# Clinical Trials by Using NIRS: Clinical Relevance and Prognostic Implication


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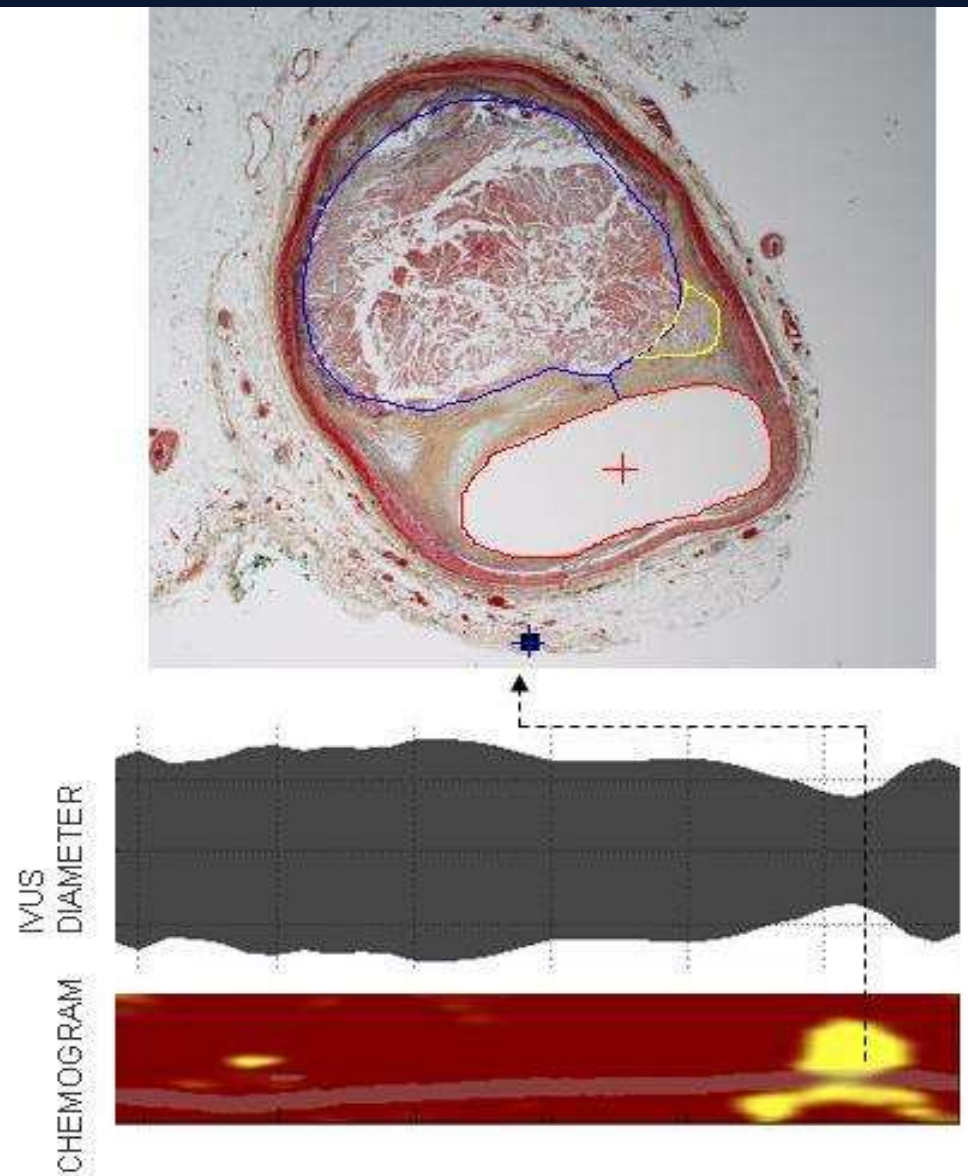
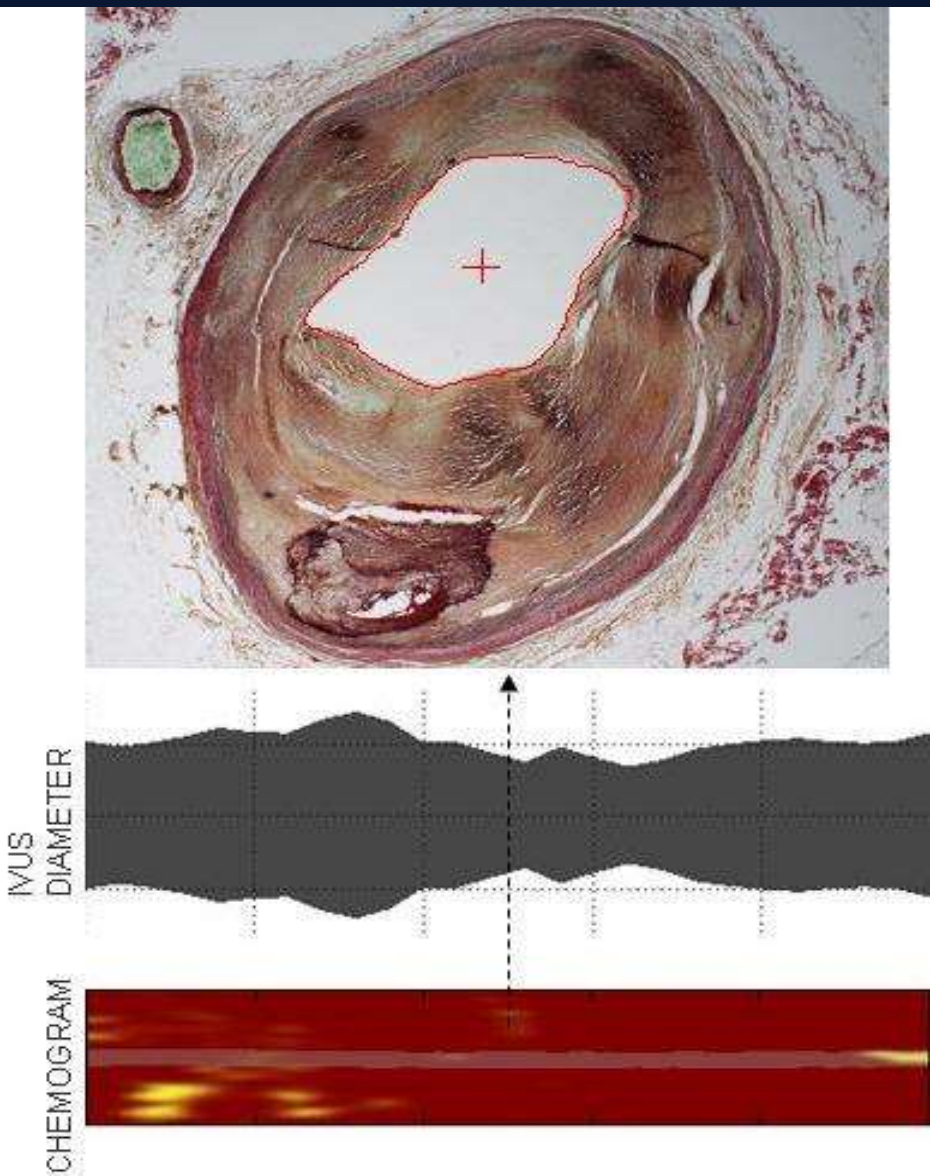
NewYork-Presbyterian

# Conflict of Interest Disclosure

- Akiko Maehara
  - Personal: Consultant for ACIST, Boston Scientific Corporation
  - Cardiovascular Research Foundation: Boston Scientific Corporation

# NIR can Distinguish Lipid-rich from Fibrotic Plaques



# COLOR Registry




infraredx
Sound Insight Into Vascular Disease

# Extent of lipid rich plaque by NIRS may predict DES restenosis

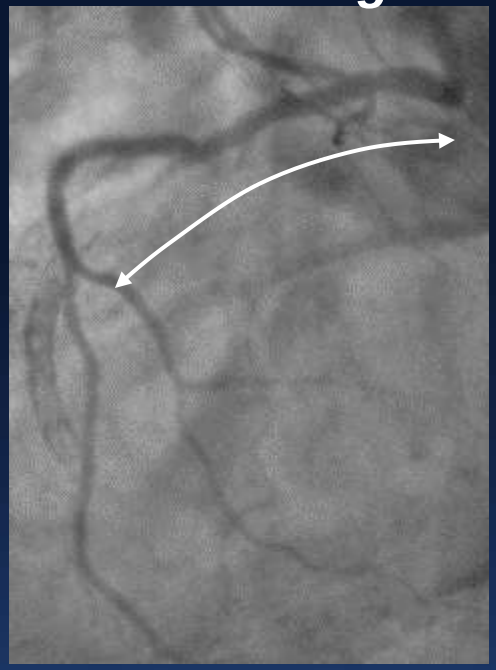
- From a total of 478 patients with complete data between February 2009 and November 2011, we identified 14 patients with stent failure.
- Of 14 patients with restenosis, ISR was found in 13 patients (9 focal, 3 diffuse, 1 total occlusion), and proximal edge restenosis was found in 1 patient.
- All implanted stents were DES, and the median follow-up time was 392 days (IQR: 300 to 418) after index PCI.
- Thirty case-matched controls were identified.

Dohi T. TCT 2013

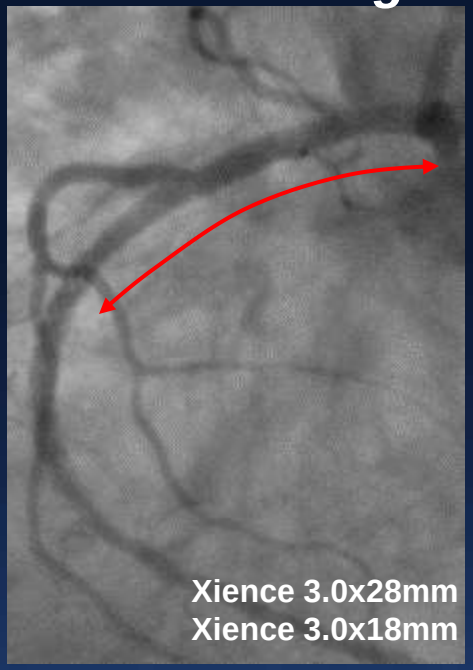
# Case 1- Restenosis in Mid RCA-

Index PCI

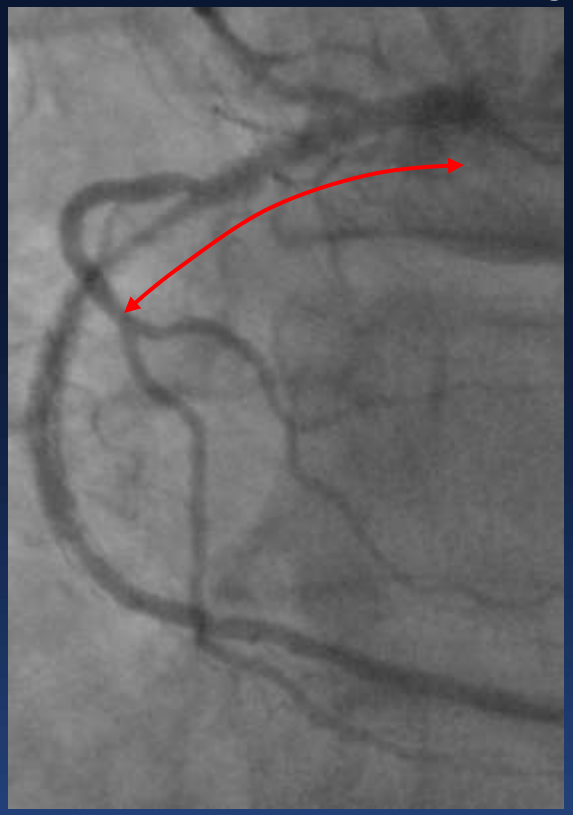
*Pre Stenting*



*Post Stenting*




*In-stent Restenosis after 1 year*



Stent segment

**Pre PCI NIRS findings**

LCBI in stent segment: **196**

MaxLCBI4mm in stent segment: **940**

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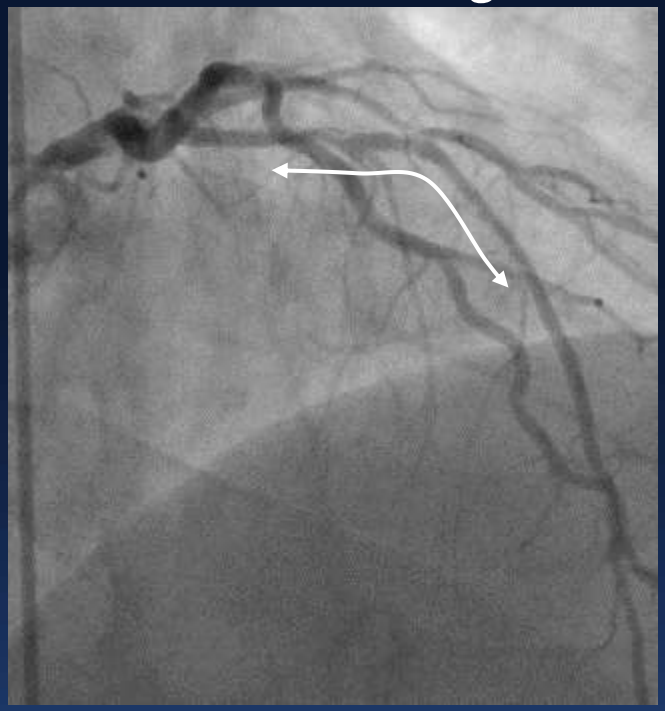
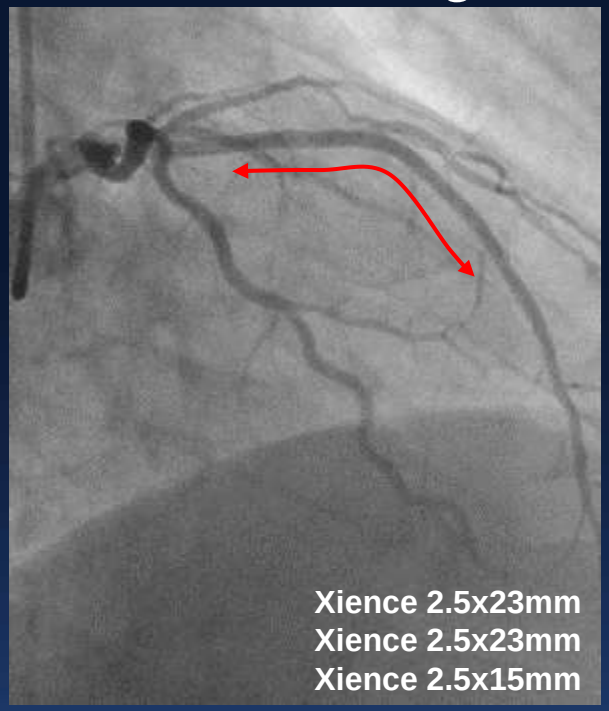
# Case 2 - Control case in Middle LAD-

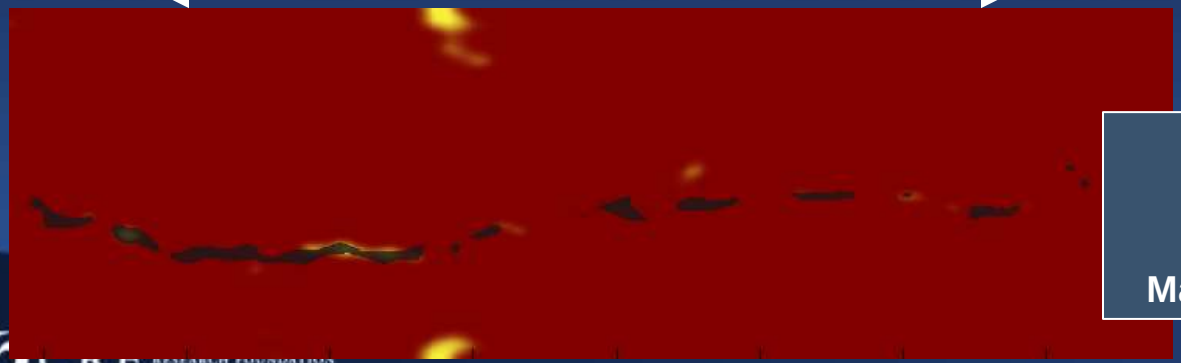
*Pre Stenting*



*Post Stenting*




Stent segment

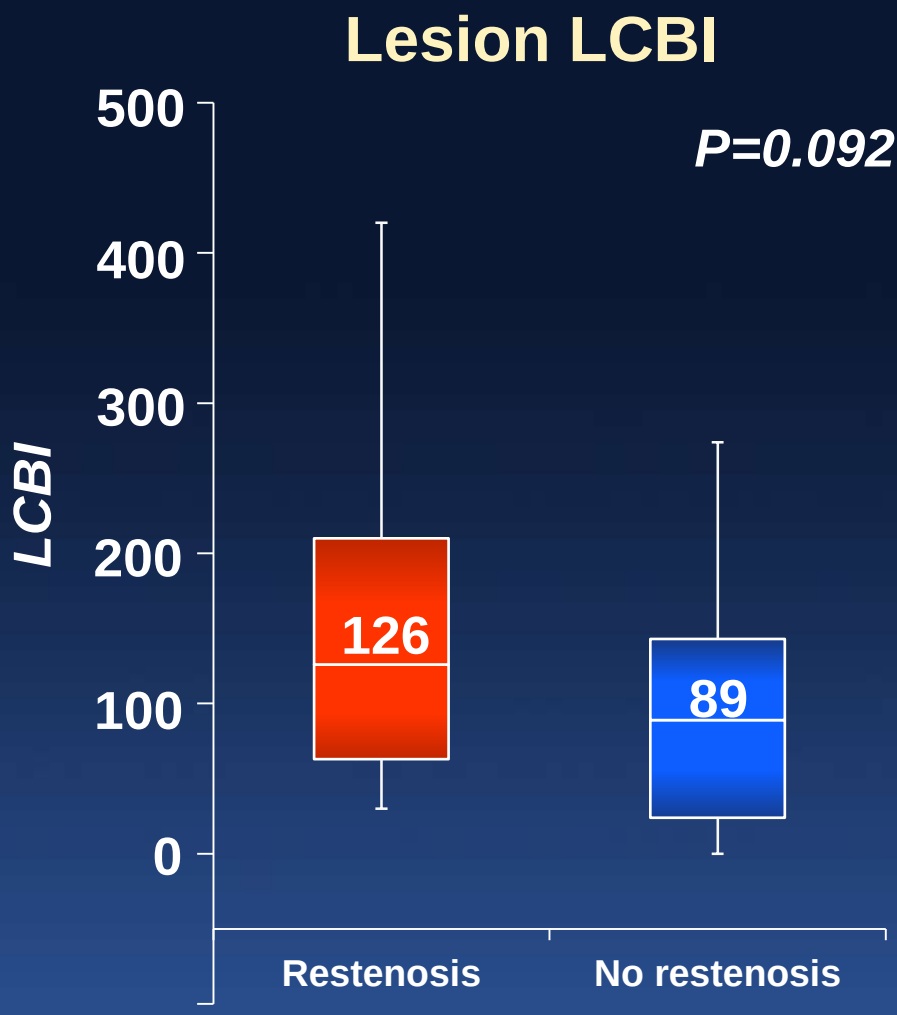


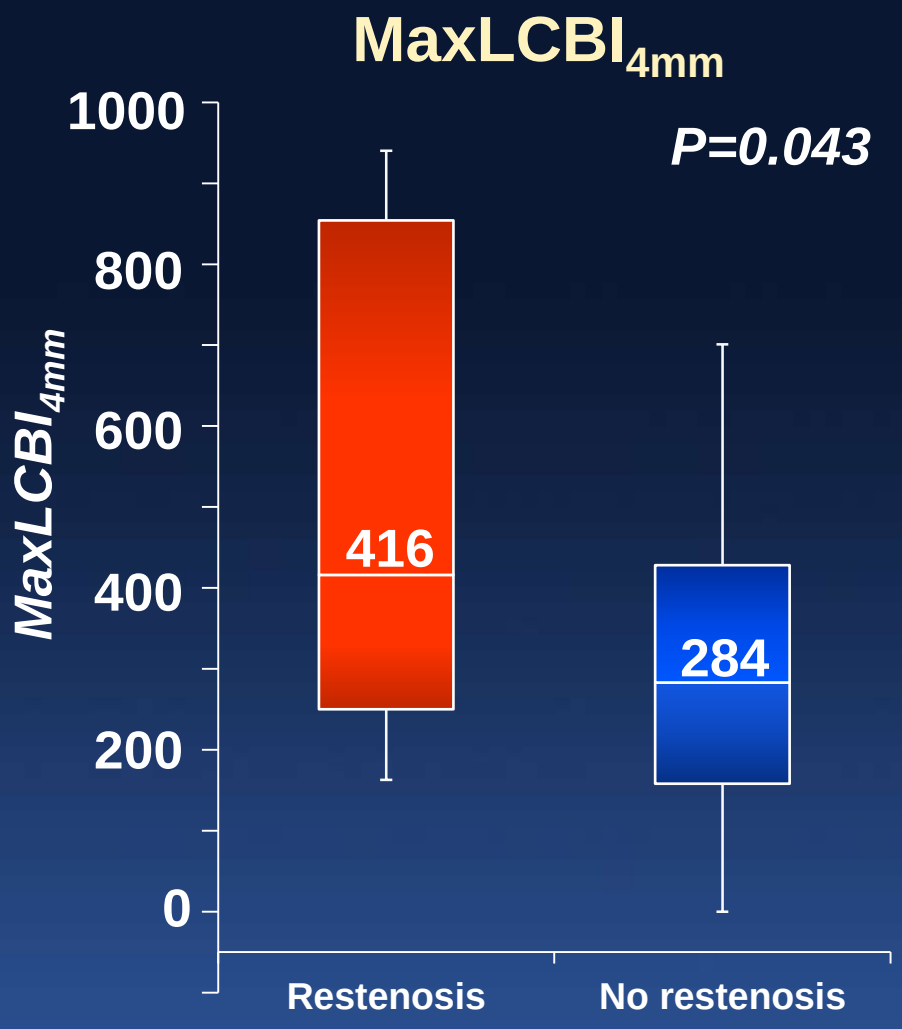
**Pre PCI NIRS findings**

LCBI in stent segment: **14**

MaxLCBI4mm in stent segment: **157**

# Comparison of LCBI and maxLCBI$_{4mm}$
## in the Stented Segment Grouped by Occurrence of Restenosis




# Two/Three Vessel CAD
# (n= 87)


**After stenting the target vessel**
**The non-target lesion underwent FFR**

**FFR≤0.8 ➔IVUS, NIRS**

**Randomized**

| **Standard** | **Aggressive** |
|---|---|
| n = 43 | n = 44 |
| Continue statin the patient was taking | Rosuvastatin 40 mg daily |
| Dual antiplatelet therapy for 1 year | Dual antiplatelet therapy for 1 year |

**Follow up Cath (6-8 weeks)**
**FFR, IVUS and NIRS repeated.**
**If FFR ≤0.8, lesion stented and imaging repeated.**
**If FFR > 0.8 the patient was treated medically.**

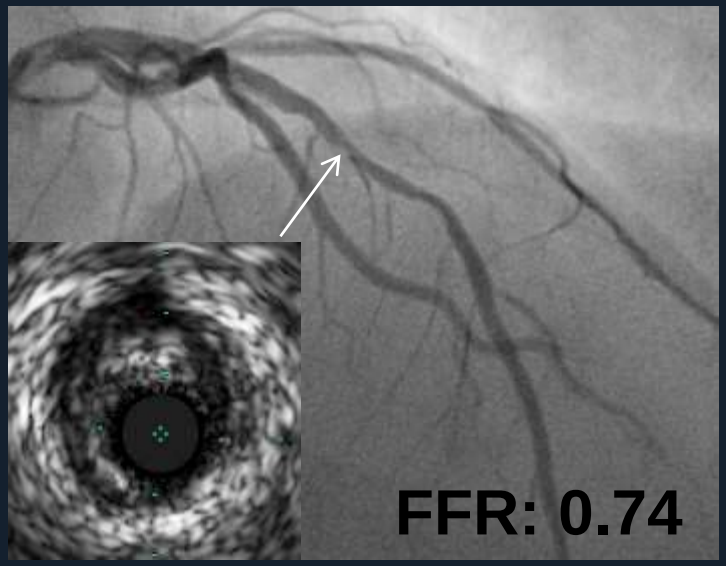
**Imaging data analyzed by CRF Core Lab**
**Data analysis for primary outcome analyzed by MSH independent Core Lab**

***Optimal medical therapy for all patients**

Kini A et al. *JACC* 2013; 62: 21-9.

# Case Example

## Baseline

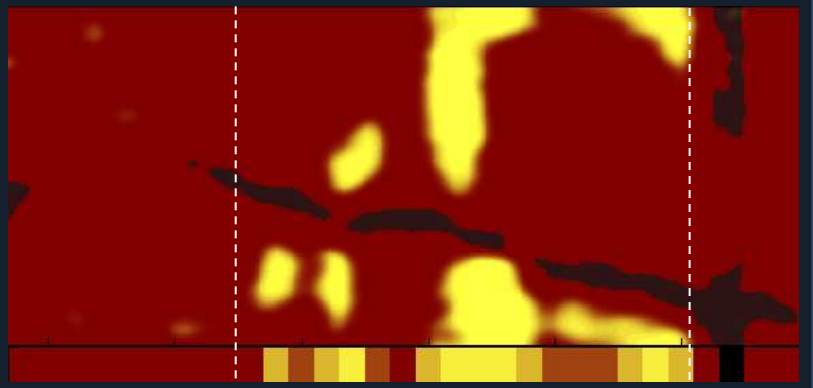



Plaque Area
5.6mm$^2$

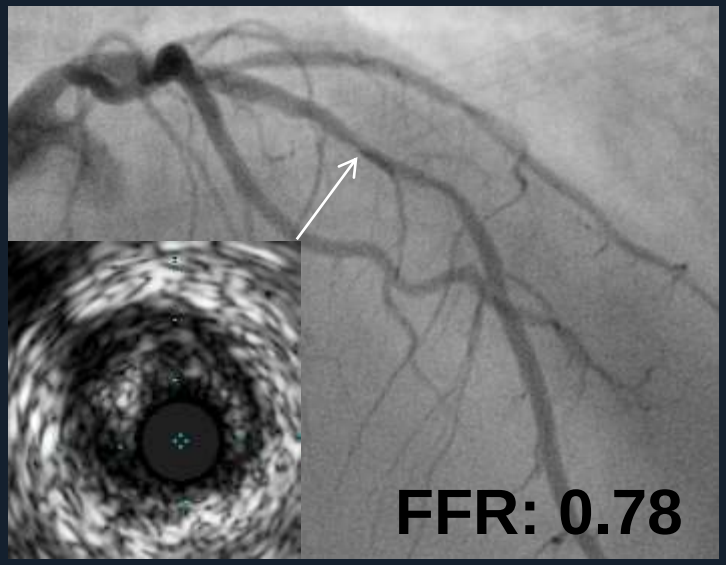
Lesion LCBI: 259

Max10mm LCBI: 511

Max4mm LCBI: 802



## Follow-up

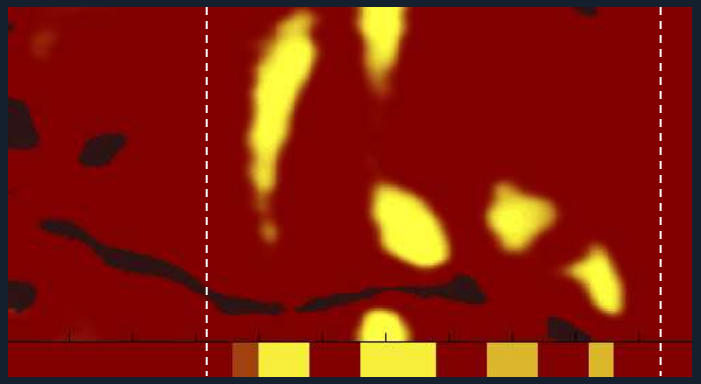



Plaque Area
5.5mm$^2$

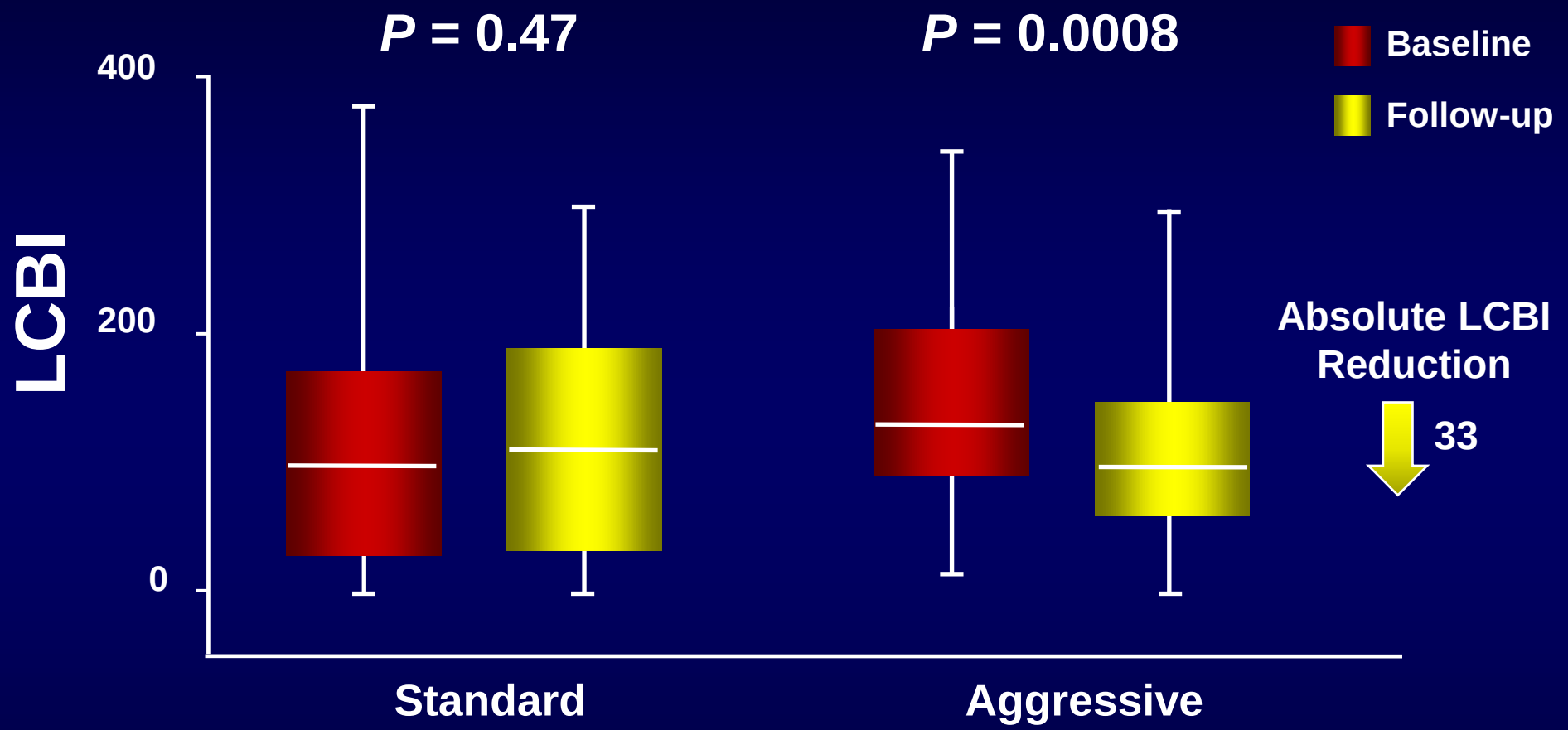
Lesion LCBI: 177

Max10mm LCBI: 289

Max4mm LCBI: 474



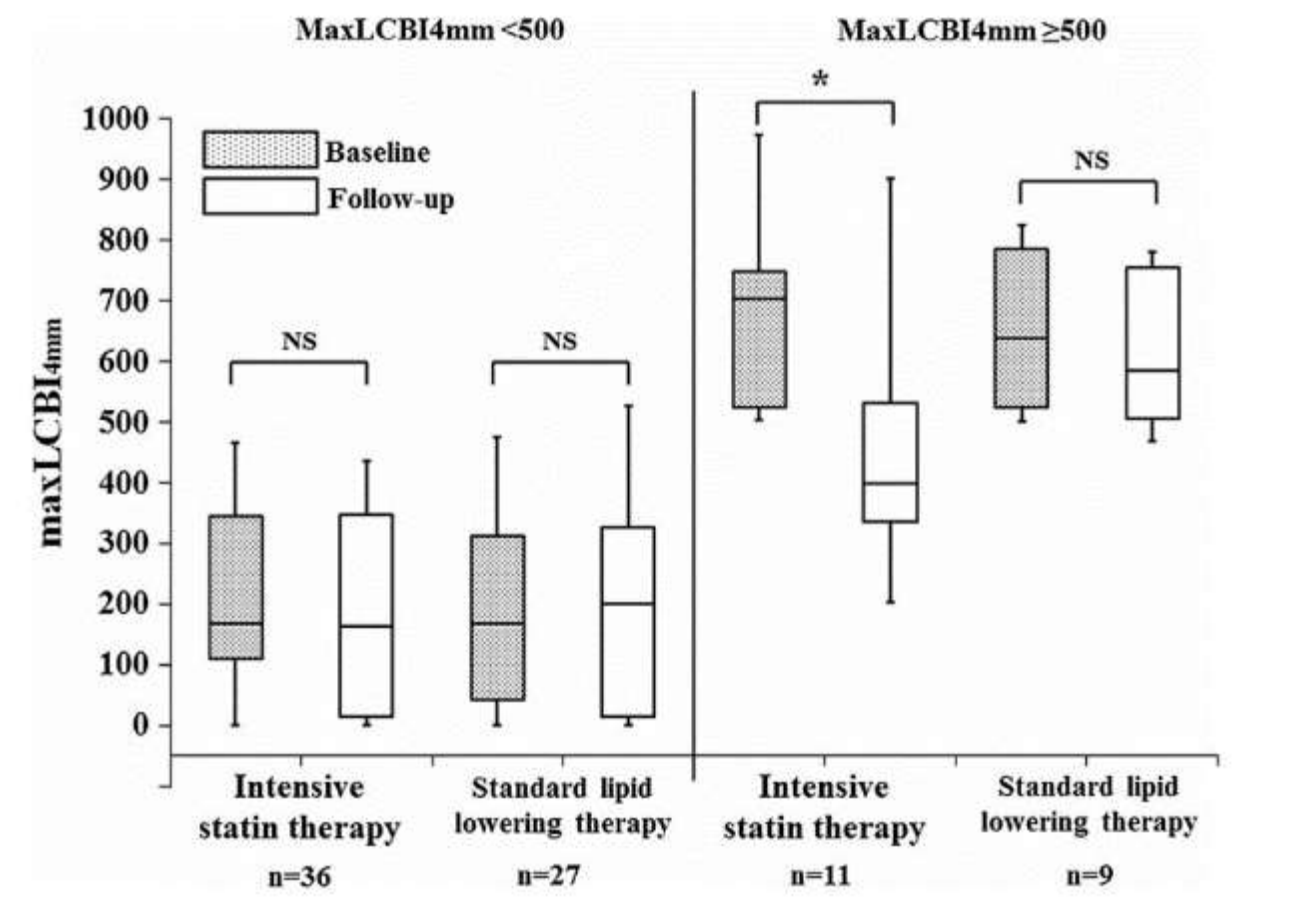
# Paired Analysis – Lesion LCBI




| Variable | Standard (n = 43) | Aggressive (n = 44) | *P* |
|---|---|---|---|
| Percent atheroma volume | 0.26% | 0.24% | 0.98 |

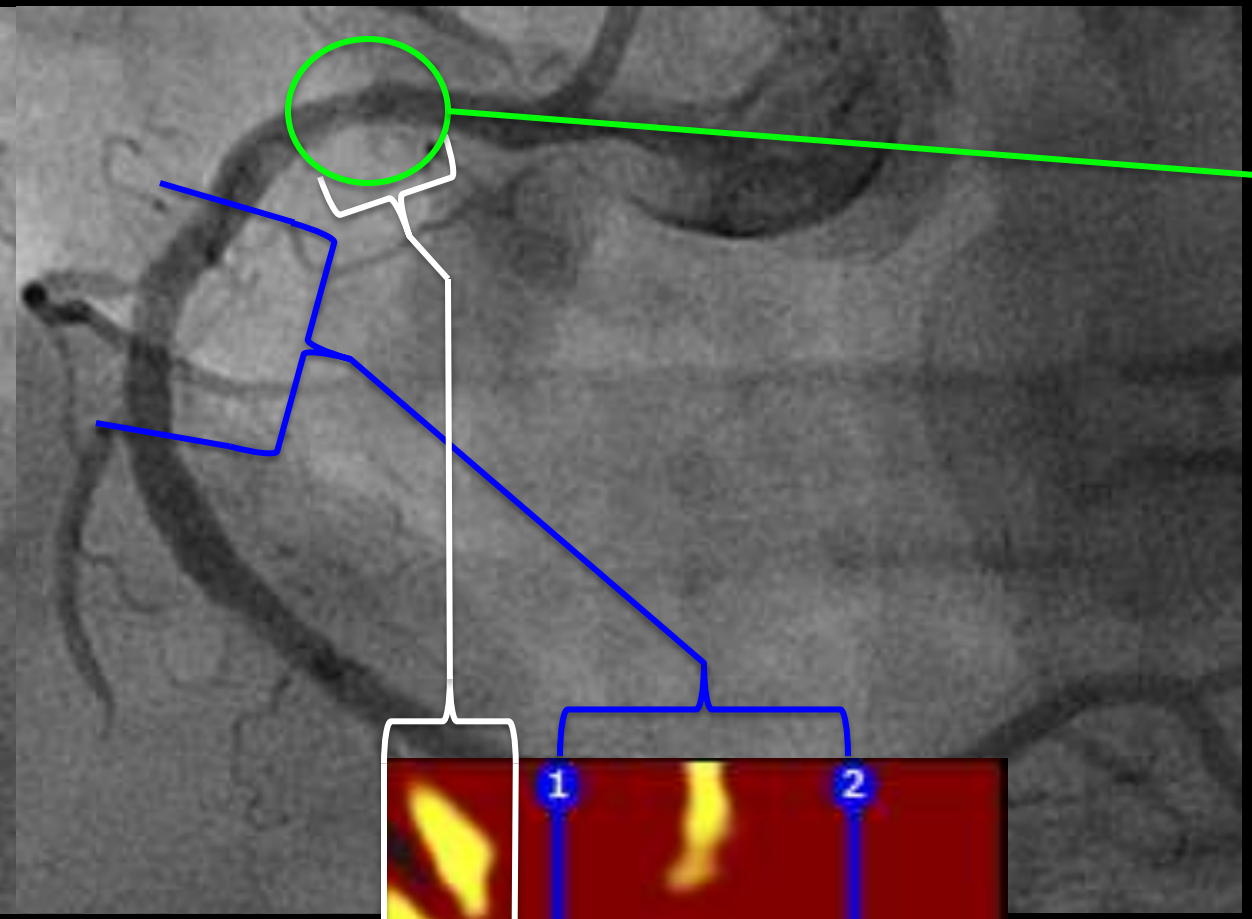
Kini A et al. *JACC* 2013; 62: 21-9.

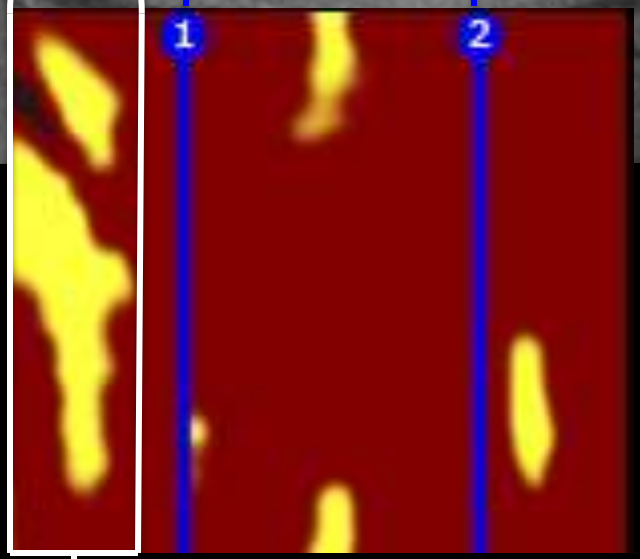
# Relationship between Lipid Regression and maxLCBI$_{4mm}$




Dohi T et al. *Eur Heart J Imaging* 2014

64 year old presents with STEMI in March 2012 → Unstable angina October 2012






$maxLCBI_{4mm}$
694

R. Madder, Spectrum Health



# Methods

## Spectrum NIRS-IVUS Registry

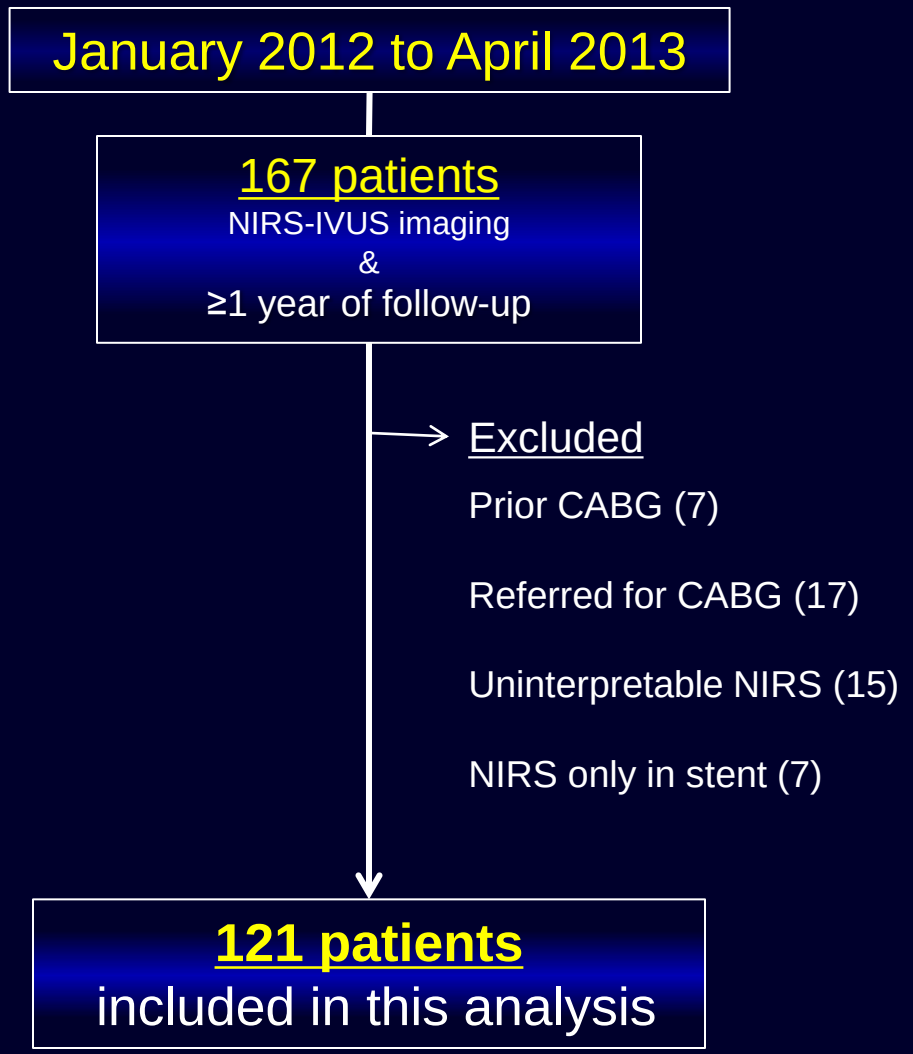
- Single center, observational
- Prospectively enrolled patients undergoing NIRS-IVUS

## Inclusion criteria

- Patients completing ≥1 year of follow-up

## Exclusion criteria

- Prior CABG/referred for CABG
- Uninterpretable NIRS
- NIRS imaging performed only within a stented segment



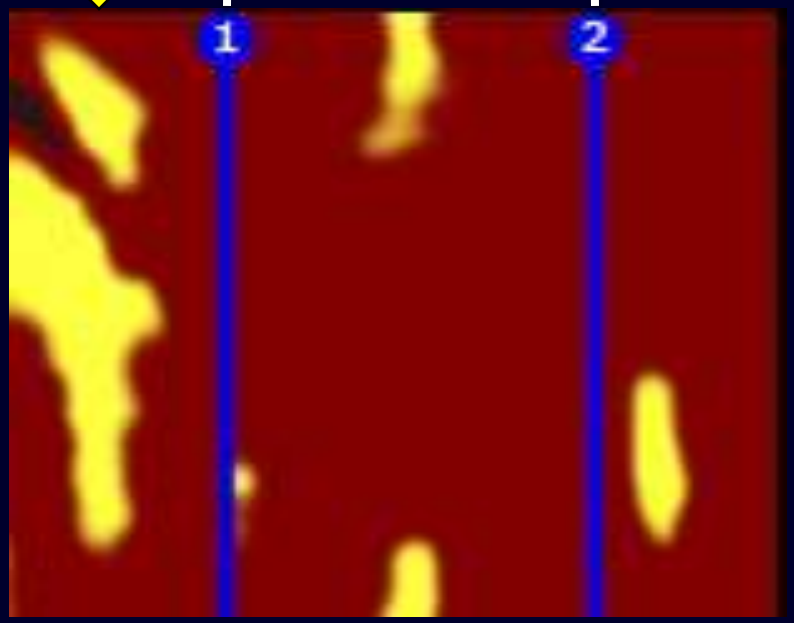


# Methods

- Evaluated non-stented coronary segments for large LRP
  - defined as a maxLCBI$_{4mm}$ ≥500
- Patients followed for MACCE
  - Composite of all-cause mortality, recurrent ACS requiring revascularization, or acute cerebrovascular events
- Events related to previously stented segments were excluded
- All events adjudicated blinded to the NIRS-IVUS imaging

Large LRP in non-stented segment

Stented segment excluded from analysis

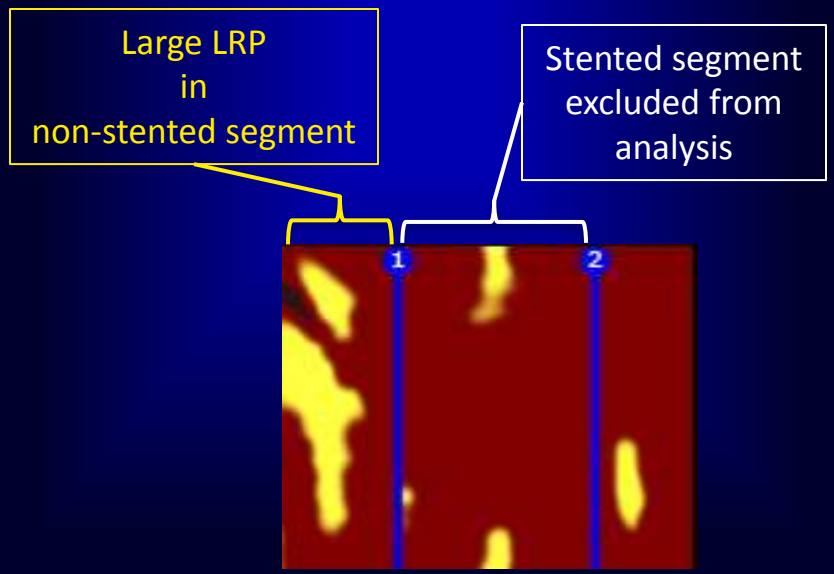




# Results

## Baseline NIRS Findings

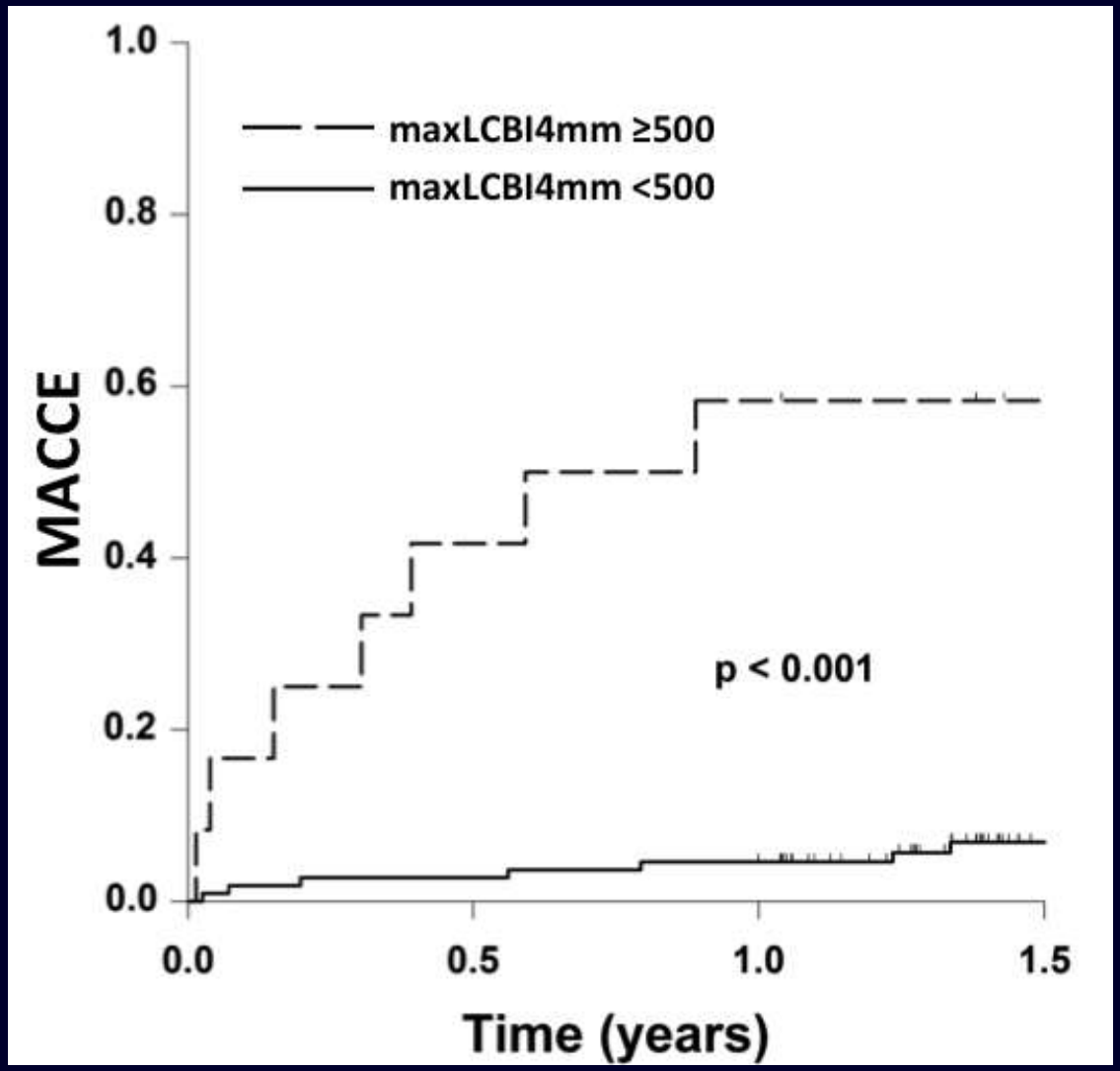
- 462 non-overlapping 10-mm coronary segments analyzed
- A large LRP was detected in 15 (3.2%) segments & in 12 (9.9%) patients




## Follow Up Events

- Average follow-up duration was 603 ± 145 days (1.7 years)
- MACCE (unrelated to previously stented segments) occurred in 11.6% of patients during follow up
  - ⇒ All-cause death 4.1%
  - ⇒ ACS requiring revascularization 6.6%
  - ⇒ CVA 0.8%

# Large LRP by NIRS and MACCE




**MACCE Rate**

Large LRP 58.3%

vs

No large LRP 6.4%

(p<0.001)

**ACS Requiring Revascularization**

Large LRP 25.0%

vs

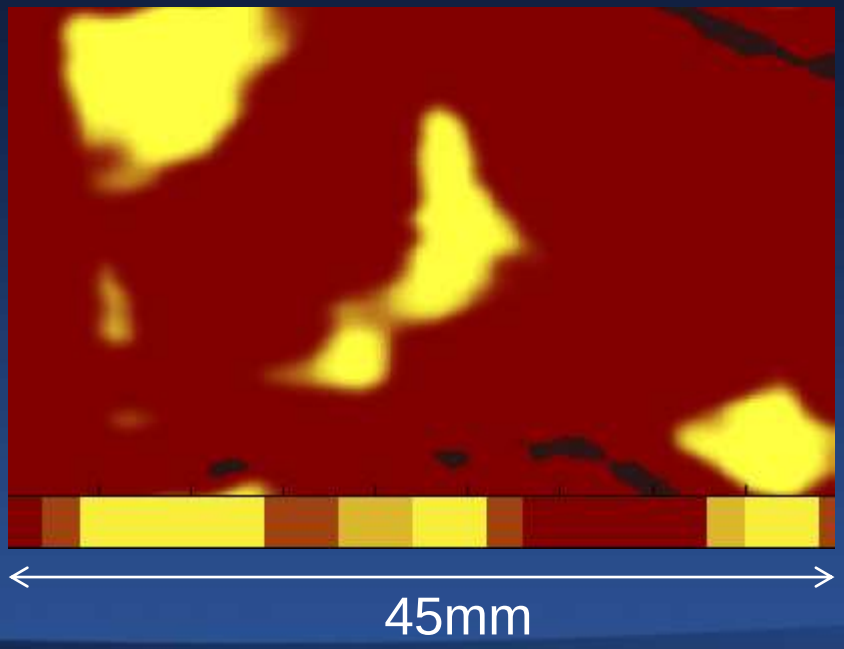
No large LRP 4.6%

(p<0.001)

# Relationship between Lipid Rich Plaque detected by NIRS and Outcomes

- Prospective Single Center Study, 206 patients (ACS47%)
- Primary Endpoint: Composite of all-cause mortality, non-fatal ACS, stroke and unplanned PCI during one-year FU
- >40mm non culprit segment of NIRS

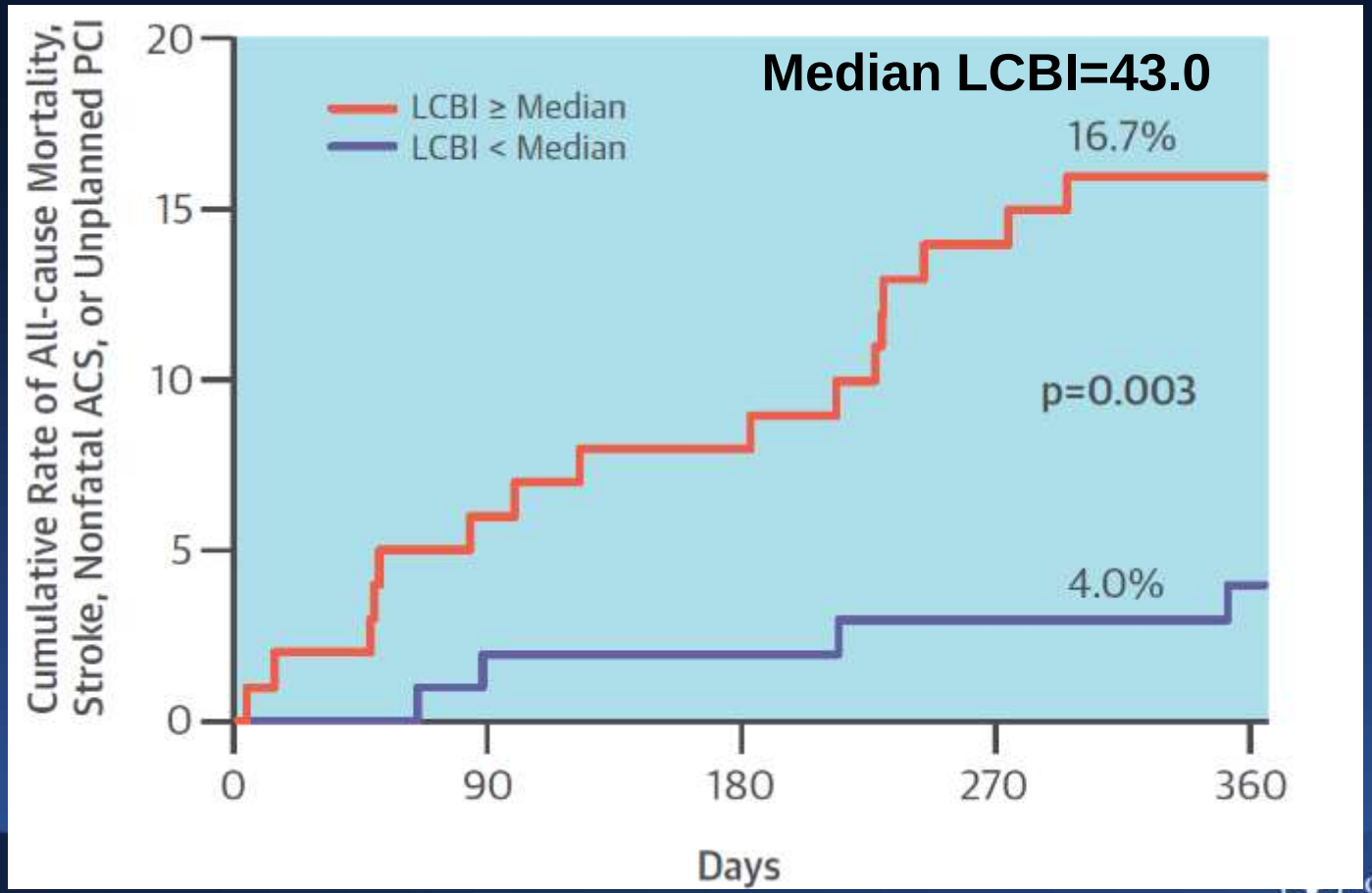
Lipid Core Burden Index (LCBI)=188




Oemrawsingh RM et al, *JACC 2015*

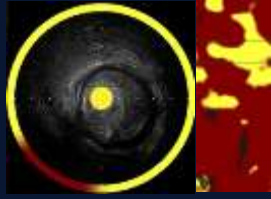
# Relationship between Lipidic Plaque detected by NIRS and Outcomes

Primary Endpoint: Adjusted Hazard Ratio = 4.0 (1.3-12.3), p=0.01




Oemrawsingh RM et al, *JACC 2015*

# PROSPECT II Study



## 900 pts with ACS at up to 20 hospitals in Sweden, Denmark and Norway (SCAAR)

NSTEMI or STEMI >12º

IVUS + NIRS (blinded) performed in culprit vessel(s)

Successful PCI of all intended lesions (by angio ±FFR/iFR)

↓

## Formally enrolled

↓

## 3-vessel imaging post PCI

Culprit artery, followed by non-culprit arteries

Angiography (QCA of entire coronary tree)

IVUS + NIRS (blinded) (prox 6-8 cm of each coronary artery)

↓

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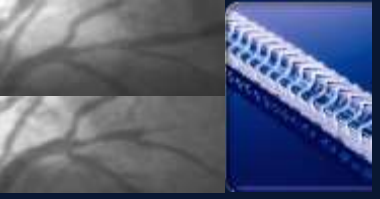
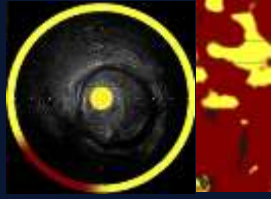


# PROSPECT II Study
# PROSPECT ABSORB RCT



## 900 pts with ACS after successful PCI

3 vessel IVUS + NIRS (blinded)

≥1 IVUS lesion with ≥65% plaque burden present?

**Yes** (N=300)

**No** (n=600)

R 1:1

**ABSORB BVS + GDMT** (N~150)

**GDMT** (N=150)

Routine angio/3V IVUS-NIRS FU at 2 years

Clinical FU for ≥3 years

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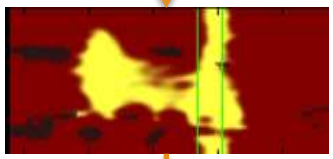
# PI: Dr.Ron Waksman

"To evaluate the relationship between non-obstructive lipid-rich plaque and a new coronary events"

Index
N=9000

Suspected Index Culprit Lesion -or- Index Culprit Lesion



BLINDED

Index Non Culprit Artery (IVUS is un-blinded)

Send to Core Lab

*Core Lab will Un-blind NIRS data*

BLINDED

N= 3000
Large LRP
(MaxLCBI4mm ≥ 250)

2yr Follow-Up

BLINDED

N= 6000
Small/No LRP
(MaxLCBI4mm < 250)

N= 3000

2yr Follow-Up

N= 3000

Terminate upon Discharge

LRP CLINICAL STUDY

The ***PREVENT***ive Implantation of Bioresorbable Vascular Scaffold on Stenosis With Functionally Insignificant Vulnerable Plaque

# SJ Park PREVENT Trial

## *Any Epicardial Coronary Stenosis*

**with *FFR ≥0.80* and with *Two* of the following**

1. IVUS MLA≤4.0mm$^2$
2. IVUS Plaque Burden >70%
3. Lipid-Rich Plaque on NIRS ($_{max}LCBI_{4mm}$>500)
4. OCT-TCFA or VH-TCFA


Primary endpoint *at 2 years*:
CV death, MI, Hospitalization d/t unstable angina

OCT sub-study/ NIRS sub-study, (300 patients in each arm at 2 years)

# Take Home Message

1. An accumulation of data shows the relationship between NIRS and clinical outcomes.
2. On-going prospective, multicenter studies will provide a definitive answer.
3. The risk assessment of future events (hazard ratio) using NIRS may not be good enough to exceed the benefit of current optimal medical therapy and further clarification of vulnerable plaque (ie. fibrous cap) is still needed.