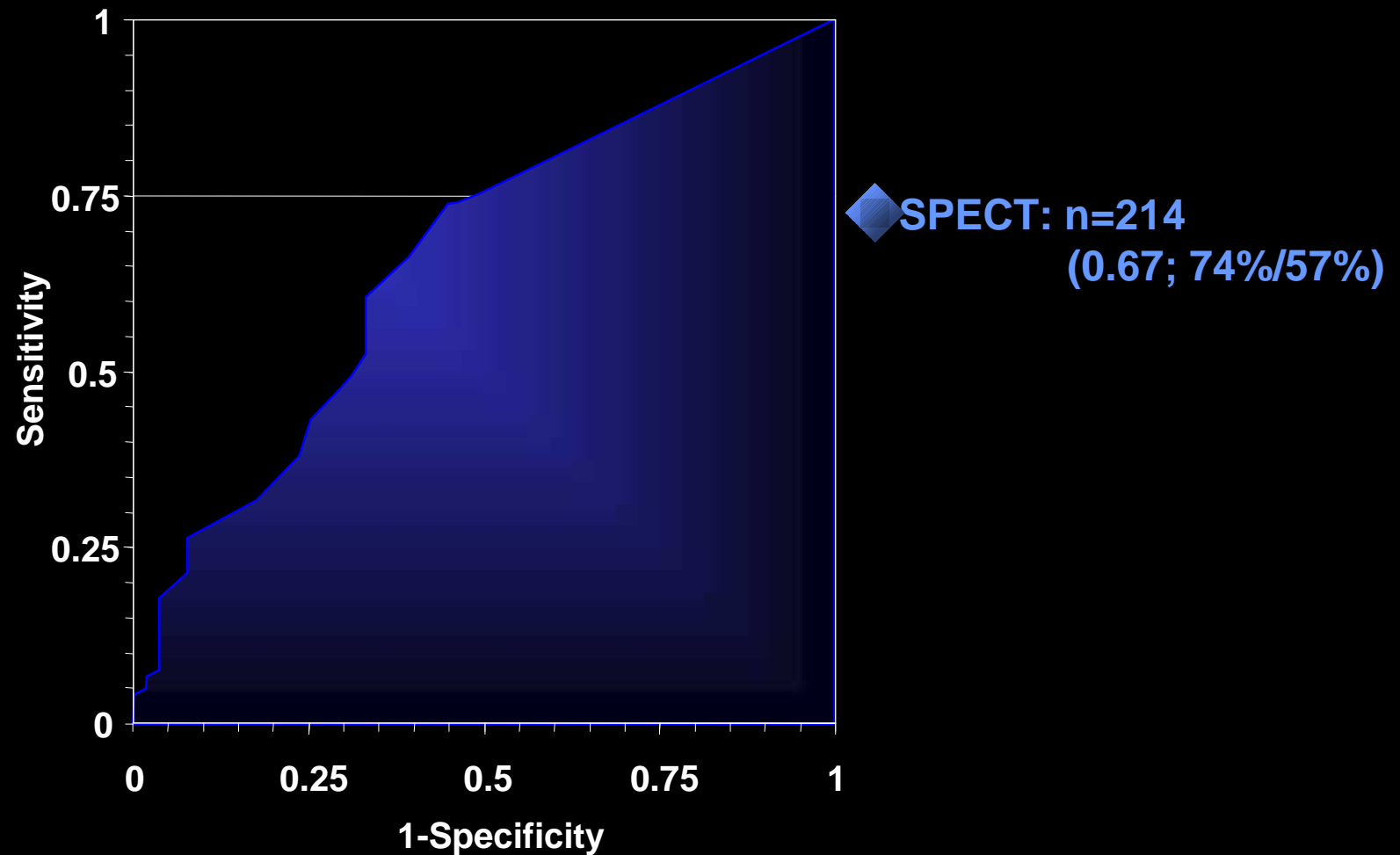
Dose of 0.01 mmol/kg yielded lowest accuracy (combined analysis of all 3 readers).



* $p < 0.05$ vs 0.01 mmol/kg

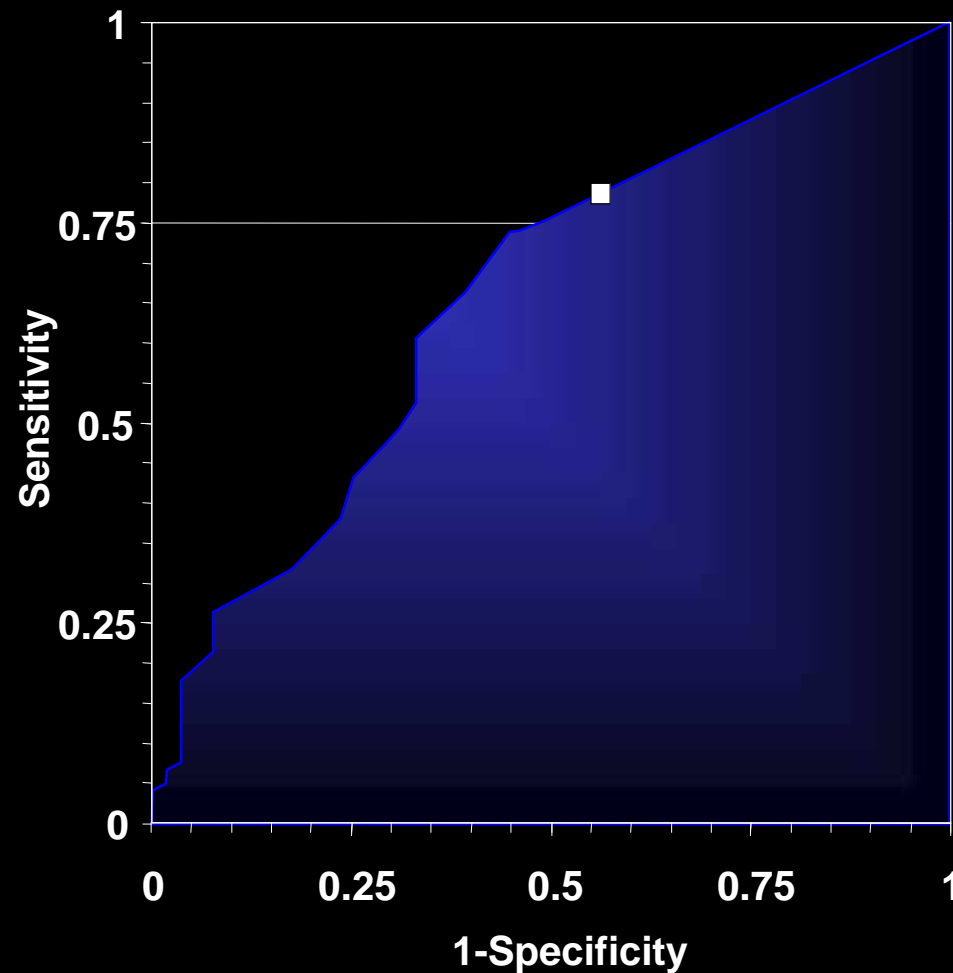
MR Perfusion vs SPECT:

18 Centers - Multivendor / Dose 0.1 mmol/kg Gd-DTPA-BMA



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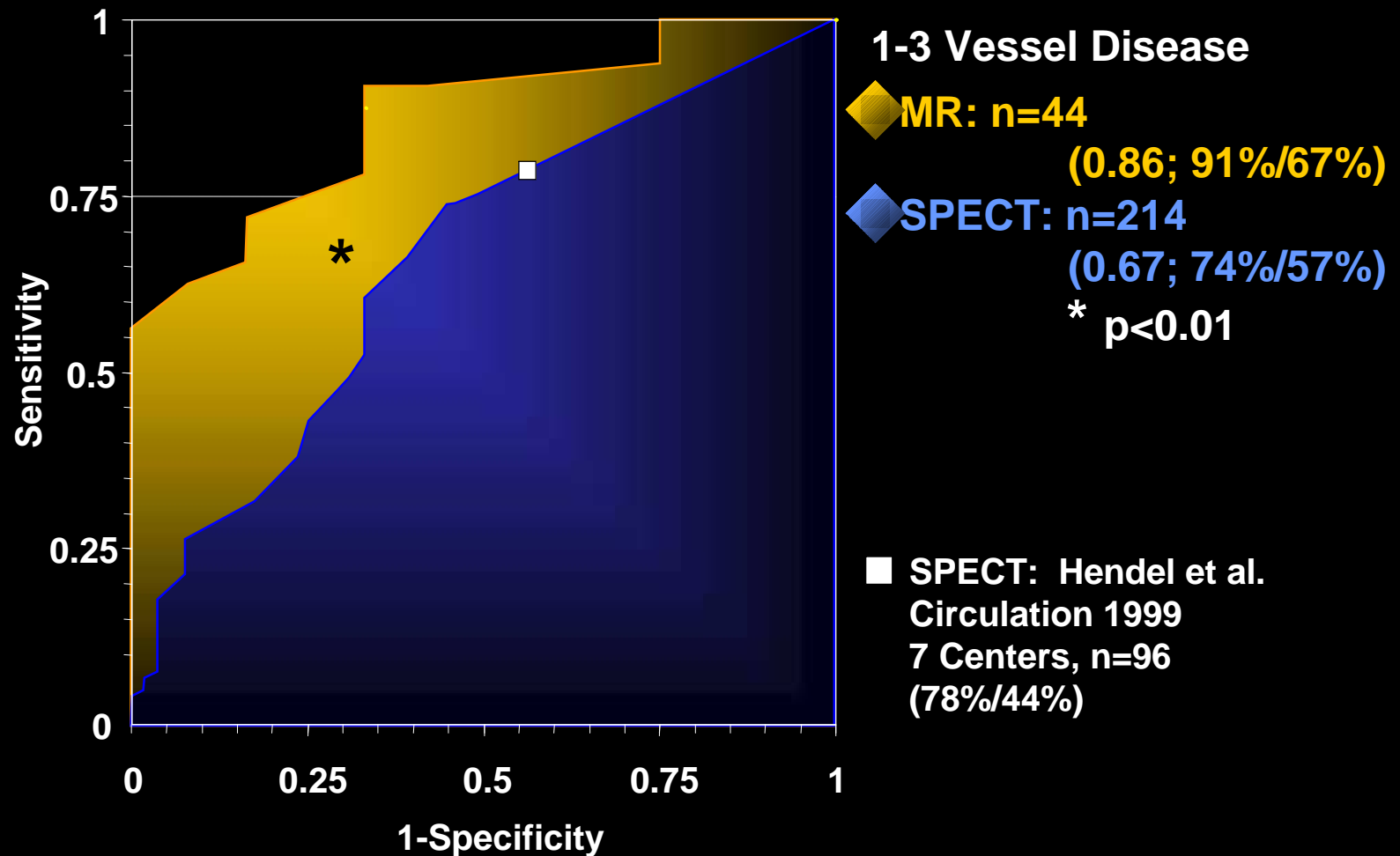
◆ SPECT: n=214
(0.67; 74%/57%)

MR-Impact: largest
Multicenter SPECT Trial

■ SPECT: Hendel et al.
Circulation 1999
7 Centers, n=96
(78%/44%)

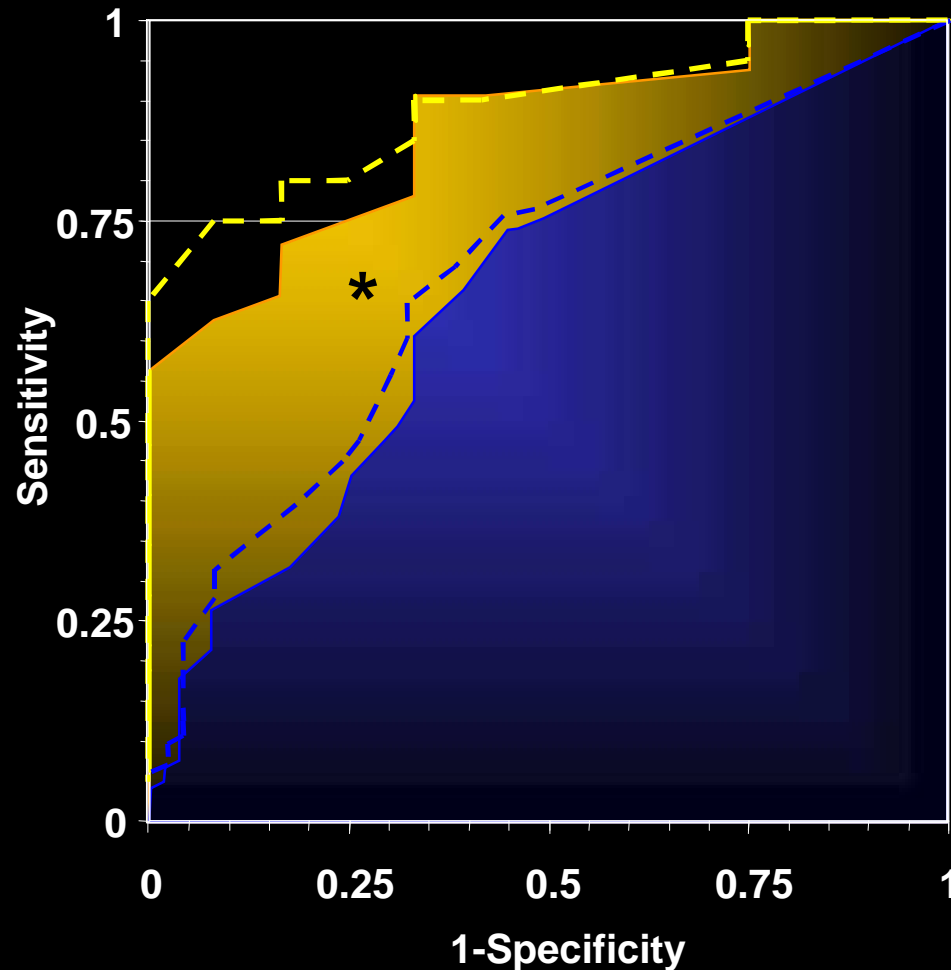
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Multivessel-Disease: MR vs SPECT

18 Centers - Multivendor / Dose 0.1 mmol/kg Gd-DTPA-BMA



1-3 Vessel Disease

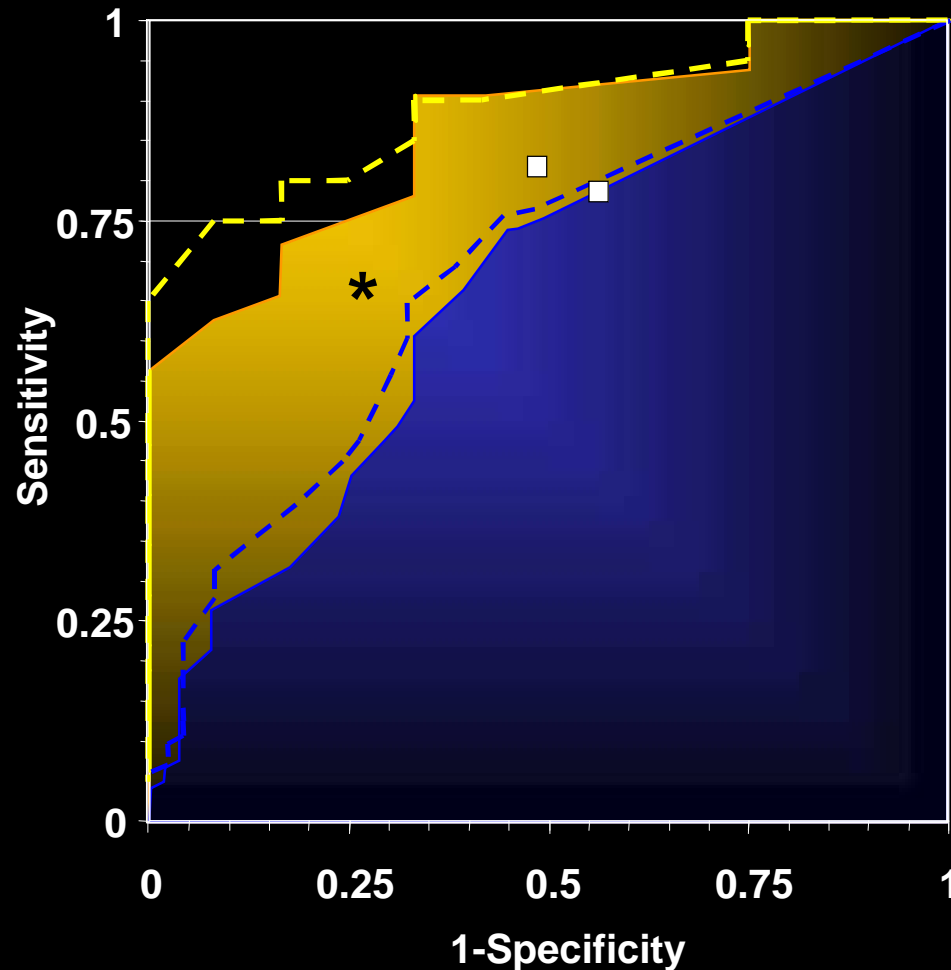
◆ MR: n=44
(0.86; 91%/67%)
◆ SPECT: n=214
(0.67; 74%/57%)
* p<0.01

2-3 Vessel Disease

- - MR: n=32
0.89, 90%/67%
- - SPECT: n=162
0.70, 76%/57%
* p<0.01

Multivessel-Disease: MR vs SPECT

18 Centers - Multivendor / Dose 0.1 mmol/kg Gd-DTPA-BMA



1-3 Vessel Disease

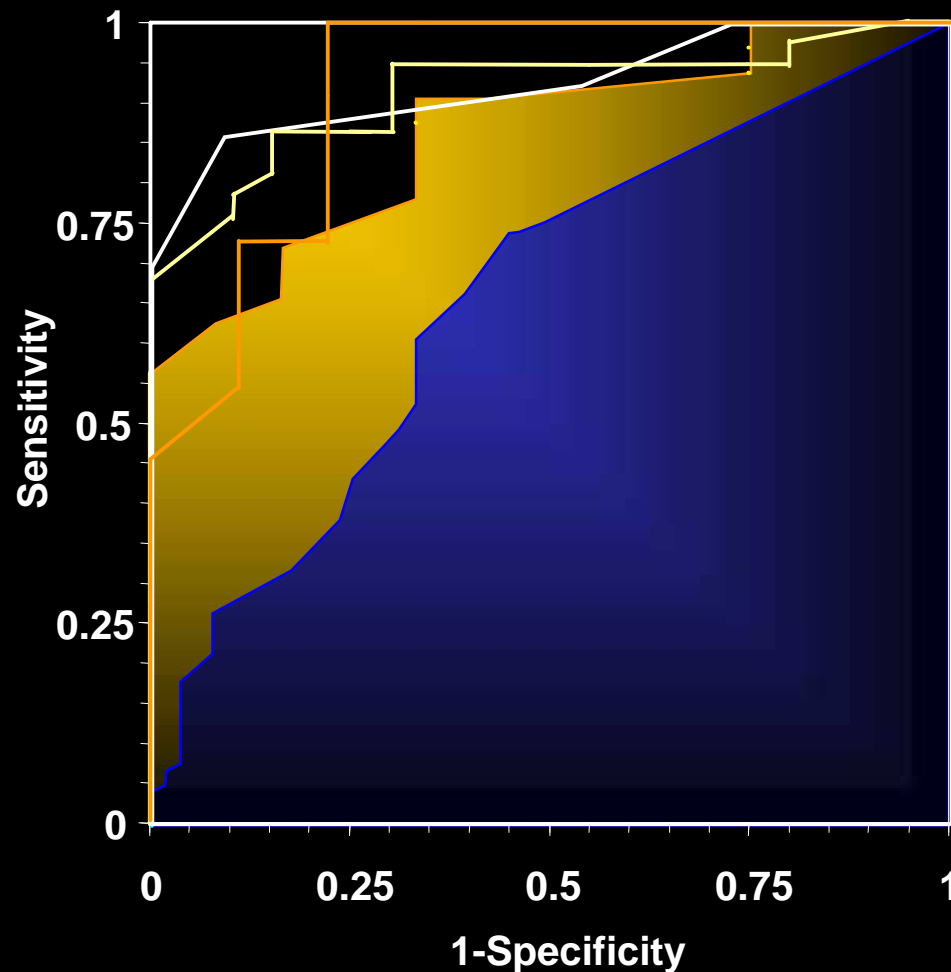
◆ MR: n=44
(0.86; 91%/67%)
◆ SPECT: n=214
(0.67; 74%/57%)
* p<0.01

2-3 Vessel Disease

- - MR: n=32
0.89, 90%/67%
- - SPECT: n=162
0.70, 76%/57%
* p<0.01

MR Perfusion vs SPECT:

18 Centers - Multivendor / Dose 0.1 mmol/kg Gd-DTPA-BMA



— 1 Center
Semi-automatic, stress
Schwitter et al.
Circ. 2001

— 3 Centers – 1 Vendor
Visual, stress-rest
Wolff, Schwitter et al.
Circ. 2004

— 3 Centers – 1 Vendor
Semi-Automatic, stress
Giang et al.
Eur. Heart J. 2004

Safety

234 subjects received Gd-DTPA-BMA (> 30'000 data points)
21 subjects experienced 23 AEs (9.0%)

- 20 AEs (87%) considered not related to Gd-DTPA-BMA
19 mild AEs, 1 severe AE (angina)
most common AE: Angina (resolved during study period)
- no AEs resulted in subject withdrawal
- no deaths, no serious AEs
- no relationship between Gd-DTPA-BMA dose and overall AE profile

„MR-Impact“ Conclusions

This Large Multicenter–Multivendor Trial shows
at 0.1 mmol/kg Gd-DTPA-BMA (Omniscan™):

- **The MR perfusion test is superior to SPECT for the detection of coronary artery disease**
- MR first-pass perfusion imaging as a short test and without radiation, is safe, is sensitive and specific, and can be recommended as an alternative for SPECT imaging in experienced centers