

# **IVUS Preferred-Stick with What Works**

*Cors at the Shore*

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# ***Disclosure Statement of Financial Interest***

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

## **Affiliation/Financial Relationship**

- *Consulting Fees/Honoraria*

## **Company**

- *BSC, Abbott Vascular, Medtronic*

# *Modalities*

- FFR
- iFR (and other resting indices)
- IVUS
- RF-IVUS (VH-IVUS, iMAP, or IB-IVUS)
- OCT
- NIRS
- Some combination of the above

# *Clinical questions*

- Is this lesion flow-limiting?
  - Non-LMCA
  - LMCA
- Pre-intervention lesion assessment (ie., what is the culprit?)
- Is this “other” lesion a vulnerable plaque that is at risk for future events?
- What is the likelihood of embolization during stent implantation?
- How do I effectively treat an CTO?
- How do I guide and optimize acute stent results (size, length, expansion, edge coverage)?
  - Is this jailed sidebranch significant?
- Why did this stent thrombose or restenose?

# IVUS vs “Ischemia” in Non-LMCA Lesions

Reference	Versus	# of lesions	% abn	Inclusion criteria	Mean MLA (mm <sup>2</sup> )	MLA cut-off (mm <sup>2</sup> )	Other independent IVUS anatomic determinants	PPV	NPV
Abizaïd AJC 1998	CFR<2.0	112	40%		4.4	<b>4.0</b>			
Nishioka JACC 1999	SPECT	70	65%		4.3	<b>4.0</b>			
Takagi Circulation 1999	FFR<0.75	51	49%		3.9	<b>3.0</b>			
Briguori AJC 2001	FFR<0.75	53	23%	40-70% DS	3.9	<b>4.0</b>	Lesion length	<b>46%</b>	<b>96%</b>
Takayama CCI 2001	FFR	14	50%	>2.5mm vessels	3.5		MLA divided by lesion length		
Lee AJC 2010	FFR<0.75	94	40%	30-75% DS <3mm vessels	2.3	<b>2.0</b>	Lesion length Plaque Burden		
Kang Circ Interv 2011	FFR<0.8	236	21%	30-75% DS	2.6	<b>2.4</b>	LAD Plaque burden	<b>37%</b>	<b>96%</b>
Ahn JACC Interv 2011	SPECT	170	26%		2.1	<b>2.1</b>		<b>39%</b>	<b>91%</b>
Kang AJC 2012	FFR<0.8	784	29%	30-90% DS		<b>2.4</b>	LAD Lesion length Plaque rupture Plaque burden	<b>48%</b>	<b>90%</b>
Ben-Dor EuroInterv 2011	FFR<0.75	92	19%	40-70% DS >2.5mm vessels	3.6	<b>2.8</b>	Lesion length		
	FFR<0.8					<b>3.2</b>			
Ben-Dor CRM 2012	FFR<0.8	205	26%	40-70% DS >2.5mm vessels		<b>3.1</b>			
Koo JACC Interv 2011	FFR<0.8	267	33%	30-70% DS Proximal or Mid	3.0	<b>3.0</b>	Proximal or Mid LAD	<b>47%</b>	
Koh JACCInterv 2012	FFR<0.8	38	37%	40-70% DS Ostial MV		<b>3.5</b>			<b>87%</b>
		55	27%	40-70% DS Ostial SB			<b>&lt;50%</b>		
Usui. EuroIntervention 2018	FFR<0.8	203	69%	30-80%	2.4	<b>2.7</b>		<b>78%</b>	<b>46%</b>
	FFR<0.75		35%			<b>2.6</b>	<b>42%</b>	<b>76%</b>	
Brown. Int J Cardiol 2017	FFR<0.8	92	74%		2.7	<b>2.6</b>	Plaque burden		
Matsushita. Heart and Vessels 2018	FFR<0.8	80	51%		2.2	<b>2.0</b>			
	iFR<0.89		26%			<b>1.8</b>			

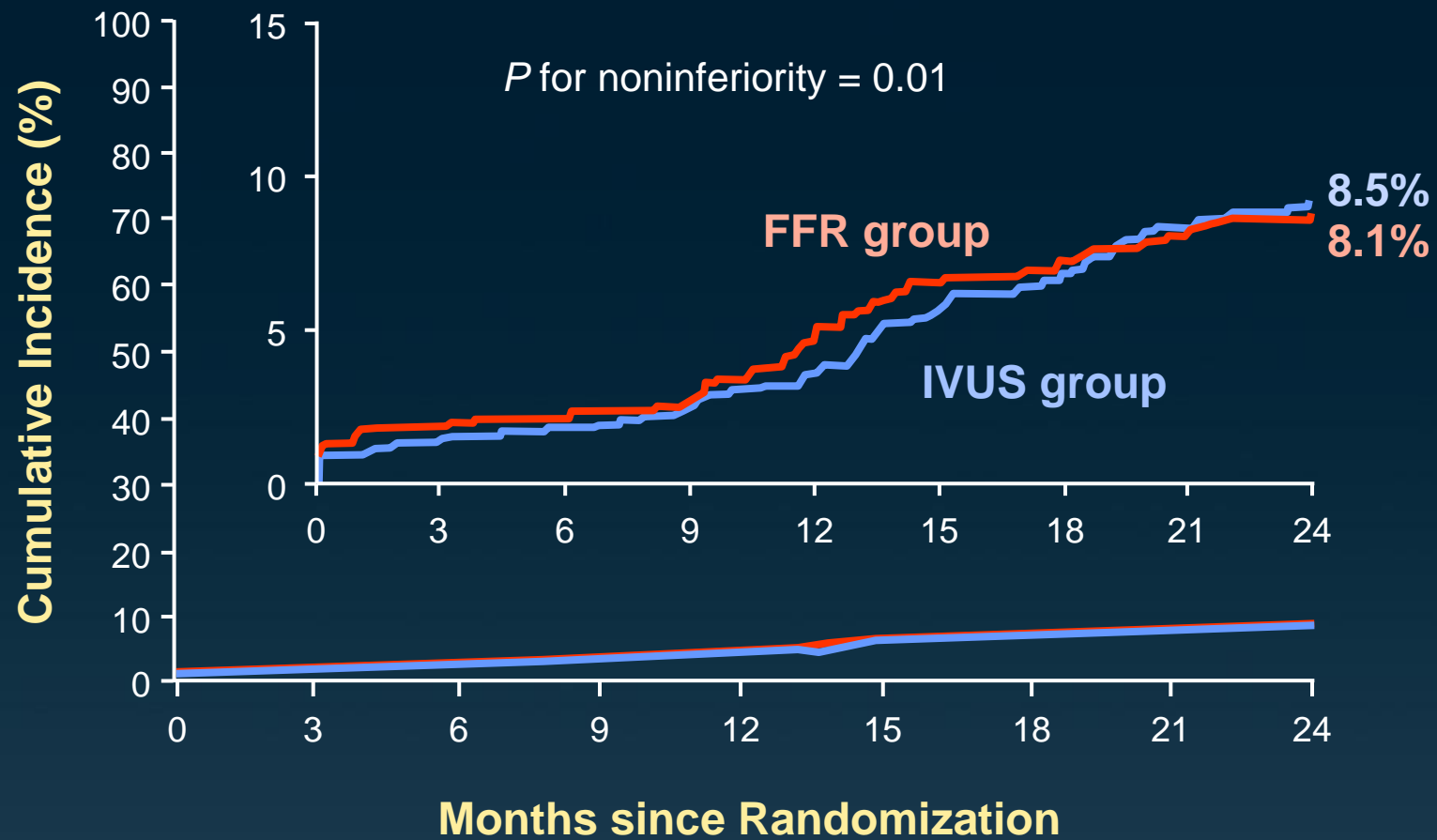
Reference	Versus	# of lesions	% abn	Inclusion criteria	Mean MLA (mm <sup>2</sup> )	MLA cut-off (mm <sup>2</sup> )	Other independent IVUS anatomic determinants	PPV	NPV
Waksman JACC 2013	FFR<0.8	334	25%	40-80% DS >2.5mm vessels	5.6	<b>3.1</b>	LAD Plaque burden	<b>40%</b>	<b>83%</b>
Stone TCT 2013	FFR<0.80	544	31%	40-80% DS >2.75mm vessels		<b>2.9</b>	LAD vs LCX RCA vs LCX	<b>47%</b>	<b>81%</b>
Kwan CMJ 2012	FFR<0.8	169	59%	40-99% DS LAD	3.0	<b>3.0</b>	Plaque burden	<b>84%</b>	<b>82%</b>
Chen IJC 2013	FFR<0.8	323	54%	≥40% DS	2.9	<b>3.0</b>	Plaque burden LAD	<b>73%</b>	<b>76%</b>
Yang CCI 2014	FFR<0.8	206	44%	40-70% DS Prox/mid LAD >3.0mm vessel	3.1	<b>3.2 (Prox) 2.5 (Mid)</b>	Lesion length		
Kang JACCInterv 2013	FFR<0.8	207 females	27% females	>30% DS LAD	2.6	<b>2.5</b>		<b>63% male</b>	<b>81% male</b>
					2.5	<b>2.5</b>		<b>42% female</b>	<b>93% female</b>
Lopez-Palop REspCard 2013	FFR<0.8	61	49%	40-70% DS ≥20mm length	2.7	<b>3.1</b>	Lesion length	<b>67%</b>	<b>93%</b>
Naganuma CRM 2014	FFR<0.8	169	30%	40-70% DS	3.0	<b>2.7</b>	Plaque burden	<b>59%</b>	<b>90%</b>
Voros AJC 2014	FFR<0.75	323	27%	40-99% DS	3.7	<b>2.7</b>		<b>39%</b>	<b>93%</b>
Cui CMJ 2013	FFR<0.8	206	26%	40-70% DS >2.5mm vessels	3.9	<b>3.2</b>	Plaque burden	<b>53%</b>	<b>85%</b>
Han Cardiology 2014	FFR<0.8	169	39%		3.1	<b>2.8</b>		<b>49%</b>	<b>73%</b>
Cho Eurointervention 2015	FFR <0.8	945	40%	30-70% DS	3.1	<b>3.0</b>		<b>50%</b>	<b>72%</b>
Gonzalo JACC 2012	FFR <0.8	51	46%	40-70% DS	2.6	<b>2.4</b>		<b>67%</b>	<b>65%</b>
Kang AJC 2016	FFR<0.8	103	41%	30-80% DS	3.6	<b>2.8</b>	Subtended myocardium	<b>71%</b>	
Kang AJC 2016	FFR<0.75	101	45%	20-80%	3.5	<b>2.8</b>	Subtended myocardium	<b>62%</b>	<b>91%</b>
Sakurai Int J CVI 2015	FFR<0.8	114	85%	26-90%	2.0		Plaque burden IB-IVUS lipid		
Nishi J Cardiol 2016	FFR<0.8	42	67%	40-80% DS	1.5	<b>2.2</b>			
Lee. Rev Esp Cardiol 2019	FFR<0.8	365	51-58%	53 ± 15% DS	4.1	<b>3.4-3.8</b>		<b>59-66%</b>	<b>62-69%</b>



# FLAVOUR: Randomized FFR vs IVUS in 1682 patients with intermediate lesions (angiographic DS 40-70%)

	FFR	IVUS
Stent implantation criteria	<0.80	MLA <3mm <sup>2</sup> (or 3-4mm <sup>2</sup> plus plaque burden >70%)
%PCI	44.4%	65.3%
Stents per patient	0.6±0.9	0.9±1.0
Stent optimization criteria	≥0.88 or a difference <0.05 across the stent	MLA ≥5.5mm <sup>2</sup> and plaque burden at stent edge ≤55% or in-stent MLA ≥ distal reference lumen
% optimized	50.1%	54.8%
24-month MACE	8.1%	8.6%
PCI-optimized	12.3%	8.5%
Suboptimal PCI	11.8%	9.8%
Medical therapy	5.0%	5.9%

Each individual component of the primary endpoint was not different between FFR- and IVUS-guided PCI (all-cause death: 1.3% vs. 2.3%; MI: 1.9% vs. 1.7%; 5.7% vs. 5.3%; repeat revascularization: 5.7% vs. 5.3%) or periprocedural MI (1.2% vs. 0.9%).



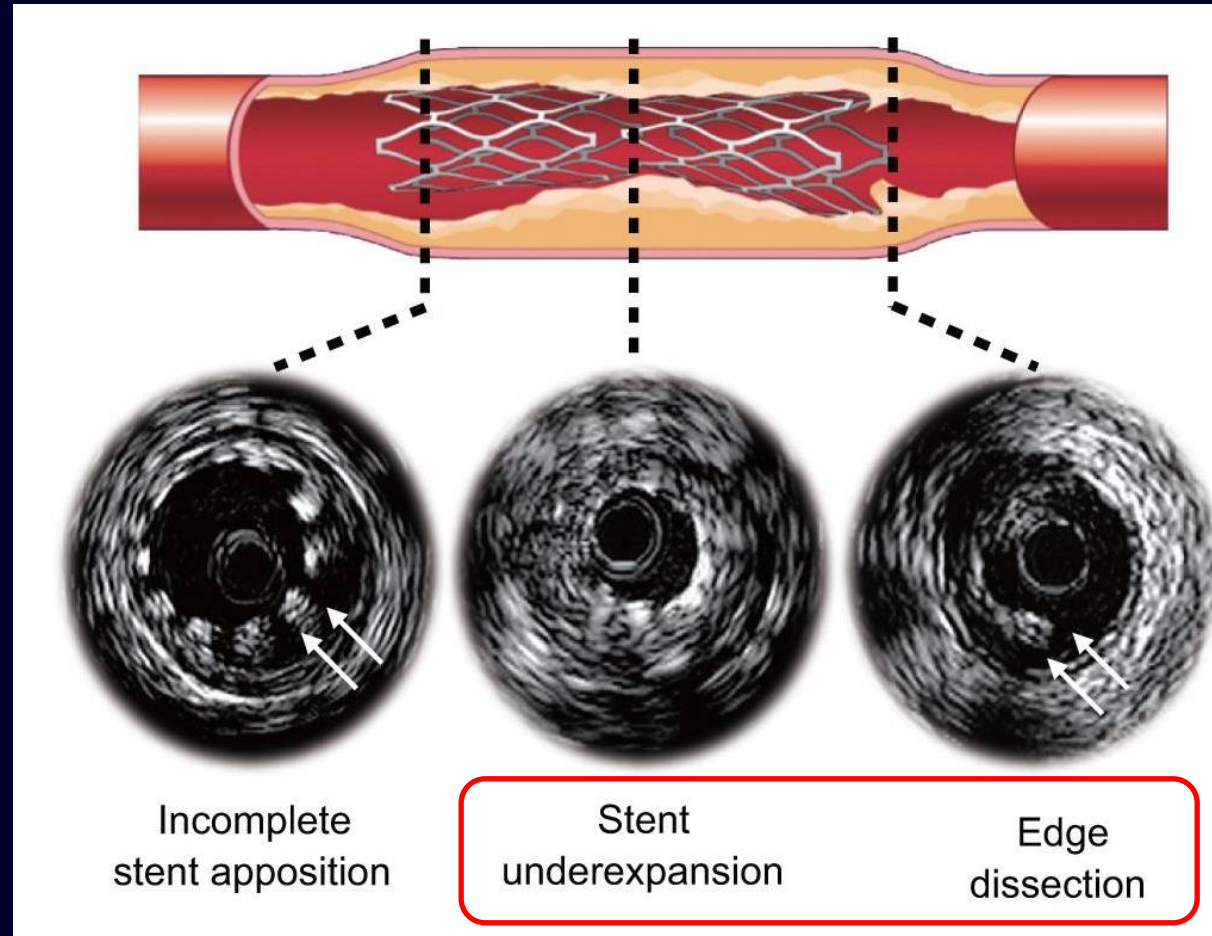
No. at Risk	0	3	6	9	12	15	18	21	24
IVUS group	844	828	825	820	809	792	784	771	690
FFR group	838	818	816	812	796	781	778	770	699

# IVUS Predictors of DES Early Thrombosis & Restenosis

Small MSA, MLA,  
or underexpansion

Edge problems

- Geographic miss
- Secondary lesion
- Large plaque burden
- Dissections, etc



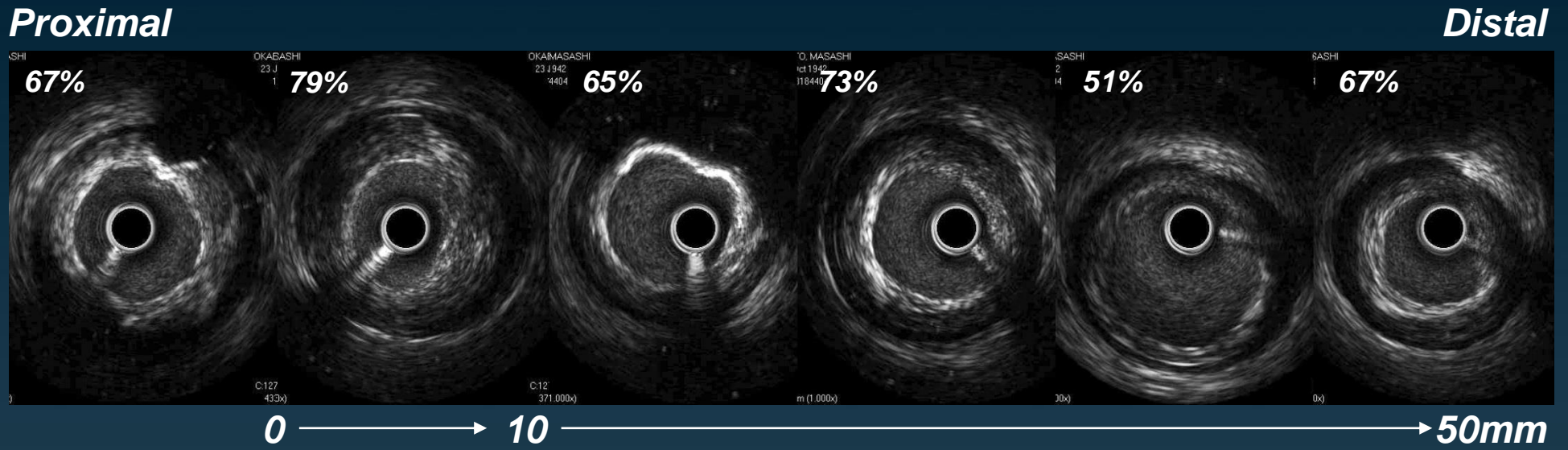
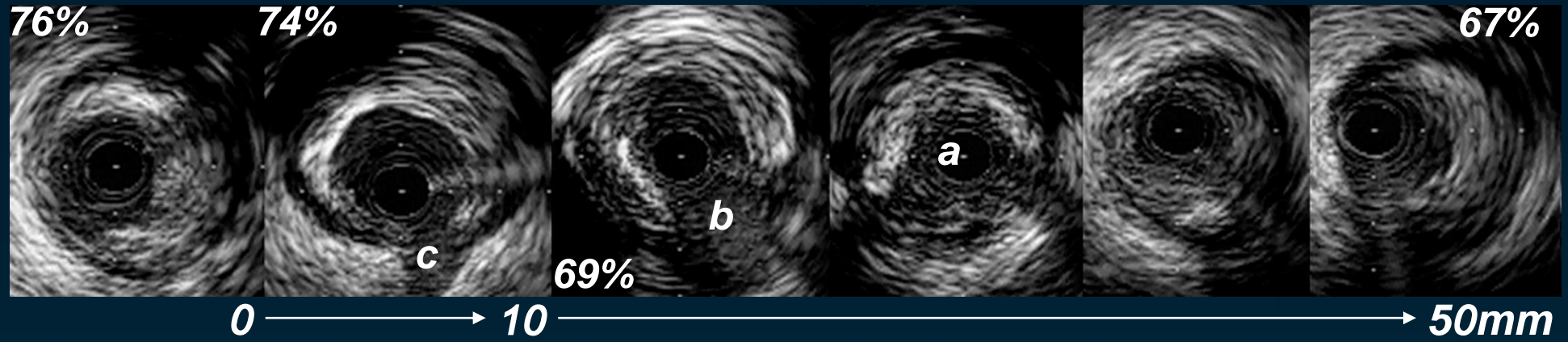
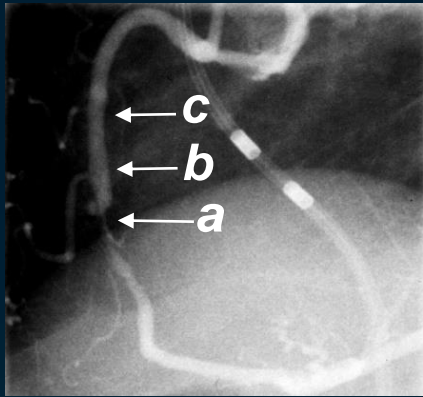
# Predictors of DES Early ST, Restenosis, MACE, or DoCE

	IVUS		OCT
	Early ST	Restenosis/MACE	Restenosis/MACE/DoCE
<p>Small MSA or underexpansion in stable lesions</p> <p>Small MLA in ACS/MI lesions</p>	<ul style="list-style-type: none"> <li>•Fujii et al. J Am Coll Cardiol 2005;45:995-8</li> <li>•Okabe et al. Am J Cardiol. 2007;100:615-20</li> <li>•Liu et al. JACC Cardiovasc Interv. 2009;2:428-34</li> <li>•Choi et al. Circ Cardiovasc Interv 2011;4:239-47</li> </ul>	<ul style="list-style-type: none"> <li>•Sonoda et al. J Am Coll Cardiol 2004;43:1959-63</li> <li>•Hong et al. Eur Heart J 2006;27:1305-10</li> <li>•Doi et al JACC Cardiovasc Interv. 2009;2:1269-75</li> <li>•Fujii et al. Circulation 2004;109:1085-1088</li> <li>•Kang et al. Circ Cardiovasc Interv 2011;4:9-14</li> <li>•Choi et al. Am J Cardiol 2012;109:455-60</li> <li>•Song et al. Catheter Cardiovasc Interv 2014;83:873-8</li> <li>•Kang et al. PLoS One 2015;10(10):e0140421</li> <li>•Hong et al. JAMA 2015;314(:2155-63.</li> <li>•Lee et al. Rev Esp Cardiol 2017;70:88-95</li> <li>•Katagiri et al. Catheter Cardiovasc Interv. 2019 Jan 31. doi: 10.1002/ccd.28105.</li> <li>•Kim et al. EuroIntervention. 2020;16:e480-e488</li> <li>•Park et al. JACC Cardiovasc Interv 2020;13:1403-13</li> <li>•Ladwiniec et al. EuroIntervention 2020;16:201-9</li> <li>•Sugane et al. Atherosclerosis 2021;318:70-5</li> <li>•Kwon et al. EuroIntervention 2021;17:e639-e646</li> <li>•Cha et al. Coron Artery Dis 2021;32:1541-8</li> <li>•Fujimura et al. JACC Cardiovasc Interv 2021;14:1639-50</li> <li>•Lee et al. Circ Cardiovasc Interv. 2021;14:e011124.</li> <li>•Komaki et al. Int J Cardiol 2021;334:31-36</li> </ul>	<ul style="list-style-type: none"> <li>•Prati et al. JACC Cardiovasc Imaging 2015;8:1297-305</li> <li>•Prati et al. Circ Cardiovasc Interv. 2016;9. pii: e003726.</li> <li>•Soeda et al. Circulation 2015;132:1020-9</li> <li>•Matsuo et al. Cathet Cardiovasc Interv 2015;87:E9-14</li> <li>•Prati et al. EuroIntervention 2018;14:e443-e451</li> <li>•Katsura et al. Catheter Cardiovasc Interv 2020;96:E501-E507</li> <li>•Kim et al. JACC Cardiovasc Imaging 2022;15:126-37</li> <li>•Lee et al. Sci Rep. 2023;13:3781. doi: 10.1038/s41598-023-30717-6</li> </ul>
<p>Edge problems (geographic miss, secondary lesions, large plaque burden, dissections, etc)</p>	<ul style="list-style-type: none"> <li>•Fujii et al. J Am Coll Cardiol 2005;45:995-8</li> <li>•Okabe et al., Am J Cardiol. 2007;100:615-20</li> <li>•Liu et al. JACC Cardiovasc Interv. 2009;2:428-34</li> <li>•Choi et al. Circ Cardiovasc Interv 2011;4:239-47</li> </ul>	<ul style="list-style-type: none"> <li>•Sakurai et al. Am J Cardiol 2005;96:1251-3</li> <li>•Liu et al. Am J Cardiol 2009;103:501-6</li> <li>•Costa et al, Am J Cardiol, 2008;101:1704-11</li> <li>•Kang et al. Am J Cardiol 2013;111:1408-14</li> <li>•Kobayashi et al. Circ Cardiovasc Interv. 2016;9:e003553</li> <li>•Calvert et al. Catheter Cardiovasc Interv 2016;88:340-7</li> <li>•Park et al. JACC Cardiovasc Interv 2020;13:1403-13</li> </ul>	<ul style="list-style-type: none"> <li>•Prati et al. JACC Cardiovasc Imaging 2015;8:1297-305</li> <li>•Prati et al. Circ Cardiovasc Interv. 2016;9. pii: e003726.</li> <li>•Ino et al. Circ Cardiovasc Interv. 2016;9:e004231</li> <li>•Prati et al. EuroIntervention 2018;14:e443-e451</li> <li>•van Zandvoort et al. Circ Cardiovasc Interv. 2020;13:e008685</li> </ul>
<p>Protrusion in ACS/MI</p> <p>Irregular Protrusion</p>	<ul style="list-style-type: none"> <li>•Choi et al. Circ Cardiovasc Interv 2011;4:239-47</li> <li>•Hong et al. Int J Cardiol 2013;168:1674-5</li> </ul>		<ul style="list-style-type: none"> <li>•Prati et al. Circ Cardiovasc Interv. 2016;9. pii: e003726.</li> <li>•Soeda et al. Circulation 2015;132:1020-9</li> </ul>
<p>Stent length (&gt;40mm)</p>		<ul style="list-style-type: none"> <li>•Hong et al. Eur Heart J 2006;27:1305-10</li> </ul>	
<p>Asymmetry/Eccentricity</p>		<ul style="list-style-type: none"> <li>•Suwannasom et al. JACC Cardiovasc Interv 2016;9:1231-42 (not significant at long term follow-up: JACC Cardiovasc Interv 2018;11:1013-5)</li> </ul>	



# Early IVUS observations regarding angiography during PCI that are still true today

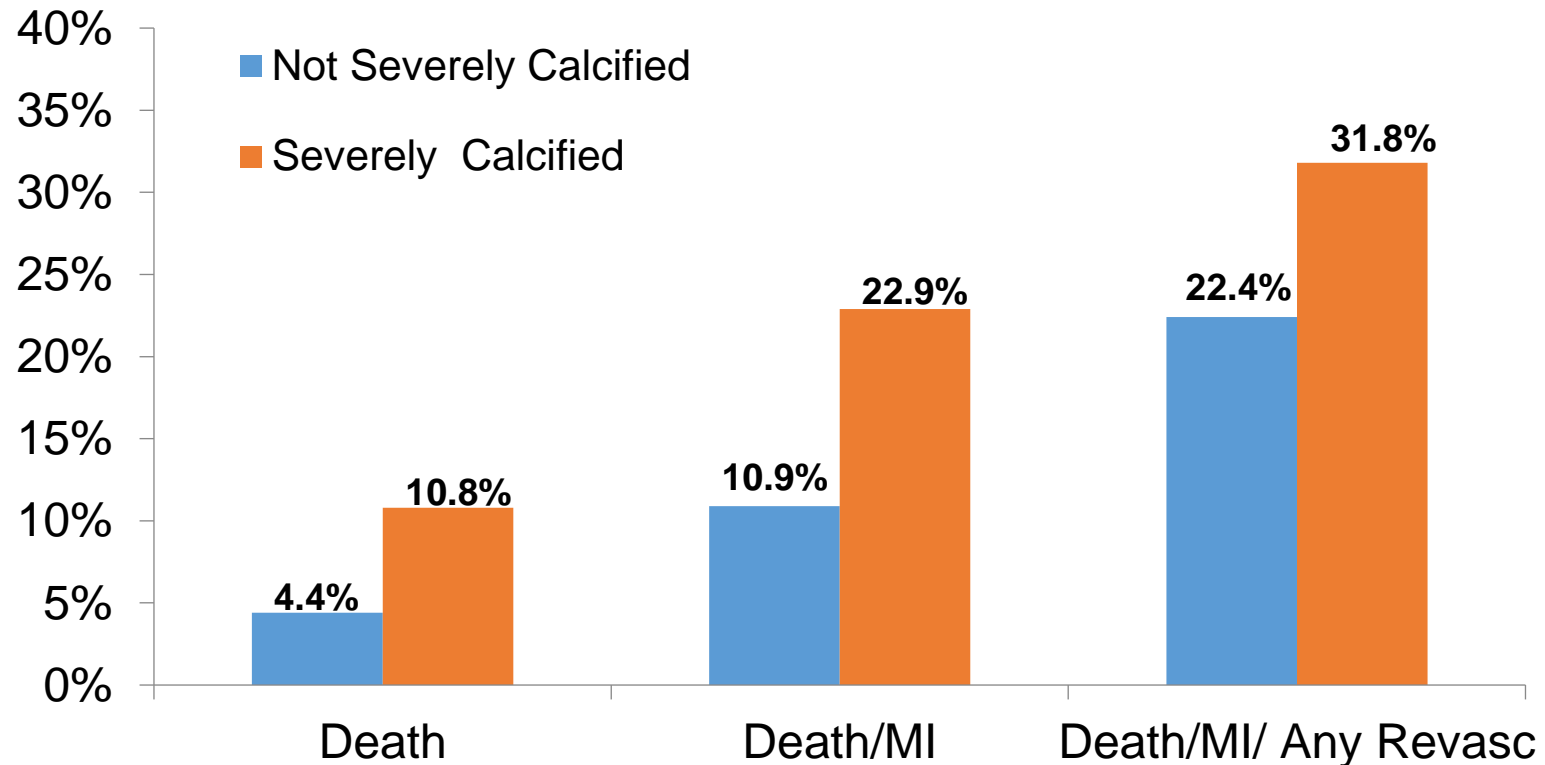
- Atherosclerosis is ubiquitous and most of it is angiographically silent
- The angiogram is often misleading in assessing vessel size
- The angiogram is often misleading in assessing calcification
- A good angiographic result is not a guarantee of a good anatomic result



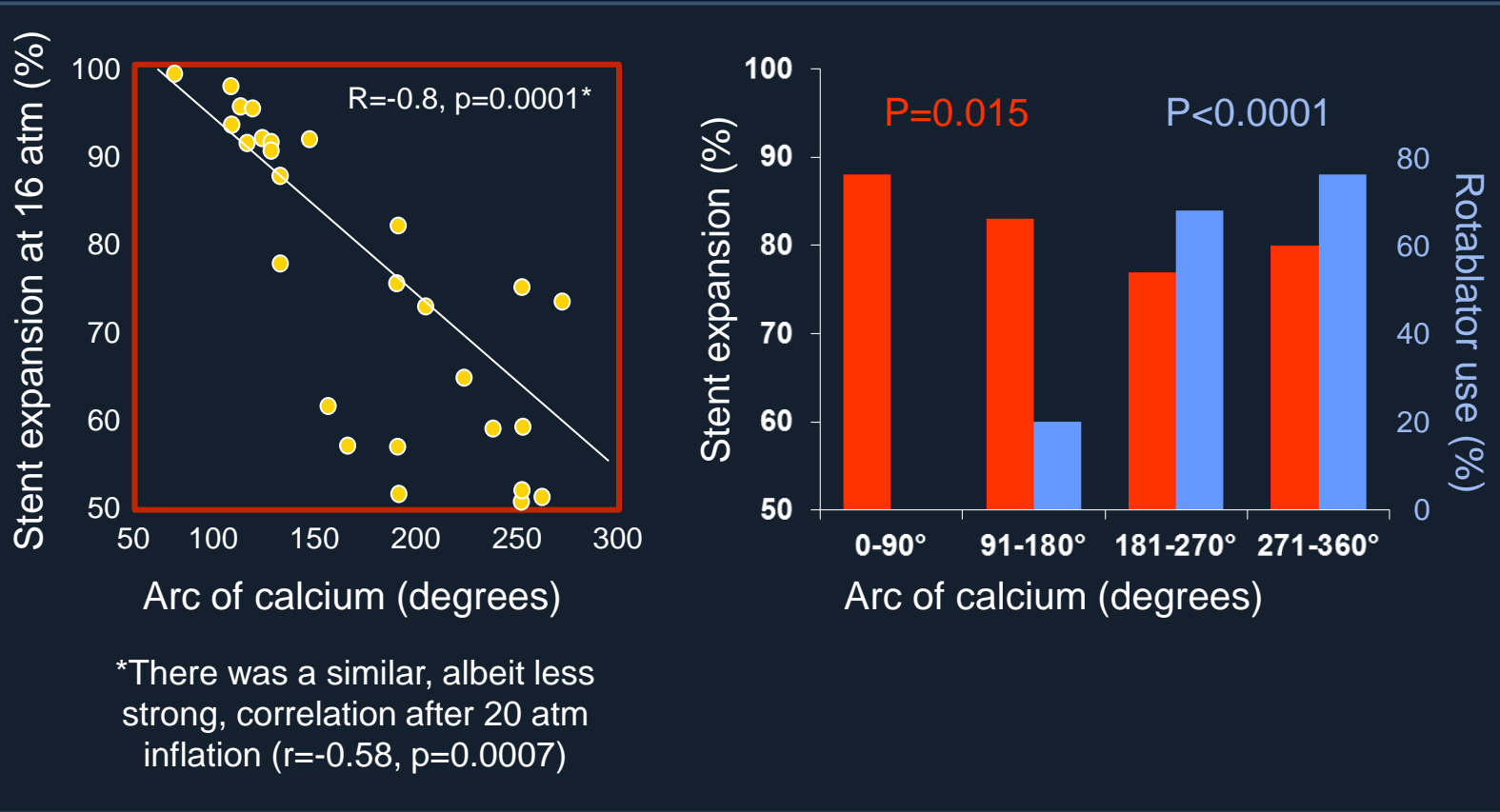
**In 884 native coronary arteries, the plaque burden in the angiographically “normal” reference segment was  $51 \pm 13\%$ ; and only 6.8% were truly normal.**

# Coronary calcium is a predictor of worse prognosis after PCI with DES

7 DES Trials - 6296 patients  
Independent core lab (Cardioanalysis, Rotterdam)  
20% of patients had severe coronary calcification  
Outcomes at 3 years



# Stent Expansion in Calcified Lesions



Vavarunakis et al. Catheter Cardiovasc Interv 2001;52:164-172

Hoffmann et al. Eur Heart J 1998;19:1224-31

# In 1155 lesions, angiography was only moderately sensitive for detection of extensive lesion calcium (sensitivity 60% and 85% for 3- and 4-quadrant calcium)

1959

## Patterns of Calcification in Coronary Artery Disease

### A Statistical Analysis of Intravascular Ultrasound and Coronary Angiography in 1155 Lesions

Gary S. Mintz, MD, Jeffrey J. Popma, MD, Augusto D. Pichard, MD, Kenneth M. Kent, MD, PhD, Lowell F. Satler, MD, Ya Chien Chuang, PhD, Christine J. Dittrano, BS, Martin B. Leon, MD

**Background.** Target lesion calcium is a marker for significant coronary artery disease and a determinant of the success of transcatheter therapy.

**Methods and Results.** Eleven hundred fifty-five native vessel target lesions in 1117 patients were studied by intravascular ultrasound (IVUS) and coronary angiography. The presence, magnitude, location, and distribution of IVUS calcium were analyzed and compared with the detection and classification (none/mild, moderate, and severe) by angiography. Angiography detected calcium in 440 of 1155 lesions (38%); 306 (26%) moderate calcium and 134 (12%) severe. IVUS detected lesion calcium in 841 of 1155 (73%,  $P < .0001$  versus angiography). The mean arc of lesion calcium measured  $115 \pm 110^\circ$ ; the mean length measured  $3.5 \pm 3.7$  mm. Target lesion calcium was only superficial in 48%, only deep in 28%, and both superficial and deep in 24%. The mean arc of superficial calcium measured  $85 \pm 108^\circ$ ; the mean length measured  $2.4 \pm 3.4$  mm. Three hundred seventy-three of 1155 reference segments (32%) contained calcium ( $P < .0001$  compared with lesion site). The mean arc of reference calcium measured  $42 \pm 80^\circ$ ; the mean

length measured  $1.7 \pm 3.6$  mm. Only 44 (4%) had reference calcium in the absence of lesion calcium. Angiographic detection and classification of calcium depended on arcs, lengths, location, and distribution of lesion and reference segment calcium. By discriminant analysis, the classification function for predicting angiographic calcium included the arc of target lesion calcium, the arc of superficial calcium, the length of reference segment calcium, and the location of calcium within the lesion. This model correctly predicted the angiographic detection of calcification in 74.4% of lesions and the angiographic classification (none/moderate/severe) of calcium in 62.8% of lesions.

**Conclusions.** IVUS detected calcium in  $>70\%$  of lesions, significantly more often than standard angiography. Although angiography is moderately sensitive for the detection of extensive lesion calcium (sensitivity, 60% and 85% for three- and four-quadrant calcium, respectively), it is less sensitive for the presence of milder degrees. (Circulation. 1995;91:1959-1965.)

**Key Words:** coronary disease • calcium • ultrasonics • angiography

Selective coronary arteriography has been the "gold standard" for guiding revascularization in coronary artery disease. Despite its widespread acceptance, it has many inherent limitations, including its inability to assess plaque composition with negative contrast imaging. Recently, it has been suggested that coronary arteriography has a limited ability to detect and localize target lesion calcium.<sup>1,2</sup> Target lesion calcium is both a marker for significant coronary artery disease and the major determinant of the success of various transcatheter therapies.<sup>2-11</sup>

Intravascular ultrasound (IVUS) provides transmural images of coronary arteries in vivo. The normal coronary arterial wall, the major components of the atherosclerotic plaque, and the changes that occur during the atherosclerotic disease process, after transcatheter therapy, and during restenosis can be studied in humans in a

manner previously not possible. The purpose of this study is (1) to use IVUS to evaluate the patterns (eg, magnitude, location, and distribution) of coronary artery calcium in a large number of patients undergoing transcatheter therapy for coronary artery disease and (2) to compare IVUS and coronary angiography in the evaluation of coronary artery calcification.

#### Methods

##### Patient Population

From July 1, 1991, to March 1, 1994, 1155 target lesions in 1117 patients were studied by IVUS and coronary angiography. These lesions met the following criteria: (1) native vessel location (thereby excluding vein graft and internal mammary lesions) and (2) ability to assess target lesion morphology by both IVUS and coronary angiography (therefore excluding lesions with previous stent placement). There were 862 men and 255 women  $61 \pm 11$  years old. Target lesion location was left main in 47, left anterior descending in 487, left circumflex in 180, and right coronary artery in 441; diagonal branches were considered part of the left anterior descending, and marginal branches were considered part of the left circumflex artery. One hundred ninety-six lesions were ostial in location. No catheter-based intervention was performed in 149 lesions (21 of which were treated instead with operative revascularization); balloon angioplasty was performed in 127 lesions; directional coronary atherectomy (Devices for Vascular Intervention) in

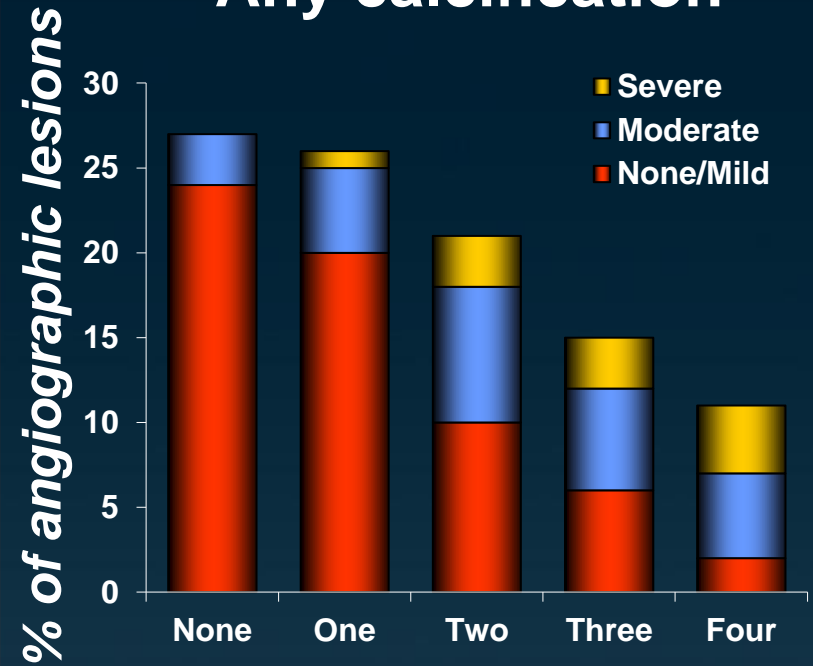
Received August 1, 1994; revision received October 12, 1994; revision accepted November 13, 1994.

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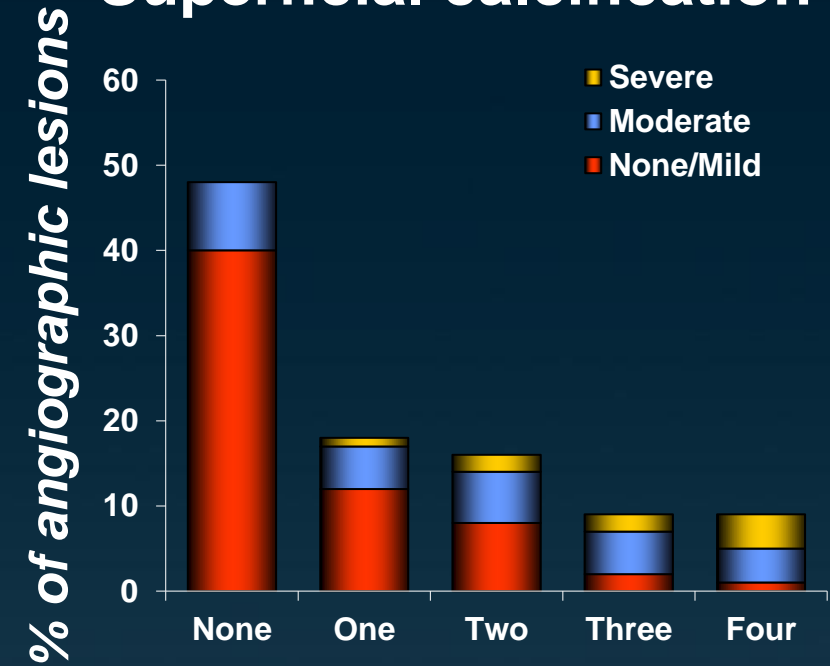
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## Any calcification



## IVUS quadrants of calcium

## Superficial calcification



## IVUS quadrants of superficial calcium

**The only predictor of IVUS calcium was angiographic calcification elsewhere in the coronary tree.**

(Tuzcu et al. *J Am Coll Cardiol* 1996;27:832-8)

# IVUS Calcium Score

1) Calcium  $>270^\circ$  over length  $>5\text{mm}$

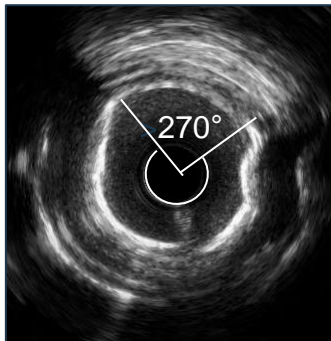
2) Calcium  $360^\circ$

3) Calcified nodule

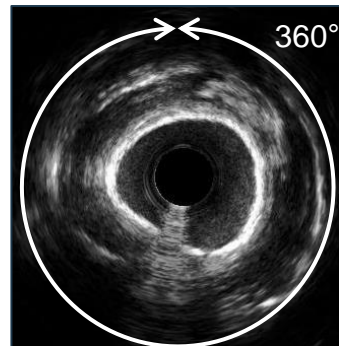
4) Vessel diameter  $<3.5\text{mm}$

Calcium Score: If  $\geq 2$  modification

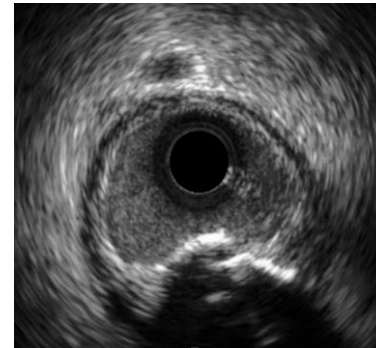
Calcium  $>270^\circ$  over  $>5\text{mm}$



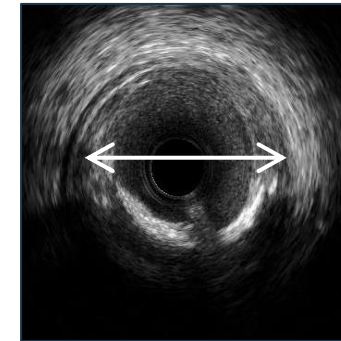
$360^\circ$  of calcium



Calcified nodule



Vessel diameter  $<3.5\text{mm}$



# IVUS calcium score predicting stent expansion (as a continuous variable) in lesions with calcium >270°

## Test cohort of 97 pts

	Regression Coeff	95% CI	P-value	Cut-off	Calcium Score	
Length of calcium >270° (per 5mm)	-5.5	-9.7, -1.2	0.01	5.0	≤5mm	0
					>5mm	1
Calcium Nodule	-10.2	-16.3 to -4.2	0.0009		absent	0
					present	1
Vessel diameter (per 1mm)	8.6	2.7 to 14.4	0.004	3.5	>3.5mm	0
					≤3.5mm	1
Circumferential calcium	-14.3	-25.0 to -3.5	0.009		absent	0
					present	1

## Stent underexpansion (<70%) in the validation cohort of 97 pts

	Cut-off	C-statistics	Sensitivity	Specificity	PPV	NPV
Score	≥2	0.85 [0.77, 0.93]	89%	63%	48%	94%

*In 67 lesions without angiographically visible calcium, but with a maximum IVUS angle of superficial calcium >270°, there were none with a calcium score of 4 and only 1 with stent underexpansion.*

*Zhang et al. Circ Cardiovasc Interv. 2021;14:e010296. doi: 10.1161/CIRCINTERVENTIONS.120.010296*

# Meta-analysis of 10 IVUS vs Angio-guided DES-implantation RCTs (5160 pts)

(weighted mean follow up  $13.8 \pm 1.4$  mos)

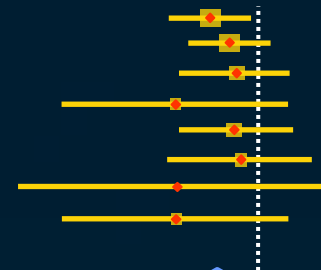
IVUS-guided PCI was associated with a lower incidence of

- Cardiac mortality (0.3% vs 1.1%, OR 0.44, 95% CI 0.26-0.75,  $P=0.003$ )
- MI (0.2% vs 0.9%, OR 0.55, 95% CI 0.32-0.94,  $P=0.03$ )
- TLR (2.4% vs 4.5%, OR 0.57, 95% CI 0.42-0.77,  $P<0.001$ )
- Stent thrombosis (0.3% vs 0.8%, OR 0.44, 95% CI 0.24-0.79,  $P=0.006$ ).

Elgendy et al. Circ J 2019;83:1410-13

## Cardiovascular mortality

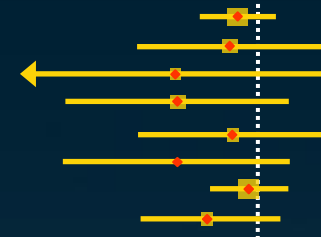
Liu et al	2019
ULTIMATE	2018
IVUS-XPL	2015
CTO-IVUS	2015
AIR-CTO	2015
Tan et al	2015
Kim et al	2013
AVIO	2013
Zhang et al	2016



OR [95% CI]	IVUS	Angio
0.33 (0.11, 1.00)	3/167	10/169
0.51 (0.18, 1.41)	5/724	10/724
0.61 (0.15, 2.43)	3/700	5/700
0.13 (0.01, 2.16)	0/201	2/201
0.60 (0.15, 2.44)	3/115	5/115
0.67 (0.11, 4.00)	2/61	3/62
0.14 (0.00, 6.95)	0/269	1/274
0.13 (0.01, 2.16)	0/142	2/142
Excluded	0/42	0/42
<b>0.44 (0.26, 0.75)</b>	<b>16/2421</b>	<b>38/2429</b>

## MI

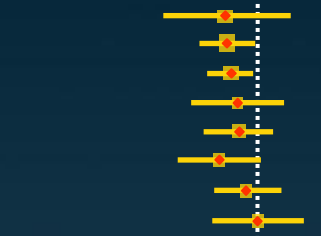
ULTIMATE	2018
Zhang et al	2016
IVUS-XPL	2015
CTO-IVUS	2015
Tan et al	2015
Kim et al	2013
AVIO	2013
HOME DES IVUS	2010



0.64 (0.25, 1.62)	7/724	11/724
0.51 (0.05, 4.99)	1/42	2/42
0.14 (0.00, 6.82)	0/700	1/700
0.13 (0.01, 2.16)	0/201	2/201
0.52 (0.05, 5.06)	1/61	2/62
0.14 (0.01, 2.20)	0/269	2/274
0.82 (0.34, 1.96)	10/142	12/142
0.29 (0.05, 1.73)	1/105	4/105
<b>0.55 (0.32, 0.94)</b>	<b>20/2244</b>	<b>36/2250</b>

## Target lesion revascularization

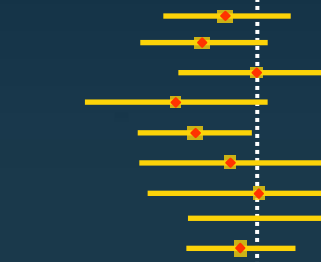
Liu et al	2019
ULTIMATE	2018
IVUS-XPL	2015
CTO-IVUS	2015
AIR-CTO	2015
Tan et al	2015
AVIO	2013
HOME DES IVUS	2010



0.42 (0.09, 1.89)	2/167	5/169
0.48 (0.23, 1.02)	9/724	19/724
0.52 (0.29, 0.91)	17/700	33/700
0.62 (0.21, 1.87)	5/201	8/201
0.65 (0.26, 1.61)	8/115	12/115
0.39 (0.14, 1.10)	5/61	12/62
0.74 (0.35, 1.58)	13/142	17/274
1.00 (0.31, 3.20)	6/105	6/105
<b>0.57 (0.42, 0.77)</b>	<b>66/2215</b>	<b>112/2218</b>

## Definite/probable stent thrombosis

Liu et al	2019
ULTIMATE	2018
IVUS-XPL	2015
CTO-IVUS	2015
AIR-CTO	2015
Tan et al	2015
Kim et al	2013
AVIO	2013
HOME DES IVUS	2010

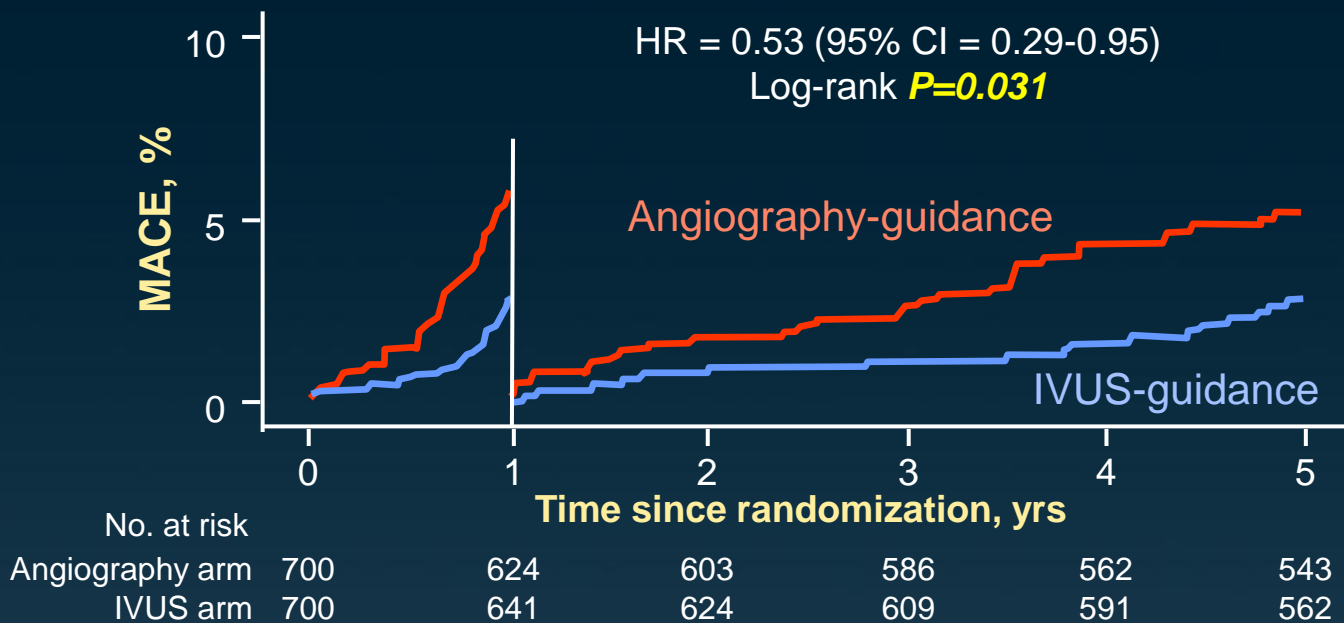


0.42 (0.09, 1.89)	2/167	5/169
0.26 (0.05, 1.30)	1/724	5/724
1.00 (0.14, 7.11)	2/700	2/700
0.13 (0.01, 1.30)	0/201	3/201
0.21 (0.05, 0.87)	1/115	7/115
0.52 (0.05, 5.06)	1/61	2/62
1.02 (0.06, 16.33)	1/269	1/274
7.39 (0.15, 372.38)	1/142	0/142
0.66 (0.19, 2.34)	4/105	6/105
<b>0.44 (0.24, 0.79)</b>	<b>13/2484</b>	<b>31/2492</b>

IVUS use is associated with better outcome

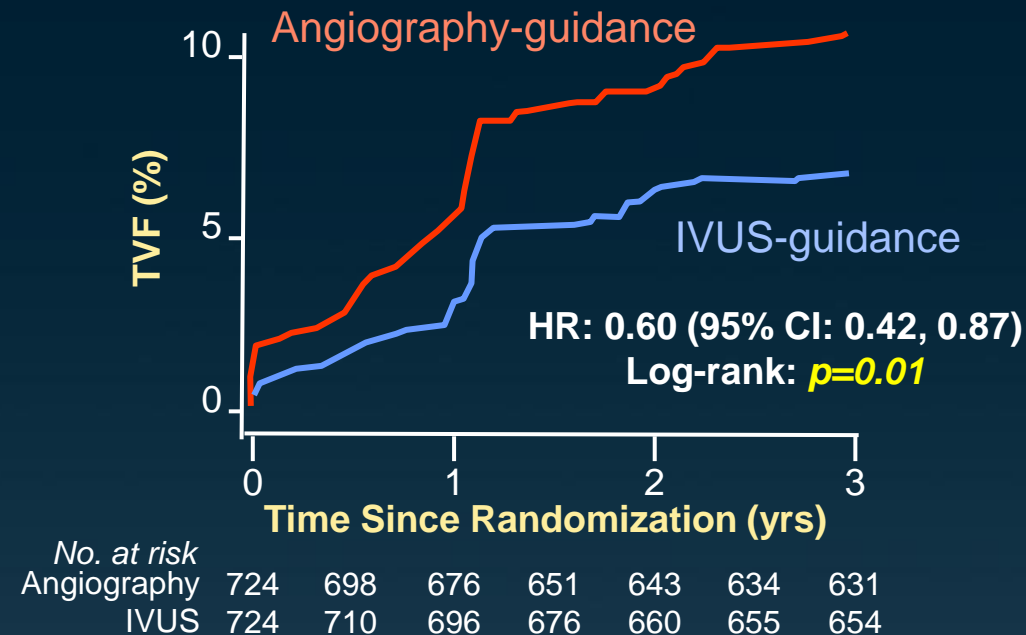
IVUS use is associated with worse outcome

# IVUS-XPL: Five year follow-up



Hong et al. JACC Cardiovasc Interv 2020;13:67-71

# ULTIMATE: Three year follow-up



Gao et al. JACC Cardiovasc Interv 2021;14:247-57

ORIGINAL ARTICLE

**Intravascular Imaging–Guided or Angiography-Guided Complex PCI**

J.M. Lee, K.H. Choi, Y.B. Song, J.-Y. Lee, S.-J. Lee, S.Y. Lee, S.M. Kim, K.H. Yun, J.Y. Cho, C.J. Kim, H.-S. Ahn, C.-W. Nam, H.-J. Yoon, Y.H. Park, W.S. Lee, J.-O. Jeong, P.S. Song, J.-H. Doh, S.-H. Jo, C.-H. Yoon, M.G. Kang, J.-S. Koh, K.Y. Lee, Y.-H. Lim, Y.-H. Cho, J.-M. Cho, W.J. Jang, K.-J. Chun, D. Hong, T.K. Park, J.H. Yang, S.-H. Choi, H.-C. Gwon, and J.-Y. Hahn, for the RENOVATE-COMPLEX-PCI Investigators\*

ABSTRACT

**BACKGROUND**

Data regarding clinical outcomes after intravascular imaging–guided percutaneous coronary intervention (PCI) for complex coronary-artery lesions, as compared with outcomes after angiography-guided PCI, are limited.

**METHODS**

In this prospective, multicenter, open-label trial in South Korea, we randomly assigned patients with complex coronary-artery lesions in a 2:1 ratio to undergo either intravascular imaging–guided PCI or angiography-guided PCI. In the intravascular imaging group, the choice between intravascular ultrasonography and optical coherence tomography was at the operators' discretion. The primary end point was a composite of death from cardiac causes, target-vessel–related myocardial infarction, or clinically driven target-vessel revascularization. Safety was also assessed.

**RESULTS**

A total of 1639 patients underwent randomization, with 1092 assigned to undergo intravascular imaging–guided PCI and 547 assigned to undergo angiography-guided PCI. At a median follow-up of 2.1 years (interquartile range, 1.4 to 3.0), a primary end-point event had occurred in 76 patients (cumulative incidence, 7.7%) in the intravascular imaging group and in 60 patients (cumulative incidence, 12.3%) in the angiography group (hazard ratio, 0.64; 95% confidence interval, 0.45 to 0.89; P=0.008). Death from cardiac causes occurred in 16 patients (cumulative incidence, 1.7% in the intravascular imaging group and in 17 patients (cumulative incidence, 3.8% in the angiography group; target-vessel–related myocardial infarction occurred in 38 (cumulative incidence, 3.7%) and 30 (cumulative incidence, 5.6%), respectively; and clinically driven target-vessel revascularization in 32 (cumulative incidence, 3.4%) and 25 (cumulative incidence, 5.5%), respectively. There were no apparent between-group differences in the incidence of procedure-related safety events.

**CONCLUSIONS**

Among patients with complex coronary-artery lesions, intravascular imaging–guided PCI led to a lower risk of a composite of death from cardiac causes, target-vessel–related myocardial infarction, or clinically driven target-vessel revascularization than angiography-guided PCI. (Supported by Abbott Vascular and Boston Scientific; RENOVATE-COMPLEX-PCI ClinicalTrials.gov number, NCT03381872).

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Hahn can be contacted at jyhahn@skku.edu or at the Heart Vascular Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, South Korea.

\*A list of the RENOVATE-COMPLEX-PCI Investigators is provided in the Supplementary Appendix, available at NEJM.org.

Drs. J.M. Lee and K.H. Choi and Drs. Y.B. Song and Hahn contributed equally to this article.

This article was published on March 5, 2023, at NEJM.org.

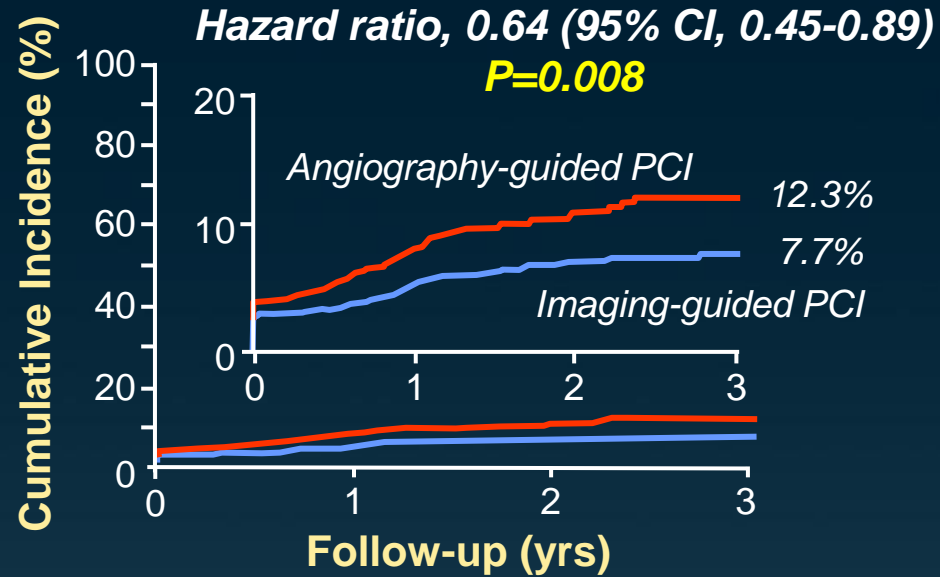
DOI: 10.1056/NEJMoa2216607  
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# RENOVATE-COMPLEX-PCI: 1639 pts with complex lesions were randomized (2:1) to IVI (74.2% IVUS or 25.8% OCT) vs angiography-guided PCI

Primary end point: composite of cardiac death, TV-MI, or clinically driven TVR

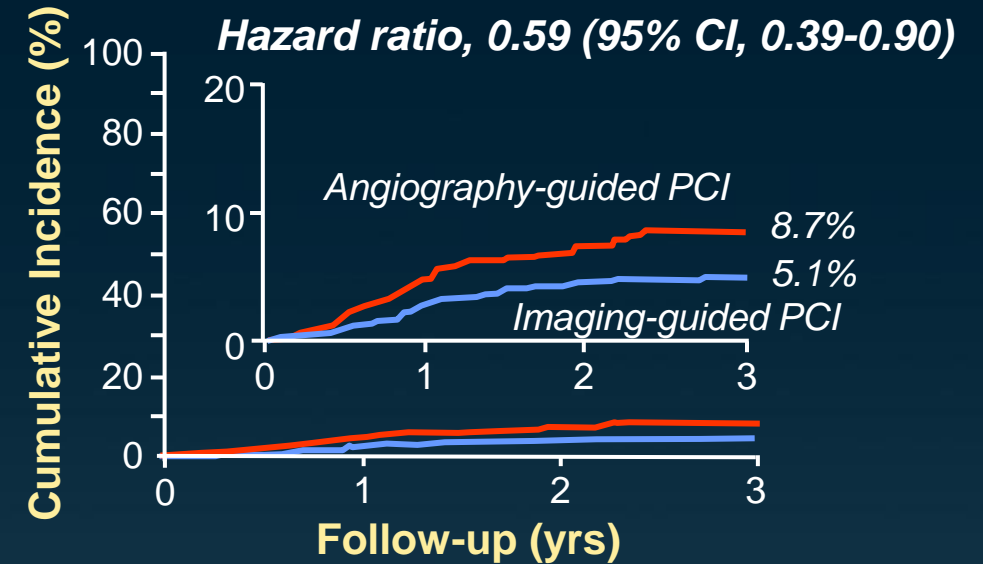
	IVI-guidance (n=1092)	Angiography-guidance (n=547)
Stable CAD	48.7%	50.3%
ACS	51.3%	49.7%
True bifurcations	21.3%	23%
CTO	20.1%	18.1%
Unprotected LMCA	12.6%	9.9%
Diffuse long lesion	56.5%	51.4%
Multivessel PCI (>2 arteries)	37.5%	38.9%
≥3 stents	19.0%	17.7%
ISR	15.5%	14.3%
Severe calcium	14.4%	13.5%
Ostial lesions	16.7%	12.6%
≥3 complex lesions	32.2%	28.0%

## Target-vessel Failure



Angiography-guided	547	496	280	120
Imaging-guided	1092	1023	591	255

## Target-Vessel Failure without Procedure-related MI



Angiography-guided	547	516	284	121
Imaging-guided	1092	1051	596	256

Lee et al. N Engl J Med 2023;338, in press

## Intravascular ultrasound in the evaluation and treatment of left main coronary artery disease: a consensus statement from the European Bifurcation Club



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This paper also includes supplementary data published online at [http://www.pcronline.com/eurointervention/137th\\_issue/81](http://www.pcronline.com/eurointervention/137th_issue/81)

### KEYWORDS

- bifurcation
- left main
- intravascular ultrasound

### Abstract

Interventional cardiology and coronary stent insertion have an increasing role in the optimal management of left main coronary artery (LMCA) stenosis. Assessing the extent of obstructive disease of the LMCA by angiography alone can be challenging. However, in contrast to the two-dimensional, shadow graphic nature of coronary angiography, intravascular ultrasound (IVUS) is an accurate tomographic technique for assessing both the coronary lumen and the vessel wall characteristics. Consequently, it is a particularly useful technique in imaging the LMCA before, during and after intervention. The European Bifurcation Club (EBC) recommends the use of IVUS during most LMCA interventions. The purpose of this consensus document is to review the available IVUS data on LMCA disease evaluation and treatment. It is a practical guide to show "how and when" to use the imaging modality. It is hoped that a standardisation of the practical approach to imaging may allow consolidation of learning and, ultimately, improve patient outcomes.

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- The normal LMCA
- Pathogenesis of LMCA disease
- Plaque distribution
- Assessment of LMCA severity and indications for treatment
- Step-by-step IVUS-guided LMCA PCI and optimization
- Evidence that IVUS guidance during LMCA intervention improves outcomes
- IVUS vs OCT



Contents lists available at ScienceDirect  
International Journal of Cardiology

journal homepage: [www.elsevier.com/locate/ijcard](http://www.elsevier.com/locate/ijcard)



## Intravascular ultrasound guidance in the evaluation and treatment of left main coronary artery disease

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Percutaneous coronary intervention

### ABSTRACT

Percutaneous coronary intervention (PCI) of left main coronary artery (LMCA) disease has become an acceptable revascularization strategy. Evaluating the extent and characteristics of obstructive disease of the LMCA by angiography is challenging and limited in its accuracy. In contrast, intravascular ultrasound (IVUS) provides accurate imaging of the coronary lumen as well as quantitative measurements and quantitative assessment of the vessel wall components. IVUS for LMCA PCI should be performed before, during, and after intervention; IVUS enhances every step in the procedure and is associated with a mortality advantage in comparison with angiographic guidance alone. In this review, we provide an update on LMCA PCI and the role of IVUS for lesion assessment and stent optimization. In addition, the latest clinical evidence of the benefits of IVUS-guided LMCA PCI as compared to angiography is reviewed.

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### 1. Introduction

Atherosclerotic obstruction of the left main coronary artery (LMCA) is present in approximately 4% of all coronary angiograms [1]. Patients with obstructive LMCA disease left untreated have a particularly poor prognosis [2]. Recent trials have demonstrated the role of LMCA stenting, especially in patients with less complex disease or those unsuitable for surgery [3,4]. Revascularization of obstructive LMCA with percutaneous coronary intervention (PCI) requires careful consideration, as the artery provides blood supply to >75% of the left ventricle [5], and complications may lead to rapidly progressive hemodynamic instability [6].

Angiographic assessment of the LMCA can be difficult [7,8]. Because of its two-dimensional shadowgraphic nature, coronary angiography cannot provide an accurate evaluation of the extent of disease or insight into the vessel-wall characteristics [9]. Limitations include lack of a well-defined reference, diffuse atherosclerosis in the LMCA with involvement of the bifurcation [10], and angiographically silent calcific

disease, which makes lesions more difficult to dilate and can lead to stent under-expansion [11,12]. In addition, coronary angiography has limitations in assessing ostial LMCA involvement, in which the operator is required to rely on indirect signs of lesion severity, such as pressure damping during catheter engagement or lack of contrast dye backflow during selective injection. Even using more "modern" equipment or incorporating fractional flow reserve (FFR), LMCA assessment remains challenging [13,14].

As compared to coronary angiography, intravascular ultrasound (IVUS) is an accurate technique for assessment of both the lumen and wall characteristics and dimensions [15], making it particularly useful for imaging the LMCA, and this is reflected in the guidelines [16,17]. In this review, we discuss indications for obstructive LMCA PCI, the role of IVUS guidance, and the impact of IVUS on clinical outcomes.

### 2. Coronary Artery Bypass Grafting versus PCI in LMCA Disease

Coronary artery bypass grafting (CABG) has been the mainstay of treatment for obstructive LMCA disease [5], with a well-documented prognostic benefit related to the very high rate of long-term patency of the left internal mammary artery [18,19]. However, advancements in stent devices, technique refinements, and adjunctive medical therapy have led to improved PCI outcomes [20]. Recent data have demonstrated that LMCA PCI can be as safe as CABG in certain patients [21–23]. The Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) study demonstrated that for patients with SYNTAX scores that are low (≤22) or intermediate (23–32), CABG and PCI had similar

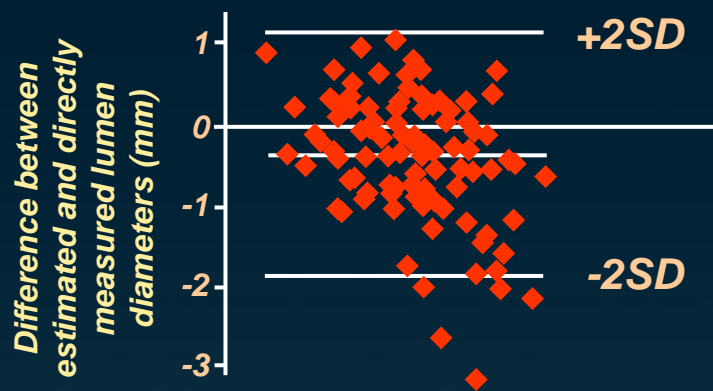
Abbreviations: CABG, Coronary artery bypass grafting; FFR, Fractional flow reserve; IFR, Intra-aortic restenosis; IVUS, Intravascular ultrasound; LAD, Left anterior descending artery; LCA, Left circumflex artery; LMCA, Left main coronary artery; MLA, Minimal lumen area; PCI, Percutaneous coronary intervention; TLR, Target lesion revascularization; TWR, Target vessel revascularization.

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E-mail address: [ron.waksman@medstar.net](mailto:ron.waksman@medstar.net) (R. Waksman).

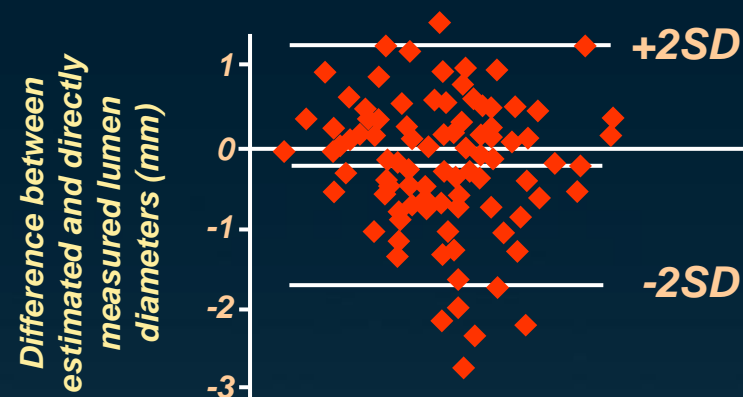
<https://doi.org/10.1016/j.ijcard.2020.10.028>  
0167-5273/© 2020 Published by Elsevier B.V.

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## Evaluation of the LAD from the LM-LCX Pullback



## Evaluation of the LCX from the LM-LAD Pullback

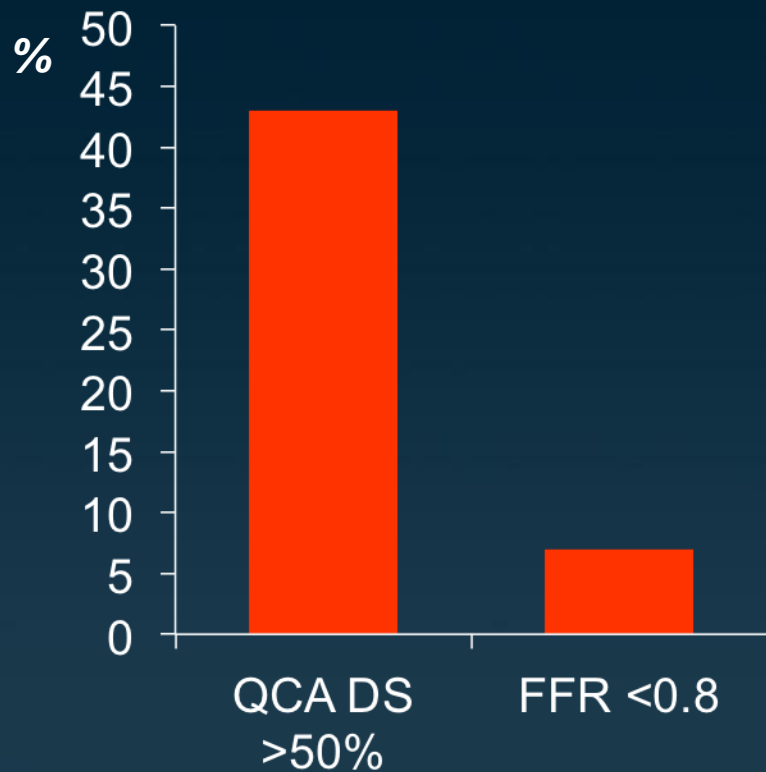


	Sensitivity	Specificity
Plaque burden >40%	59%	45%
Plaque burden >70%	78%	42%

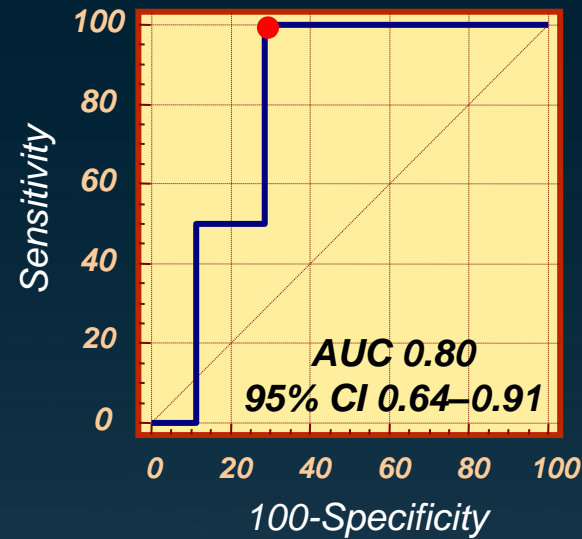
	Sensitivity	Specificity
Plaque burden >40%	67%	55%
Plaque burden >70%	88%	42%

# One stent vs two stents?

Frequency and IVUS predictors of  $FFR < 0.8$  after 43 LMCA bifurcation lesions with a pre-PCI LCX ostial DS  $< 50\%$  were treated by single-stent cross-over

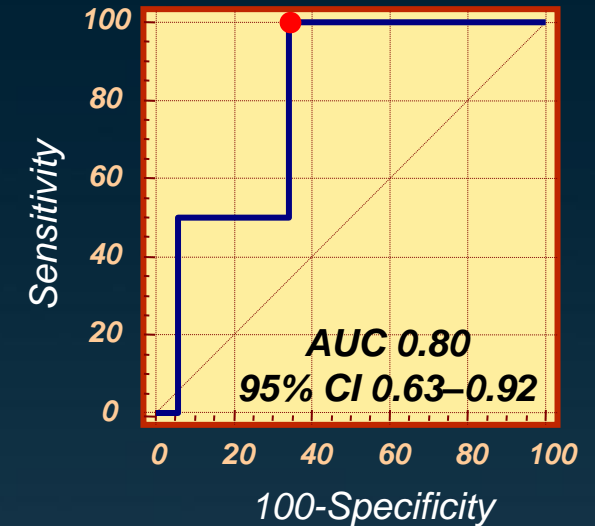


Kang et al. *Catheter Cardiovasc Interv* 2014;83:545-52



## MLA $< 3.7\text{mm}^2$

- Sensitivity 100%
- Specificity 71%
- PPV 16%
- NPV 100%

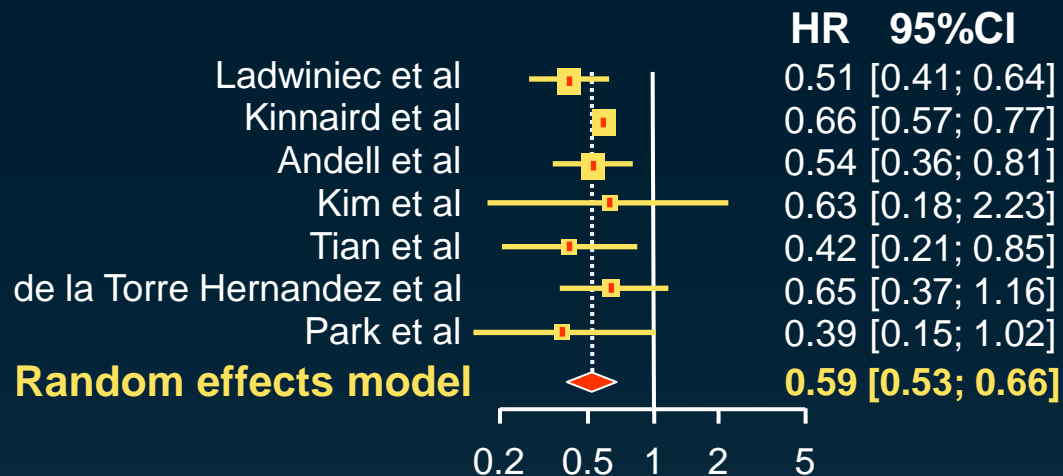


## Plaque Burden $> 56\%$

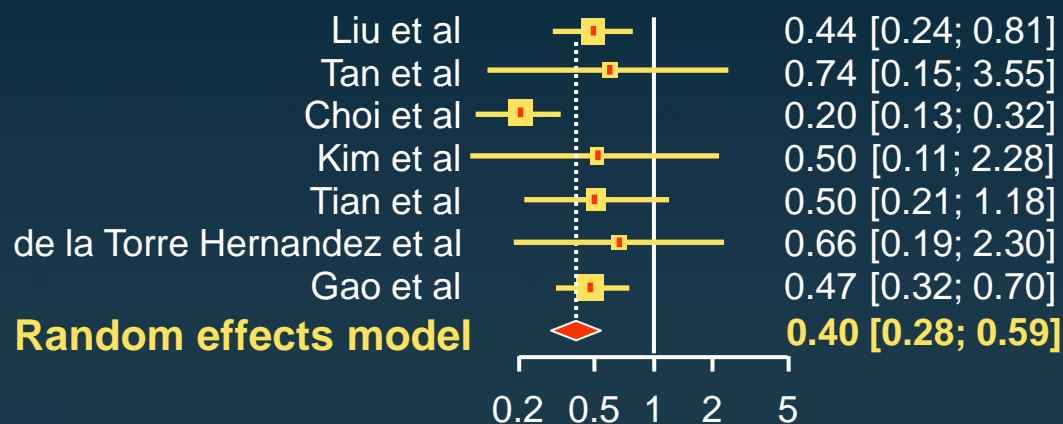
- Sensitivity 100%
- Specificity 65%
- PPV 14%
- NPV 100%

# Meta-Analysis of 11 LMCA DES Studies

## All Cause Mortality

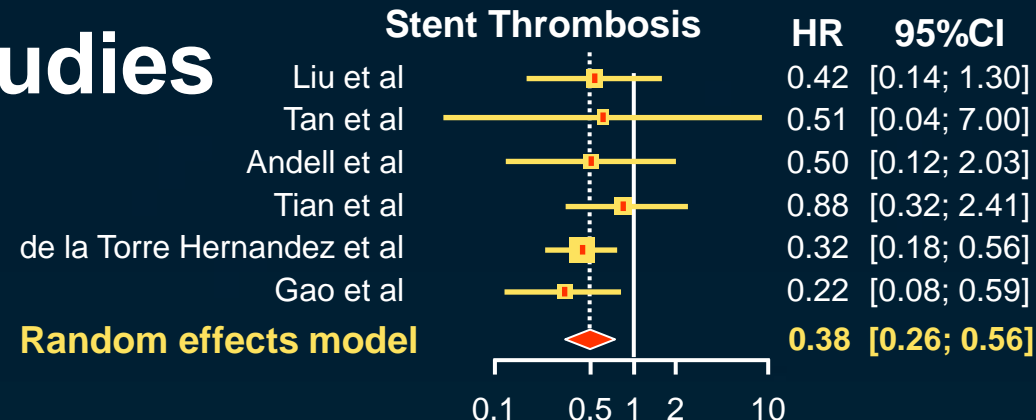


## Cardiovascular Mortality



Elgendy et al. Am J Cardiol 2019;124:1652-3  
Elgendy et al. Am J Cardiol 2020;128:92-93

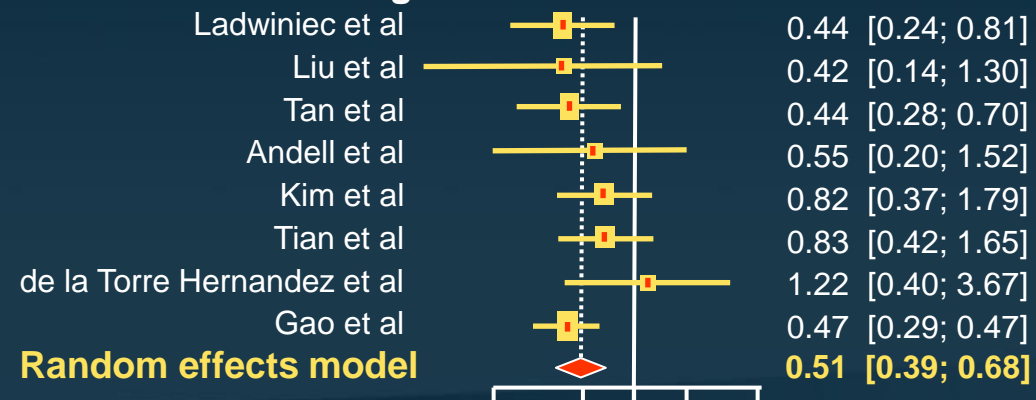
## Stent Thrombosis



## Myocardial Infarction

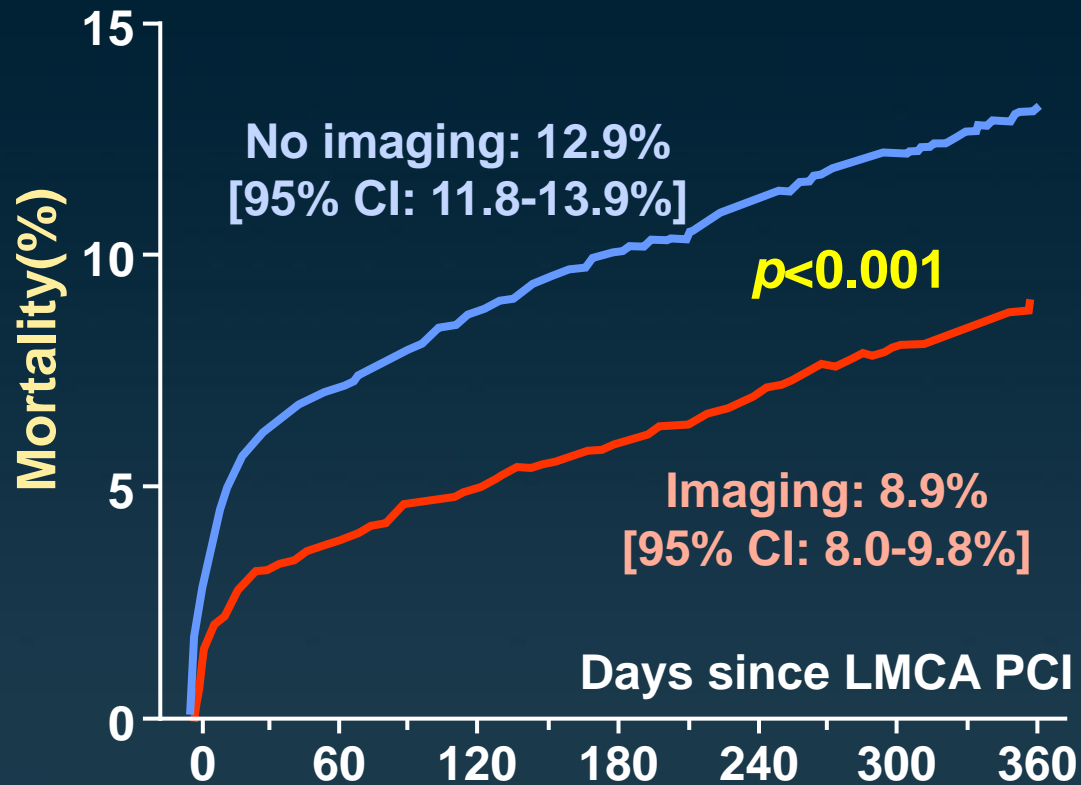


## Target Lesion Revascularization



# British Cardiovascular Intervention Society (BCIS) Registry

*(11,264 LMCA PCI, 5056 imaging [98% IVUS]-guided, with imaging use increasing from 30% in 2007 to 50% in 2014)*



*Kinnaird et al. JACC Cardiovasc Interv 2020;13:346-357*

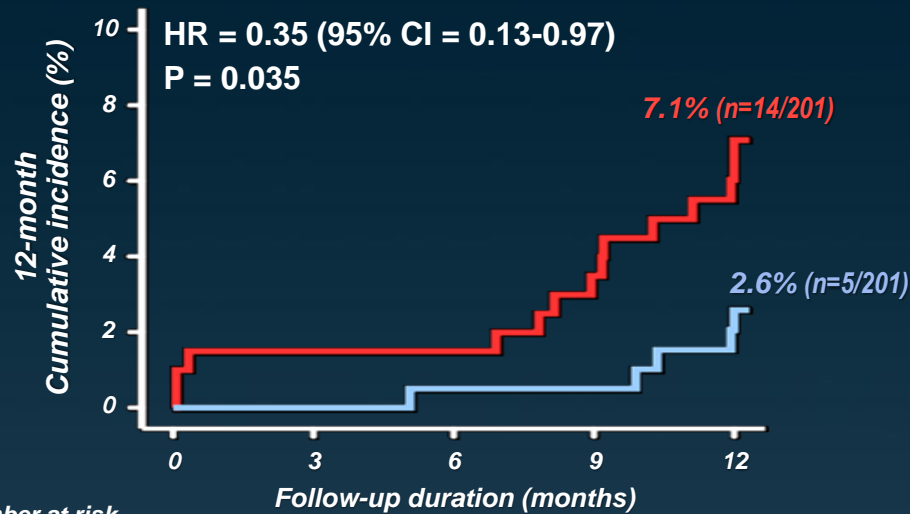
- Overall, there was a 34% mortality reduction with IVUS guidance.
- Operators with greater LMCA-PCI volumes had better outcomes and greater mortality benefit with IVUS guidance.
- There was a 59% mortality benefit among operators in the quartile with the highest number of LMCA procedures

# Randomized IVUS vs Angiographic Guided CTO Intervention

Primary endpoint (Cardiac death, MI, TVR)

— Angiography-guided group  
— IVUS-guided group

## Intention to Treat



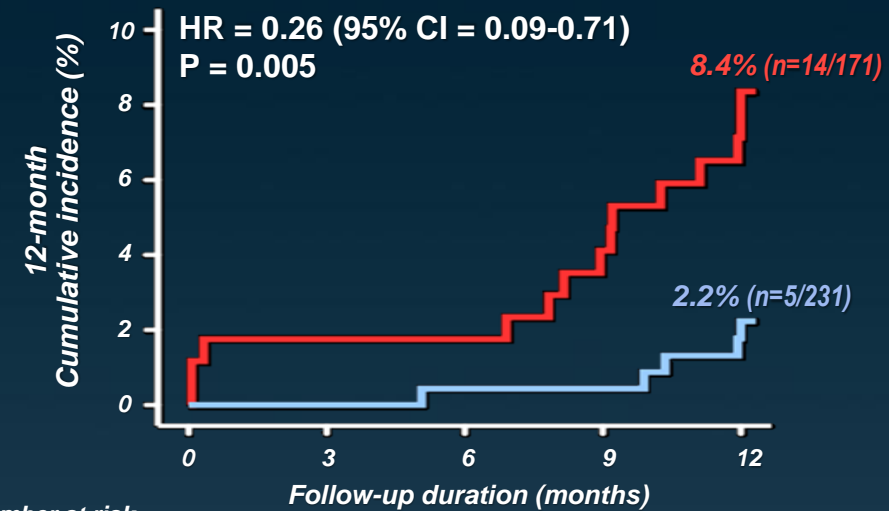
Number at risk

Angiography	201	198	179
IVUS	201	198	186

	IVUS	Angio	P-value
Cardiac death/MI	0%	2%	0.045
TVR	2.6%	5.2%	0.186

## Per Protocol

(30 pt x-over from angio to IVUS-guidance)



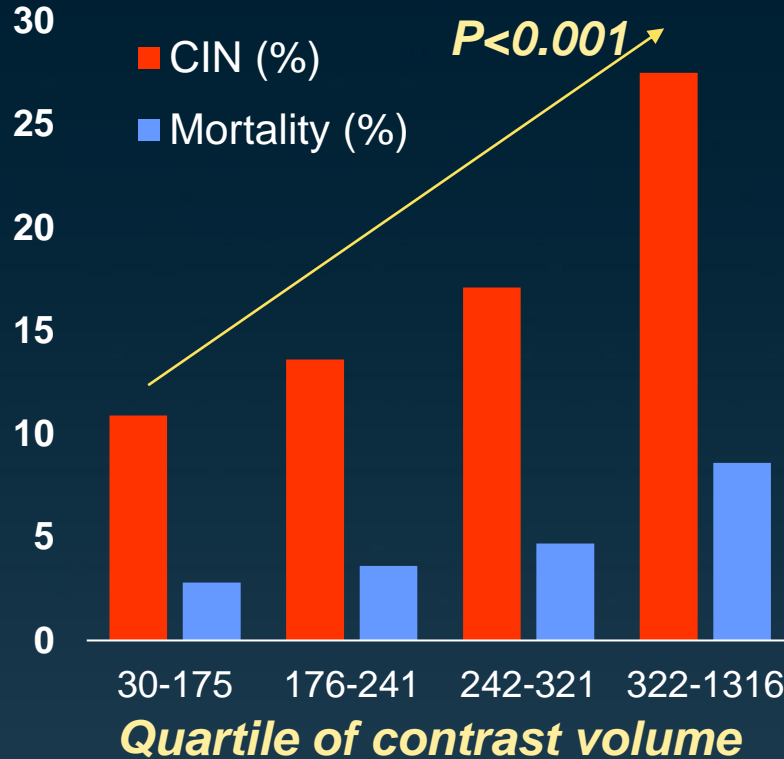
Number at risk

Angiography	171	167	151
IVUS	231	229	214

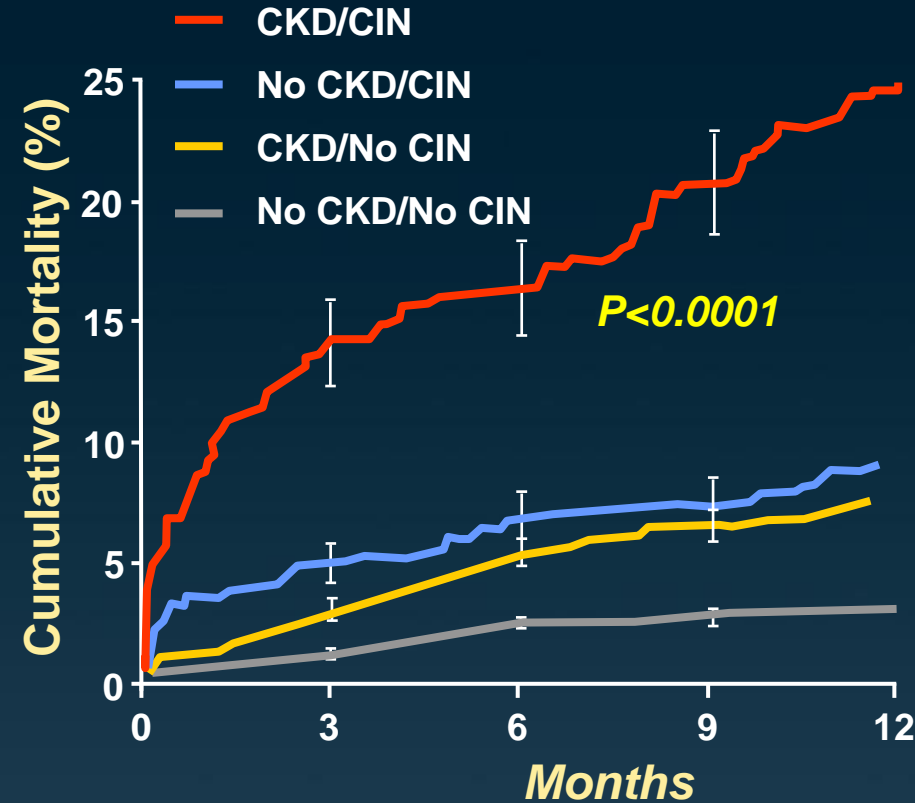
	IVUS	Angio	P-value
Cardiac death/MI	0%	2.3%	0.019
TVR	2.2%	6.1%	0.049

# Prevalence of and Mortality from Contrast-Induced Nephropathy

NCDR database  
(n=1.3 million PCIs)



In-hospital mortality was 21.4% among pts with CIN vs 0.9% without CIN ( $p < 0.001$ ).



# Zero Contrast PCI

- Ali et al. Eur Heart J. 2016;37:3090-3095
  - 31 pts with median creatinine of 4.2mg/dL (IQR 3.1-4.8)
  - Successful zero contrast PCI was performed at least 1 week after diagnostic angiography using real-time IVUS guidance and pre- and post-PCI FFR and CRF to confirm physiologic improvement
  - No MACE and preservation of renal function in all pts at a median follow-up of 79 days (IQR 33-107).
- Rahim et al. TCT2019
  - 99 pts with creatinine of 3.6±1.6mg/dL
  - 18% PCI performed at time of diagnostic angio and 82% PCI were staged
  - Staged PCI used 1.3±2.8ml contrast with zero contrast in 72%
  - One guidewire perforation requiring pericardiocentesis
- Na ***Also useful for patients with contrast allergy*** days.
- Kumar et al. Int J Cardiol Heart Vasc 2022 May 16;40:101052. doi: 10.1016/j.ijcha.2022.101052
  - 42 pts (66 vessels)
  - Zero contrast in 61 vessels (92.4%) and the remaining 7.6% were completed with ultra-low volume contrast.
  - 5 (11.9%) pts developed AKI, but none required dialysis
- Shibata et al. Circ J 2022;86:787-96
  - 55 pts (78 PCIs)
  - Zero contrast in 78 PCIs
  - No AKI.
  - Follow-up of 437-1460 days, 4 pts required RRT

Clinical problem	FFR	NHPR	IVUS	RF-IVUS	OCT	NIRS
<b>Assessing lesion severity</b>						
Non-LMCA*	++	++	+		+	
Tandem lesions	+	++				
<b>LMCA*</b>	++		++			
Identifying the culprit lesion			±		++	±
Identifying vulnerable plaque				+	+	+
<b>PCI Guidance</b>						
Predicting distal embolization			+	+	+	+
Calcium			+		++	
Guiding CTO intervention			++			
<b>Routine DES optimization*</b>			++		++	
Jailed sidebranch	++					
LMCA stenting			++			
Minimizing contrast			++			
Assessing stent failure			+		++	

iREVIEW

STATE-OF-THE-ART PAPER

## Clinical Utility of Intravascular Imaging

Past, Present, and Future

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**ABSTRACT**

Although it is the tool used by most interventional cardiologists to assess the severity of coronary artery disease and guide treatment, coronary angiography has many limitations because it is a shadowgraph, depicting planar projections of the contrast-filled lumen that are often foreshortened rather than imaging the diseased vessel itself. Currently available intravascular imaging technologies include grayscale intravascular ultrasound (IVUS), optical coherence tomography (OCT) (the light analogue of IVUS), and near-infrared spectroscopy that detects lipid within the vessel wall and that has been combined with grayscale IVUS in a single catheter as the first combined imaging device. They provide tomographic or cross-sectional images of the coronary arteries that include the lumen, vessel wall, plaque burden, plaque composition and distribution, and even peri-vascular structures—information promised, but rarely provided angiographically.

Extensive literature shows that these tools can be used to answer questions that occur during daily practice as well as improving patient outcomes. Is this stenosis significant? Where is the culprit lesion? What is the anatomy of an unusual or ambiguous angiographic lesion? What is the right stent size and length? What is the likelihood of distal embolization or periprocedural myocardial infarction during stent implantation? Has the intervention been optimized? Why did this stent thrombose or restenose? This review summarizes these uses of intravascular imaging as well as the outcomes data supporting their incorporation into routine clinical practice. (J Am Coll Cardiol Img 2022;■:■-■)

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**I**ntravascular imaging (IVI)—intravascular ultrasound (IVUS), optical coherence tomography (OCT), and near infrared spectroscopy—have moved beyond research to aid in decision making during diagnostic catheterization, percutaneous coronary interventions (PCIs), and when assessing stent failure.

IVI image quality is defined by spatial and contrast resolution and penetration. Spatial resolution affects the sharpness of an image and the ability to detect small structures and is classically measured as the smallest distance between line pairs that can be distinguished as separate objects in the axial or lateral direction, assuming that the IVI beam is stationary and not rotating (Figures 1A to 1B). However, today spatial resolution is calculated using engineering formulas. In

addition to axial and lateral resolution, there are 2 resolutions that are rarely acknowledged and never reported: 1) spatial resolution along the circumference of the artery when a cross-sectional image is generated; 2) and spatial resolution along the length of the artery during pull back (Figures 1C to 1D).

Contrast resolution—the ability to distinguish between objects having different backscatter (Figures 1E to 1G)—depends on both the dynamic range as well as the number of shades of “gray.” Poor contrast resolution is also associated with image artifacts, noise, blurring, and the inability to differentiate adjacent structures.

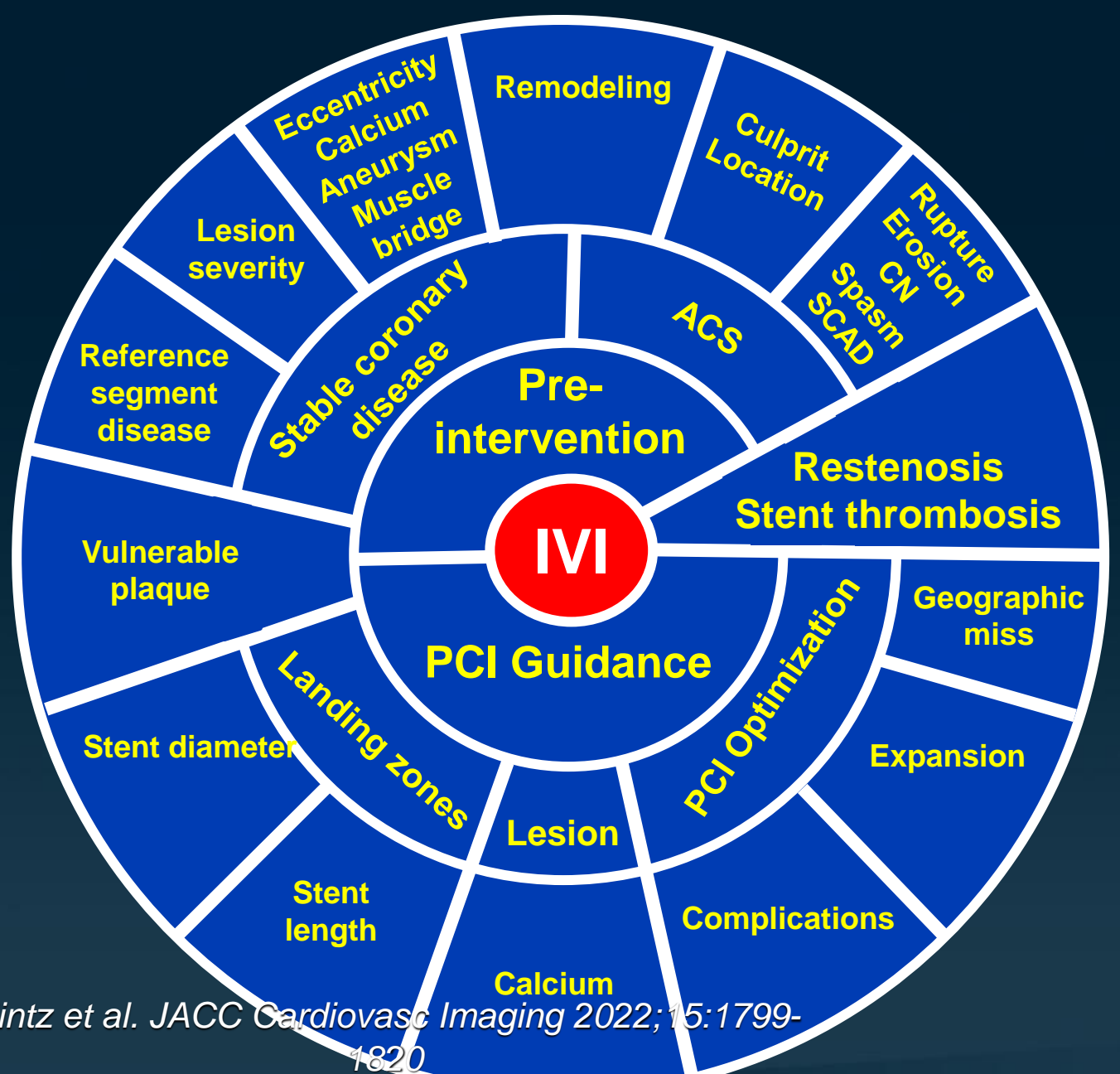
Superior resolution and obligatory flushing to clear blood from the lumen combine to create a clear interface so that automatic OCT lumen measurements

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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