New Method to
Detect Myocardial Ischemia

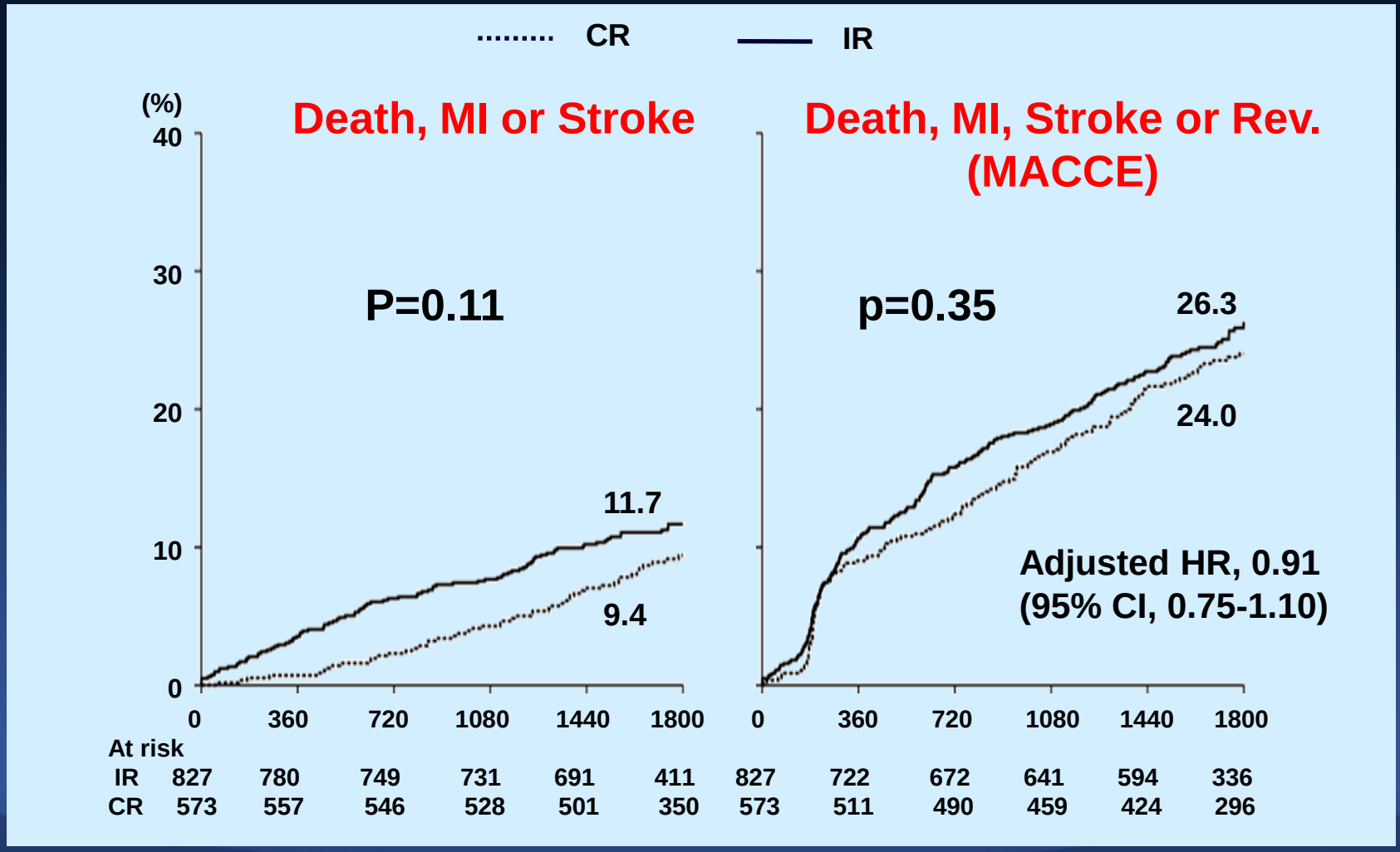
Stress Myocardial Perfusion CT

Young-Hak Kim, MD, PhD

Heart Institute, University of Ulsan College of Medicine,
Asan Medical Center, Seoul, Korea

Angiographic Complete Revascularization (CR)

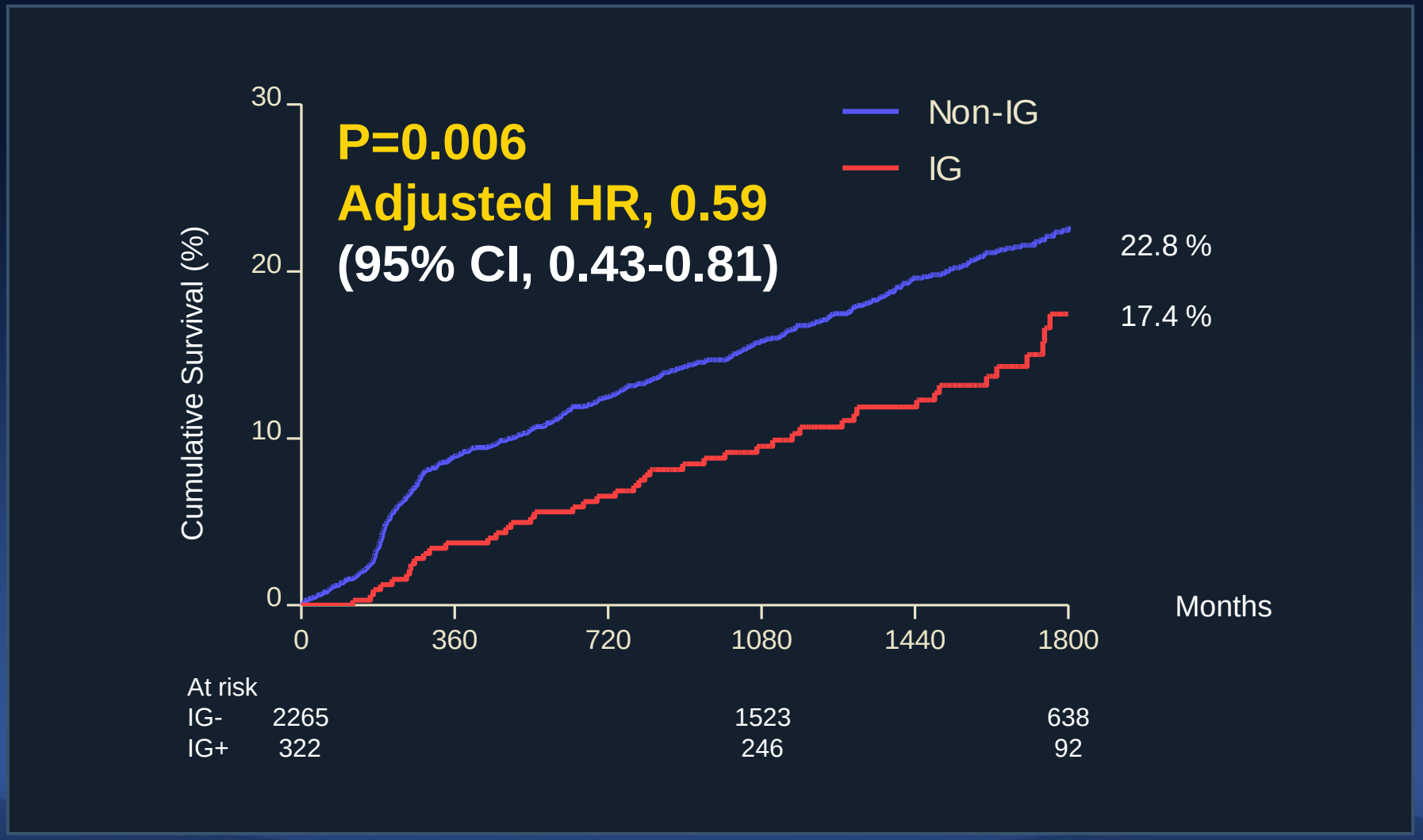
1914 Angina MVD (1400 PCI, 514 CABG) in AMC



Kim YH et al. Circulation. 2011;123:2373

Ischemia-guided PCI using SPECT in AMC

MACCE for 5 Years



Kim YH et al. J Am Coll Cardiol 2012;60:181

Ischemia-guided Revascularization
for appropriate use of PCI and optimized outcomes

Kim YH, Park SJ.
Circulation. 2013;128:95-7.

Kim YH, Park SJ.
Circ J. 2013;77:1967-74.

Editorial

Paradigm Has Already Shifted to Ischemia-Guided Functional Approach

Seung-Jung Park, MD, PhD; Young-Hak Kim, MD, PhD

The anatomic Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery (SYNTAX) score is a stratification score illustrating the complexity of angiographic stenosis. It was considered a surrogate for poor prognosis after percutaneous coronary intervention (PCI).[1] Accordingly, in patients with a high baseline SYNTAX score (bSS) requiring coronary revascularization, analysis of the SYNTAX study by Farooq et al[6] in this issue of *Circulation* provides important information on whether the rSS has a good discriminatory power for predicting outcomes in patients presenting with relatively stable symptoms. Patients with an rSS of >8 had a higher risk of 5-year mortality (35.3%) than those with an rSS of 0 (8.5%), >0 to 4 (8.7%), and >4 to 8 (11.4%). Given these findings, rSS appears to be

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REVIEW

Ischemia-Guided Percutaneous Coronary Intervention for Patients With Stable Coronary Artery Disease

Young-Hak Kim, MD, PhD; Seung-Jung Park, MD, PhD

Current evidence and guidelines support the strategy of ischemia-guided revascularization for treatment of patients with stable coronary symptoms. However, anatomical stenosis is often targeted in revascularization treatment using percutaneous coronary intervention or coronary artery bypass surgery without seriously considering objective evidence of myocardial ischemia. Particularly, for patients with multivessel disease, angiographic complete revascularization was traditionally considered an ideal objective of revascularization treatment. Recently, however, observational studies contradict the concept of angiographic complete revascularization and support the benefit of ischemia-guided selective revascularization based on noninvasive and invasive functional evaluation detecting ischemia-producing coronary lesions. In the absence of a trial specifically designed to assess the relative benefit of either strategy, the present review explores the current concepts about the strength and weakness of anatomical vs. functional revascularization. (*Circ J* 2013; **77:** 1967–1974)

Key Words: Coronary artery disease; Ischemia; Stents

What is the best tool to detect ischemic lesion and vessel ?

- **Noninvasive method**
  - SPECT
  - PET
  - MRI
  - CT

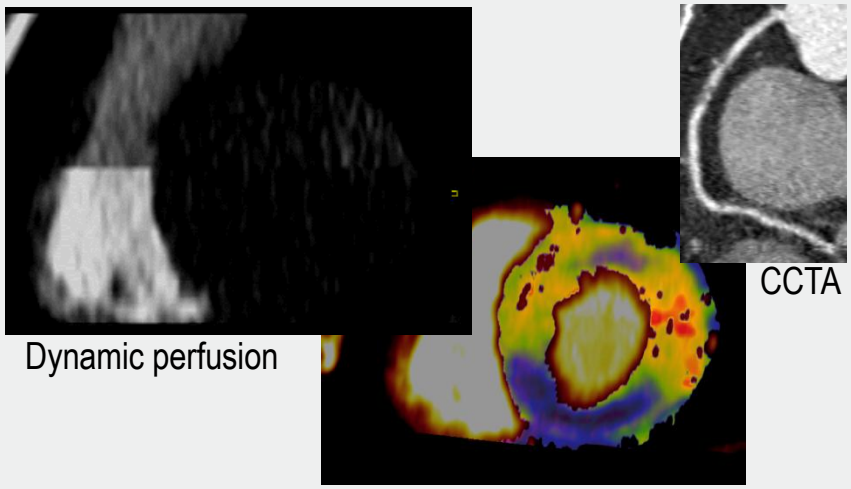
Relatively high F(-) rate in multivessel and LM disease due to the balanced ischemia, low spatial resolution

- **Invasive method**
  - FFR

Fractional Flow Reserve

- The best modality so far to detect ischemic lesions.
- But it has limitations of invasiveness and inaccuracy in very tortuous, diffuse, CTO lesions…

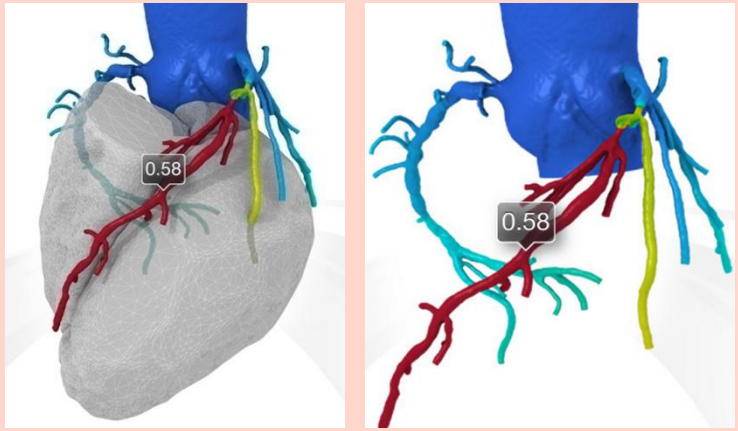
CT-based Ischemia Diagnosis



CT Perfusion (CTP)

Pros	✓ Direct view of myocardium ✓ Easy to perform ✓ No special software
Cons	✓ Radiation dose concern (two scans; stress + rest) ✓ Requirement of adenosine

Computational fluid dynamics simulation



CT-FFR

Pros	✓ No additional scan ✓ No requirement of adenosine
Cons	✓ Indirect view of ischemia ✓ Need supercomputer ✓ No information on perfusion.

Published Data about CT Perfusion

Institution	Year	Pts	Sens / Spec (%)	Ref.	CT
MGH	2009 2010	33 35	94 / 74 91 / 91	QCA/SPECT QCA	64 DSCT (Siemens), Static
Johns Hopkins	2009 2012	27 50	81 / 85 72 / 91	QCA/SPECT QCA/SPECT	64 ch, 320 ch (Toshiba), Static
Monash H (Australia)	2012 2012	42 40	91 / 72 95 / 87	FFR FFR	320 ch , Static (Toshiba)
Centro H. (Portugal)	2013	101	55 / 95 (CTP) 71 / 90 (CTP/CTA)	FFR	64 ch, single source (Siemens), Static
Grosshadern (Germany)	2012	36	93 / 87	FFR	128 DSCT, Dynamic (Siemens)
MUSC (South Carolina)	2010 2012	10 20	86 / 98 86 / 98	MRI MRI/SPECT	128 DSCT, Dynamic (Siemens)
Mount Alvernia H. (Singapore)	2011	35	83 / 78	SPECT	128 DSCT, Dynamic (Siemens)
Cedars-Sinai, LA	2010	30	92 / 86	SPECT	64 DSCT (Siemens), Static
Korea (Kunkook U.)	2011	41	91 / 72	MRI	64 DSCT-DE mode (Siemens), Static
Innsbruck (Austria)	2012	39	96 / 95	MRI/QCA	128 DSCT-FLASH mode (Siemens)

CTP Protocol in AMC

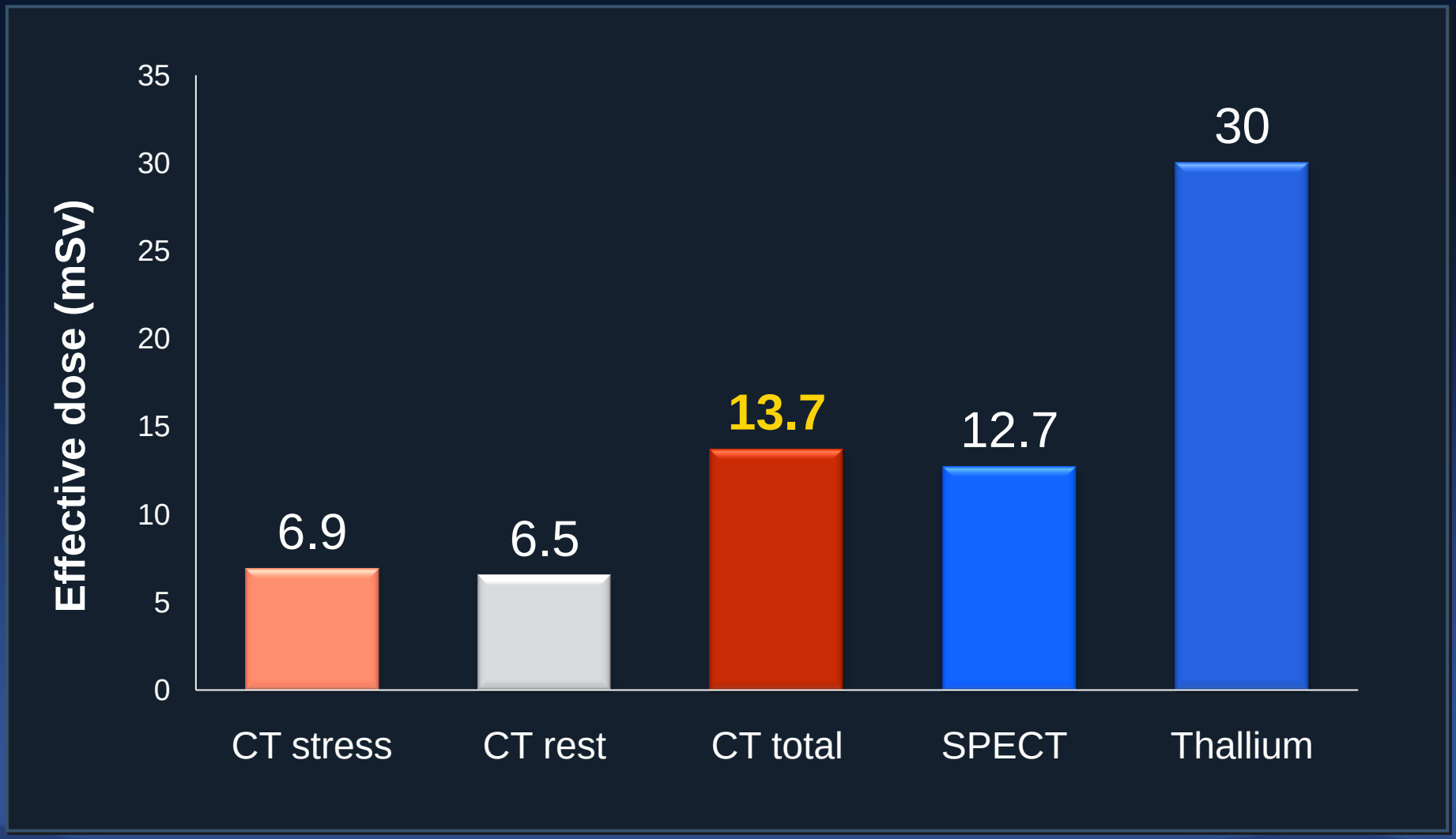
25 minutes
using second-generation dual-source 126 ch. CT

		10 min. interval		
Calcium scoring	**Adenosine infusion**	**Stress perfusion**	**Sublingual NTG**	**Rest perfusion (CTA)**
Scan range	4 min. 30 sec	Retrospective ECG-gating	2 min. before	Retrospective ECG-gating

Option
1. **Static perfusion**
2. Dynamic perfusion

Option
1. Retrospective mode
2. Prospective mode
3. High-pitch mode

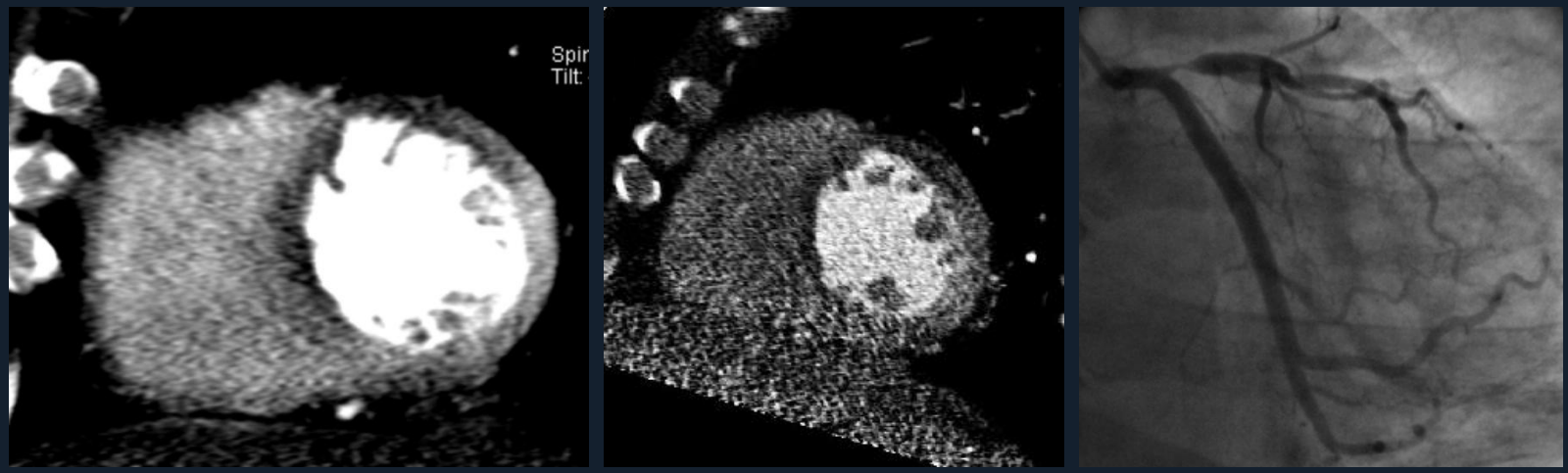
Radiation Dose



SPECT, Blankstein et al . 2009 JACC 54:1072-84

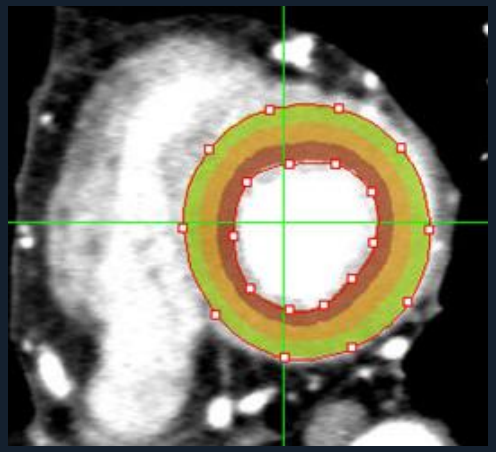
Visual Analysis of CTP

- Diagnostic indicator of myocardial ischemia
  - Low density lesion conforming coronary territory
  - Persistent lesion on cine image at systole and diastole
    - DDx) Transient motion or beam-hardening artifact



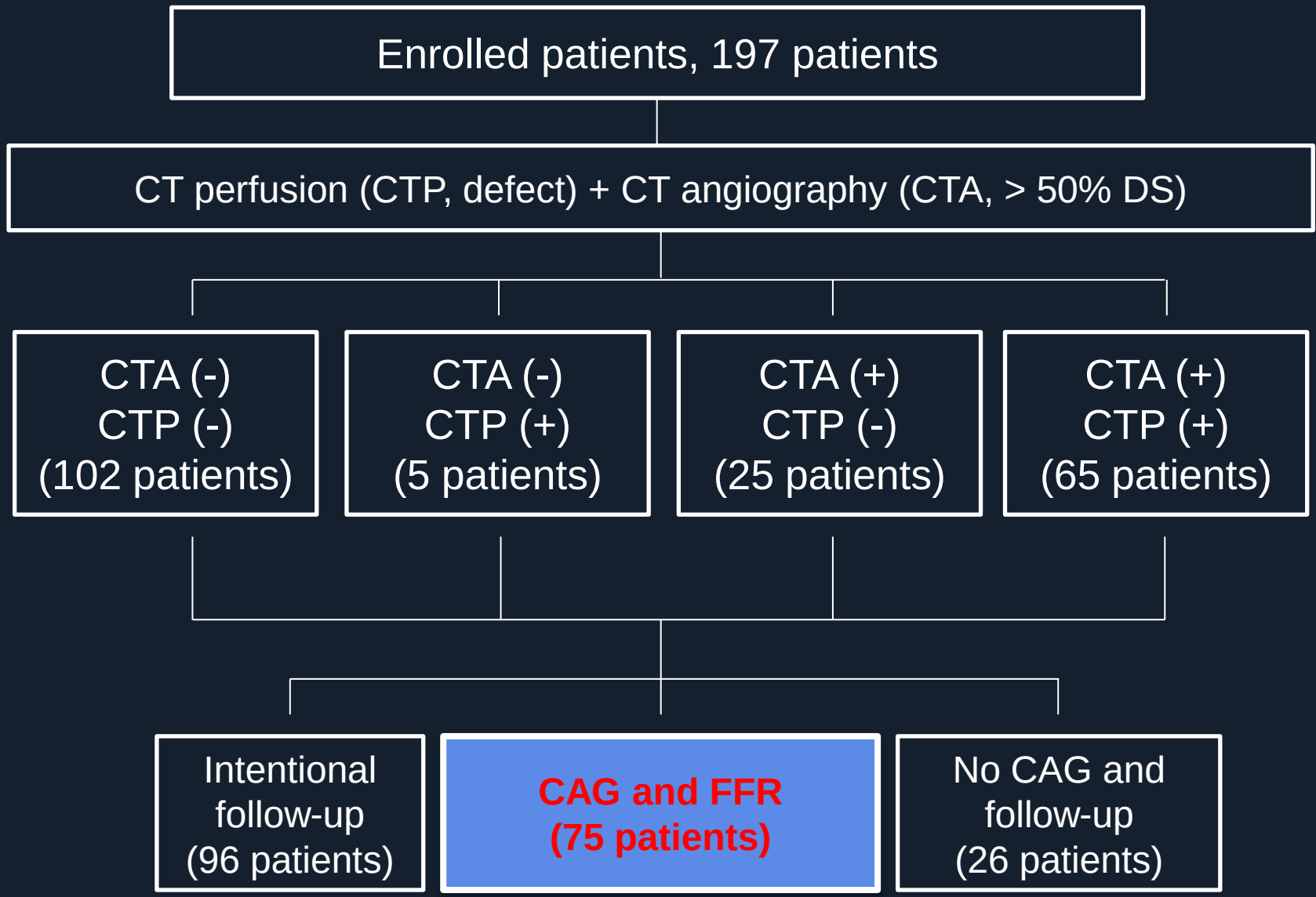
Quantitative Analysis

- Using customized software
  - Classification of whole myocardium into 16 segments and three layers



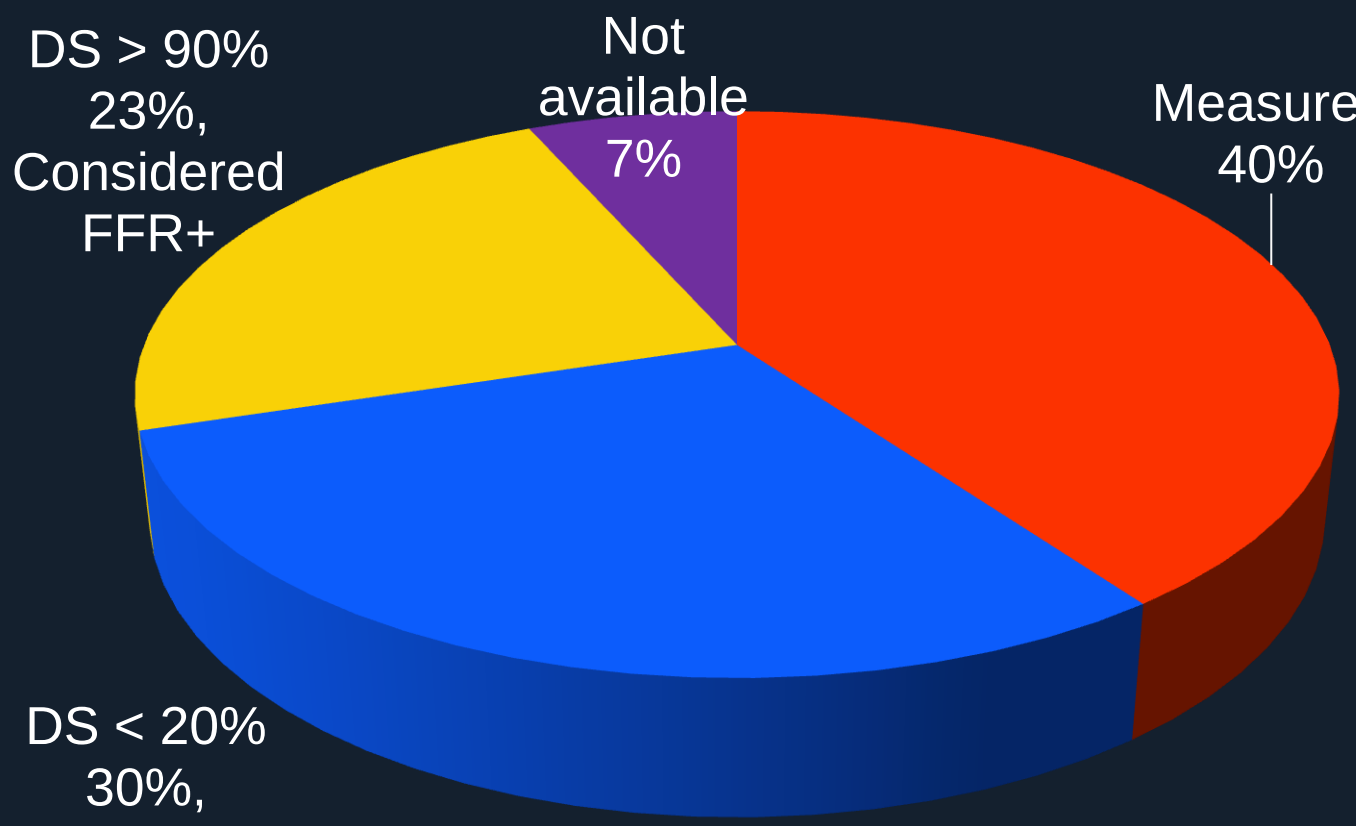
- Evaluation parameters
  - CT density on stress / rest CT
    - $Density_{stress}$ / $Density_{rest}$, HU
  - Transmural perfusion ratio (TPR)
    - $Density_{endocardial}/Density_{epicardial}$
  - Myocardial perfusion reserve index (MPRI),%
    - $(Density_{stress} – Density_{rest})/Density_{rest}$ X 100

CTP Analysis in AMC



Measurement of FFR

Of the 225 vessel territories,



Statistical Analysis

- Per-vessel-territory analysis to compare CTP with FFR
- Kappa statistics to measure the degree of agreement between a certain diagnostic modality and FFR
- McNemar test to compare the diagnostic performance between each modality
- AUC of ROC curve to find best cut-off value for each quantitative parameter of CTP

Baseline Clinical Characteristics

Patients	N=75
Age, yr	63.1±10.3
Male gender	126 (64)
BMI, kg/m^2	25.7 ± 3.1
Diabetes	44 (22)
Hyperlipidemia	31 (16)
Hypertension	98 (50)
Family history	12 (6)
Current smoking	31 (16)
Typical chest pain	94 (48)
Pre-test probability of CAD	
Low (< 10%)	3 (2)
Intermediate (10-90%)	107 (54)
High (>90%)	87 (44)

Per-vessel Visual Assessment

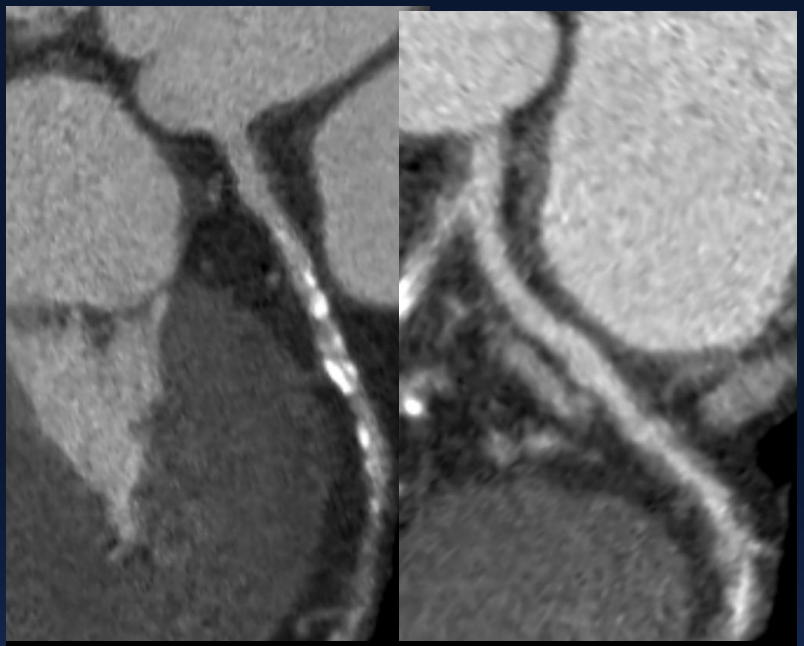
	CTA, DS ≥ 50%		CTP, perfusion defect		QCA, DS ≥ 50%	
	Value	95% CI	Value	95% CI	Value	95% CI
Sensitivity,%	**99**	94, 100	**80**	70, 88	**86**	76, 92
Specificity,%	**73**	65, 81	**95**	90, 98	**91**	84, 95
PPV,%	**72**	63, 80	**92**	83, 97	**87**	78, 93
NPV,%	**99**	94, 100	**87**	81, 92	**90**	83, 94
Kappa statistic	0.68	0.59, 0.78	0.77	0.68, 0.86	0.77	0.69, 0.86
Accuracy	84		89		88	

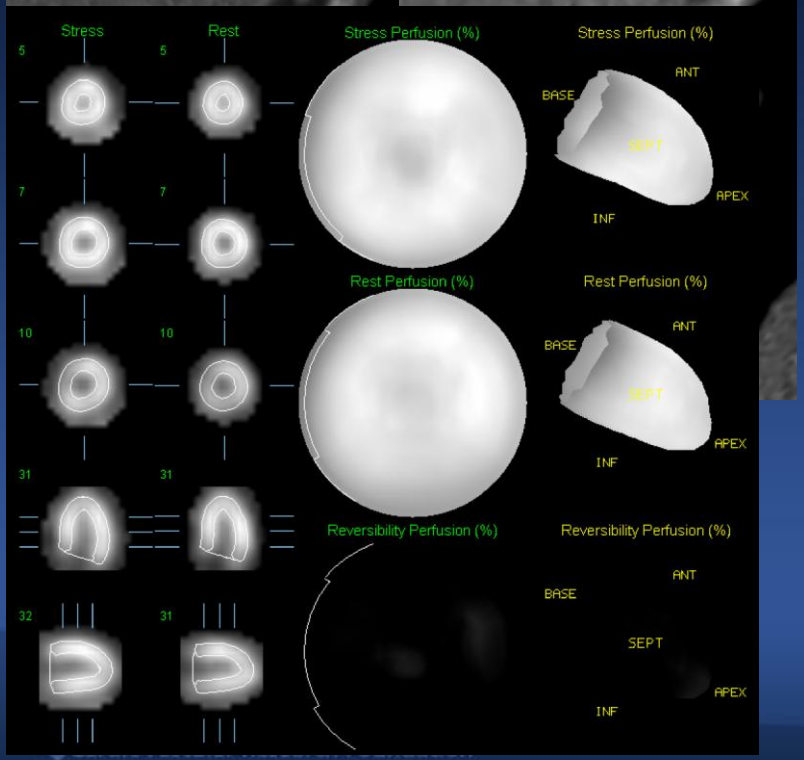
Visual Assessment: CTP or CTA

	CTP	CTA or CTP	
	Values	Value	95% CI
Sensitivity,%	**80**	**100**	96, 100
Specificity,%	**95**	**73**	64, 80
PPV,%	**92**	**71**	63, 80
NPV,%	**87**	**100**	96, 100
Kappa statistic	0.77	0.68	0.59, 0.78
Accuracy	89	83	

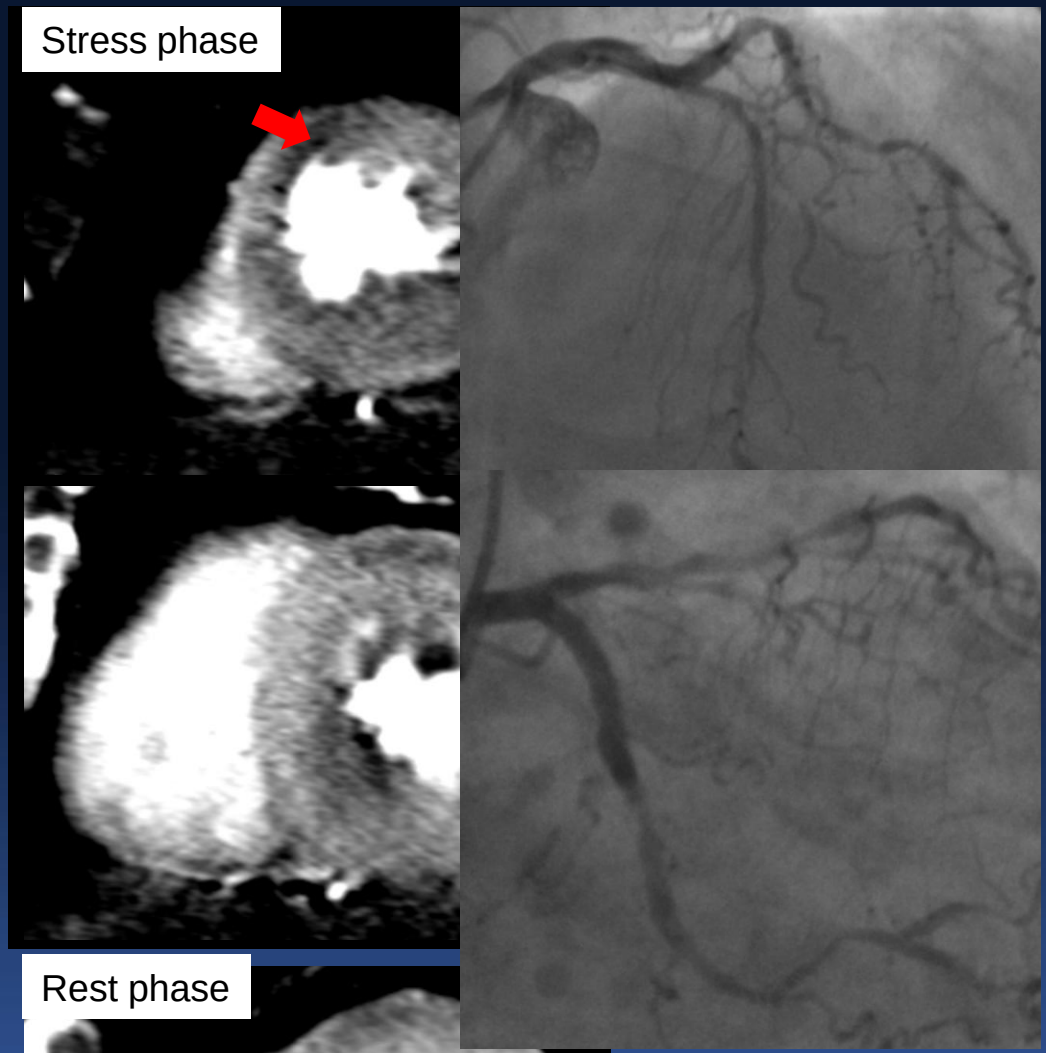
Subgroups

	All patients (N=210)		High calcium score >400 (N=63)		Multivessel (N=54)	
Per vessel	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
CTP	80	95	**85**	**100**	**76**	**91**
CTA	99	73	100	50	100	45
CTP or CTA	100	73	100	50	100	45
CTP and CTA	90	89	94	87	89	82
QCA	86	91	87	83	84	73

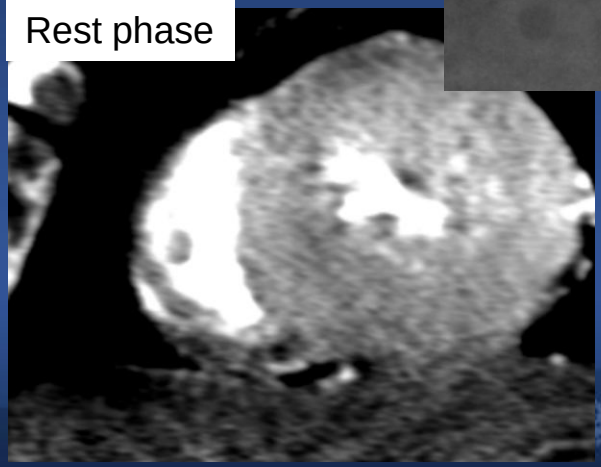




Stress phase



Rest phase

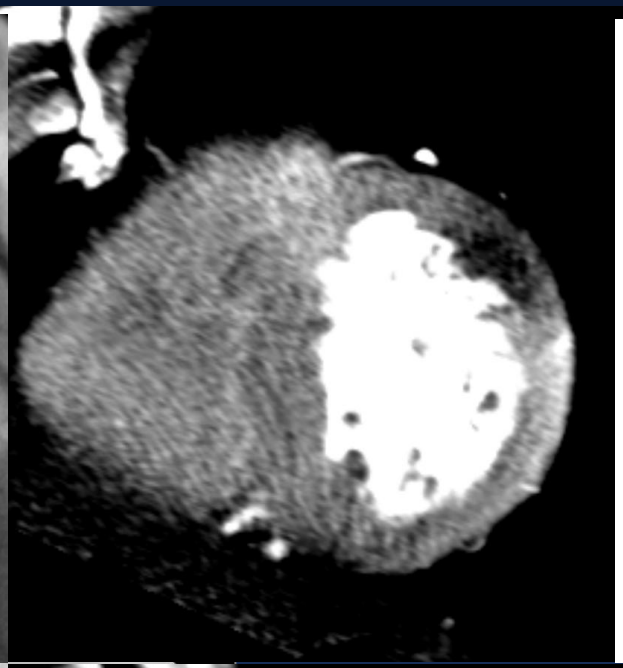


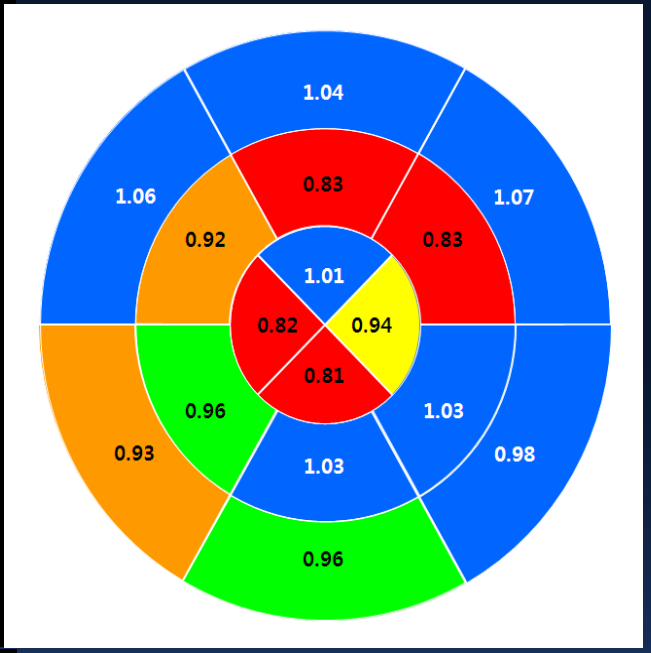
Quantitative Assessment

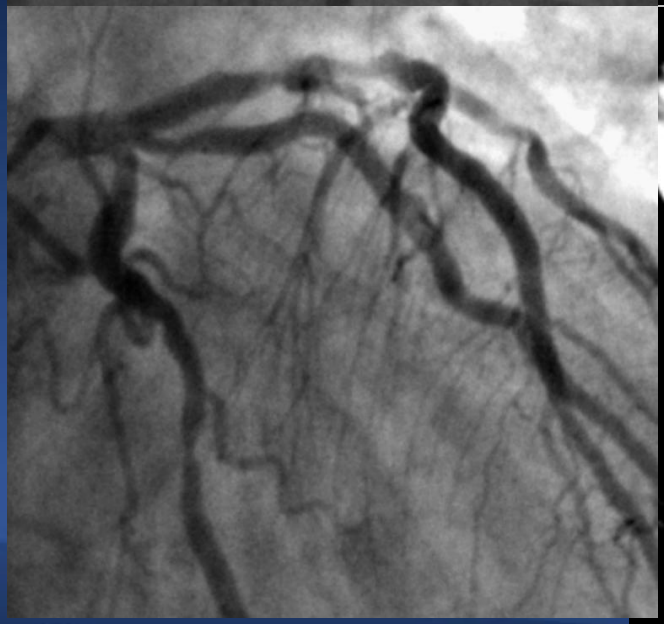
	AUC	Cut Off	Sensitivity	Specificity
TPR	**0.759**	0.98	**75**	**71**
$Density_{stress}$	0.687	102.1	**77**	**56**
$Density_{rest}$	0.559	113.9	**65**	**51**
MPRI	0.691	-4.0	**67**	**62**
Combined quantitative results (TPR, $Density_{stress}$, MPRI)	0.746	-	**63**	**75**
Integration of qualitative and quantitative results	**0.878**	-	**89**	**73**

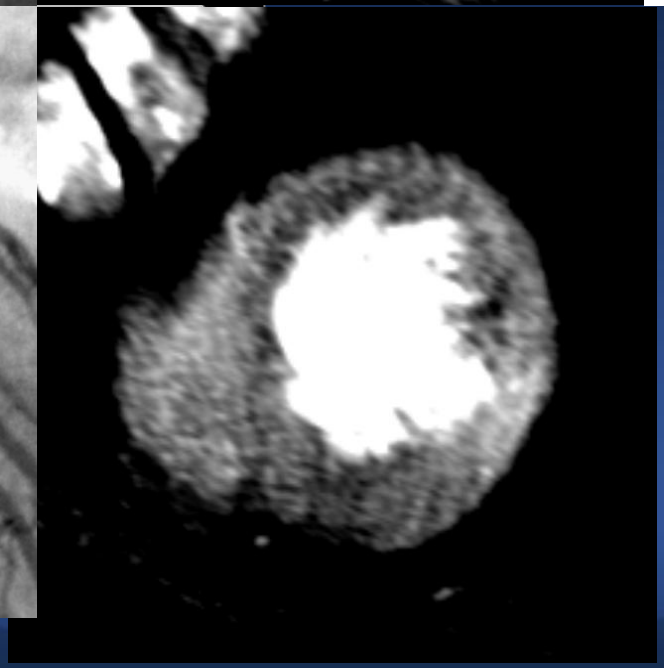
Quantitative Assessment: Multivessel

N=20	AUC	Cut Off	Sensitivity	Specificity
TPR	**0.7209**	0.97	**71**	**67**
$Density_{stress}$	0.6260	113.56	**59**	**67**
$Density_{rest}$	0.6423	109.19	**51**	**67**
MPRI	0.6243	5	**73**	**56**
Combined quantitative results (TPR, $Density_{stress}$, MPRI)	0.7433	-	**68**	**78**
Integration of qualitative and quantitative results	**0.8266**	**-**	**81**	**89**



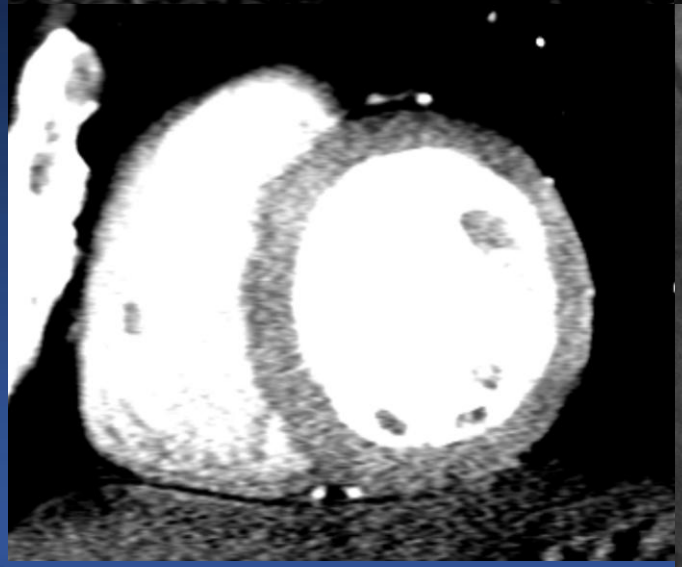


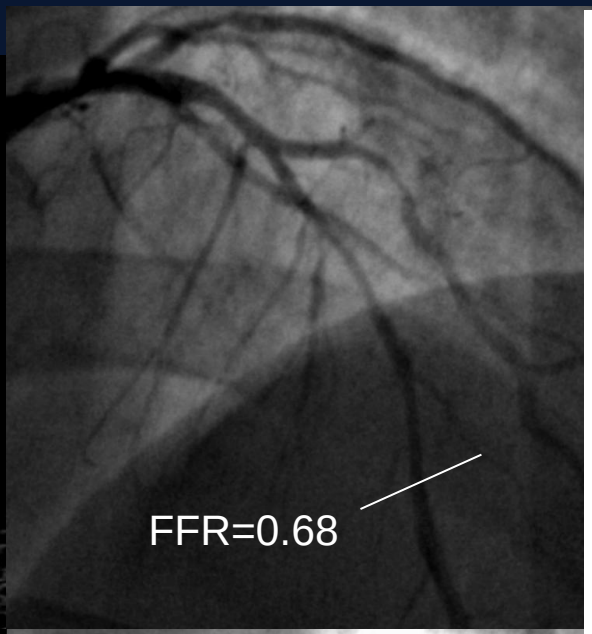




TPR map

- **LAD**
- **LCX**

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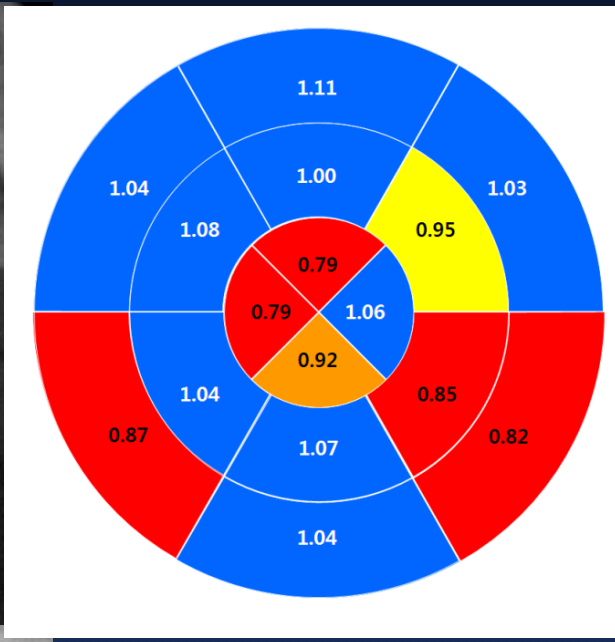
1.11
1.00
1.03
1.04
1.08
0.95
0.79
0.79
1.06
0.92
1.04
0.85
0.87
0.82
1.07
1.04

TPR map

Conclusions

- CTP showed a good diagnostic accuracy for detection of myocardial ischemia.
- Diagnostic accuracy of CTP in localizing ischemic territory was preserved in patients with high calcium score but relatively decreased in those with multivessel diasease.
- Quantitative analysis did not show superior accuracy than visual assessment.
- Integrated interpretation using qualitative and quantitative analysis may provide a better diagnostic accuracy.
- Creation of a diagnosis algorhythm based on qualitative and quantitative measurement and its validation are required in future studies.

25 Korean Multicenters CTP Research Group

PERFUSE Registry and RCT