Why Current DES Should NOT be Used Routinely During Primary AMI Angioplasty

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Slides prepared by the help of Gaku Nakazawa

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DES Pathology

- Drug Eluting Stents (DES) have shown increased risk of late stent thrombosis (LST) compared to bare metal stents (BMS) *(Pfisterer M, et al. JACC 2006;48:2584)*
- Significant delayed arterial healing characterized by incomplete endothelialization and persistent fibrin deposition has been reported in DES at autopsy. *(Joner M, et al. JACC 2006;48:193)*

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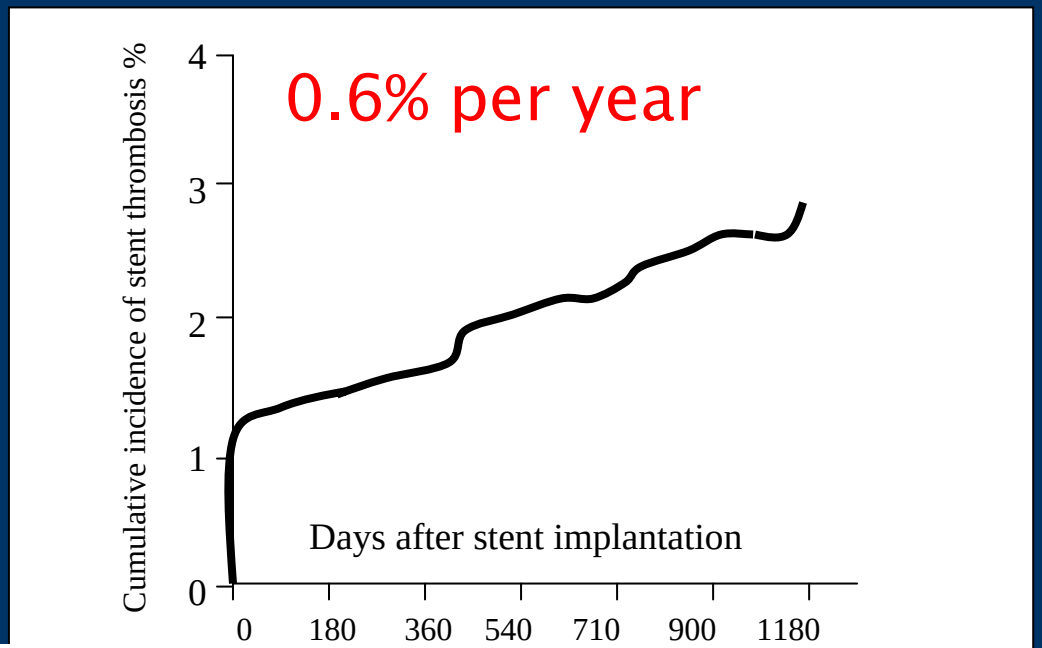
Clinical Studies raise concern!!

- Initial clinical results of DES implantation in patients with acute myocardial infarction (AMI) have shown either no significant differences in late thrombosis, a benefit at 9 months, or an increase in the incidence of death *(Laarman GJ, et al.New Engl J Med 2006;355:1105. Spaulding C, et al. New Engl J Med 2006;355:1093. Steg G, ESC 2007)* however, long-term safety remains a concern
- Recently, AMI is being recognized as one of the predictors for LST following DES implantation (Daemen J et al. Lancet 2007; 369: 667. Daemen J et al. ESC 2007.)
- Presence of a large necrotic core (>30% of plaque area), often observed in AMI lesions, is a likely risk factors for LST

- Drug-Eluting Stents (DES) dramatically reduced restenosis as compared to bare-metal stents (BMS) in man.
- However, late stent thrombosis (LST), a life threatening complication, has emerged as a major safety concern.



Days after PCI	9	30	365	710	1095
Cummulative incidence (%)	1.1	1 2	1.7	2.3	2.9
Cumulative events (n)	79	90	116	141	152
Full number at risk (n)	7173	7041	5549	2857	999

Daemen J et al. Lancet 2007; 369: 667

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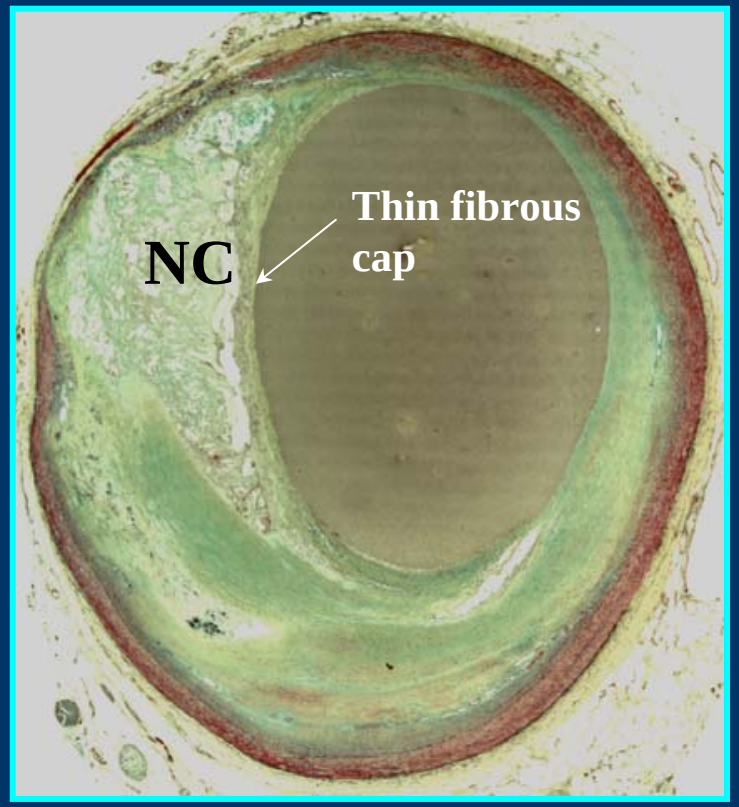
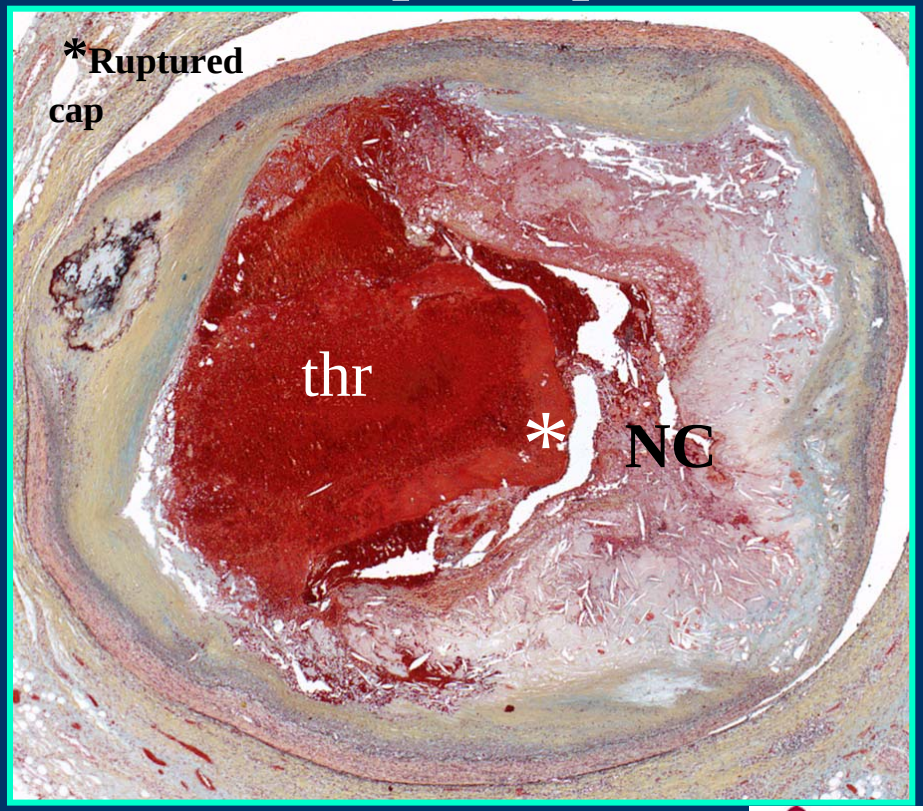
Underlying Plaque Morphology in Acute Myocardial Infarction Lesions

Underlying plaque in ACS patients

TCFA



Plaque Rupture



* = rupture site

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Only method available today that can accurately evaluate plaque morphology and DES response is histology

1. Culprit vs. non-Culprit within the same lesion in response to DES
   - in AMI culprit and non-culprit sites, respectively
2. Culprit site Stent pathology Comparison between
   - AMI vs. Stable patients
3. Comparison of stent healing in DES at plaque rupture site versus non-ruptured site within culprit section (AMI).

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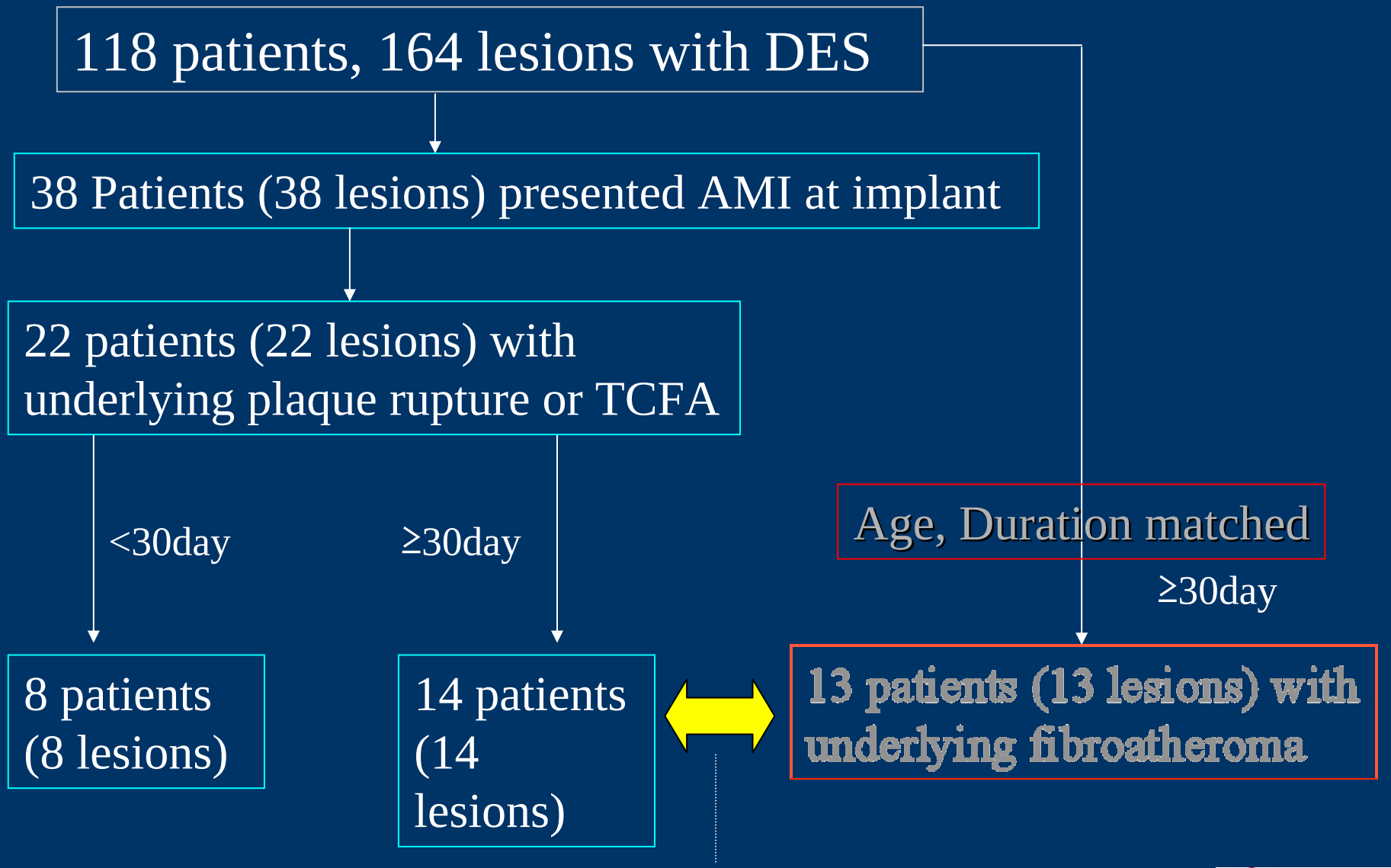
Study design



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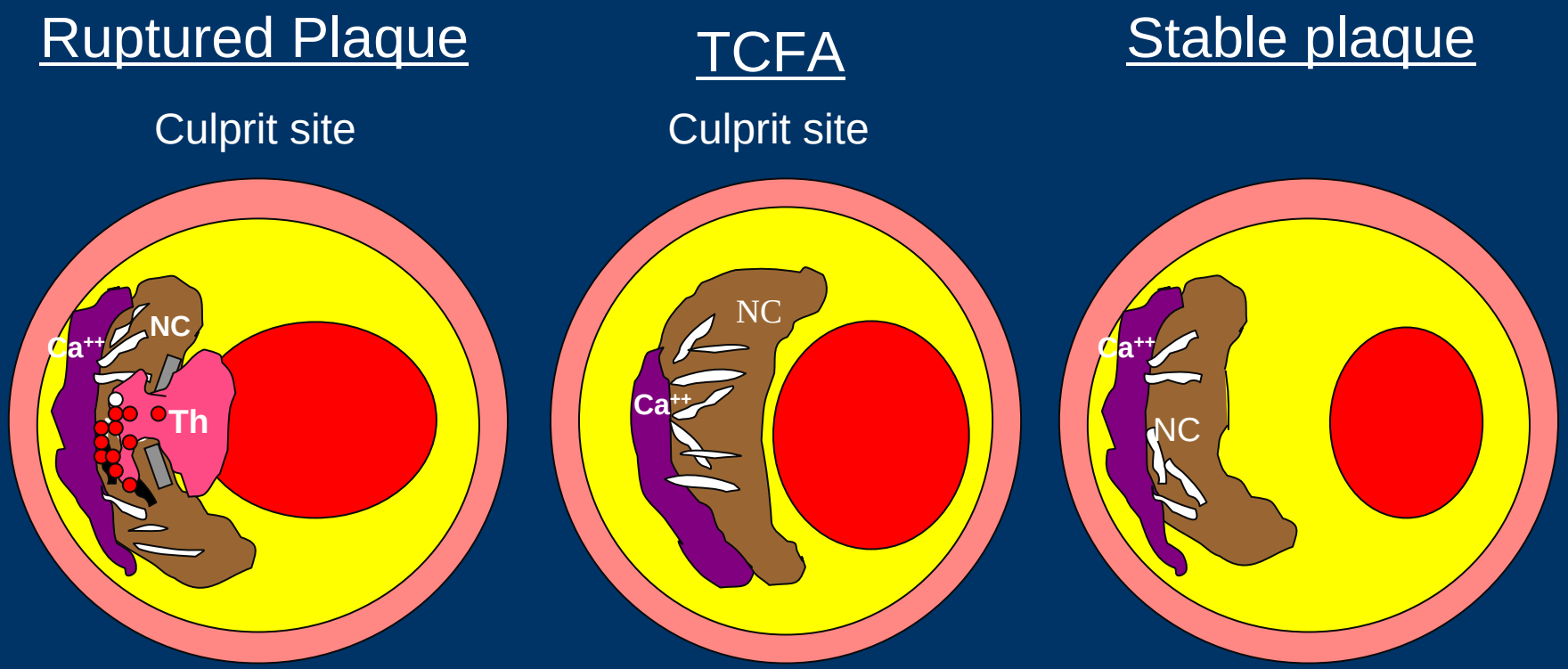
Should DES stents be implanted in AMI patients?



Abbreviations: TCFA = thin cap fibroatheroma/vulnerable plaque; NC =necrotic core; Th = thrombus; Ca++ = calcium

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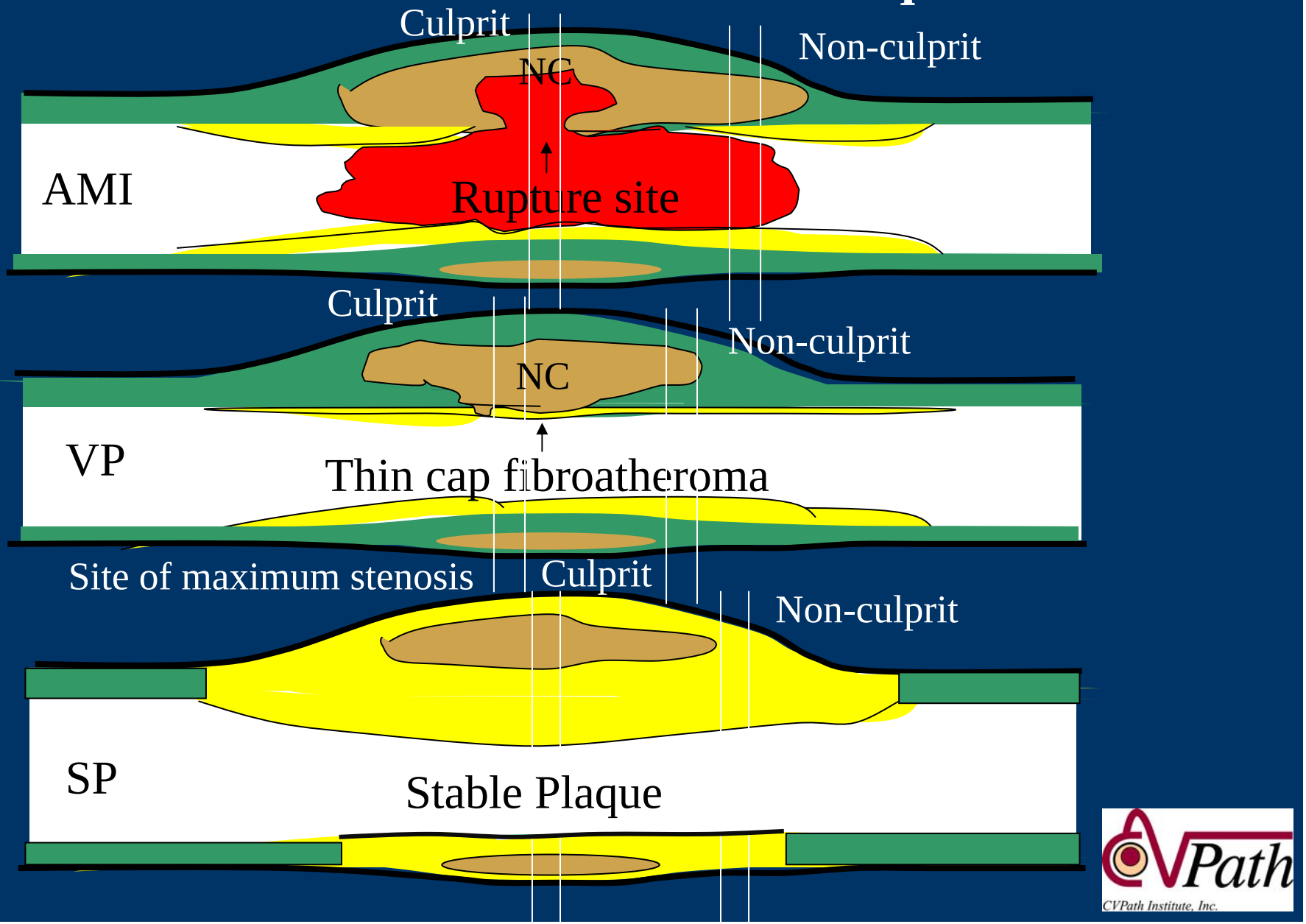
Acute Myocardial Infarction, Thin-cap Fibroatheroma and Stable Plaque



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Morphometric assessment of vessel area, stentosis, necrotic core size, and macrophage density from 72 pts with SCD

Plaque Type	IEL mm^2	Stenosis %	Necrotic core %	Macrophage (%CD68)
Fibroatheroma (n=262)	9.2±4.9	64.5±17.8	11.2±13.2	1.1±1.5
Thin-cap Fibro-atheroma (n=46)	12.8±7.9	67.0±15.5	21.6±23.7	2.0±1.9
Plaque rupture (n=55)	13.2±6.4	79.8±14.4	29.0±19.0	5.3±5.4
P value	<0.0001**	<0.0001*	<0.0001***	<0.0001*

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Patient / Lesion Characteristics

	AMI Patients with Rupture or TCFA		Stable Patients with fibroatheroma	p value AMI vs Non-AMI
	≤30 days (n=8)	>30 days (n=14)	(>30 days, n=13)	
Age, yrs	70 ± 11	59 ± 16	59 ± 12	>0.99
Male gender, %	88	79	92	0.32
Stent duration, day	5 ± 4	285 ± 277	299 ± 237	0.89
Cypher / Taxus	2 / 6	5 / 9	7 / 6	0.34
Number of stents	1.5 ± 0.5	1.5 ± 1.0	1.2 ± 0.4	0.26
Stent length, mm	28.9 ± 14.3	27.8 ± 12.8	21.2 ± 9.2	0.14
Thrombosis, %	50	50	8	0.016
Restenosis, %	0	0	0	NA

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Lesion Characteristics (Culprit Comparison In Patients With AMI and without AMI >30 days)

	AMI Patients (n=14)	Stable Patients (n=13)	p value
EEL, mm^2	19.82 ± 7.71	15.48±4.94	0.10
Stent Area, mm^2	8.63 ± 3.36	6.72±1.84	0.08
Plaque Area, mm^2	11.19 ± 4.78	8.76±3.76	0.16
Necrotic Core Area, mm^2	3.15 ± 1.94	1.07±0.76	0.0015
Max %NC area	31 ± 12	14 ± 8	0.0002
Max NC Arc, º	228 ± 59	114 ± 47	<0.0001
Fibrous cap thickness, µm	58 ± 18*	250 ± 94	<0.0001
Longitudinal NC length, mm	13.9 ± 6.9	8.8 ± 4.2	0.03
Rupture site length, mm	5.3 ± 4.0	0	<0.0001
% Struts penetrating NC	31 ± 12	0	0.0001

* = remnants of fibrous cap

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Morphometry and Pathologic Assessment (Culprit stent Comparison; AMI vs. Non-AMI)

	AMI Patients (n=14)	Non-AMI Patients (n=13)	p value
Neointimal thickness, mm	0.05 ± 0.04	0.12±0.10	0.03
Strut with fibrin deposition, %	67.2 ± 24.7	41.8±29.4	0.02
Strut with inflammation, %	54.7 ± 36.4	17.8±15.9	0.03
Uncovered strut, %	33.6 ± 19.6	23.8±27.4	0.02

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Morphometry and Pathologic Assessment (Culprit site vs. Non-Culprit site in AMI and Stable)

	Culprit	Non-Culprit	p value
AMI Patient with Underlying Plaque Rupture or TCFA (n=14)			
Neointimal thickness, mm	0.05±0.04	0.11±0.11	0.05
Strut with fibrin deposition, %	67.2±24.7	47.7±24.5	0.05
Strut with inflammation, %	54.7±36.4	29.7±33.0	0.03
Uncovered strut, %	33.6±19.6	23.6±14.2	0.01
Stable Patient with Underlying Fibroatheroma (n=13)			
Neointimal thickness, mm	0.12±0.10	0.12±0.08	0.75
Strut with fibrin deposition, %	41.8±29.4	47.8±30.1	0.16
Strut with inflammation, %	17.8±15.9	19.7±16.5	0.70
Uncovered strut, %	23.8±27.4	25.8±29.9	0.59

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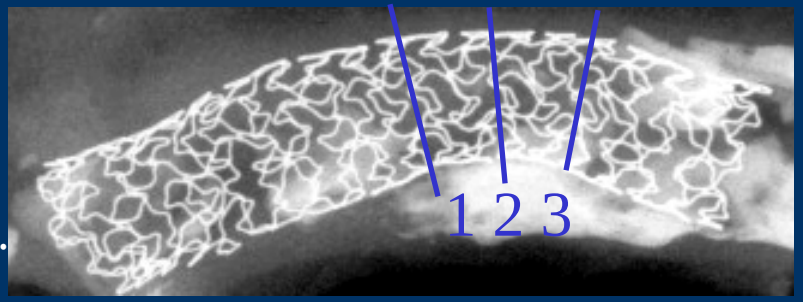
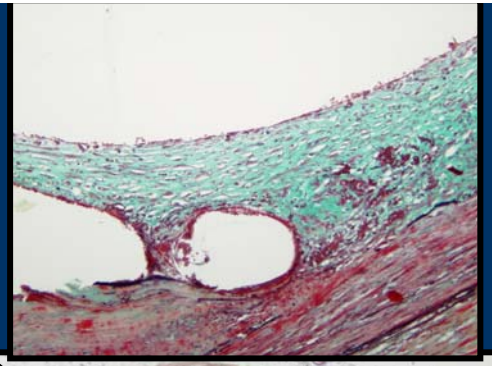
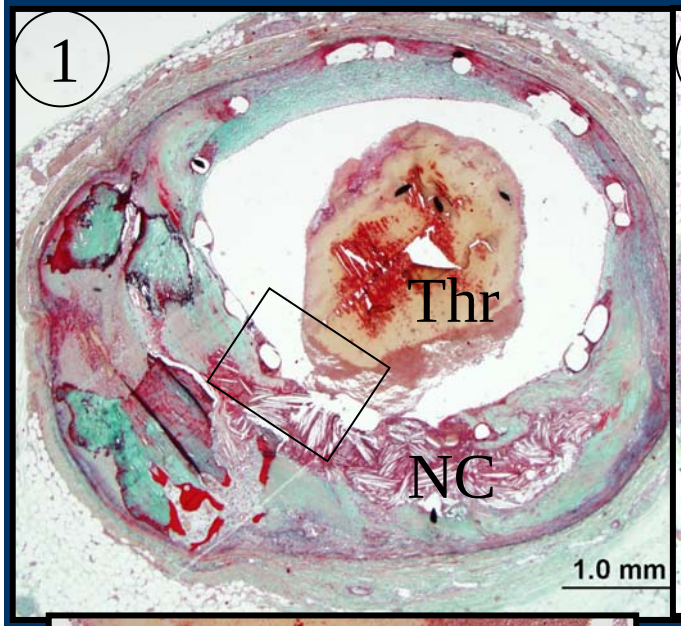
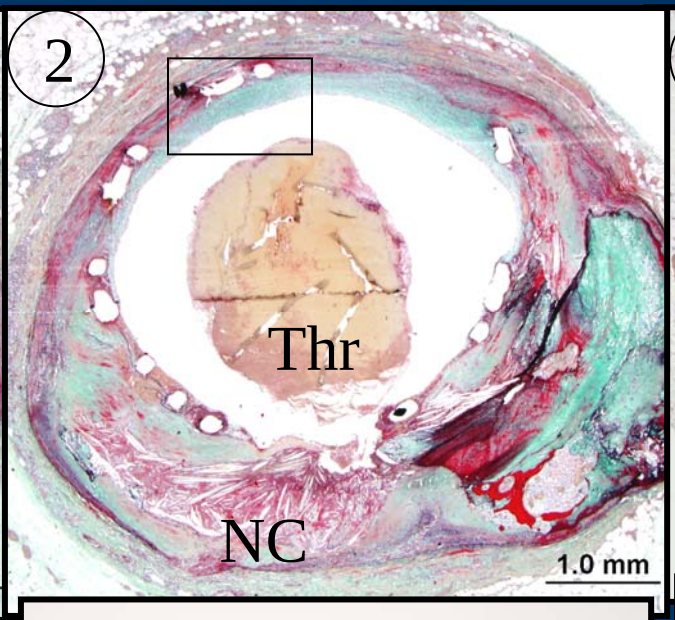
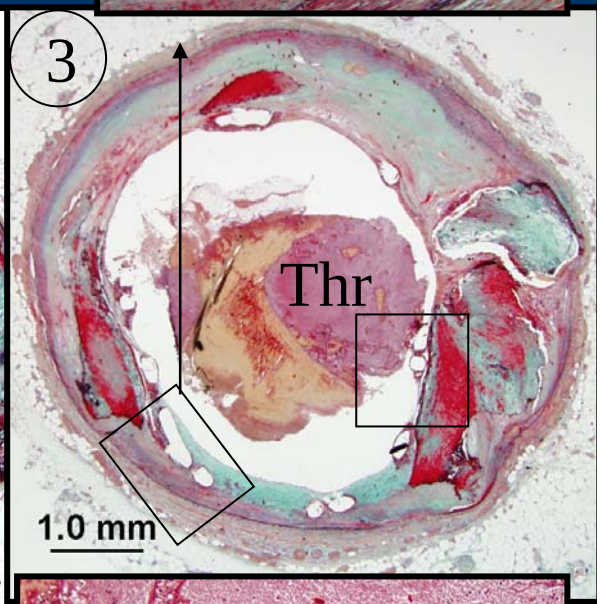
81 yrs old male, presenting MI, stent (Taxus) implantation in the LAD ostium 2 months antemortem.

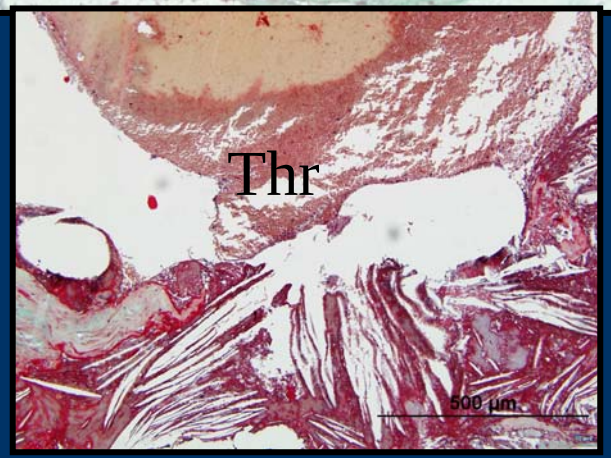


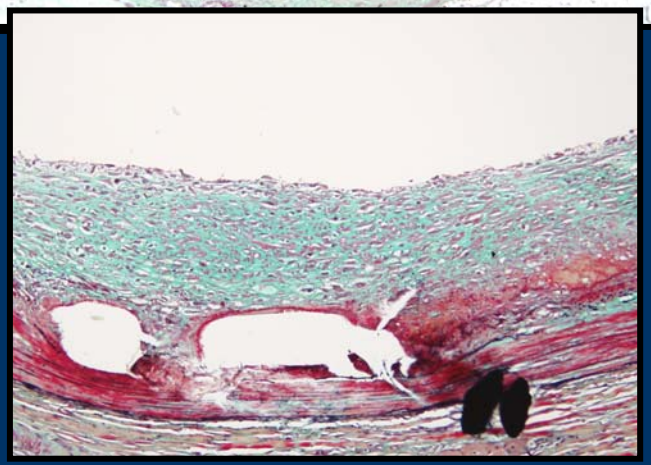












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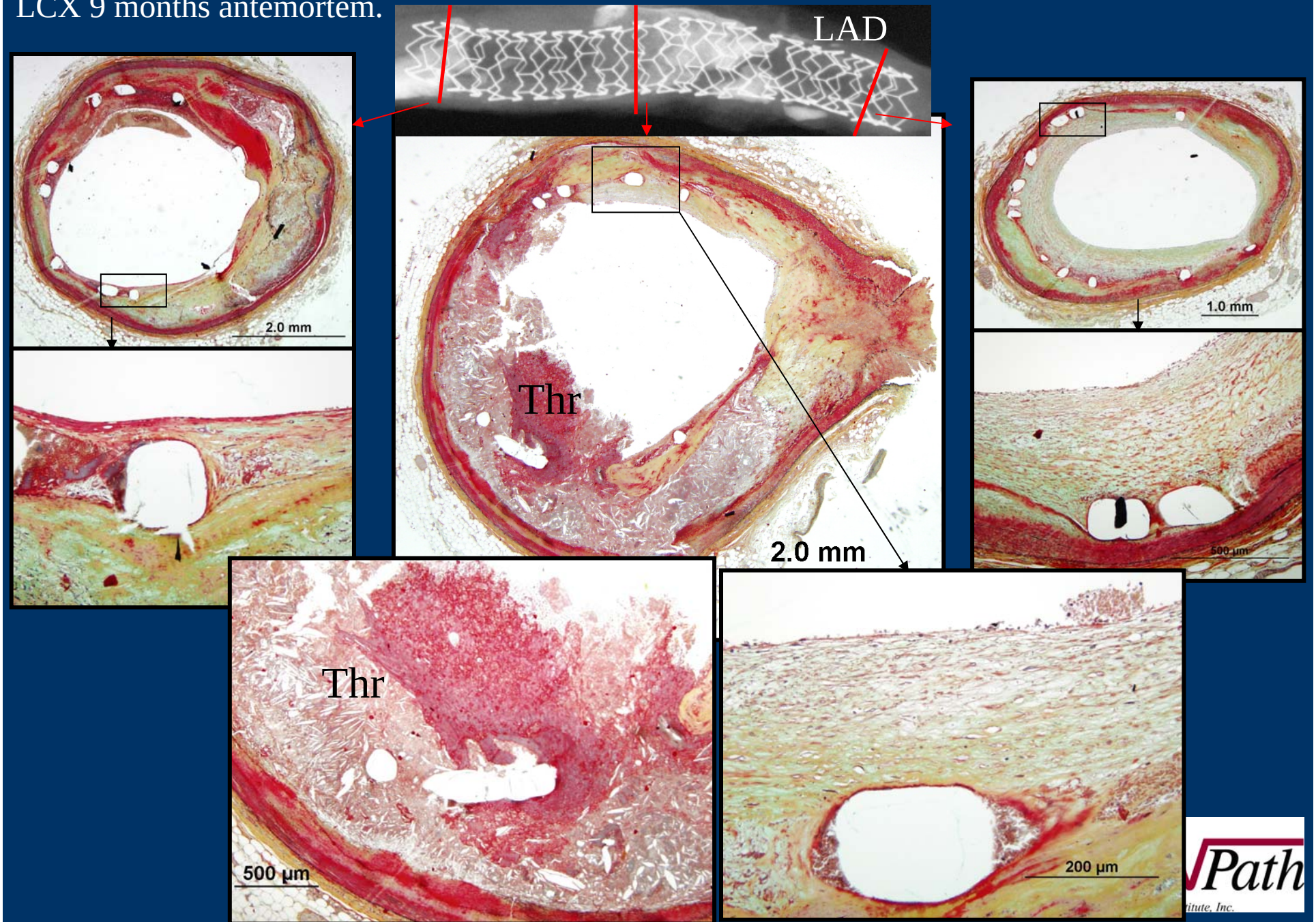
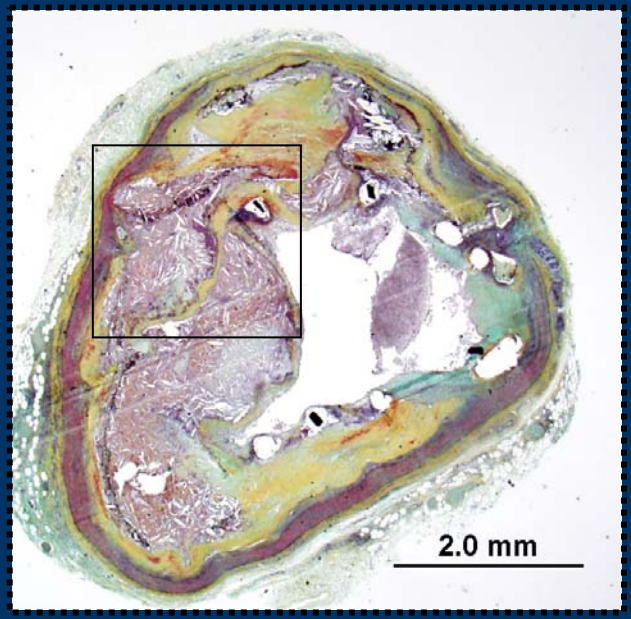
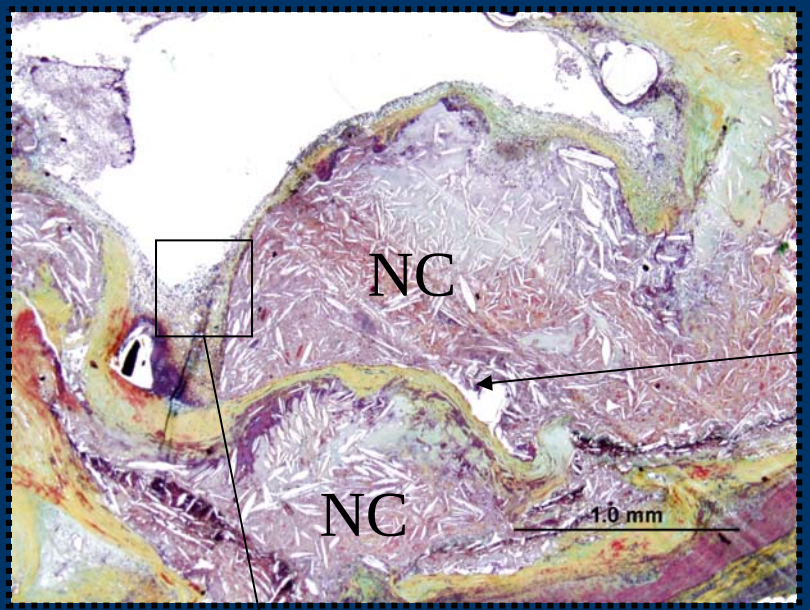
65 yrs old male, presenting acute coronary syndrome, stent (Taxus) implantation in the LAD and LCX 9 months antemortem.

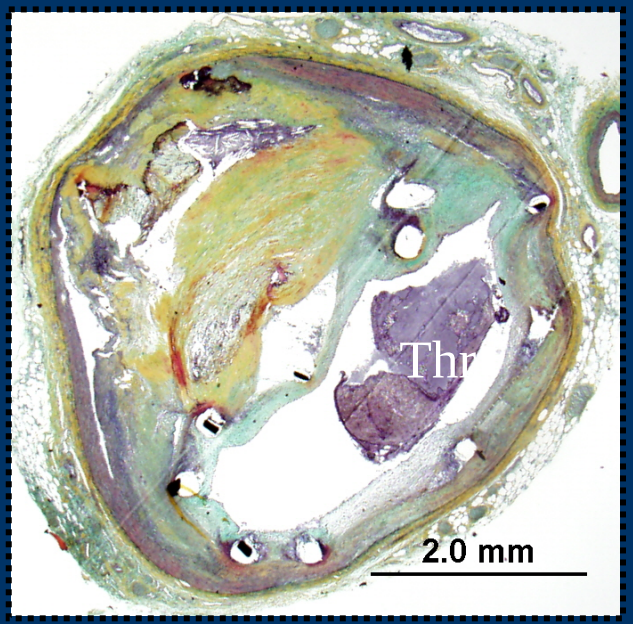


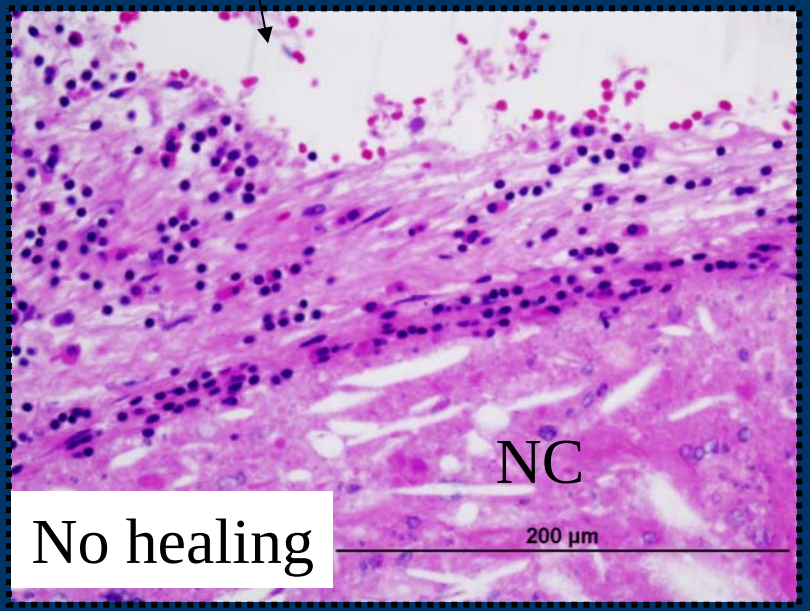
59M, 2 years following Cypher stent implantation for AMI, died suddenly





Fibrous cap





No healing

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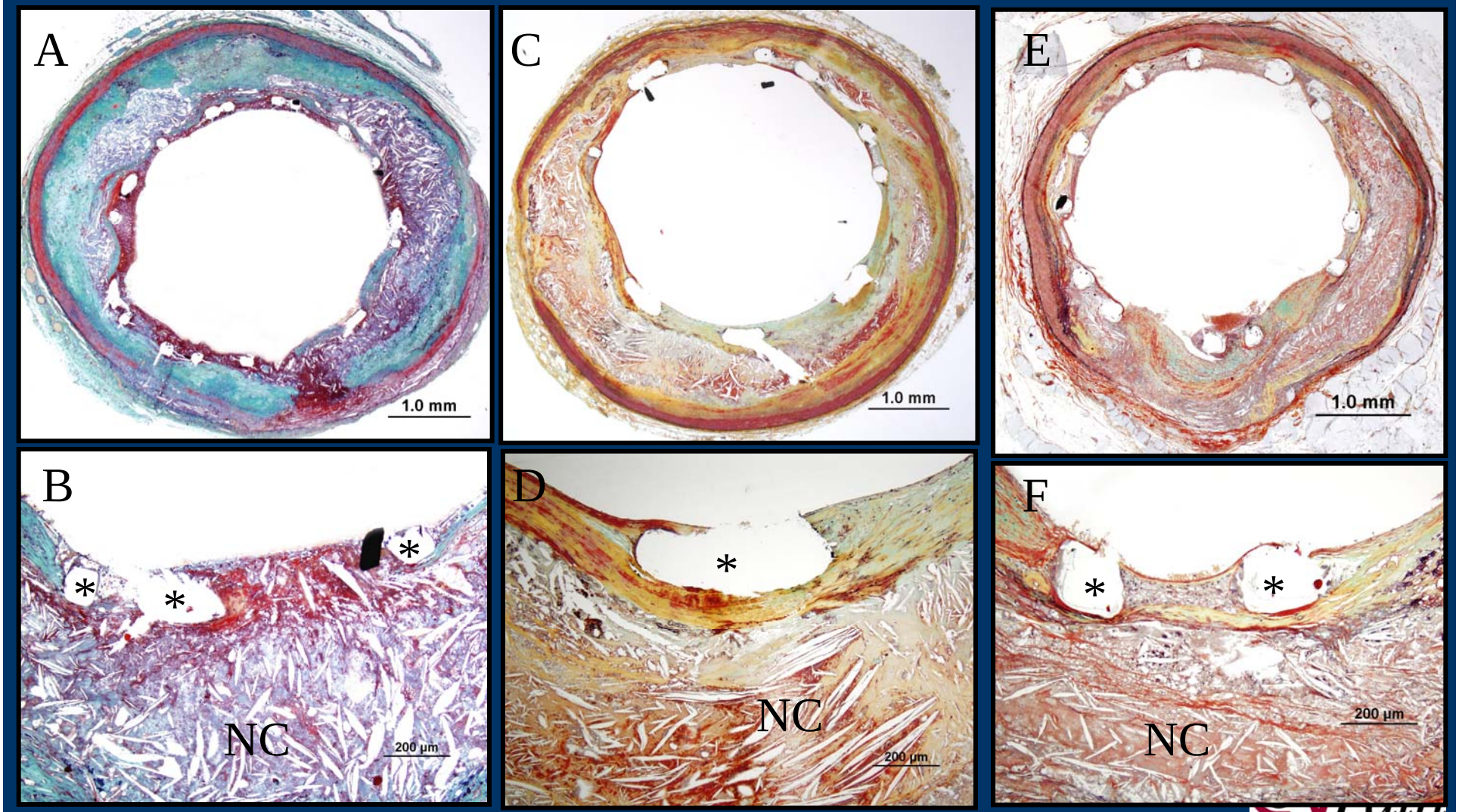
AMI lesions (with Rupture or TCFA)

9 months Taxus	13 months Cypher	24 months Cypher



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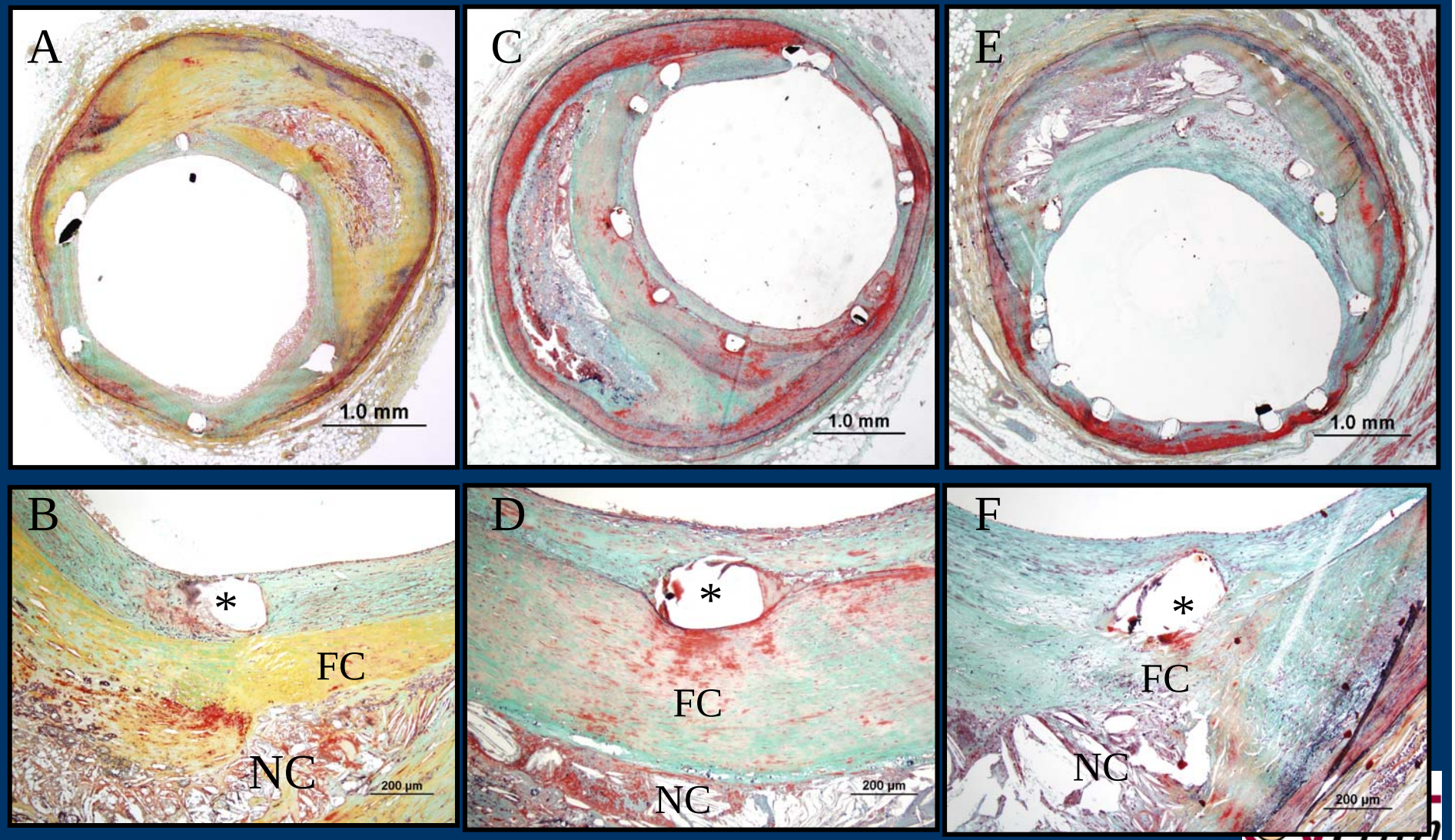
Non-AMI lesions (with underlying Fibroatheroma)

7 months	18 months	19 months
Cypher	Taxus	Cypher



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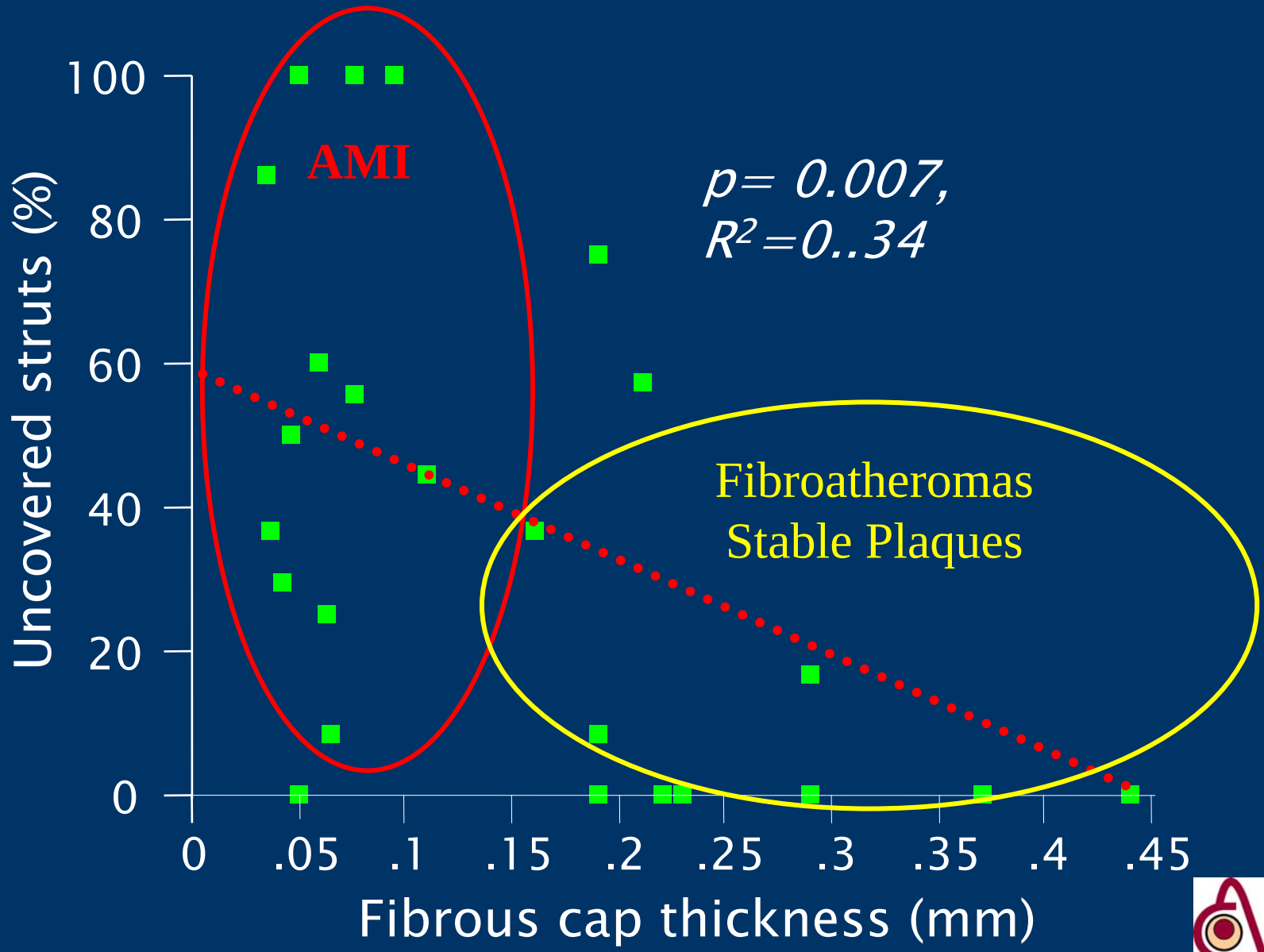
Correlation between “Cap thickness” and “Uncovered struts”



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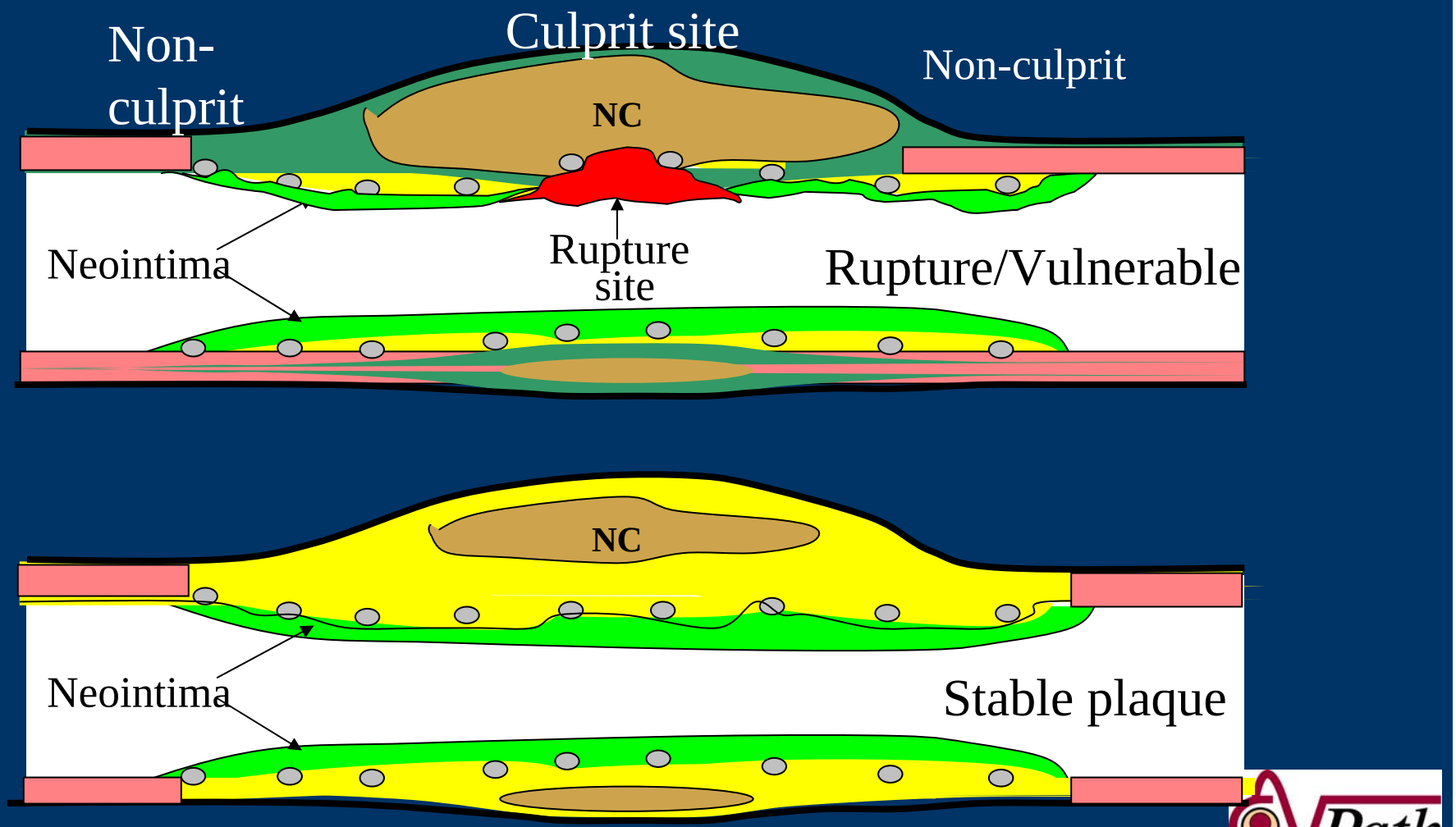
Pattern of healing at AMI cuprit /vulnerable sites vs. Stable Plaque following DES deployment



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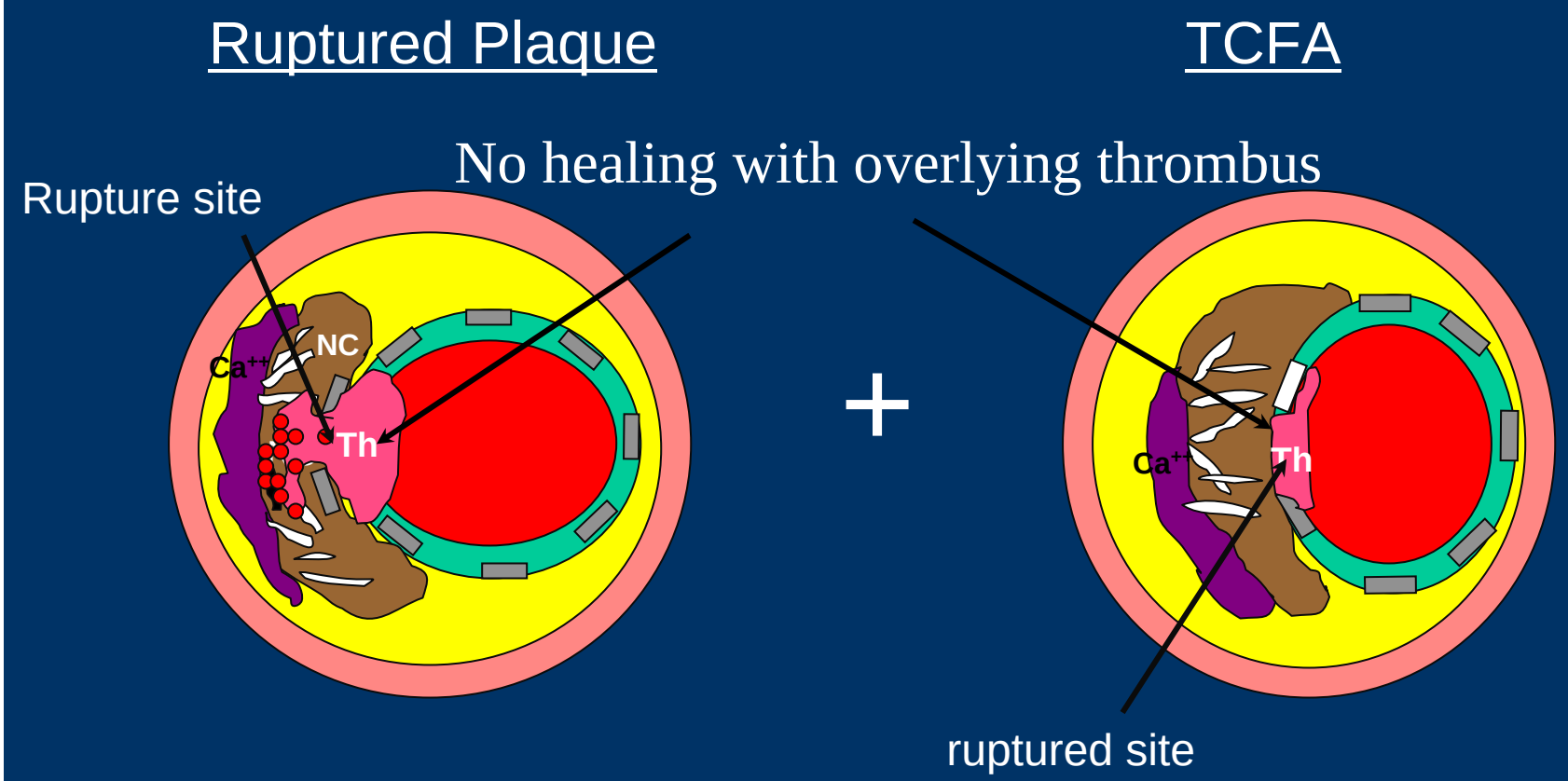
Should DES stent be implanted in AMI patients: site of ruptured and TCFA following DES implantation



Abbreviations: TCFA = thin cap fibroatheroma/vulnerable plaque; NC =necrotic core; Th = thrombus; Ca++ = calcium

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Conclusions

- Culprit site in the AMI lesions showed larger and longer necrotic core size compared to Stable plaques
- The incidence of late stent thrombosis at autopsy was significantly greater in AMI as compared to Stable patients
- Culprit sites showed greater delayed arterial healing as compared to non-culprit sites within the AMI lesions (heterogeneity of healing) while stable lesions showed similar arterial healing between culprit and non-culprit sites

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Conclusions

- Greater delayed arterial healing, evidenced by greater fibrin deposition and incomplete strut coverage, was observed in AMI lesions as compared to non-AMI lesions
- Randomized Clinical trials will result in greater thrombosis in patient treated with DES for AMI
- Treating AMI patients with DES is asking for trouble.

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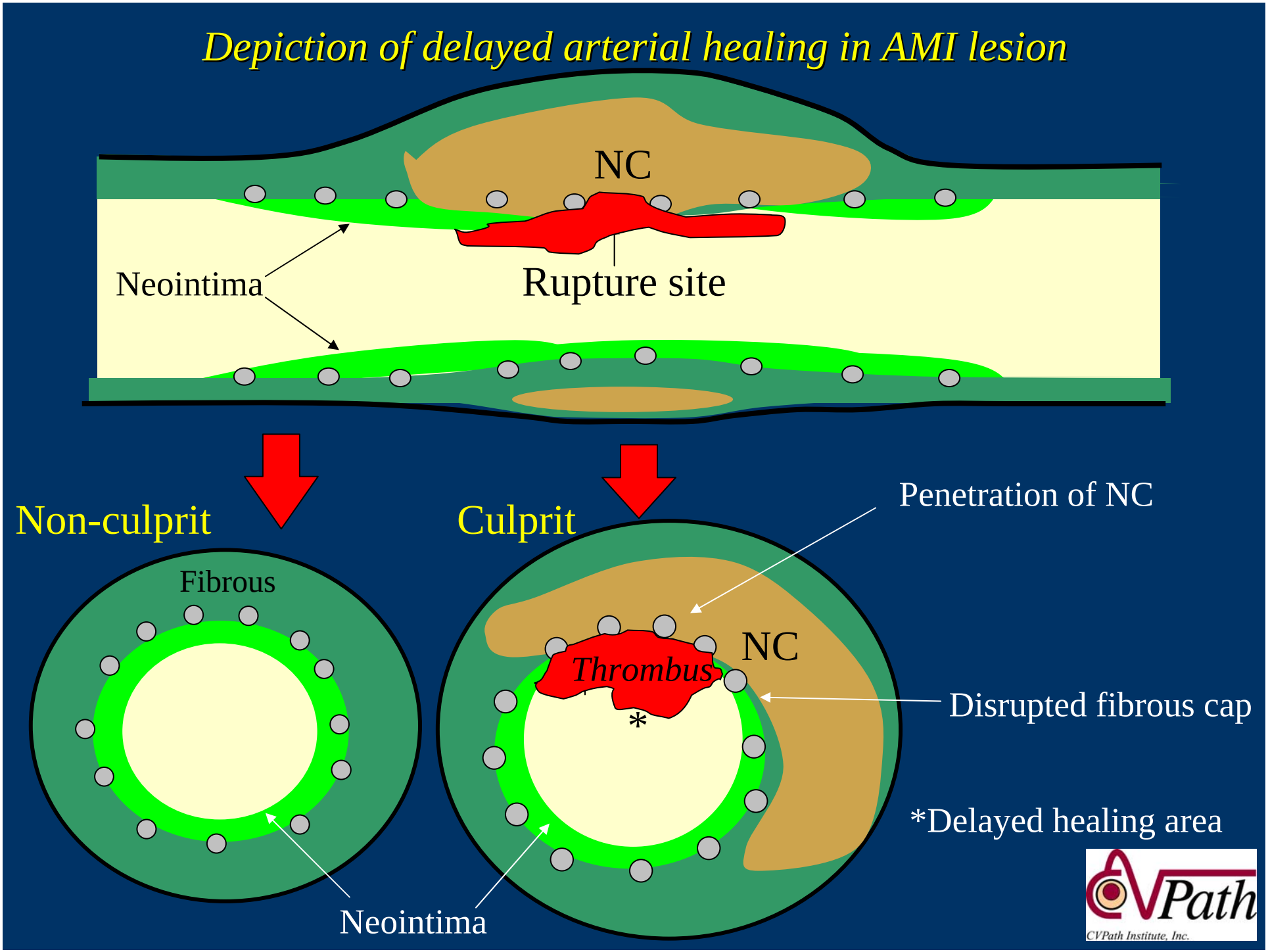
Depiction of delayed arterial healing in AMI lesion
NC
Neointima
Rupture site
Non-culprit
Culprit
Penetration of NC
Fibrous
NC
Thrombus
*
Disrupted fibrous cap
*Delayed healing area
Neointima
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