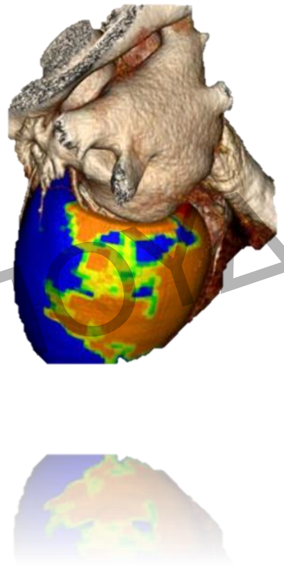
ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ

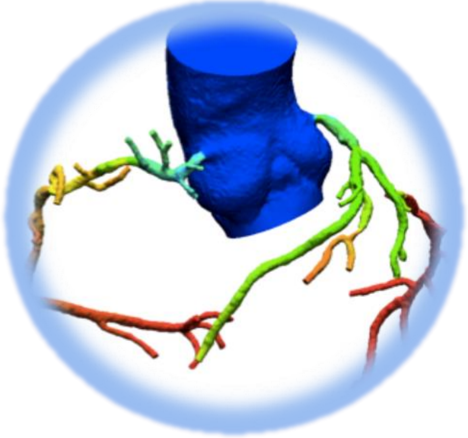
ΚΑΡΔΙΑΓΓΕΙΑΚΗ ΑΠΕΙΚΟΝΙΣΗ

March 14th 2026



CT-Perfusion

CT-Fractional Flow Reserve



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Director, *Coronary Atherosclerosis Biomechanics Lab, University Hospital Zurich*
EACVI Board Member, *Councilor CCT & Nuclear*
Chair, *EACVI Research Committee*

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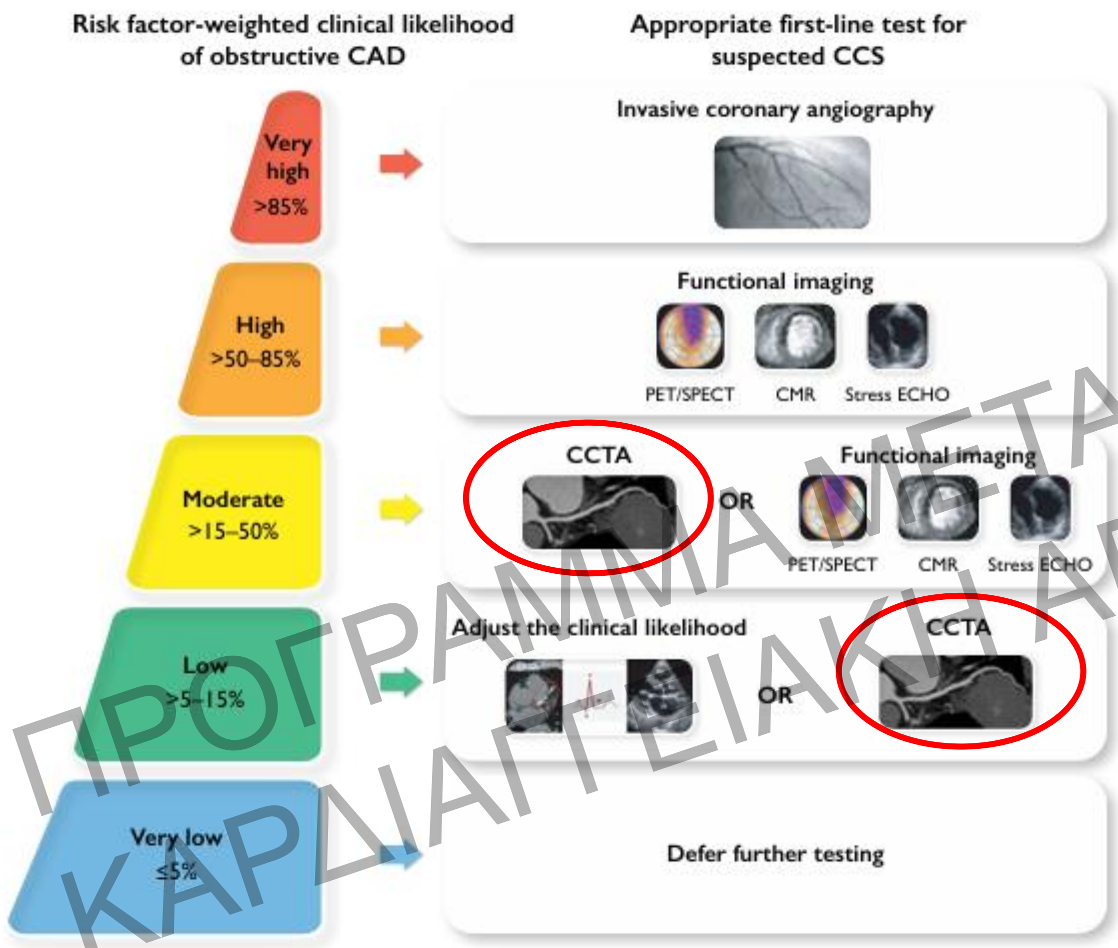
Coronary CTA holds key role

First-Line test



UniversityHospital Zurich

2024 ESC guidelines on the management of chronic coronary syndromes, Eur Heart J 2024

Coronary CTA holds key role

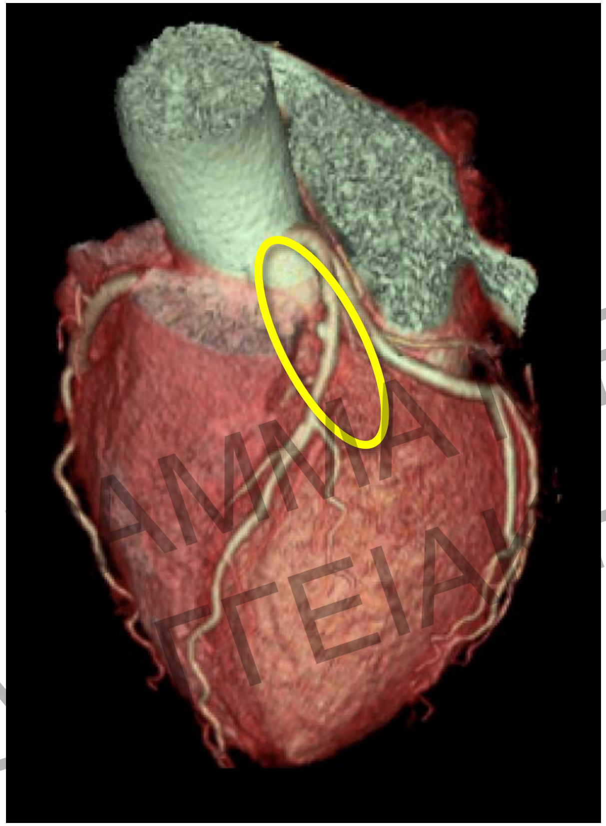
Anatomically significant CAD				
Test	Sensitivity (%), (95% CI)	Specificity (%), (95% CI)	+LR (95% CI)	−LR (95% CI)
Stress ECG	58 (46–69)	62 (54–69)	1.53 (1.21–1.94)	0.68 (0.49–0.93)
Stress echo	85 (80–89)	82 (72–89)	4.67 (2.95–7.41)	0.18 (0.13–0.25)
CCTA	97 (93–99)	78 (67–86)	4.44 (2.64–7.45)	0.04 (0.01–0.09)
SPECT	87 (83–90)	70 (63–76)	2.88 (2.33–3.56)	0.19 (0.15–0.24)
PET	90 (78–96)	85 (78–90)	5.87 (3.40–10.15)	0.12 (0.05–0.29)
Stress CMR	90 (83–94)	80 (69–88)	4.54 (2.37–8.72)	0.13 (0.07–0.24)

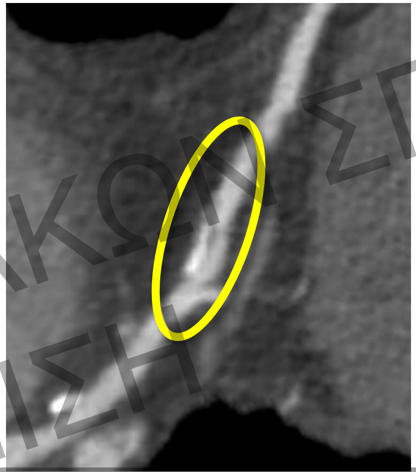
Functionally significant CAD				
Test	Sensitivity (%), (95% CI)	Specificity (%), (95% CI)	+LR (95% CI)	−LR (95% CI)
ICA	68 (60–75)	73 (55–86)	2.49 (1.47–4.21)	0.44 (0.36–0.54)
CCTA	93 (89–96)	53 (37–68)	1.97 (1.28–3.03)	0.13 (0.06–0.25)
SPECT	73 (62–82)	83 (71–90)	4.21 (2.62–6.76)	0.33 (0.24–0.46)
PET	89 (82–93)	85 (81–88)	6.04 (4.29–8.51)	0.13 (0.08–0.22)
Stress CMR	89 (85–92)	87 (83–91)	7.10 (5.07–9.95)	0.13 (0.09–0.18)

Knuuti J et al. European Heart Journal (2018) 39, 3322-3330

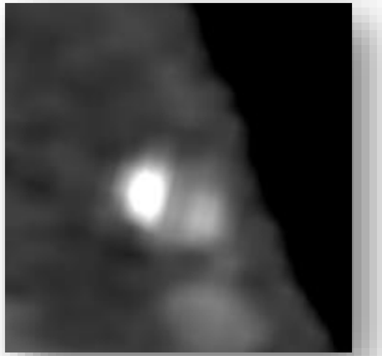
Clinical Background

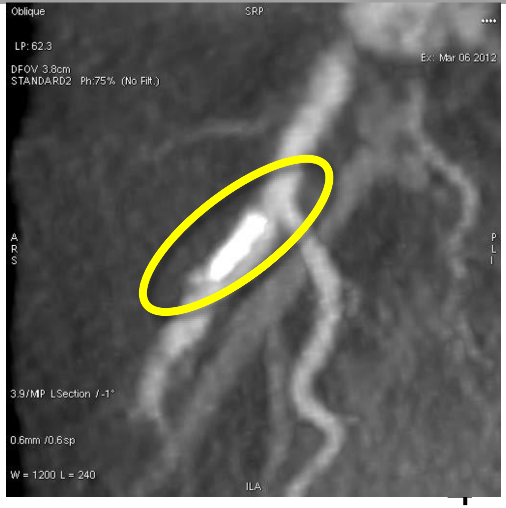
CCTA





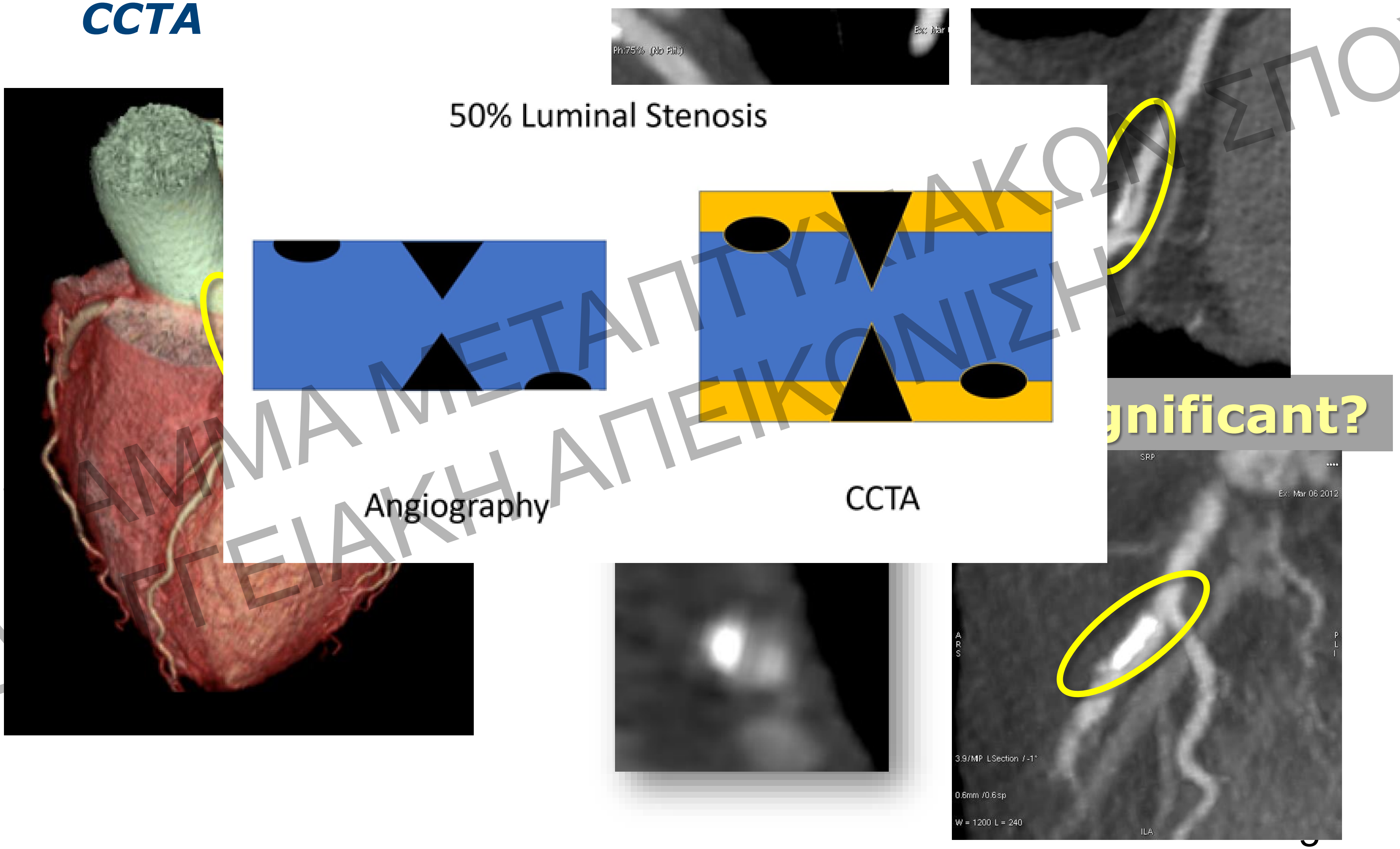
Is this stenosis significant?





Clinical Background

CCTA



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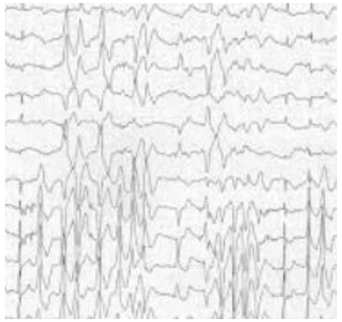
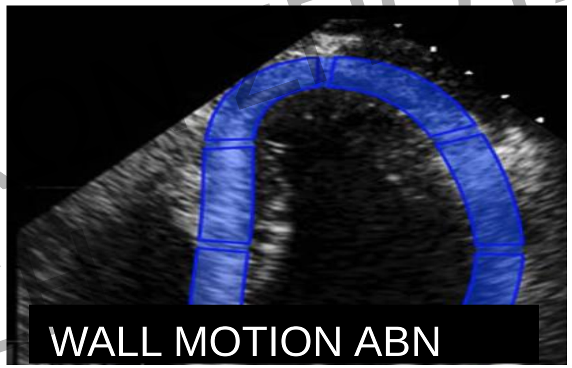
Myocardial Ischemia

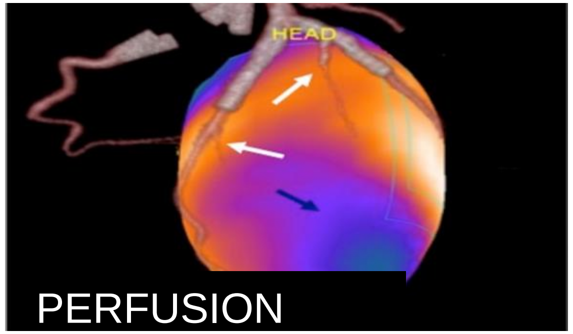
Physical Stress Test



Echo



SPECT



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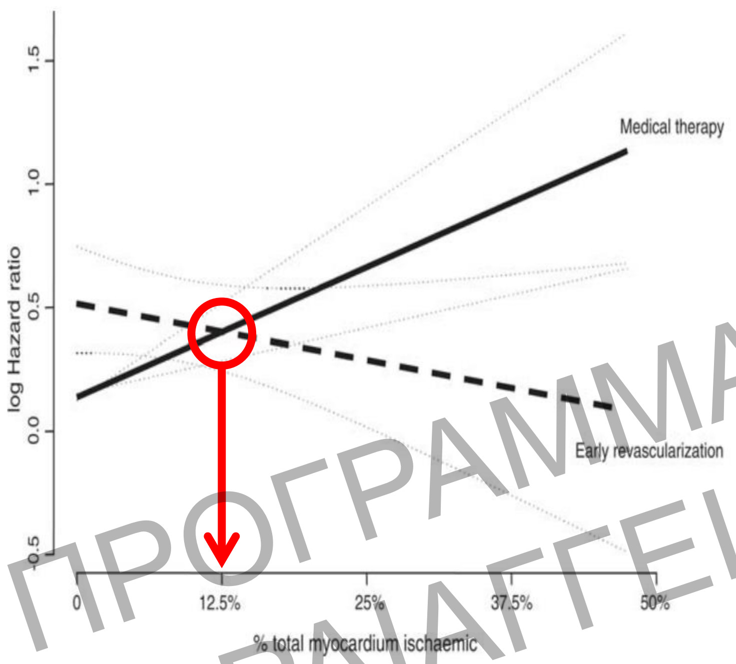
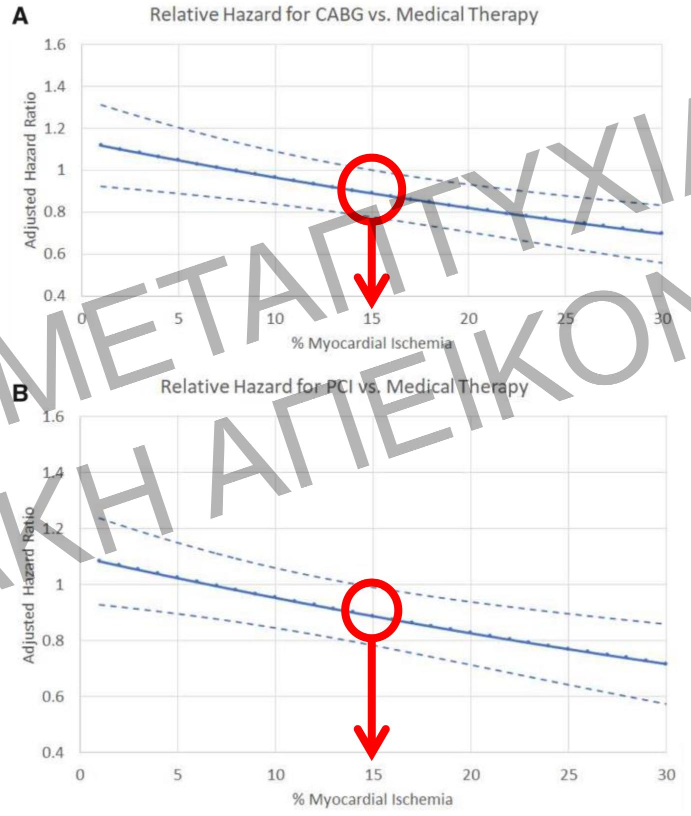
The Benefit of Revascularisation is correlated to the Ischemia-Burden

SPECT

n = 14‘627

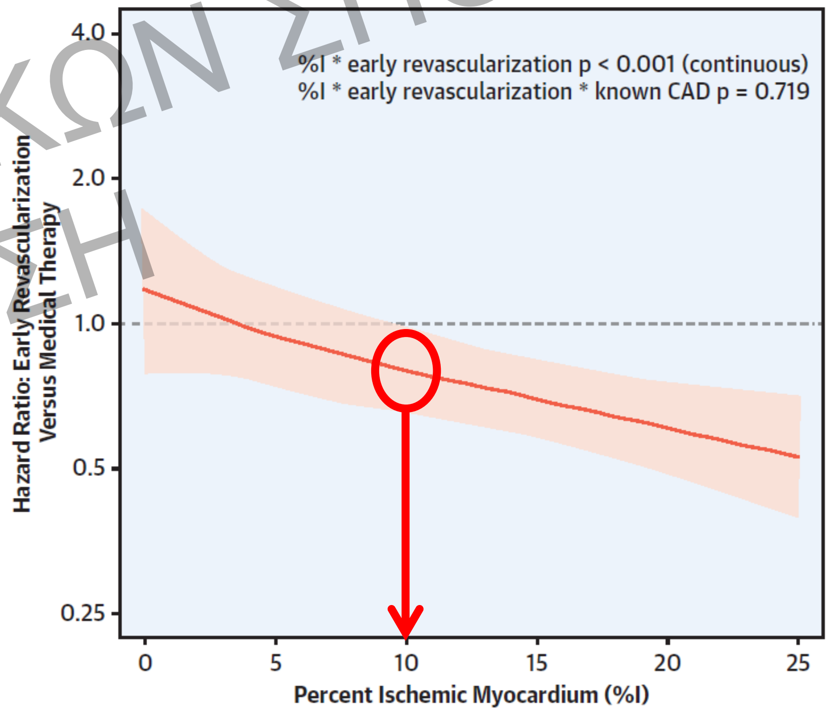


n = 7’832



Rubidium-82 PET

n = 16‘029



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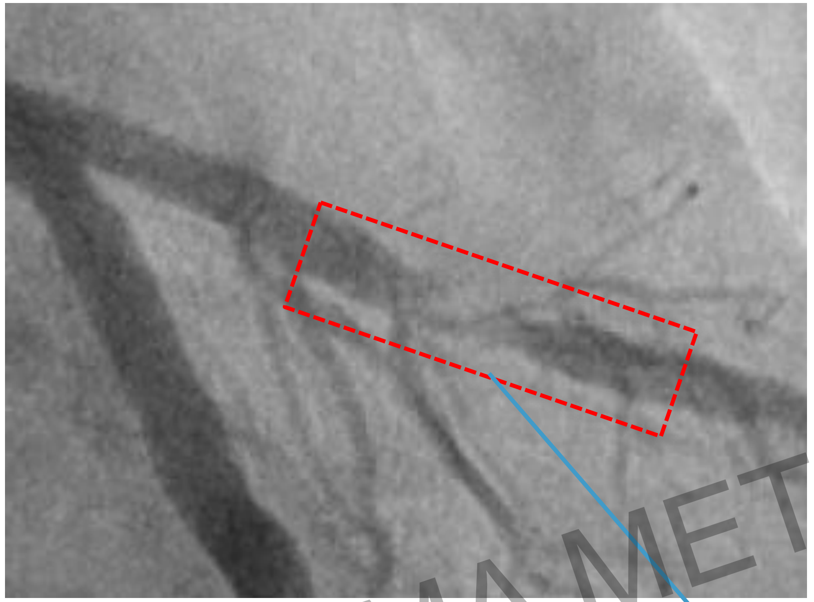
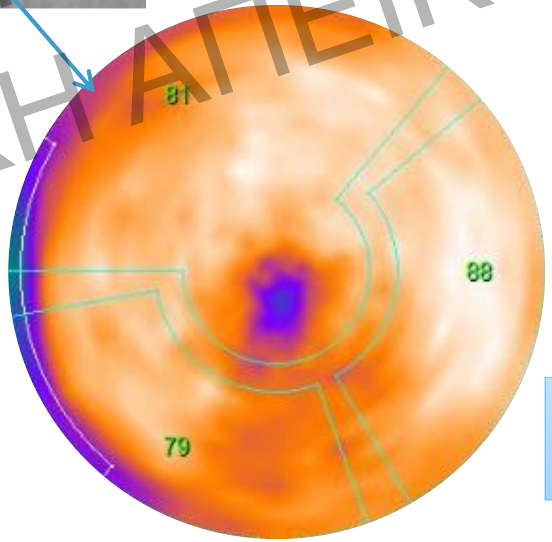
Hachamovitch R et al. Eur Heart J. 2011 Apr;32(8):1012-24
Miller et al. Eur Heart J Cardiovasc Imaging. 2020 Sep 1;21(9):961-970.
Patel KK et al. J Am Coll Cardiol. 2019 Oct; 74(13):1645-1654.

Coronary Stenosis ≠ Myocardial Ischemia



The degree of stenosis is a poor predictor of ischemia

This principle applies to all angiographic techniques



Normal Stress Myocardial Perfusion

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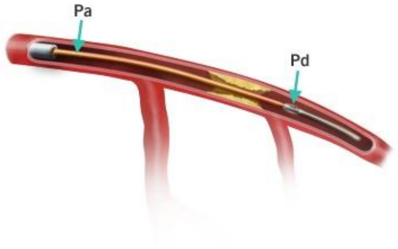
Lesion Specific Ischemia

Invasive Fractional flow reserve (FFR)

An invasive measurement of hemodynamic stenosis severity

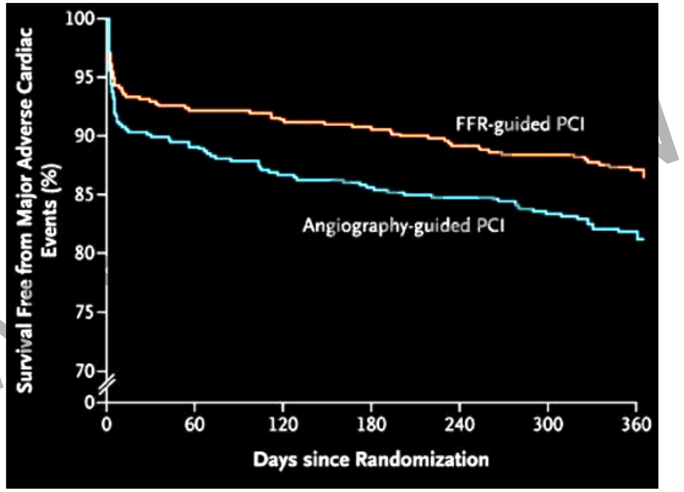


$$FFR = \frac{\text{Distal Coronary Pressure (Pd)}}{\text{Proximal Coronary Pressure (Pa)}}$$

(During Maximum Hyperemia)

FFR <= 0.8 → ischemia (spec 100%)

FFR > 0.8 → ischemia unlikely (sens 88%)



Ischaemia guided revascularization reduces major cardiovascular events with significant cost savings, whereas angiographic strategies alone are ineffective for guiding revascularization

- Use of FFR is **recommended** in all **intermediate** coronary lesions to determine the **need** for **revascularization**
- Use of FFR **reduces** the **number** of **unnecessary revascularization** procedures and **improves** patient **outcomes**
- ***FFR is underutilized***

(FFR guidance integrated in only 10%–20% of revascularization procedures)

- *invasive procedure*
- *additional costs*
- *regional variations in reimbursement*

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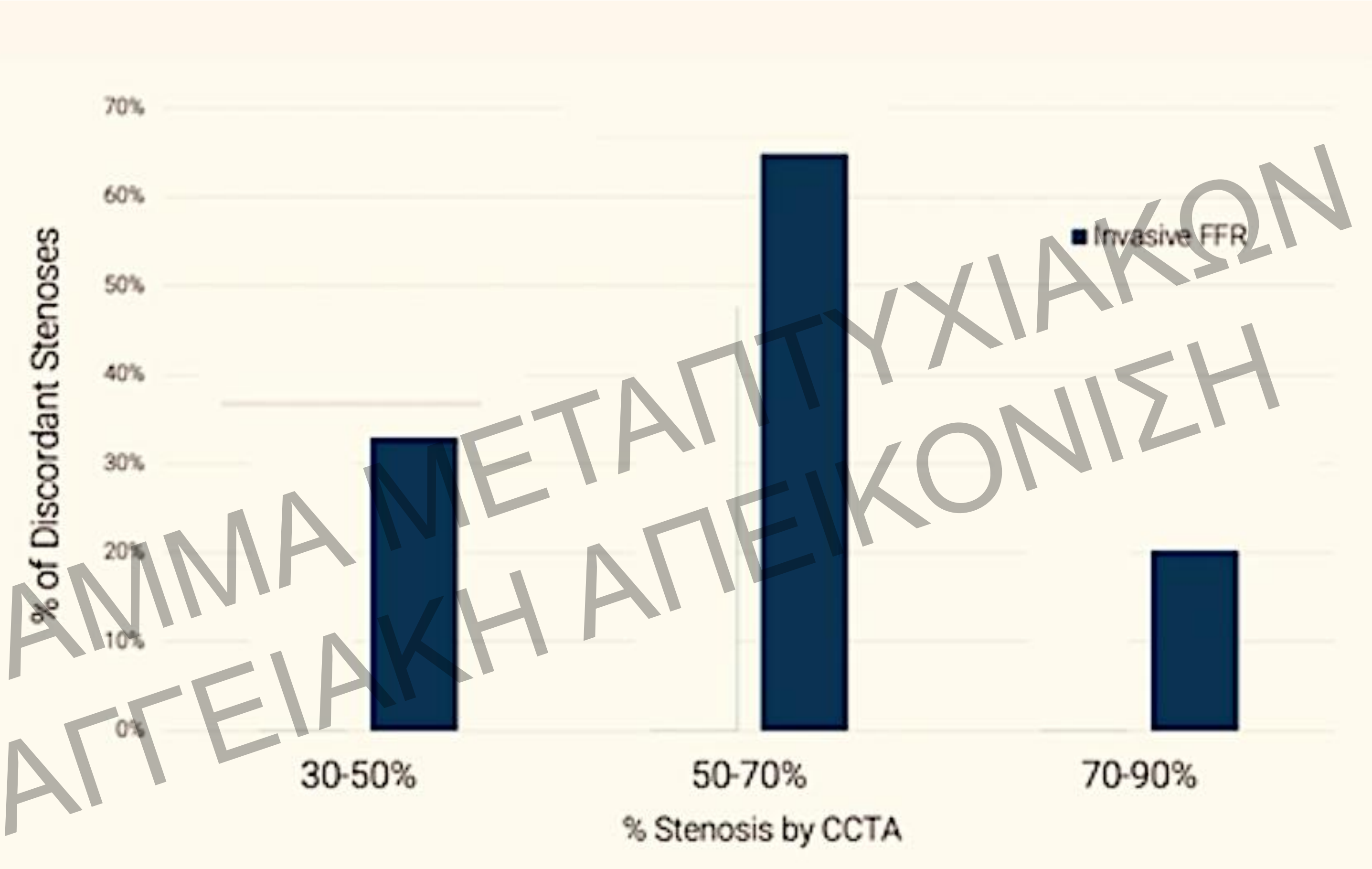
Tonino AL P *et al,* *N Engl J Med 2009*
De Bruyne B *et al.* *N Engl J Med, 2012*

DISCORDANCE ANATOMY-PHYSIOLOGY



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Tonino *et al*, *JACC, 2010*
Curzen *et al*. *Circ Int, 2014*

What do the guidelines say?

ESC European Society of Cardiology
European Heart Journal (2019) **40**, 87–165
doi:10.1093/eurheartj/ehy394
ESC/EACTS GUIDELINES

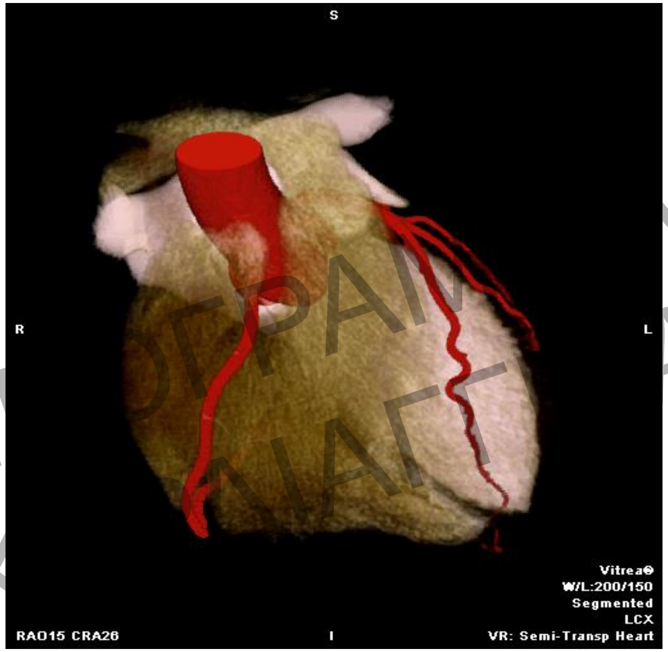
2018 ESC/EACTS Guidelines on myocardial revascularization

Indications for revascularization in patients with stable angina or silent ischaemia

Extent of CAD (anatomical and/or functional)		Class[a]	Level[b]
For prognosis	Left main disease with stenosis >50%.[c] [68–71]	I	A
	Proximal LAD stenosis >50%.[c] [62,68,70,72]	I	A
	Two- or three-vessel disease with stenosis >50% with impaired LV function (LVEF ≤35%).[c] [61,62,68,70,73–83]	I	A
	Large area of ischaemia detected by functional testing (>10% LV) or abnormal invasive FFR.[d] [24,59,84–90]	I	B
	Single remaining patent coronary artery with stenosis >50%.[c]	I	C
For symptoms	Haemodynamically significant coronary stenosis[c] in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical therapy.[e] [24,63,91–97]	I	A

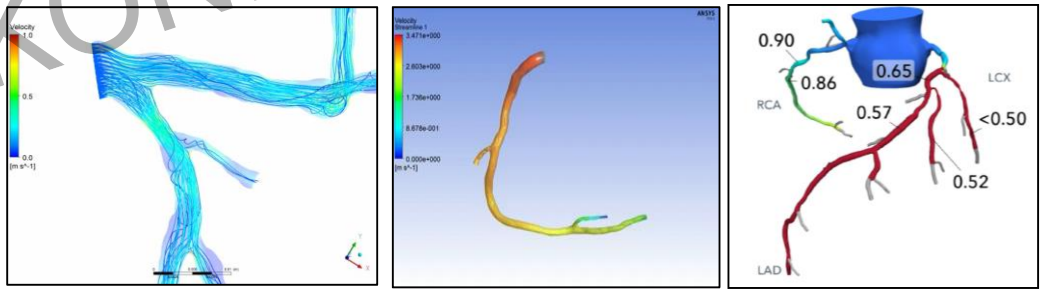
CAD = coronary artery disease; FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; LAD = left anterior descending coronary artery; LV = left ventricular; LVEF = left ventricular ejection fraction.
[a]Class of recommendation.
[b]Level of evidence.
[c]With documented ischaemia or a haemodynamically relevant lesion defined by FFR ≤0.80 or iwFR ≤0.89 (see section 3.2.1.1), or >90% stenosis in a major coronary vessel.
[d]Based on FFR <0.75 indicating a prognostically relevant lesion (see section 3.2.1.1).
[e]In consideration of patient compliance and wishes in relation to the intensity of anti-anginal therapy.

One-Stop Shop with cardiac CT
Anatomical and Functional Diagnostic



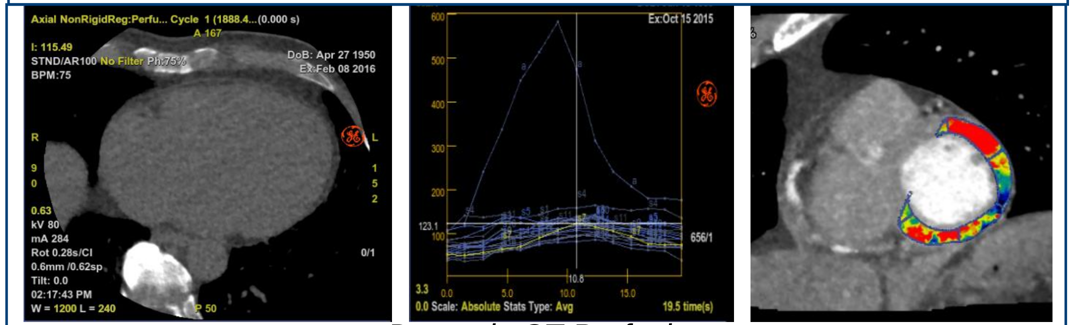
Plaque Assessment

CT-FFR



Computational Simulations

CTP



Dynamic CT Perfusion

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Courtesy of Drs Dweck and Buechel

Cardiac CT Perfusion

- Assessment of Myocardial Perfusion by CT w/o computational simulations; similar to common MPI approaches
- Contrast Enhanced Imaging of Myocardial Perfusion using **qualitative, semi-quantitative or quantitative methods**

PRINCIPLE

Images are acquired during the transit of contrast from the coronary arteries to the myocardium. Since iodinated contrast attenuates x-rays proportionally to the concentration of iodine, hypoattenuated myocardial areas typically represent regions with low blood flow, or hypoperfusion.

Patel AR P *et al, JCCT* *2020*
SCCT Expert Consensus Document on CTP

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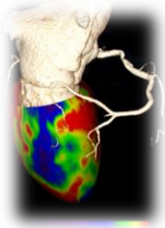
- Recommended as additional to CCTA:
  - Pts at high atherosclerotic risk for obstructive CAD (prior intervention, high calcification, indeterminant functional significance)
    - If knowledge regarding ischemia is expected to impact patient management
    - If CTP is feasible

Patel AR P *et al, JCCT* *2020*
SCCT Expert Consensus Document on CTP

Cardiac CT Perfusion

Static CT Perfusion

Single-Energy

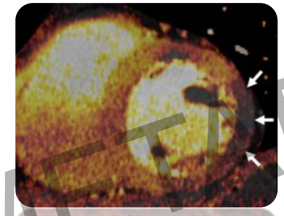


Single data sample of myocardial contrast enhancement during first-pass.

Qualitative-compares attenuation in ischaemic area to remote myocardium or normalizes it to LV-cavity.

Hypoattenuating myocardial areas represent hypoperfused myocardium

Dual-Energy



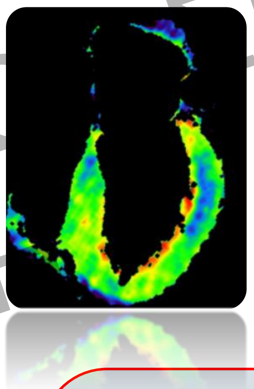
Combines lower noise of higher energy images, with high contrast resolution of lower energy images

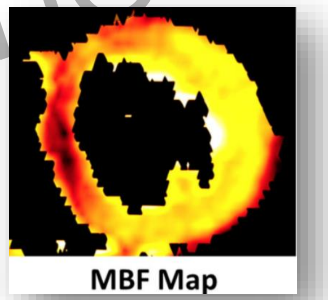
Should create **better definition between hypoperfusion and remote myocardium**

Creation of **iodine maps**

Snapshot of Perfusion

Dynamic CT Perfusion





Dynamic sample of first pass of contrast

Arterial input function

Time-attenuation curves in each myocardial voxel

Fitting: two compartment model relates contrast concentration (HU) to **quantitative perfusion parameters** (MBF, MBV, etc)

Dynamic Assessment of Perfusion

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Cardiac CT Perfusion

Advantages and Disadvantages

Static CT Perfusion

Single-Energy

Pros
- Technically Simple
- Can use CCTA images for rest CTP
- Low radiation exposure

Cons
- Qualitative/Semiquantitative analysis
- Timing of CTP acquisition critical
- Need normal segment to identify abnormal
- Frequently artifacts (beam hardening)

Dual-Energy

Pros
- Higher contrast differentiation than other modalities
- Beam hardening correction possible
- Additional quantification approaches possible

Cons
- Specific scanner hardware requirements
- Additional software requirements

Dynamic CT Perfusion

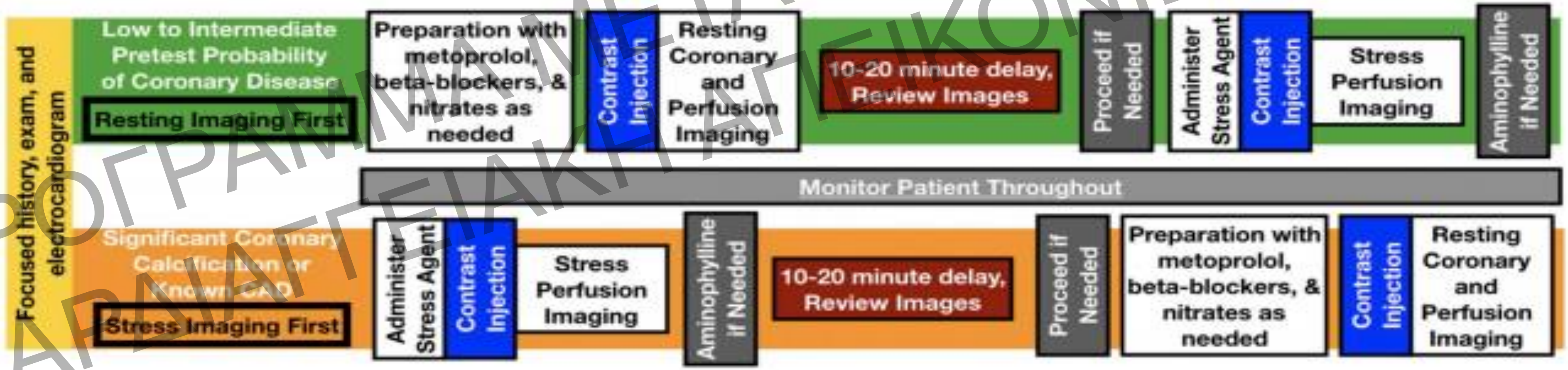
Pros
- Quantitative MBF and MBV assessment possible
- Timing less critical than static CTP
- Potential to detect balanced and microvascular ischemia

Cons
- Lower detector systems may require shuttle mode
- Common artifacts (longer breath hold)
- Higher radiation exposure
- Additional software requirements
- Increased scanner hardware requirements

Cardiac CT Perfusion

Protocols> Stress and Rest Scans

- **Pharmacological** Stress: adenosin, regadenoson, dypiridamole (CAVE>off-label and Nitroglycerin)
- **CT Contrast**: 70-120ml of iodinated contrast is injected at a rate of 5–6 ml/sec followed by saline bolus (40–50ml)
- **Optimal order/sequencing of imaging** should be individualized (Calcium-Scoring might be helpful)



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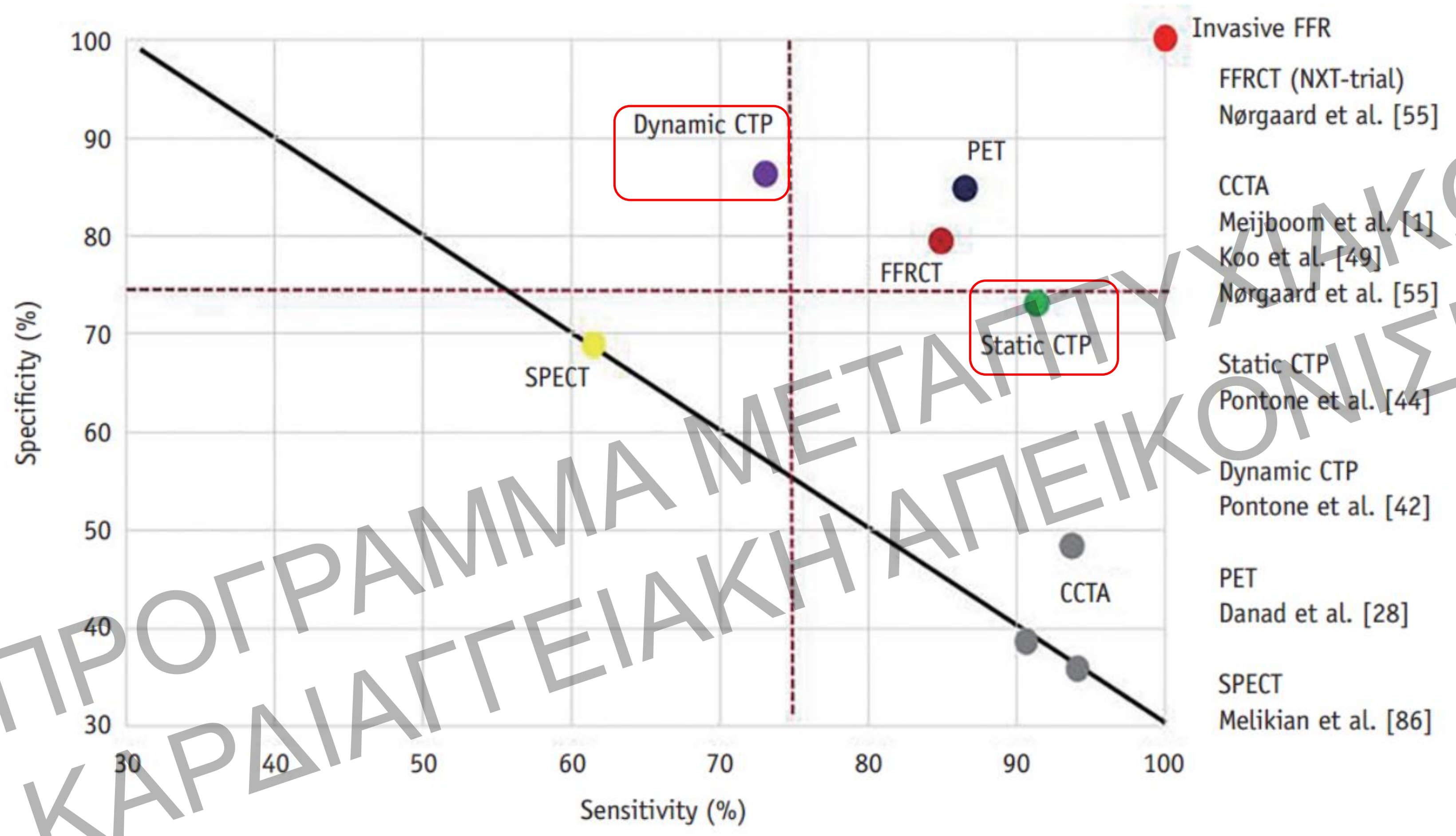
Patel AR P *et al, JCCT* *2020*
SCCT Expert Consensus Document on CTP

Cardiac CT Perfusion

Specificity versus sensitivity plots of different imaging modalities for assessment of functional coronary artery disease.



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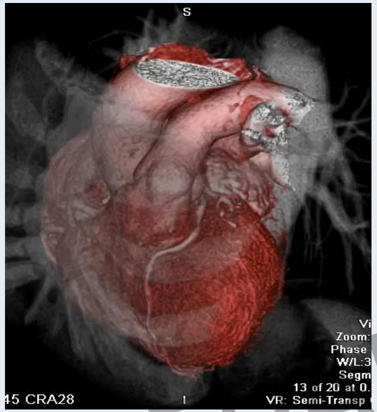
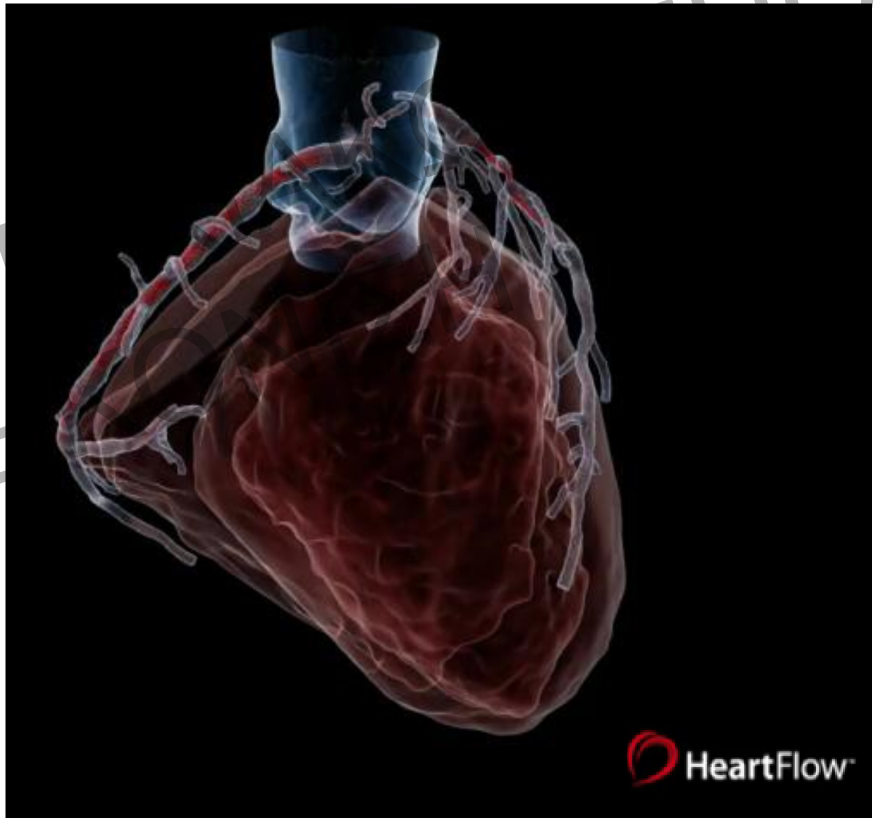
Yun CH P *et al*, *Korean J Radiol 2021;22(11):1749-1763*

Coronary CT- derived FFR



Computed Tomography Angiography (CTA)

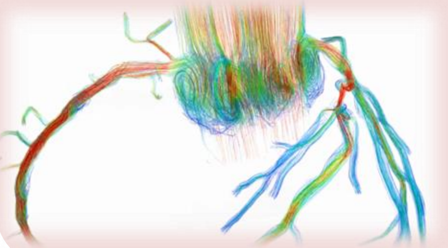
Computational Fluid Dynamics (CFD)



Technical background and physiological models

FDA approved

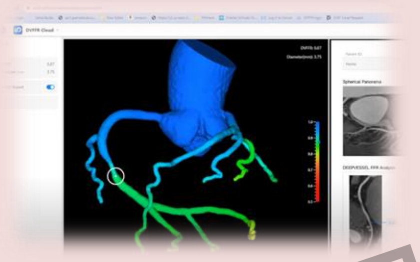
FFR_{CT} HeartFlow®



Min J *et al* *JAMA, 2012*

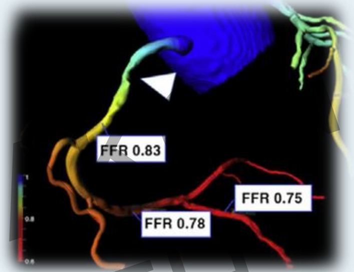
FDA approved

DVFFR-Keya



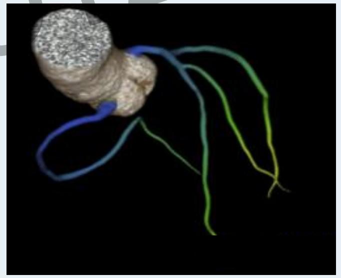
Yang J *et al Circulation*, *2023*

cFFR Siemens®



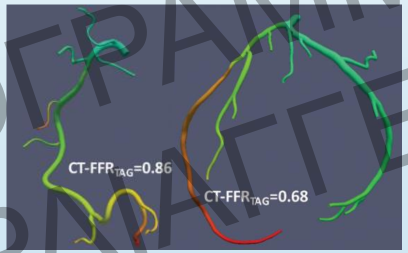
Coenen A *et al* *Radiology, 2015*

Toshiba CT-FFR



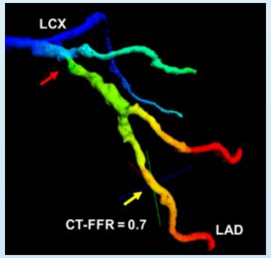
Ko BS *et al* *JACC Img, 2017*

Research CT-FFR (DIY)



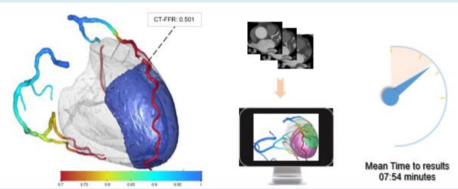
Kishi S, Giannopoulos AA *et al* *Radiology, 2018*

LBM-CT-FFR



Giannopoulos AA *et al* *EuroIntervention, 2017*

Deep Learning-CT-FFR



Giannopoulos AA *et al* *AJR, 2023*

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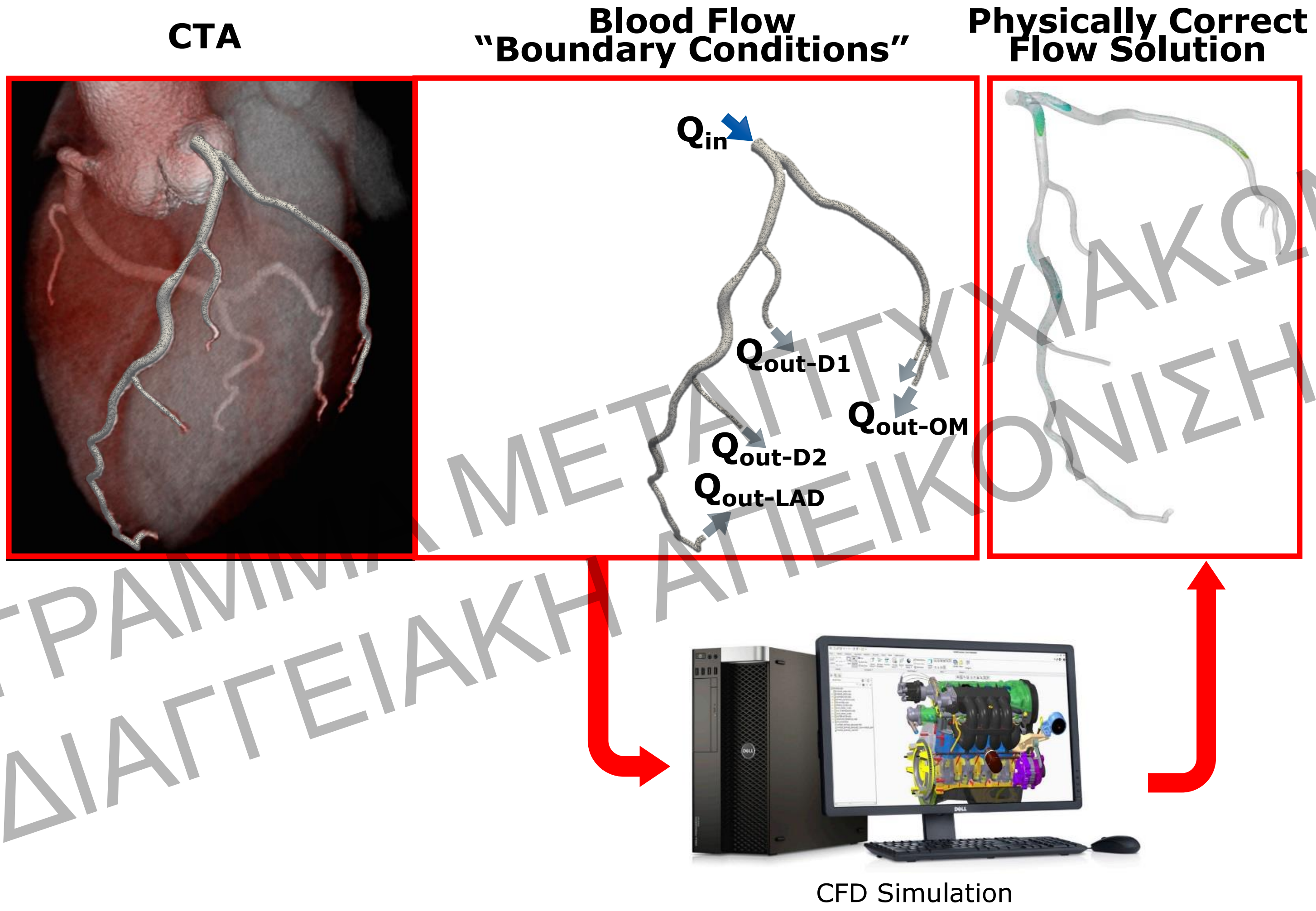
FFR estimated from a Rest CTA



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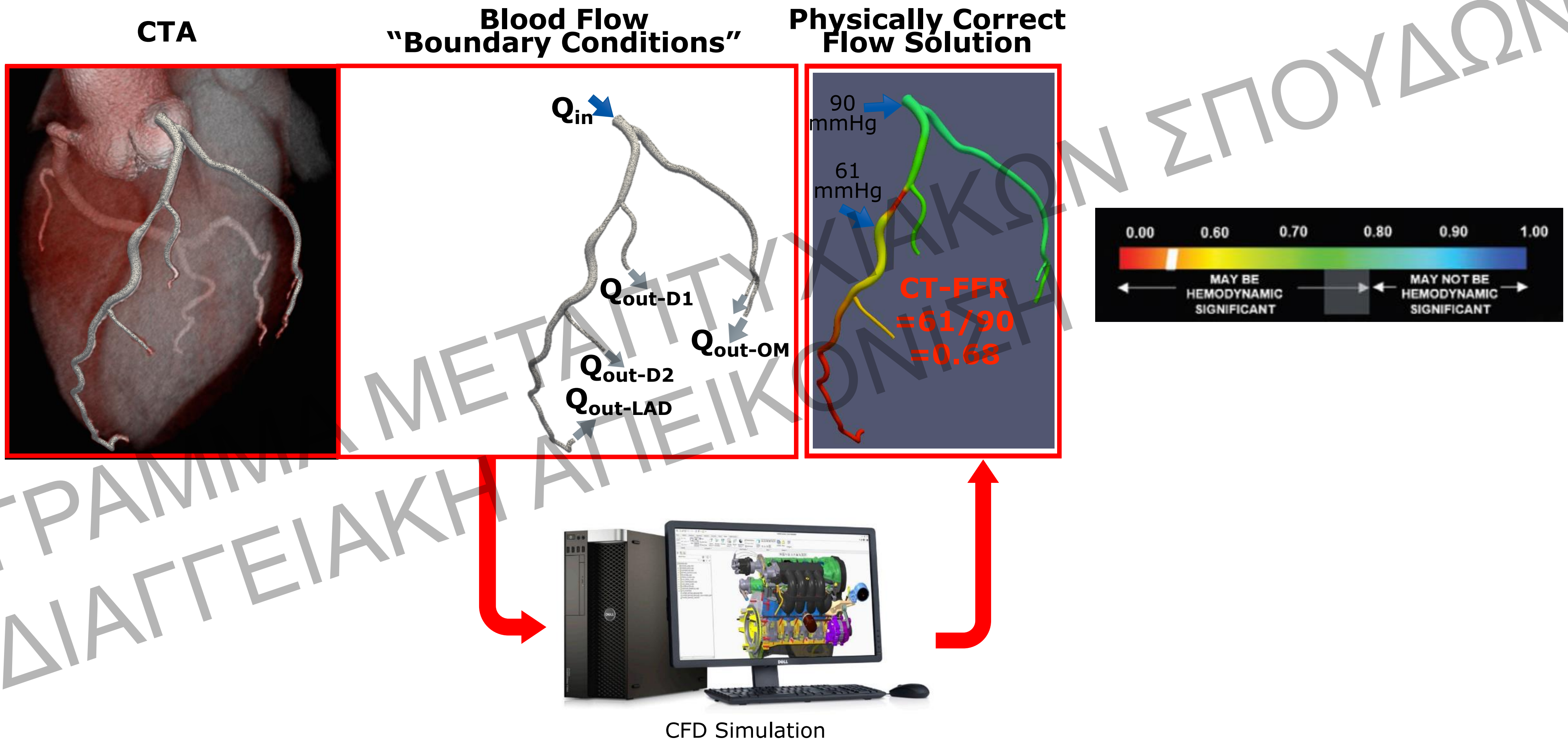
Courtesy of Dr Mitsouras D, AISL, BWH

FFR estimated from a Rest CTA



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Courtesy of Dr Mitsouras D, AISL, BWH

Limitations of CT-FFR

◆Limitations from inaccurate anatomical models:

- Poor CT image quality (calcifications, motion, misregistration)

◆Intrinsic limitations of physiological models:

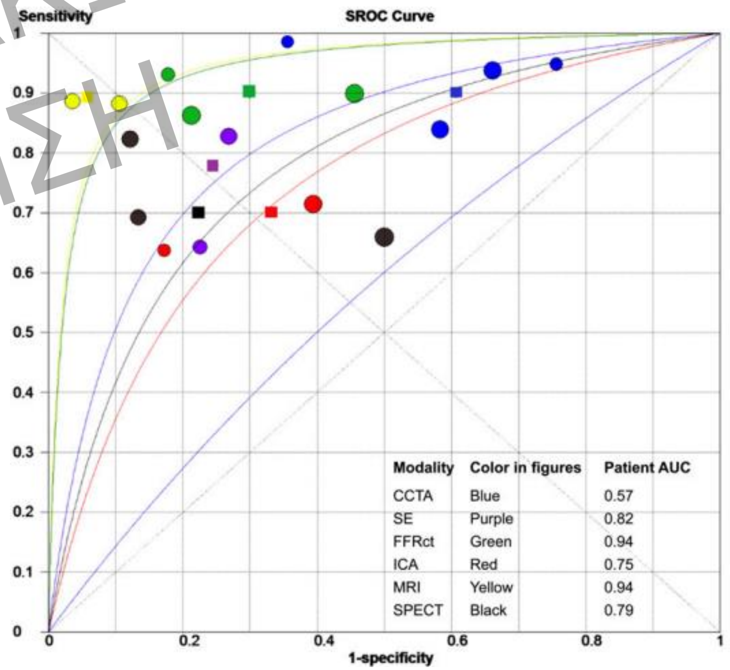
- Individual variability in relationship between **myocardial mass and total coronary flow**
- Individual variability in relationships between **vessel branch diameter and local microvascular resistance**
- **Predictability** of **coronary hyperemia**

CT – FFR current landscape

- The technology is **well validated** against **invasive FFR**
- **Incremental value** over CCTA demonstrated in several studies

Article	Technology	# of patients/# of lesions	ROC AUC	Sensitivity	Specificity	Diagnostic Accuracy	Correlation (Pearson r or Spearman ρ)	Bland-Altman Bias	Bland-Altman LA	Bland-Altman Δ of limits
Norgaard et al (NXT) (JACC 2014)	Heartflow FFRct	251/484	**0.93**	0.84	0.86	**0.86**	r=0.82	0.03	-0.115 – 0.175	0.29
Min et al (DeFACTO) (JAMA. 2012)	Heartflow FFRct	252/407	**0.81**	0.80	0.61	**NR**	r=0.63	0.06	NR	NR
Koo et al (DISCOVER-FLOW) (JACC)	Heartflow FFRct	103/159	**0.90**	0.879	0.822	**0.84**	r=0.72	0.02	-0.249 – 0.205	0.454
Kruk et al (JACC: Cardiovasc Imaging. 2016)	Siemens cFFR	90/96	**0.84**	NR	NR	**NR**	ρ = 0.67	-0.01	-0.21 – 0.18	0.39
Coenen et al (Radiology. 2015)	Siemens cFFR	106/189	**0.83**	0.875	0.651	**0.75**	r = 0.59	-0.04	-0.31 – 0.22	0.53
Renker et al (Am J Cardiol. 2014)	Siemens cFFR	53/67	**0.92**	0.85	0.85	**NR**	r = 0.66	NR	-0.18 – 0.2	0.38
Ko et al (JACC: Cardiovasc Imaging. 2017)	Toshiba 4D CT-FFR	42/78	**0.88**	0.778	0.868	**0.84**	r = 0.57	0.07	-0.204 – 0.334	0.538
Giannopoulos et al (EuroIntervention. 2017)	LBM CT-FFR	60/73	**0.89**	0.793	0.977	**0.90**	r = 0.60	-0.01	-0.223 – 0.206	0.429
Kishi et al (Radiology 2017)	“Open CT-FFR” (CT-FFR_{TAG})	61/61	**0.95**	0.949	0.864	**0.918**	r=0.73	-0.02	-0.182 – 0.147	-0.33

NR: not reported



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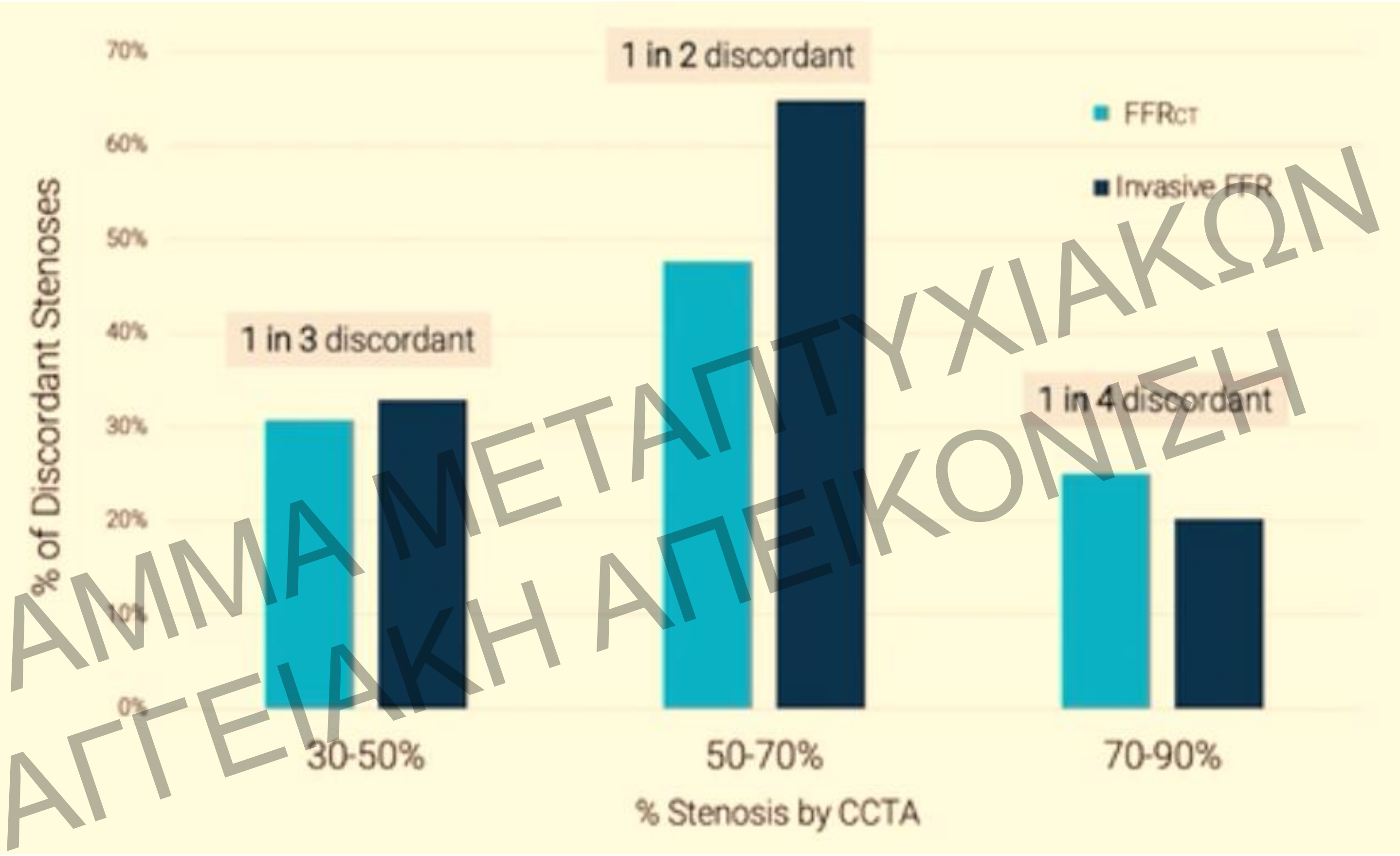
Danad I et al, Eur Heart J. 2017 Apr 1;38(13):991-998
Deng SB et al. Int J Cardiol. 2015

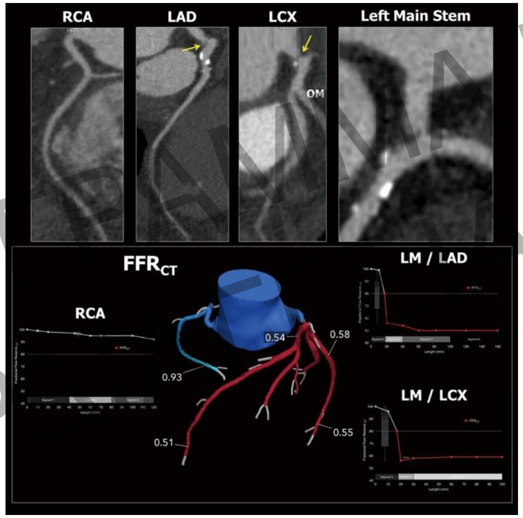
DISCORDANCE ANATOMY-PHYSIOLOGY



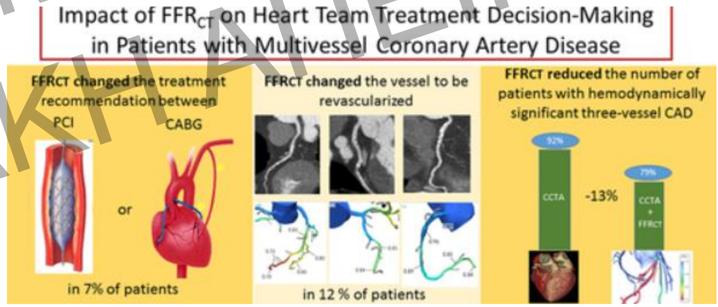
Advance Registry
Tonino *et al*, *JACC, 2010*
Curzen *et al.* *Circ Int, 2014*

CT – FFR current landscape

- The technology is **well validated** against **invasive FFR**
- **Incremental value** over CCTA demonstrated in several studies
- Depends primarily on the **CCTA image quality**
- **Calcifications** might be an issue, less with software improvement



SYNTAX III REVOLUTION Trial



HIGHLY CALCIFIED MULTIVESSEL DISEASE
ONLY 4/222 PATIENTS EXCLUDED DUE TO CALCIFICATIONS
AND FFRCT FEASIBLE IN TOTAL 88% OF CASES

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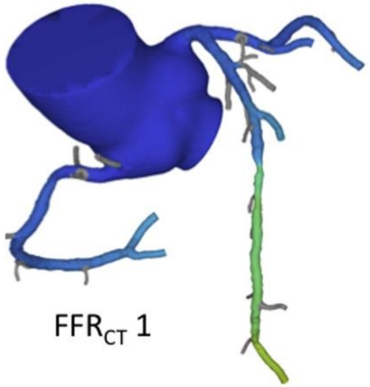
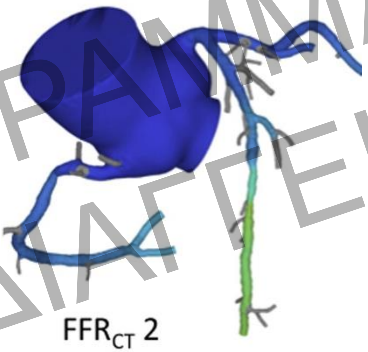
Andreini D et al. Circulation: Cardiovascular Interventions. 2019

Reproducibility of FFR_{CT}

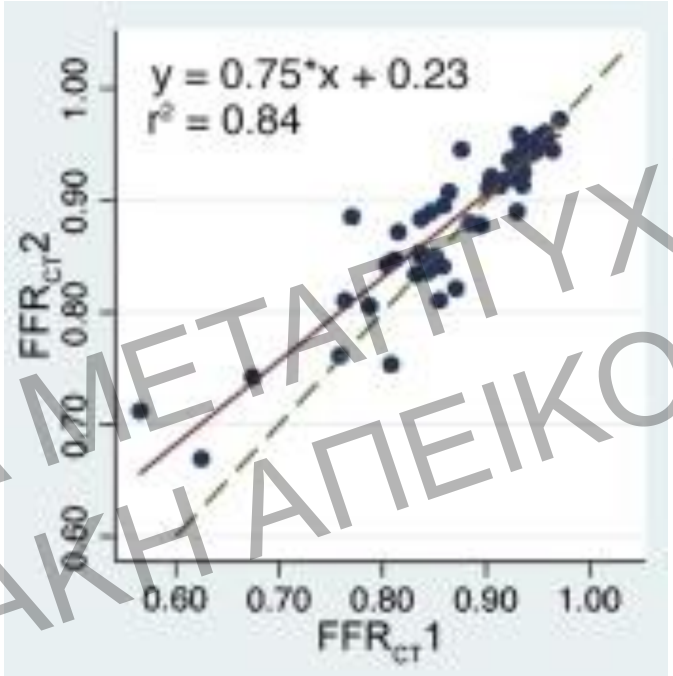
HeartFlow Analyst 1



HeartFlow Analyst 2

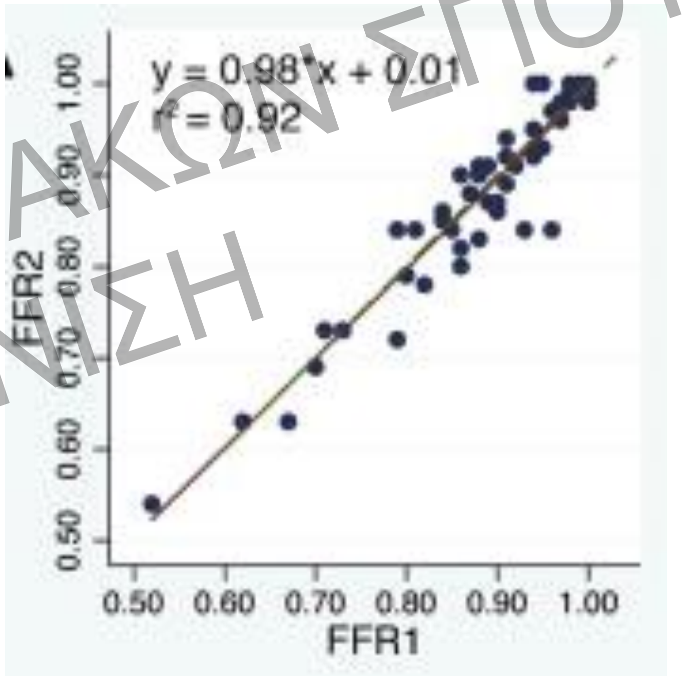


Repeated FFR_{CT}



	Mean	Standard deviation
FFR_{CT}		
Difference	0.011	0.034

Repeated Invasive FFR



	Mean	Standard deviation
FFR		
Difference	−0.004	0.033

n=28 pts, 58 vessels

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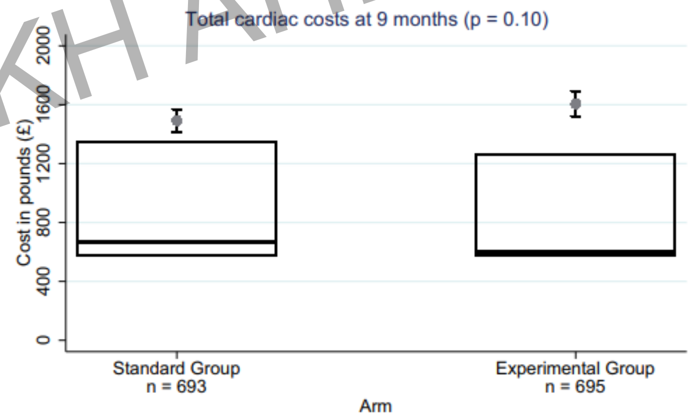
Gaur S *et al.* *JCCT, 2014*

CT – FFR current landscape

- The technology is **well validated** against **invasive FFR**
- **Incremental value** over CCTA demonstrated in several studies
- Depends primarily on the **CCTA image quality**
- **Calcifications** might be an issue, less with software improvement
- Observational trials have shown the ability of CT – FFR to **reduce ICA**
- **Lowering costs** has **not** been demonstrated



Study arm	Median (25th and 75th centile)	Mean (+/- 1 standard error)
Standard Group	£670 (£574 to £1,346)	£1,491 (£1,414 to £1,569)
Experimental Group	£600 (£572 to £1,263)	£1,605 (£1,521 to £1,690)

Douglas PS et al. Eur Heart J. 2015
Hlatky MA et al. JACC. 2015
Norgaard BL, Heart. 2022
Curzen N et al. Eur Heart J. 2021
Hlatky MA et al. JCCT. 2023

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CT – FFR intergration into guidelines

- 2016/2017 NICE Guidelines
  - ***CCTA First Line test*** for CAD regardless of risk factor or pre-test probability
  - ***FFR_{CT} recommended*** as add on predicting ***costs savings*** of £ 9.1 Million

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  - ***CCTA First Line test*** for CAD regardless of risk factor or pre-test probability
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- 2018 Japanese Circulation Society Guidelines

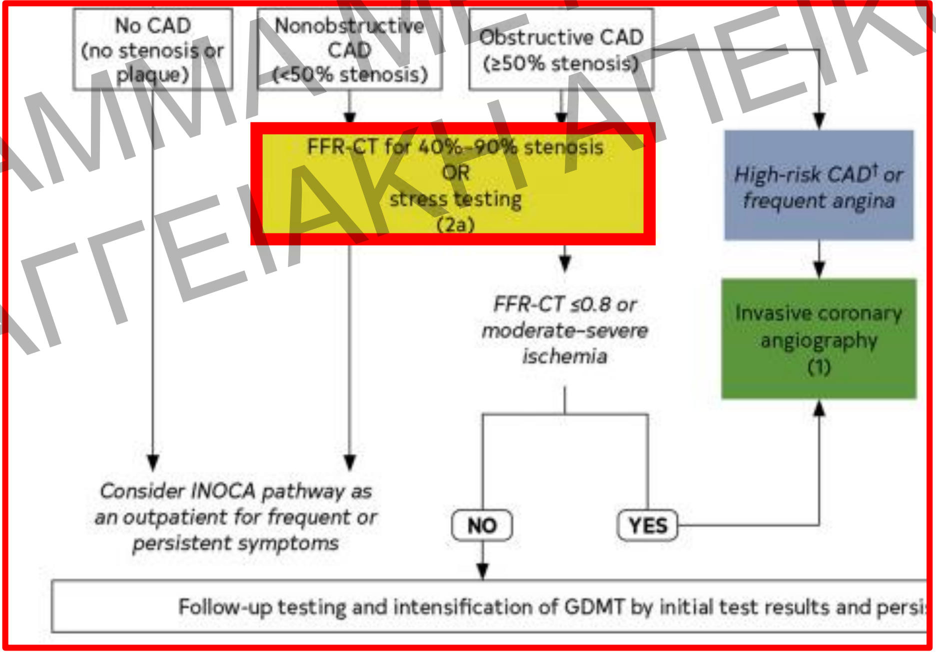
Table 36. Recommendations and Levels of Evidence for FFR-CT

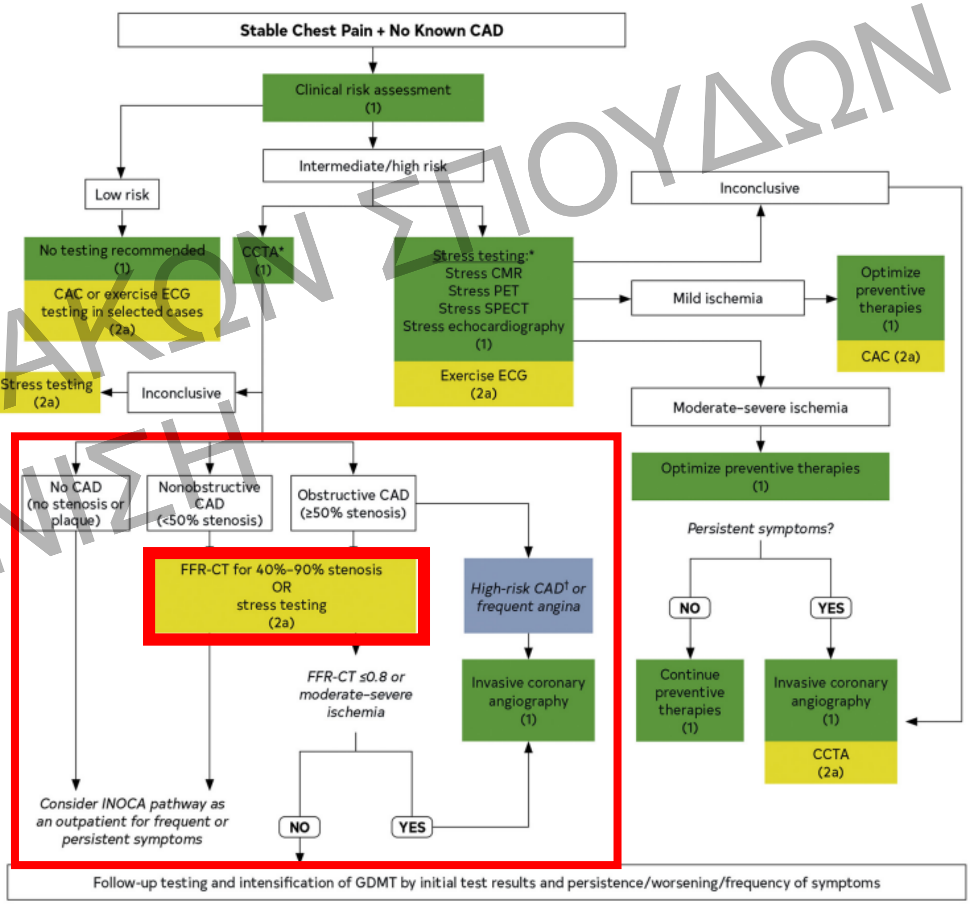
	COR	LOE	GOR (MINDS)	LOE (MINDS)
Angina patients with more than a moderate degree of coronary stenosis on cardiac CT; patients whose overall definitive diagnosis for myocardial ischemia is difficult; moreover, patients who are candidates for revascularization once myocardial ischemia is detected	IIb	B	B	II

Yamagishi M et al. Circ J. 2021

CT – FFR intergration into guidelines

- 2016/2017 NICE Guidelines
  - ***CCTA First Line test*** for CAD regardless of risk factor or pre-test probability
  - ***FFR_{CT} recommended*** as add on predicting ***costs savings*** of £ 9.1 Million
- 2018 Japanese Circulation Society Guidelines
- 2021 ACC AHA/AHA Chest Pain Guidelines





Gulati M et al. J Am Col Cardiol. 2021

CT – FFR intergration into guidelines

- 2016/2017 NICE Guidelines
  - ***CCTA First Line test*** for CAD regardless of risk factor or pre-test probability
  - ***FFR_{CT} recommended*** as add on predicting ***costs savings*** of £ 9.1 Million
- 2018 Japanese Circulation Society Guidelines
- 2021 ACC AHA/AHA Chest Pain Guidelines
- 2024 ESC CCS Guidlines

Recommendation Table 13 — Recommendations for selection of initial diagnostic tests in individuals with suspected chronic coronary syndrome (see also Evidence Table 13)

Recommendations	Class[a]	Level[b]
Selection of non-invasive testing		
It is recommended to select the initial non-invasive diagnostic test based on pre-test likelihood of obstructive CAD, other patient characteristics that influence the performance of non-invasive tests,[c] and local expertise and availability.[29,148]	I	C
In symptomatic patients in whom the pre-test likelihood of obstructive CAD by clinical assessment is >5%, CCTA or non-invasive functional imaging for myocardial ischaemia is recommended as the initial diagnostic test.[33,148,178,187,189,211,212,219,222,390]	I	B
To rule out obstructive CAD in individuals with low or moderate (>5%–50%) pre-test likelihood, CCTA is recommended as the preferred diagnostic modality.[29,148]	I	B
CCTA is recommended in individuals with low or moderate (>5%–50%) pre-test likelihood of obstructive CAD if functional imaging for myocardial ischaemia is not diagnostic.[391]	I	B
Functional imaging for myocardial ischaemia is recommended if CCTA has shown CAD of uncertain functional significance or is not diagnostic.[392–394]	I	B
In patients with a known intermediate coronary artery stenosis[d] in a proximal or mid coronary segment on CCTA, CT-based FFR may be considered.[395–401]	IIb	B

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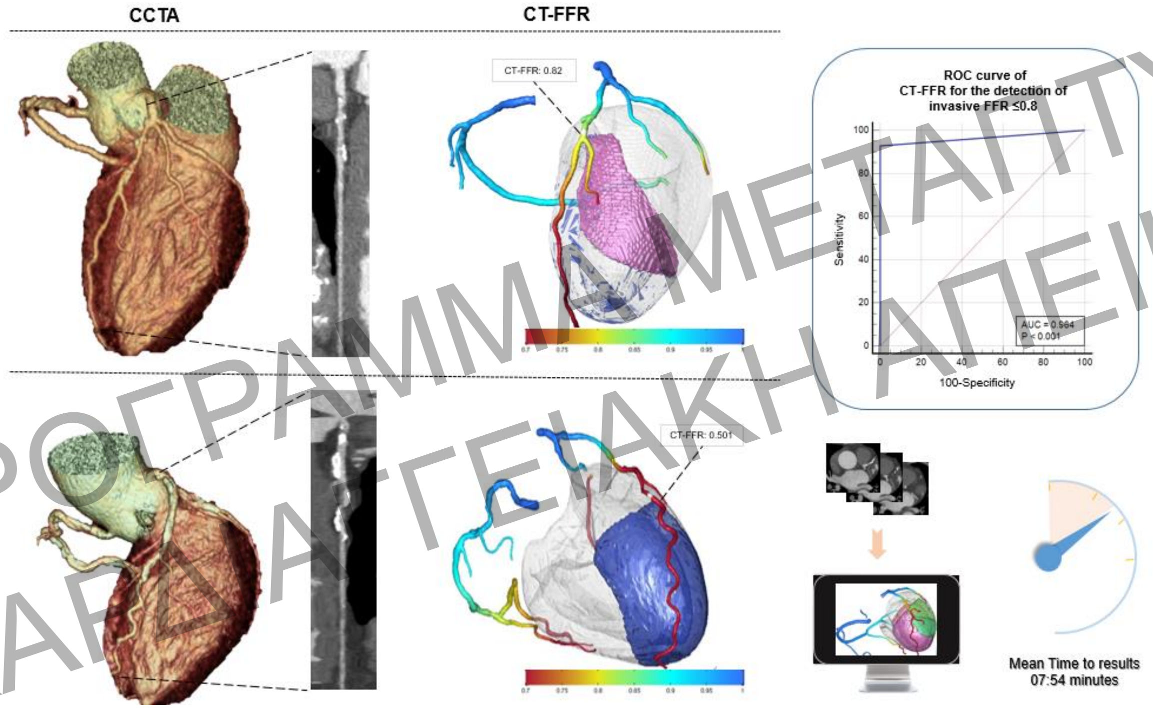
2024 ESC guidelines on the management of chronic coronary syndromes, Eur Heart J 2024

CT – FFR Issues

- Technological Advancements
  - Universally available CT-FFR technology
  - Faster, more accurate and on-site



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Giannopoulos AA et al. EutoIntervention. 2017
Giannopoulos AA et al AJR 2023

CT – FFR clinical intergration

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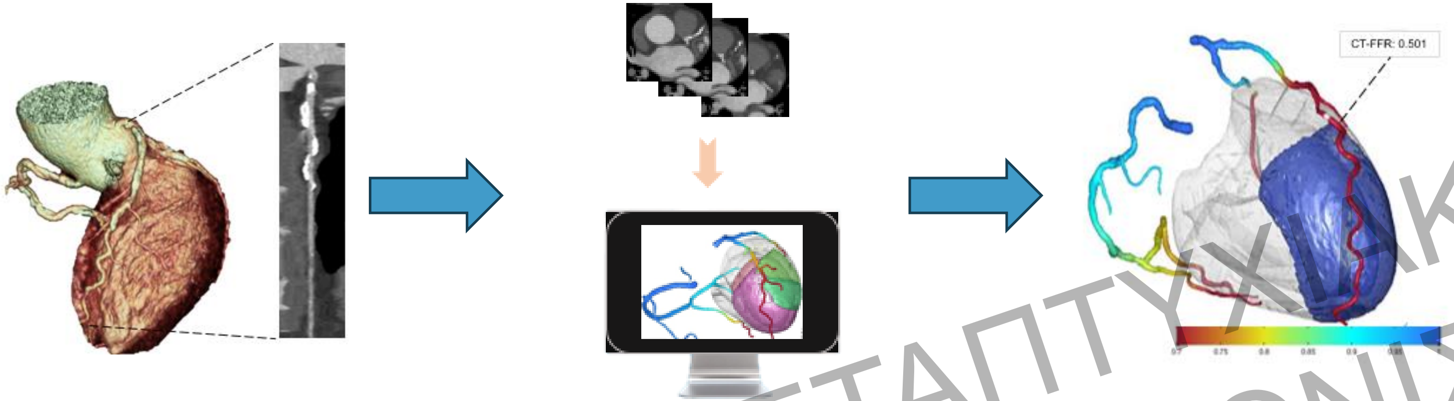
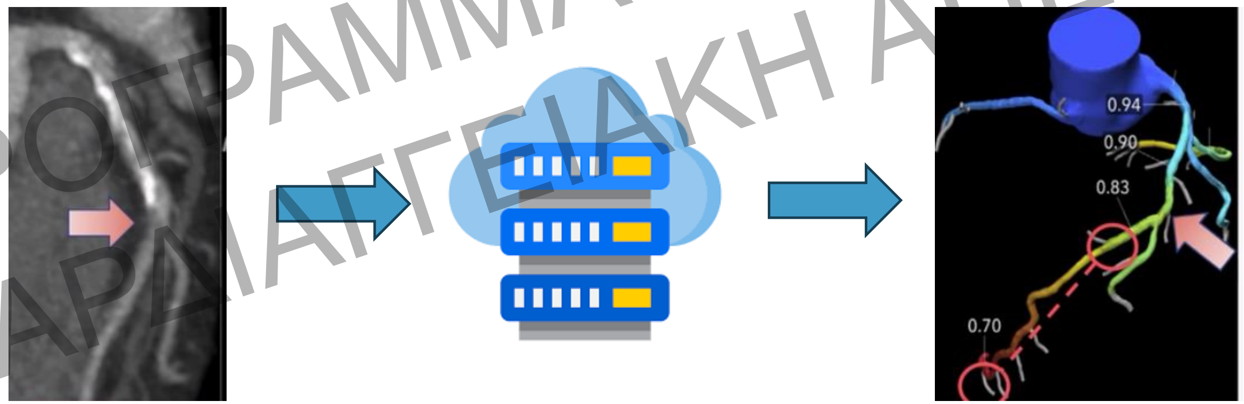


- In all stenoses >50% < 90%
- Preferential solitary stenosis
- Not in severe coronary calcification (CACS>1000)
- 7-10 minutes/patient
- Report integrated in CCTA report with potential suggestion for downstream testing or not

MGH 1811



- CCTA interpreted and reported at once
- Decision for FFR_{CT}
- Data transfer to HeartFlow cloud
- 12-24 hours turnaround time
- Review of FFR_{CT} results
- Separate report on hemodynamic significance

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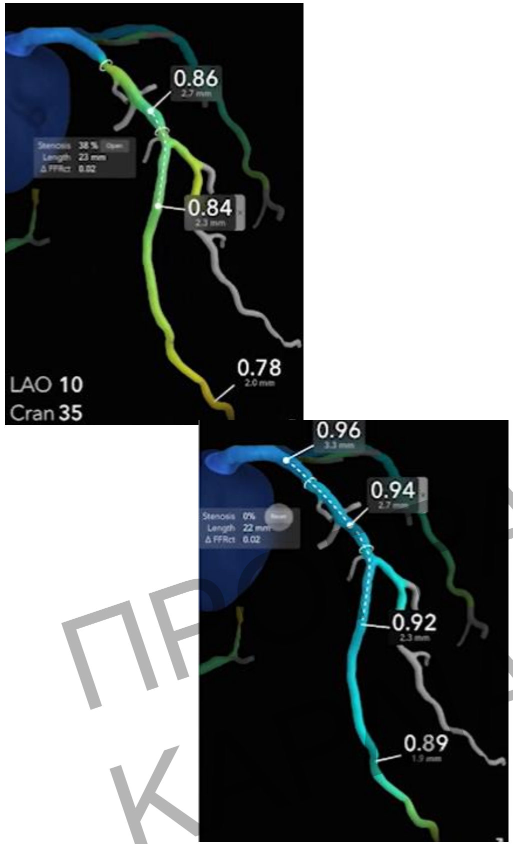
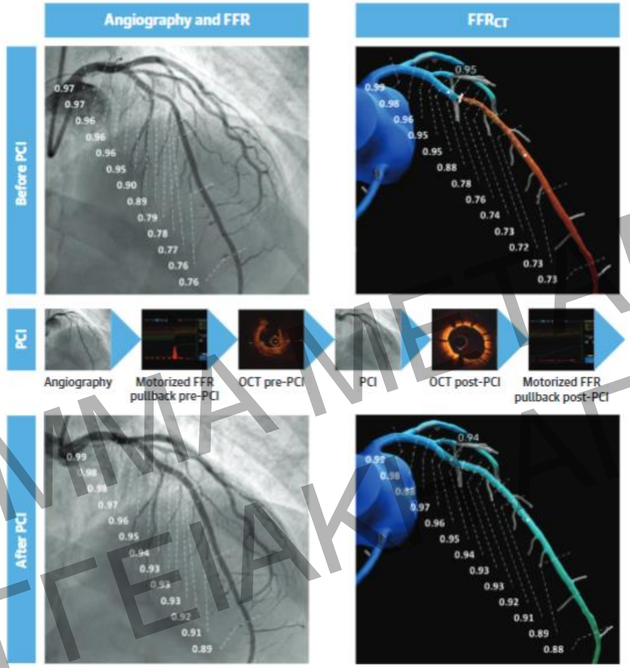
Courtesy Dr. Brian Ghoshhajra

CT – FFR Future Applications

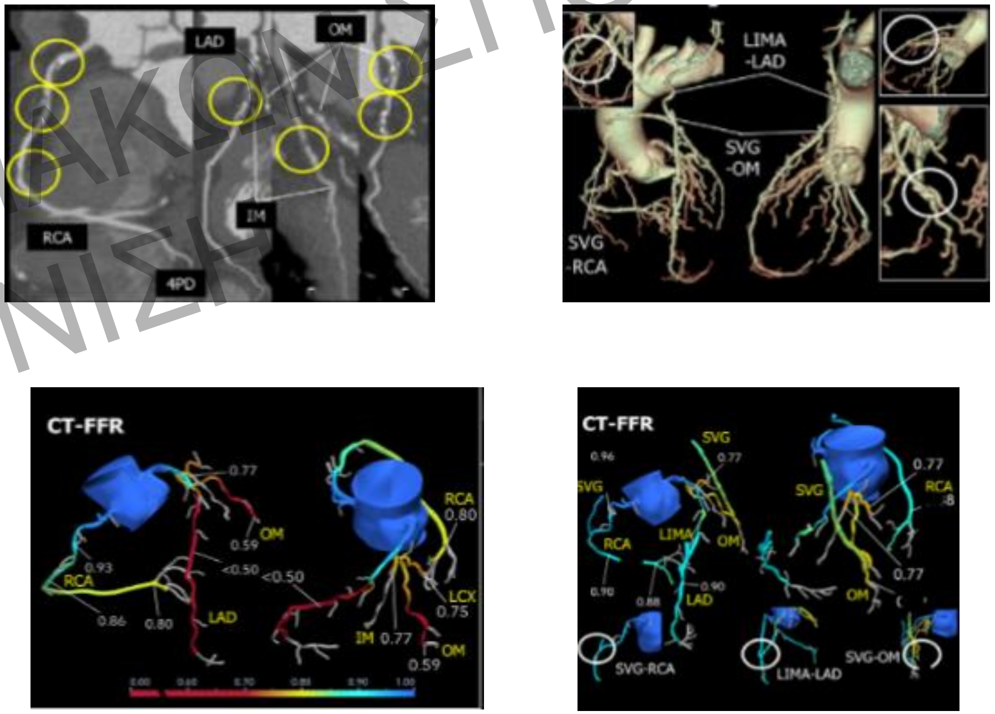
Virtual Stenting PCI Planning





CABG Patients

Planning *Post-CABG*



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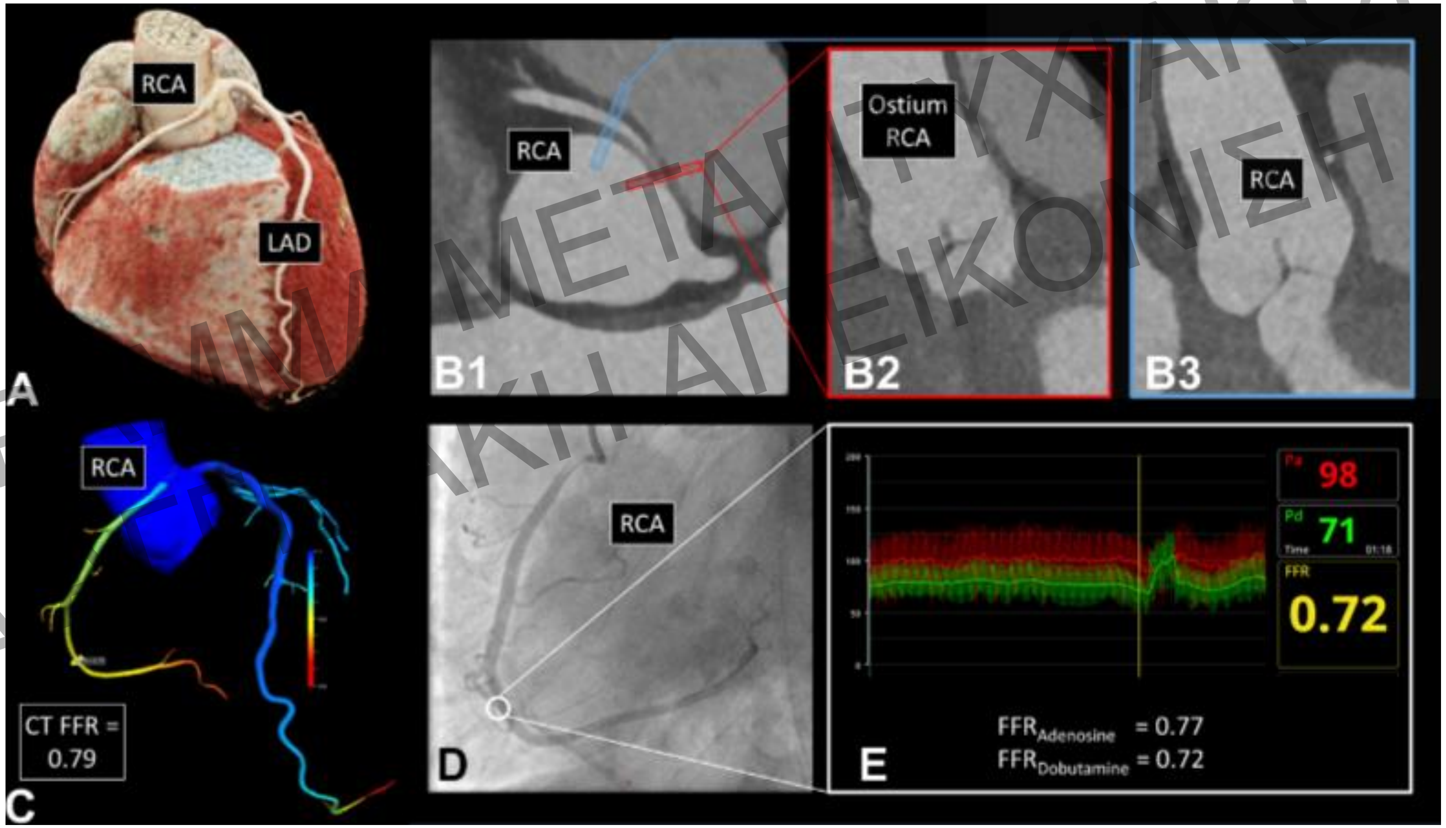
Ihdayhid AR et al. JACC Interventions. 2017
Sonck J et al. J Am Col Cardiol Img. 2022
Andreini D et al JCCT. 2022

CT – FFR Future Applications

- **Coronary anomalies**
  - Beyond simulation of vasodilation
  - Assessing dynamic component



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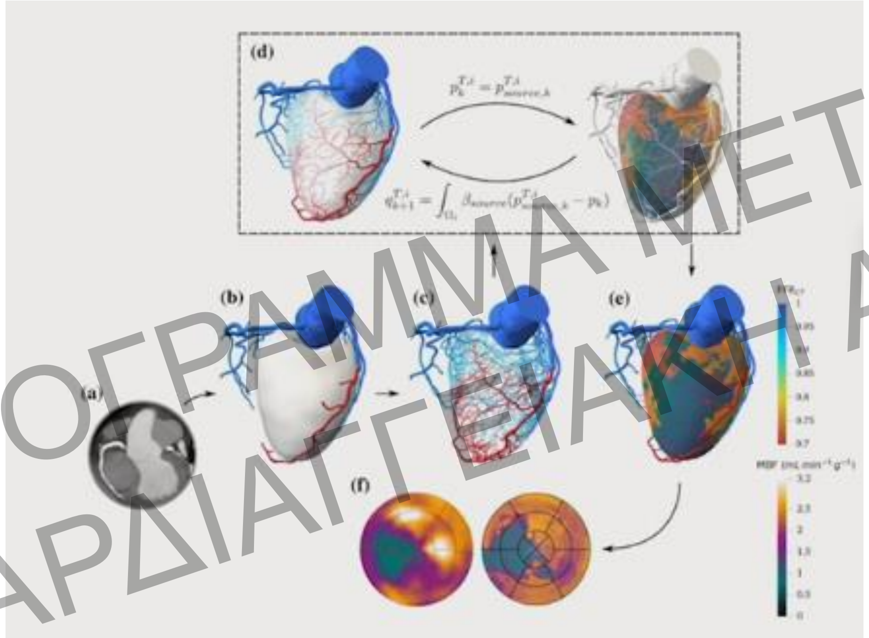
Bigler MR, Giannopoulos AA, et al. JACC:Case Reports. 2022

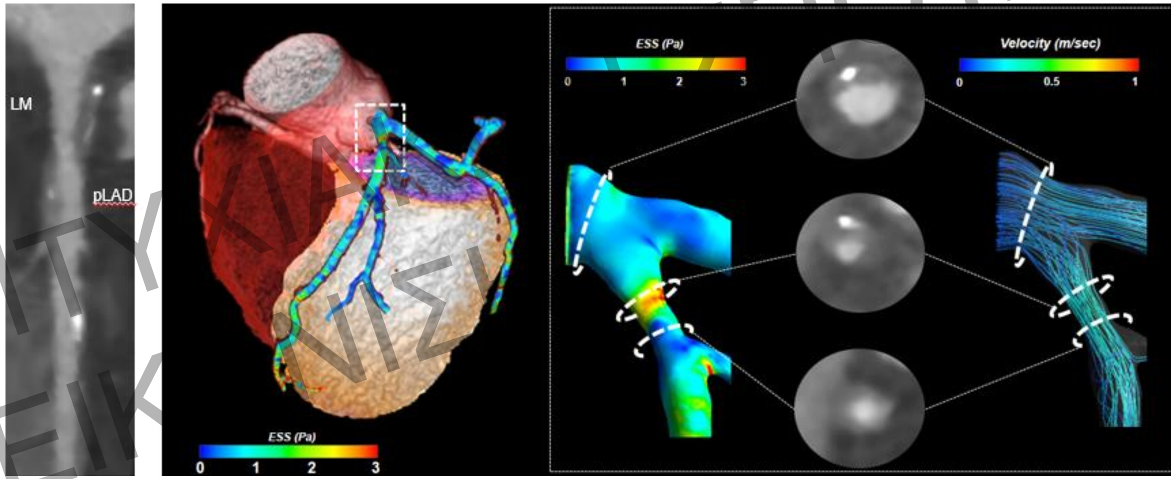
CT – FFR Future Applications

- **Research Applications**

Assessment of Microcirculation



Insights into Pathophysiology of Atherosclerosis



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Giannopoulos AA et al. Eur Hear J. 2018
Papamanolis et al Annals of Biomedical Engin. 2021

Take home messages

- CTP is a **robust** and **accurate** method to assess myocardial ischemia, although **less well studied** as CT-FFR
- CTP has not yet found widespread clinical use, due to **relative complexity** of the test and **radiation** issues
- **Newer-g** … P
- CT-FFR is … ns on CCTA
- CT-FFR is an already, **FDA-approved**, but still developing technology
- CT-FFR allows to **select appropriate** patients/lesions for **revascularization** procedures and **cut costs (?)**
- CT-FFR still has **limitations** from poor anatomical models and intrinsic limitations from physiological models applied

KNOWN SEVERE CAD> CTP
LESS SEVERE CAD / SINGLE LESIONS> CT-FFR

Thank you for your attention

EACVI Cardiac Computed Tomography Course 2026

16 April - 18 April 2026

Seminar

AC Hotel (Nice, FR)

EACVI 2026

03 Dec 2026 - 05 Dec 2026

Milan, Italy

Organised by:

EACVI

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