

2012 Insights into Plaque Vulnerability and Identification: From VH-IVUS to OCT to NIRS

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How common are vulnerable plaques?



The Limits of Opening Arteries

NYTimes March 28, 2004

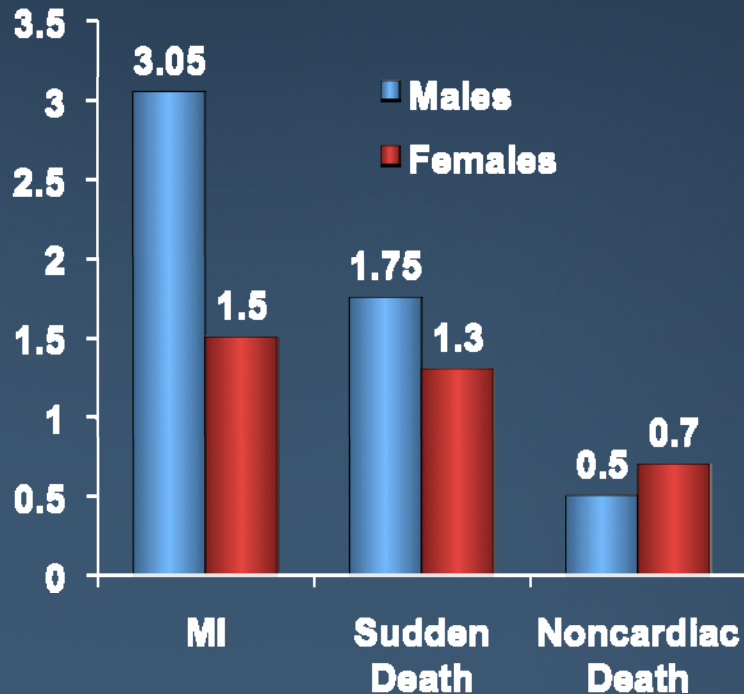
Experts agree that artery-opening methods -- like bypass surgery, or insertion of a balloon to mash down plaque and a wire-cage stent to keep the channel open - - can alleviate crushing chest pain and save some lives. But patients should not assume that their cardiovascular problems are "fixed" by such procedures, and patients without symptoms whose arteries are narrowing should be wary about

undergoing these procedures to ward off a potential heart attack. **They may have hundreds of vulnerable plaques elsewhere that are more apt to burst and trigger a heart attack than are the more stable plaques in the narrow section.** Most such patients might better be treated with drugs to lower their cholesterol levels, control their blood pressure and prevent blood clots, or should adopt a healthier life style by giving up smoking, eating heart-healthy foods and exercising.



Number of thin-cap fibroatheromas in patients dying with MI, sudden death, or noncardiac causes and studied at necropsy

Cross-sectional analysis

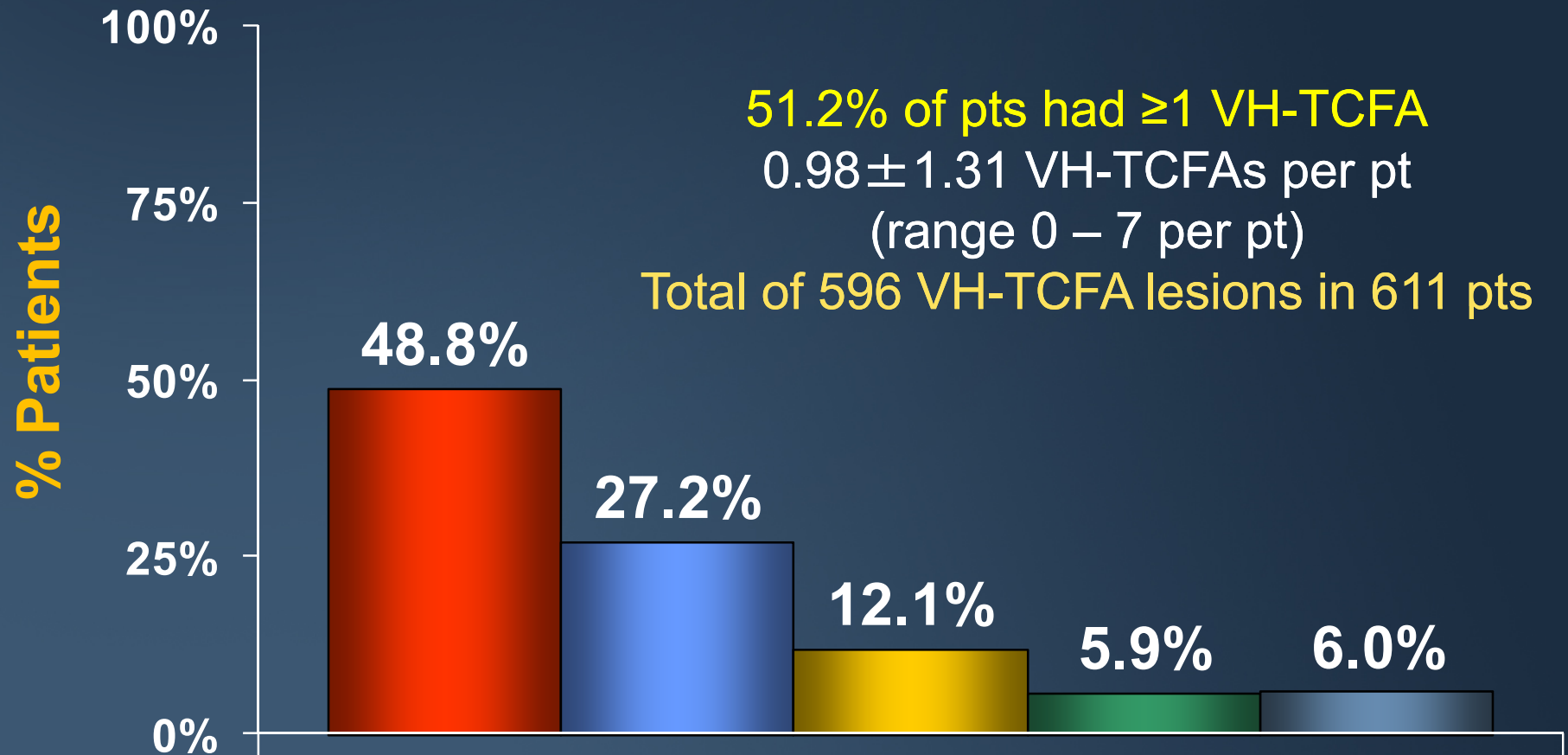


Longitudinal analysis

	All pts	Pts with ≥ 1 ruptured plaque	Pts with ≥ 1 TCFA or ruptured plaque	Pts with CV death
# of patients	50	14	20	33
# of ruptured plaques	19 (0.38/pt)		19 (0.95/pt)	15 (0.45/pt)
# fibroatheromas	193			
# TCFAs	23 (0.46/pt)	15 (1.21/pt)	23 (1.15/pt)	18 (0.55/pt)

PROSPECT: Per patient incidence of VH-TCFAs

lesions/pt per coronary tree: ■ 0 ■ 1 ■ 2 ■ 3 ■ ≥4



Predictors of non-culprit events

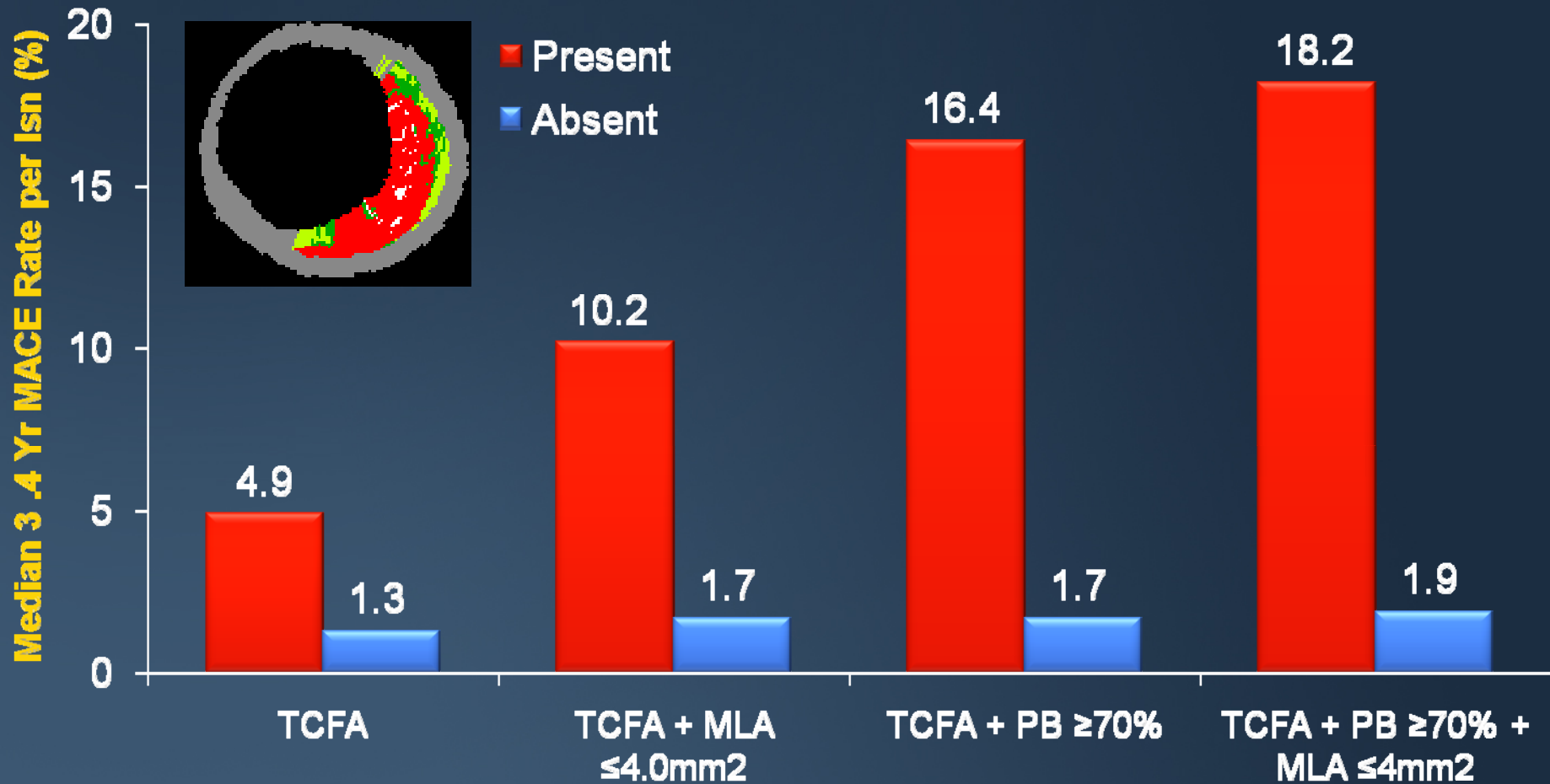


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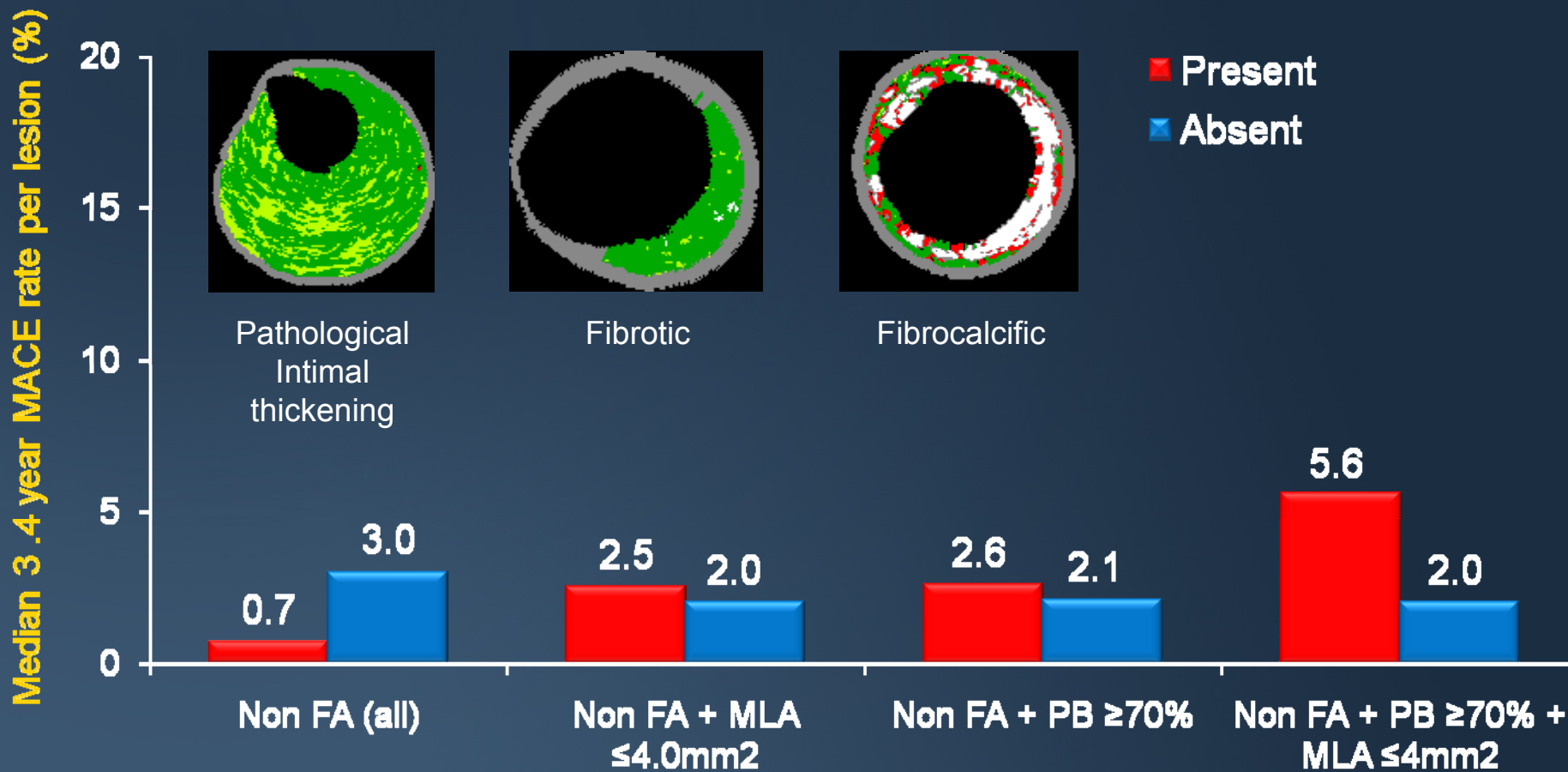
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VH-TCFA and Non Culprit Lesion Events in PROSPECT



Lesion HR	3.90 (2.25, 6.76)	6.55 (3.43, 12.51)	10.83 (5.55, 21.10)	11.05 (4.39, 27.82)
P value	<0.0001	<0.0001	<0.0001	<0.0001
Prevalence*	46.7%	15.9%	10.1%	4.2%

Non Fibroatheromas and Non Culprit Lesion Events



Lesion HR	0.22 [0.10, 0.49]	1.49 [0.44, 3.39]	1.25 [0.17, 9.01]	2.60 [0.36, 18.84]
P-value	0.0002	0.70	0.83	0.34
Prevalence	67.9%	19.7%	5.6%	2.7%

VIVA: Virtual Histology in Vulnerable Atherosclerosis

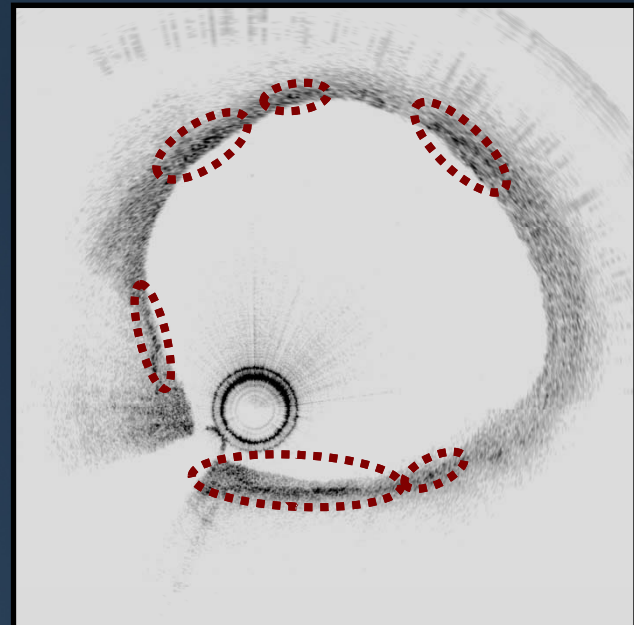
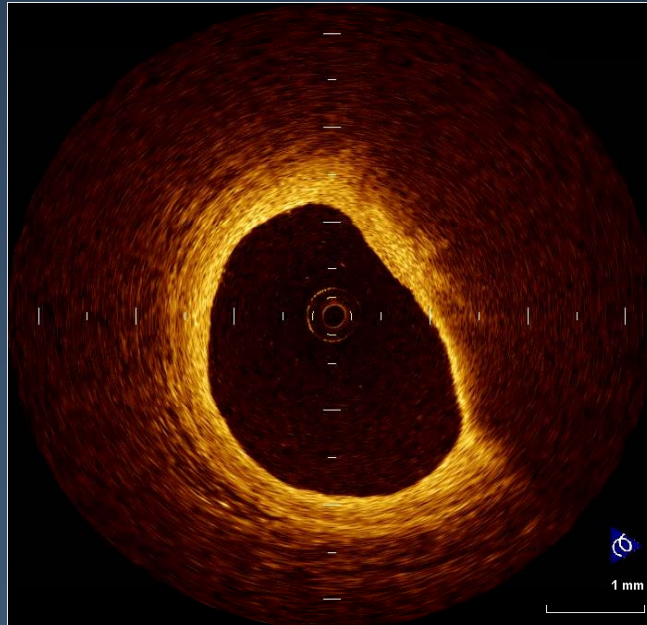
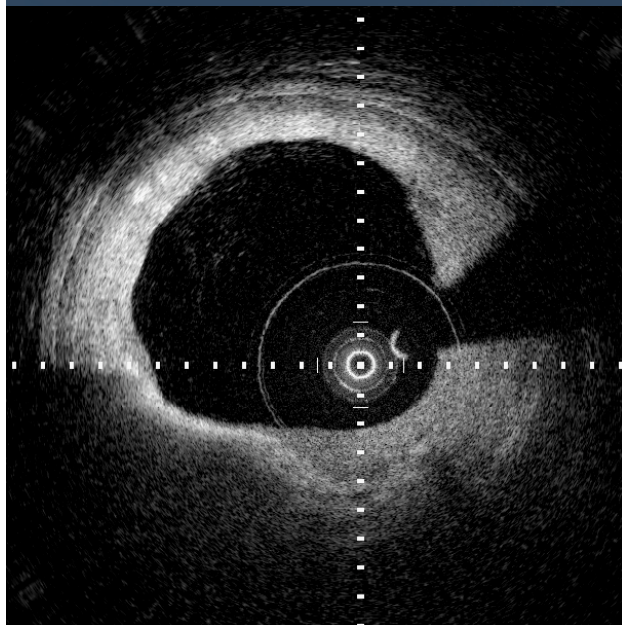
- 932 non-culprit lesions in 170 pts were identified with 3-vessel IVUS imaging
- At a median follow-up of 625 days, there were 18 culprit and non-culprit MACE in 16 pts
 - 14 revascularizations, 2 MIs, and 2 deaths
- Univariate predictors of non-culprit MACE
 - Non-calcified VH-TCFA (p=0.025)
 - MLA <4mm² (p=0.021)
 - Plaque burden >70% (p<0.001)
 - Remodeling index (p=0.014)

Optical Coherence Tomography

Fibroatheroma

TCFA

**Macrophage
Accumulations**



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White



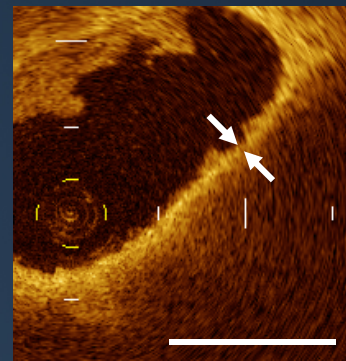
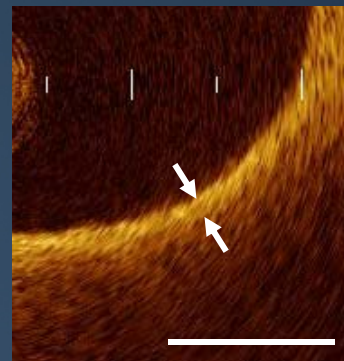
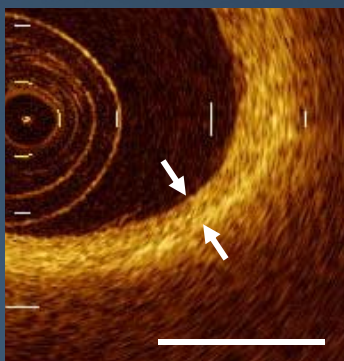
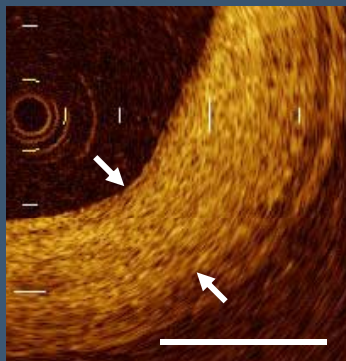
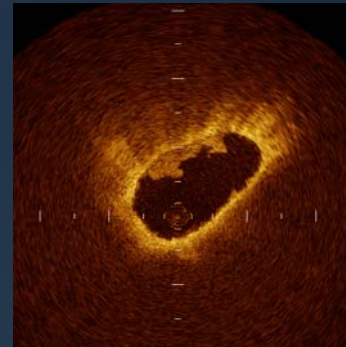
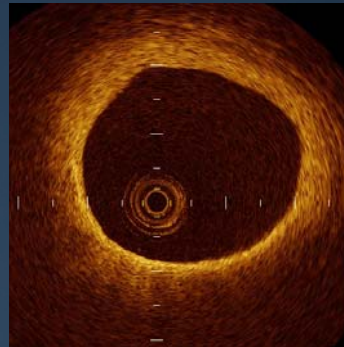
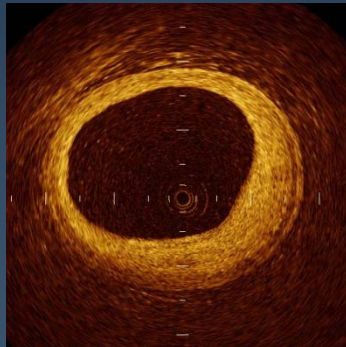
Light Yellow



Yellow



Intense Yellow



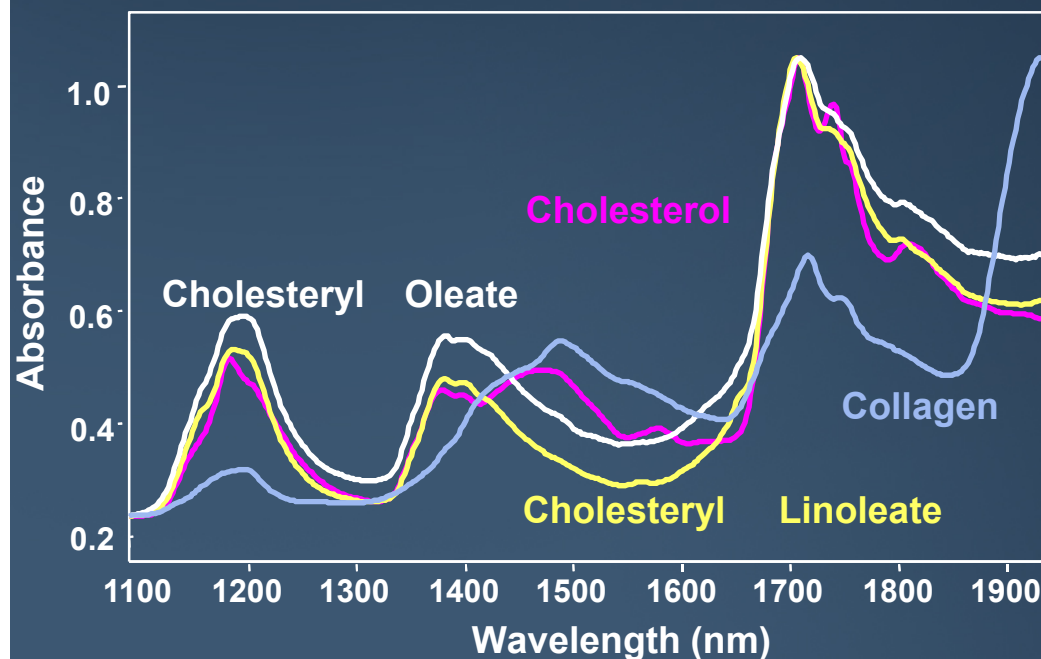
OCT findings and lesion progression

	Progression*	No Progression	P-value	OR	P-value
Plaque rupture	61.5%	8.9%	<0.01	10.2	<0.001
Microchannels	76.9%	14.3%	<0.01	20.0	<0.001
Lipid pools	100%	60.7%	0.02	2.16	0.2
TCFA	76.9%	14.3%	<0.01	20.0	<0.001
Macrophages	61.5%	14.3%	<0.01	9.0	0.001
Thrombus	30.8%	1.8%	<0.01	12.0	0.002

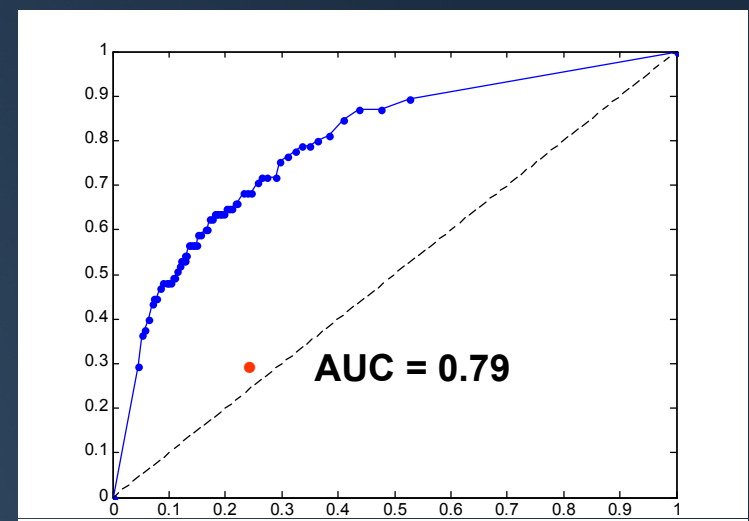
**decrease in QCA
MLD >0.4mm*

Univariate analysis showed that OCT-TCFA and microchannels (both OR=20.0, p<0.01) correlated with progression

Identification lipid core plaque (LCP) is based on distinction of cholesterol spectral features. ROC Analysis of validation of NIR spectroscopy in 51 autopsy hearts for detection of confluent [$>0.2\text{mm}$ thick and $>60^\circ$ in circumference] and relatively superficial necrotic core [overlying fibrous cap thickness $<0.45\text{microns}$]



Percent Positive Agreement



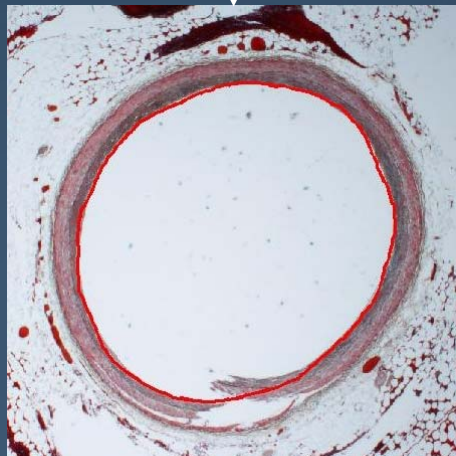
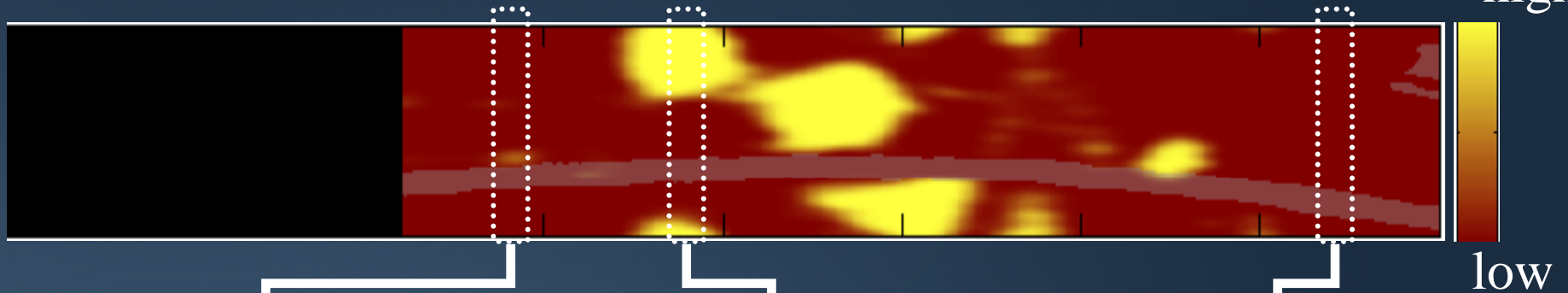
1-Percent Negative Agreement



LipiScan NIRS vs Histology

mm of
pullback

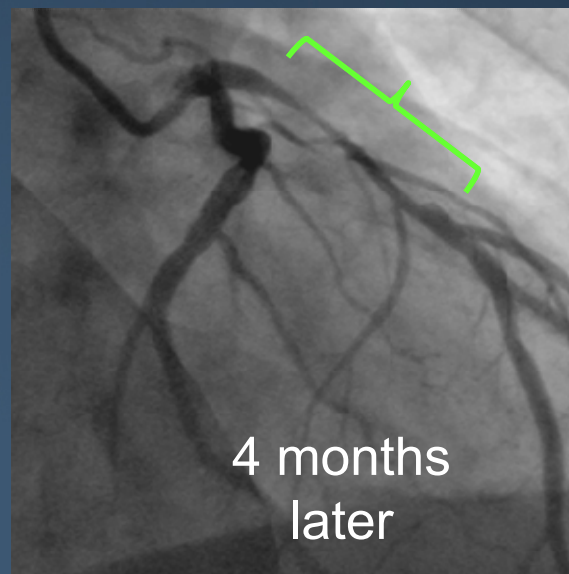
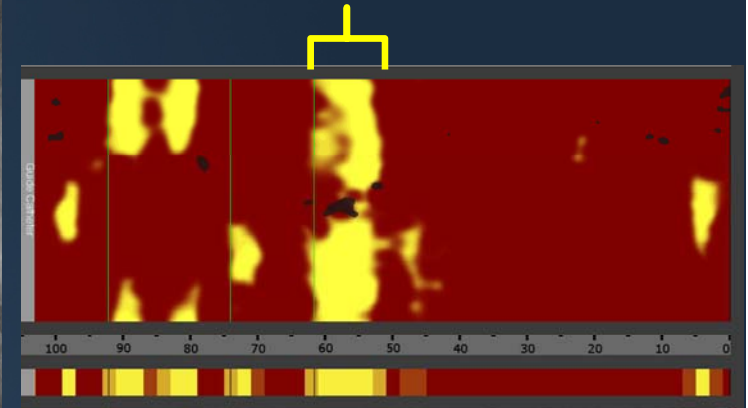
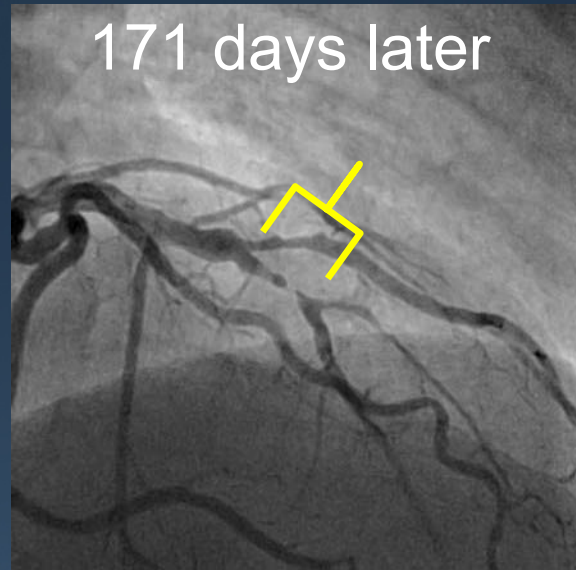
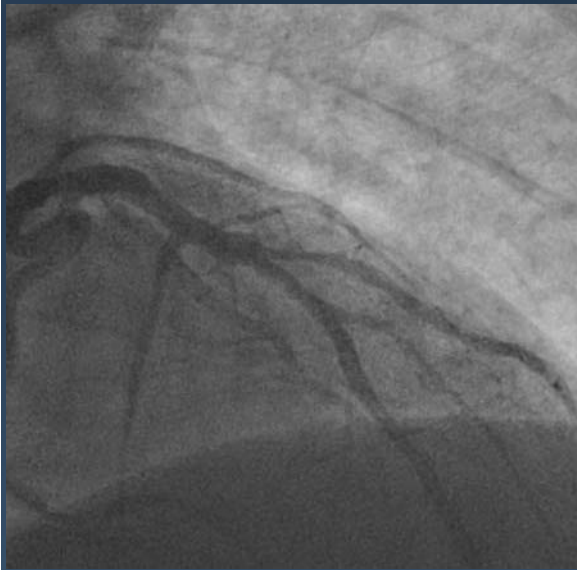
high



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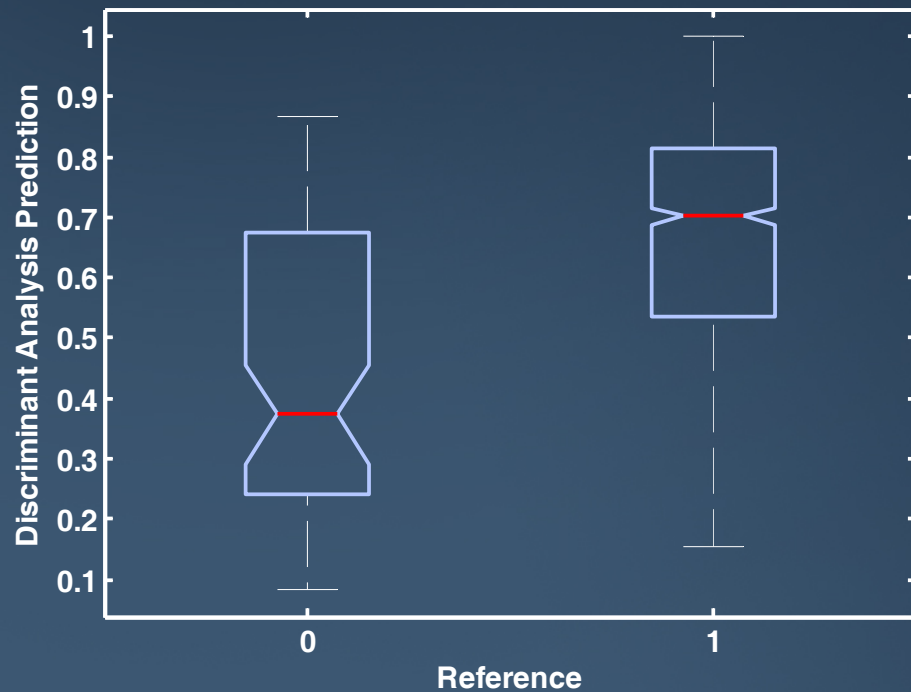


4 months later

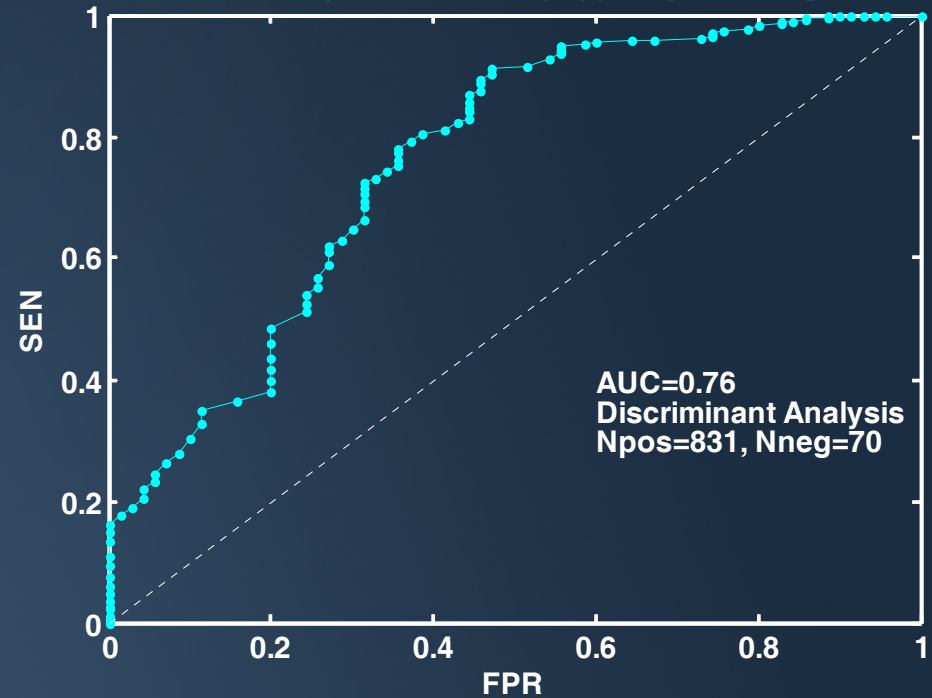


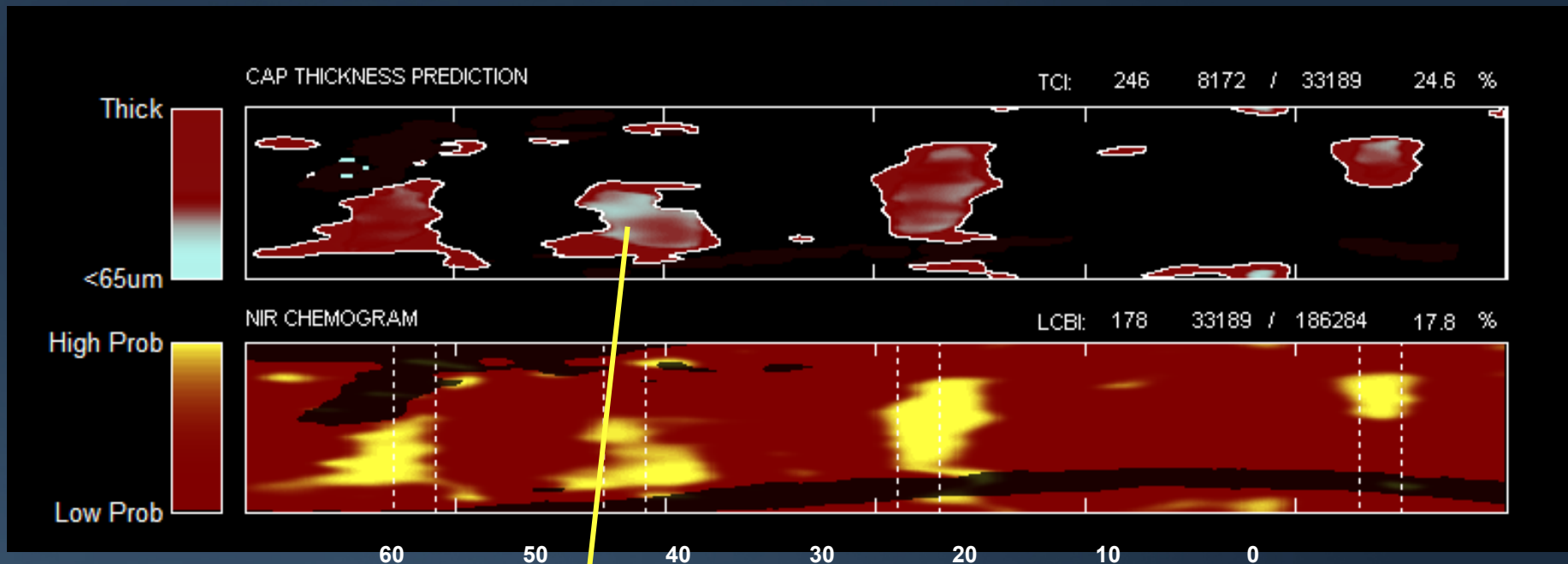
Ability to Predict Thin Cap (<0.065mm)

Capmeth=min, Neg=Cap<0.065mm,
Pos=Cap>0.065mm, CapTypes=[LCNCCC]



Capmeth=min, Neg=Cap<0.065mm,
Pos=Cap>0.065mm, CapTypes=[LCNCCC]





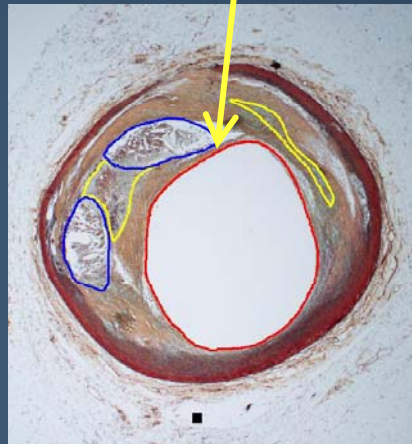
60 50 40 30 20 10 0

52mm

42mm

28mm

6mm



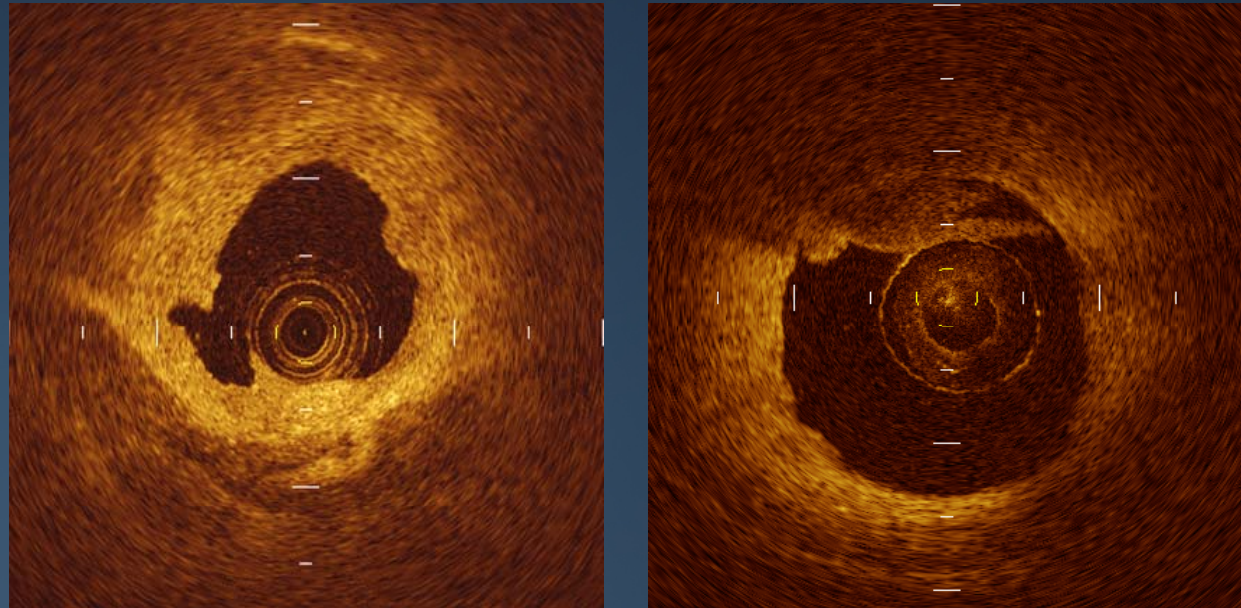
Other techniques for detection of a thin-cap fibroatheroma

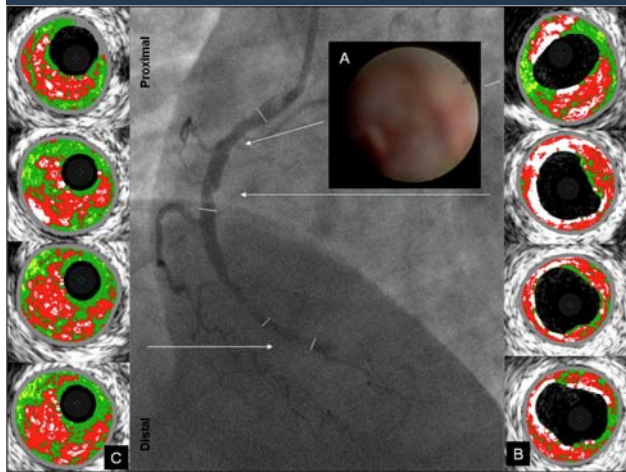
- **IB-IVUS**
- **iMAP**
- **Palpography**
 - **Predictors of fibrous cap strain**
- **Shear stress**
- **Angioscopy**
- **Thermography**
 - **Temperature is related to inflammation**
- **Contrast vasovascular imaging**
 - **Assess neovascularization**



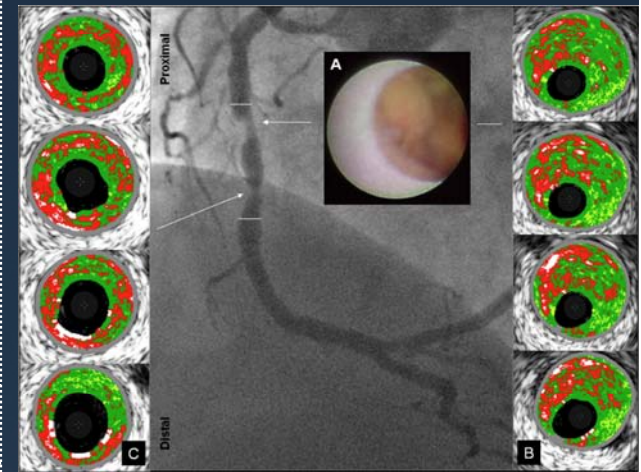
OCT Erosion

Thrombus is superimposed on a de-endothelialized, but otherwise intact plaque.





	Angioscopic thrombosis	
	- Rupture (n=23)	+ Rupture (n=19)
VH-TCFA	17	11
ThCFA	5	7
PIT	1	1



The similarity of VH-IVUS plaque composition (% NC and % VH-TCFA) in thrombotic lesions with or without angioscopic plaque rupture suggest a spectrum of underlying morphologies to explain thrombosis in the absence of a ruptured plaque including erosions, small (and undetectable) plaque ruptures, and potentially unruptured TCFA with superimposed thrombosis.

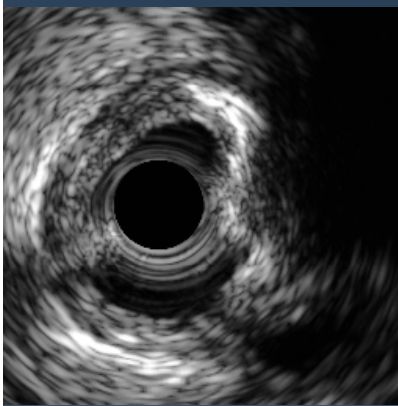
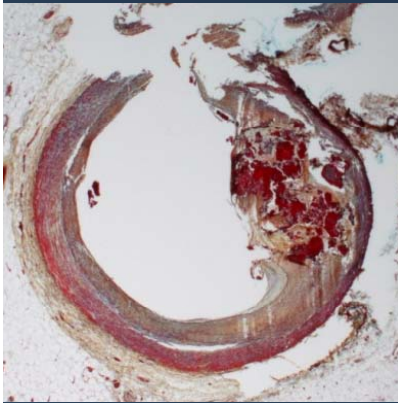
Characteristics of culprit lesions in ACS not related to plaque rupture as defined by OCT and angioscopy

	Rupture	Erosion	Stable	P-value
#	27	11	25	
OCT				
Fibrous cap thickness, μ	45 \pm 12	132 \pm 54	318 \pm 140	0.001
Lipid >180°	93%	45%	24%	0.001
TCFA	93%	18%	8%	0.001
Thrombus	100%	100%	16%	0.001
Angioscopy				
Yellow plaque	85%	72%	56%	0.066
Deep yellow plaque	19%	27%	28%	
Light yellow plaque	67%	45%	28%	
White plaque	15%	27%	44%	0.066
Thrombus	89%	100%	16%	0.001

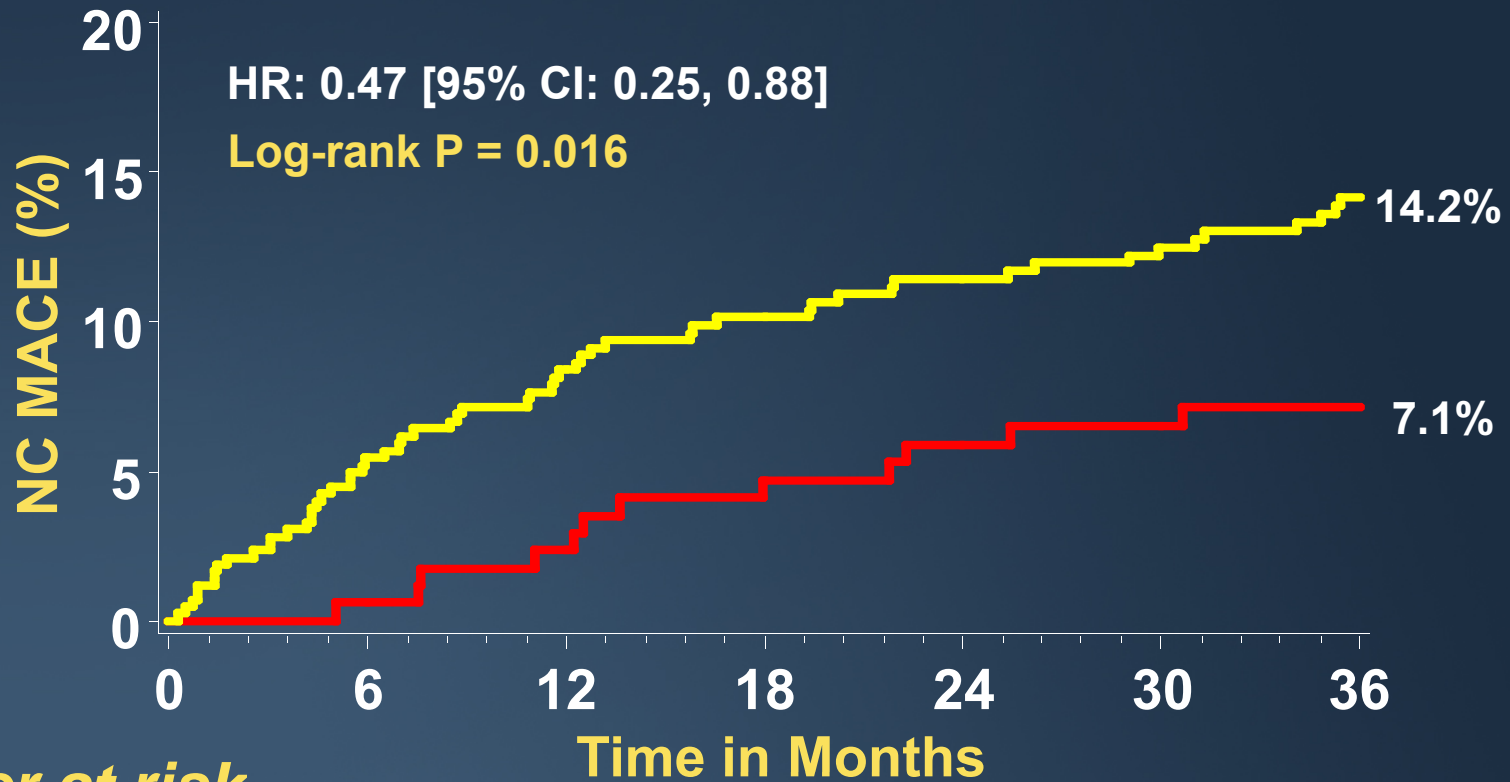
Superficial calcified nodule can protrude through and rupture the fibrous cap

314 calcified nodules in PROSPECT

- At least one calcified nodule: 16% per artery (250 of 1573), 30% per pt (185 of 623).
- Two or more calcified nodules: 48 arteries (3%), 76 patients (12%).
- The angiographic appearance was severe calcium in 3, moderate calcium in 35, hazy in 19, and normal in 257
- The VH-IVUS appearance was a fibroatheroma in 42% (116 of 276) , but only a VH-TCFA in 5.



— Calcified nodule cohort
 — Non-calcified nodule cohort



Number at risk

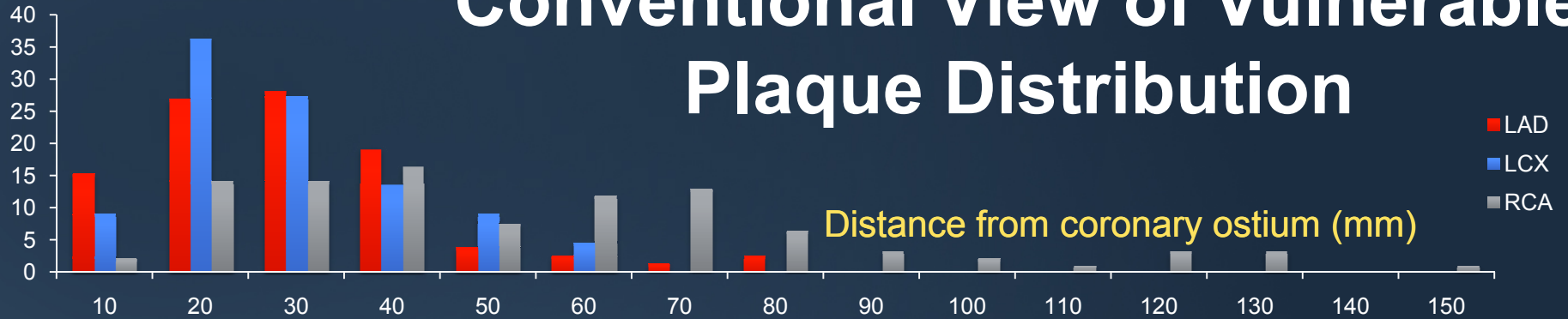
CN cohort	185	170	166	162	156	150	90
Non-CN cohort	438	389	370	352	338	324	190

In patients treated with statins who have undergone primary PCI (secondary prevention), there appears to be a shift in location of vulnerable plaque location.



Conventional View of Vulnerable Plaque Distribution

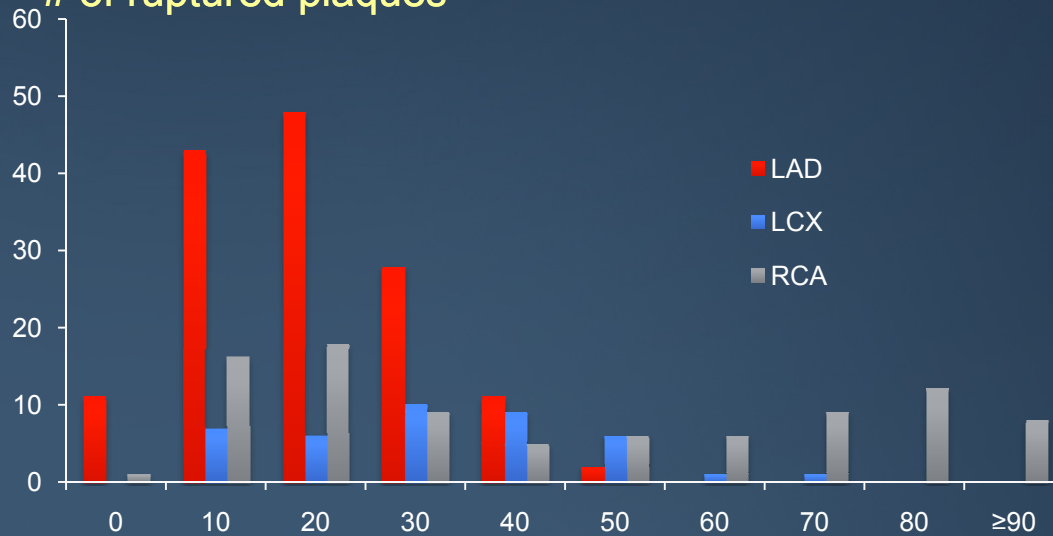
% acute occlusions



(Wang et al., Circulation 2004;110:278-84)

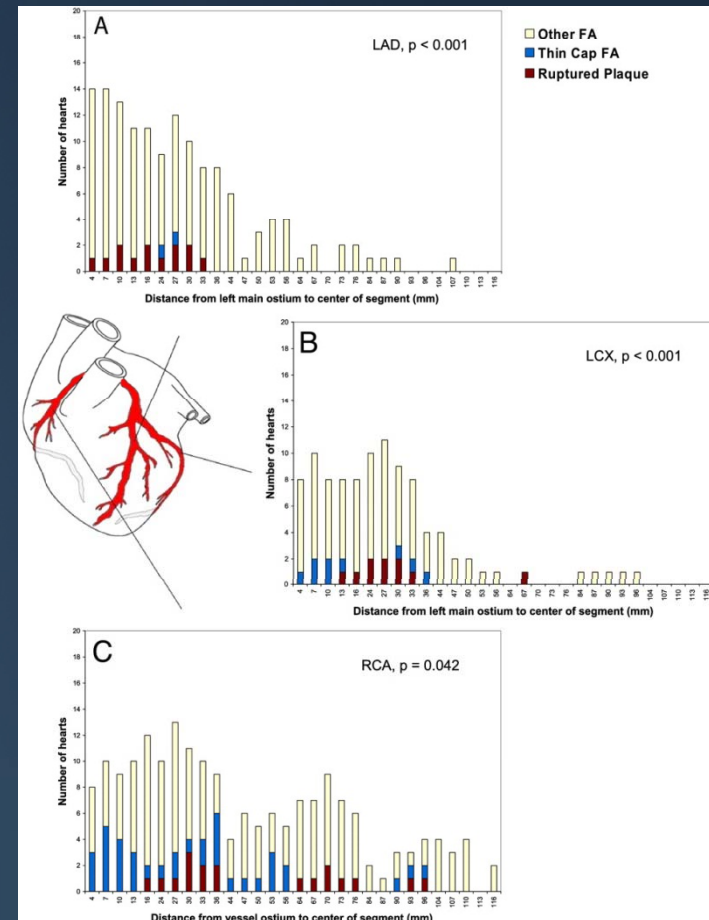
(Cheruvu et al. J Am Coll Cardiol 2007;50:940-9)

of ruptured plaques



Distance from coronary ostium (mm)

(Hong et al J Am Coll Card 2005;46:261-5)



PROSPECT: Location of MACE

	All (n=228)	Culprit lesion related (n=121)	Non culprit lesion related (n=107)
LM	4 (1.8%)	1 (0.8%)	3 (2.8%)
LAD	82 (36.0%)	48 (39.7%)	34 (31.8%)
LCX	63 (27.6%)	30 (24.8%)	33 (30.8%)
RCA	79 (34.6%)	42 (34.7%)	37 (34.6%)
Proximal vessel	69 (30.3%)	43 (35.5%)	26 (24.3%)
Mid vessel	51 (22.4%)	30 (24.8%)	21 (19.6%)
Distal vessel	35 (15.4%)	18 (14.9%)	17 (15.9%)
Branch*	73 (32.0%)	30 (24.8%)	43 (40.2%)

Excludes indeterminate lesions. Includes, diagonal, ramus, obtuse marginal, R/L PDA, R/L PLAS.

PROSPECT: Completeness of 3-vessel IVUS and VH-IVUS imaging

Event type	Total # of events	Baseline QCA at event site	Baseline IVUS at event site	Baseline VH at event site
All MACE	245	227	140	132
Culprit lesion related	120	120	84	76
Non culprit lesion related	107	107	56	56
- With RLP	51	51	31	31
- Without RLP	56	56	25	25
Indeterminate	18	0	0	0



Is three vessel invasive imaging safe?



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PROSPECT: Complications attributed to the 3-vessel IVUS imaging procedure (n=697, non-hierarchical)

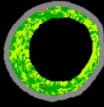
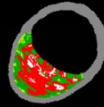
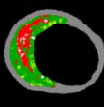
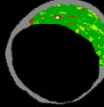
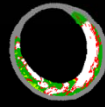
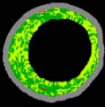
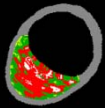
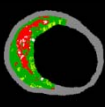
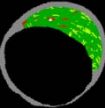
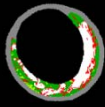
Death	0 (0%)
MI	3 (0.4%)
- Q-wave (from dissection)	1
- non Q-wave (from dissection)	2
PCI or CABG	10 (1.4%)
- CABG (from perforation)	1
- CABG (from dissection)	2
- PCI (from dissection)	9
Any imaging complication*	11 (1.6%)

*Some pts had more than one complication

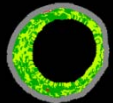
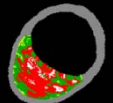
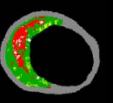
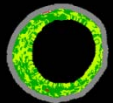
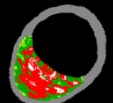
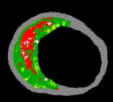
Safety becomes an even more important concern if imaging must be repeated periodically.



Change in non-culprit lesion phenotype in 106 pts (201 lesions) with plaque burden >40% from the Global VH Registry with baseline and 8-month follow-up VH analysis

		<i>Follow-up</i>					
		PIT (n=48)	TCFA (n=17)	ThCFA (n=109)	Fibrotic (n=23)	Fibrocalcific (n=20)	
<i>Baseline</i>							
	PIT (n=62)		44	6	12	0	0
	TCFA (n=20)		0	5	14	2	0
	ThCFA (n=93)		0	6	83	3	1
	Fibrotic (n=22)		4	0	0	18	0
	Fibrocalcific (n=19)		0	0	0	0	19

Change in non-culprit lesion phenotype in 100 pts (100 lesions: plaque burden >40%) from HORIZONS: Baseline and 13-month follow-up VH-IVUS

		<i>Follow-up</i>			
		PIT (n=11)	TCFA (n=54)	ThCFA (n=32)	
<i>Baseline</i>					
	PIT (n=16)		6	3	7
	TCFA (n=43)		2	33	8
	ThCFA (n=40)		1	19	20

And some vulnerable plaques rupture asymptotically and are detected incidentally while others heal and contribute disease progression

- *Maehara et al. J Am Coll Cardiol 2002;40:904-10*
- *Rioufol et al. Circulation. 2002;106:804-8*
- *Hong et al. Circulation 2004;110:928-33*
- *Fuji et al. Circulation 2003;108:2473-8*
- *Burke et al. Circulation 2001;103:934-40*
- *Rioufol et al. Circulation 2004;110:2875-80*
- *Hong et al. Atherosclerosis. 2007;19:107-14*



Conclusion

- We can now say with confidence that we are able to detect TCFAs and, perhaps more importantly, exclude the presence of a vulnerable plaque.
- However, that does not mean that searching for a vulnerable plaque in patients will ever make clinical sense unless we can identify a truly high risk patient population or one that does not respond to conventional medical therapy in order to justify invasive imaging – especially, since we do not have a focal therapy to offer.

Reference: Vancraeynest et al. Imaging the vulnerable plaque. J Am Coll Cardiol 2011;57:1961-79

