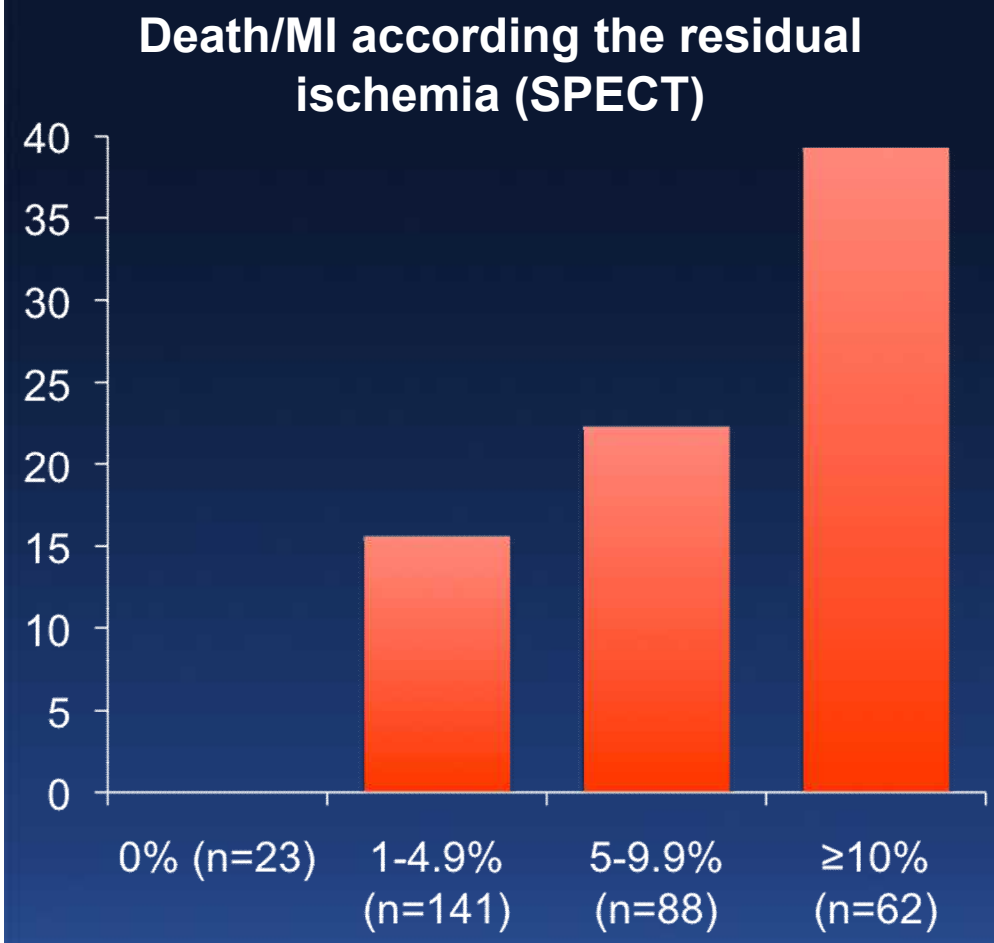
Integrating IVUS, FFR, and Noninvasive Imaging to Optimize Outcomes

Gary S. Mintz, MD

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell
CARDIOVASCULAR RESEARCH FOUNDATION

COURAGE Nuclear Substudy (n=314)

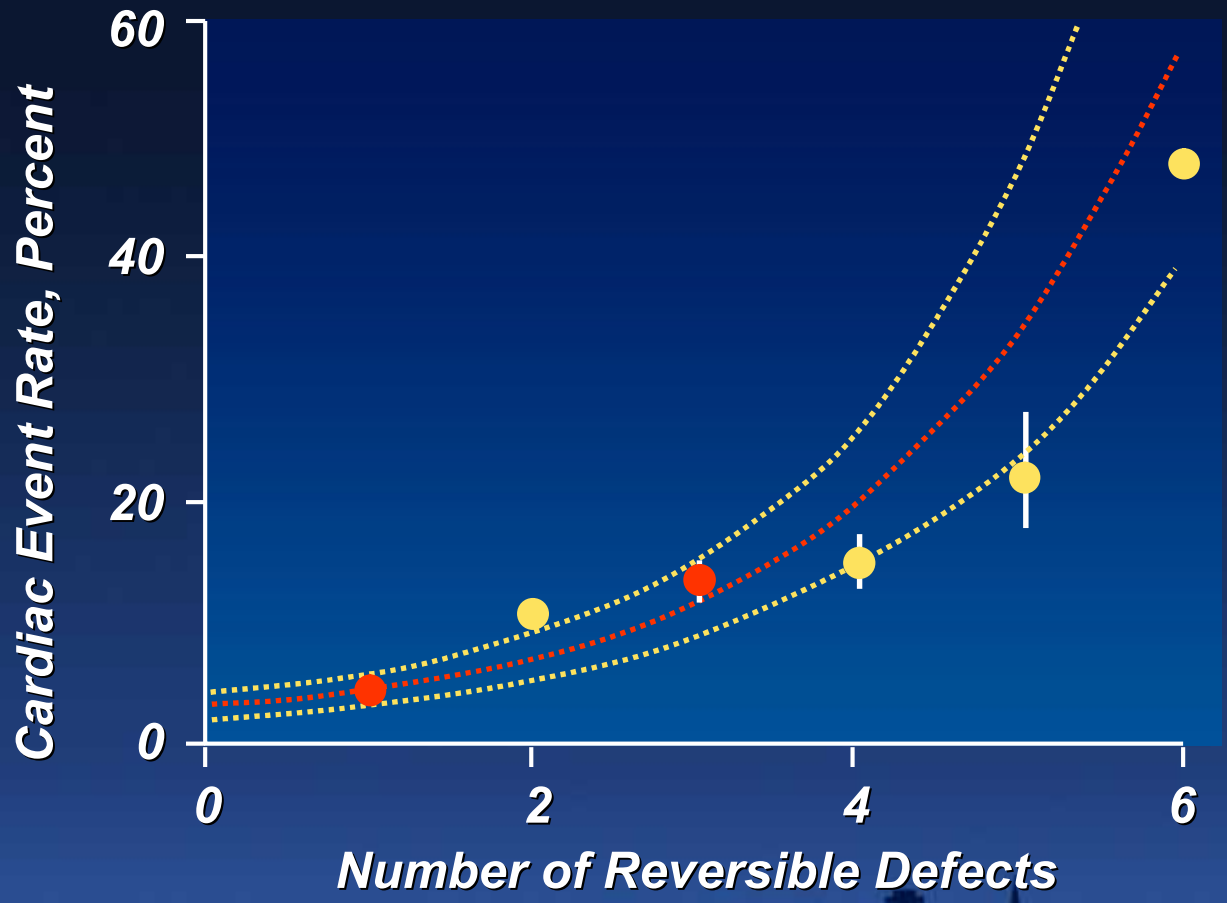


- PCI+optimal medical therapy was associated with greater ischemia reduction overall and in pts with moderate/severe pre-treatment ischemia
- ≥5% ischemia reduction was associated with reduced death/MI compared to no ischemia reduction: 13.4% vs 27.4%, p=0.037 (overall) and 16.2% vs 32.4%, p=0.001 (in patients with moderate/severe pretreatment ischemia)

Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell
CARDIOVASCULAR RESEARCH FOUNDATION

(Shaw et al. Circulation 2008;117:1283-91)

Relationship Between Extent of Ischemia and Cardiac Events (n=1689)

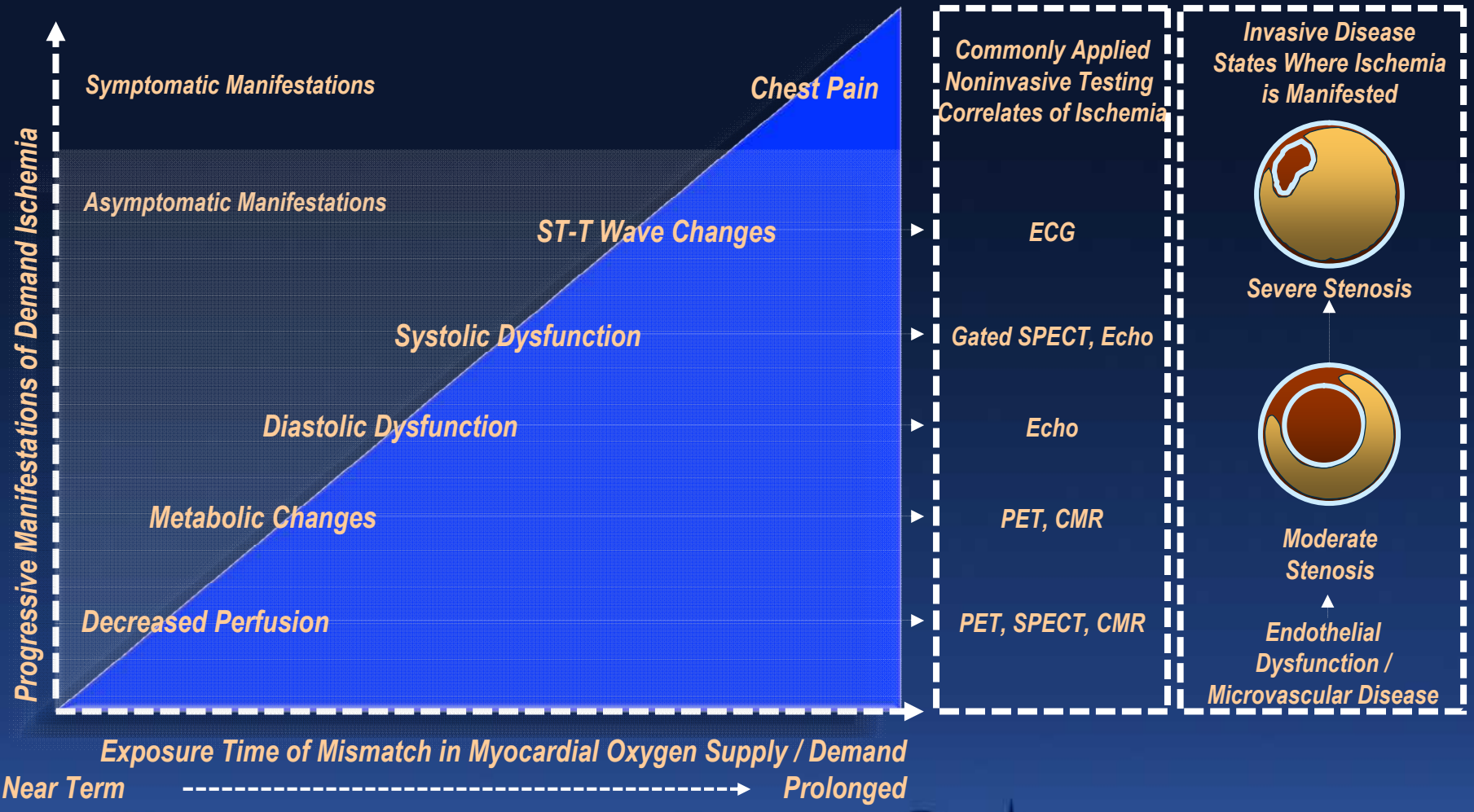


Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

CARDIOVASCULAR RESEARCH FOUNDATION

(adapted from Ladenheim, et al. J Am Coll Cardiol. 1986;7:464–71)

Progressive Manifestations of Myocardial Ischemia as Illustrated by Ischemic Cascade

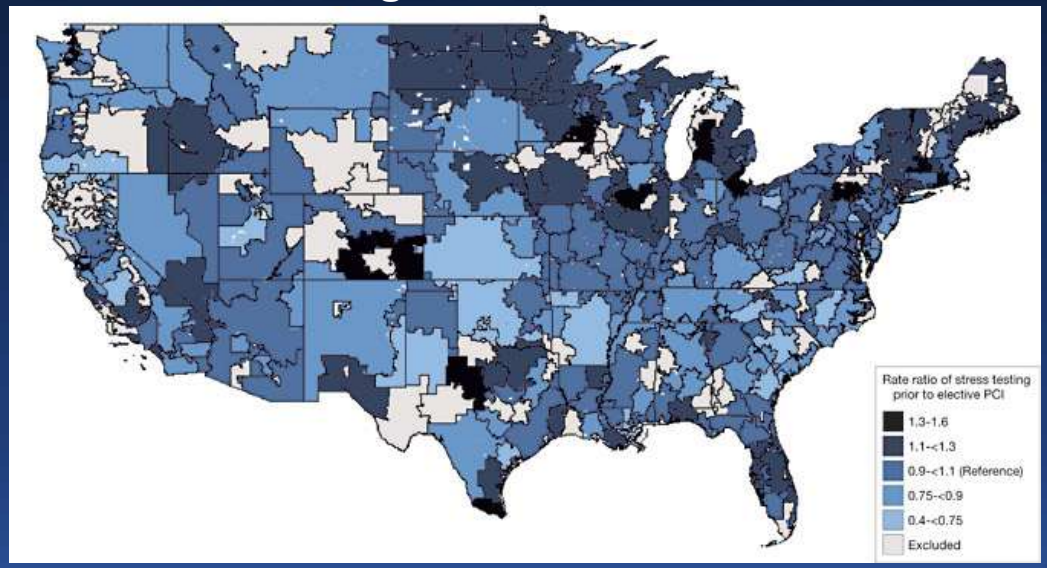


(Shaw. TCT 2008)

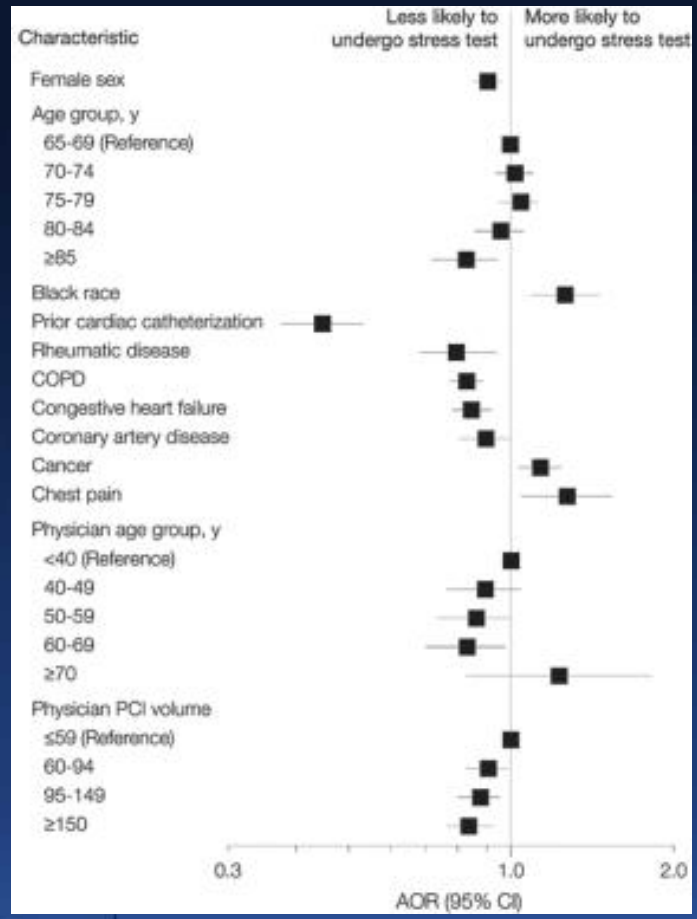
Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell
Cardiovascular Research Foundation

In the United States, 44.5% of medicare pts underwent stress testing within the 90 days prior to elective PCI.

Geographic Variation of Rates of Stress Testing Prior to Elective PCI



Factors Predicting Stress Test Prior to Elective PCI



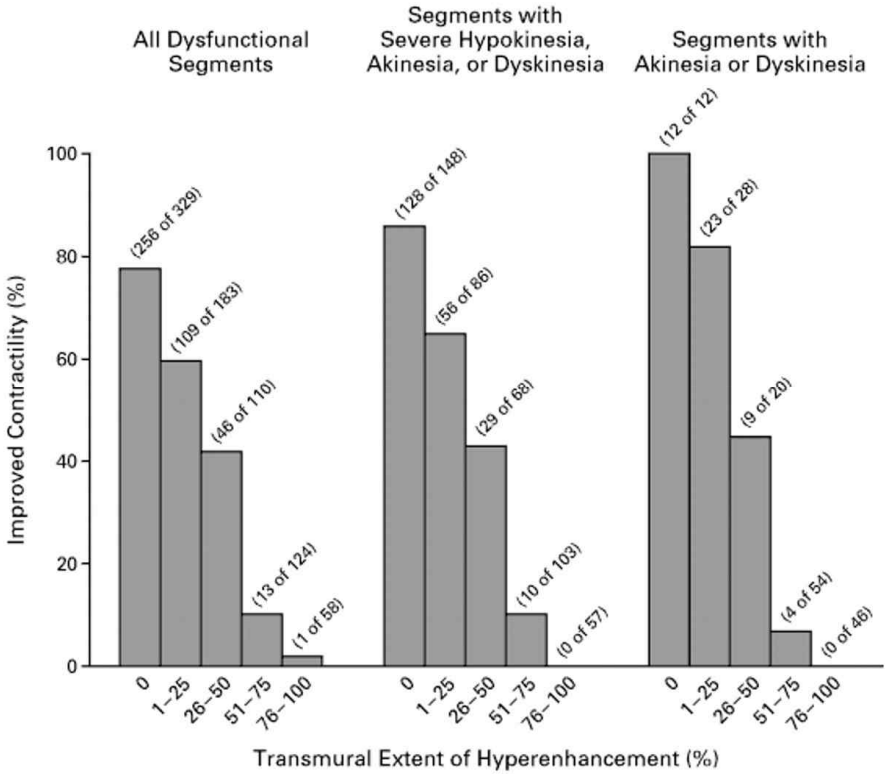
(Lin et al. JAMA 2008;300:1765-1773)

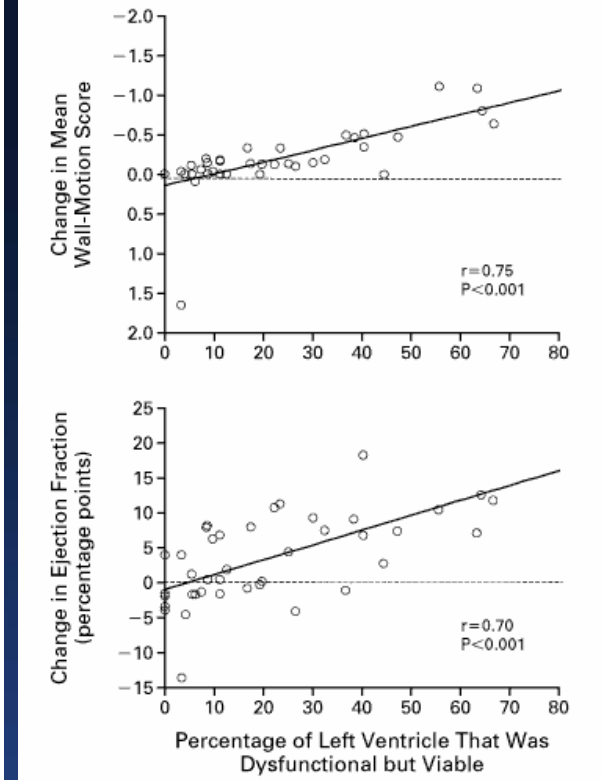
Use of MPS to localize CAD

	LAD		RCA		LCX	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
DePasquale et al. Circulation 1988;77:316-27	78%	83%	89%	87%	65%	95%
Borges-Neto et al. J Am Coll Cardiol. 1988;11:962-9	80%	84%	87%	92%	51%	92%

As best at I have been able to determine, the use of myocardial perfusion scanning to guide PCI especially in the setting of multivessel disease is anectodal, is extrapolated from DEFER and FAME and the fact that FFR was originally validated against MPS, and is not supported by the literature

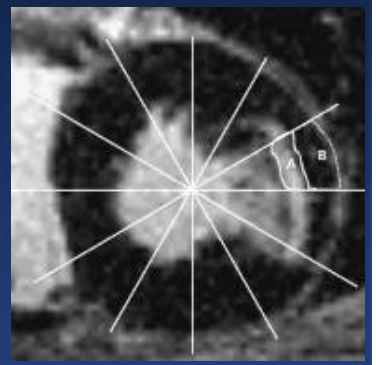
Cardiac MR and Viability: *Prediction of improved LV function by MRI*





Cine image

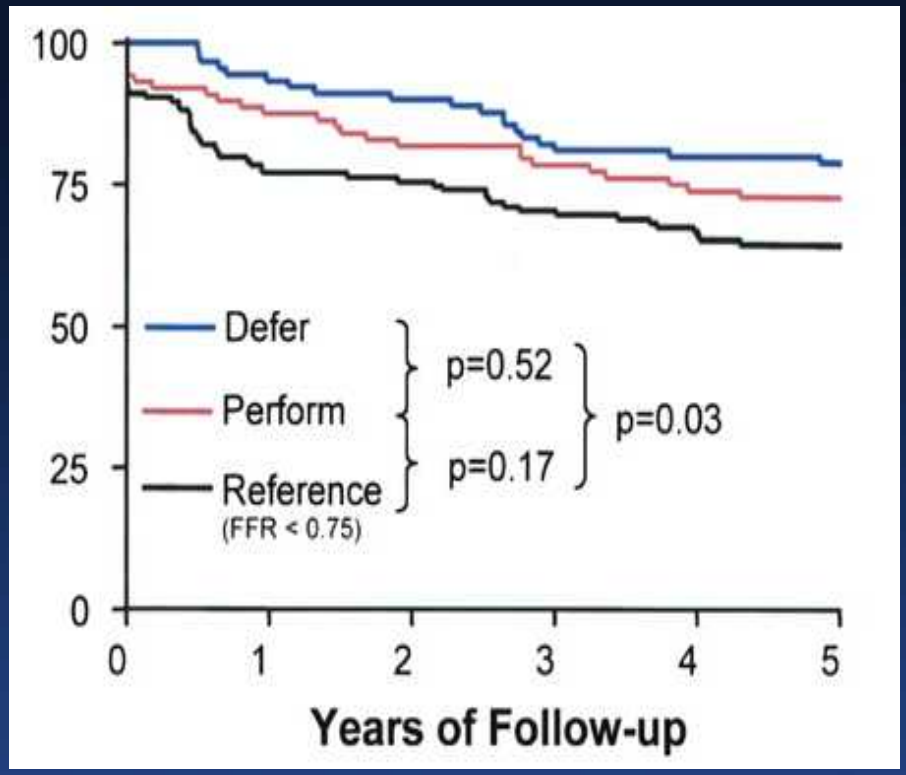
Enhanced



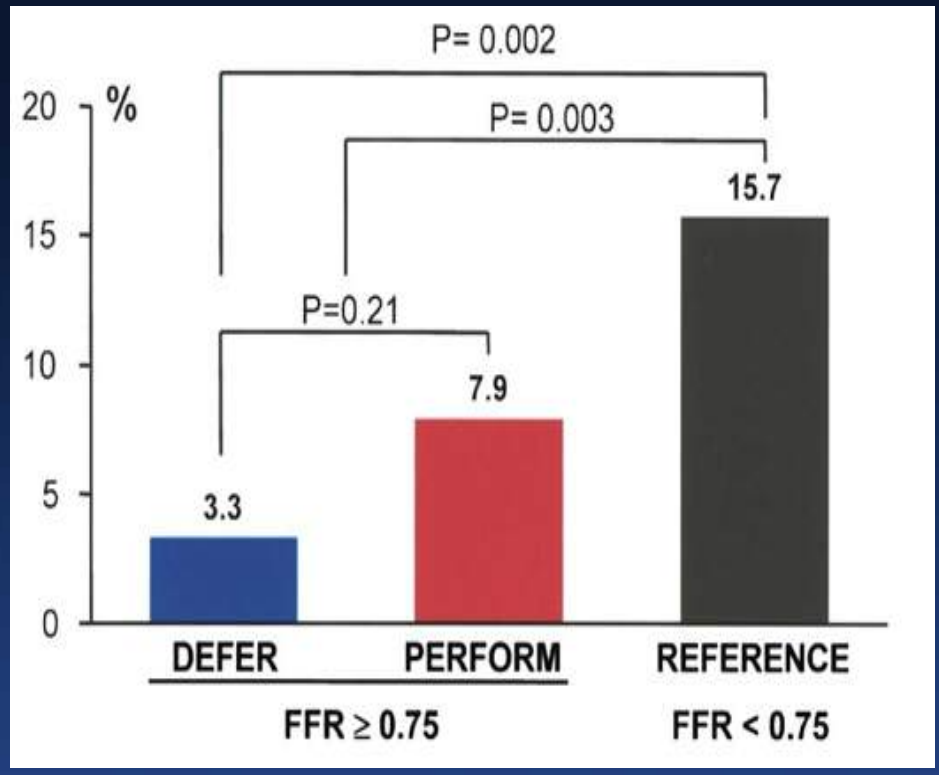
(Kim et al. N Engl J Med. 2000;343:1445-53)

DEFER 5 Year Results

Event Free Survival



Cardiac Death and MI



Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

CARDIOVASCULAR RESEARCH FOUNDATION

(Pijls et al. J am Coll Cardiol 2007;49:2105-11)

FAME: FRACTIONAL FLOW RESERVE versus ANGIOGRAPHY FOR GUIDING PCI IN PATIENTS WITH MULTIVESSEL CORONARY ARTERY DISEASE

Late Breaking Trial at TCT, October 14 th , 2008

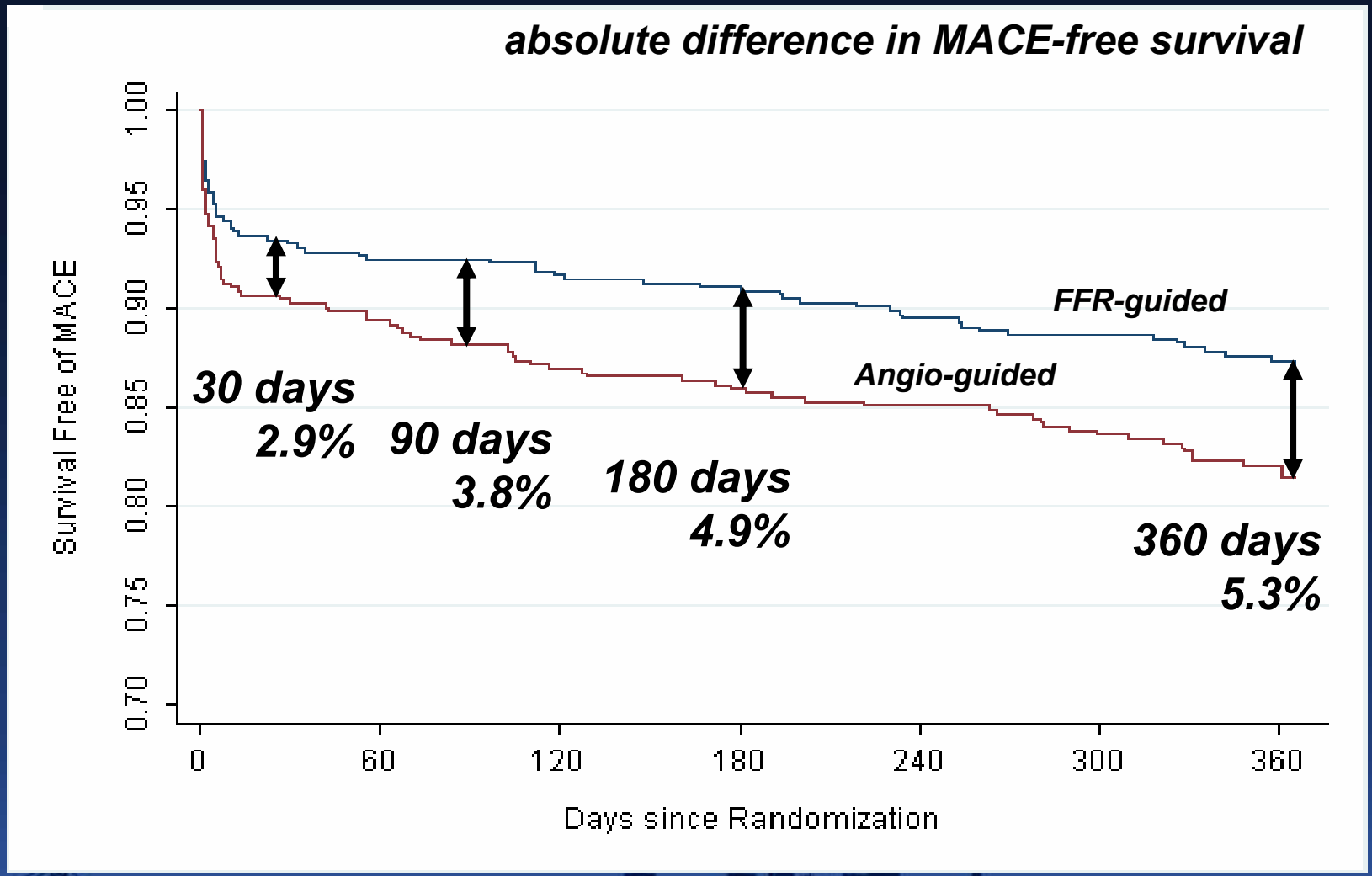
Nico H.J.Pijls, MD, PhD
Catharina Hospital, Eindhoven
The Netherlands,
on behalf of the FAME investigators

Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell
CARDIOVASCULAR RESEARCH FOUNDATION

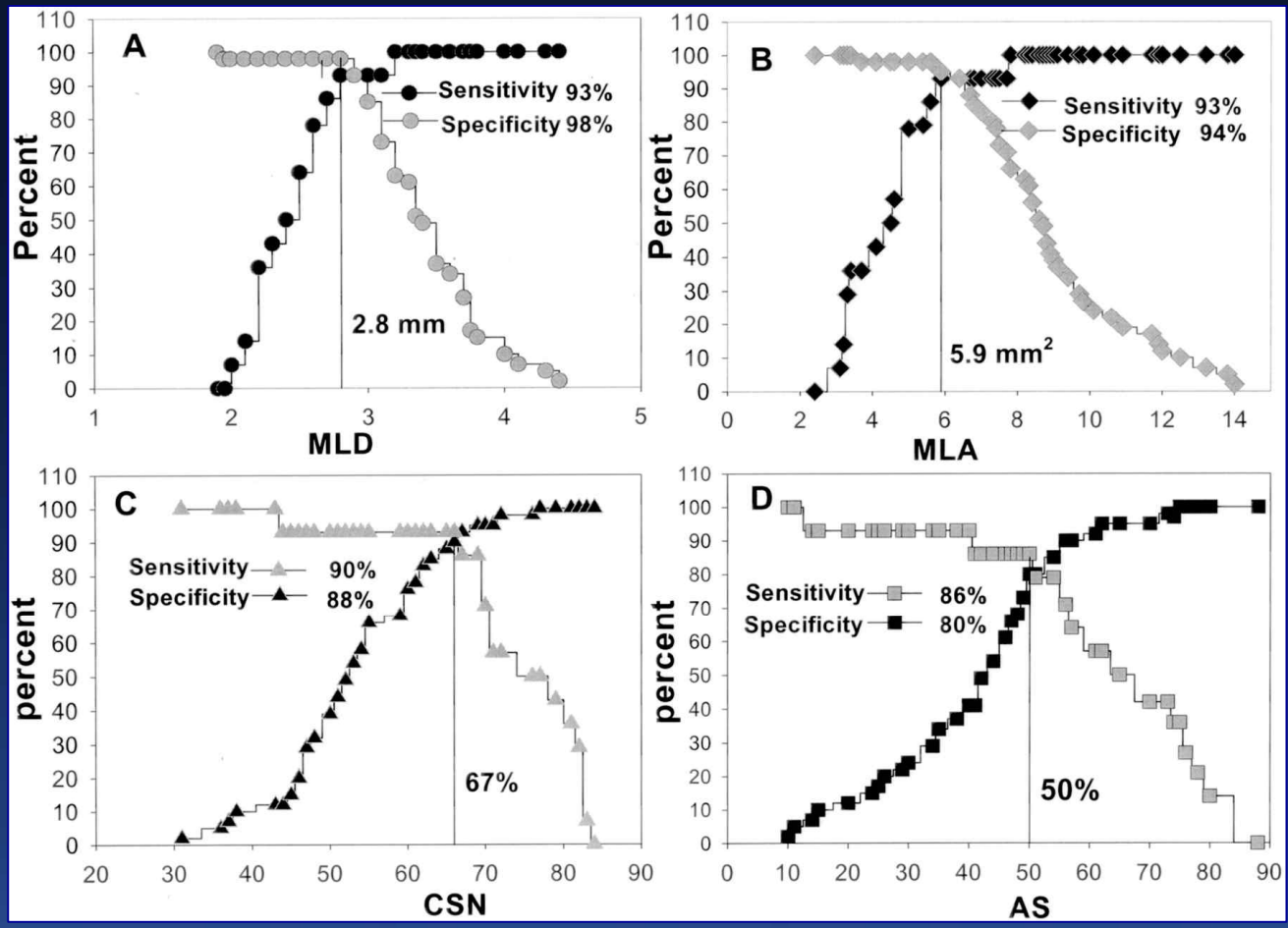
FAME study: Procedural Results

	ANGIO-group N=496	FFR-group N=509	P-value
# indicated lesions per patient	**2.7 ± 0.9**	**2.8 ± 1.0**	0.34
FFR results			
Lesions succesfully measured, No (%)	-	**1329 (98%)**	-
Lesions with FFR ≤ 0.80, No (%)	-	**874 (63%)**	-
Lesions with FFR > 0.80, No (%)	-	**513 (37%)**	-
Stents per patient	**2.7 ± 1.2**	**1.9 ± 1.3**	<0.001
Lesions succesfully stented (%)	**92%**	**94%**	-
DES, total, No	**1359**	**980**	-

FAME study: Event-free Survival



IVUS determinants of LMCA FFR <0.75

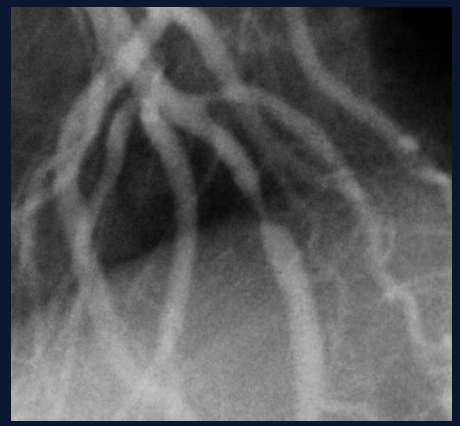


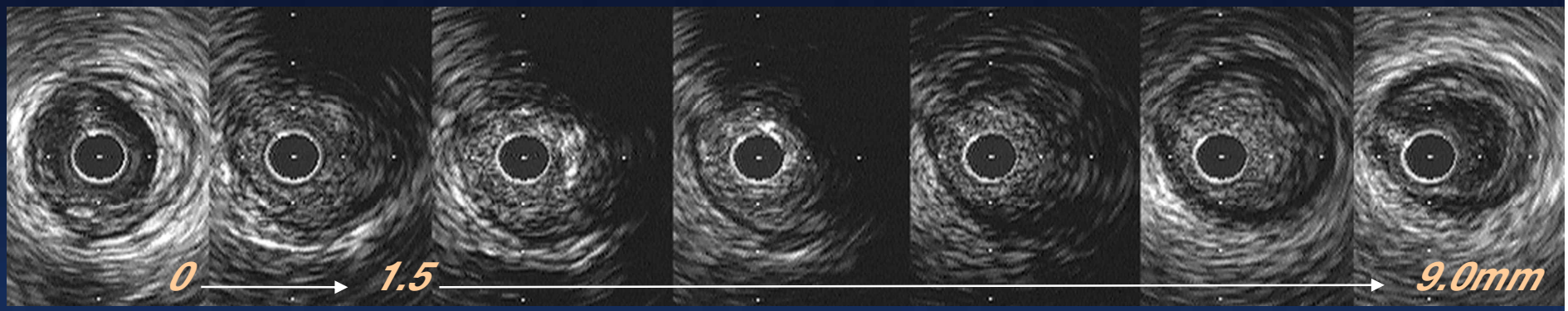
(Jasti et al. Circulation 2004;110:2831-6)

IVUS Criteria for a 'Significant' LMCA Stenosis

- Most IVUS LMCA studies show either insignificant disease or critical disease
- Absolute lumen CSA <6.0mm^2 (or MLD <3.0mm) is the suggested criterion for a significant LMCA stenosis
  - Correlates with a LMCA FFR<0.75
  - Murray's Law ($_{LMCA}r^3 = {}_{LAD}r^3 + {}_{LCX}r^3$)
  - Does not depend on finding a disease-free reference segment

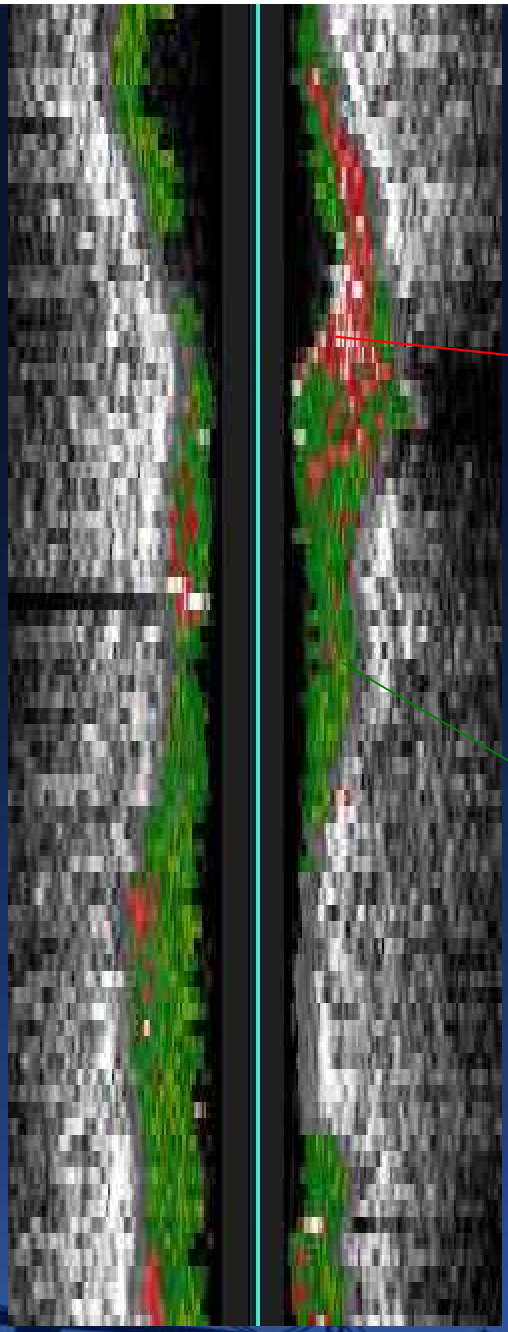
Attenuated Plaque

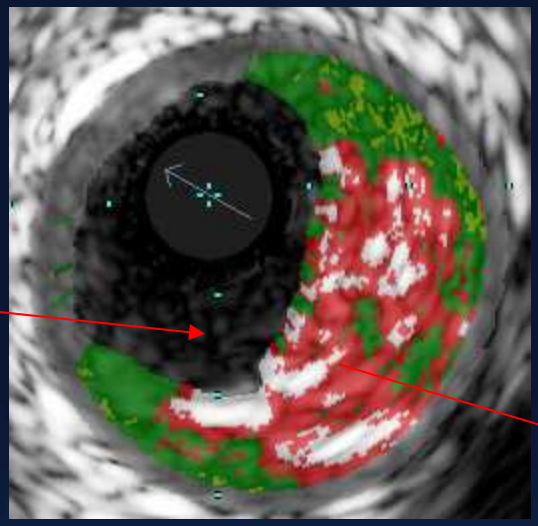




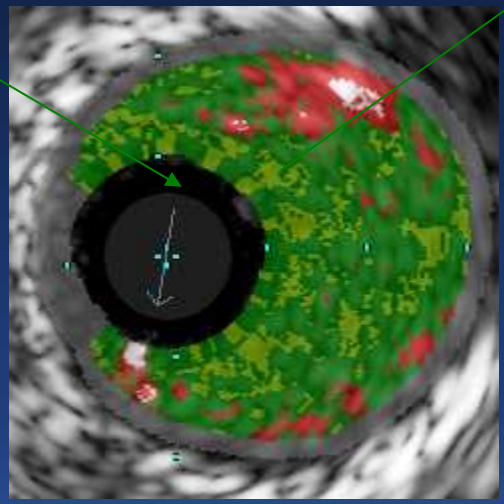
- *Attenuated plaques were observed in 39.6% of STEMI, 17.6% of NSTEMI, and 0% of stable angina.*
- *Attenuate plaques were associated with more fibroatheromas and a larger necrotic core (on VH-IVUS).*
- *In ACS patients with attenuated plaques (1) the level of CRP was higher, (2) angiographic thrombus and initial coronary flow <TIMI 2 were more common, and (3) no-reflow or flow deterioration post-PCI were more common.*

(Lee et al. JACC Cardiovasc Interv. 2009;2:65-72)
(Wu et al, Am J Cardiol 2010;105:48-53)

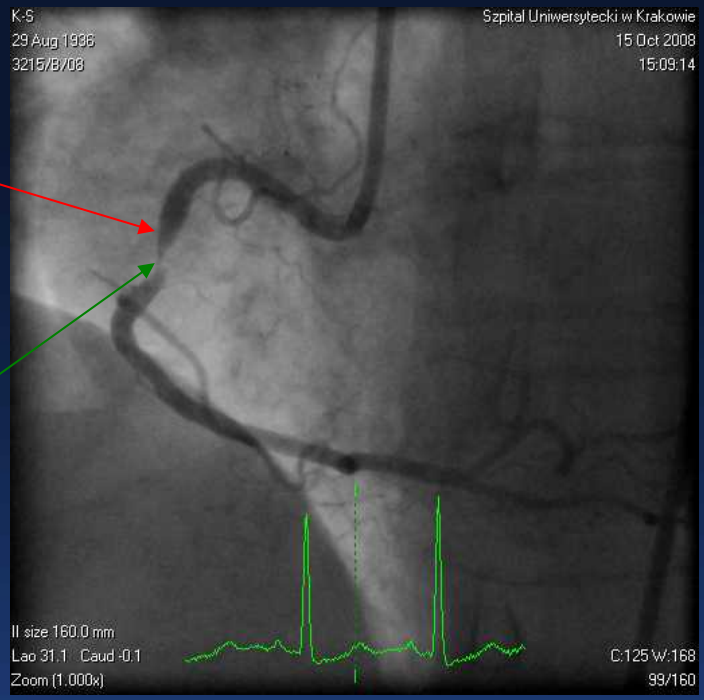




culprit of the culprit proximal to MLA



MLA

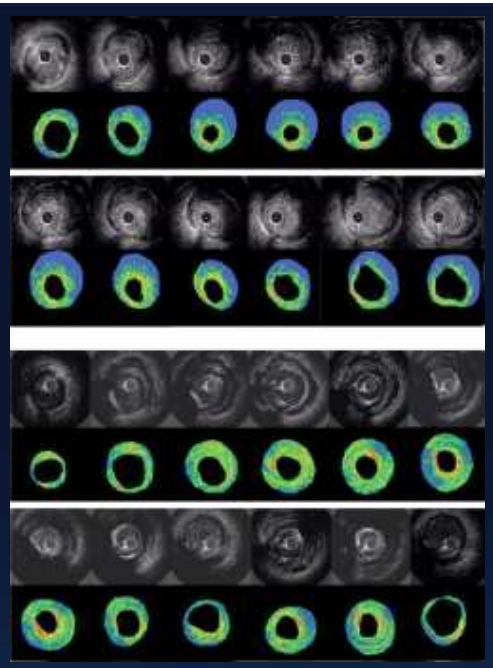


Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

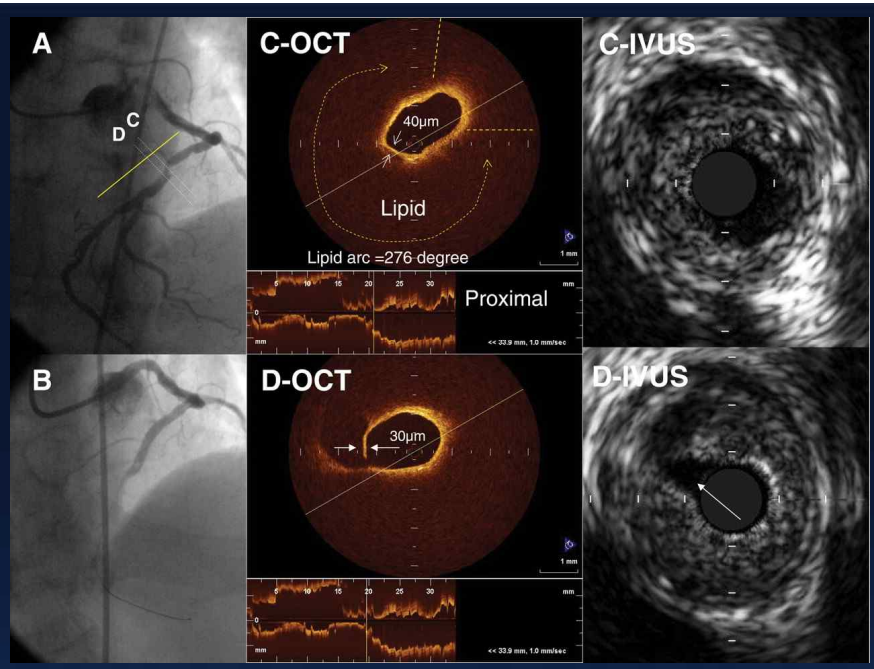
CARDIOVASCULAR RESEARCH FOUNDATION

Numerous studies have shown a relationship between the maximum necrotic core and post-PCI distal embolization

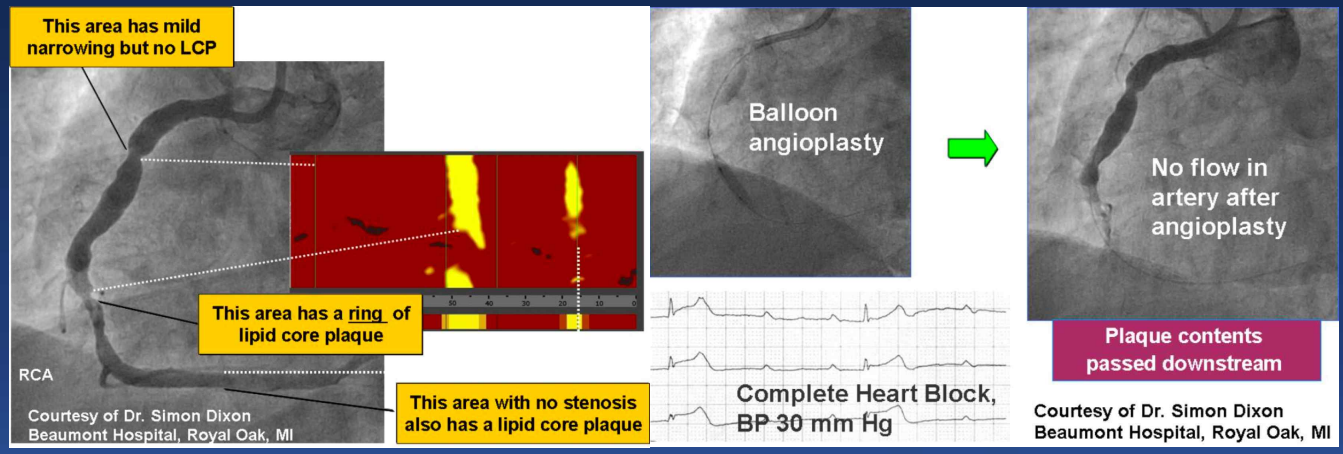
- Kawaguchi et al. J Am Coll Cardiol. 2007;50:1641-6
  - ST re-elevation in 71 pts with STEMI
- Kawamoto et al. J Am Coll Cardiol. 2007;50:1635-40
  - Doppler FloWire high intensity transit signals in 44 pts undergoing elective stenting resulting in poor recovery of CVFR
- Park et al. VH Summit 2007 (unpublished)
  - Largest NC independent predictor of CK-MB release (n=332)
- Hong et al. J Am Coll Cardiol Img, 2009;2:458-468
  - Troponin post elective stenting in 80 pts (29 stable and 51 unstable angina)
- Bose et al. Basic Res Cardiol 2008;103:587-97
  - CK and TnI in 55 pts undergoing direct stenting. Patients in the 4th quartile of NC volume had a particularly high increase in biomarkers.
- Higashikuni et al. Circ J 2008; 72: 1235-41
  - No reflow in 49 pts with ACS undergoing PCI
- Hong et al. Eur Heart J, in press
  - No reflow in 190 pts with ACS undergoing stenting



Uetani et al. Eur Heart J 2008;29:1714-20



Tanaka, A. et al. Eur Heart J 2009;30:1348-1355



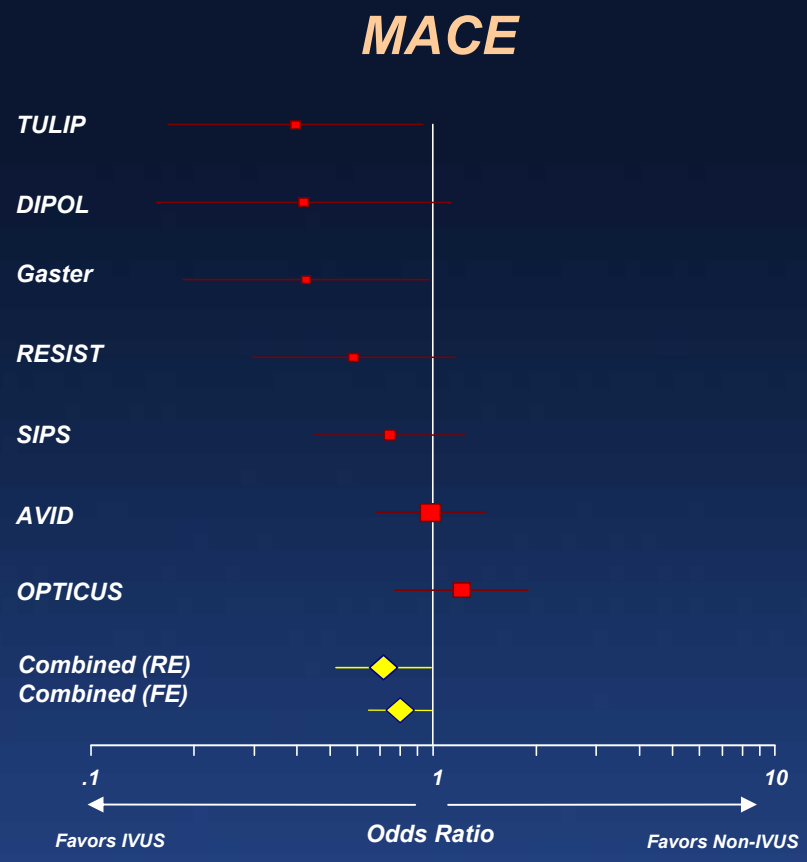
Goldstein et al. JACC Cardiovasc Imaging. 2009;2:1420-4

Meta-analysis of IVUS guidance of BMS implantation

IVUS guidance was associated with significantly lower rate of

- *Angiographic restenosis (22.2% vs. 28.9%; OR 0.64, p=0.02)*
- *Repeat revascularization (12.6% vs. 18.4%; OR 0.66, p=0.004)*
- *Overall MACE (19.1% vs. 23.1%; OR 0.69, p=0.03)*

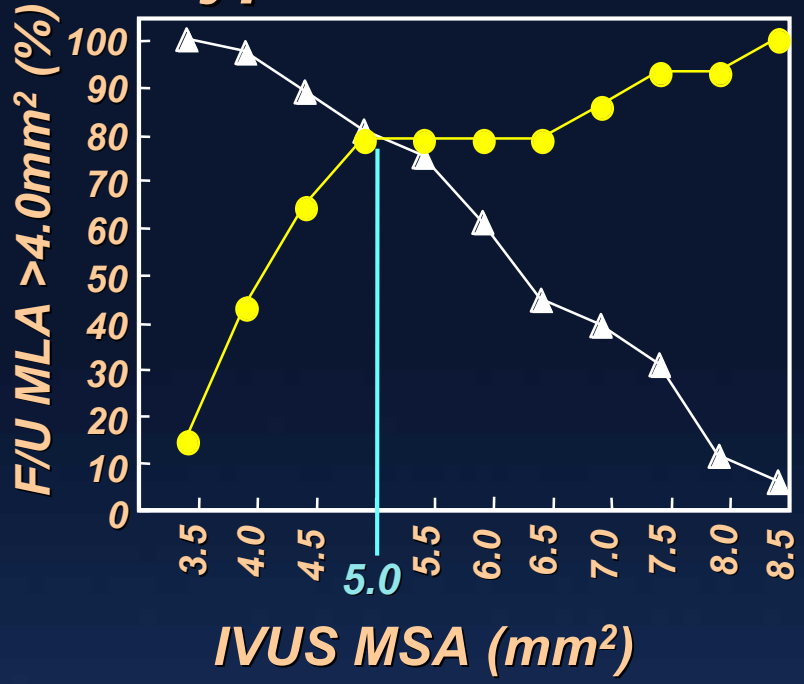
but no significant effect on MI (p=0.51) or mortality (p=0.18).



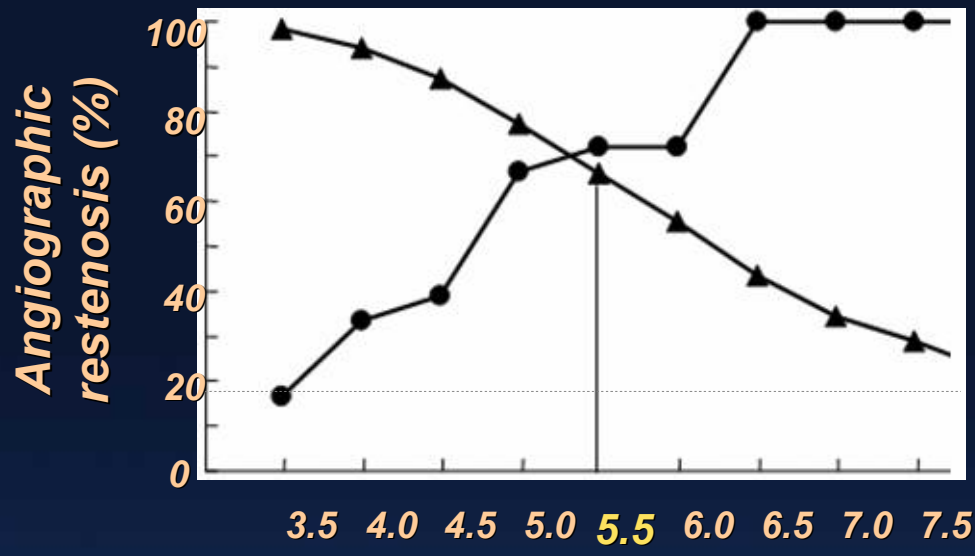
Predictors of DES Thrombosis & Restenosis

	DES Thrombosis	DES Restenosis
Underexpansion	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8)* •*Okabe et al., Am J Cardiol. 2007;100:615-20* •*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34*	•*Sonoda et al. J Am Coll Cardiol 2004;43:1959-63* •*Hong et al. Eur Heart J 2006;27:1305-10* •*Doi et al. JACC Cardiovasc Interv. 2009;2:1269-75* •*Fujii et al. Circulation 2004;109:1085-1088* •*Rathore et al. EuroIntervention. 2009;5:349-54.*
Edge problems (geographic miss, secondary lesions, large plaque burden, etc)	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8)* •*Okabe et al., Am J Cardiol. 2007;100:615-20* •*Liu et al. JACC Cardiovasc Interv. 2009;2:428-34*	•*Sakurai et al. Am J Cardiol 2005;96:1251-3* •*Liu et al.Am J Cardiol 2009;103:501-6* •*Costa et al, Am J Cardiol, 2008;101:1704-11*

Cypher in SIRIUS

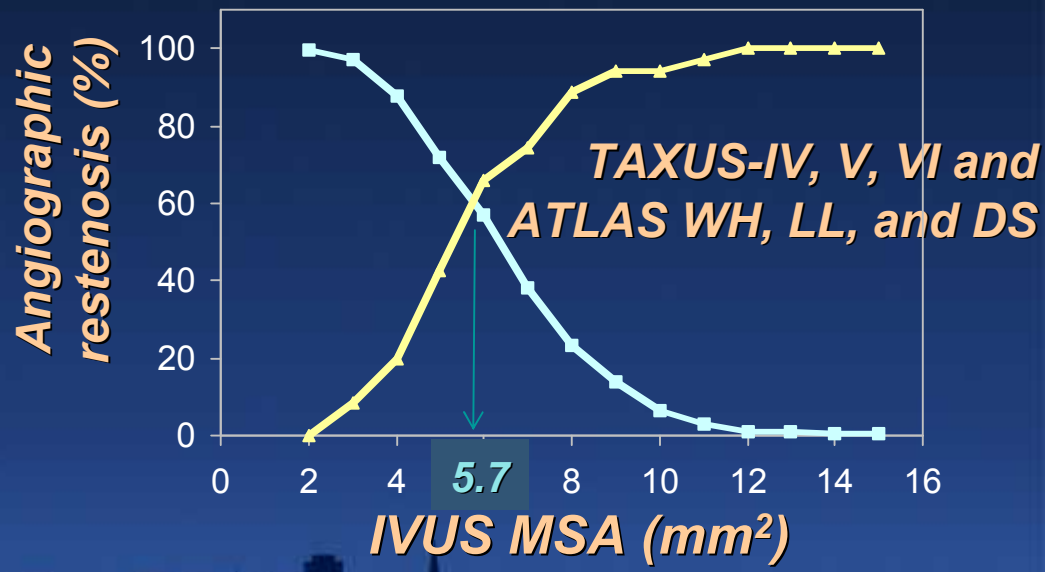


Cypher at AMC



By definition, sensitivity/specificity curve analysis "must" identify a single MSA that best separates restenosis from no restenosis

C-statistic for TAXUS was only 0.64



(Sonoda et al. J Am Coll Cardiol 2004;43:1959-63)
(Hong et al. Eur Heart J 2006;27:1305-10)
(Doi et al. JACC Cardiovasc Interv. 2009;2:1269-75)

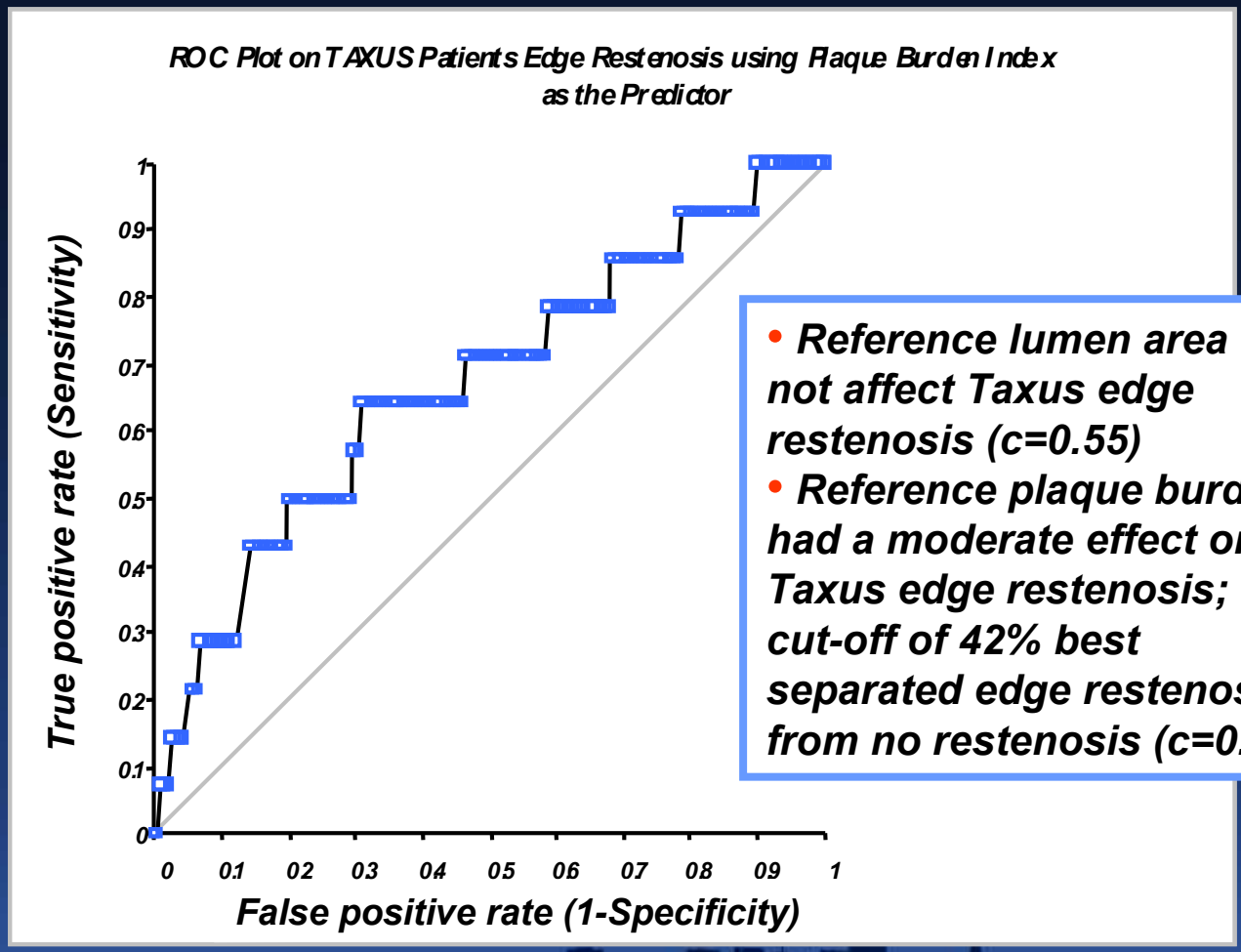
Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

CARDIOVASCULAR RESEARCH FOUNDATION

Does one size (MSA=5.0-5.5mm^2) fit all?

- Is an MSA of 5.0-5.5mm^2 enough in big arteries? Probably not. There is a step-wise decrease in restenosis with increasing stent expansion (MSA)
- Is it achievable in small arteries? Also, probably not.
- If so, manufacturers would only need to make one size DES – i.e., a 2.75mm stent - and it would suffice in all situations.

Comparison of 9-month QCA edge restenosis vs reference lumen area and plaque burden in TAXUS-IV, V, and VI (n=810)



- *Reference lumen area did not affect Taxus edge restenosis (c=0.55)*
- *Reference plaque burden had a moderate effect on Taxus edge restenosis; a cut-off of 42% best separated edge restenosis from no restenosis (c=0.67)*

Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell
CARDIOVASCULAR RESEARCH FOUNDATION

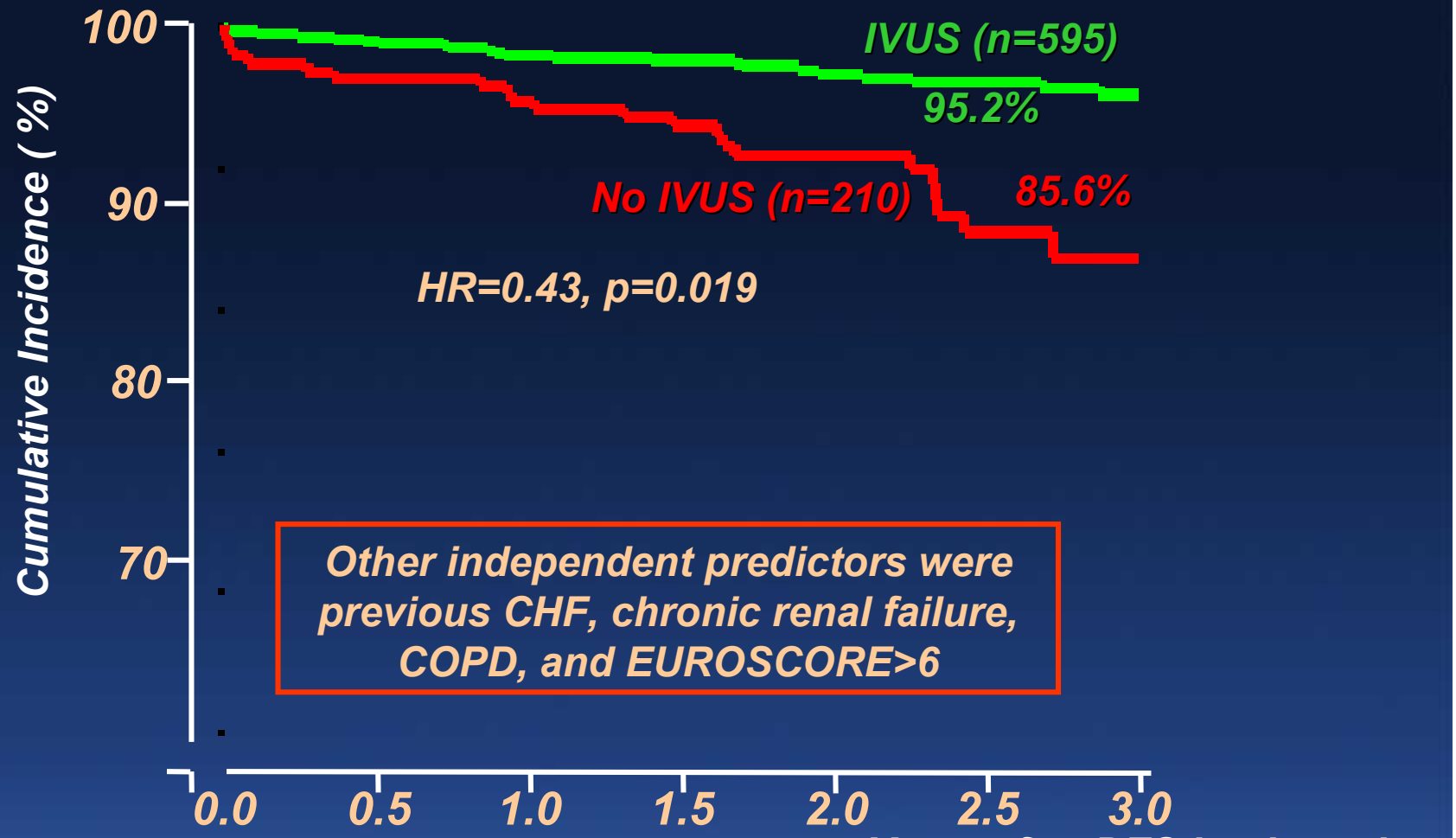
(Liu et al, Am J Cardiol 2009;103:501-6)

1296 IVUS-guided, DES-treated lesions in 884 pts vs 1312 propensity-score-matched, angio-guided, DES-treated lesions in 884 pts

	IVUS-guided	Angio-guided	p
30 day			
MACE	2.8%	5.2%	0.01
Stent thrombosis	0.5%	1.4%	0.045
TLR	0.7%	1.7%	0.045
1 year			
MACE	14.5%	16.2%	0.3
Definite stent thrombosis	0.7%	2.0%	0.014
Probably stent thrombosis	4.0%	5.8%	0.08
TLR	5.1%	7.2%	0.06
Late definite stent thrombosis	0.2%	0.7%	0.3

(Roy et al. Eur Heart J 2008;29:1851-7)

All-Cause Mortality After LMCA DES Implantation: Impact of IVUS Guidance

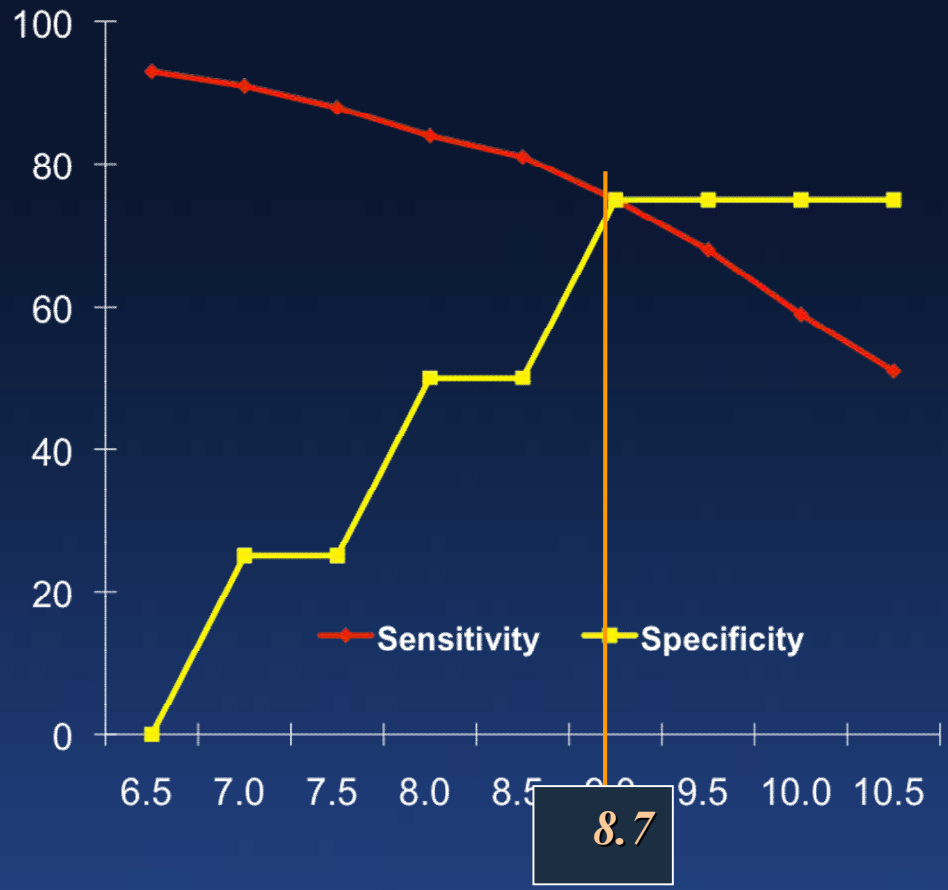


Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

CARDIOVASCULAR RESEARCH FOUNDATION

(Park et al. Circ Cardiovasc Intervent 2009;2:167-77)

"Optimal" MSA and TLR after LMCA DES Implantation (n=595)

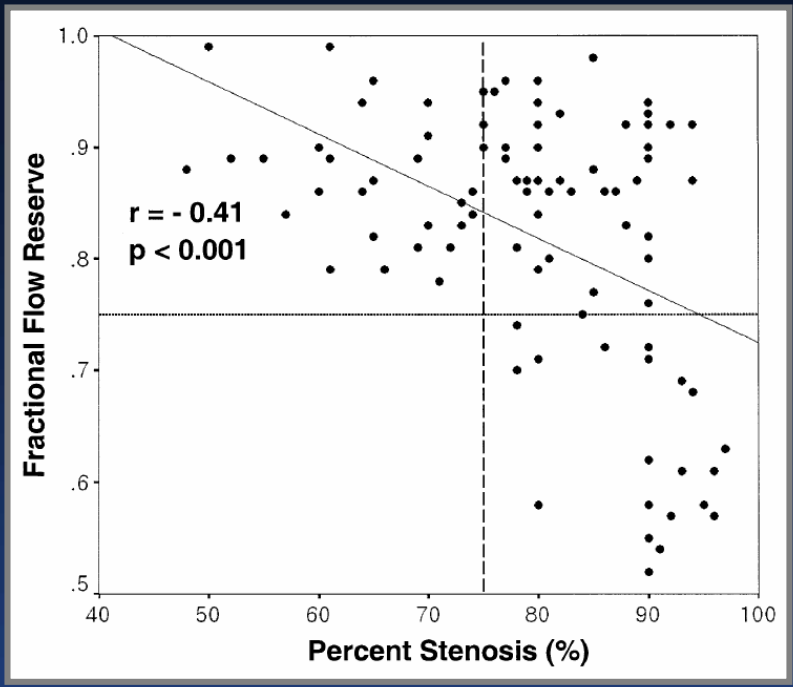


Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

CARDIOVASCULAR RESEARCH FOUNDATION

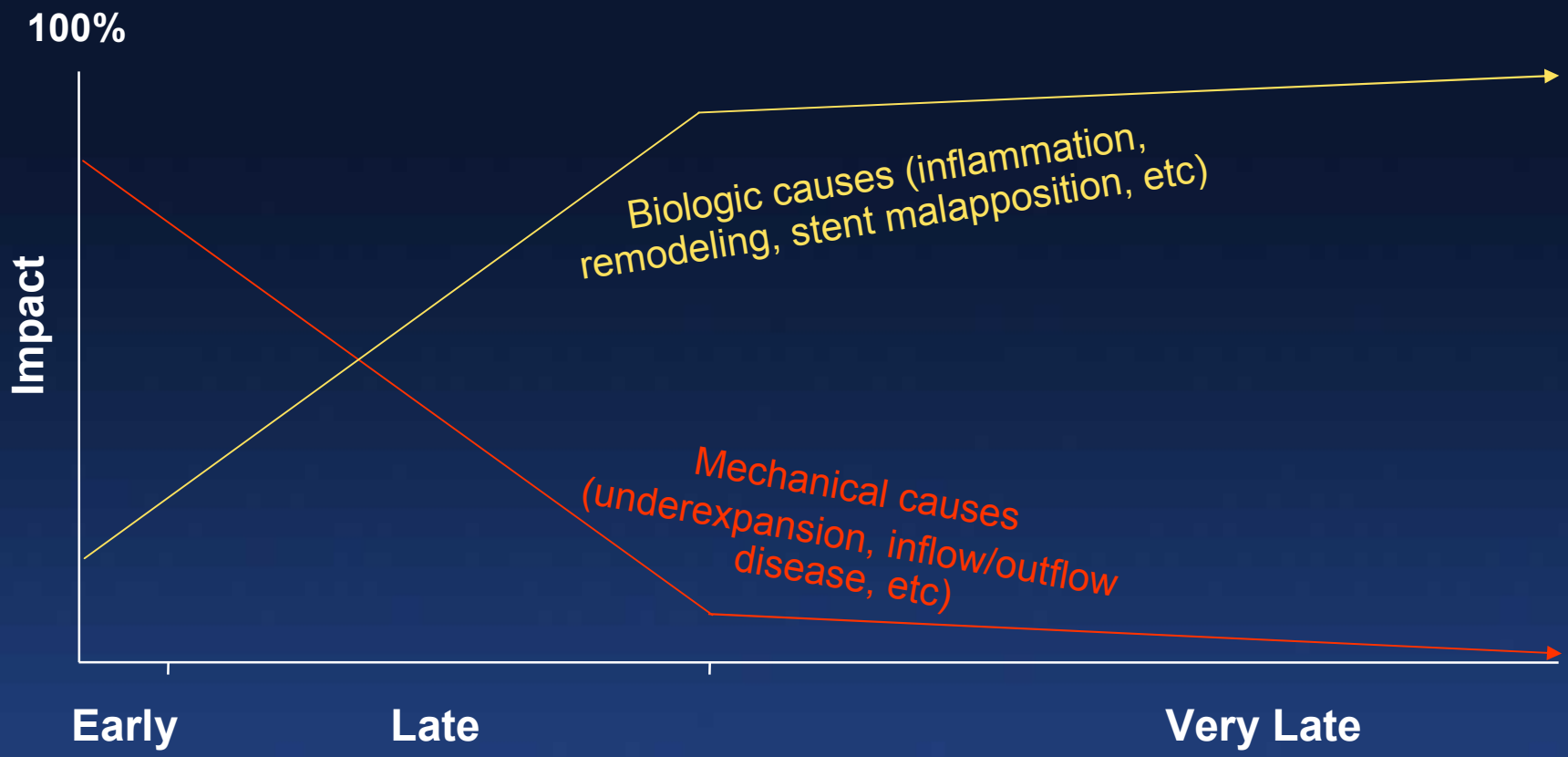
(SJ Park. TCT 2007)

FFR Assessment of 97 Jailed Side Branch Lesions

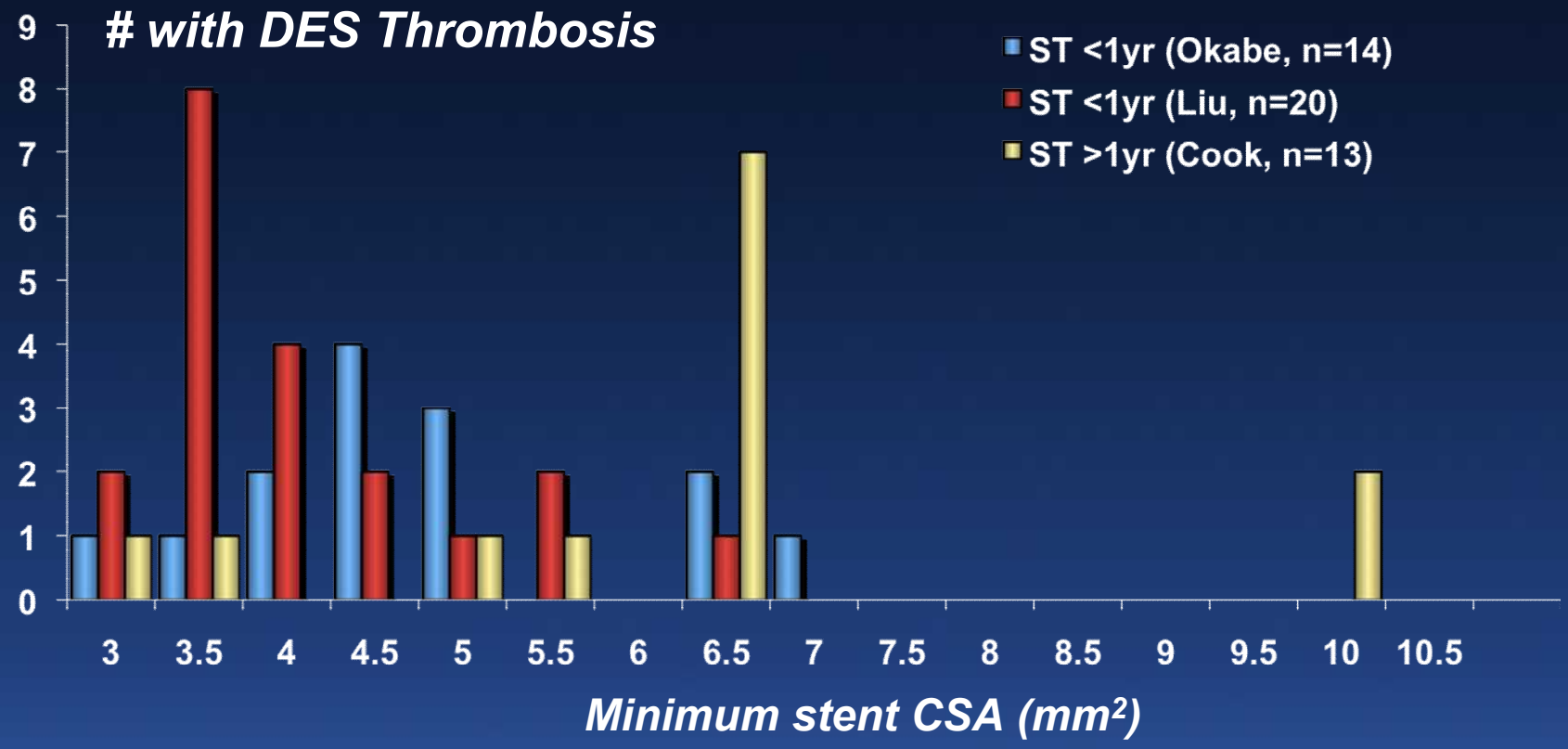


- *There was a negative correlation between the % stenosis on QCA and FFR (r=-0.41, p<0.001).*
- *Only 27% of lesions with QCA DS >75% were functionally significant as assessed by FFR (<0.75).*

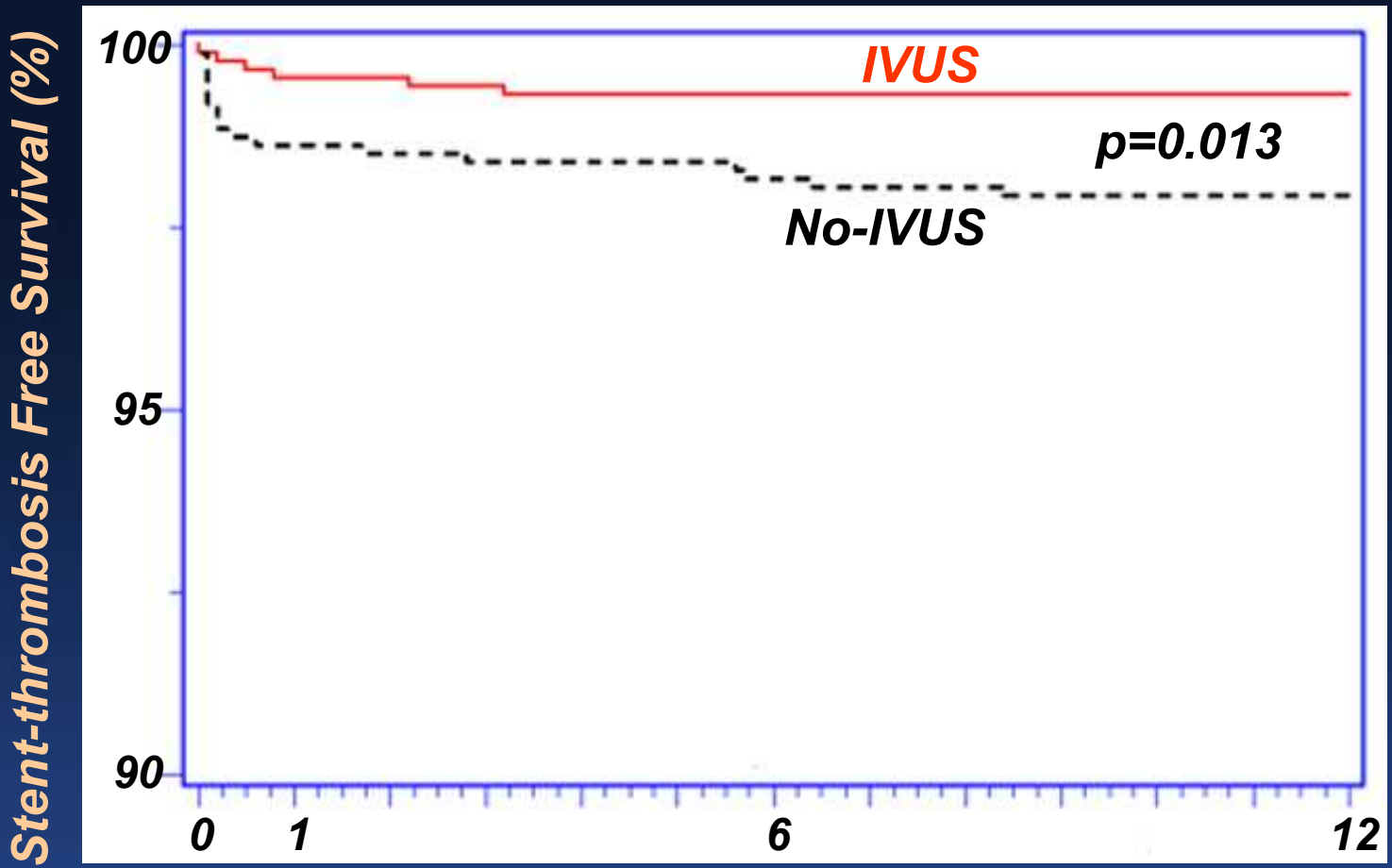
(Koo et al. J Am Coll Cardiol 2005;46:633-7)


100%
Impact
Biologic causes (inflammation, remodeling, stent malapposition, etc)
Mechanical causes (underexpansion, inflow/outflow disease, etc)
Early
Late
Very Late

Impact of DES underexpansion on early/late and very late thrombosis



(Okabe et al. Am J Cardiol 2007;100:615-20)
(Liu et al. JACC Cardiovasc Interv. 2009;2:428-34)
(Cook et al. Circulation 2007;115:2426-34)



(Roy et al. Eur Heart J. 2008;29:1851-7)

Meta-Analysis of Late Stent Malapposition (LSM) Frequency

- 17 studies with 4648 patients
  - 2453 BMS and 2195 DES
  - 4 SES, 4 PES, 1 EES, 2 ZES, 3 DES vs DES, and 3 BMS only
- LSM more common in DES than BMS
  - OR=2.5, p=0.02 when both RCT and observational studies were included
  - OR=4.4, p=0.002 when only RCT were included
  - SES > PES > ZES > EES

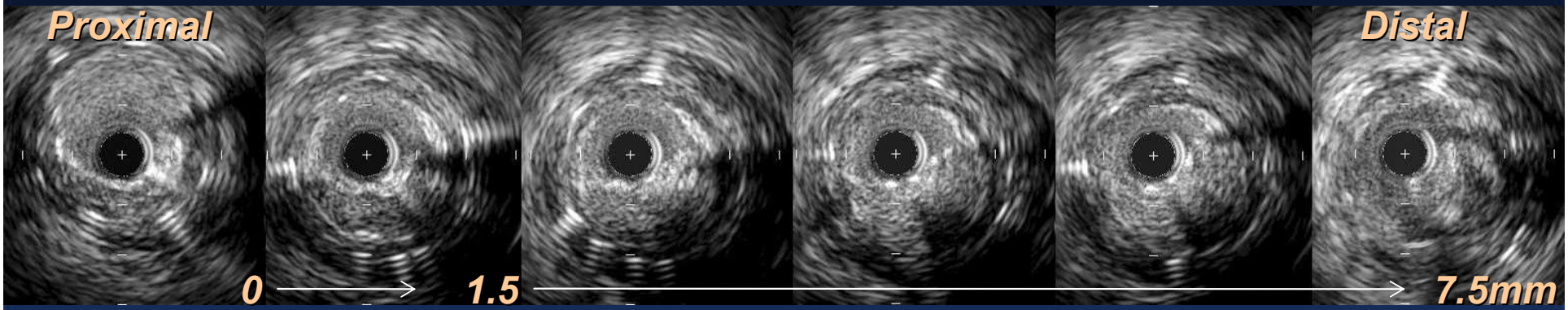
(Hassan et al. Eur Heart J, in press)

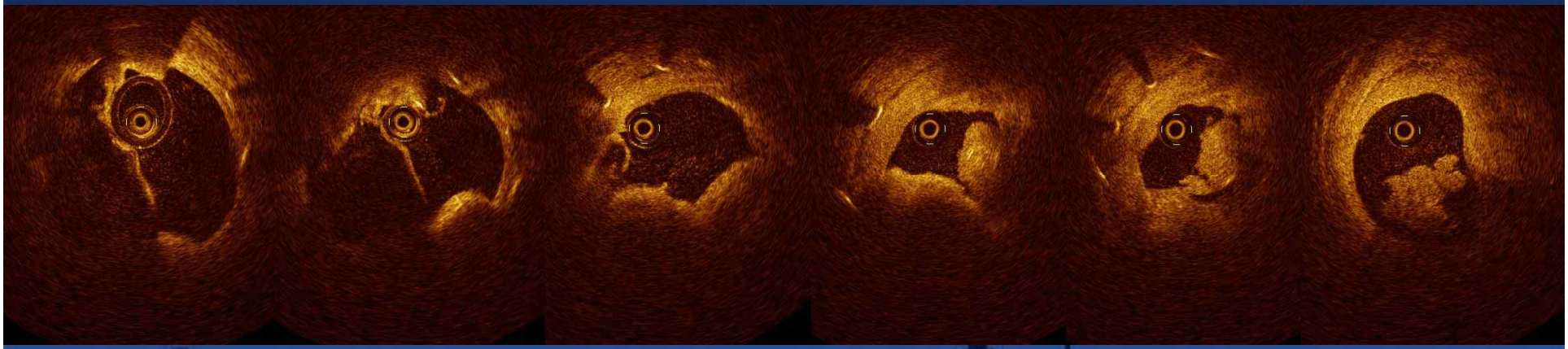
Meta-Analysis of Very Late ST in LSM

- 5 studies with 2080 patients
  - 228 LSM and 1852 no LSM
  - 3 Late ST (<12 mos), none in LSM
  - 6 Very late ST (>12 mos), 4 in LSM
- Risk of very late ST was higher in LSM patients (OR=6.5, p=0.02).
- Based on the expected numbers of very late ST, 3 of 5 studies favored the relationship between LSM and very late ST.

(Hassan et al. Eur Heart J, in press)

Neoatherosclerosis with neointimal rupture was observed in 62.5% of DES patients with VLST and 100% of BMS patients with VLST





Columbia University Medical Center
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

CARDIOVASCULAR RESEARCH FOUNDATION

(Lee et al. J Am Coll Cardiol 2010;55:1936-42)

Follow-up

- A decrease in specificity has been observed when myocardial perfusion imaging (MPI) is performed <2 months of PCI.
- The overall sensitivity and specificity of MPI for detecting myocardial ischemia ≥2 months after PCI are both 79%, and are roughly equivalent in all three vascular territories
- Following PCI, progression of disease in untreated vessel segments occurs at rates approaching 7% per year in both symptomatic and asymptomatic patients. More than one-half of pts presenting with chest pain >1 year after PCI have a new lesion or significant worsening of a previously nonobstructive stenosis. During late follow-up, outcomes are more strongly correlated with disease progression than restenosis.
- Asymptomatic patients should initially be followed clinically and undergo MPI at 6-9 months. Patients with normal, low-risk, or intermediate-risk scans (small or medium-sized defects of mild-to-moderate severity) can be managed medically. Patients with high-risk scans (medium-sized severe defects, large defects of any severity, or scans showing stress-induced left ventricular failure) should undergo angiography.

(Giedd & Bergmann. J Am Coll Cardiol 2004;43:328-36)

In the ideal world. . .

- Pts would be screened pre-PCI using a technique that assessed stress-induced myocardial ischemia (or viability when treating CTOs).
  - Although the various techniques have their systematic differences, my experience is that the dedication of an institution to expertise in an individual technique is most important
- FFR would be used to identify ischemia-producing lesions, especially in the setting of intermediate lesions or multivessel disease. The exception being intermediate LM lesions where IVUS has certain advantages over FFR, especially in the setting of LAD and/or LCX disease
- Stent implantation would be IVUS-guided to optimize expansion and full lesion coverage, especially in high-risk pt and lesion subsets
- After 6 months pts would have repeat assessment of stress-induced myocardial ischemia