CT Perfusion

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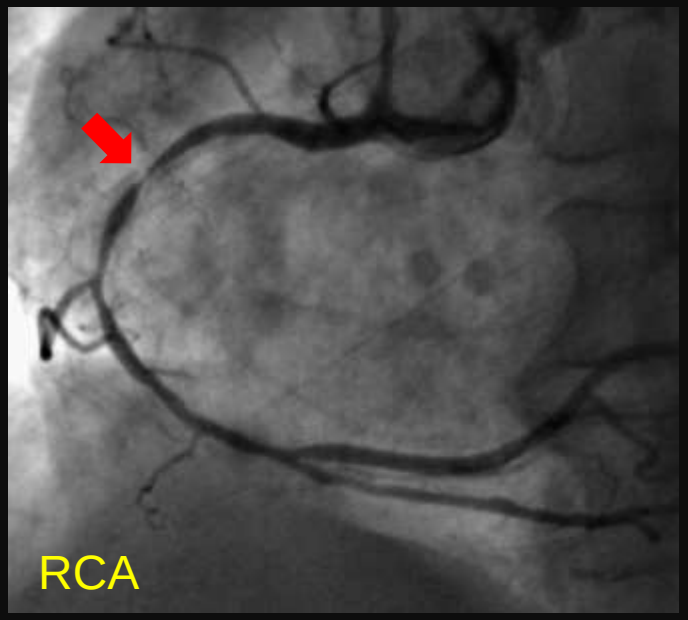
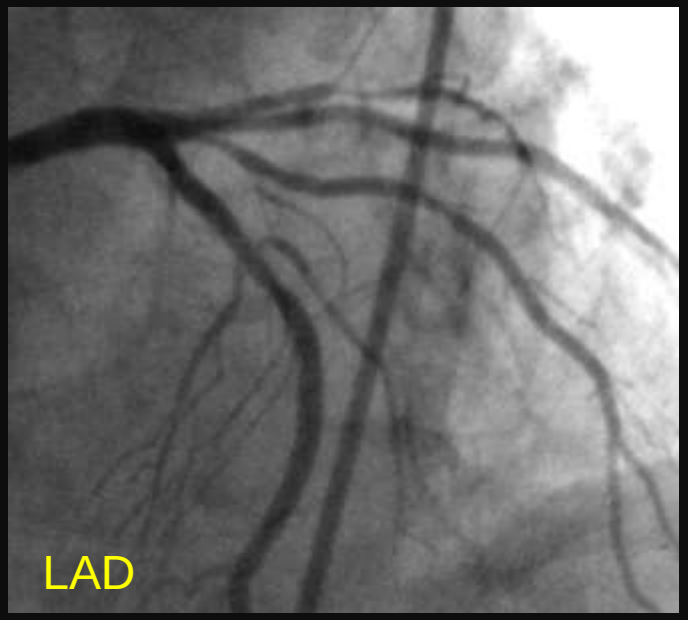
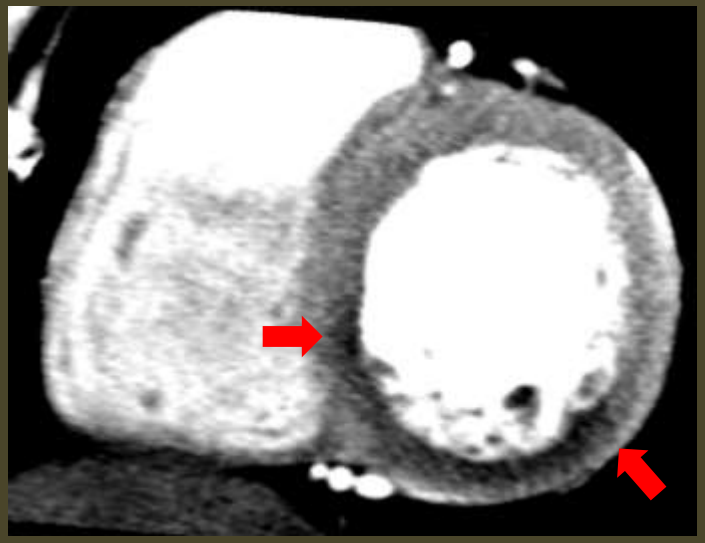
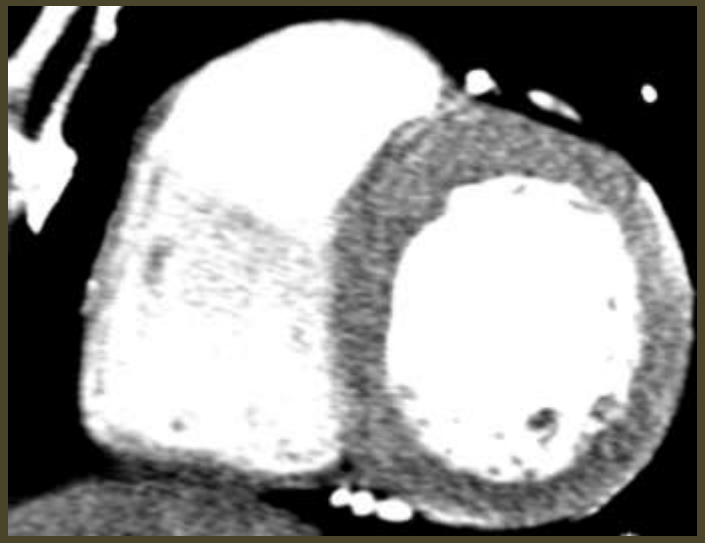
69/M, Effort chest pain

Heavily calcified plaque



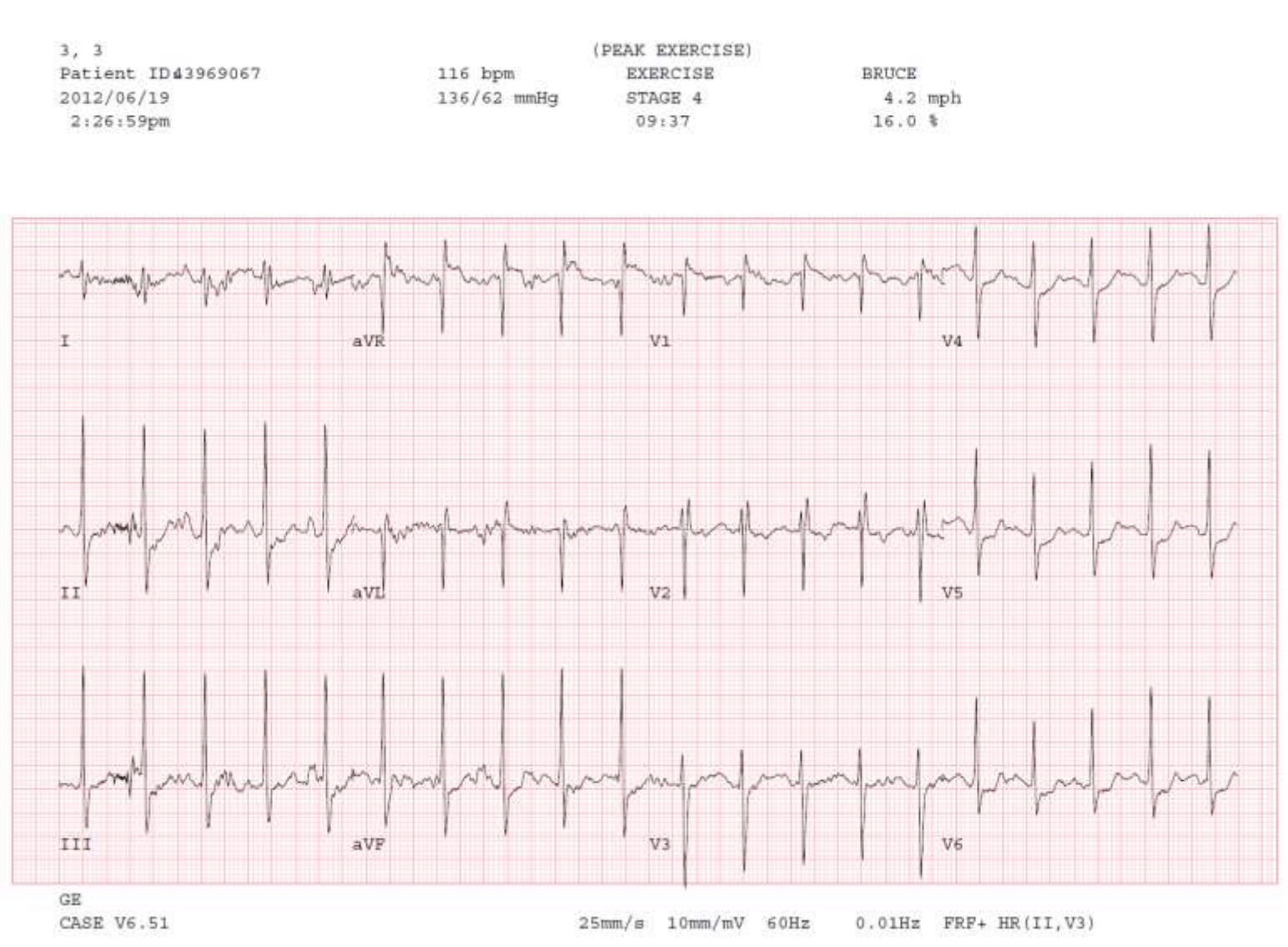






Reversible perfusion defect in RCA territory

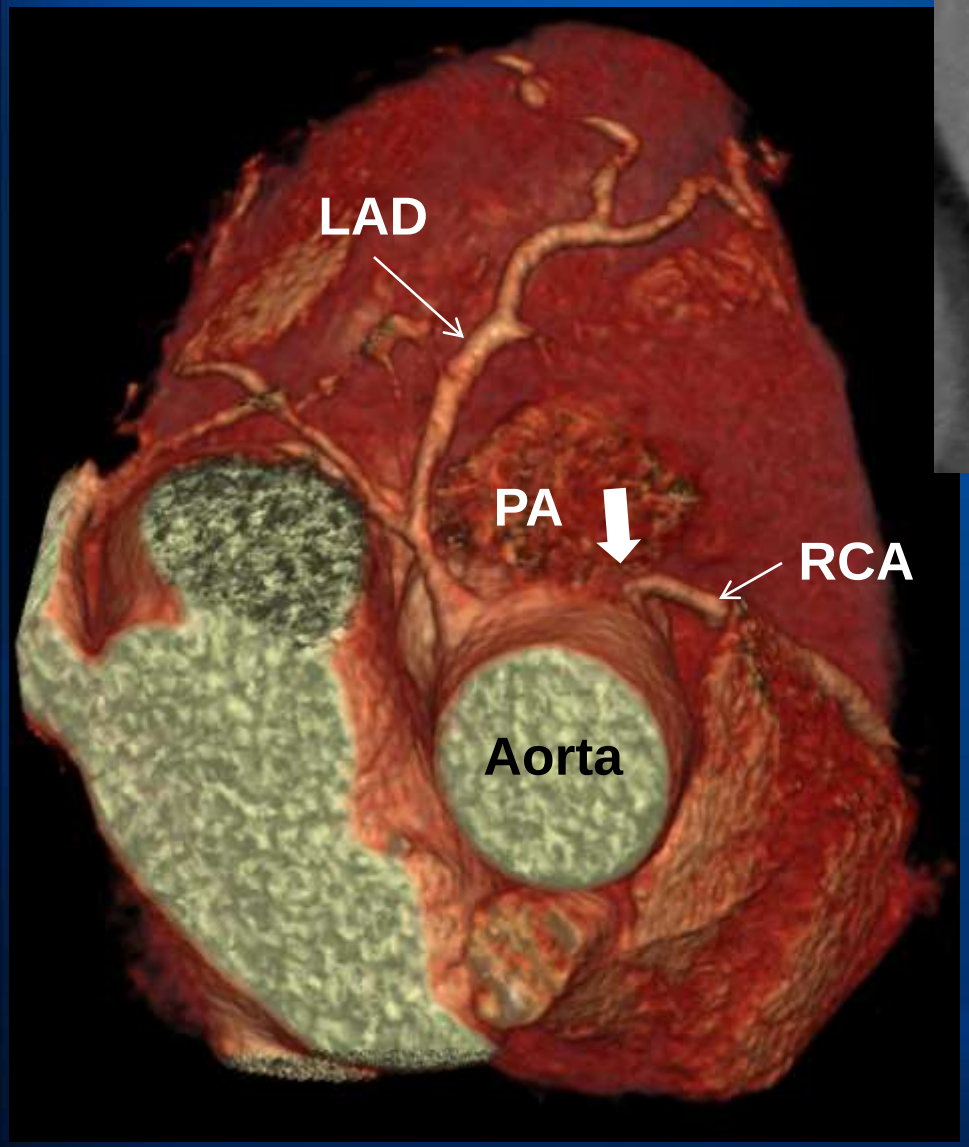
42/M, Effort chest pain
Positive TMT, stage 4 (II, III, aVF, V4-6)



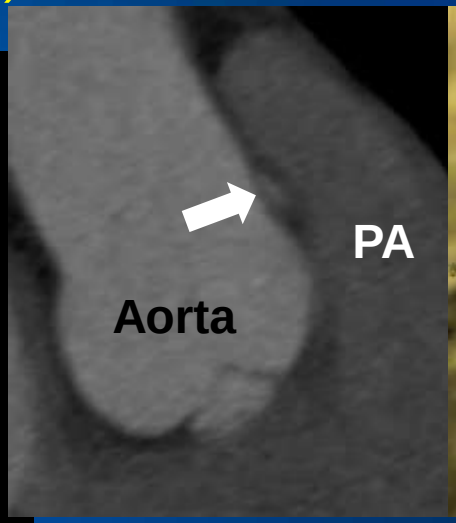
Others

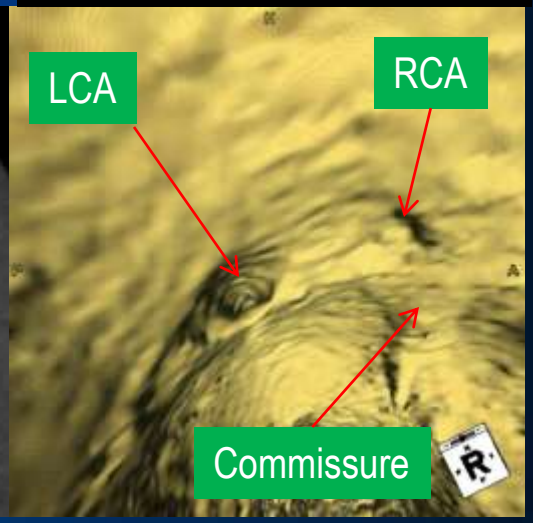
42/M, Effort chest pain

Positive TMT, stage 4 (II, III, aVF, V4-6)

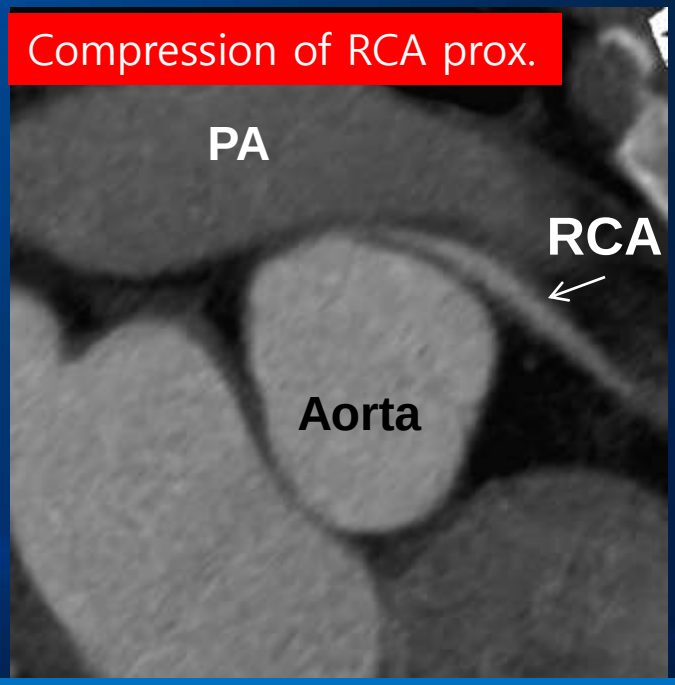


CT virtual angioscopy





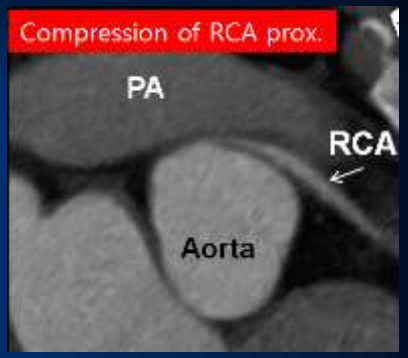
Compression of RCA prox.

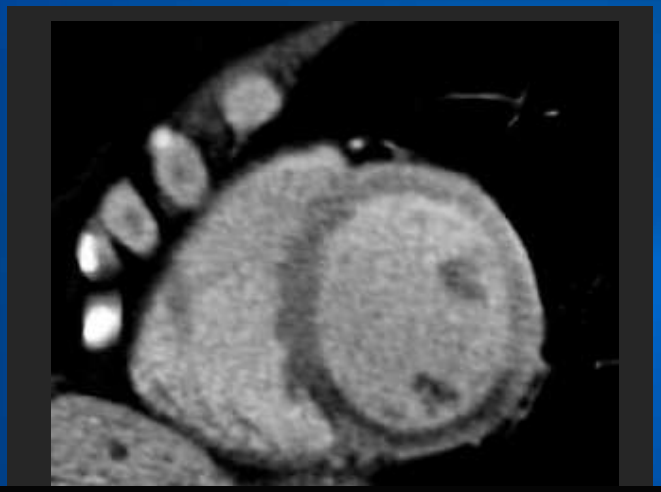


Aberrant origin of RCA from left coronary sinus with interarterial course

42/M, Effort chest pain

Positive TMT, stage 4 (II, III, aVF, V4-6)





Ab

Characteristics of tests commonly used to diagnose the presence of CAD

	Diagnosis of CAD	
	Sensitivity (%)	Specificity (%)
Exercise ECG[a]	45-50	85-90
Exercise stress echocardiography	80-85	80-88
Exercise stress SPECT	73-92	63-87
Dobutamine stress echocardiography	79-83	82-86
Dobutamine stress MRI[b]	79-88	81-91
Vasodilator stress echocardiography	72-79	92-95
Vasodilator stress SPECT	90-91	75-84
Vasodilator stress MRI[b]	67-94	61-85
Coronary CTA[c]	95-99	64-83
Vasodilator stress PET	81-97	74-91

CAD = coronary artery disease; CTA = computed tomography angiography; ECG = electrocardiogram; MRI = magnetic resonance imaging; PET = positron emission tomography; SPECT = single photon emission computed tomography.
[a]Results without/with minimal referral bias; [b]Results obtained in populations with medium-to-high prevalence of disease without compensation for referral bias; [c]Results obtained in populations with low-to-medium prevalence of disease.
This slide corresponds to Table 12 in the full text.

Eur Heart J 2013;34:2949–3003. doi:10.1093/eurheartj/eht296

Diagnostic Accuracy

> 50% stenosis, Per-segment analysis

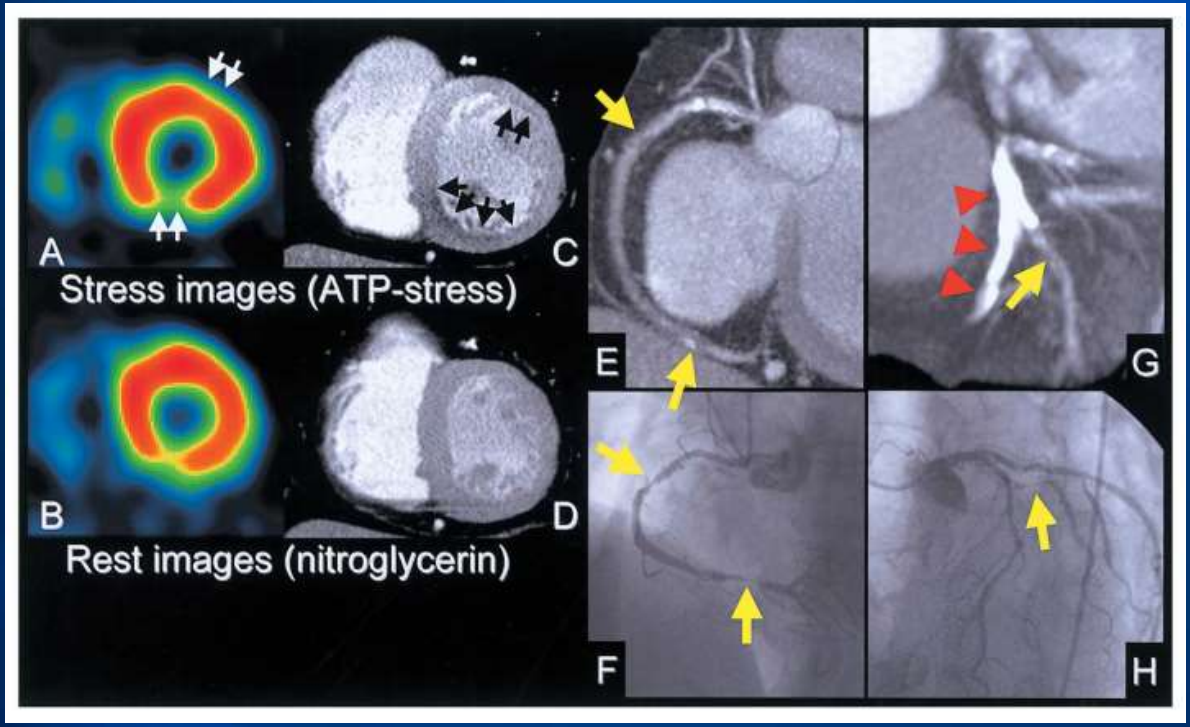
Small diameter of artery, poor image quality, and high calcium are cause of inaccuracy !

>2	10	419	50	89%	90%	49%	99%
1.5-2	3	40	3	77%	91%	20%	99%
<1.5	3	12	6	**45%**	96%	29%	98%
Image quality							
Good	9	206	34	89%	94%	58%	99%
Moderate	11	117	15	84%	85%	40%	98%
Poor	10	148	10	86%	**78%**	30%	98%
Calcium							
None	5	108	37	78%	97%	54%	99%
Moderate	17	197	17	92%	81%	49%	98%
High	25	166	5	**95%**	**47%**	38%	97%

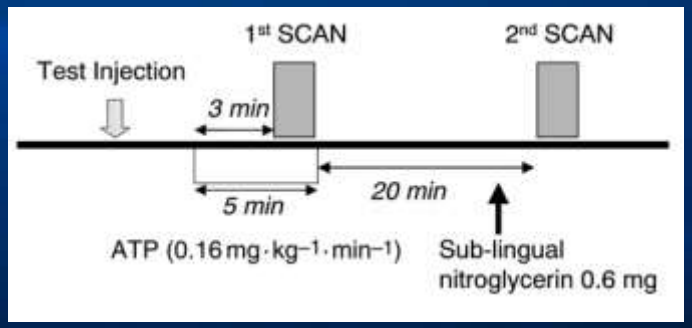
- Sensitivity decreased with vessel diameter and increased with high calcium.
- Specificity decreased with poor image quality and severe calcification.

Meijboom W.B. JACC 2008;52:2135-44

First Article of CTP, 2005



Summary
16-ch CT (GE, LightSpeed 16)
12 patients
Reference: Thallium SPECT
Population: suspected CAD
Sensitivity (per-vessel): 90%
Specificity (per-vessel): 79%
First article



Kurata A. Mochizuki T. et al . 2005 Cir J 69:550-557

Published Data: Early Results

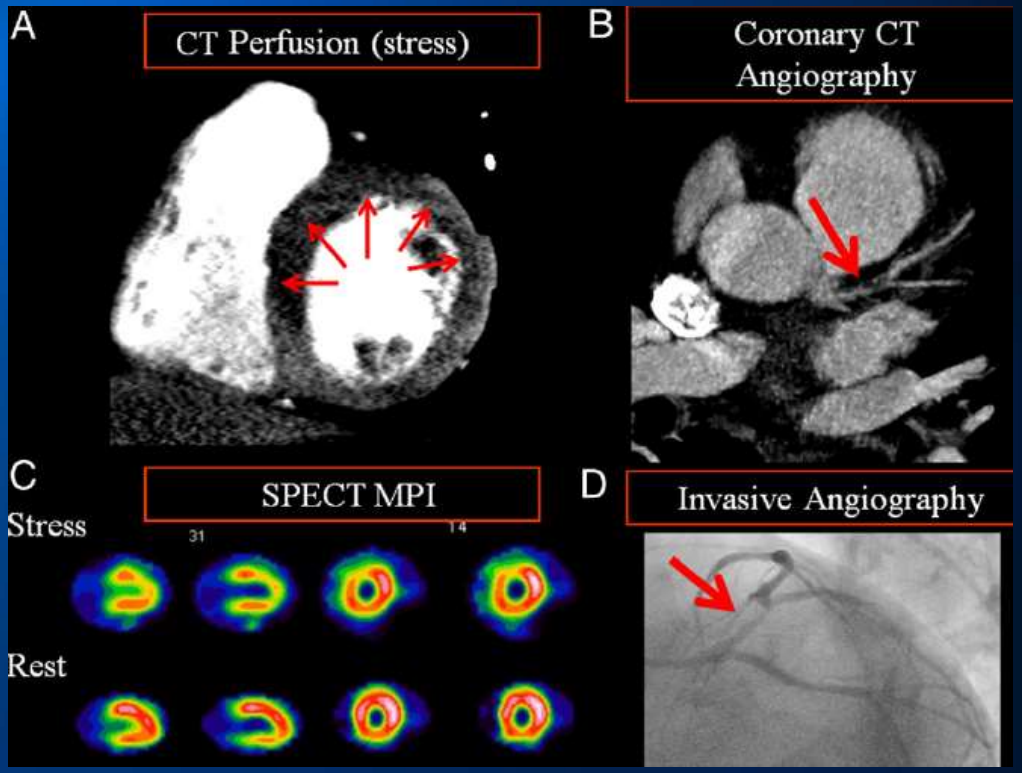
Group	PI	Year	Pts	Sens/Spec (%)	Ref.	CT
MGH	Cury,RC Hoffmann, U	2009 2010	33 35	94/74 91/91	QCA/SPECT QCA	64 DSCT (Siemens)
Johns Hopkins	George, RT	2009 2012	27 50	81/85 72/91	QCA/SPECT QCA/SPECT	64 ch, 320 ch (Toshiba)
Monash H (Australia)	Sujith, K	2012 2012	42 40	**91/72** **95/87**	**FFR** **FFR**	320 ch (Toshiba)
Grosshadern (Germany)	Bamberg, F	2012	36	93/87	**FFR**	128 DSCT, Dynamic (Siemens)
MUSC (South Carolina)	Schoepf, J	2010 2012	10 20	86/98 86/98	MRI MRI/SPECT	128 DSCT, Dynamic (Siemens)
Mount Alvernia H. (Singapore)	Ho, KT	2011	35	83/78	SPECT	128 DSCT, Dynamic (Siemens)
Cedars-Sinai, LA	Berman, DS	2010	30	92/86	SPECT	64 DSCT (Siemens)
Korea (Kunkook U.)	Ko, SM	2011	41	91/72	MRI	64 DSCT-DE mode (Siemens)
Innsbruck (Austria)	Feuchtner, GM	2012	39	96/95	MRI/QCA	128 DSCT-FLASH mode (Siemens)

Early Result of CTP: Visual Analysis

Per-vessel, CAD (QCA, ≥50%)

	CTP	SPECT
Sensitivity	79	67
Specificity	80	83
PPV	73	74
NPV	84	78
C-statistic	0.793	0.750

No difference !

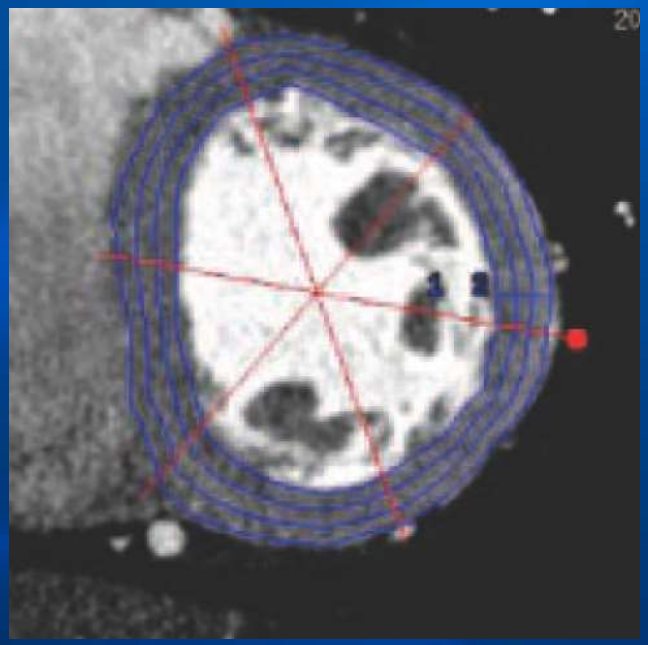


CT perfusion vs. SPECT
Comparable diagnostic accuracy !

Blankstein et al . 2009 JACC 54:1072-84

TPR: semi-quantitative method

First quantification on static CTP !



Transmural perfusion ratio (TPR)

$$\text{TPR} = \frac{\text{Subendocardial Density}}{\text{Subepicardial Density}}$$

Summary

64-ch CT or 256-ch CT (Toshiba)
Stress first protocol

27 patients

Reference: QCA plus SPECT

Population: Abnormal SPECT

Sensitivity (per-vessel): 79%

Specificity (per-vessel): 91%

1. Acceptable diagnostic accuracy of CTA/CTP combination.
2. Quantification of static CTP may be useful.

George RT et al . 2009 Circulation CV Img 2:174-182

TPR: semi-quantitative method

Per-vessel territories

	CTP vs. SPECT	CTA (>50%) vs. SPECT	CTP vs. CTA + SPECT
Sensitivity	50	25	100
Specificity	90	85	85
PPV	55	31	28
NPV	87	81	100
AUC	0.70	0.55	0.93

CTP was a better predictor !

Summary

320-ch CT (Toshiba)
Rest first protocol

50 patients

Reference: SPECT
or CTA (50% >) + SPECT

Population: Suspected CAD who underwent SPECT

Sensitivity (per-vessel): 50%

Specificity (per-vessel): 89%

CTP was a better predictor

George RT et al . 2012 Circulation CV Img 5:333-340

CTP-Visual analysis vs. FFR

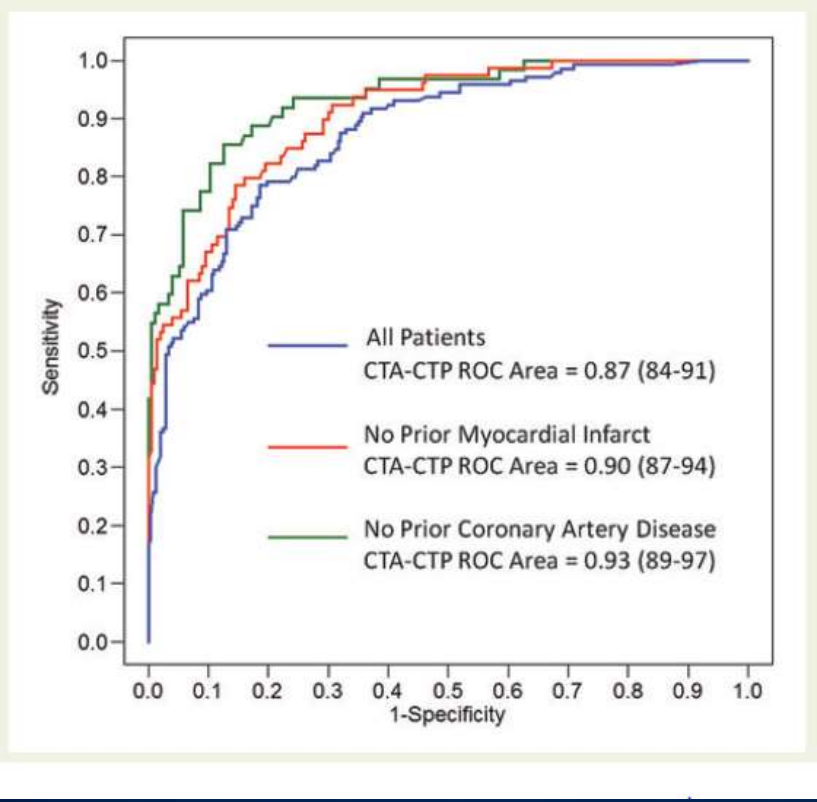
	CTA ≥ 50%	CTP (+)	CTA ≥ 50% & CTP(+)	CTA ≥ 50% OR CTP(+)	QCA ≥ 50%
Sensitivity	93	76	68	100	71
Specificity	60	84	**98**	47	62
PPV	68	82	97	63	63
NPV	90	79	77	**100**	70
Accuracy	76	80	84	73	66

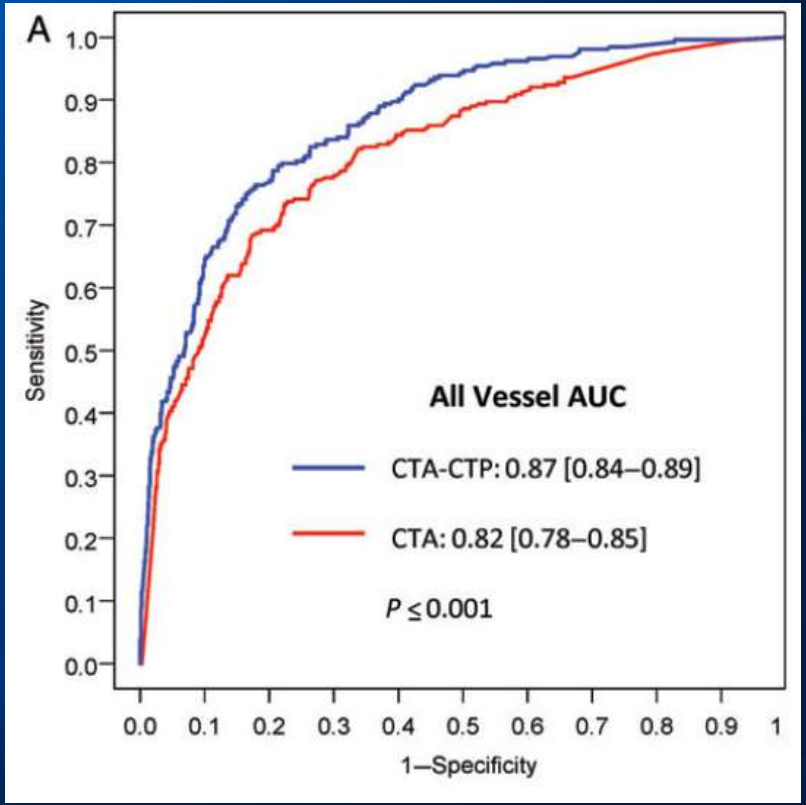
CTA ≥ 50% & CTP(+) was 98% specific for ischemia.
CTA < 50% and normal CTP was 100% specific for ischemia.

Ko BS et al . 2012 Eur Heart J 33:67-77

CORE320 Study: CT perfusion

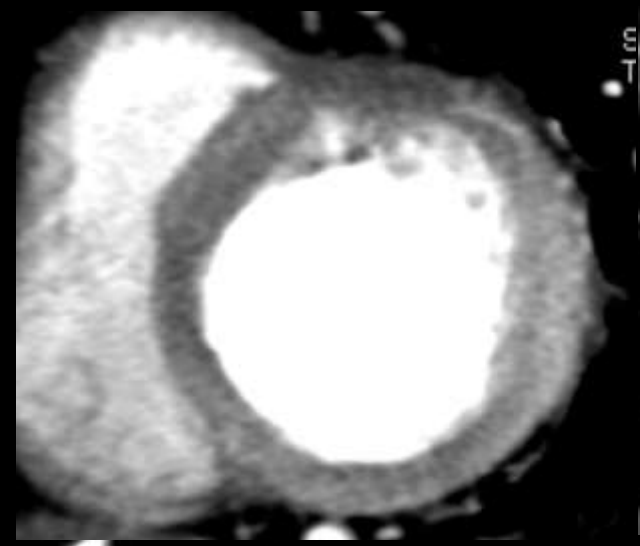
- Multicenter studies (n=391)
- Validation of CT perfusion using QCA / SPECT as a reference standard

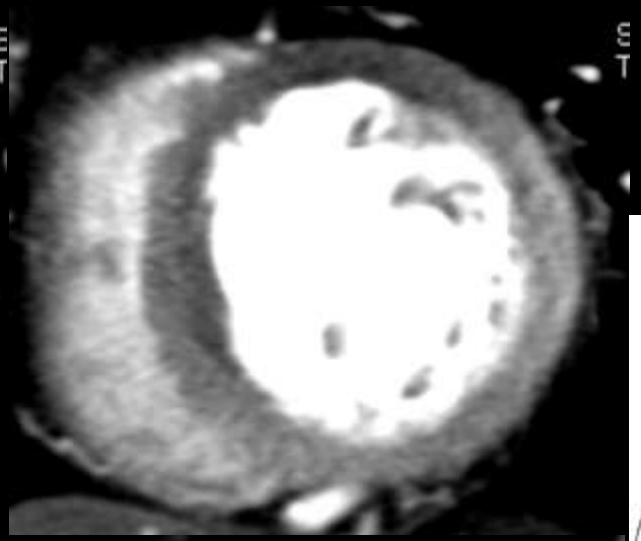


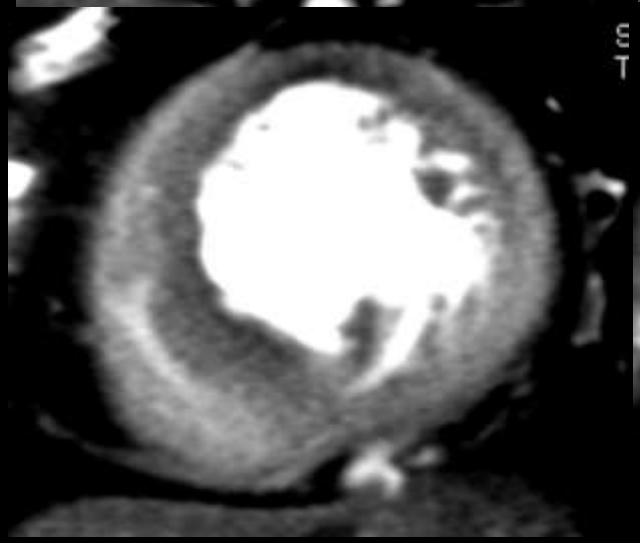


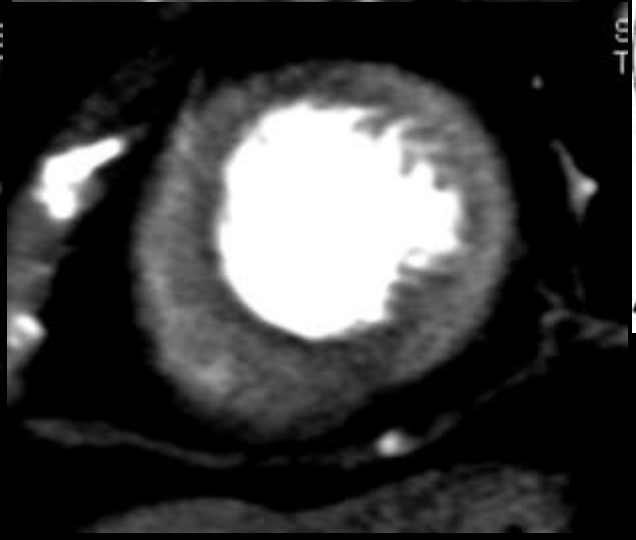
Rochitte CE, et al. Eur Heart J 2013

First CT Perfusion Case at AMC





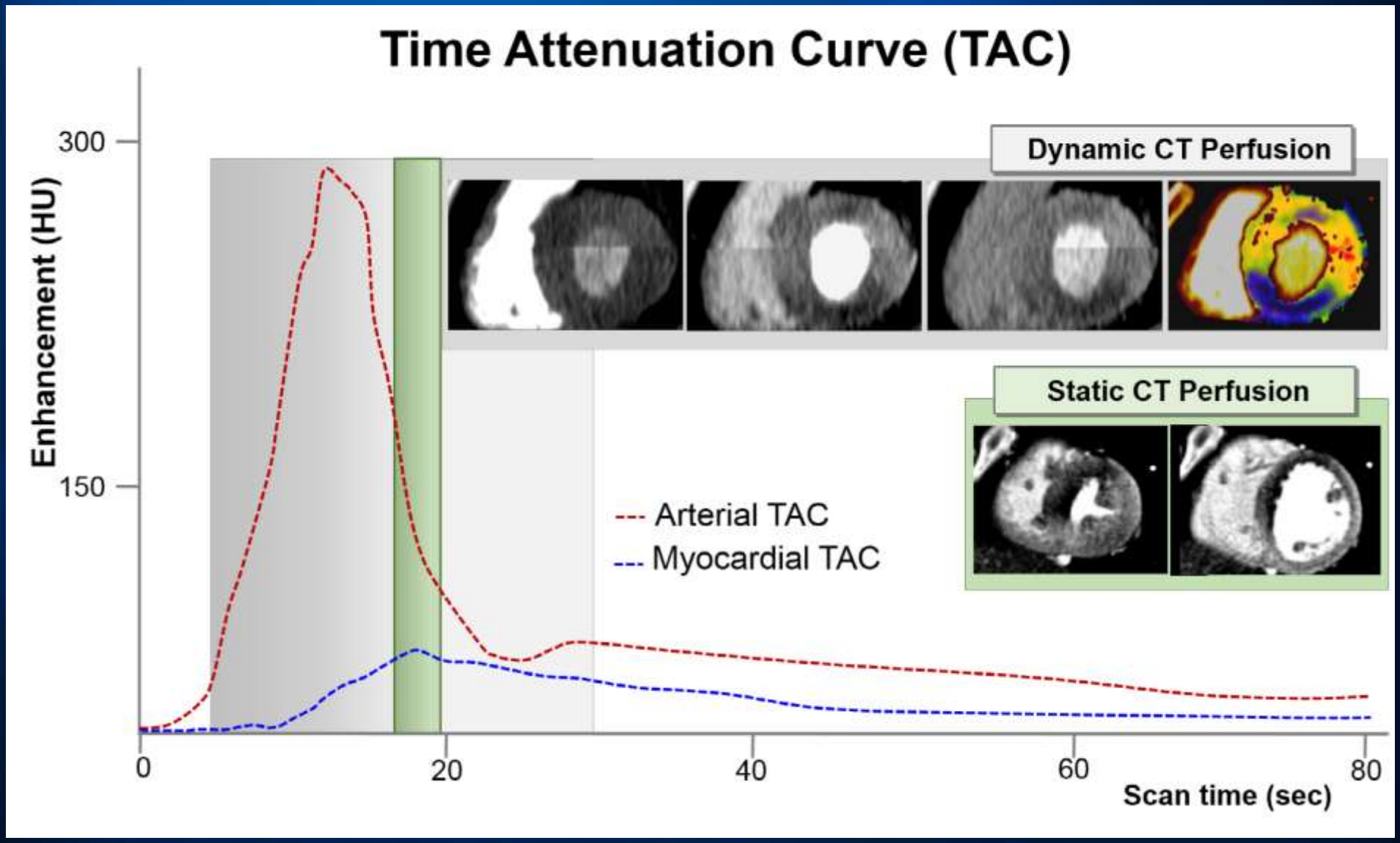




2011-12-22

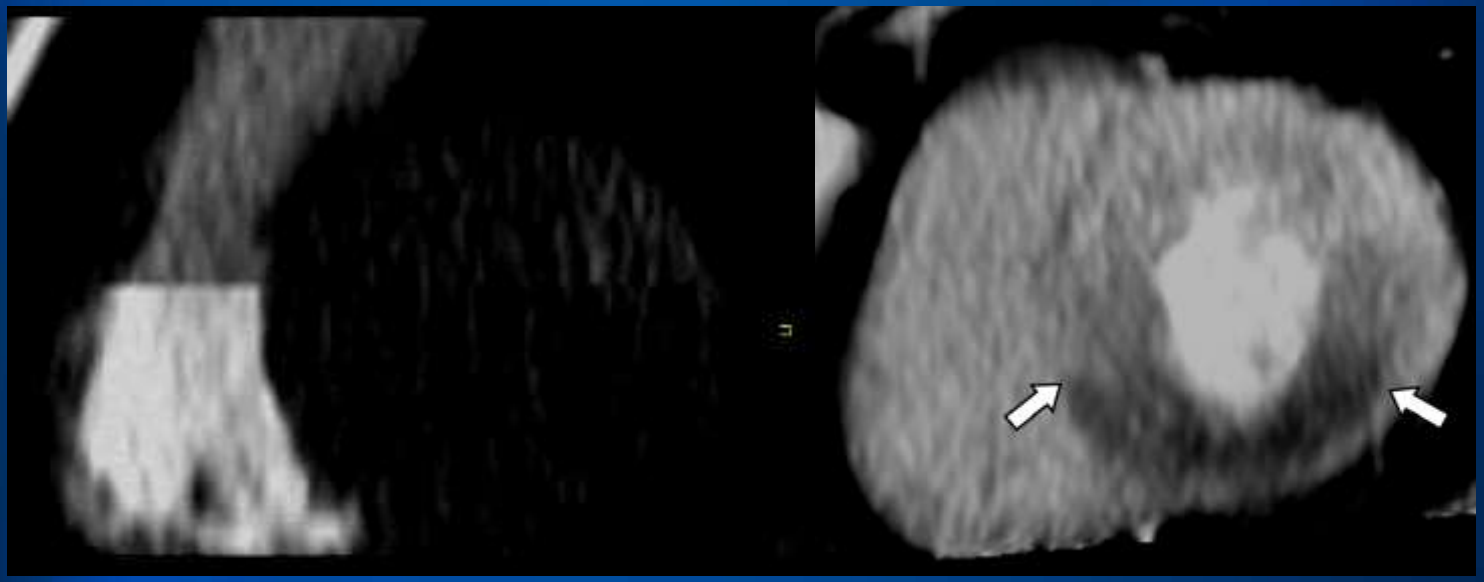
73/F

Static vs. Dynamic Scan

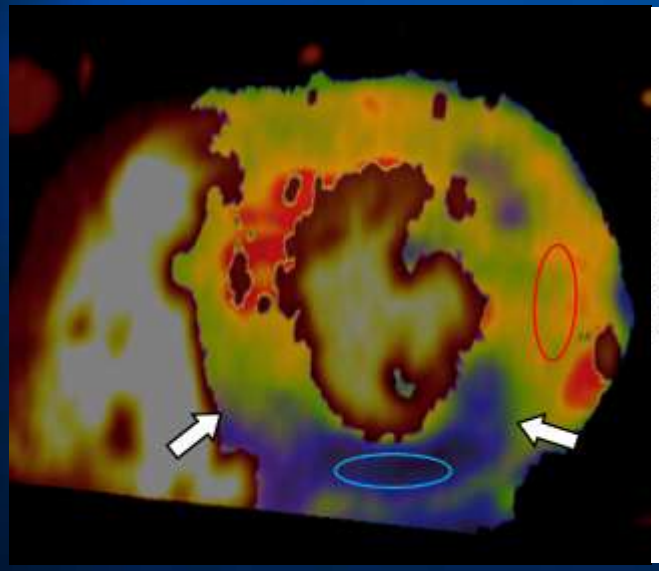


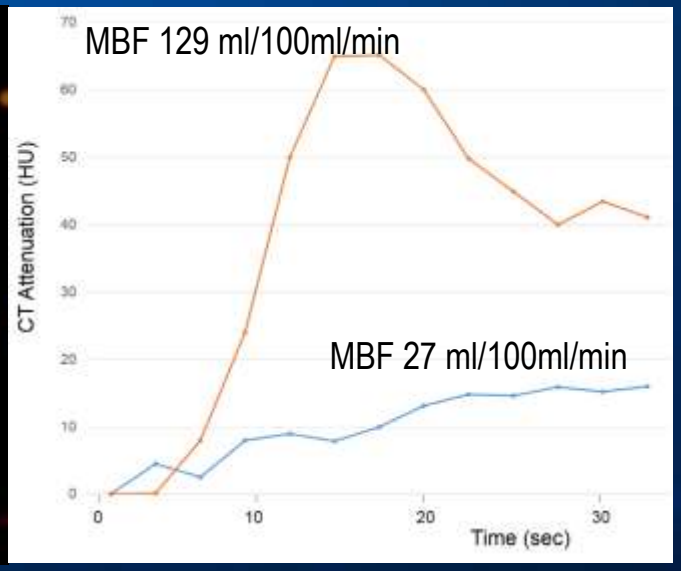
Koo HJ, Yang DH et al. In submission

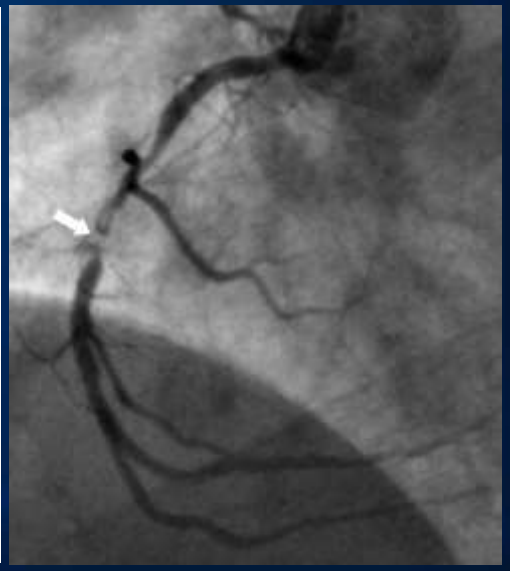
Dynamic Scan



40 / M
Effort chest pain
for 1 month







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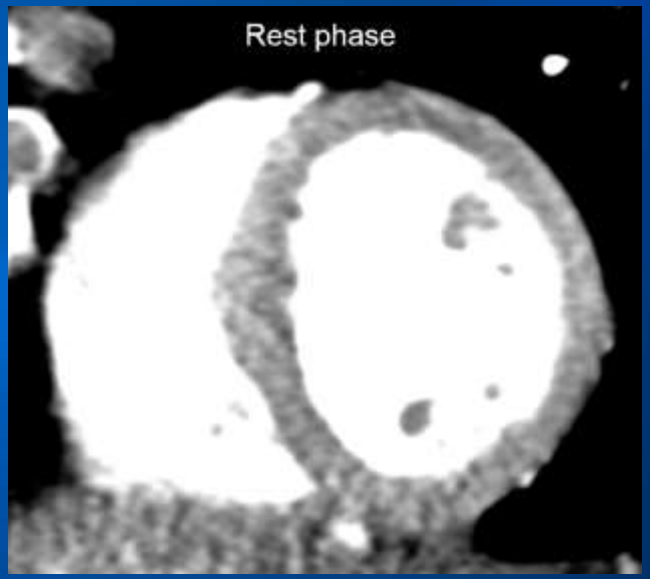
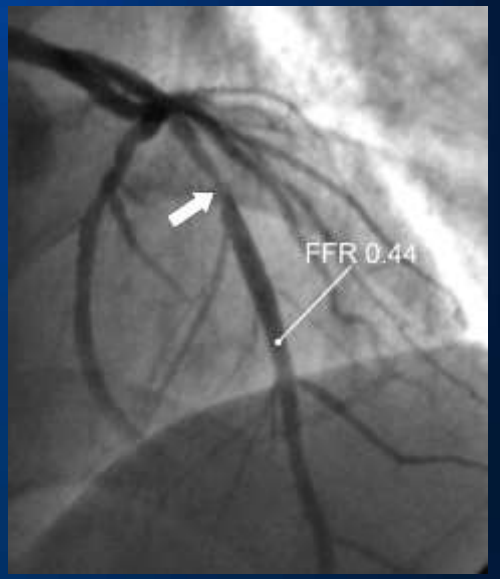
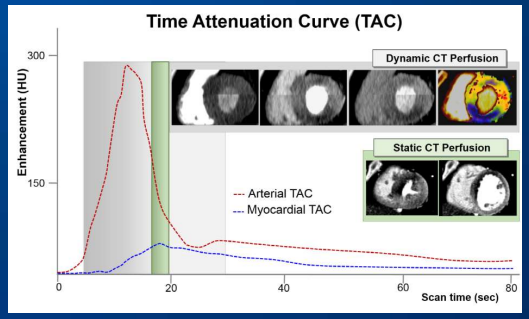
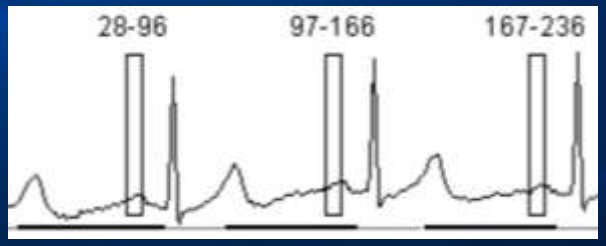
Static Scan







Contrast enhancement:
Static



Motion
Dynamic
(Retrospective ECG-gating)

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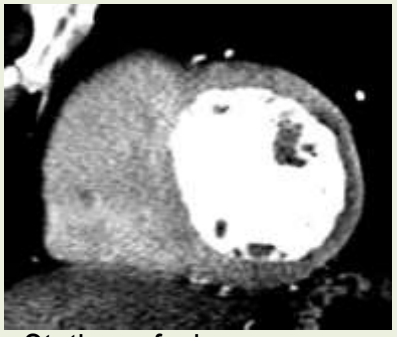
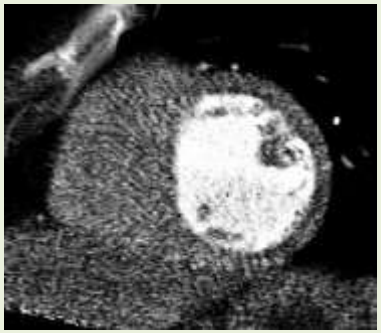
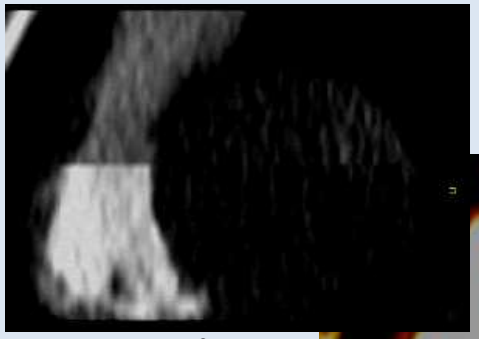
Static vs. Dynamic Scan



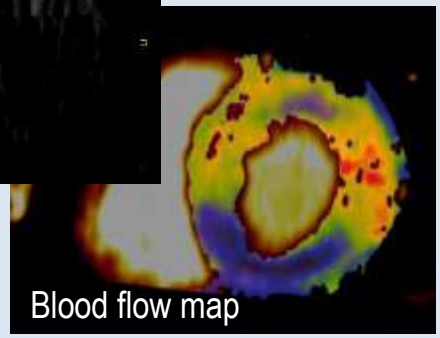
Static perfusion



Cine CT



Dynamic perfusion



Blood flow map

Static scan

Pros

- ✓ Low radiation dose
- ✓ Easy to perform
  - Same with CCTA
- ✓ Wall motion abnormality

Cons

- ✓ No quantification of blood flow
- ✓ Suboptimal enhancement time
  → low lesion detectability

Dynamic scan

Pros

- ✓ Blood flow quantification
- ✓ Better detectability (not validated)

Cons

- ✓ High radiation dose
- ✓ Hard to perform
  - Need high-end CT machine
  - Long breath hold time (30 s)
- ✓ Systolic phase only

CTP/CTA protocol at AMC

- 128-ch dual source CT or 64-ch dual source CT
  - Siemens, Definition (FLASH)
- Single energy, static protocol
- Stress-first
- No beta-blocker
- Nitroglycerin: 2 min. before rest CTP (CTA)
- 100 kV for reduce radiation dose
- Tube current modulation and ECG-pulsing
- Bolus triggering method (NOT test bolus)
- NO Delayed enhancement scan

CT Perfusion Protocol at AMC

- AMC protocol (25 minutes)
  - Second degeneration dual-source 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

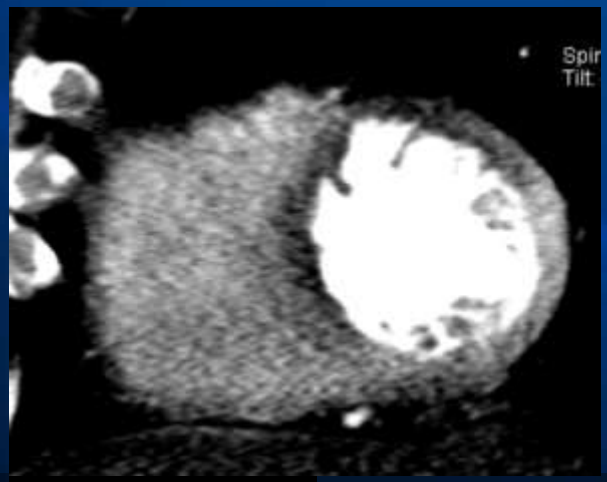
Option
1. **Retrospective mode**
2. Prospective mode
3. High-pitch mode

Published Data: CTP vs. FFR

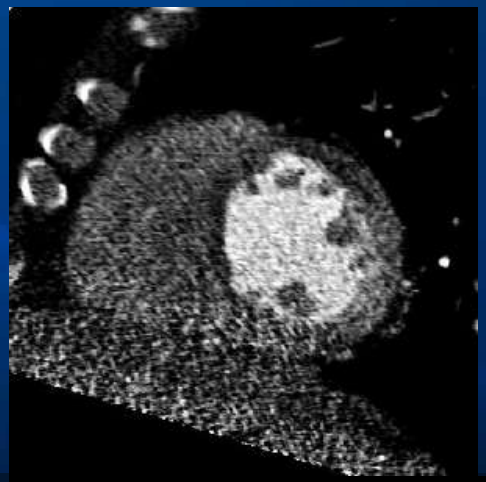
Year	Author	Pts NO. (Vessels)	Technique	Effective dose, mSv	Reference standard	Parameters	Sensitivity,%	Specificity,%
2011 RAD	Bamberg et al.	33 (96)	Dynamic / Rest first	CTA 3.1 CTP 10.0	FFR ≤ 0.75	CTA	100	51
						CTA plus CTP	93	87
2012 JACC img	Ko et al.	40 (103)	Static / Rest first	CTA 4.7 CTP 4.5	FFR ≤ 0.80	CTA	95	78
						CTP (TPR)	74	66
						CTA plus CTP (visual)	87	95
2012 EHJ	Ko et al.	42 (86)	Static / Stress first	CTA 5.3 CTP 4.8	FFR ≤ 0.80	CTA	93	60
						CTP (visual)	76	84
2013 JACC	Bettencourt et al.	101 (303)	Static / Stress first	CTA-CTP 5.0	FFR ≤ 0.80	CTA	95	67
						CTA plus CTP (visual)	71	90
2013 Heart	Greif et al.	65 (195)	Dynamic/ Rest first	CTA 2.9 CTP 9.7	FFR ≤ 0.80	CTA	97	53
						CTA plus CTP (MBF)	95	74
2014 EHJ	Rochitte et al. (CORE320)	381 (1143)	Static/ Rest first	CTA-CTP 9.3	SPECT plus CAG ≥ 50%	CTA	92	51
						CTP (TPR + Visual)	80	74
2014 JACC	Wong et al.	75 (97)	Static/ Rest first	CTA 4.6 CTP 4.8	FFR ≤ 0.80	CTA	89	65
						CTA plus CTP (visual)	76	89

CT Perfusion Analysis: Qualitative

- Very smooth kernel (B10f) reconstruction
- Multiphase image (0% ~ 90% of R-R interval, 10% increment)
- 10-mm thick MPR image with narrow window setting
- **Diagnostic clue** of perfusion defect
  - Low density lesion conforming coronary territory
  - Persistent lesion on cine image
    - DDx) Transient motion or beam-hardening artifact
  - Complementary regional wall motion abnormality on cine image



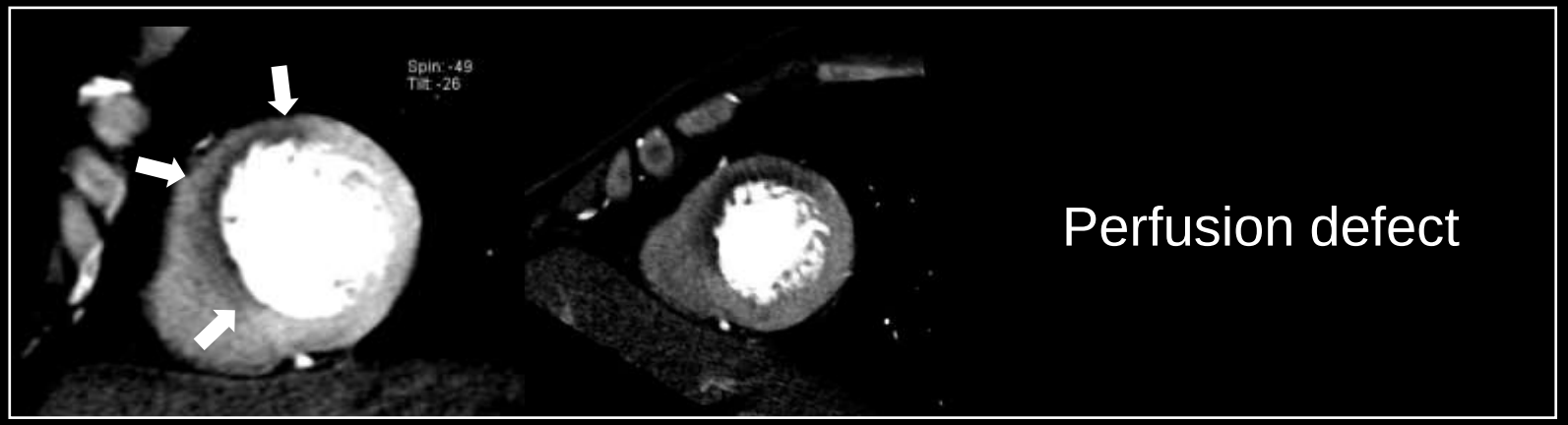
Stress phase

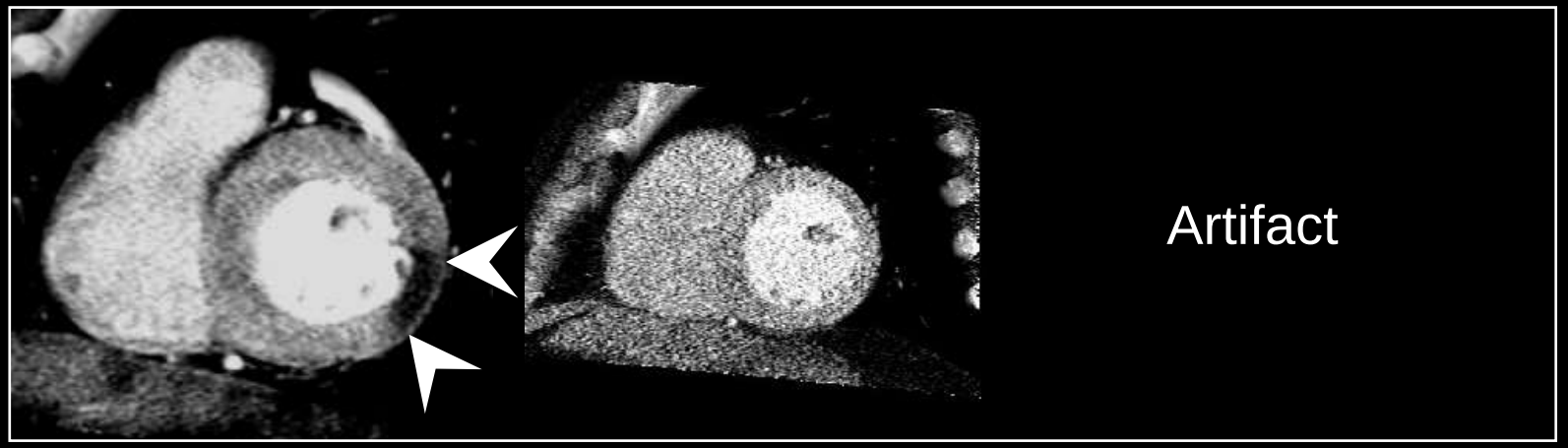


Stress phase – cine image

Visual Assessment of Perfusion Defect in CT Perfusion

AMC protocol – Static CT perfusion





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PERFUSE Registry

***P*rospective *E*valuation of**
St*R*ess Coronary Per*FUS*ion CT R*E*gistry

PERFUSE registry

- PI: Young-Hak Kim
- Co-PI: Dong Hyun Yang

DSMB

Executive Committee (EC)

- Chair: PI
- Co-chair: co-PI
- Cardiologist: total 3
- Radiologist: total 3

Steering Committee (SC)

- Each site: 1 cardiologist
  1 radiologist

Core Laboratory

- Angiography
- CT

Statistical Department

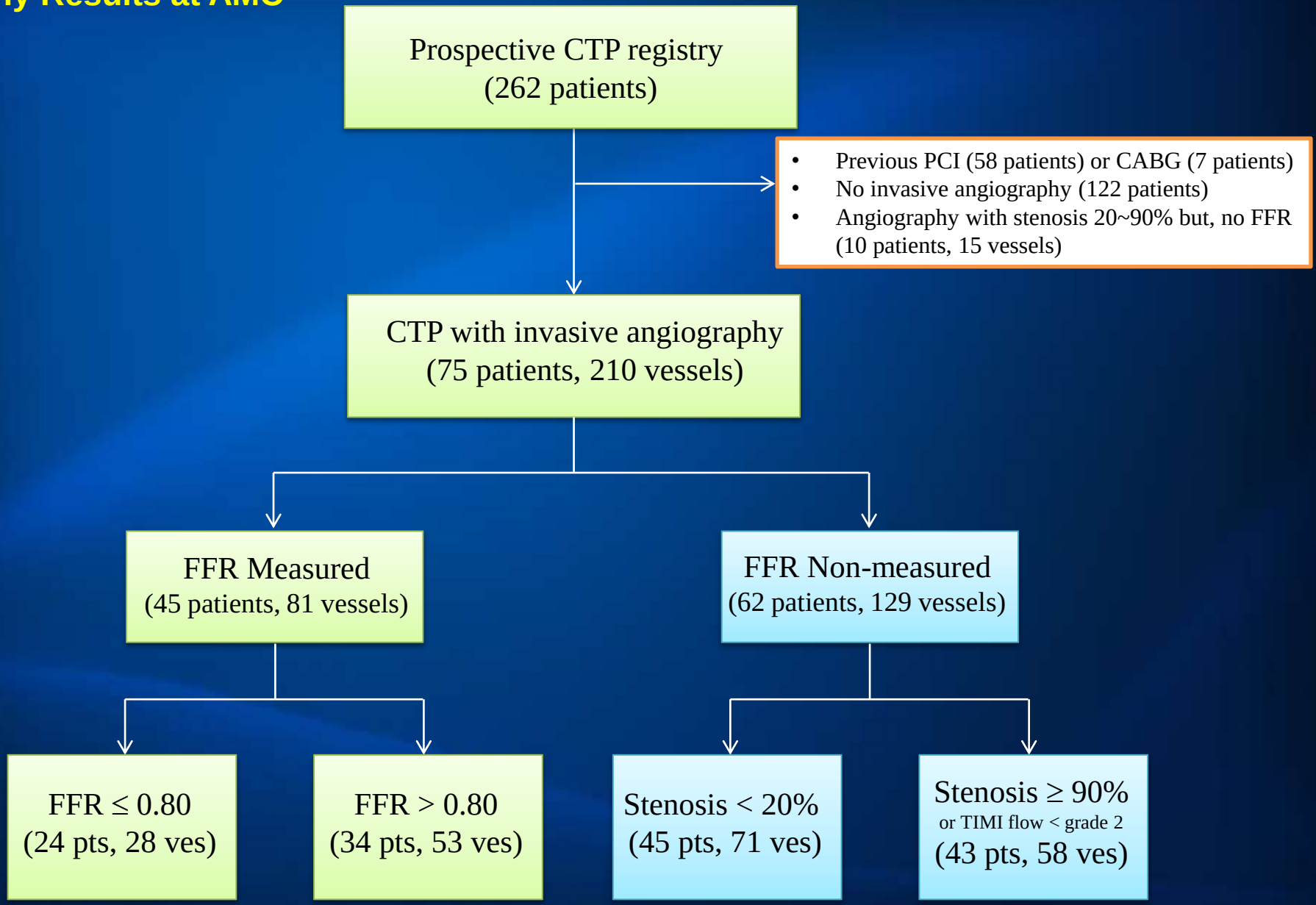
- Statistician

Data Coordinating Department (DCD)

- Research nurses
- CRF producer
- DB manager

> 1300 cases (2015.02)

Early Results at AMC



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Early Results: CTP visual assessment

	CTP	CTA	CTP / CTA Integration	QCA, DS ≥ 50%
True positive	69	85	77	74
False positive	6	33	14	11
True negative	118	91	110	113
False negative	17	1	9	12
Sensitivity,%	**80**	**99**	**90**	**86**
Specificity,%	**95**	**73**	**89**	**91**
PPV,%	**92**	**72**	**85**	**87**
NPV,%	**87**	**99**	**92**	**90**
Kappa statistic	0.77	0.68	0.78	0.77
Accuracy	89	84	89	88

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Subgroup Analysis

	High Agastone calcium score > 400 (N=63)			Multivessel disease (N=56)		
	Sensitivity	Specificity	IDI index	Sensitivity	Specificity	IDI index
CTP visual assessment	85	100	**0.38***	76	91	-0.10
CTA, DS ≥ 50%	100	50	-	100	45	-
Integration of CTP and CTA	94	87	**0.31***	89	82	0.01
QCA, DS ≥ 50%	87	83	-	84	73	-

IDI, integrated discrimination improvement

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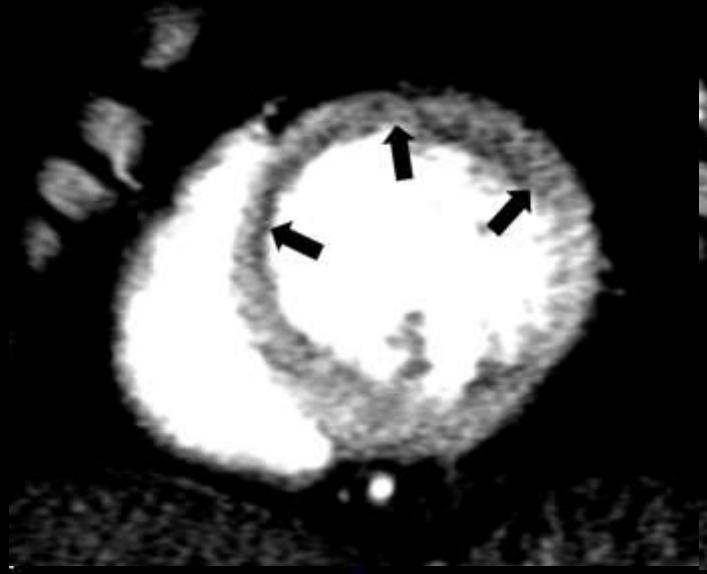
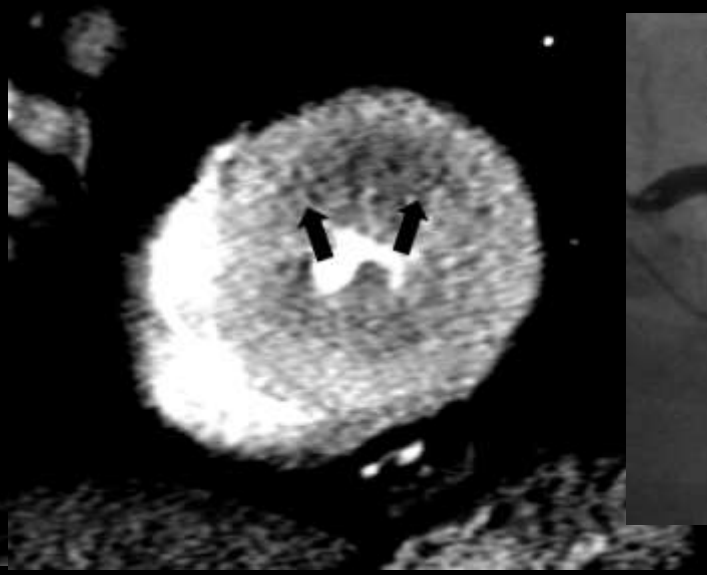
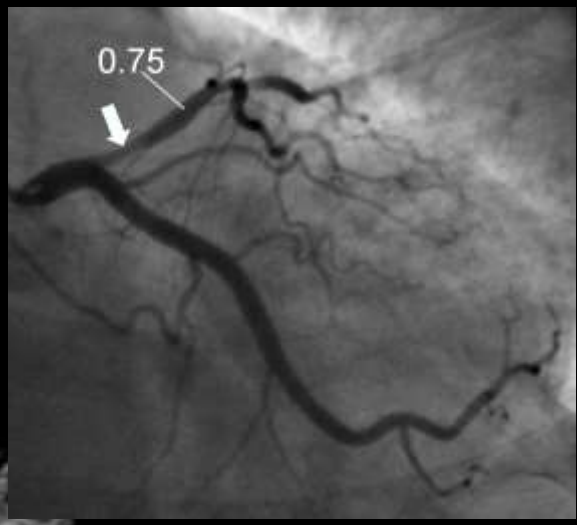
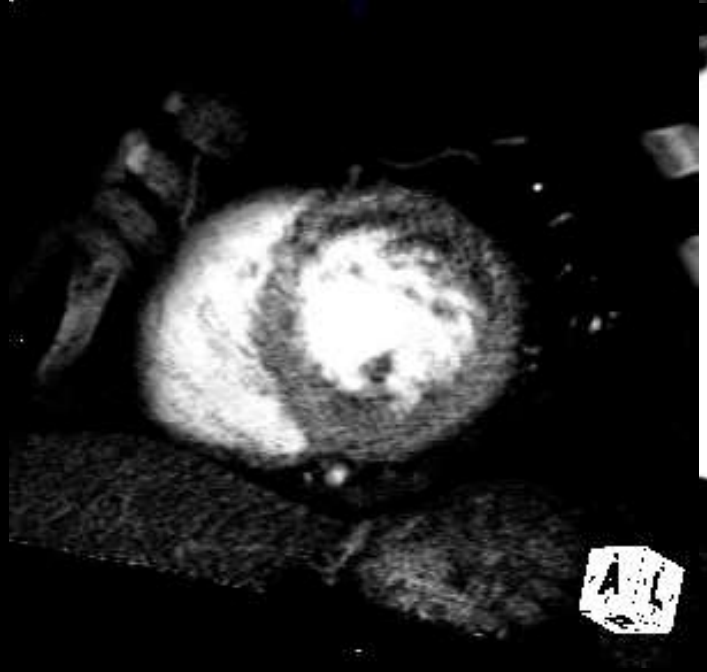
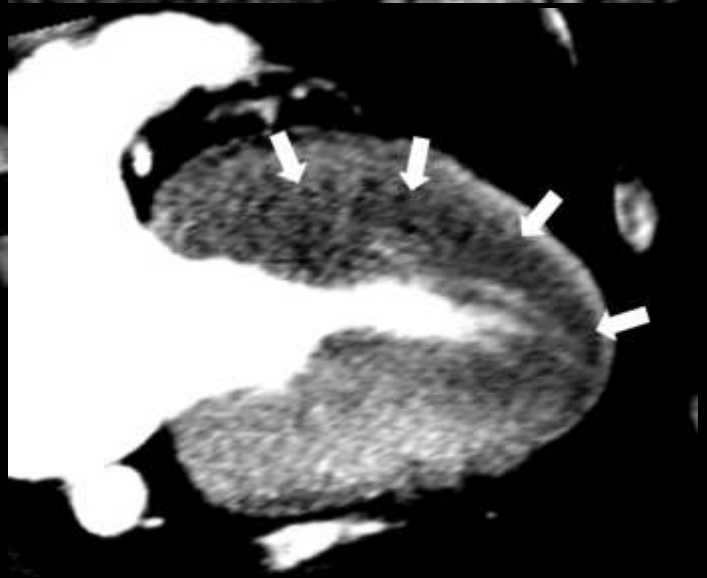
Borderline Coronary Stenosis: FFR 0.75





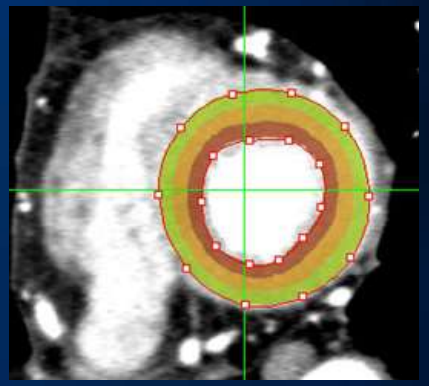






CT Perfusion Analysis: Quantitative

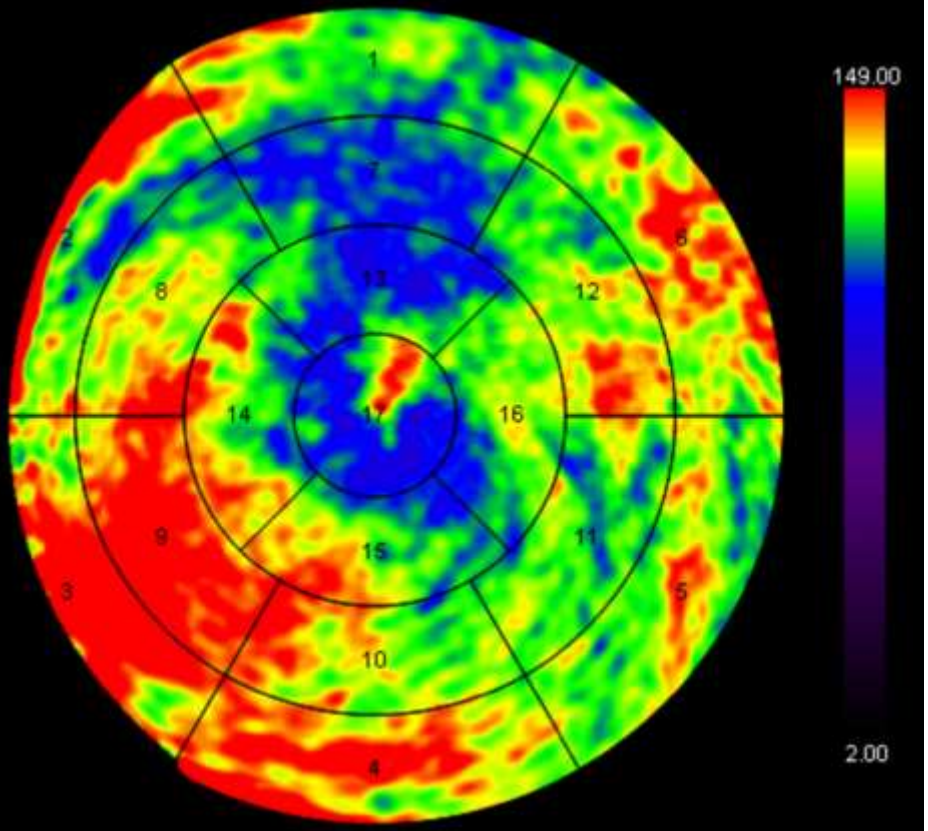
- Diastolic phase with the least motion artifact
- *Customized software*
  - Classification of whole myocardium into 16 segments and into three myocardial layers
- Assignment of myocardial segments to vessel territories (LAD, LCX, RCA)



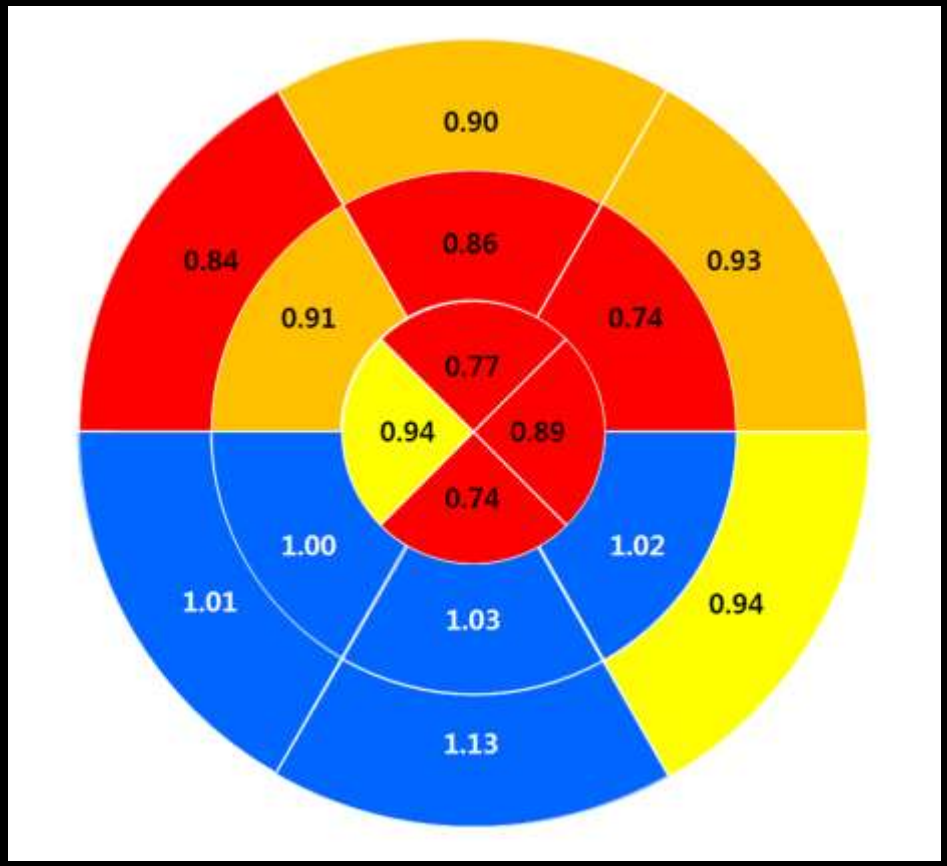
- **Evaluation parameters**
  - CT density on stress / rest CT ($Density_{stress}$ / $Density_{rest}$, HU)
  - Transmural perfusion ratio (TPR)
    - $Density_{endocardial}/Density_{epicardial}$
  - Myocardial perfusion reserve index (MPRI),%
    - $(Density_{stress} – Density_{rest})/Density_{rest}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

Intermediate stenosis

Quantitative Analysis



Density map
Syngo, Siemens



TPR map
Home-made, AMC

Quantitative Analysis

Parameter	AUC	Cut off	Sensitivity	Specificity
All patients (n=75)				
TPR	0.759	**0.98**	75	71
$Density_{stress}$, HU	0.687	102.1	77	56
$Density_{rest}$, HU	0.559	113.9	65	51
MPRI, %	0.691	-4.0	67	62
Quantitative composite of TPR, $Density_{stress}$, or MPRI *	0.746	-	63	75
Combination of visual and quantitative composite **	**0.878**	-	89	73
Multivessel disease group (n=20)				
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	5.0	73	56
Quantitative composite of TPR, $Density_{stress}$, or MPRI *	0.7433	-	68	78
Combination of visual and quantitative composite **	**0.8266**	-	81	89

TPR: transmural perfusion ratio
MPRI: myocardial perfusion reserve index

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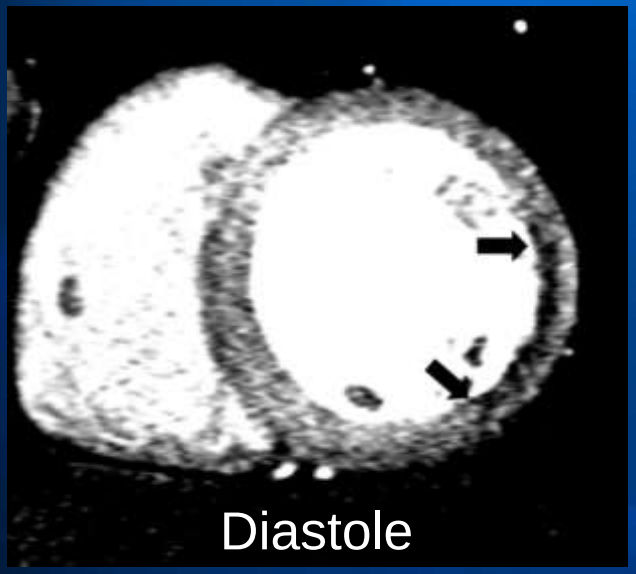
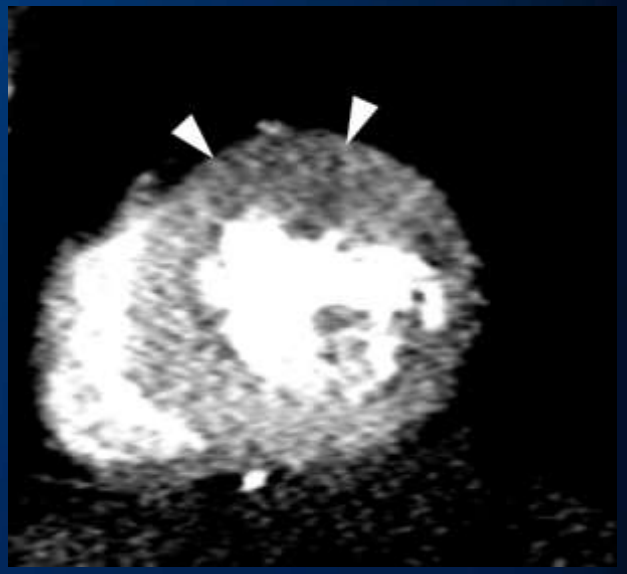
Case: Assistance with Density Quantitation

Step 1

Visual Assessment

Low density lesion conforming coronary territories in both systolic and diastolic phases





LCX (+)

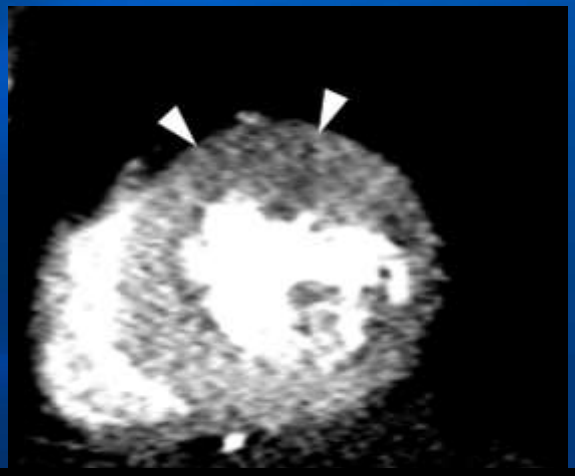
LAD (-)

Case: Assistance with Density Quantitation

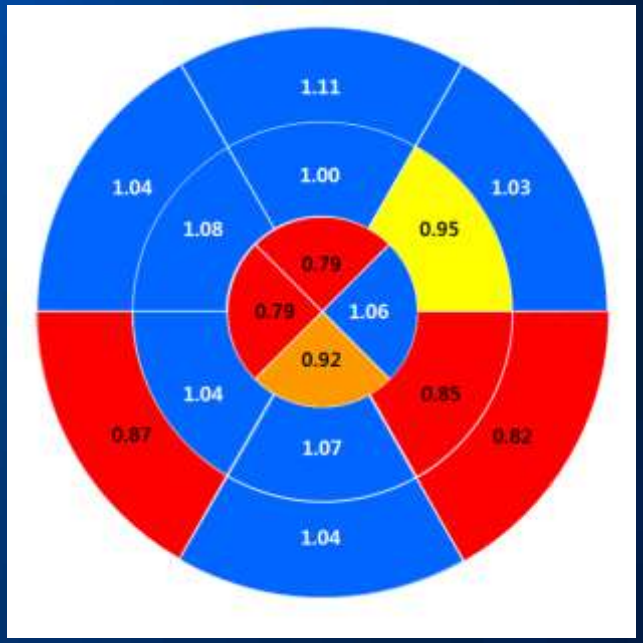
Step 2

Density quantitation

Positive quantitative parameters in *Two or more consecutive* myocardial segments



LAD (-) visual assessment



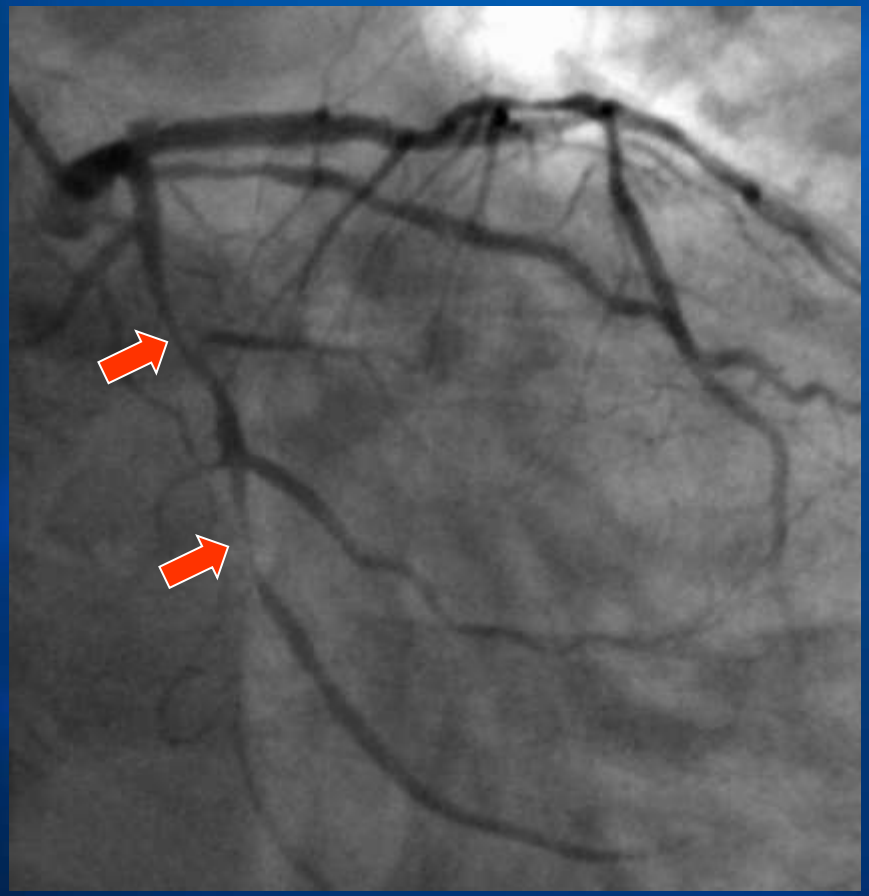
TPR map

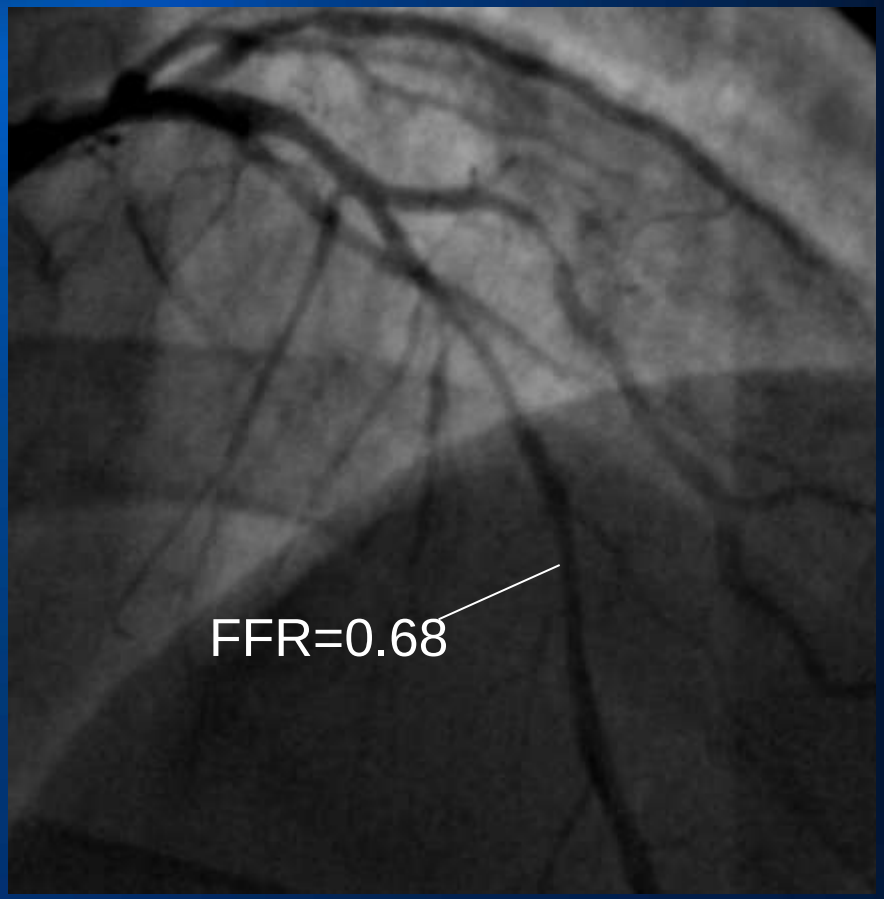
LCX (+)

LAD (+)

Case: Assistance with Density Quantitation

Angiography & FFR





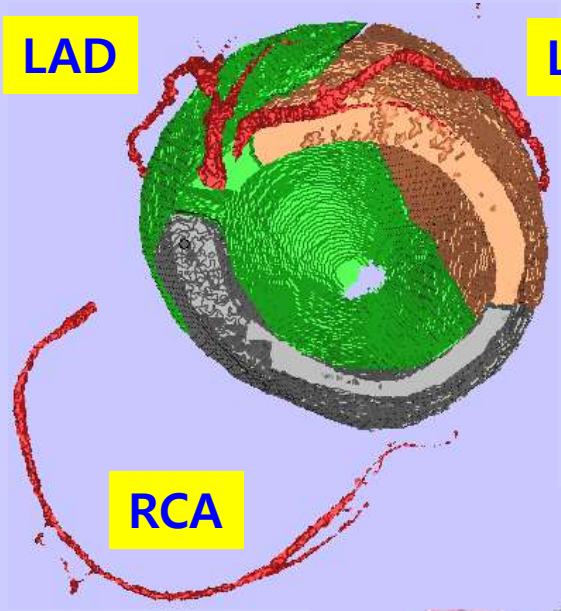
LCX (+)

LAD (+)

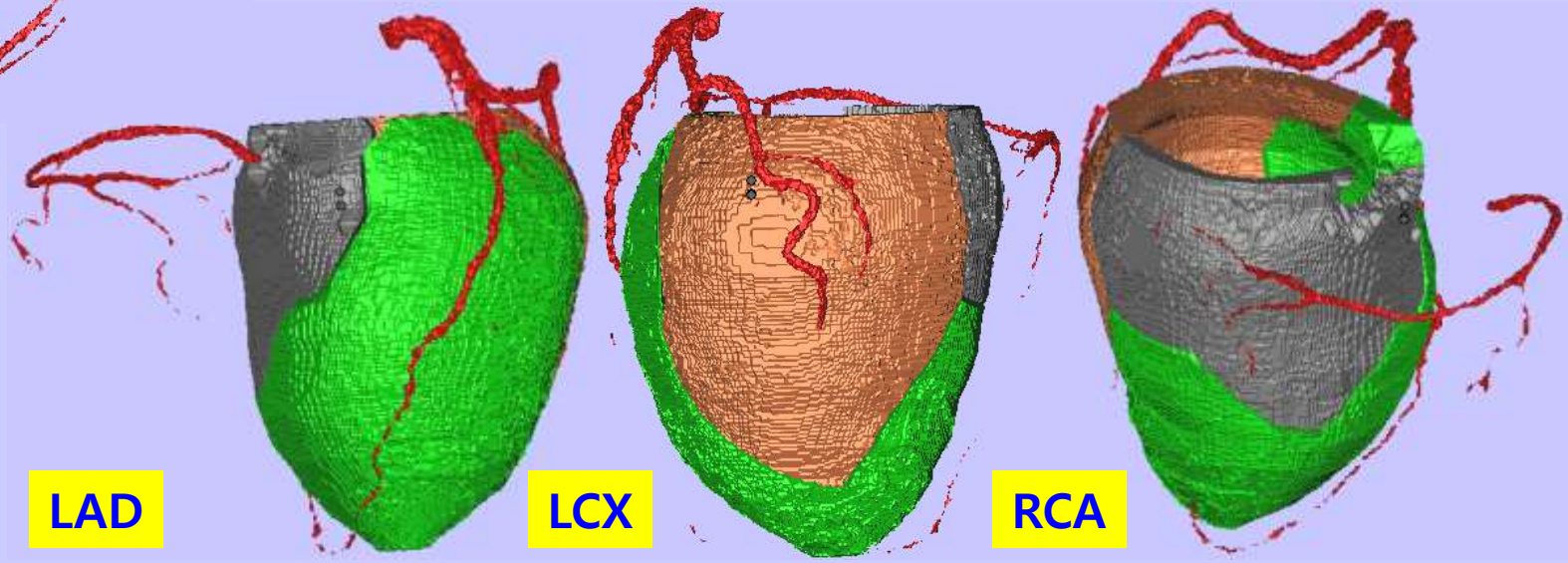
Quantitative Analysis of CTP: Potential Role

- Improvement of diagnostic accuracy
  - Intermediate lesion
  - Multi-vessel disease (balanced ischemia)
- Quantification of ischemic burden
- Vascular territory assignment

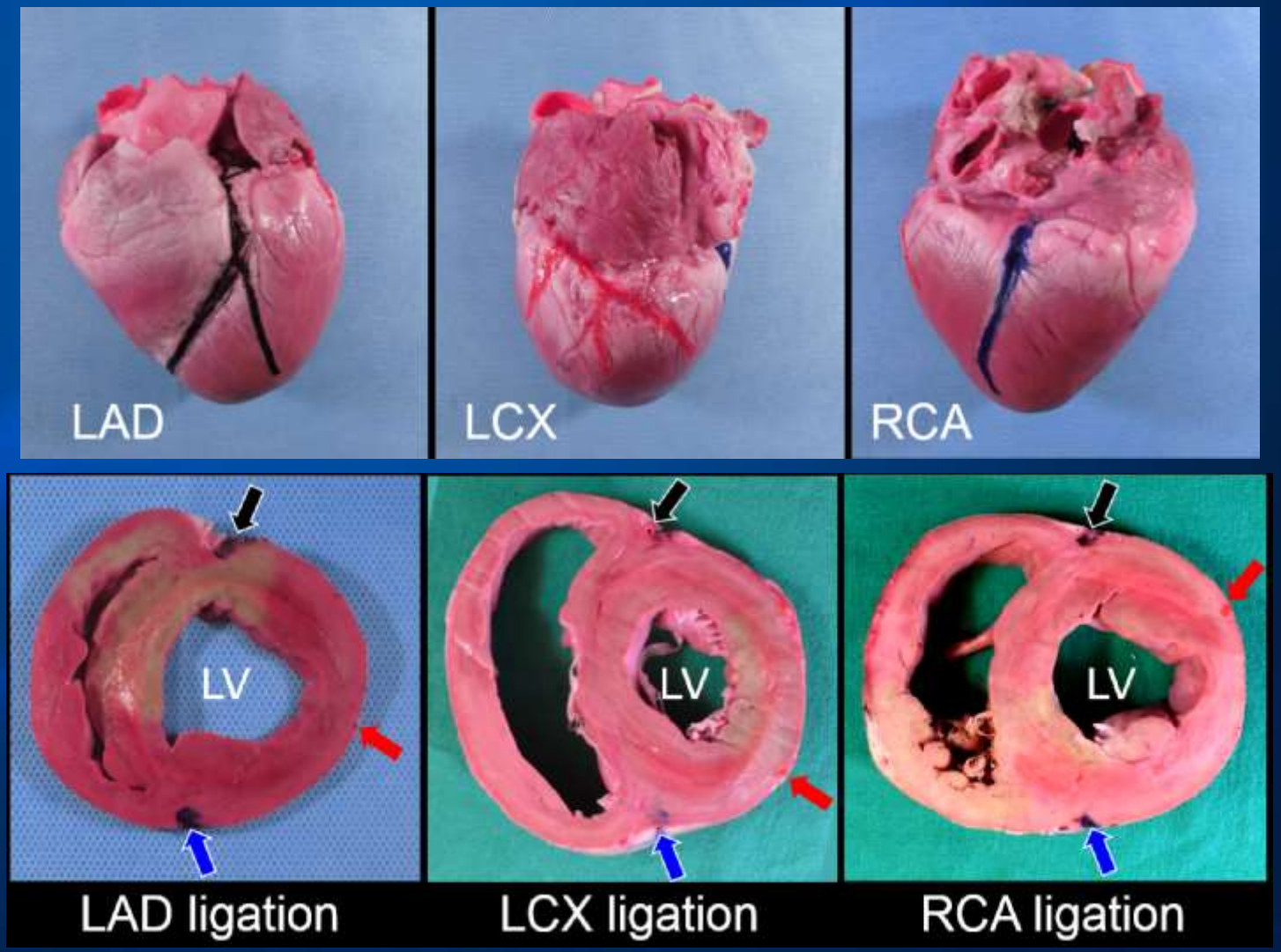
Coronary artery based myocardial segmentation (CAMS) method



Final result of CAMS method



CAMS – Animal Validation



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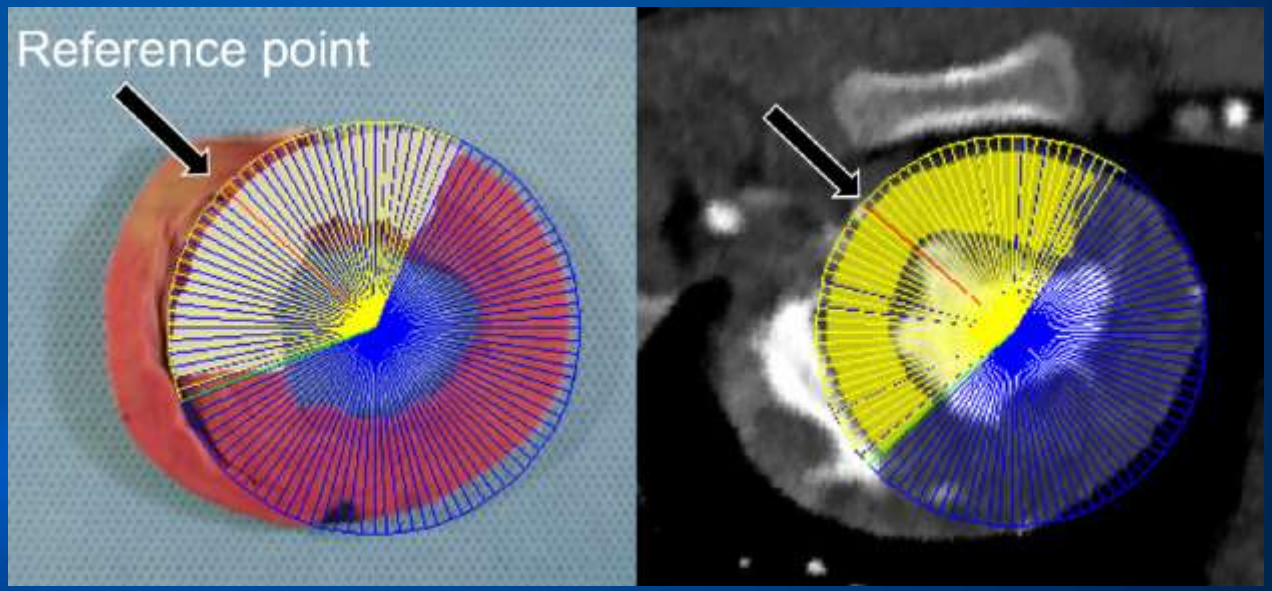
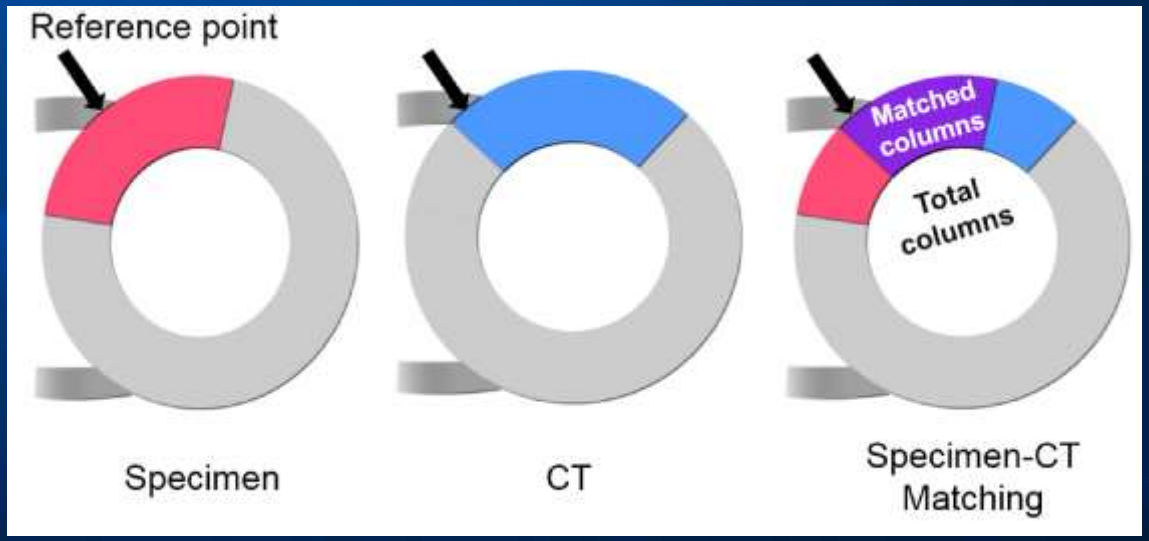
CAMS – Animal Validation





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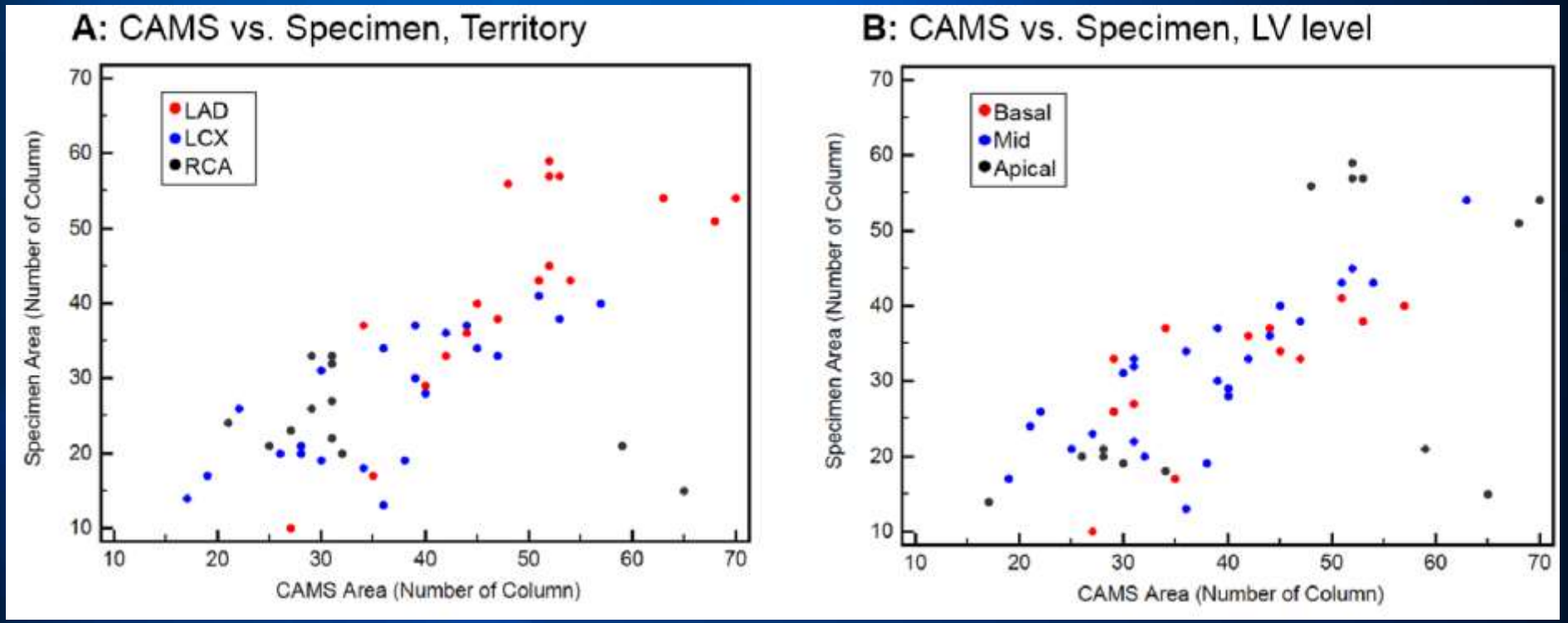
CAMS vs. Specimen



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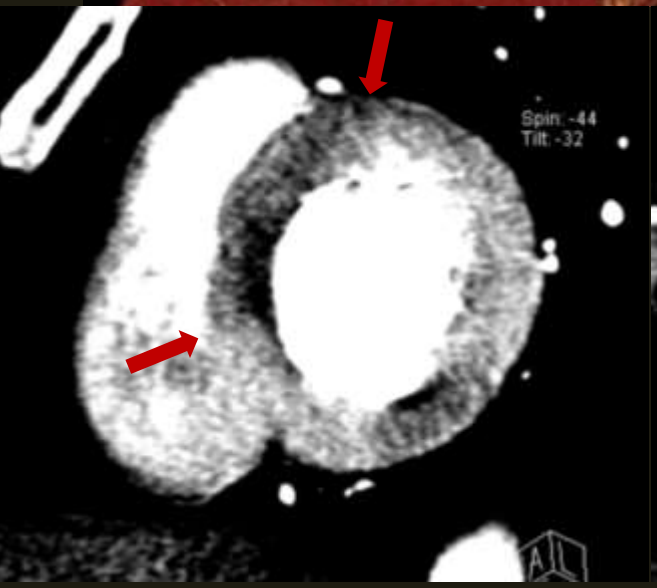
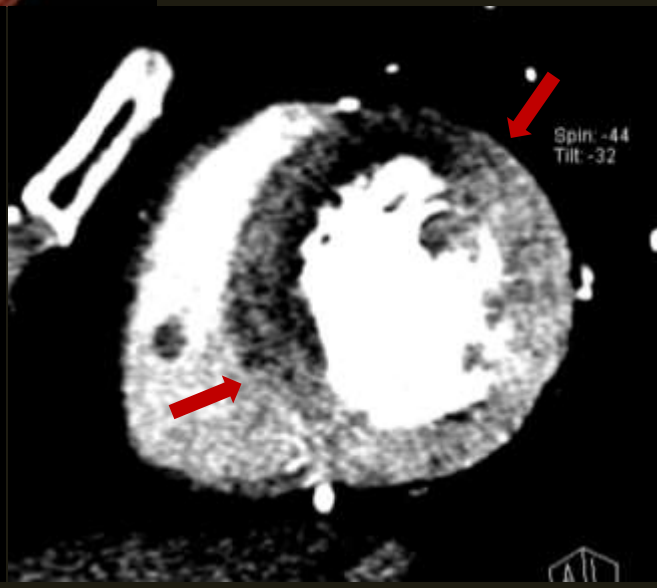
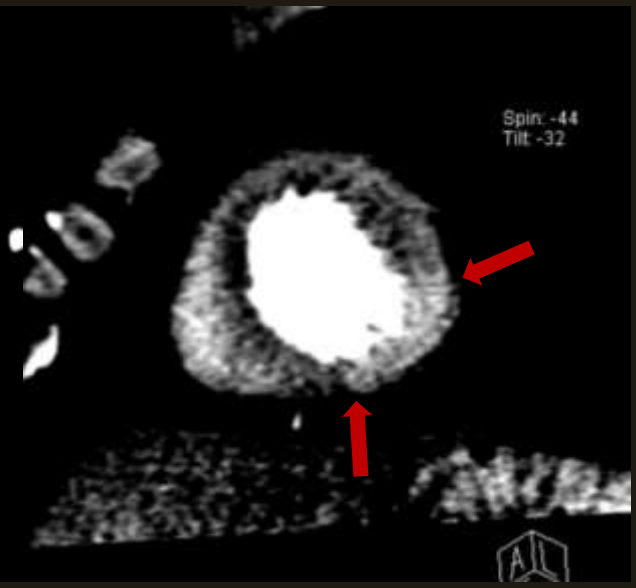
Case: LAD Territory Ischemia

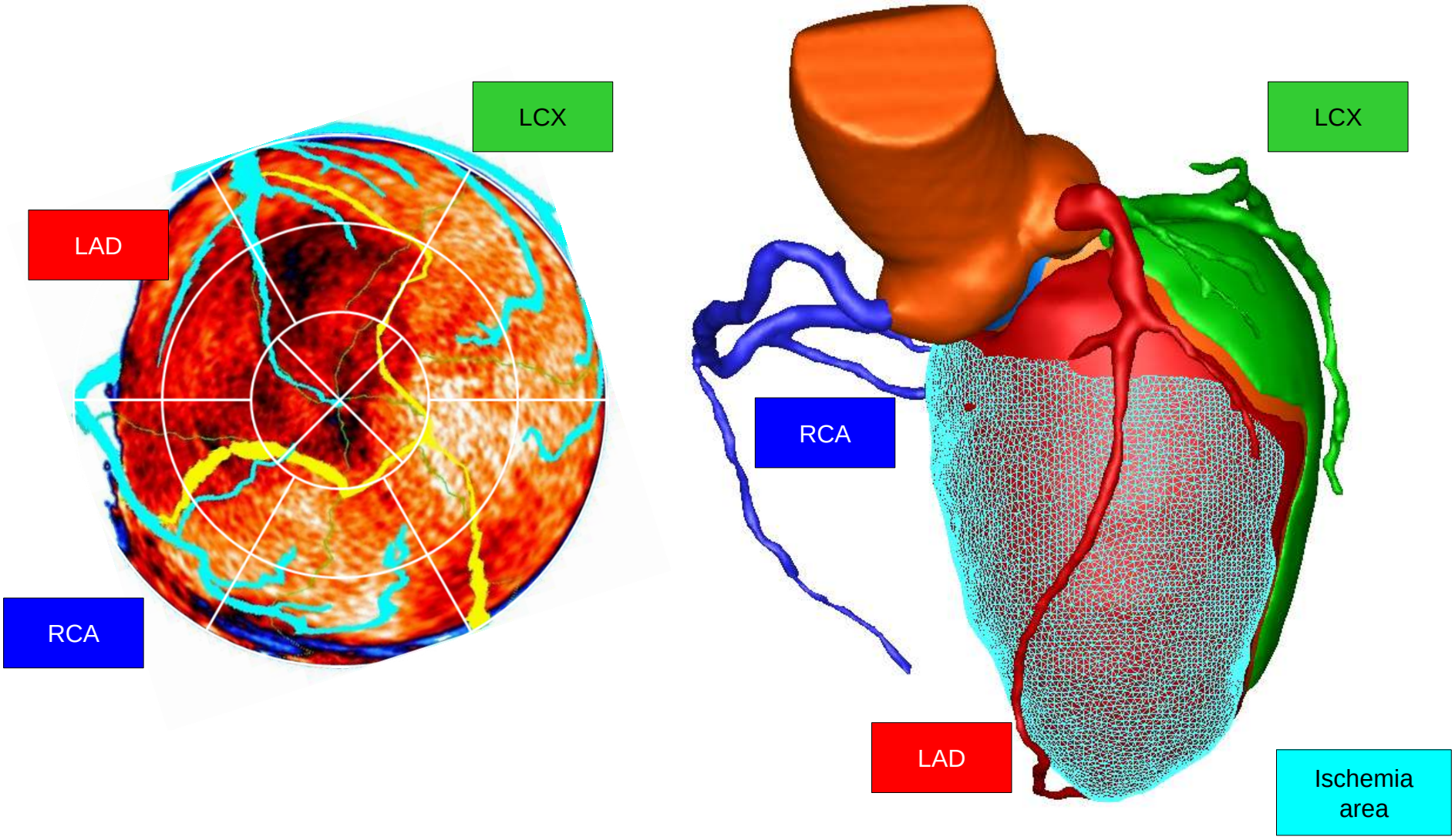
- Tight stenosis in proximal LAD
- Reversible perfusion defect in LAD territory, larger than conventional myocardial segmentation than apical area



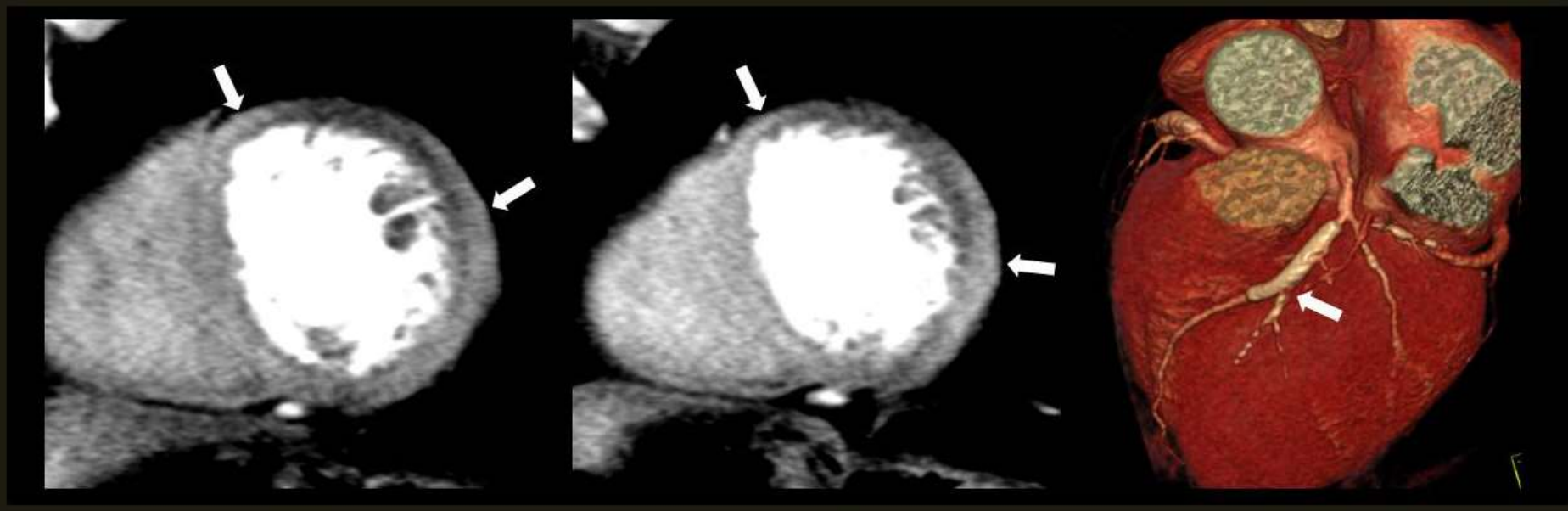


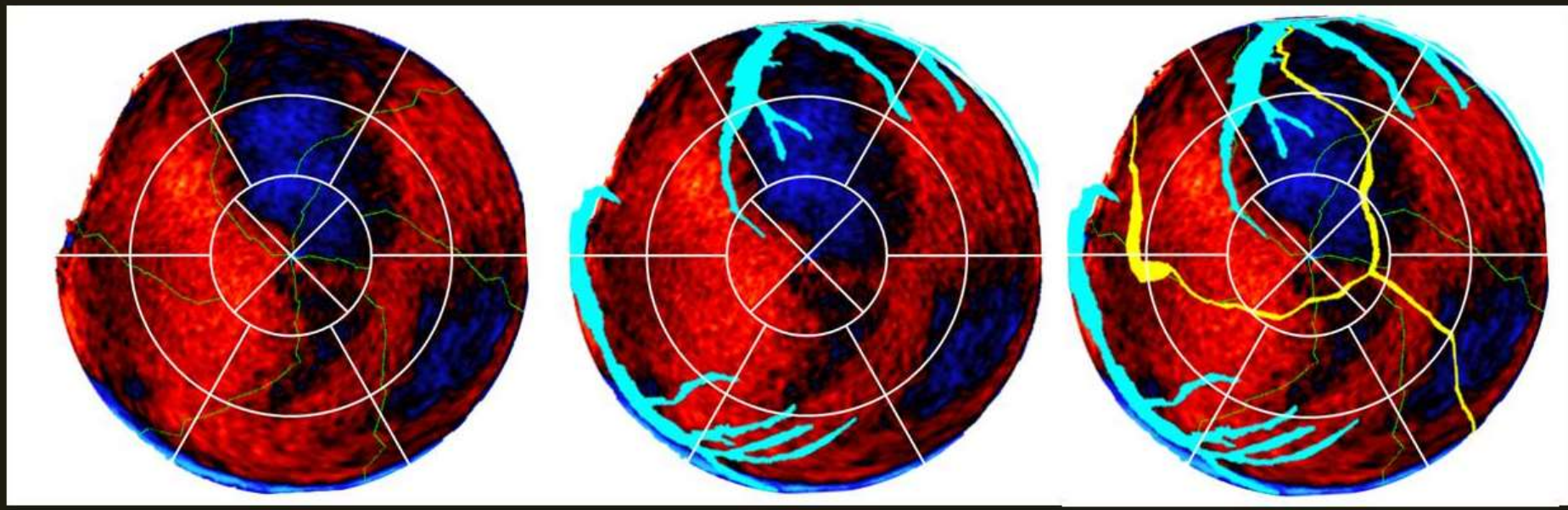


Ischemic Area: **42%** of LV myocardium

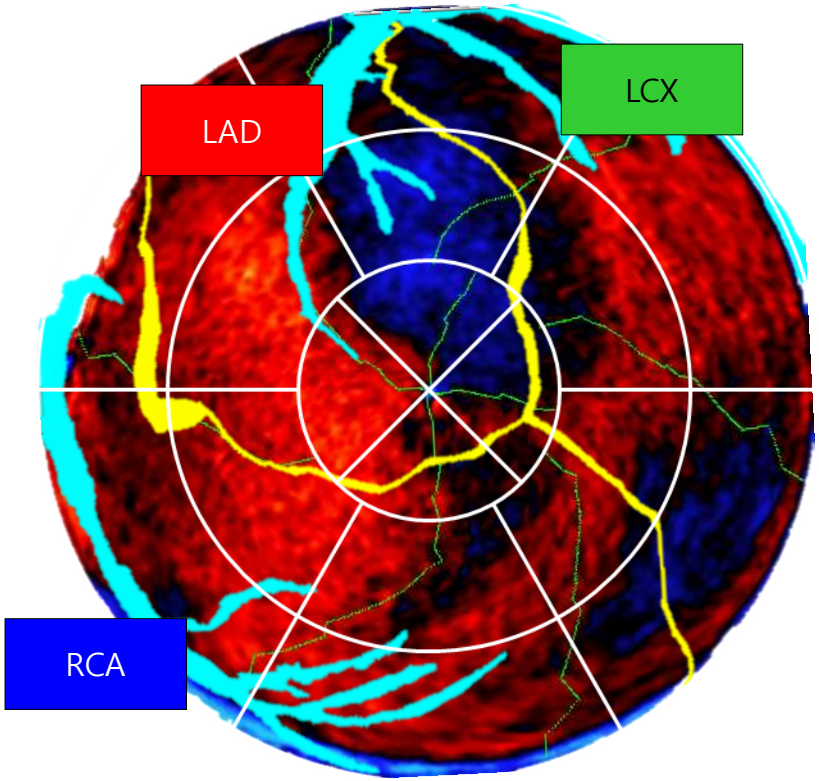


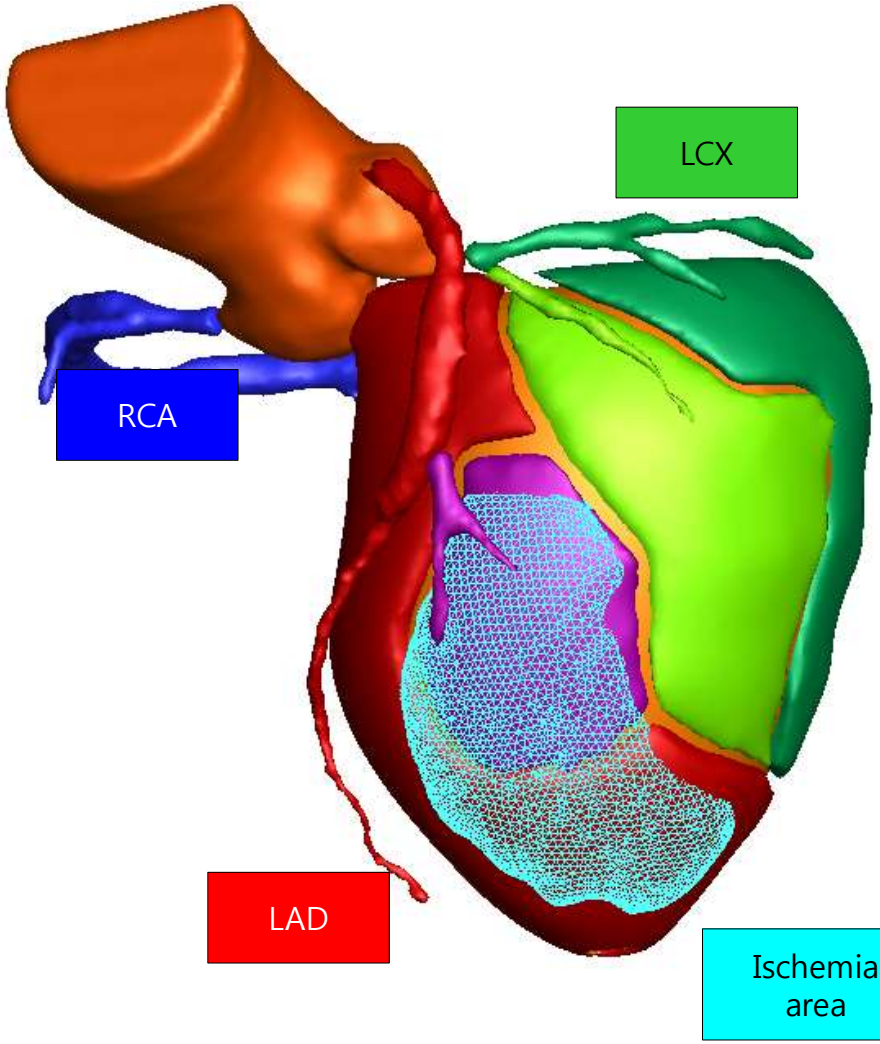
Anterior wall Ischemia





Ischemic Area: **8%** of LV myocardium





Cardiac CT: One Stop Shop

Imaging Target	Conventional Technique	Limitation of CT
1. Coronary artery stenosis	CAG	• Temporal resolution • Spatial resolution • Radiation exposure • Use of contrast material • Blooming artifact from calcified plaque
2. Plaque evaluation	IVUS, OCT	
3. Ventricular function	ECHO, MRI	
4. Myocardial ischemia **(CT perfusion)**	SPECT, MRI	
5. Fractional flow reserve **(CT-FFR)**	Invasive FFR	
6. Valve, Structural abnormality	ECHO, MRI	

KSCMR

CMR Seoul

Thank you !

KSCMR & CMR SEOUL 2015

May 16 (Sat) – 17 (Sun), 2015

Asan Medical Center, Seoul, Korea