

Beyond Stenosis: Ischemia and Plaque Assessments in Coronary CTA



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Controversies in Cardiovascular Disease
2016



DISCLOSURE

Daniel S. Berman, M.D.

declares the following relationships:

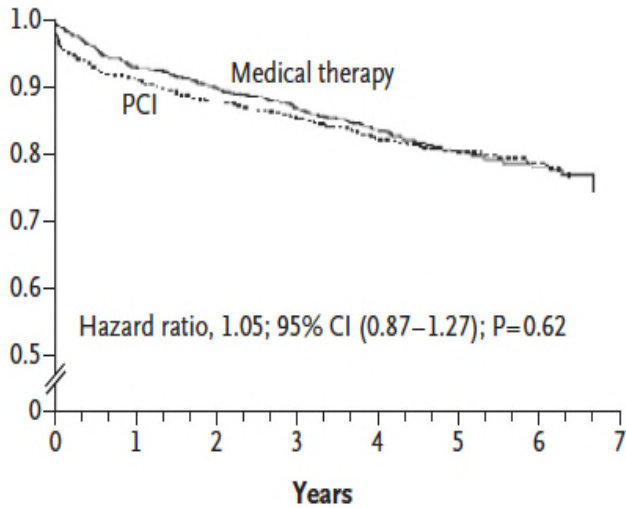
Consultant:	Molecular-Dynamics
Royalties:	Cedars-Sinai Medical Center

Beyond Stenosis: Ischemia and Plaque Assessments in Coronary CTA

- General considerations
- Stenosis
- Ischemia
- Plaque

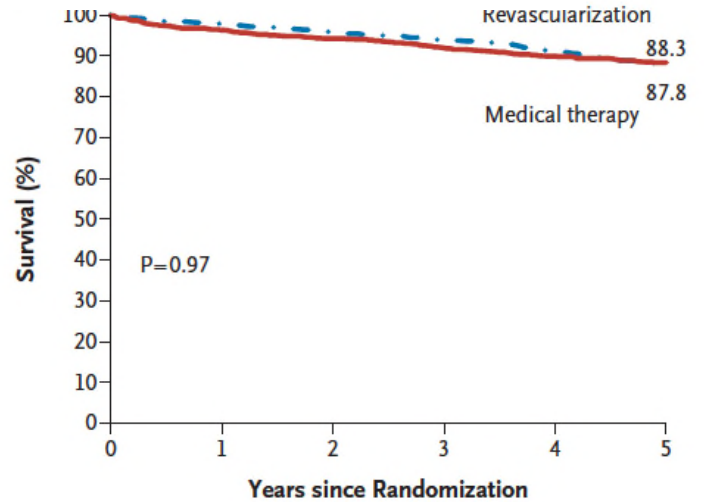
Decisions of coronary revascularization should not be based upon anatomic stenosis alone

COURAGE Trial (D/MI/CVA)



2,287 individuals with angiographically obstructive CAD and ischemia assigned to PCI or medical tx and followed for 4.6 years

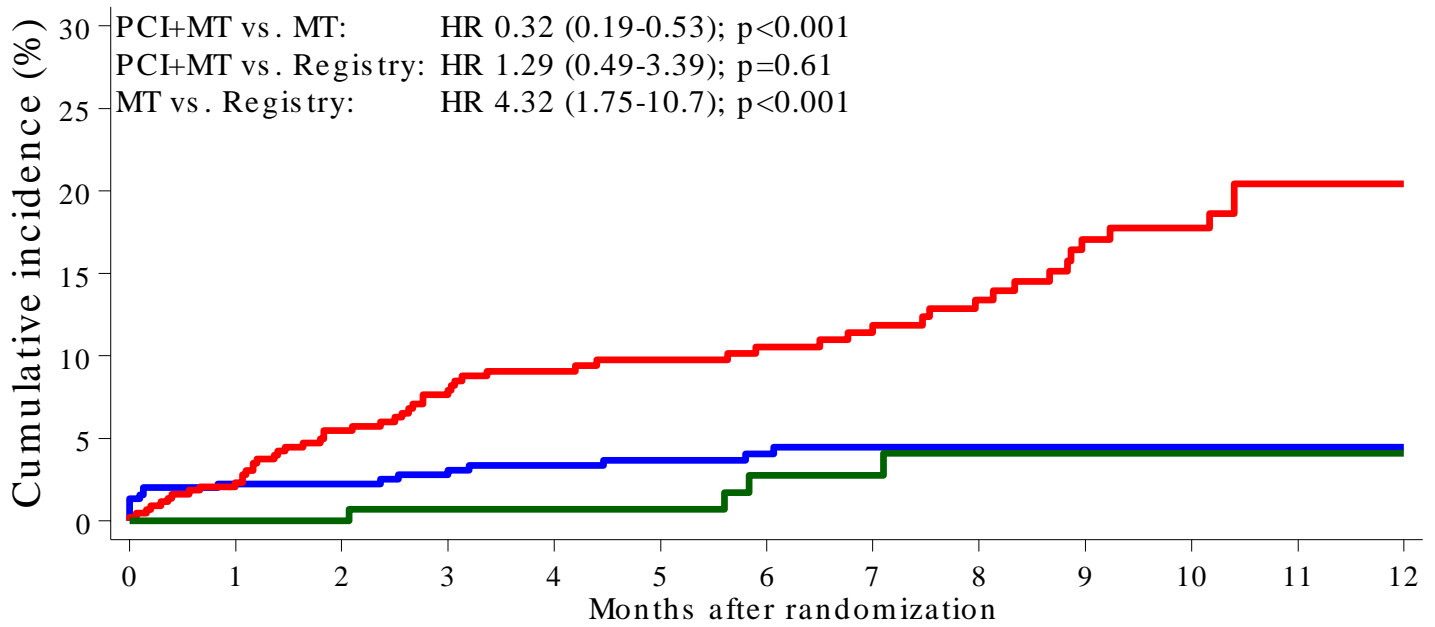
BARI 2D Trial (D/MI/CVA)



2,368 diabetic patients assigned to revascularization or medical tx and followed for 5 years

Primary Outcome

All-cause death, MI, or urgent revascularization

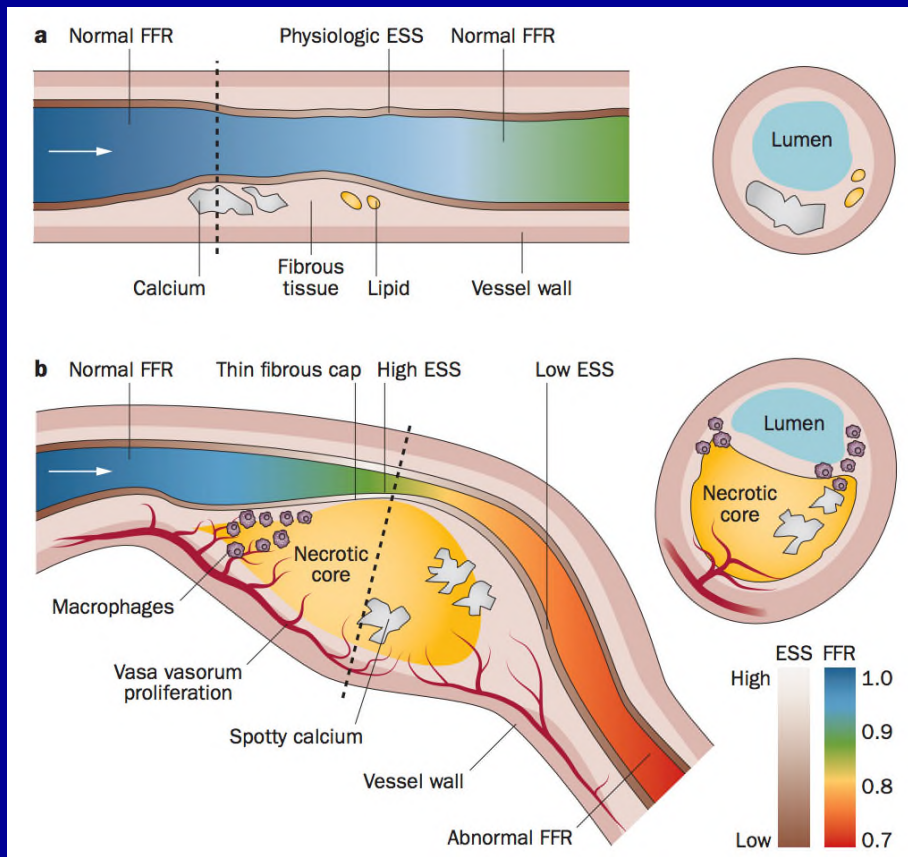


No. at risk

MT	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI+MT	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

De Bruyne B et al. NEJM 2012

Multiple Features Beyond Stenosis Contribute to High-Risk Plaque



Assessable by OCTA

- Plaque burden
- Lipid core
- Spotty calcification
- Low endothelial shear stress (ESS)
- FFR

Beyond Stenosis: Ischemia and Plaque Assessments in Coronary CTA

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Risk-stratification in CAD

Stenosis has been given a bad rap

Risk-stratification in CAD

Stenosis has been given a bad rap

- Most MI's are caused by event in plaque with mild stenosis; but,
 - Mild stenoses: far more numerous
- Occlusive thrombosis: more likely in severely stenosed artery

Arbab-Zadeh, Fuster JACC 2015
Alderman, et al: CASS, JACC 1993

CASS: Rate of Segment Occlusion by Baseline Stenosis Severity

Stenosis at Baseline

- 5-49%
- 50-80%
- 81-95%

Occlusion at Follow-up

- 2.3%
- 10.1%
- 23.6%

Follow-up angio (n=298):

42-66 months after randomization

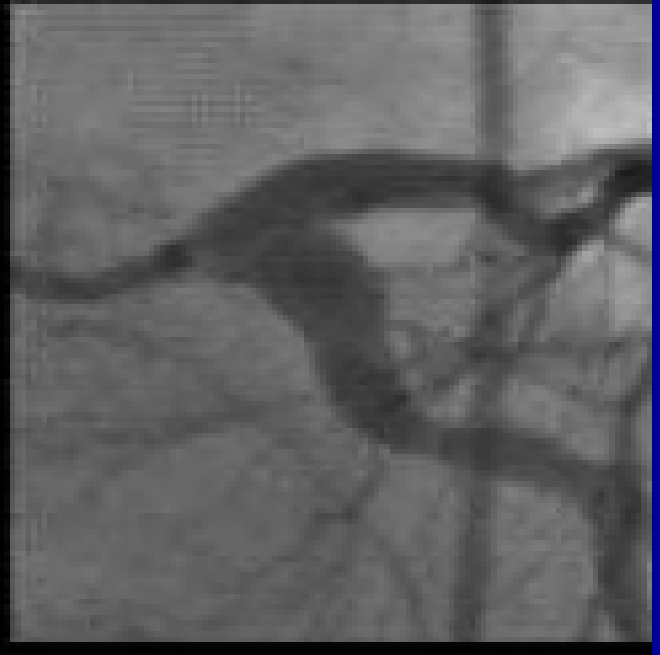
3049 non-bypassed segments

Alderman, et al: JACC 1993

Left Main Coronary Stenosis



CTA



CATH

BLUROB

Left Main Coronary Stenosis



- Left main CAD: excluded in COURAGE, BARI 2D, ISCHEMIA

DEKOB

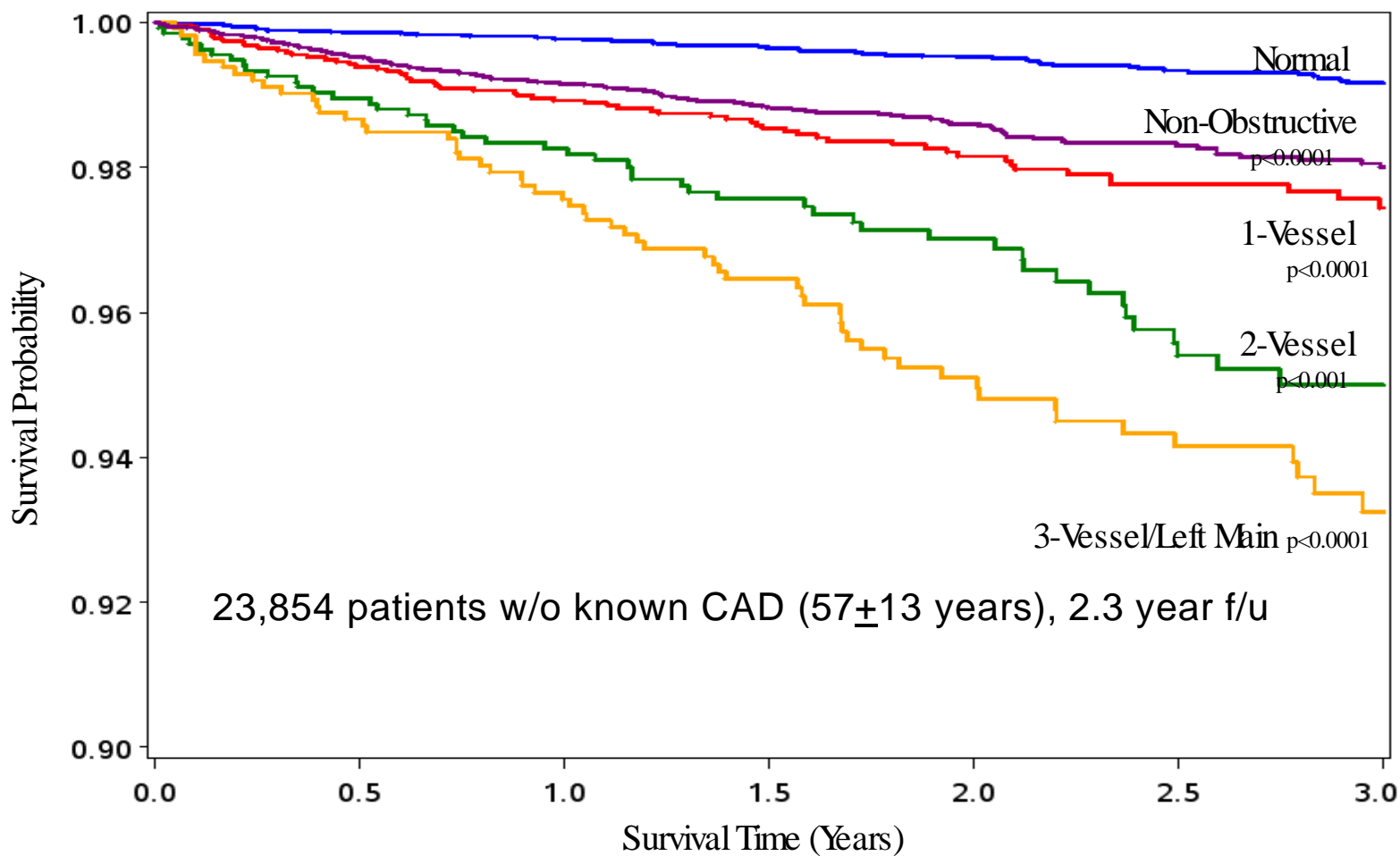
Left Main Coronary Stenosis



- Left main CAD: excluded in COURAGE, BARI 2D, ISCHEMIA
- Frequency: 5-7% of invasive coronary angiograms (Fijedet ~~E~~HJ2012)

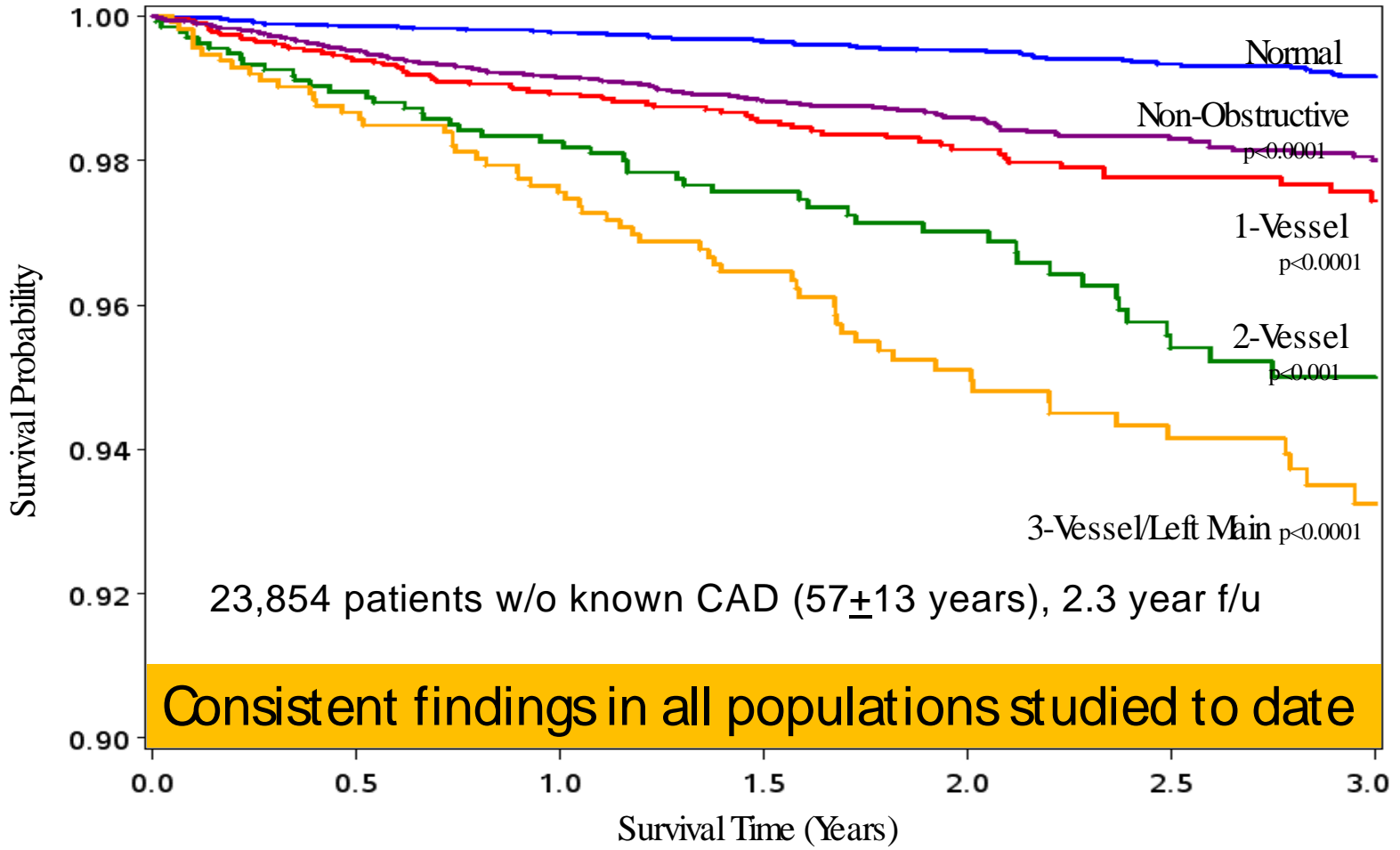
DEKOP

Prognostic Value of CCTA CAD Extent / Severity



Source: CONFIRMMin et al. J Am Coll Cardiol 2011

Prognostic Value of CCTA CAD Extent / Severity



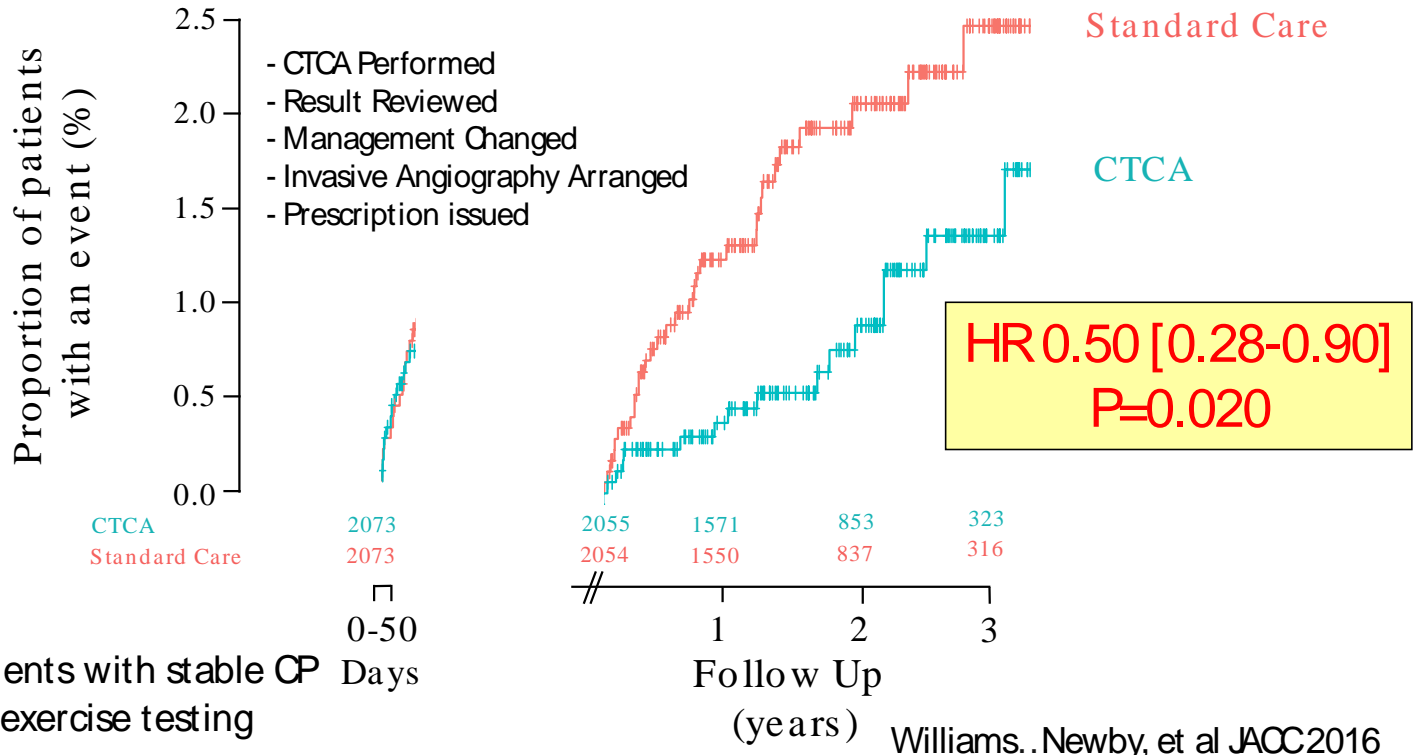
Source: CONFIRMMin et al. J Am Coll Cardiol 2011



CHD Death and MI in Scot Heart Trial

Post-hoc 50-Day Landmark Analysis

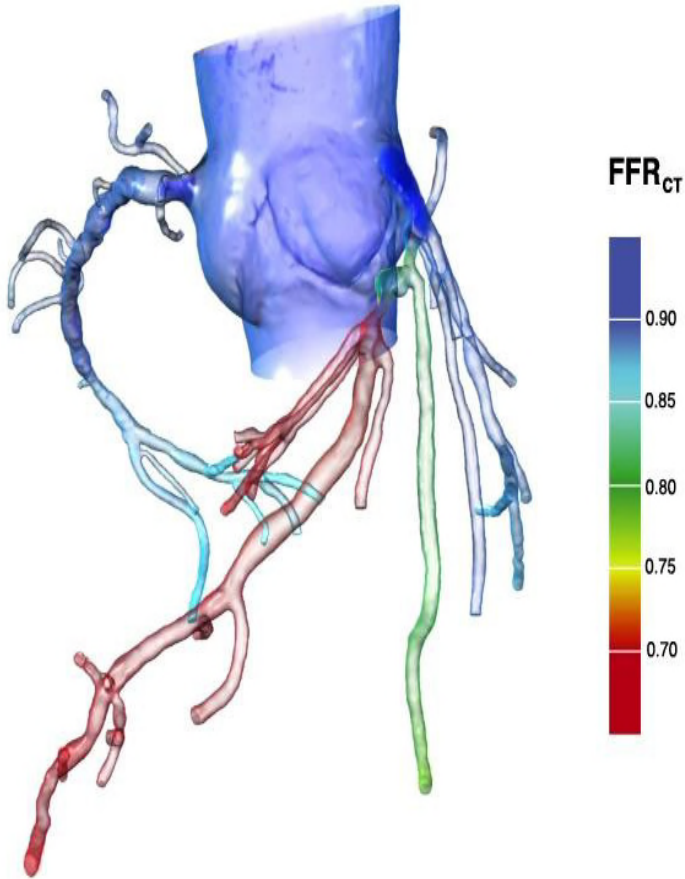
Implementation Delay	Impact of Alterations in Therapy
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Beyond Stenosis: Ischemia and Plaque Assessments in Coronary CTA

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- Ischemia
- Plaque

Non-Invasive FFR_{CT}

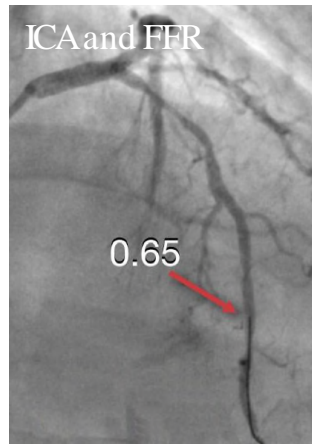


- From typically acquired CCTA
- Computational fluid dynamics
 - Stenosis
 - Vessel volume after lesion
 - Myocardial mass distal to lesion
- No additional acquisition, radiation
- No modification to imaging protocols
- No administration of medications

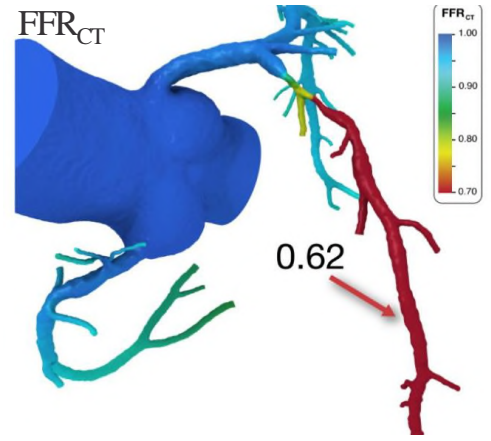
Source: Min JK et al. J Cardiovasc Comput Tomogr 2011; Min JK et al. Am J Cardiol 2012; Min JK et al. J Cardiovasc Comput Tomogr. 2012; Grunau GL et al. Curr Cardiol Report; Min JK et al. JAMA 2012; Koo et al. J Am Coll Cardiol 2012

FFR_{CT} for Lesion-Specific Ischemia

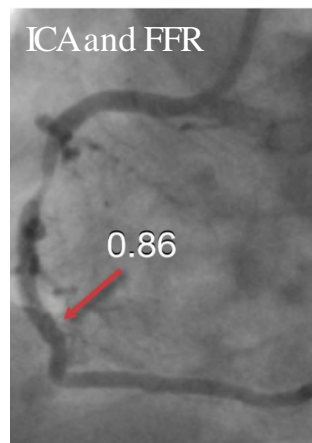
Case 1



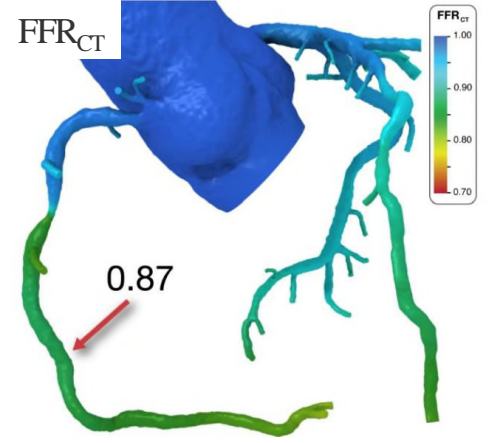
FFR 0.65
= Lesion-specific ischemia



Case 2



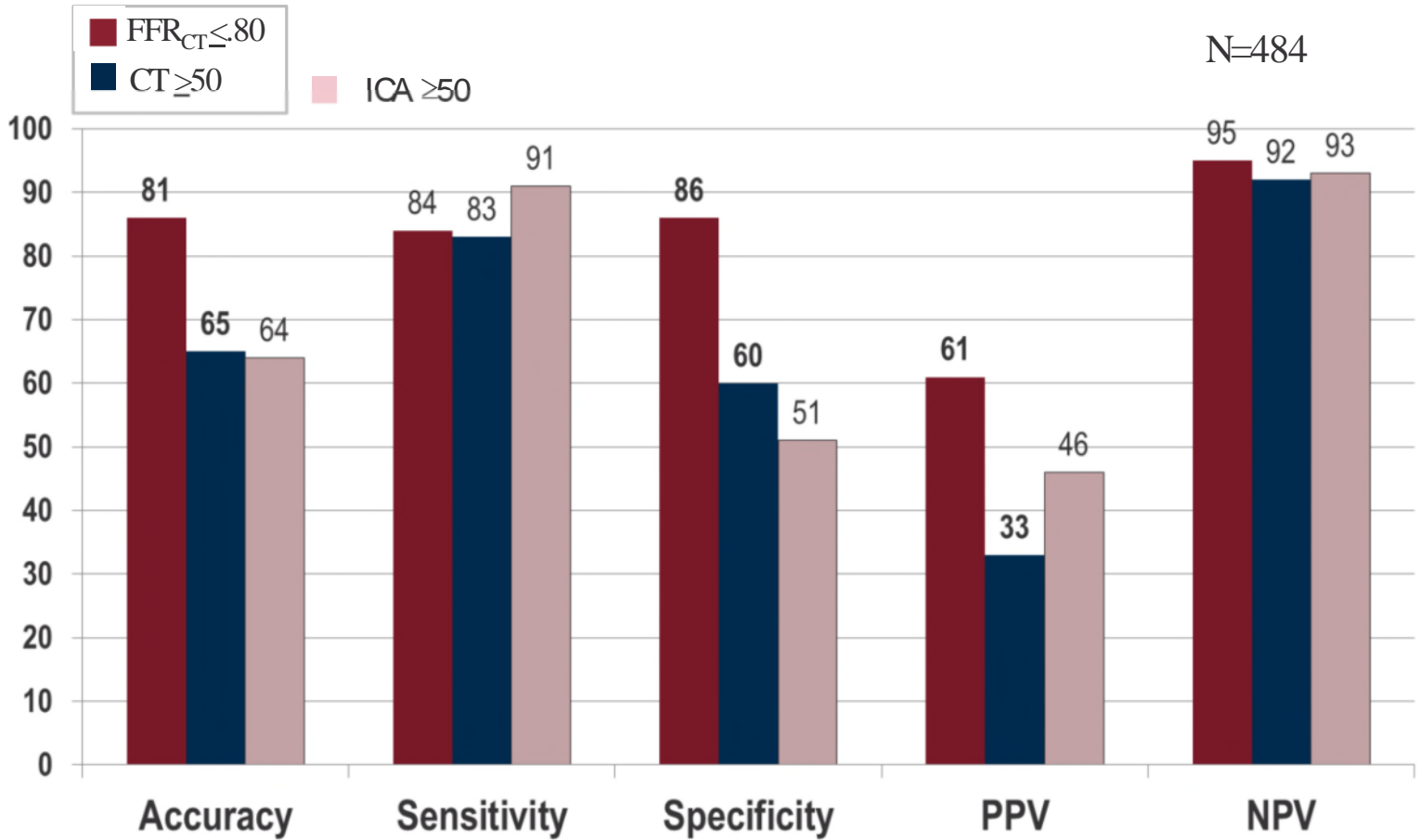
FFR 0.86
= No ischemia



FFR_{CT}: Three (3) Prospective Multicenter Trials

	DISCOVER-FLOW	DeFACTO	NXT
Primary end point	Per pt. diag accuracy	Per pt. diag accuracy; lower limit 95% CI 0.7	Per pt. AUC
Study sites/countries	4 / 3	17 / 5	10 / 8
Site expertise qualification	FFR	CT or FFR	CT plus FFR
CT training of site	Yes	No	Yes
FFR training of site	No	No	Yes
CT quality check	No	No	Yes
CT results reading	Core lab	Core lab	Site
FFR results report	Site	Site	Site with core lab overview
Vessel size for inclusion	≥ 2.0 mm	≥ 1.5 mm	≥ 2.0 mm
Use of NIG with CT	?	75%	99.6%
Software version*	V 1.0 manual	V 1.2 partial automation approx 6 hours (this is specified in manuscript)	V 1.4 increased automation <4 hours
	Koo et al JACC 2011	Min et al JAMA 2013	Norgaard et al JACC 2014

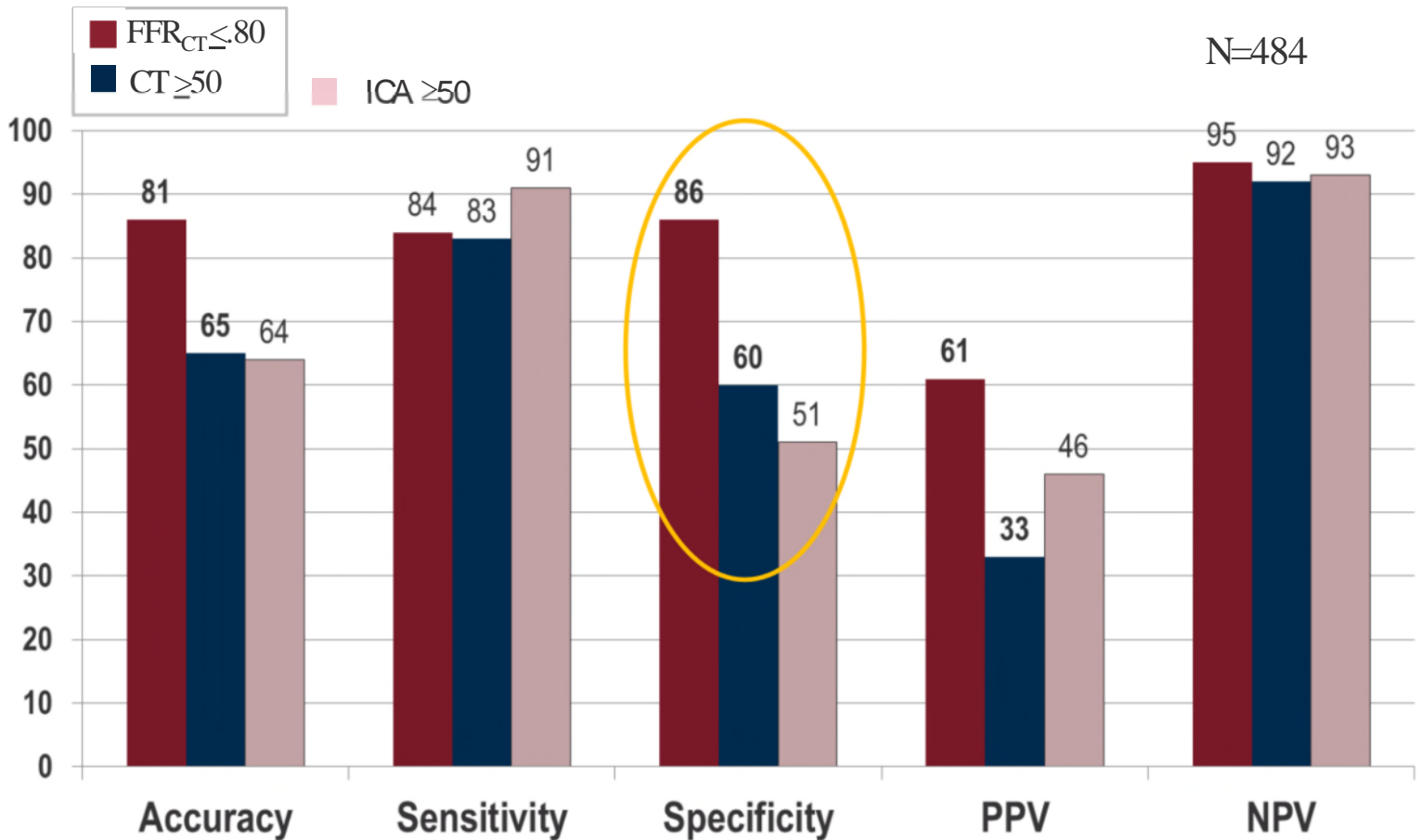
NXTPer-Vessel: FFR_{CT} vs. FFR and ICA



FFR_{CT} diagnostic accuracy superior to both CT and ICA stenosis

Norgaard et al JACC 2014

NXTPer-Vessel: FFR_{CT} vs. FFR and ICA



FFR_{CT} diagnostic accuracy superior to both CT and ICA stenosis
Norgaard et al JACC2014

The FFR_{ct} RIPCORDER Study

- 200 consecutive patients with stable chest pain undergoing CCTA then FFR by ICA) (from NXT)
- Management plans: consensus of 3 interventionalists
- Assumed that patients were suitable for any treatment:
 - OMT, PCI, CABG, more information needed
- Plan 1: based on CCTA
- Plan 2: based on CCTA + FFR_{ct}

Recommended Management Plan on the Basis of CCTA with and without FFR_{CT}

TABLE 1 Summary of Overall Changes to Management in Patients According to Treatment Plan on the Basis of CT Angiography Alone and of FFR_{CT} Data in Addition to CT Angiography

	CT Angiography Alone	CT Angiography With FFR _{CT}	Strategy Change
More data required	38 (19.0)	0	19 (14 to 24)
Optimal medical therapy	67 (33.5)	113 (56.5)	23 (18 to 29)
Percutaneous coronary intervention	87 (43.5)	78 (39.0)	-5 (-2 to -8)
Coronary artery bypass graft surgery	8 (4.0)	9 (4.5)	0.5 (0.1 to 3)

Values are n (%) or % (95% confidence interval). n = 200 patients; p < 0.001 for between group change, angio alone versus FFR_{CT}.

CT = computed tomography; FFR_{CT} = computer tomography-derived fractional flow reserve.

200 patients from NXT: All had subsequent ICA

The FFR_{CT} RIPCARD study

Curzen..Rajani: JACC CV Imaging 2016

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Recommended management plan: changed in 36% of cases

200 patients from NXI: All had subsequent ICA

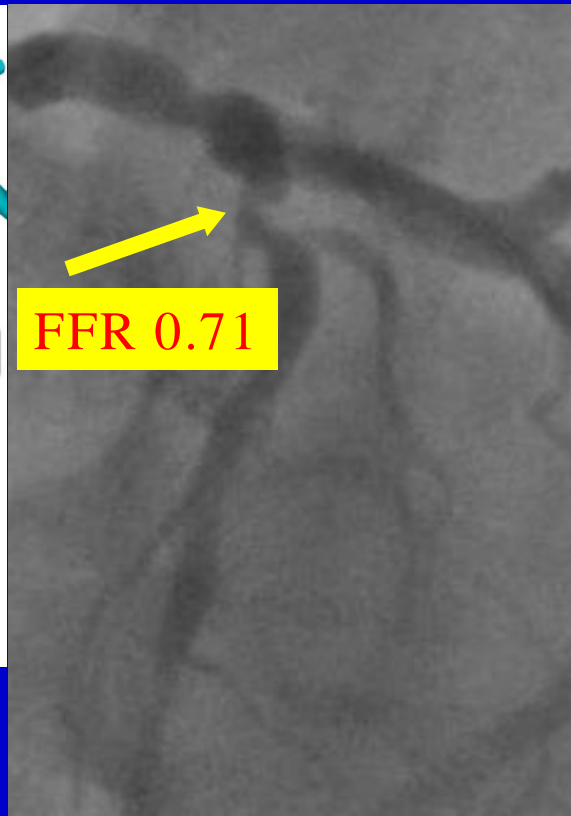
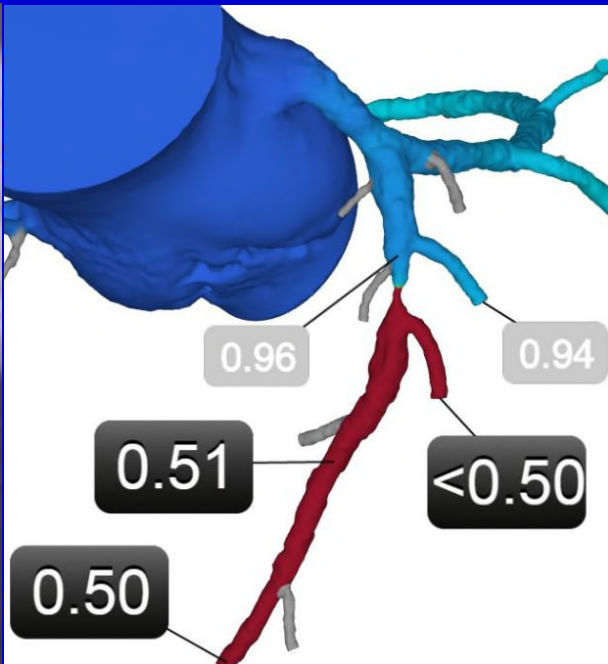
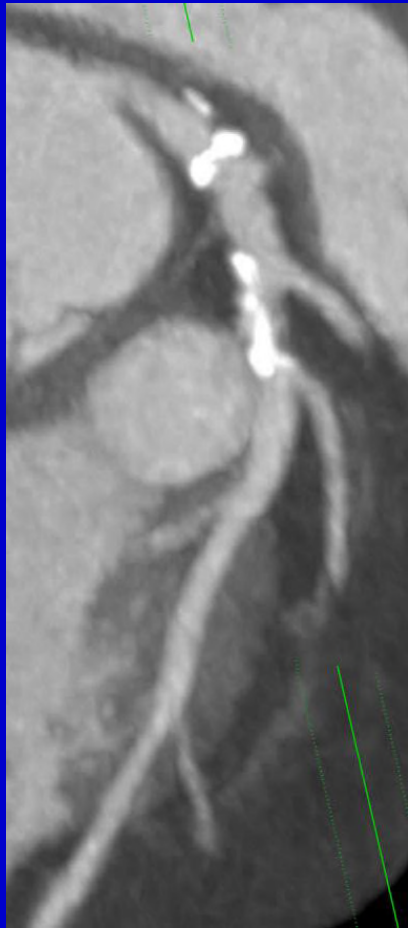
FFRct at Cedars-Sinai: Pilot Experience

- 1550 patients: CCTA from 2/19/16 to 11/4/16
- Research/hospital funding: No charge to patient or insurance
- 393 CCTA sent for FFRct (>25% stenosis)

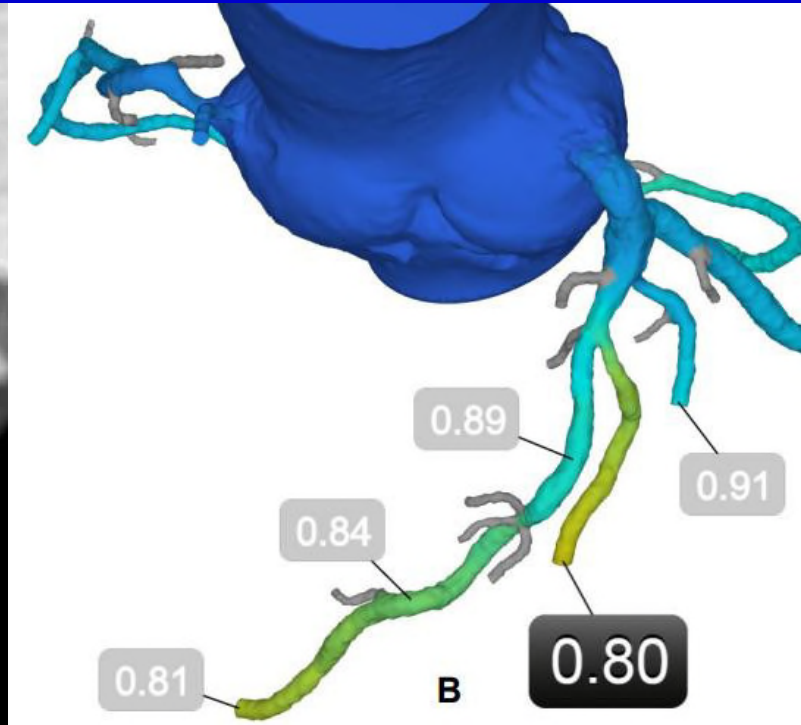
Maximal CT stenosis grade	N of Patients , %	
Grade 1: 1-24%	3	1%
Grade 2: 25-49%	193	49%
Grade 3: 50-69%	109	28%
Grade 4: 70-89%	28	7%
Grade 5: 90-99%	14	4%
Grade 6 : 100%	13	3%
Unevaluable	33	8%

Unpublished 2016

BRADER (79M): Recent onset exertional CP/SOB
Statin, ASA, ARB, BB



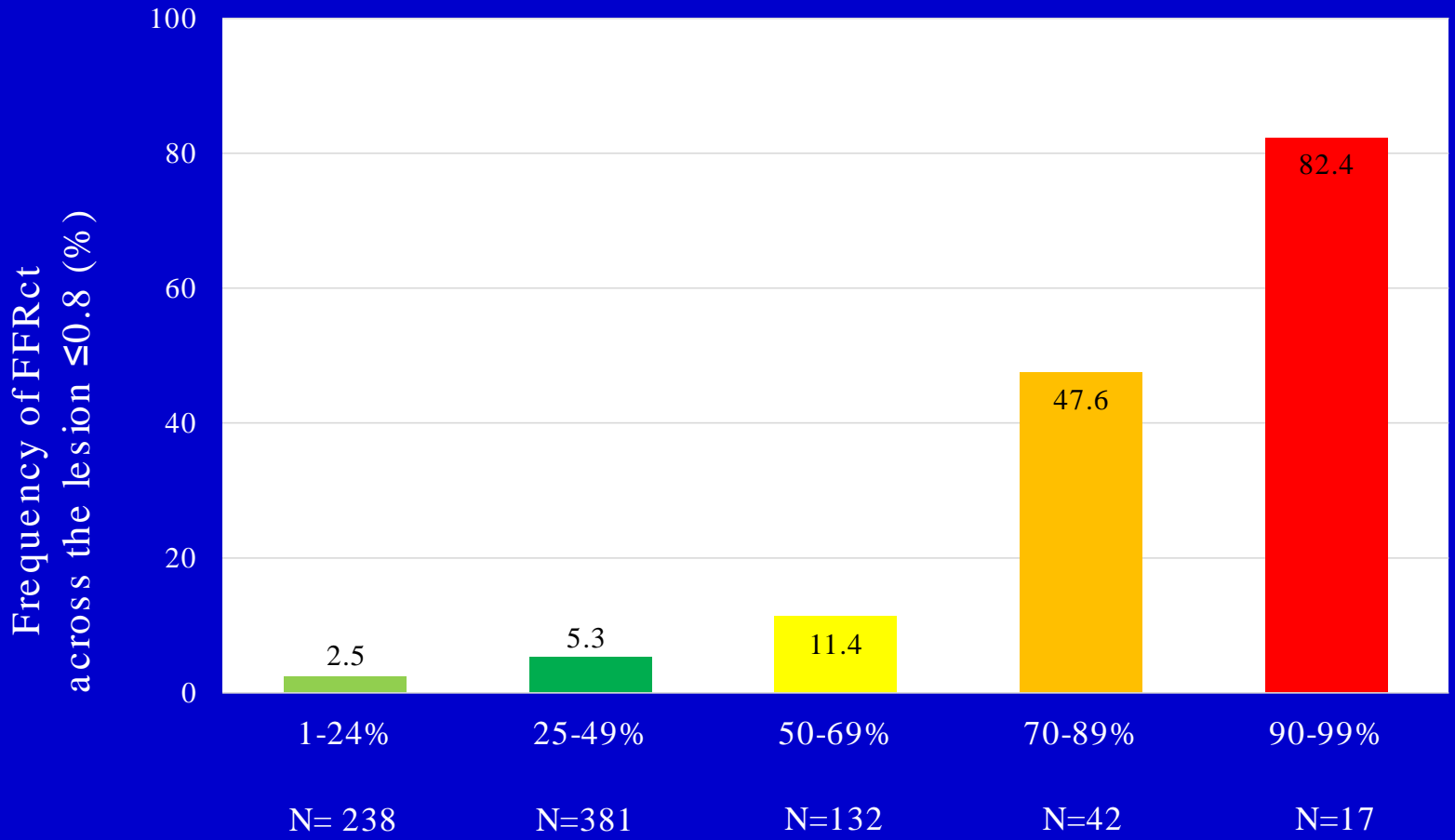
BAUSTE (59M) Non-exertional CP/SOB DM/Insulin; Hypertension



Normal SPECT-MPI



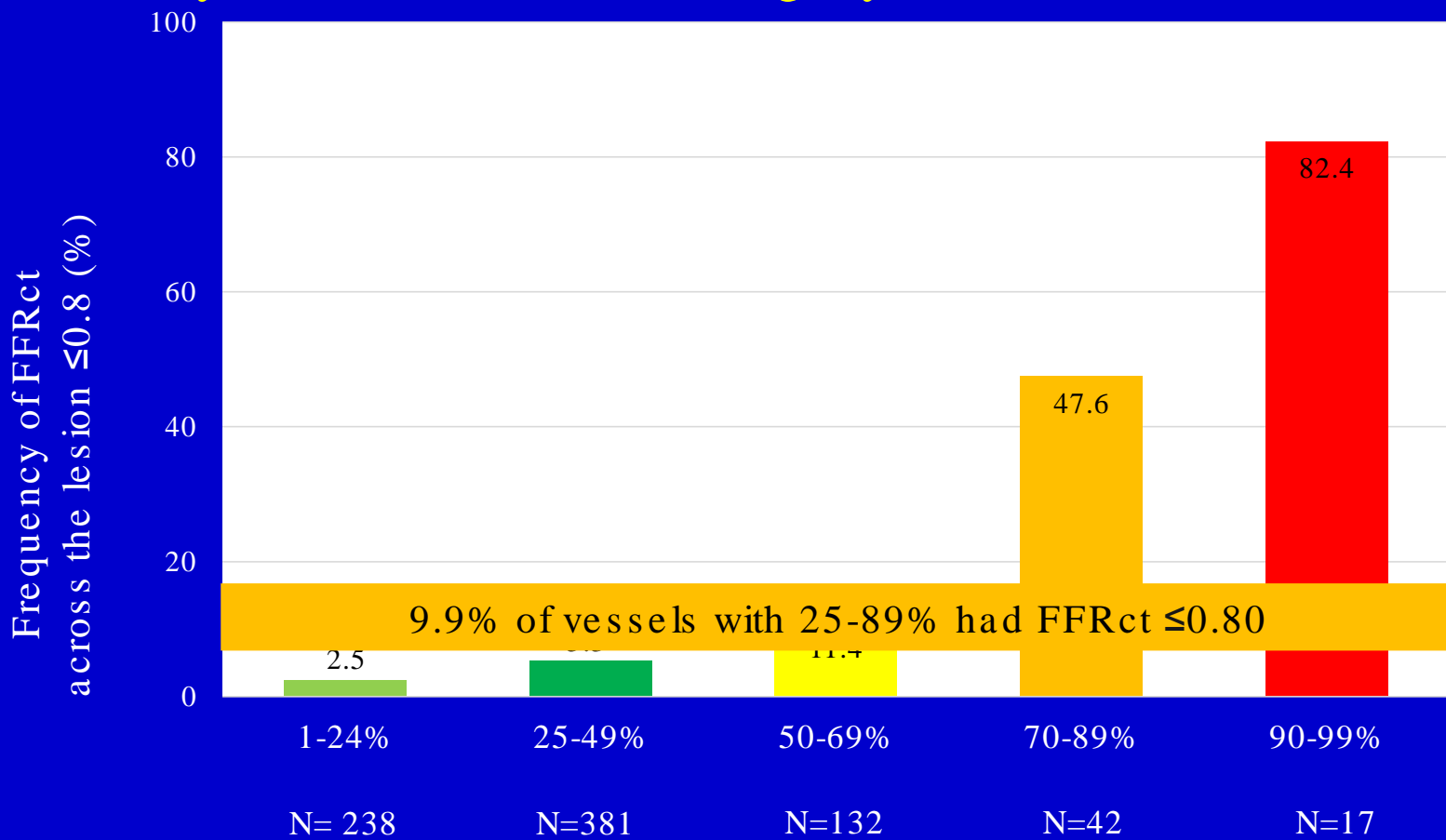
Frequency of Abnormal FFRct Across Lesion by CCTA Stenosis Category (Cedars-Sinai)



810 vessels (393 patients) Maximal CT stenosis grade

Unpublished 2016

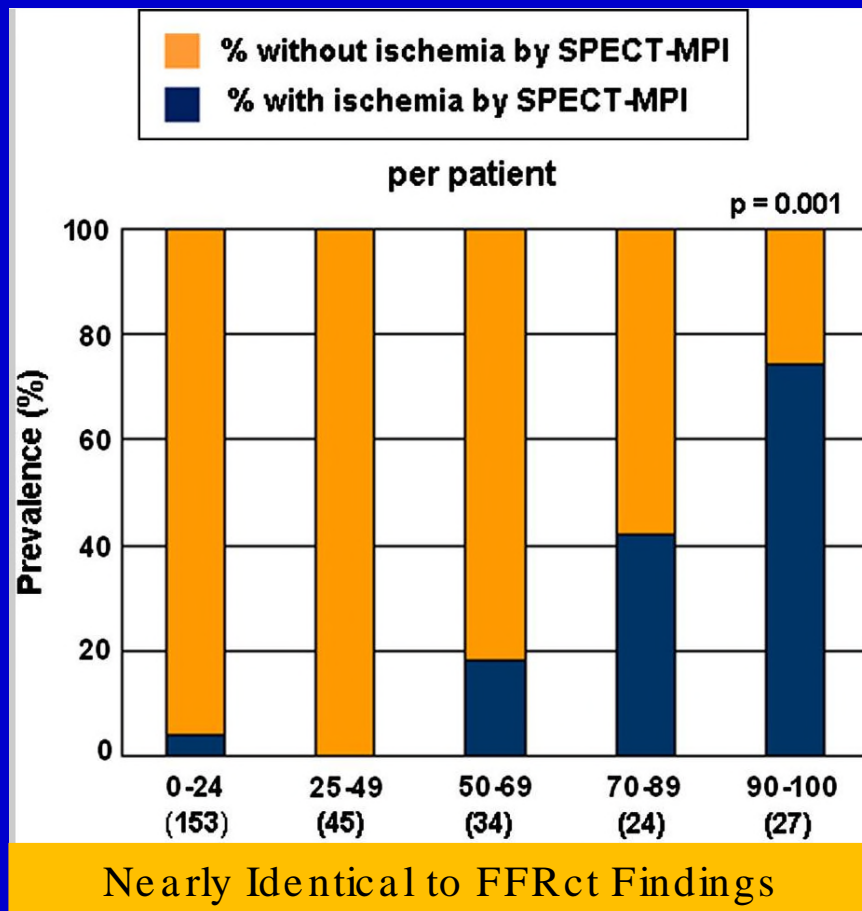
Frequency of Abnormal FFR_{ct} Across Lesion by CCTA Stenosis Category (Cedars-Sinai)



810 vessels (393 patients) Maximal CT stenosis grade

Unpublished 2016

Frequency of Abnormal SPECT by CCTA Stenosis Category



Tamarappoo, Berman et al JNC 2010

Use of FFR_{ct} at Cedars-Sinai

Algorithm According to % Stenosis and Plaque Features

Stenosis

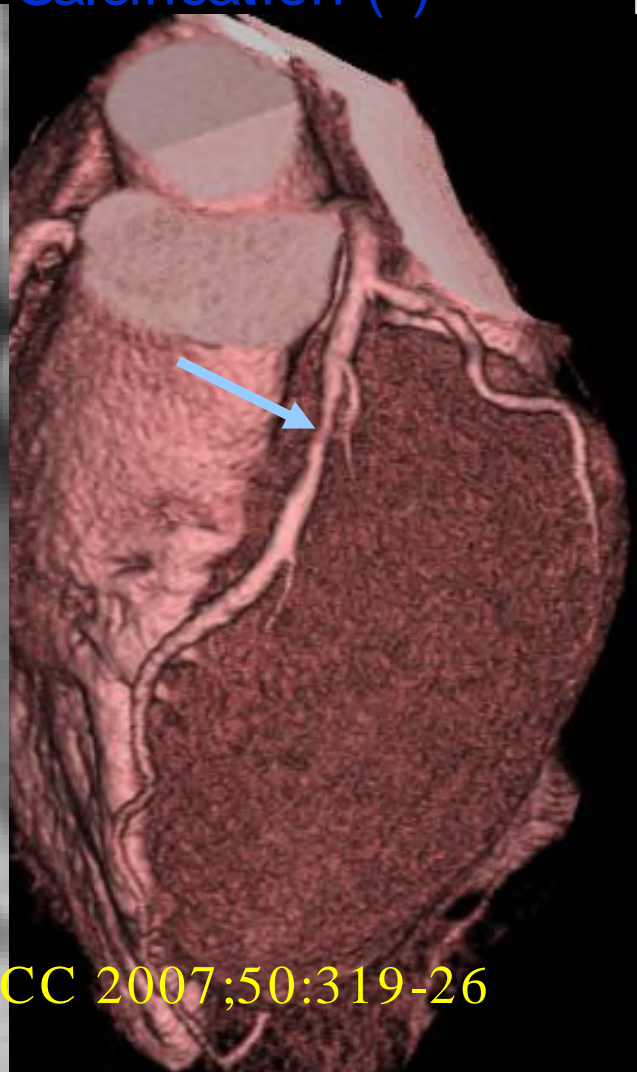
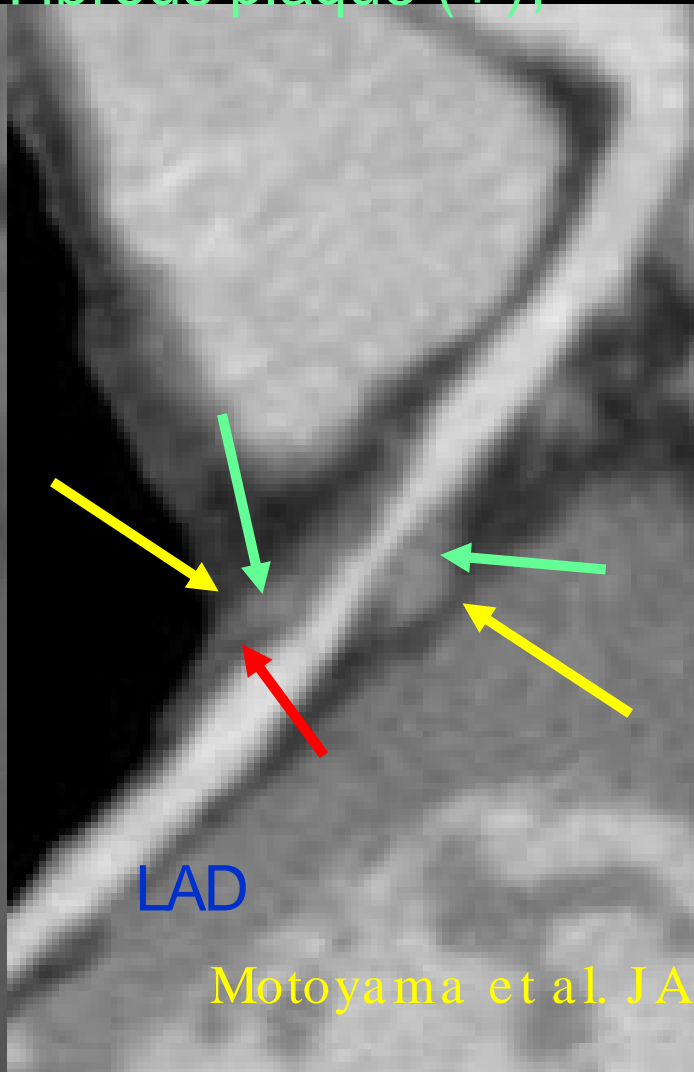
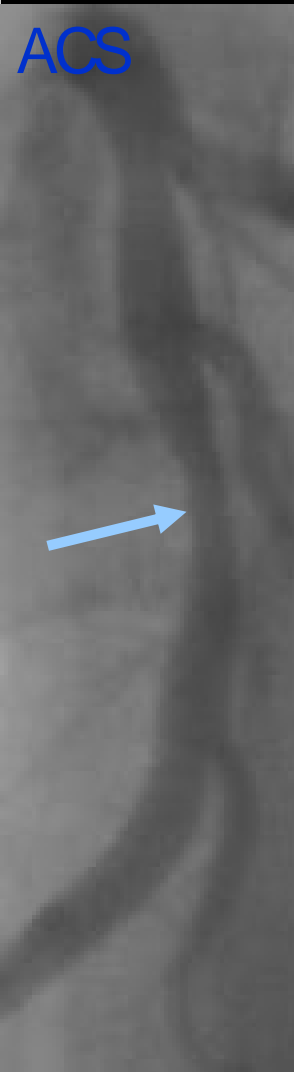
FFR_{ct}

- | | |
|----------|---|
| • <25% | • No |
| • 25-49% | • Consider if closer to 50%
and/or high risk plaque features |
| • 50-69% | • FFR _{ct} |
| • 70-89% | • Consider if closer to 50% and
no high risk plaque features |
| • ≥90% | • No |

Beyond Stenosis: Ischemia and Plaque Assessments in Coronary CTA

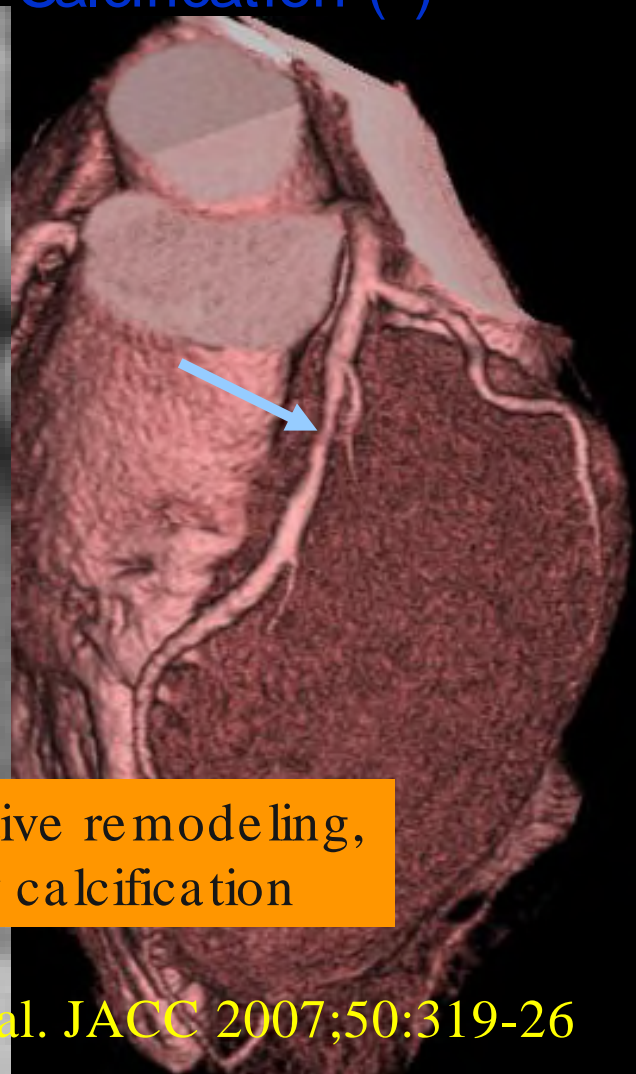
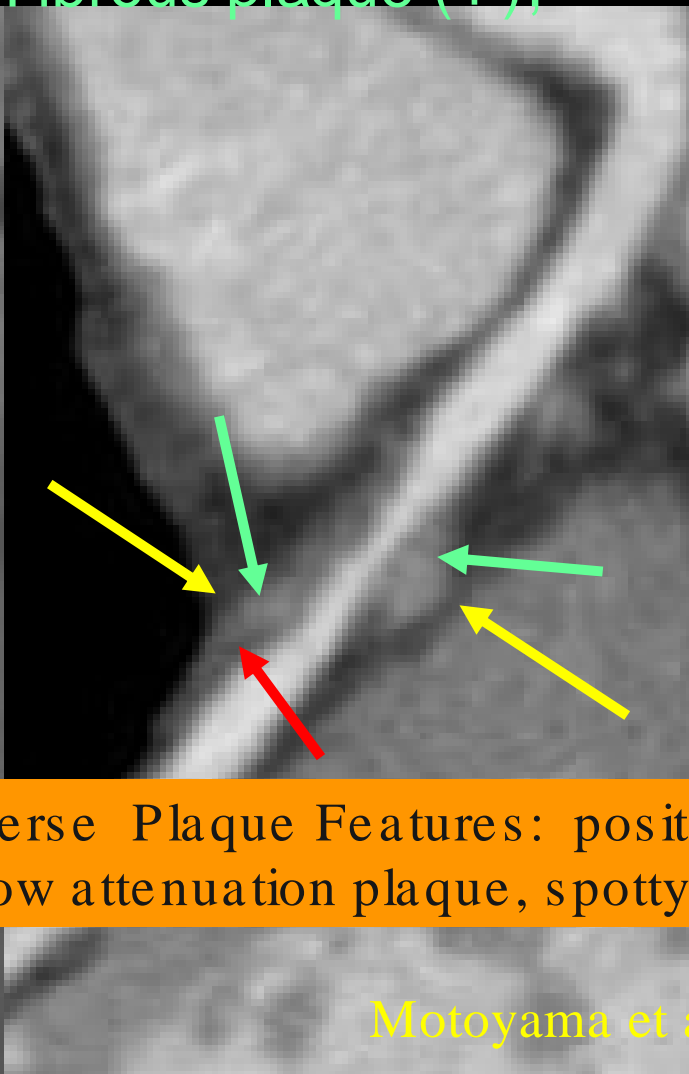
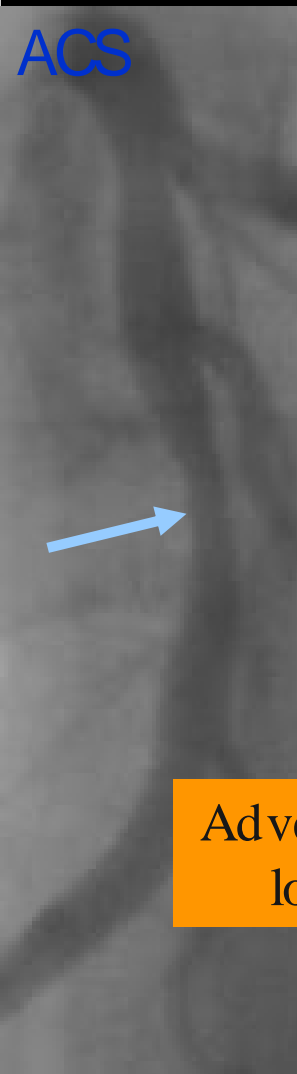
- General considerations
- Stenosis
- Ischemia
- **Plaque**

Positive remodeling (+), Soft plaque (+),
Fibrous plaque (+), Calcification (-)



Motoyama et al. JACC 2007;50:319-26

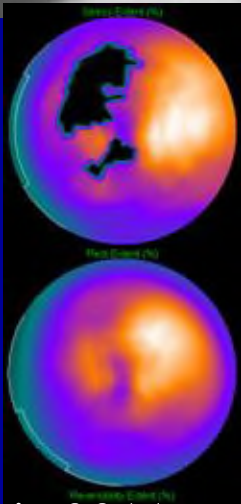
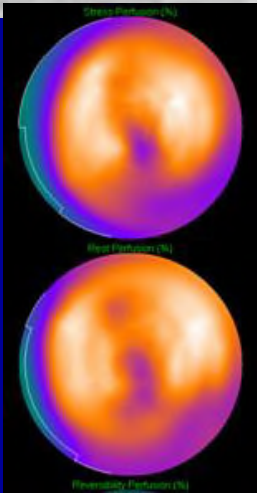
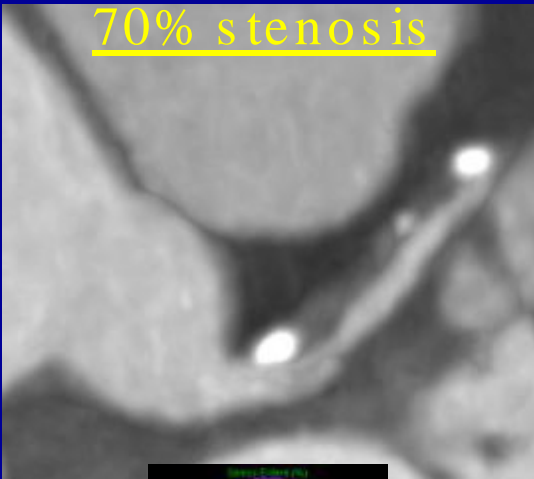
Positive remodeling (+), Soft plaque (+),
Fibrous plaque (+), Calcification (-)



Adverse Plaque Features: positive remodeling,
low attenuation plaque, spotty calcification

Motoyama et al. JACC 2007;50:319-26

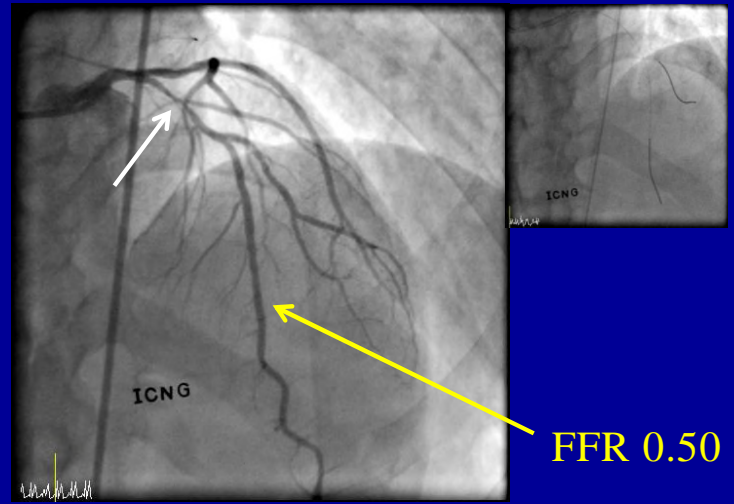
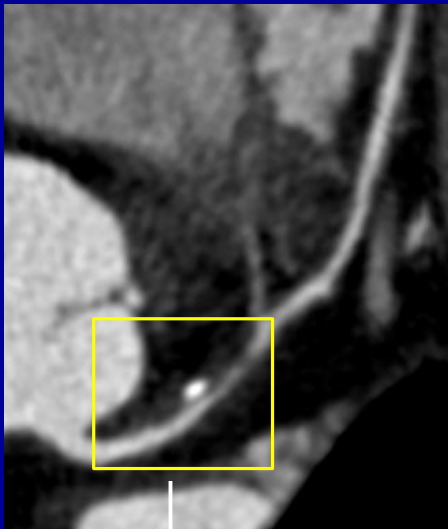
High risk plaque Features: Predict Ischemia



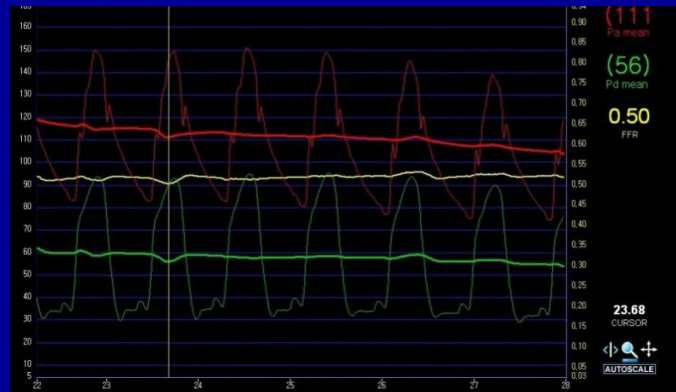
Shmilovich, Cheng, et al., Atherosclerosis 2011



Aggregate Plaque Volume: Predicts FFR Ischemia In Patients with Intermediate Stenosis



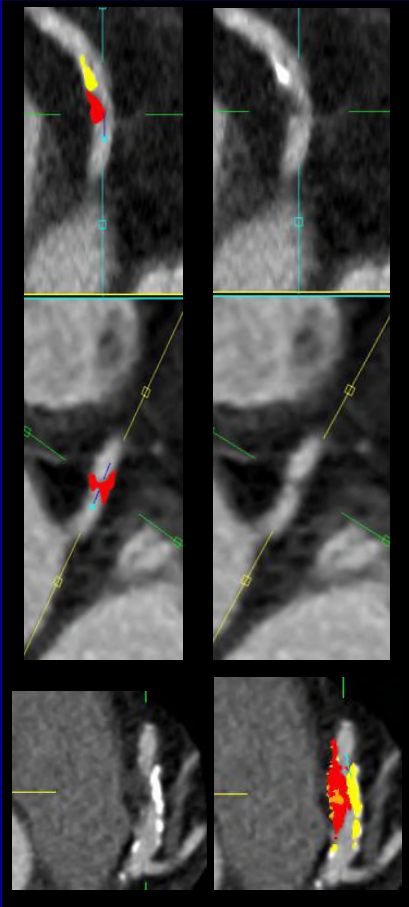
FFR 0.50



58 pts with intermediate stenosis on CCTA

Nakazato, et al JACC 2013

Automated quantitative plaque characterization*

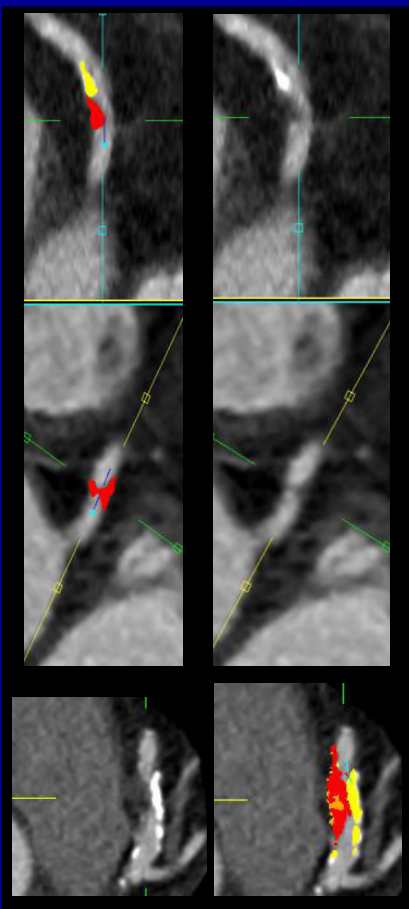


- % Diameter Stenosis
- % Area Stenosis
- Total plaque volume/burden (CP, NCP)
- Low-density NCP plaque volume/burden
- % NCP/Total plaque Volume
- % Aggregate plaque volume
- Remodeling index
- Contrast density difference
- Minimum luminal area, lesion length

* Autoplaq

Dey et al JOCT 2009, Dey et al JOCT 2014,

Automated quantitative plaque characterization*



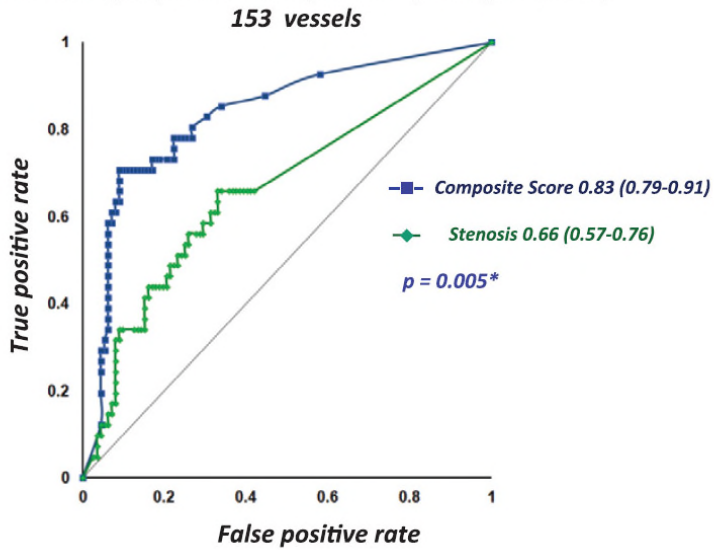
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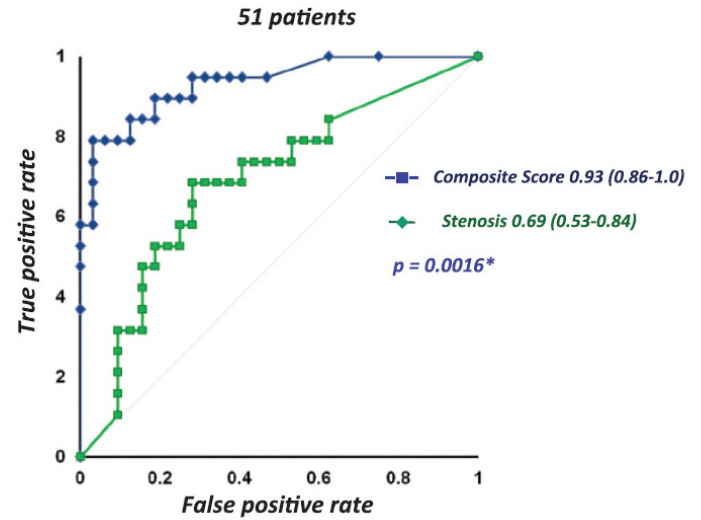
Dey et al JOCT 2009, Dey et al JOCT 2014,

Quantitative Plaque Assessment on CCTA Predicts PET Ischemia

Prediction of impaired MFR by coronary CTA (per-vessel)



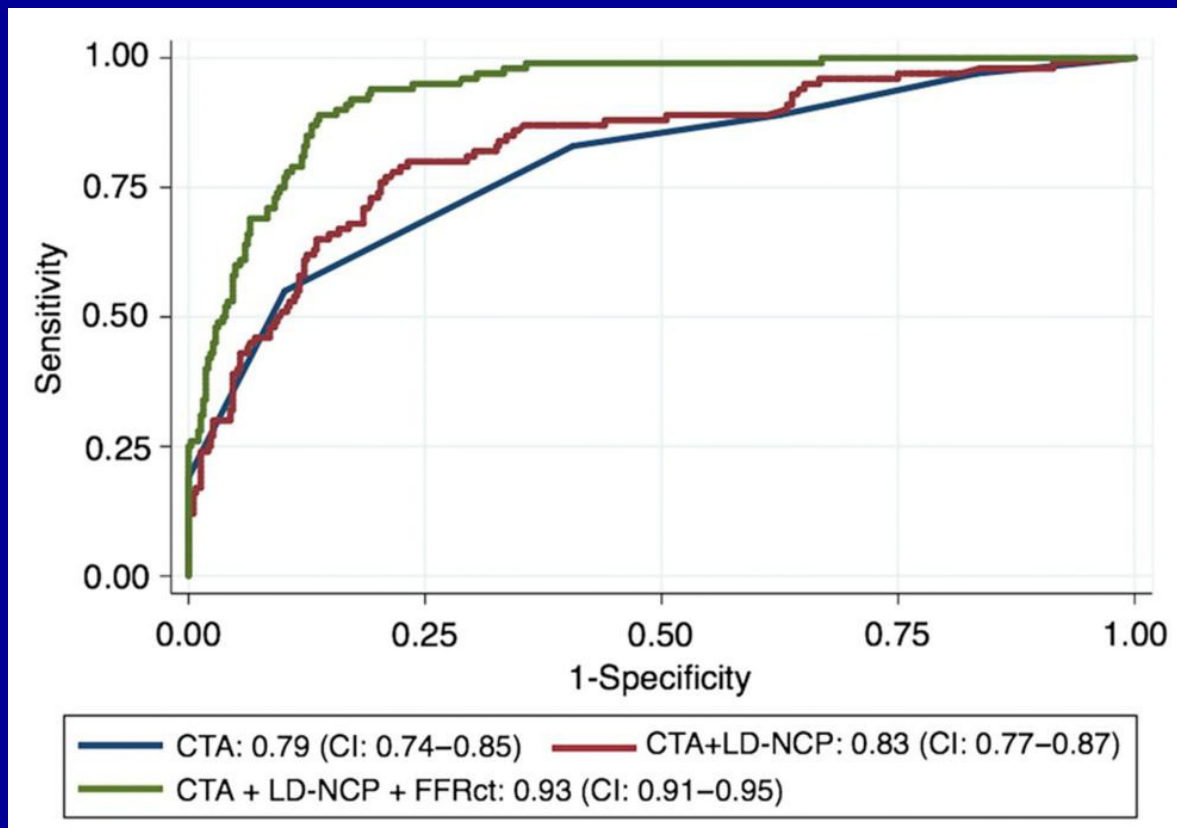
Prediction of impaired MFR by coronary CTA (per-patient)



Autoplaq vs N-13 Ammonia PET

Dey, et al Circ CV Imaging 2015

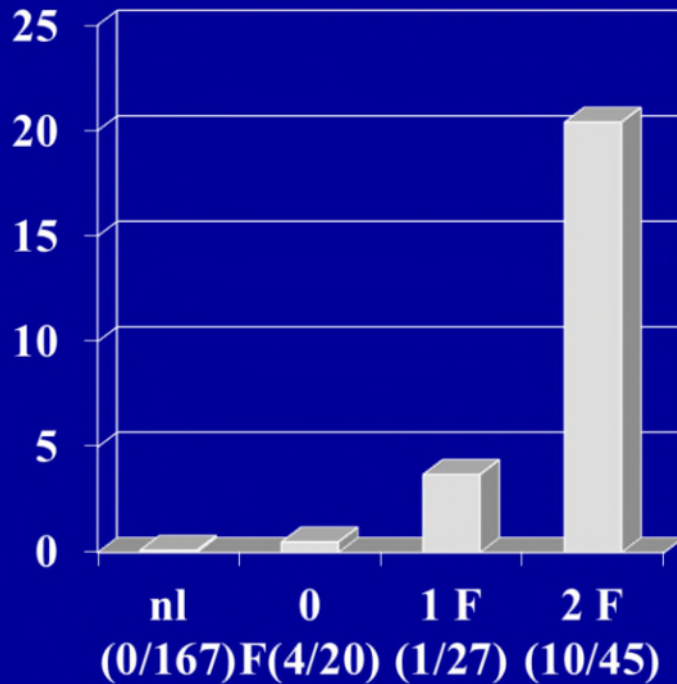
Stenosis, Low-density Plaque, and FFRct Predict of FFR-Ischemia



N=484 vessels/ 254 pts (NXT); Autoplaque

Gaur...Norgard EHJ 2016

% of Patients Subsequently Having ACS Adverse Plaque Features on CCTA



Adverse features (F):
positive remodeling
low-attenuation plaque

■ % with events

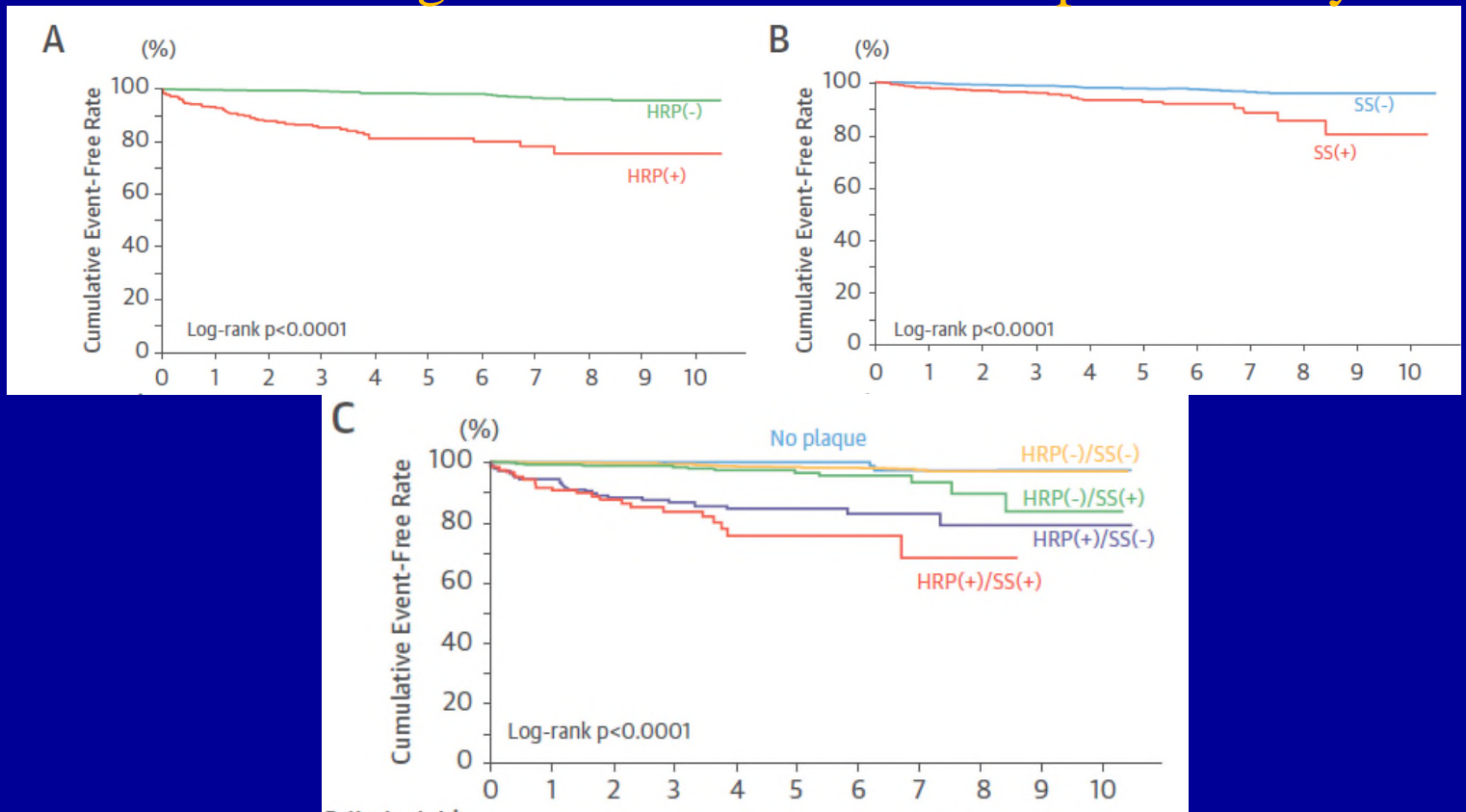
1,059 pts with CCTA followed up for 27 ± 10 months

ACS developed in 15 patients.

None had $>75\%$ stenosis in the culprit lesion at time of CCTA

Motoyama et al. JACC 2009;54:49-57

High risk plaque (HRP) Features: Predict ACS HRP and Significant Stenosis: Complementary



N=3,158; 88 ACS in mean f/u 3.9 ± 2.1 years

HRP: positive remodeling or low attenuation plaque; SS: $\geq 70\%$ stenosis

Motoyama, et al JACC 2015

Serial Quantitative Coronary Plaque Assessment

Assessing the Effects of Therapy

- Reproducible, quantitative assessments of global plaque burden and plaque features
- Potential important tool for serial assessment
 - Clinical trials
 - Clinical management
 - Could extend application of CCTA to asymptomatic patients

Endothelial Shear Stress (ESS) in Human Coronary Arteries

Left Main, Proximal LAD, and Proximal Circumflex

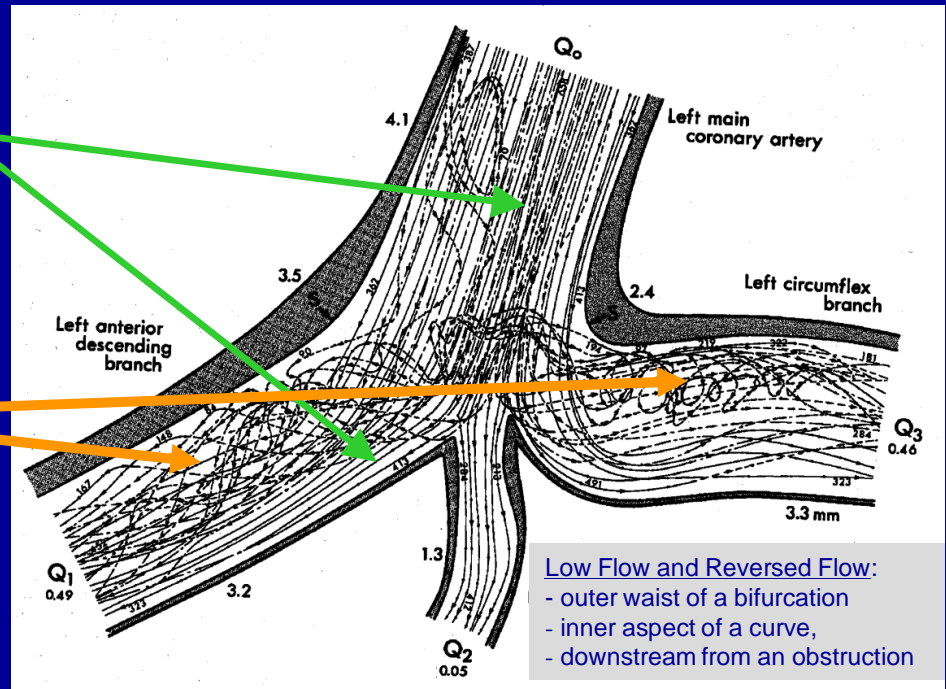
Undisturbed laminar flow
- Physiologic ESS -

vasculoprotective

Low and oscillatory
disturbed laminar flow

- Low ESS -

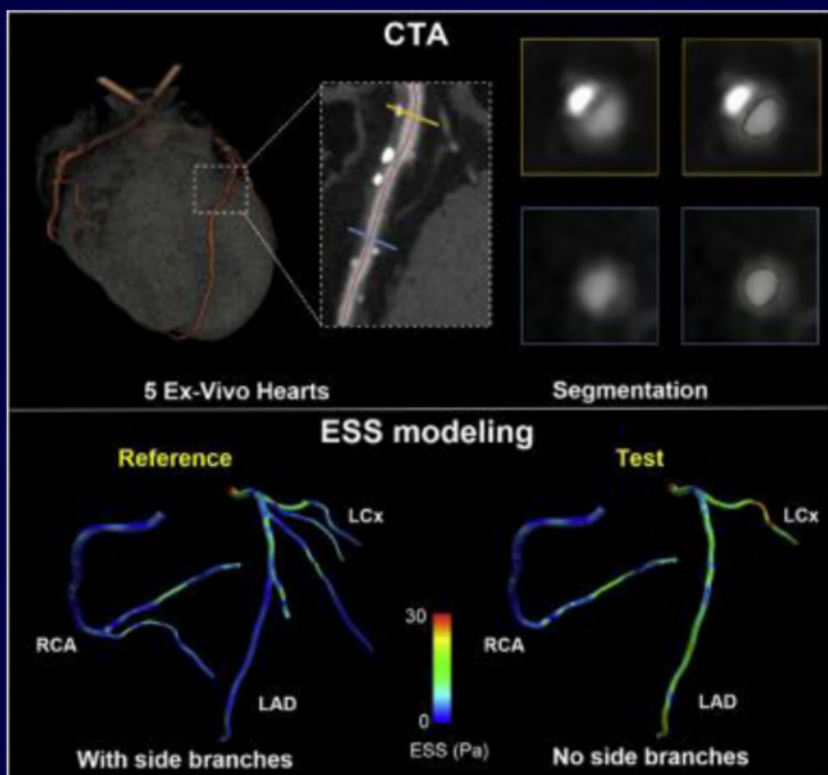
pro-inflammatory
and atherogenic



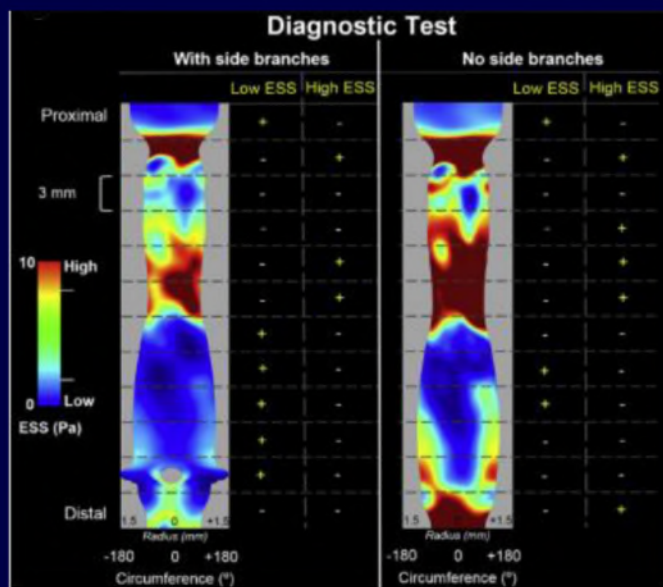
Courtesy: Peter Stone

Asakura and Karino. Circ Res 1990

Innovative Refinements to Enhance ESS Calculation by CCTA



Measuring coronary flow in major coronary artery and side branches



(Giannopoulos AA, et al. Atherosclerosis 2016;251:213)

Stenosis, Ischemia, and Plaque in CCTA

- Stenosis: Definitive when severe
- FFR_{ct}
 - Provides lesion specific ischemia
 - Reduces need for stress imaging after CCTA
 - Decreases the rate of ICA after CCTA
- Quantification of plaque:
 - Adds to prognostic assessment
 - Potential to guide revascularization in asymptomatic patients
 - Valuable tool for assessment of therapy
- Assessments of stenosis, plaque, and ischemia:
 - Complementary

WHY FEEL HELPLESS ABOUT YOUR CORONARY ARTERY DISEASE?

**HIGH TECH
ROTO-ROOTER!**

TRY

- ✓ No better than cheap heart meds
- ✓ Accounts for 10% of recent increase in Medicare spending
- ✓ Proven useless unless you're in the middle of a heart attack or have severe ischemia on stress test
- ✓ Chance of heart attack or stroke right there on the operating table

COOL!



SPECIAL:
Only \$20,000 - \$200,000
Act now, and
Medicare (your tax dollars)
or your insurance company
will pick up most of the tab!

**WAY EASIER THAN
EXERCISING OR
CHANGING YOUR DIET!**

GET THAT FEELING OF DOING SOMETHING:
The 21st Century's Answer to Leeches

by Carolyn Thomas ♥ @HeartSisters

Thank you very much