

Vulnerable Plaque Detection: What is New in 2018? - NIRS -

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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

- Grant/Research Support
- Consulting Fees/Honoraria

Company

- Boston Scientific, Abbott Vascular
- Boston Scientific, OCT Medical Imaging Inc.

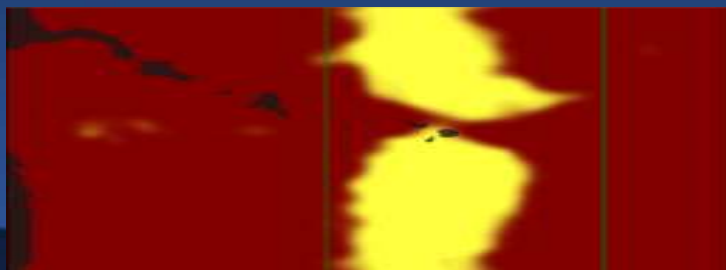
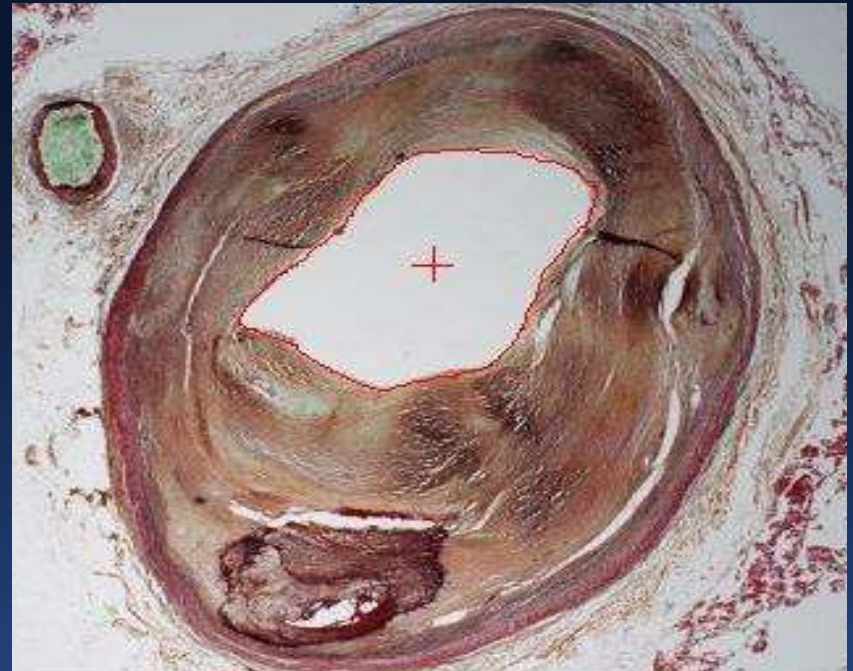
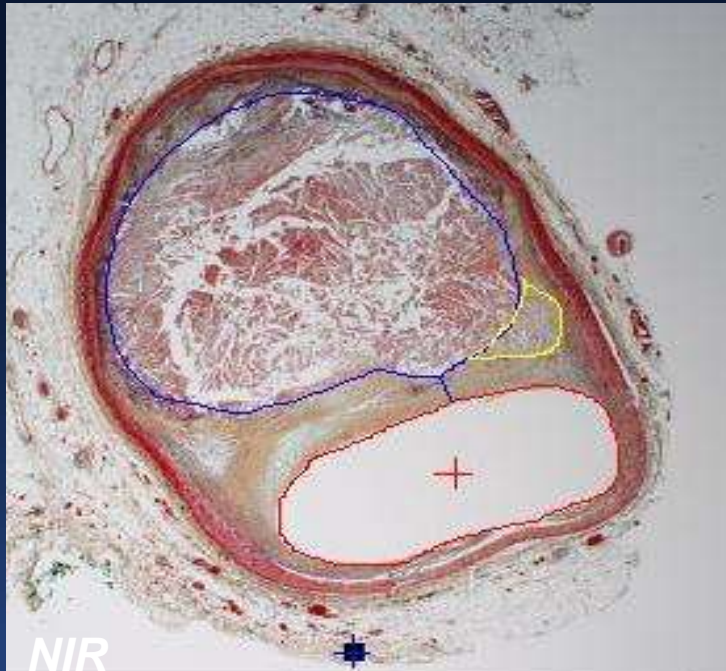
NIRS Can Differentiate Lesions with Large Plaque Burden

Large Plaque Burden + Large Lipid Core

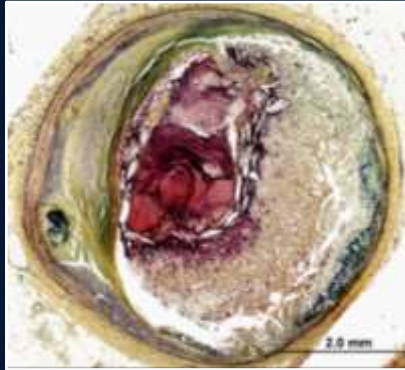
Large Plaque Burden + No Lipid Core

Large Plaque Burden +
Large Lipid Core

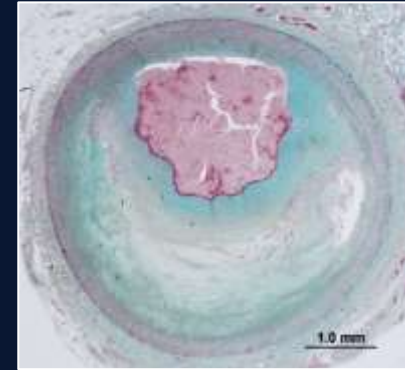
Large Plaque Burden +
No Lipid Core



Rupture



Erosion



Disruption of fibrous cap

Deficiency of endothelium

Smooth muscle cell apoptosis

Endothelial cell apoptosis

Thin fibrous cap

Proteoglycan rich thick cap

Lipid rich

Lipid poor

Abundant inflammation

Few inflammation

STEMI presentation (70%)

NSTEMI presentation (60%)

Male dominant

Female dominant

High LDL

High triglycerides

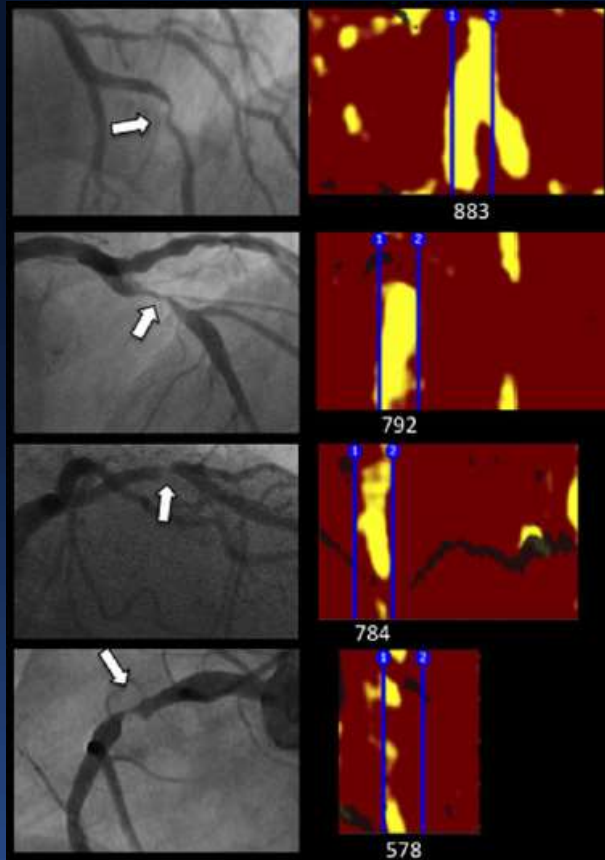
Clinical Parameters to Predict maxLCBI_{4mm}

- COLOR registry, 990 culprit lesions in 990 pts
- 64±11 yo, 77% men, 37% DM, 13% STEMI/NSTEMI, 75% on statin

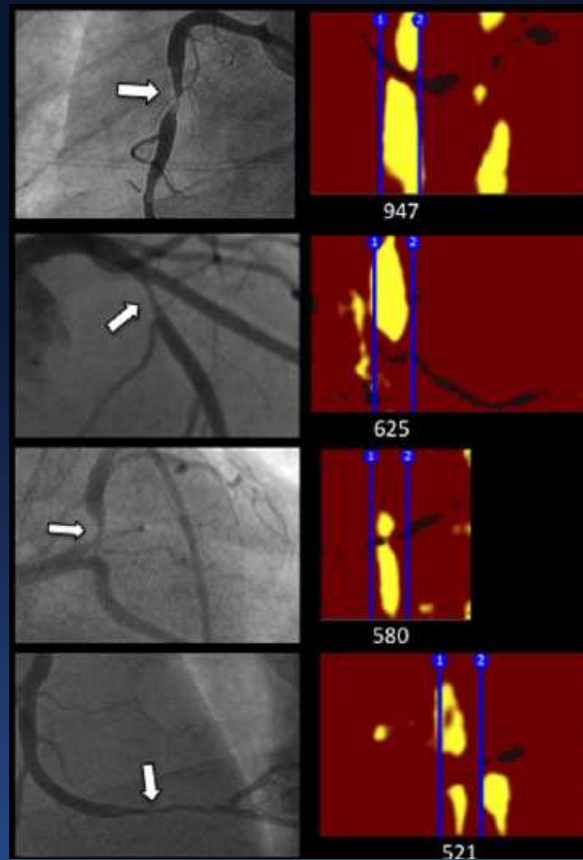
Covariates	Adjusted regression coefficient (95% confidence interval)	Adjusted p-value
Age, years	-0.2 (-2.1, 1.6)	0.82
Male	18 (-23, 59)	0.39
Body mass index, kg/m ²	0.77 (-2.4, 3.9)	0.64
Hypertension	0.9 (-54, 56)	0.97
Diabetes mellitus	10 (-27, 47)	0.59
Dyslipidemia	37 (-26, 101)	0.25
Current smoker	-12 (-52, 29)	0.57
Renal insufficiency	36 (-14, 85)	0.16
Peripheral vascular disease	-25 (-84, 33)	0.39
Prior PCI	-23 (-60, -14)	0.22
Prior CABG	-96 (-158, -34)	0.002
Prior MI	23 (-19, 66)	0.28
Clinical presentation of MI	84 (32, 136)	0.002
Statin use at admission	-48 (-92, -5)	0.03

Culprit/Non-culprit Lesion Characteristics

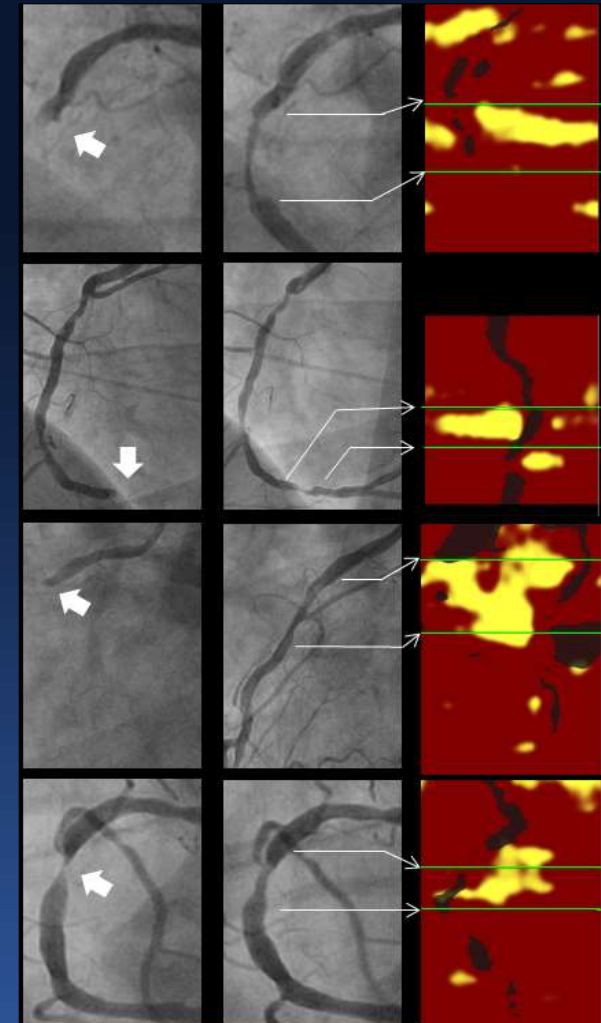
UAP



NSTEMI

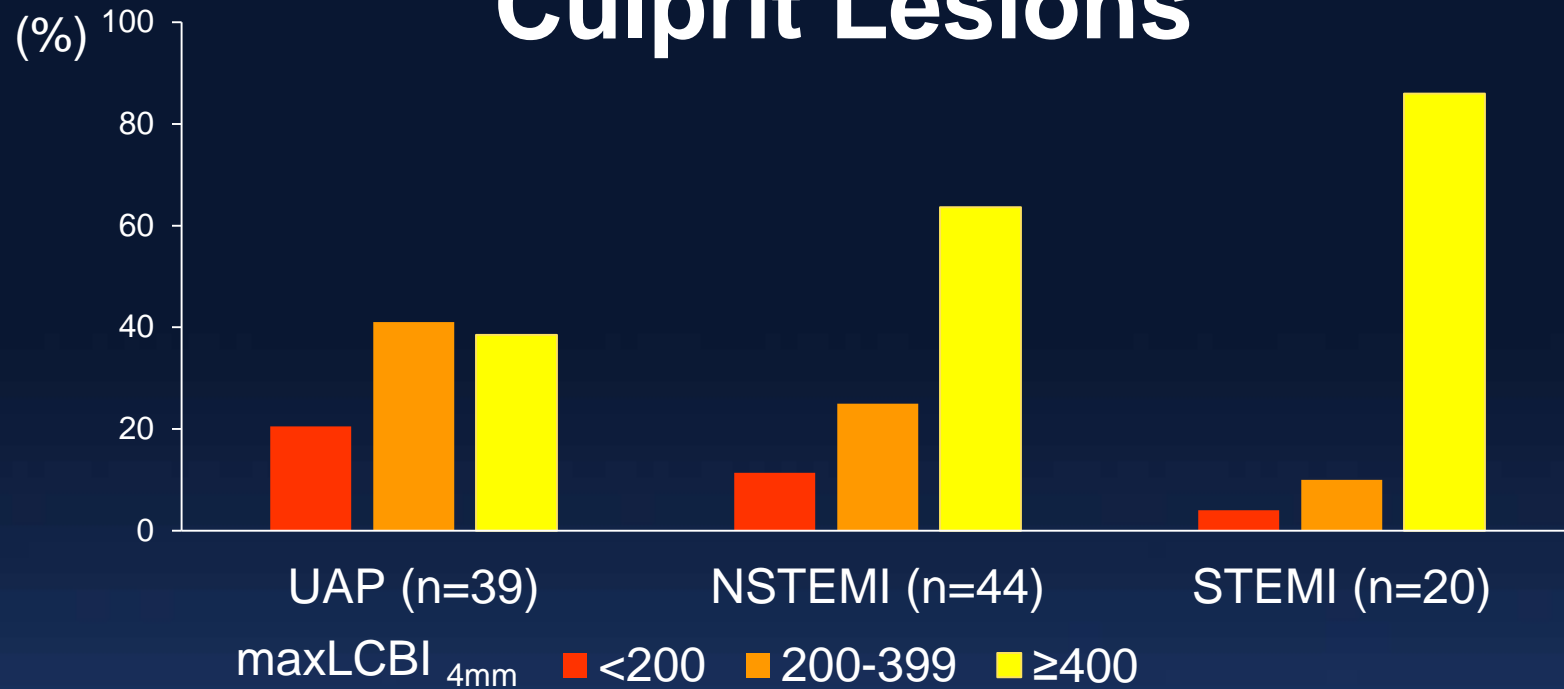


STEMI



Madder RD, Erlige, JACC Interv 2013, Cather Cardiovasc Interv 2015, Euro Atheroscl Soc 2013

Prevalence of Lipid Rich Plaque in Culprit Lesions



maxLCBI _{4mm}	UAP	NSTEMI	STEMI
Culprit lesion	381 ± 239	448 ± 229	523 (445, 821)
Non-culprit lesion	146 ± 175	132 ± 154	90 (6, 265)
Cut off of Culprit lesion	208	317	400
AUC for cut off	0.87 (0.80-0.94)	0.79 (0.70-0.87)	0.90

Madder RD, Erlige, JACC Interv 2013, Cather Cardiovasc Interv 2015, Euro Atheroscl Soc 2013

Relationship between the extent of lipid-rich plaque and clinical presentation in COLOR registry (n=800)

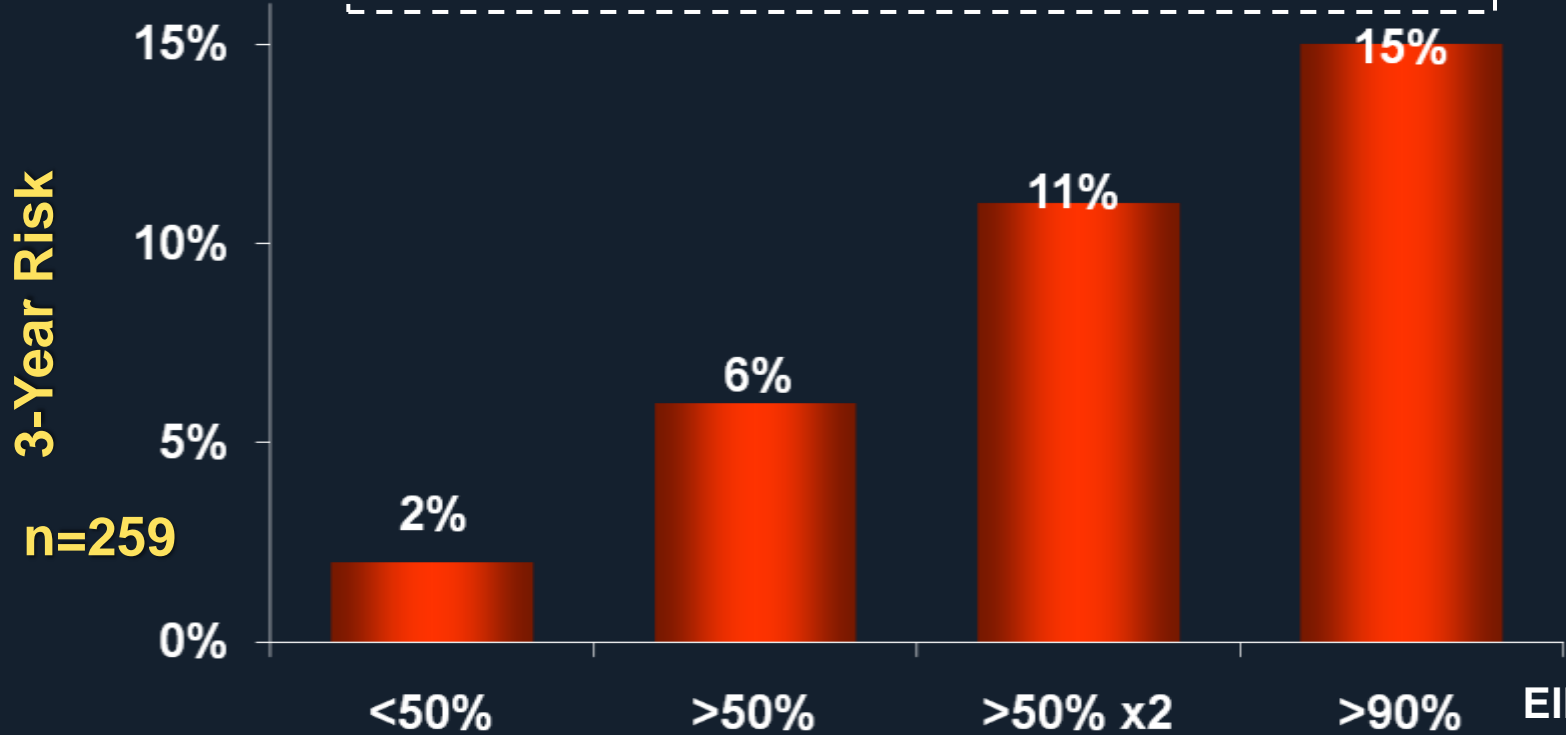
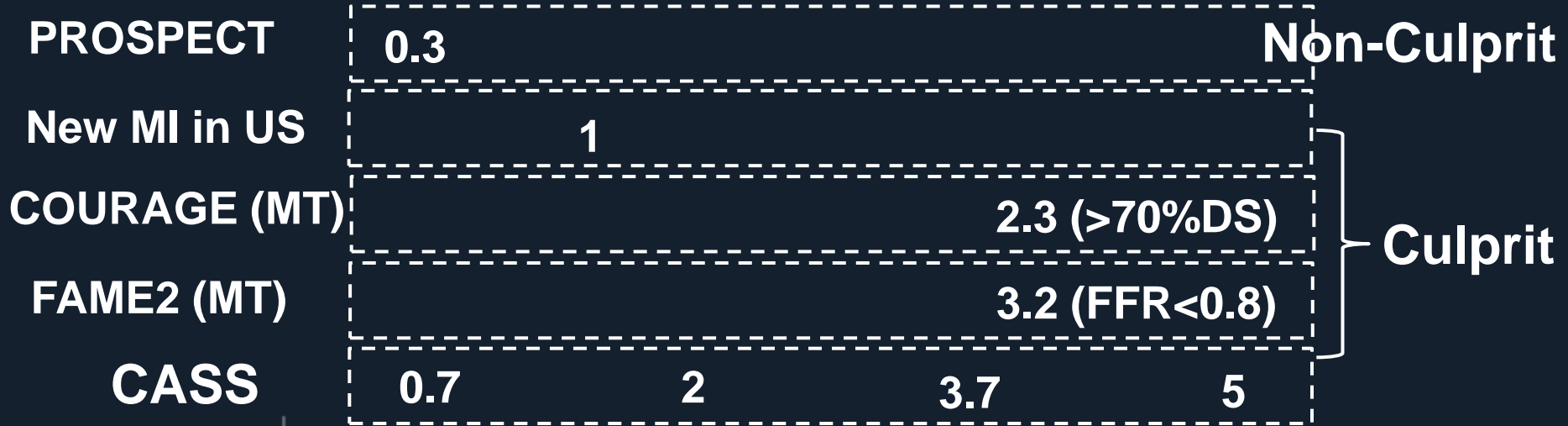
	MI (N=130)	Unstable AP (N=339)	Stable CAD (N=331)	P-value
Age, years	60 (54, 67)	65 (58, 73)	65(59, 71)	< 0.001
Male	78.9%	73.9%	82.2%	0.046
Hypertension	81.5%	91.0%	91.6%	0.01
Diabetes	30.6%	37.0%	39.3%	0.28
Dyslipidemia	80.2%	92.9%	94.3%	< 0.001
Prior PCI	33.9%	55.0%	43.0%	< 0.001
Lesion length, mm	24 (18, 30)	24 (18, 31)	24 (18, 34)	0.66
Plaque burden at MLA site, %	78.9 (72.5, 84.2)	75.4 (68.7, 82.0)	75.3 (67.0, 81.8)	0.18
LRP burden at MLA, %	35.0 (14.7, 49.1)	18.1 (0.0, 38.5)	26.0 (0.0, 47.9)	0.06
LCBI in lesion	141 (65, 247)	93 (29, 171)	98 (41, 185)	< 0.001
MaxLCBI _{4mm}	392 (205, 661)	288 (96, 478)	305 (138, 495)	0.001

Angiographic Parameters to Predict maxLCBI_{4mm}

- COLOR registry, 1073 culprit lesions in 996 pts
- 64±11 yo, 77% men, 37% DM, 13% STEMI/NSTEMI, 75% on statin

	Regression coefficient (95%CI)	Adjusted p value
Reference vessel diameter, mm	-24.7 (-48.2, -1.2)	0.04
Lesion length, mm	2.3 (1.0, 3.6)	0.0003
Diameter stenosis, %	2.8 (1.8, 3.8)	<0.0001
Eccentric lesion	15.0 (-13.9, 43.8)	0.31
True bifurcation	38.5 (-6.4, 83.4)	0.09
Ostial lesion	-41.6 (-112.3, 29.2)	0.25
Moderate calcification	4.0 (-45.4, 53.3)	0.88
Severe calcification	-62.9 (-108.9, -16.9)	0.007

Difference of the Incidence of MI/100 pts/year

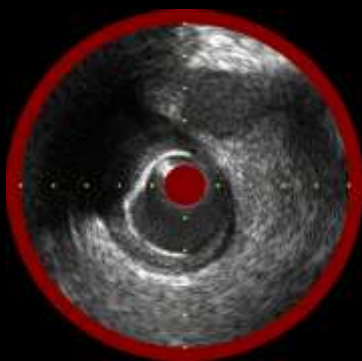


TCFA morphology with angiographic DS>30% by OCT/IVUS

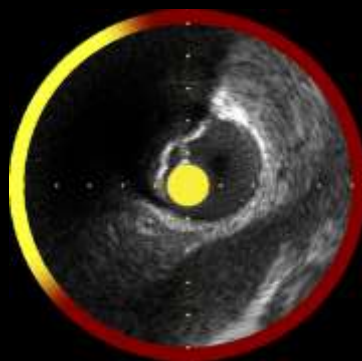
Angio DS	30-49%	50-69%	>70%
OCT			
Prevalence of TCFA	18% (58/325)	18% (40/227)	36% (33/91)
Fibrous cap thickness (µm)	57.0±6.6	56.0±7.5	49.0±9.2
Lipid arc (°)	214±56	209±55	204±59
Lipid length (mm)	9.4±4.6	10.5±5.5	9.6±4.5
IVUS			
Lumen area (mm ²)	5.8±2.4	4.5±2.1	3.2±2.3
Plaque burden (%)	58.1±8.4	67.5±9.4	80.1±7.4
Remodeling index	0.98±0.10	1.02±0.13	1.09±0.13

NIRS/IVUS Plaque Classification

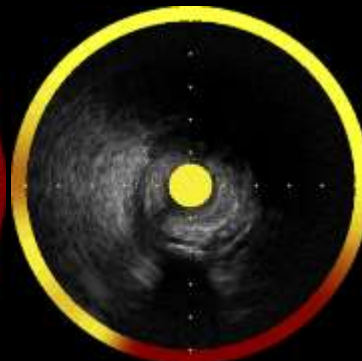
Calcified
Non-LRP



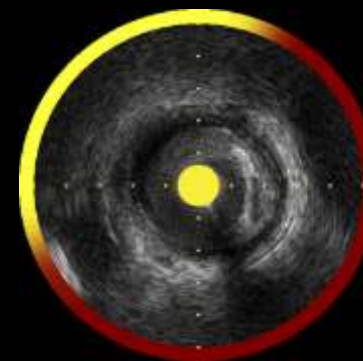
Calcified LRP



LRP with
Superficial
Attenuation



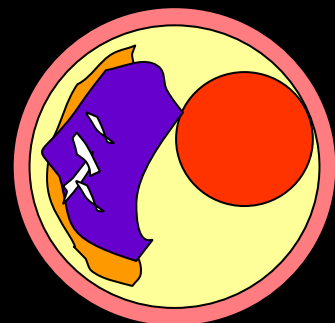
LRP without
Superficial
Attenuation



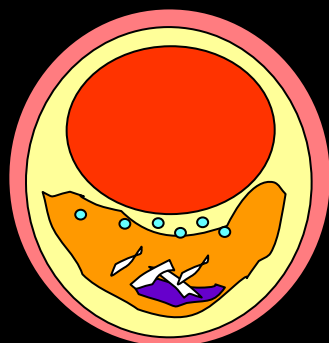
Non-LRP



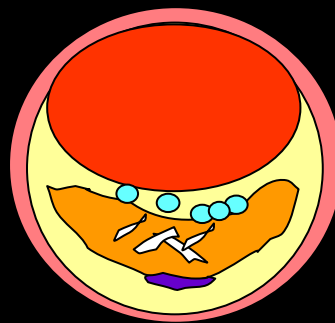
Fibrocalcific



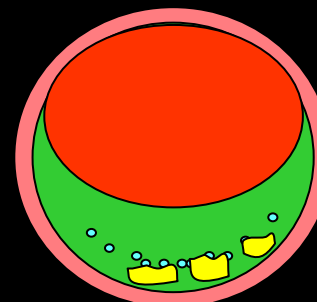
ThCFA



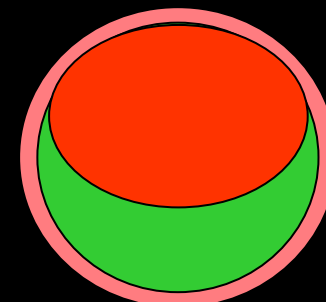
TCFA



PIT



Fibrotic



NIRS morphology stratified by angiographic diameter stenosis

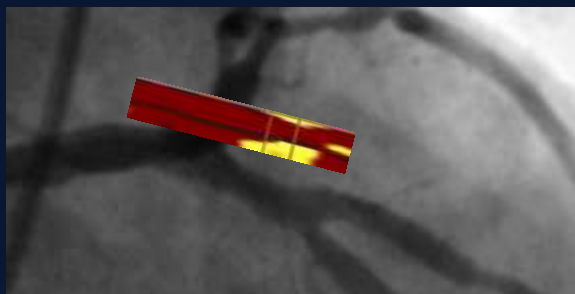
- COLOR registry, 647 *de novo* culprit lesions in 617 pts

	Lowest Tertile	Middle Tertile	Highest Tertile
Angio diameter stenosis (%)	40 (35, 45)	55 (52, 59)	73 (66, 81)
Max LCBI_{4mm}	278 (252, 304)	335 (307, 363)	421 (387, 454)
Plaque burden (%)	70 (68, 71)	75 (73, 76)	79 (78, 81)
Lipid rich plaque burden (%)	29 (25, 33)	34 (31, 37)	43 (40, 46)
LRP with superficial attenuated plaque	12.6%	17.1%	29.6%
LRP without superficial attenuated plaque	4.2%	6.5%	7.4%
Calcified LRP	23.3%	21.3%	13.4%

LRP is defined as $\text{maxLCBI}_{4\text{mm}} \geq 400$

Ishida M, et al. ACC2018

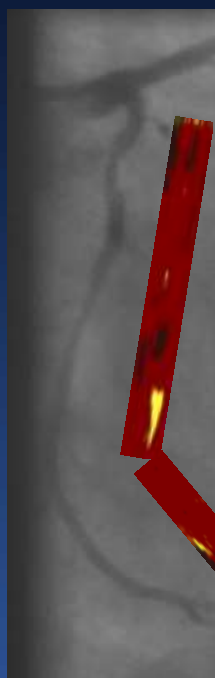
NIRS Cases with Rapid Lesion Progression and MACE, with a Pre- or Post-event Chemogram



↓ c/o D. Erlinge



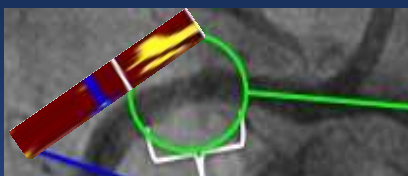
c/o D. Rizik



c/o K. Petersen



c/o J. Goldstein and S. Dixon



↓ c/o R. Madder

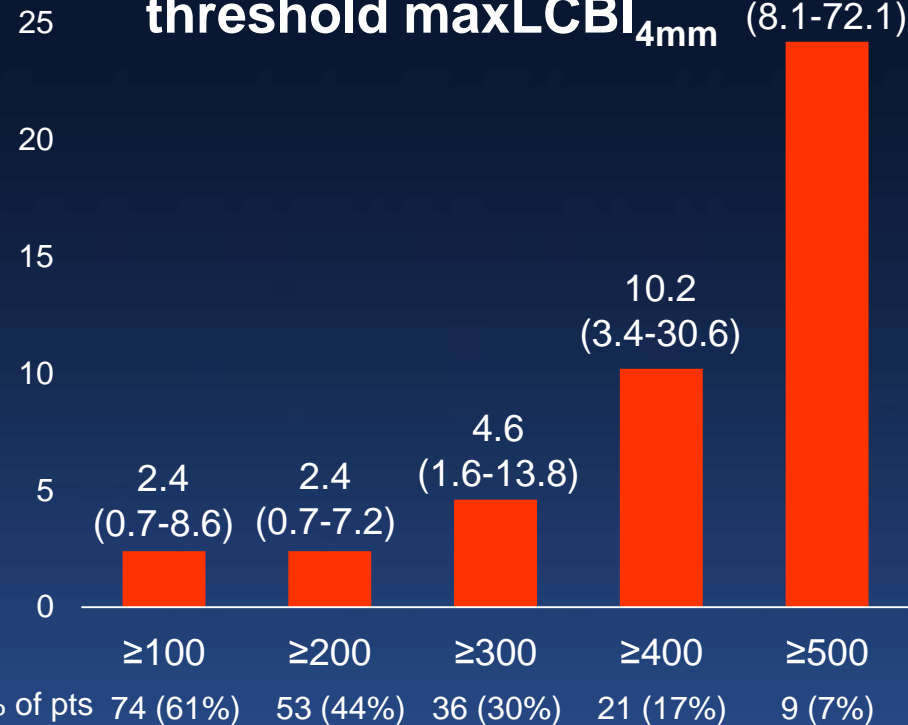
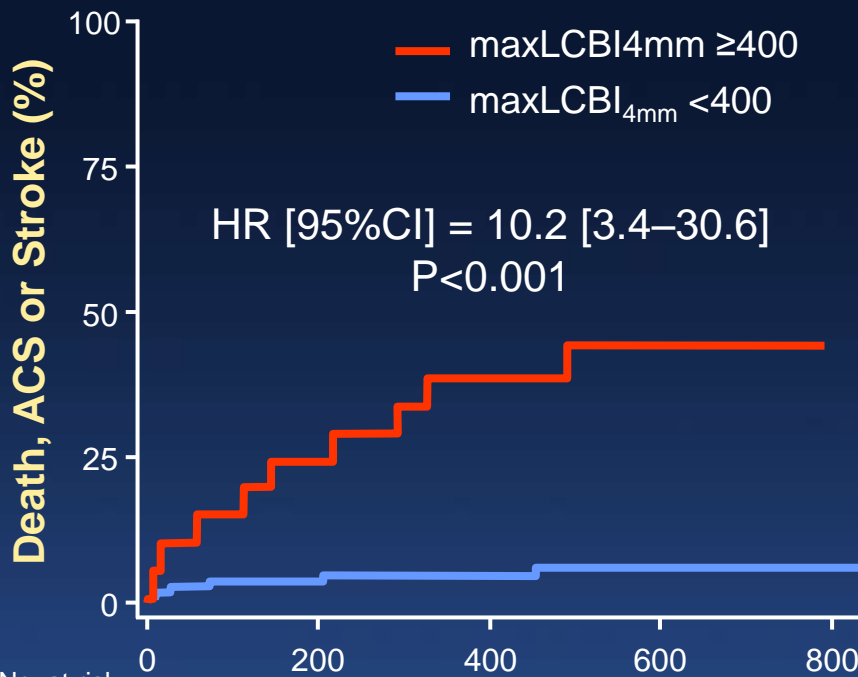


c/o G. Stone

Relationship between Lipid Rich Plaque detected by NIRS and Outcomes

- Non-target segment in culprit vessel in 121 patients, >1 year follow-up
- 14 MACCE: 5 all-cause mortality, 8 non-fatal ACS, 1 acute cerebrovascular events

Hazard ratios for various threshold maxLCBI_{4mm}

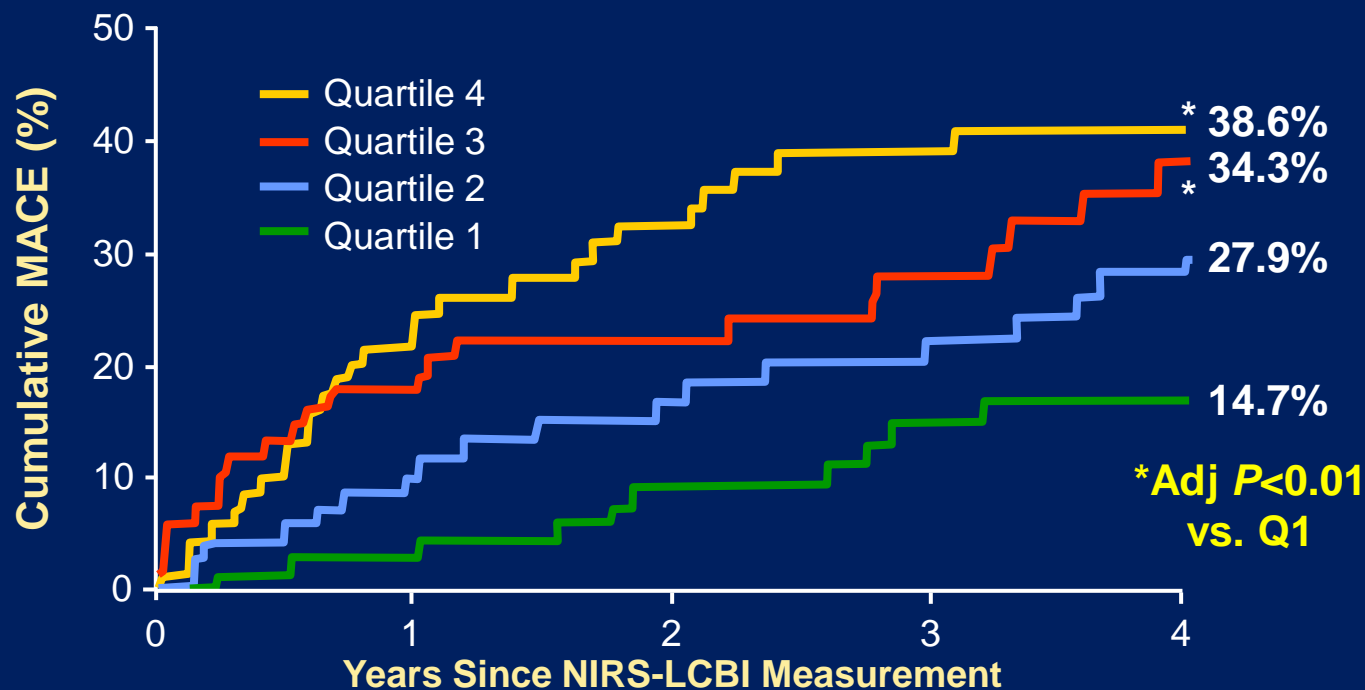


No. at risk:	0	200	400	600	800
maxLCBI _{4mm} ≥400	21	16	12	5	0
maxLCBI _{4mm} <400	100	97	87	47	13

Neither plaque burden ≥70% by IVUS (HR 1.30 [0.41-4.16], P=0.65) nor MLA ≤4.0 mm² (HR 0.80 [0.28-2.38], P=0.69) was significantly associated with MACCE

Predictive Value of NIRS: ATHEROMO-NIRS (n=203) and and IBS 3 (n=131)

- Total 286 patients, 43% ACS at Index, median FU=4.2 yrs
- Primary endpoint: All cause death, non-fatal ACS, or unplanned revascularization
- Image in non-culprit segment, median imaged length= 56.4 mm



No. at risk:

MaxLCBI _{4mm} Quartile	0	1	2	3	4
Q1 (<83.0)	68	66	52	43	29
Q2 (≥83.0-227.0)	68	61	47	40	31
Q3 (≥227.0-360.0)	67	55	42	35	22
Q4 (≥360.0)	70	53	41	30	25

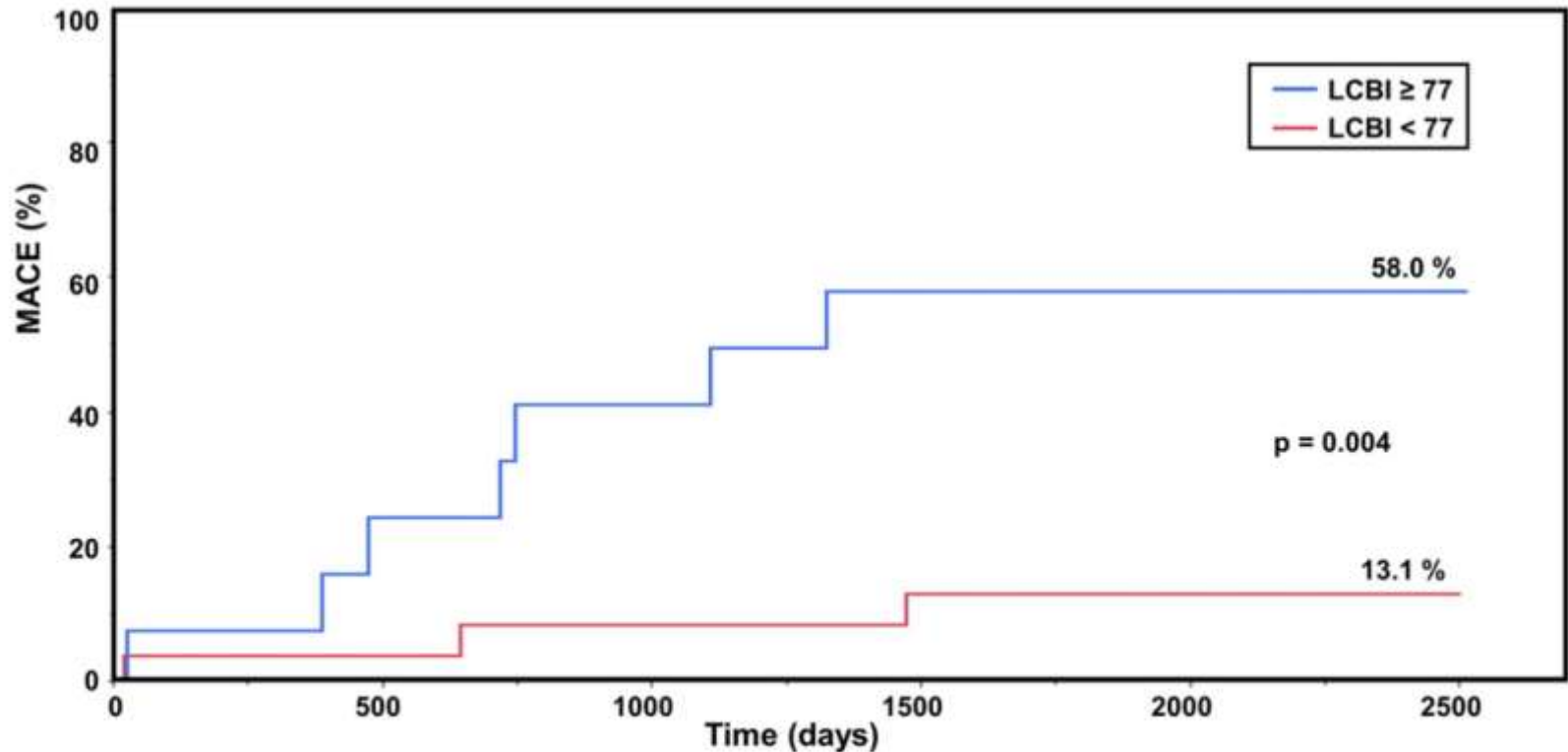
LCBI and Risk of Composite of Cardiac Death, Non-Fatal ACS, and Revascularization at 4 years

Tested Variable	Adjusted HR (95%CI)	P-value
All MACE		
MaxLCBI _{4mm}	1.21 (1.08, 1.35)	0.001
MaxLCBI _{10mm}	1.20 (1.05, 1.37)	0.007
Lesion LCBI	1.29 (0.98, 1.70)	0.06
MACE without TLR events		
MaxLCBI _{4mm}	1.24 (1.10, 1.39)	<0.001
MaxLCBI _{10mm}	1.25 (1.09, 1.44)	0.002
Lesion LCBI	1.38 (1.04, 1.83)	0.03

Adjusted for: Age, sex, ACS vs. stable CAD, diabetes, history of stroke, history of PVD, and IVUS-derived segmental plaque burden

ORACLE-NIRS Registry

- Total 239 patients, 39% ACS at Index, median FU=5.3 (1.8, 6.4) yrs
- Primary endpoint: Cardiac death, ACS, unplanned revascularization, or stroke
- Image in pre/post target vessel and non-target vessel



Number at risk

LCBI ≥ 77	13	9	8	6	5	1
LCBI < 77	26	23	21	20	17	1

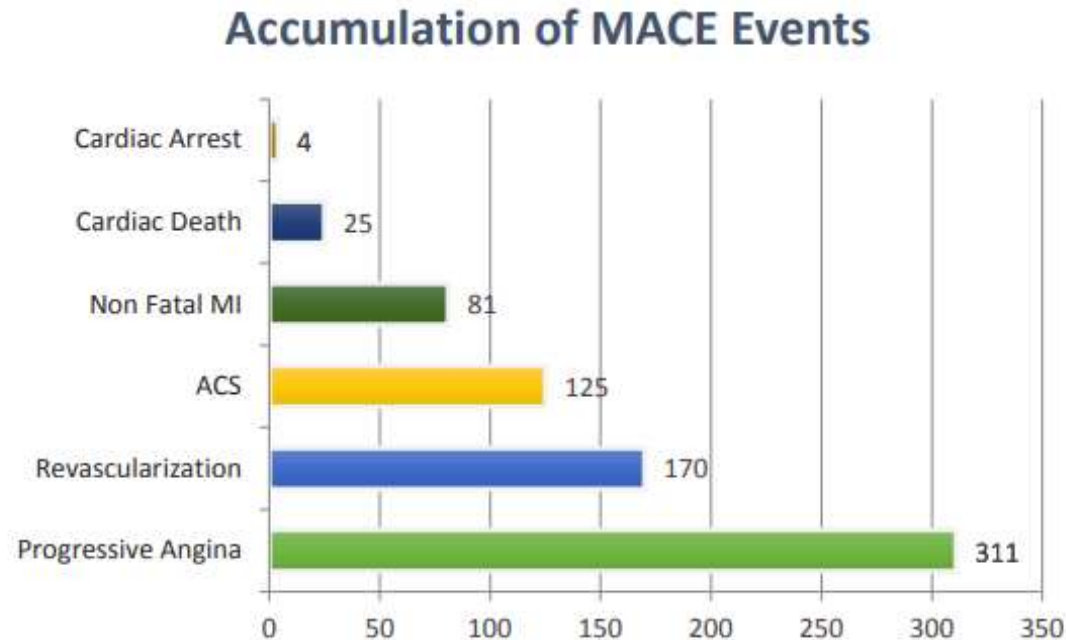
LCBI and Risk of Composite of Cardiac Death, ACS, Revascularization, and Stroke

Tested Variable	HR (95%CI)	P-value
Univariate Cox Model		
Pre-stent target vessel LCBI	1.00 (1.0, 1.0)	0.69
Post-stent target vessel LCBI	0.98 (0.99, 1.0)	0.47
Non-target vessel LCBI	1.01 (1.0, 1.02)	0.083
Multivariable Cox Model		
Non-target vessel LCBI	1.03 (1.01, 1.07)	0.007
DM	12.5 (2.0, 112.7)	0.006
Prior MI	11.6 (1.9, 103.0)	0.007
Index PCI	20.0 (2.5, 261)	0.004

Cut off of Non-target vessel LCBI=77, Adjusted HR for MACE=14.1 (2.5, 133.5), p=0.002, Adjusted HR for MACE without target vessel related events= 10.7 (1.7, 204.2), p=0.007.

LRP Study - 1562 patients with 2Y FU - Planned to report study results in Fall 2018

LRP Events Distribution



PROSPECT II Study PROSPECT ABSORB RCT

900 pts with ACS after su

3 vessel IVUS + N

≥1 IVUS lesion

ent?

**Enrollment closed in
Dec 2017 with 901 patients!
Follow-up is ongoing**

**GDMT
alone**

Routine an... IVUS-NIRS FU at 2 years

Clinical FU for 15+ years

Summary

- 1. Vulnerable plaque detection by NIRS focus lipid rich plaque (LRP).**
- 2. Clinical predictors of LRP are ACS presentation and statin usage.**
- 3. Angiographic predictors of LRP are diffuse disease and stenosis severity.**
- 4. Prior three small-modest studies (121-334) showed the association between LRP and future events.**
- 5. Large registry data will be available in 2018.**