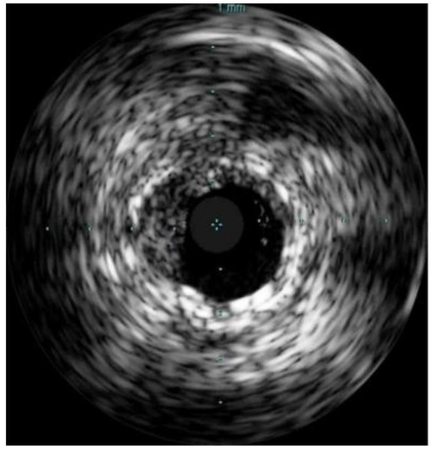
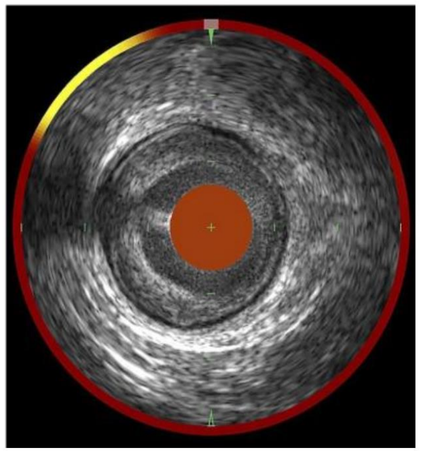
BVĐK AN GIANG – KHOA TIM MẠCH CAN THIỆP

IVUS – NIRS
IVUS QUANG PHỔ CẬN HỒNG NGOẠI
TRONG DỰ PHÒNG NO REFLOW

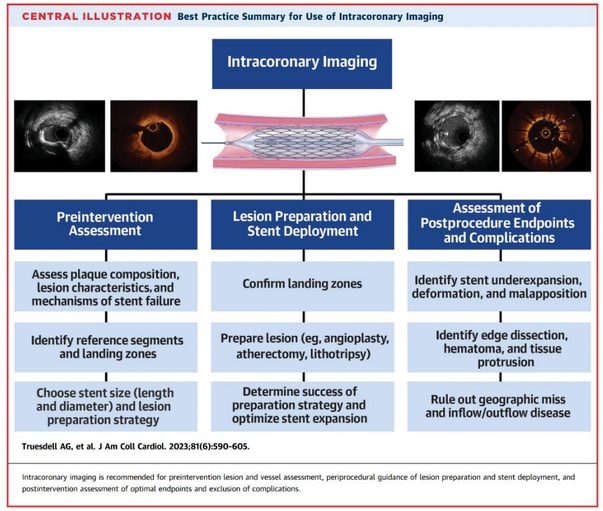
THS.BS. PHẠM HUỲNH MINH TRÍ



Competitor IVUS Image



Dualpro IVUS Image



BVĐK AN GIANG – KHOA TIM MẠCH CAN THIỆP

AGIC.VN

AN GIANG GENERAL HOSPITAL

INTERVENTIONAL CARDIOLOGY

agic

Cathlab DSA: IVUS-NIRS + OCT Gen 2nd

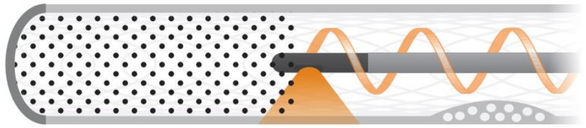
How We Create a Chemogram

A mountain of NIRS data simplified into a single image you can trust

The Makoto™ Intravascular Imaging System was designed with the primary goal of helping you make quick and informed decisions at the bedside. The easy-to-interpret chemogram provides insight into the complex plaques that complicate your interventional strategy, treatment procedures, and patient's recovery.

1 200,000 NIRS Spectra

Approximately **1,300 NIRS spectra per millimeter** are acquired as the catheter scans the vessel.[1]

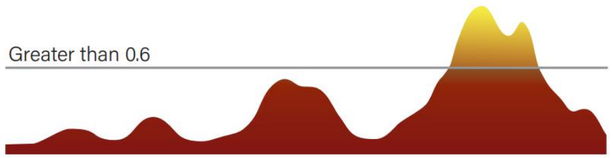


2 Analysis of Acquired Data

The acquired NIRS signals are analyzed and **each spectrum is assigned a probability score, from 0 to 1,** based on the likelihood of the presence of LCP.

3 Color Based on Probability

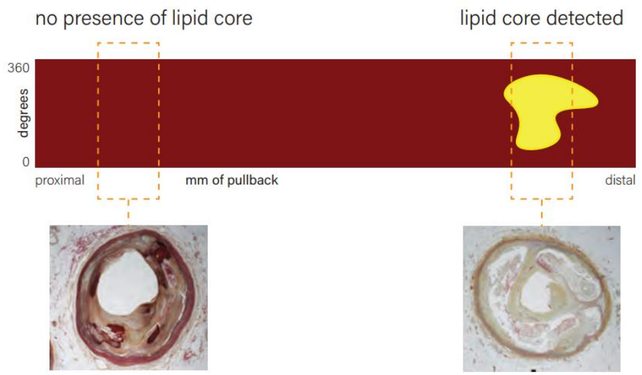
All probability scores, low to high, are mapped on **a continuous color scale from red to yellow.** Scores above 0.6 appear orange to yellow in the chemogram and contribute to the Lipid Core Burden Index (LCBI).



4 Chemogram Display

The chemogram is automatically generated within seconds, creating **a map of the LCP location** within the vessel wall. This color-coded map can be interpreted quickly, permitting informed treatment decisions.

Data you can trust:
Nearly 2,500 artery cross-sections were histologically and spectrally analyzed to validate lipid core plaque detection by NIRS. The red and yellow colors on the chemogram help differentiate normal or fibrotic plaque that is presumed to be stable (left) from those that contain lipid core plaques (right).[2]



References: **1** In a 150mm scan at 0.5 mm/s **2** Detection of lipid core coronary plaques in autopsy specimens with a novel catheter-based near-infrared spectroscopy system, Gardner et al, JACC Cardiovasc Imaging, 2008.

Pathophysiology of ACS

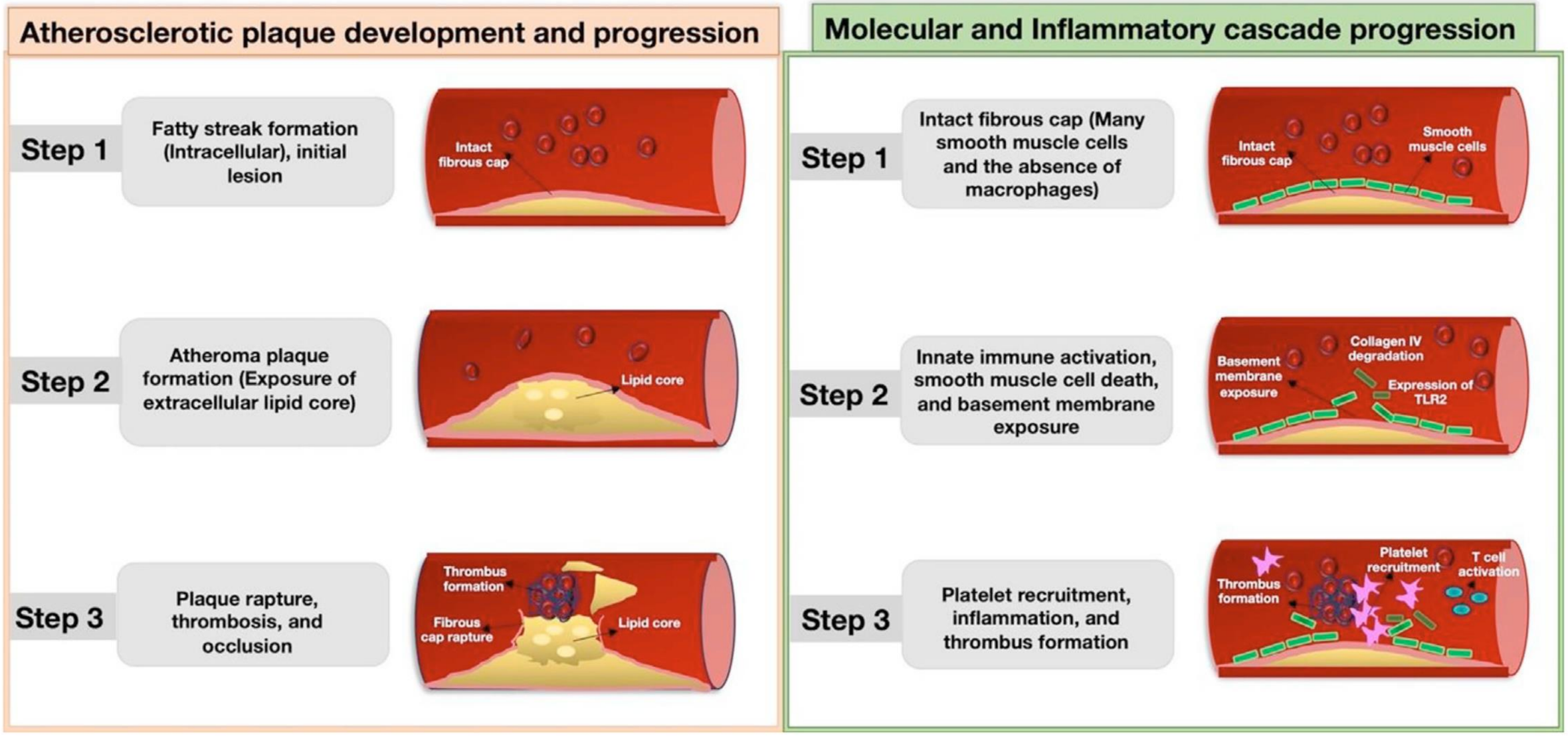


Figure 1. Pathophysiology of ACS. ACS = acute coronary syndrome; TLR2 = Toll-like receptor 2.

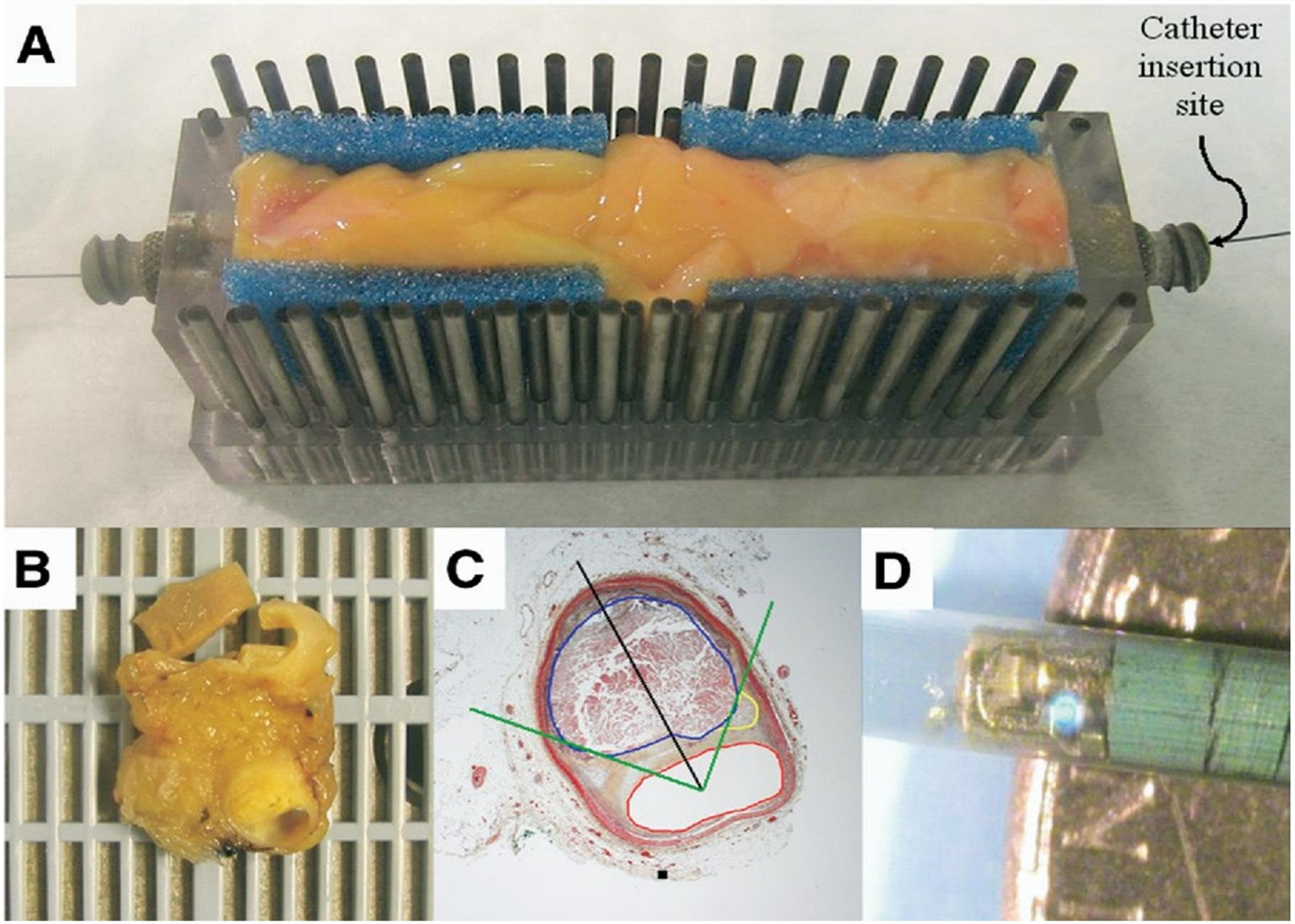
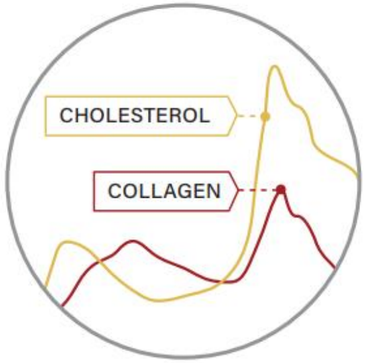


Figure 1. Apparatus for Fixing an Arterial Sample, Gross and Histologic Views, and Close-Up of NIRS Catheter

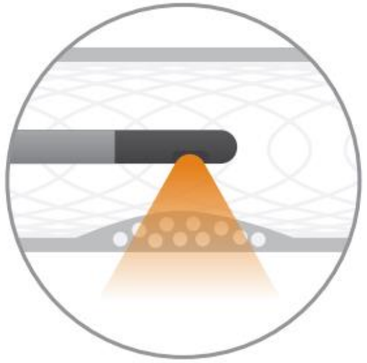
(A) A coronary artery segment mounted in a fixture to ensure registration of intraluminal near-infrared spectroscopy (NIRS) signals with histology. The vertical rods permit precise sectioning at 2-mm intervals. **(B and C)** Gross and microscopic cross-sections. Histomorphom- etry outlines show the lumen **(red)**, lipid core **(blue)**, and a small lipid pool **(yellow)**. The angle subtended by the lipid core is shown in **green**. Radii used to measure cap and core thickness are in **black. (D)** The imaging tip of the NIRS catheter lying on a U.S. penny.



Why NIR Spectroscopy?

To identify lipids such as cholesterol

Organic molecules have unique spectroscopic signatures that can be used to detect their presence in a mixture of unknown composition. NIRS allows us to **distinguish molecules, such as collagen and cholesterol,** within the vessel wall and thus identify the presence of LCP.



Where does the Light Propagate?

Through blood, tissue and interstitial spaces

The microscopic mirrors at the tip of the Dualpro™ catheter are designed to deliver near-infrared light to the vessel wall and collect the diffusely reflected light. The light propagates **through blood and tissue by scattering and absorption**, even in the presence of calcium or stents, to interrogate the plaque for its chemical fingerprint.

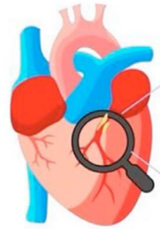
How are the Spectra Interpreted?

With the aid of advanced algorithms

Advanced algorithms analyze the returned light and calculate the probability of the presence of a lipid core plaque. Our algorithms have been **validated in a large prospective histology study** providing you with information you can trust.

BVĐK AN GIANG – KHOA TIM MẠCH CAN THIỆP

MẢNG XƠ VỮA DỄ TỔN THƯƠNG



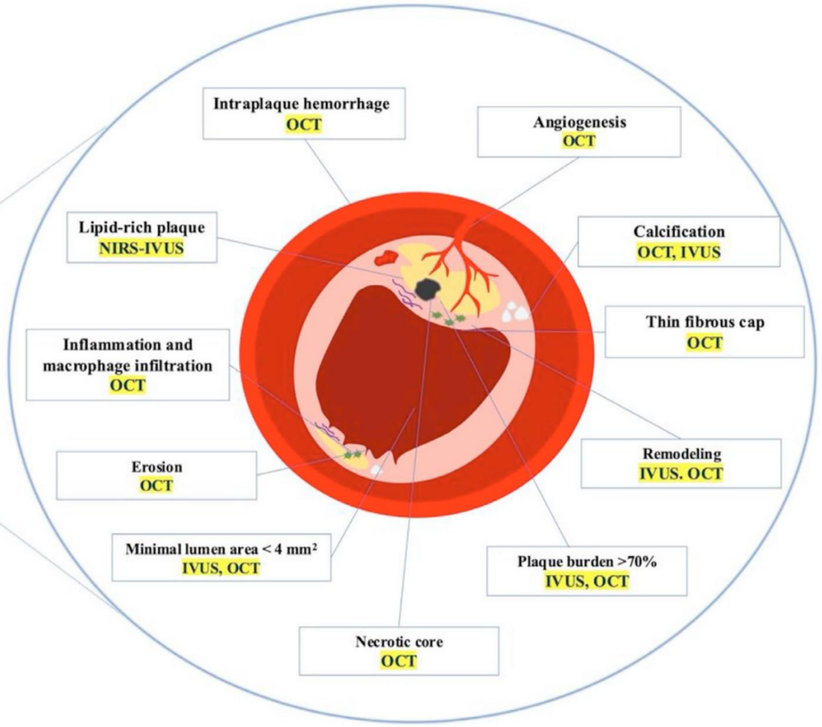


Figure 2. Concept of vulnerable plaque. IVUS = intravascular ultrasound; NIRS-IVUS = Near infrared spectroscopy-IVUS; OCT = optical coherence tomography.

Vulnerable Plaque là những tổn thương động mạch vành có nguy cơ cao vỡ và gây biến cố tim mạch cấp (nhồi máu cơ tim, tử vong).
Các đặc điểm định nghĩa Vulnerable Plaque theo mô bệnh học:
- Xơ vữa nắp mỏng (< 65 µm, là thin-cap fibroatheroma TCFA)
- Lõi hoại tử lớn (hàm lượng lipid cao)
- Bạch cầu xâm nhập vào lõi mảng xơ vữa (trong nắp xơ)
- Tái cấu trúc dương

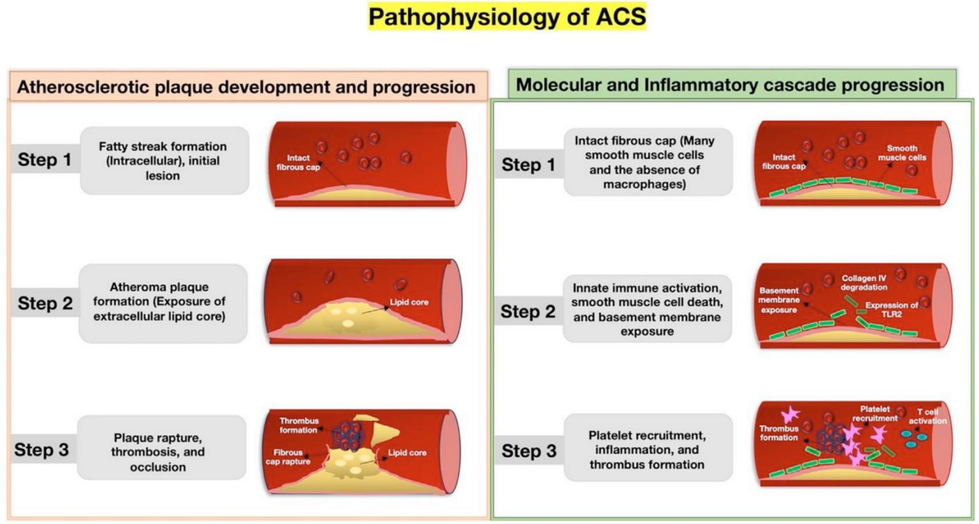
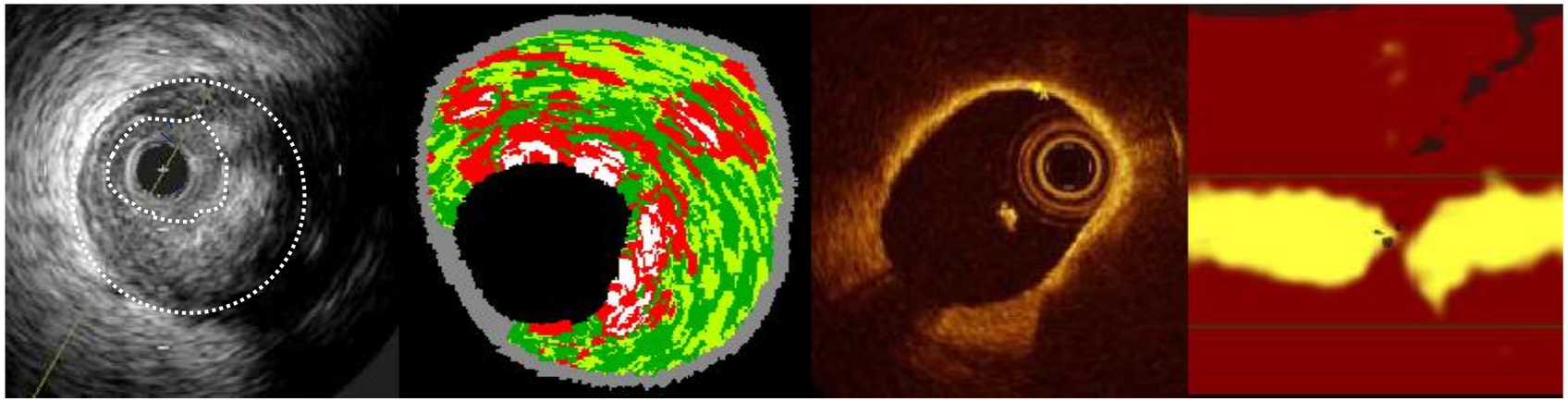


Figure 1. Pathophysiology of ACS. ACS = acute coronary syndrome; TLR2 = Toll-like receptor 2.

MẢNG XƠ VỮA DỄ TỔN THƯƠNG

PREVENT

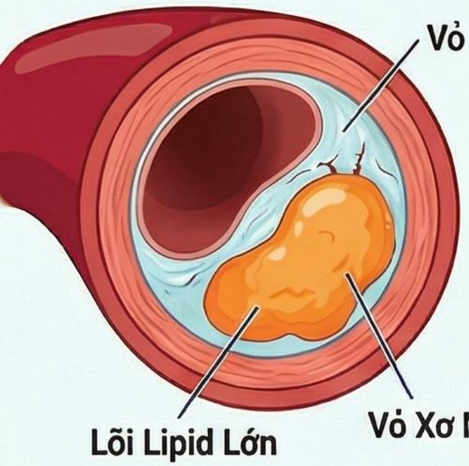
1. MLA ≤ 4.0mm^2,
2. Plaque burden >70%
3. TCFA by OCT or RF-IVUS
4. Lipid rich plaque on NIRS ($_{max}LCBI_{4mm}$>315)



MLA, minimal lumen area, TCFA (thin-cap fibroatheroma) was defined as a ≥10% confluent necrotic core with >30° abutting the lumen in 3 consecutive frames on RF-IVUS (radiofrequency intravascular ultrasonography) or a lipid plaque with arc >90° and fibrous cap thickness <65 µm on OCT (optical coherence tomography). $_{max}LCBI_{4mm}$, maximal lipid core burden index in a 4 mm segment on NIRS (near-infrared spectroscopy).

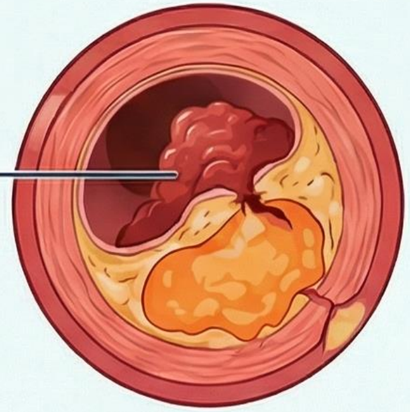
Nhận Diện Rủi Ro Tiềm Ẩn: Sức Mạnh Của Hình Ảnh Học NIRS-IVUS

VẤN ĐỀ: Mảng Xơ Vữa Dễ Vỡ



Mảng bám giàu lipid là thủ phạm chính

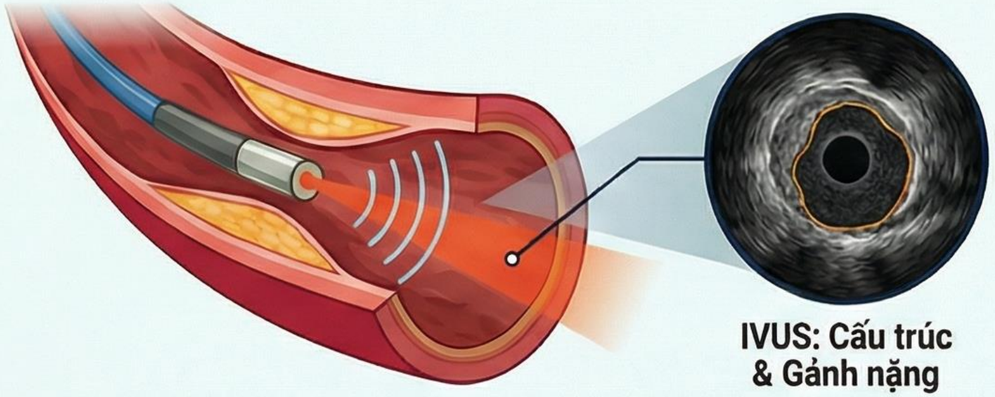
Nứt vỡ vỏ mỏng bao phủ lõi lipid gây ra khoảng 2/3 số biến cố mạch vành cấp



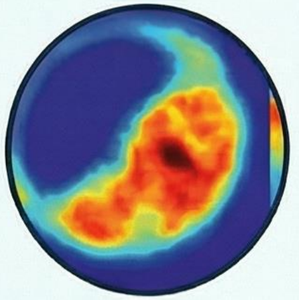
Nguy cơ cao nhất khi kết hợp lõi lipid lớn & vỏ xơ mỏng

Sự kết hợp này làm tăng nguy cơ biến cố bất lợi lên gần 5 lần

GIẢI PHÁP: Phân Tầng Nguy Cơ Bằng Hình Ảnh Học Tiên Tiến



IVUS: Cấu trúc & Gánh nặng



NIRS: Thành phần hóa học (Lipid)

Công nghệ kép NIRS-IVUS: Thấy rõ Cấu trúc & Thành phần

IVUS cho thấy cấu trúc và gánh nặng mảng bám, NIRS xác định thành phần hóa học (lipid)

Ngưỡng báo động

Chỉ Số Gánh Nặng Lõi Lipid (LCBI)

Chỉ Số Gánh Nặng Lõi Lipid (LCBI) > 400 là ngưỡng báo động

maxLCBI4mm định lượng lượng lipid tối đa trong một đoạn động mạch 4mm

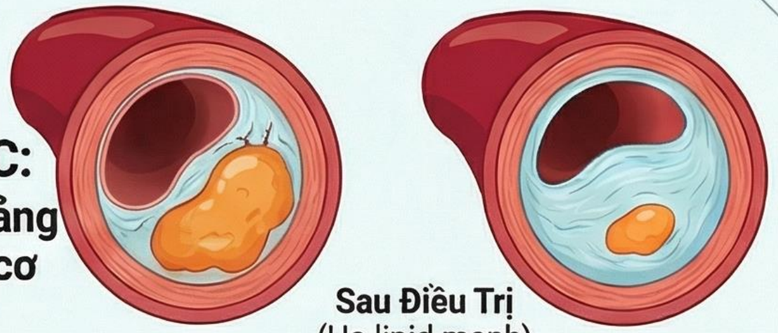
MỨC TĂNG NGUY CƠ

Nguy cơ cho Bệnh nhân (Cao hơn 89%)

Nguy cơ tại Vị trí Mảng bám (Cao hơn 322%)

ĐIỀU TRỊ TÍCH CỰC:

Ổn định mảng bám nguy cơ cao



Sau Điều Trị (Hạ lipid mạnh)

Điều trị tích cực giúp ổn định mảng bám nguy cơ cao

Liệu pháp hạ lipid mạnh làm giảm đáng kể chỉ số LCBI và làm dày vỏ xơ

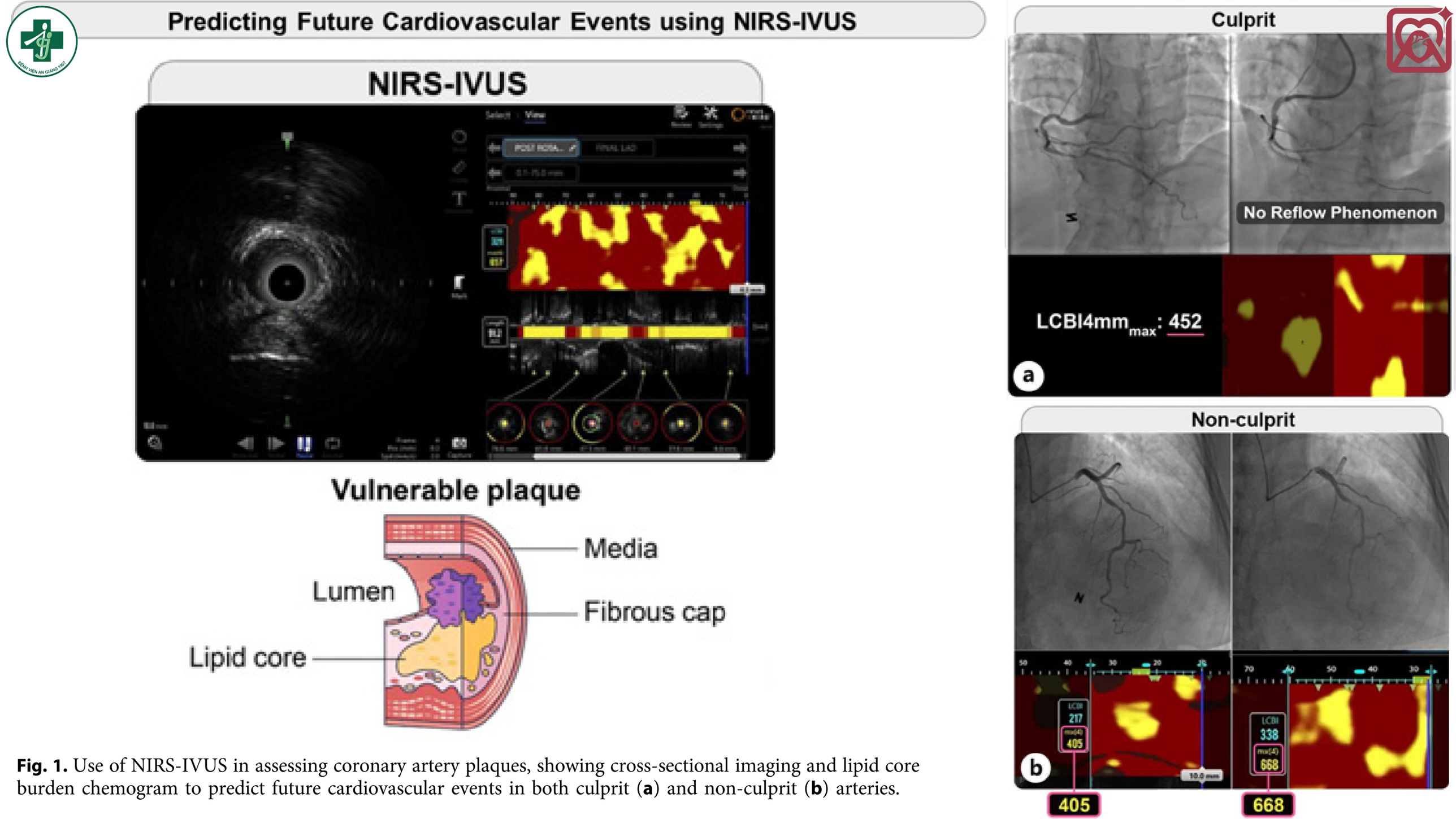
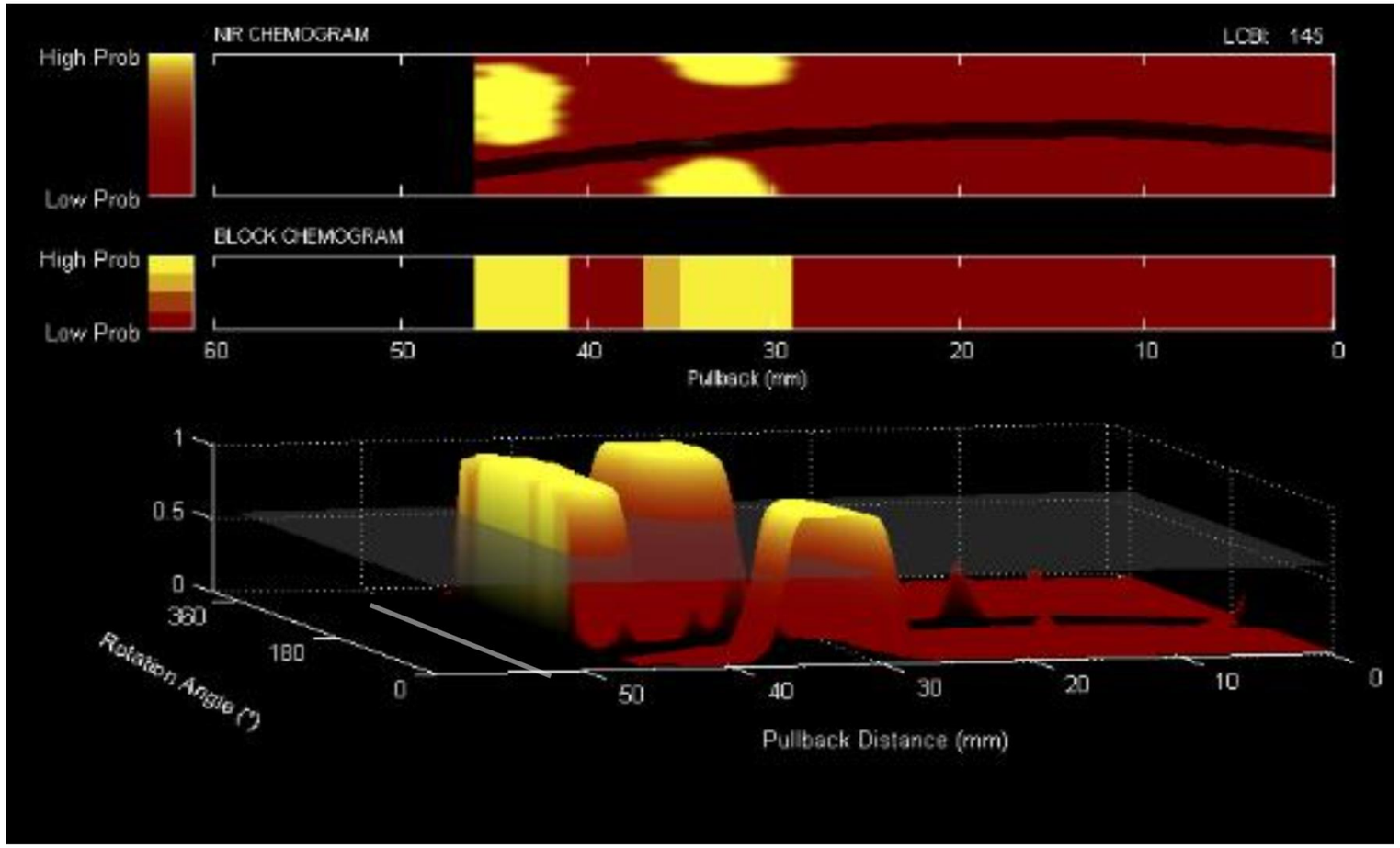


Fig. 1. Use of NIRS-IVUS in assessing coronary artery plaques, showing cross-sectional imaging and lipid core burden chemogram to predict future cardiovascular events in both culprit (**a**) and non-culprit (**b**) arteries.

“Lipid Core Burden Index” – LCBI Calculation

- Quantitative summary metric of LCP content in Chemogram
  - Potentially useful as measure of risk or of therapeutic efficacy
- Fraction of Chemogram image pixels above probability of 0.6
  - Scaled from 0 to 1000



LCBI Calculation

Image pixels > 0.6: **21239**

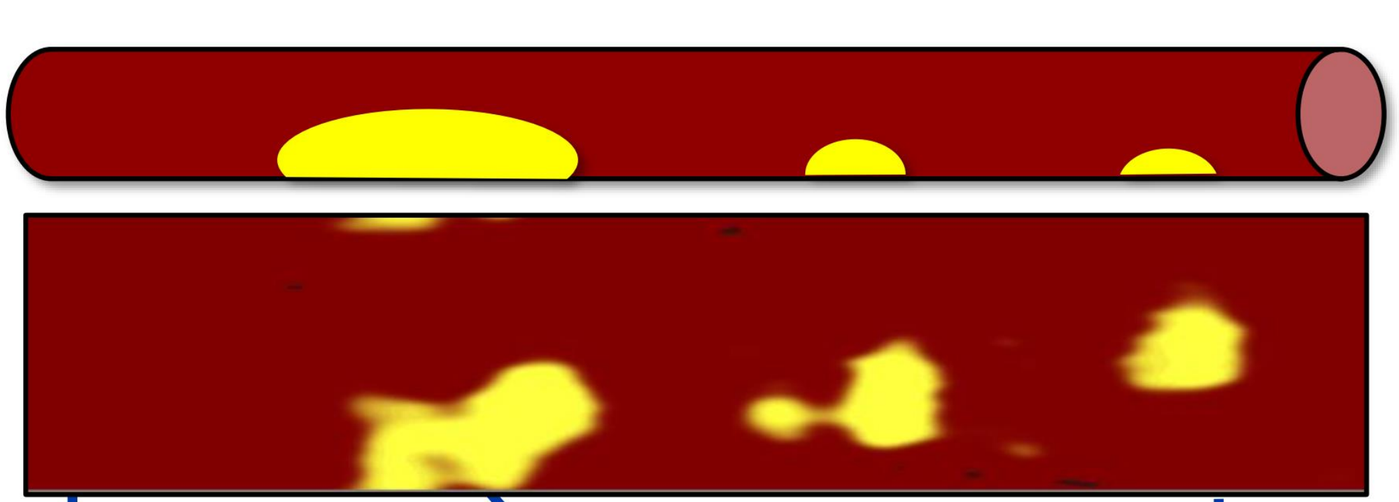
Image pixels: **145974**

$$\frac{21239}{145974} \times 1000 = 145$$

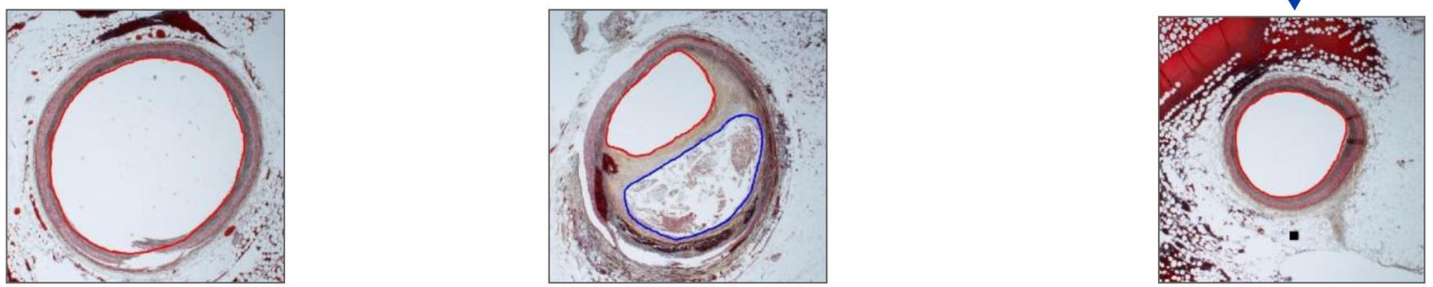
(outliers and guidewire excluded)

NIRS Detects Plaques Which May Be Vulnerable to Rupture

- A chemogram is a scanned vessel opened and laid flat
- Yellow indicates lipid core plaque (LCP)
- Histologically validated



Chemogram Color	Indication
Red	No LCP
Yellow	LCP



How We Create a Chemogram

A mountain of NIRS data simplified into a single image you can trust

1 200,000 NIRS Spectra

Approximately **1,300 NIRS spectra per millimeter** are acquired as the catheter scans the vessel.[1]

2 Analysis of Acquired Data

The acquired NIRS signals are analyzed and **each spectrum is assigned a probability score, from 0 to 1,** based on the likelihood of the presence of LCP.

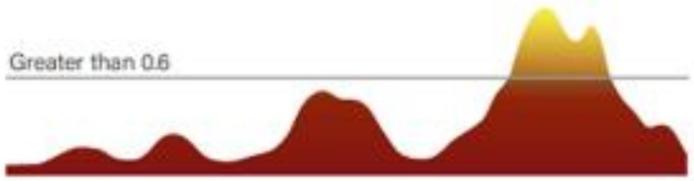
3 Color Based on Probability

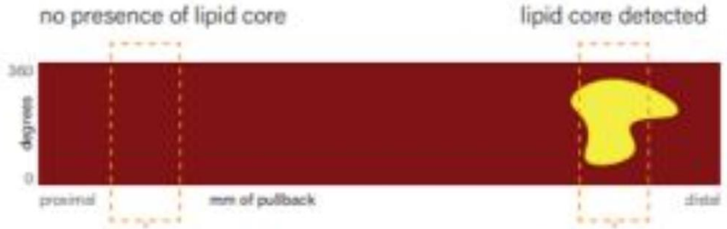
All probability scores, low to high, are mapped on **a continuous color scale from red to yellow.** Scores above 0.6 appear orange to yellow in the chemogram and contribute to the Lipid Core Burden Index (LCBI).

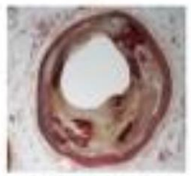
4 Chemogram Display

The chemogram is automatically generated within seconds, creating **a map of the LCP location** within the vessel wall. This color-coded map can be interpreted quickly, permitting informed treatment decisions.

Data you can trust:
Nearly 2,500 artery cross-sections were histologically and spectrally analyzed to validate lipid core plaque detection by NIRS. The red and yellow colors on the chemogram help differentiate normal or fibrotic plaque that is presumed to be stable (left) from those that contain lipid core plaques (right).[2]

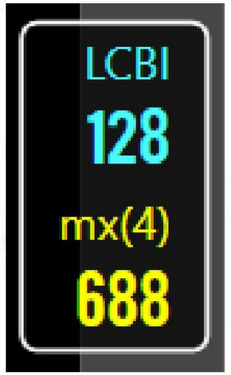


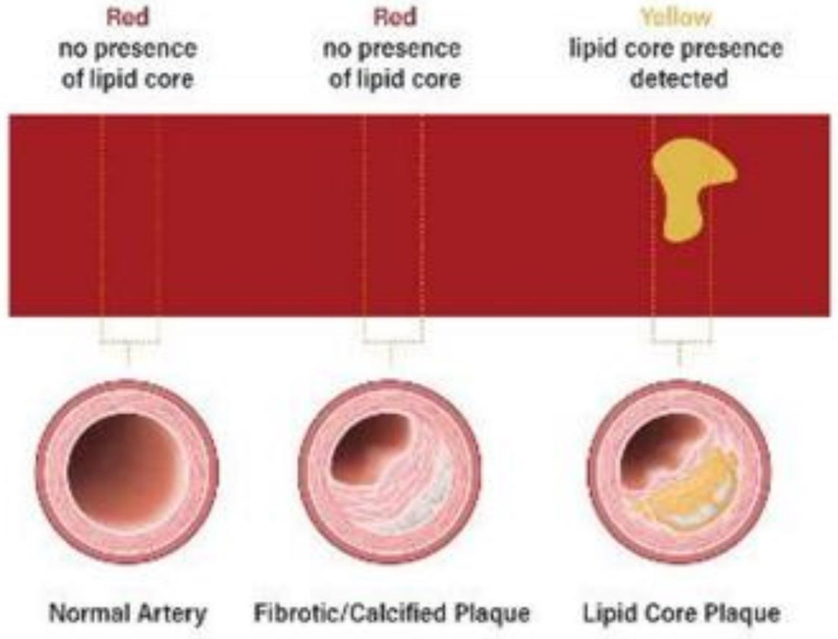



Fibrotic/Calcified Plaque

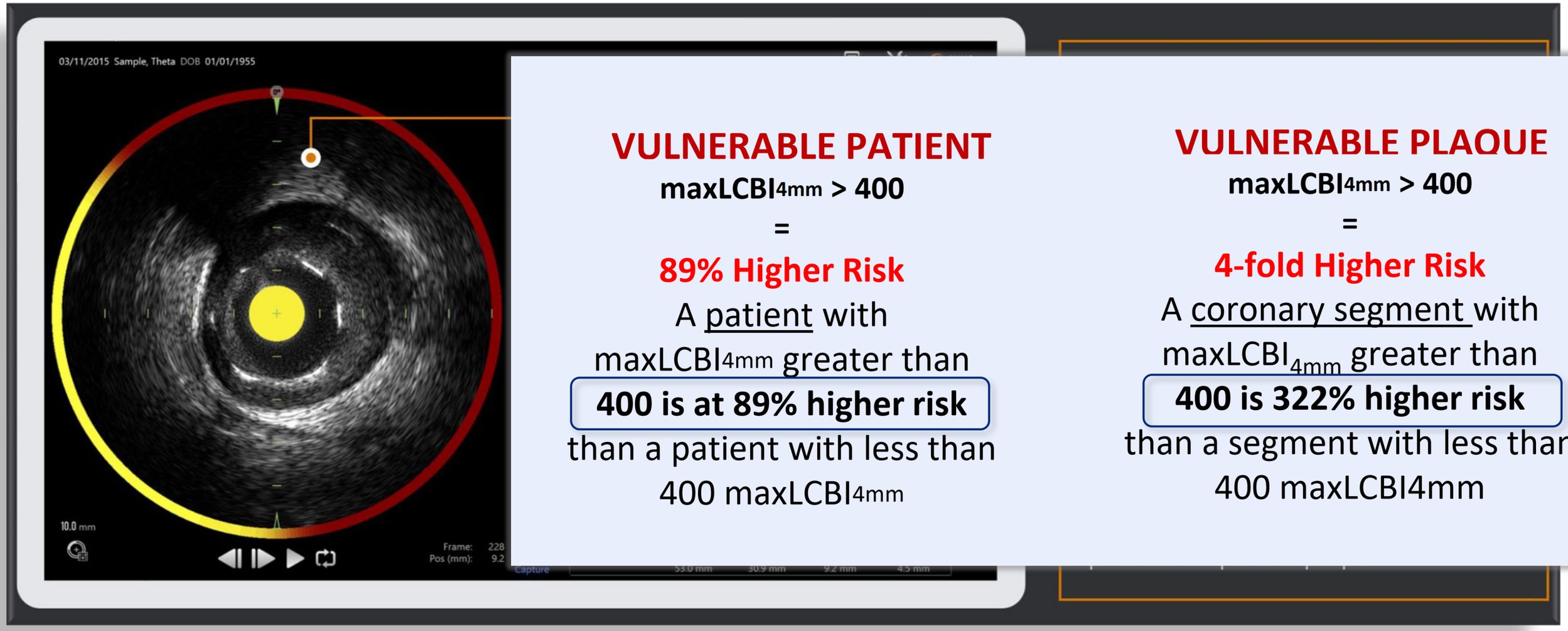

Lipid Core Plaque

NIRS





Delivering unprecedented treatment insights through the power of plaque composition analysis and high-resolution structural views



VULNERABLE PATIENT

maxLCBI4mm > 400

=

89% Higher Risk

A patient with maxLCBI4mm greater than **400 is at 89% higher risk** than a patient with less than 400 maxLCBI4mm

VULNERABLE PLAQUE

maxLCBI4mm > 400

=

4-fold Higher Risk

A coronary segment with $maxLCBI_{4mm}$ greater than **400 is 322% higher risk** than a segment with less than 400 maxLCBI4mm

Identify – Qualify – Quantify LCP (LCBI : 0 - 1000 units)

Vulnerable Threshold : > 400 units signifying an increased risk of plaque rupture and MACE.

LRP CLINICAL STUDY

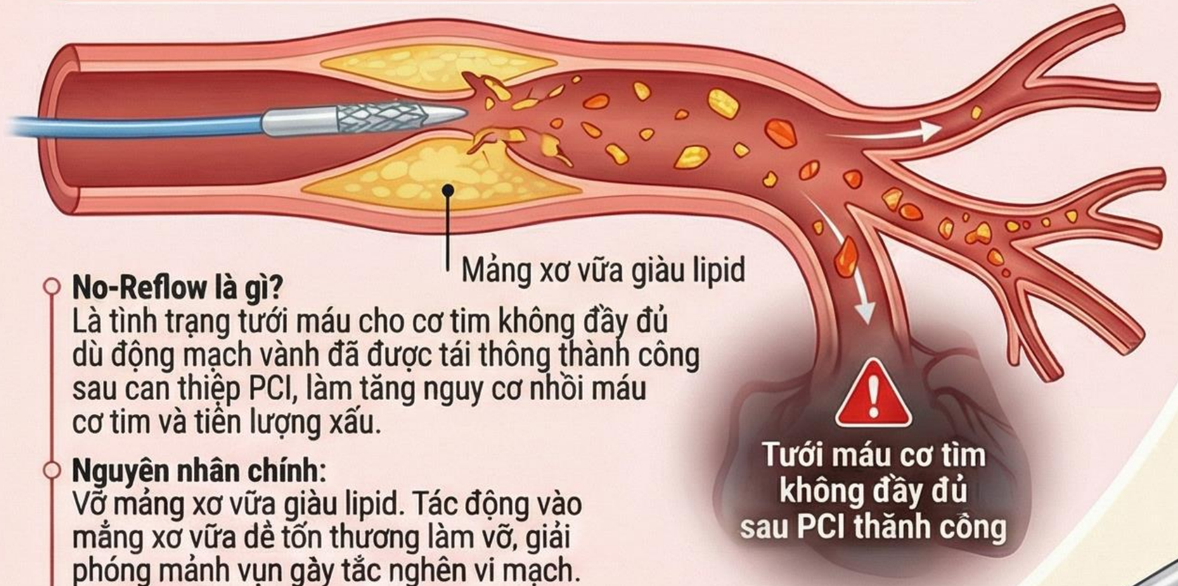
Sponsored by Infraredx

NCT02033694

NIPRO

Vai trò của IVUS-NIRS: Dự phòng sớm Biến chứng No-Reflow trong Can thiệp Mạch vành (PCI)

VẤN ĐỀ: HIỆN TƯỢNG "KHÔNG TÁI TƯỚI MÁU" (NO-REFLOW)

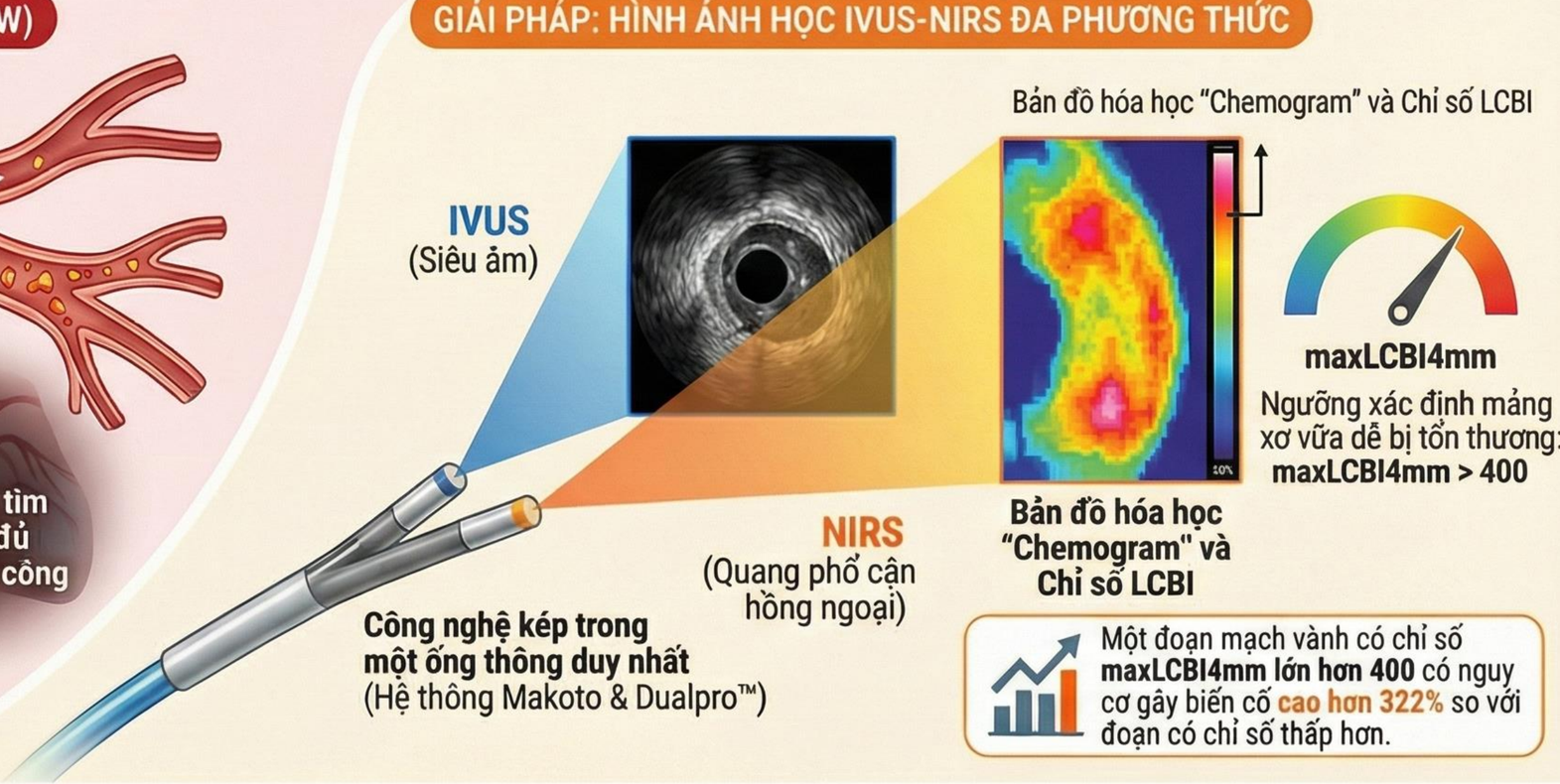


No-Reflow là gì?
Là tình trạng tưới máu cho cơ tim không đầy đủ dù động mạch vành đã được tái thông thành công sau can thiệp PCI, làm tăng nguy cơ nhồi máu cơ tim và tiên lượng xấu.

Nguyên nhân chính:
Vỡ mảng xơ vữa giàu lipid. Tác động vào mảng xơ vữa dễ tổn thương làm vỡ, giải phóng mảnh vụn gây tắc nghẽn vi mạch.

Hạn chế của Chụp mạch vành truyền thống:
Chỉ cho thấy hình ảnh 2D lumenogram, không phát hiện mảng xơ vữa nguy hiểm ẩn trong thành mạch.

GIẢI PHÁP: HÌNH ẢNH HỌC IVUS-NIRS ĐA PHƯƠNG THỨC

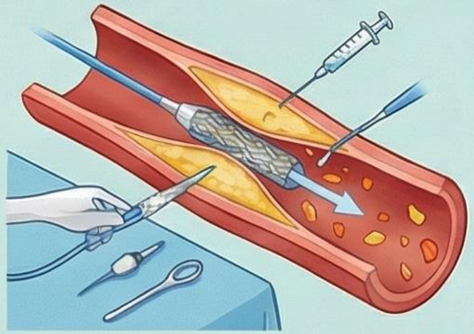


Một đoạn mạch vành có chỉ số **maxLCBI4mm lớn hơn 400** có nguy cơ gây biến cố **cao hơn 322%** so với đoạn có chỉ số thấp hơn.

ỨNG DỤNG LÂM SÀNG: CHIẾN LƯỢC DỰ PHÒNG NO-REFLOW

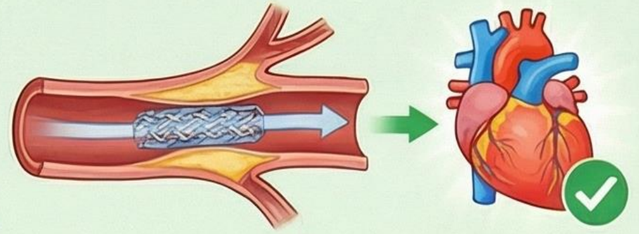
Bước 1: Sàng lọc nguy cơ trước can thiệp
Sử dụng IVUS-NIRS quét tổn thương trước stent. maxLCBI4mm > 400 cảnh báo nguy cơ cao.

Bước 2: Cá nhân hóa chiến lược can thiệp PCI



Các chiến lược can thiệp điều chỉnh

- ✓ Thiết bị bảo vệ đầu xa
- ✓ Điều trị dự phòng bằng thuốc
- ✓ Kỹ thuật đặt stent nhẹ nhàng hơn
- ✓ Tránh đặt cạnh stent vào vùng lõi lipid lớn



Cải thiện kết quả cho bệnh nhân
Xác định và quản lý mảng xơ vữa nguy cơ cao ngăn ngừa No-Reflow, giảm nhồi máu cơ tim chu phẫu và cải thiện an toàn thủ thuật.

Dual Modality … Why Makoto IVUS + NIRS?

IVUS Imaging

- Accurate vessel diameter
- Plaque burden
- Plaque morphology for optimal stent sizing
- Devices deployment

+NIRS Imaging

- Identification of lipid core plaques vulnerable to rupturing
- Future coronary events

IVUS + NIRS Catheter

- Enhanced detection of high-risk plaques
- Guidance for preventive PCI to **reduce adverse events**.

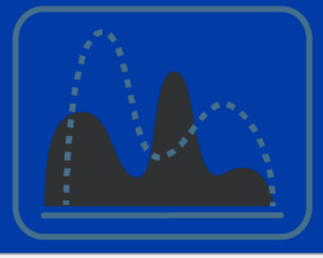
Clinical Outcomes

- Lower mortality
- Target on lesion failure
- Lower repeat revascularization
- Lower myocardial infarction rates
- Low flow and non-flow phenomenon

IVUS + NIRS Clinical Applications

- Determine degree of stenosis
- Determine size of reference vessel
- Determine landing zone for a stent
- Assure proper stent deployment
- Assess degree of calcification

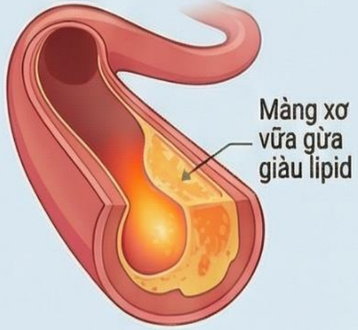
NIRS



- Detect Lipid Core Plaque (LCP)
- Identify culprit lesions
- Assess Risk of Peri-procedural MI
- Avoid landing stent edge in large lipid core
- Assess impact of lipid lowering therapy on LCP
- Identify Patients and Plaques with risk of MACE

Nhìn Thấu Mảng Xơ Vữa: Nâng Cao Tiên Lượng Tim Mạch với IVUS+NIRS

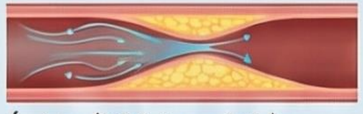
Vấn Đề Lâm Sàng: Mối Nguy Hiểm Ẩn Giấu



Khoảng 2/3 các biến cố mạch vành cấp là đo vỡ mảng xơ vữa giàu lipid.

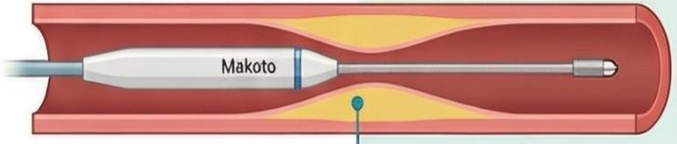
Chụp động mạch vành có thể bỏ sót các mảng xơ vữa nguy hiểm không gây hẹp đáng kể

Bệnh nhân tiểu đường có nguy co MACE tăng gấp ~2 lần

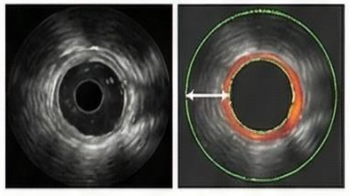


Áp lực cắt thành mạch thấp (Low Wall Shear Stress - WSS) và sự hiện diện của lipid có tác động cộng hưởng

Công Nghệ Đột Phá: Hệ Thống Makoto IVUS+NIRS



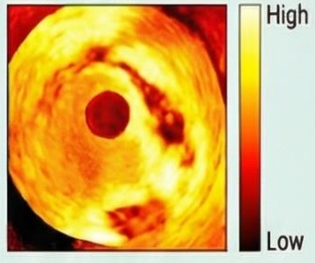
Thiết bị hình ảnh nói mạch hai phương thức duy nhất được FDA cấp phép



IVUS cho Cấu trúc

Gánh nặng mảng xơ vữa

Kích thước lòng mạch



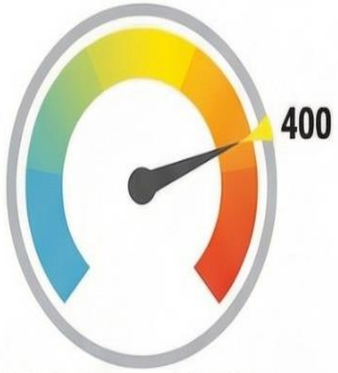
NIRS cho Thành phần

NIRS tạo ra một Chemogram trực quan. Màu vàng chỉ ra sự hiện diện của mảng xơ vữa lõi lipid

Hệ thống Makoto được chỉ định để xác định các bệnh nhân và mảng xơ vữa có nguy cơ gia tăng các Biến cổ Tim mạch Bất lợi Chính (MACE)

Bằng Chứng Lâm Sàng: Dự Đoán Rủi Ro và Cải Thiện Kết Quả

Chỉ Số Then Chốt: Chỉ Số Gánh Nặng Lõi Lipid (LCBI)



LCBI định lượng hàm lượng mảng xơ vữa lõi lipid

Ngưỡng dễ bị tổn thương: maxLCBI4mm > 400

Một chỉ số maxLCBI4mm lớn hơn 400 cho thấy nguy cơ vỡ mảng xơ vữa và MACE tăng iân đáng kể

$$\text{Tính toán LCBI} = \frac{\text{Số điểm ảnh có xác suất lipid >0.6}}{\text{Tổng số điểm ảnh có thể phân tích}} \times 1000$$

Bằng Chứng Lâm Sàng: Dự Đoán Rủi Ro và Cải Thiện Kết Quả

Nghiên cứu LRP: Bệnh nhân có maxLCBI4mm > 400 có nguy cơ MACE cao hơn 89%. Các đoan mạch xành có maxLCBI4mm > 400 có nguy cơ cao hơn 322% (gấp 4 lăn) gây ra một biến cố trong tương lai

Nghiên cứu PROSPECT II: Gánh nặng mảng xơ vữa ≥70% và maxLCBI4mm ≥324.7 làm tàng nguy co MACE lên 37 lần

Nghiên cứu PACMAN-AMI: Liệu pháp hạ lipid tích cực làm giảm lipid và ổn định mảng xơ vữa.

IVUS-PCI làm giảm tỷ lệ thất bại của mạch máu đích (6,6%) so với PCI chỉ có hướng dân của chụp mạch (10,7%) sau 3 nâm

Ứng Dụng Lâm Sàng: Tối Ưu Hóa Can Thiệp

Xác định các tổn thương thủ phạm và nguy cơ tiềm ẩn: NIRS giúp phát hiên các mảng lôi lipid (LCP) gây ra các biên cố và xác định các tổn thương không phải thủ phạm có nguy cơ cao

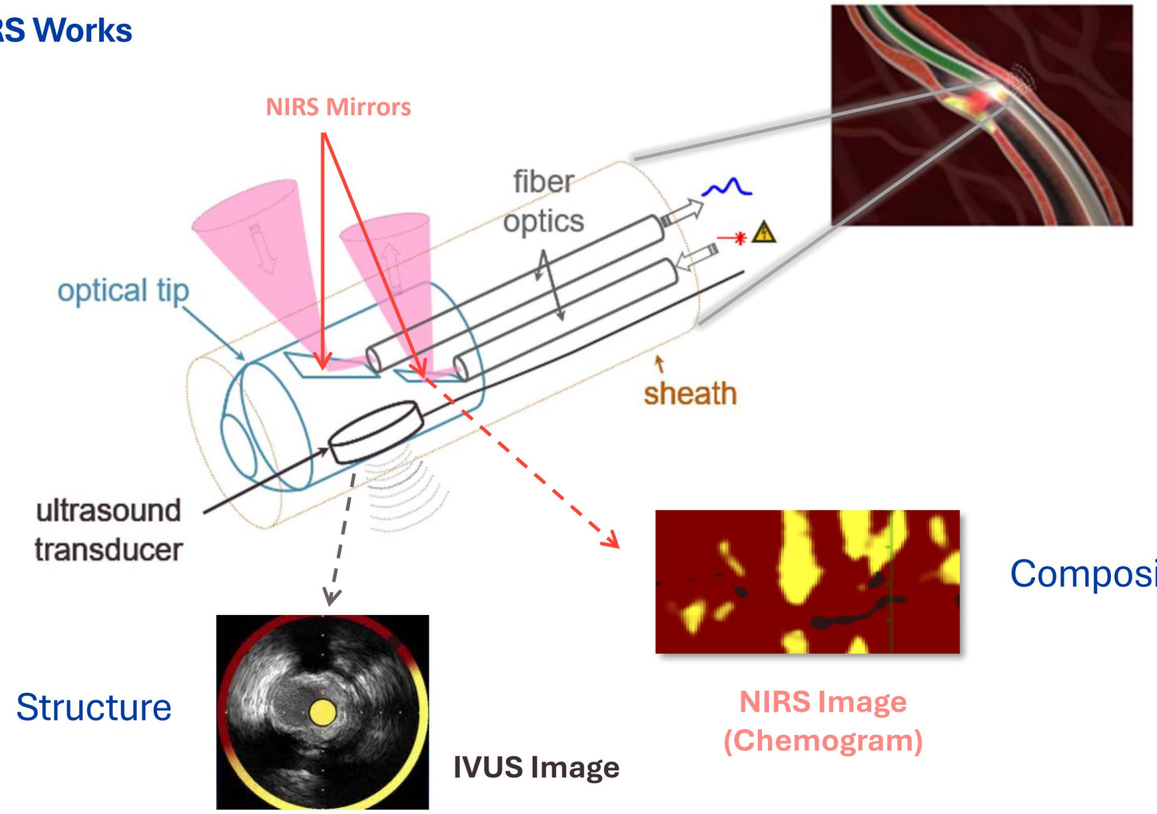
Tối uu hóa việc đăt stent: IVUS đám bảo kích thước stent phù hợp, xác định vùng tiếp cận tối ưu và xác nhận sự áp sát và bung nở hoàn toàn của stent, giảm các biến chứng

Hướng dẫn điều trị phòng ngừa: Xác định các bệnh nhân và mảng xơ vữa có nguy cơ cao - cho phập can thiệp sớm hoặc điều trị nội khoa tích cực hơn để ngăn ngừa các biến cố trong tương lai

Đánh giá hiệu quả điều trị: NIRS có thể theo đôi tác đông của các liêu phàp hạ lipid đối với thành phân mảng xơ vữa, cung cấp bằng chứng khách quan về ổn định của mảng xơ vữa

CATHETER KÉP 2 CÔNG NGHỆ IVUS+NIRS

NIRS Works



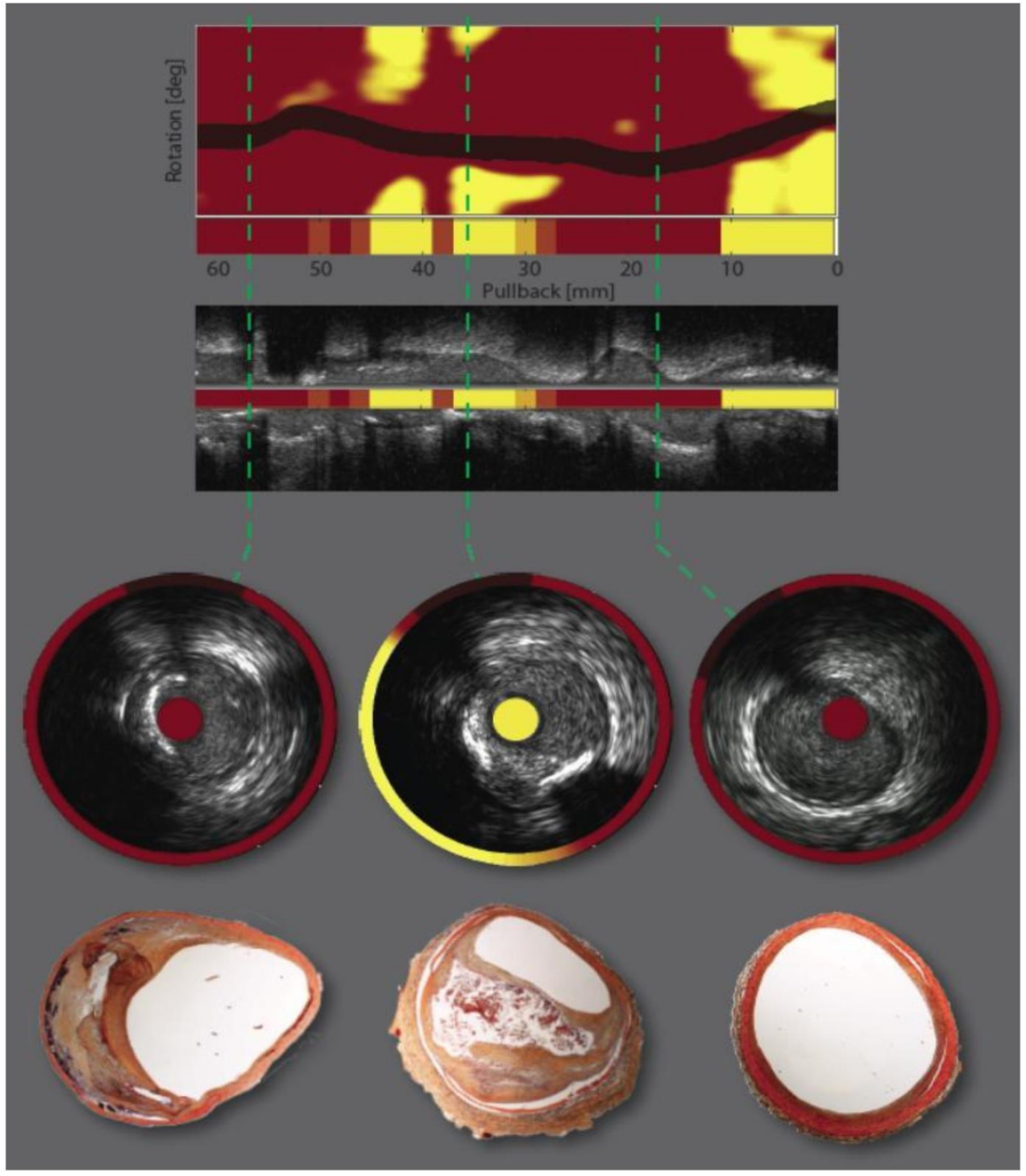
dualpro™ IVUS + NIRS

- **Catheter Specification**

HD IVUS 35 - 65Mhz Extended Bandwidth

- 160cm Working Length
- 150mm Pullback Imaging Range
- 16mm 1st Marker to IVUS Image Distance
- 6mm – 16mm IVUS Image Depth Diameter
- 6F Interventional Guide Compatible
- 0.014” Guide Wire Compatible
- 3.2F Crossing Profile
- Dual Layer Hydrophillic Coating

NIRS-IVUS with Histology



- *Left*
  - High plaque burden, calcium shadowing and signal dropout on IVUS, but no lipid core plaque by NIRS
  - Histology confirms calcified fibrous plaque
- *Center*
  - High plaque burden, calcium shadowing and signal dropout on IVUS, and substantial lipid core plaque by NIRS
  - Histology confirms large lipid core plaque
- *Right*
  - No plaque burden on IVUS and no lipid core plaque by NIRS
  - Histology confirms normal vessel

NIPRO

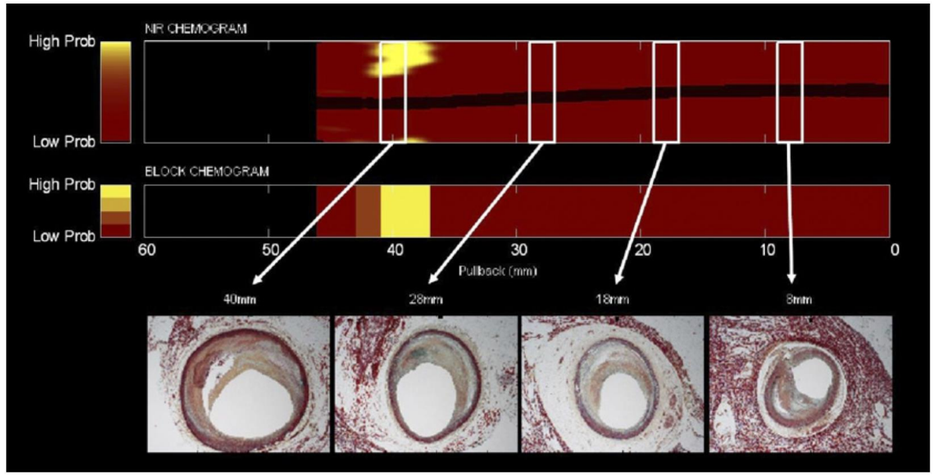
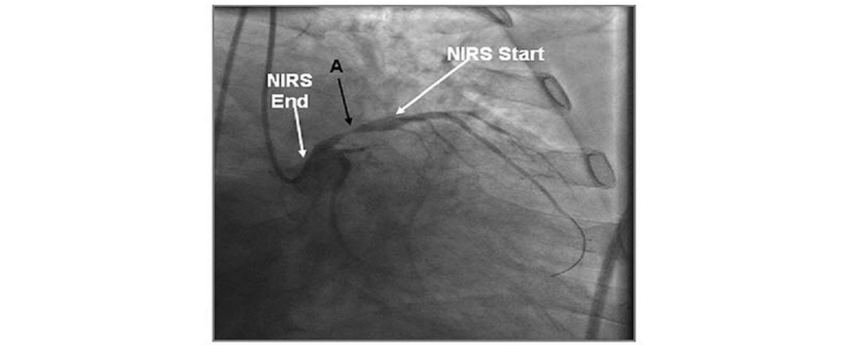


Figure 3. **A NIRS Scan From a Coronary Artery From the Autopsy Study Compared With Histology**



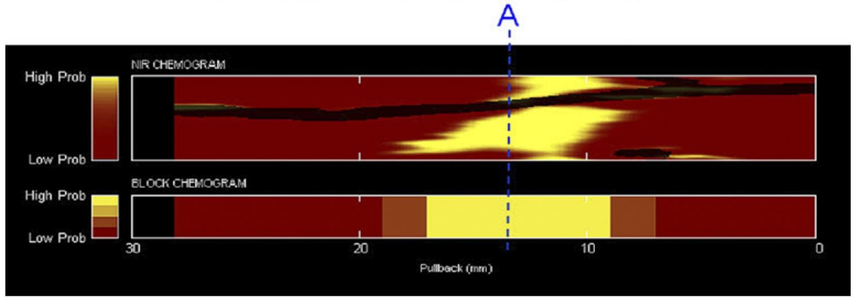
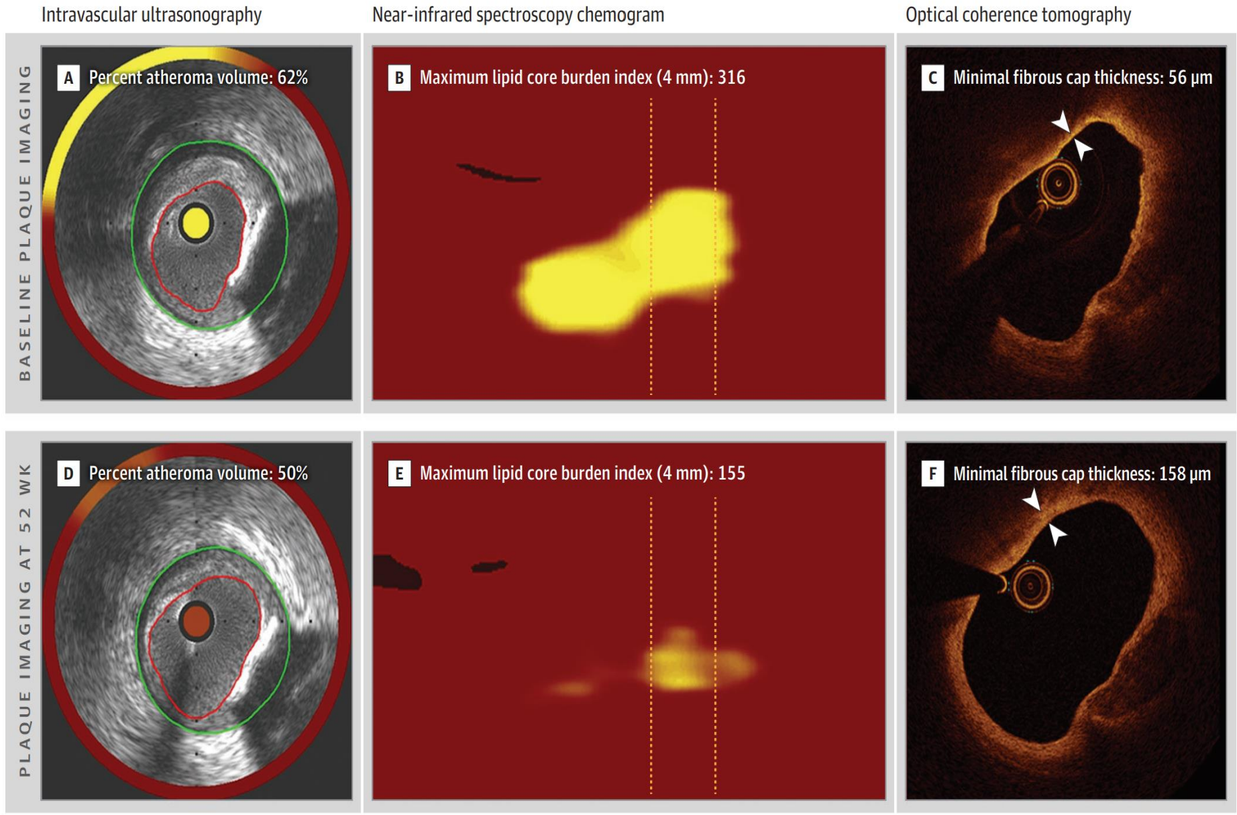


Figure 6. **NIRS Scan of a Patient and Corresponding Angiogram**

(Top) cineangiographic frame of the left coronary artery of a 71-year-old man with post-infarct angina. There is a severe culprit stenosis **(A)** in the proximal left anterior descending artery. **(Bottom)** the corresponding chemogram reveals a prominent, circumferential lipid core-containing coronary plaques (LCP) signal between 8 and 18 mm in the area of the culprit lesion. The narrowest area of luminal stenosis is approximately 14 mm and demarcated in the chemogram **(A)**. The block chemogram shows that the strongest LCP signals extend from 9 to 17 mm. NIRS = near-infrared spectroscopy.

CHEMOGRAM

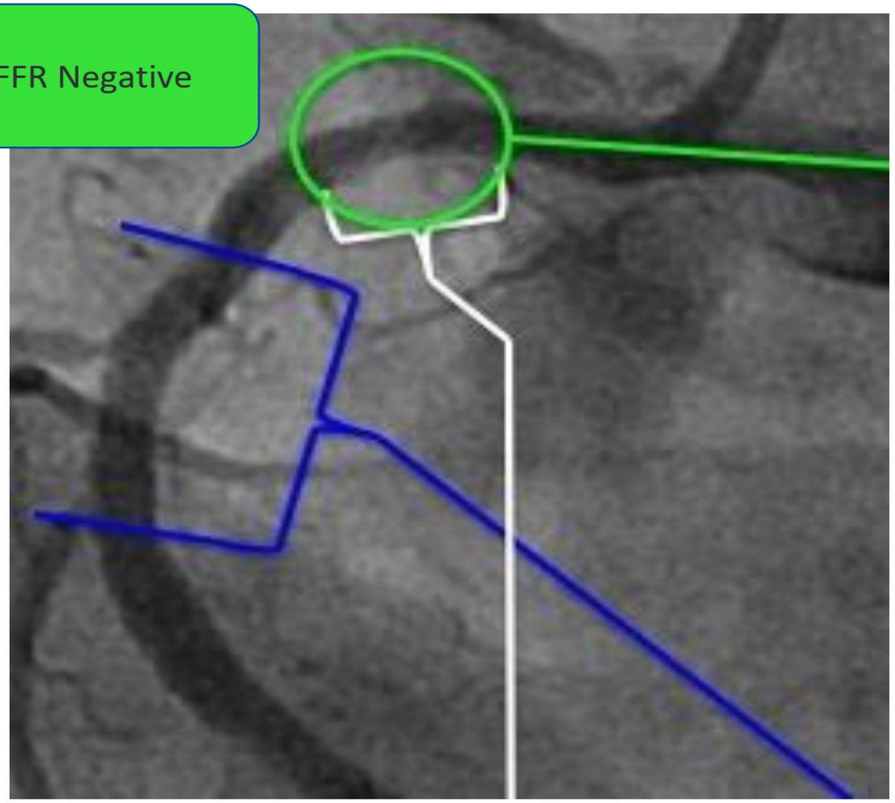
Figure 3. Example of Plaque Regression, Lipid Regression, and Fibrous Cap Thickening in a Trial Patient



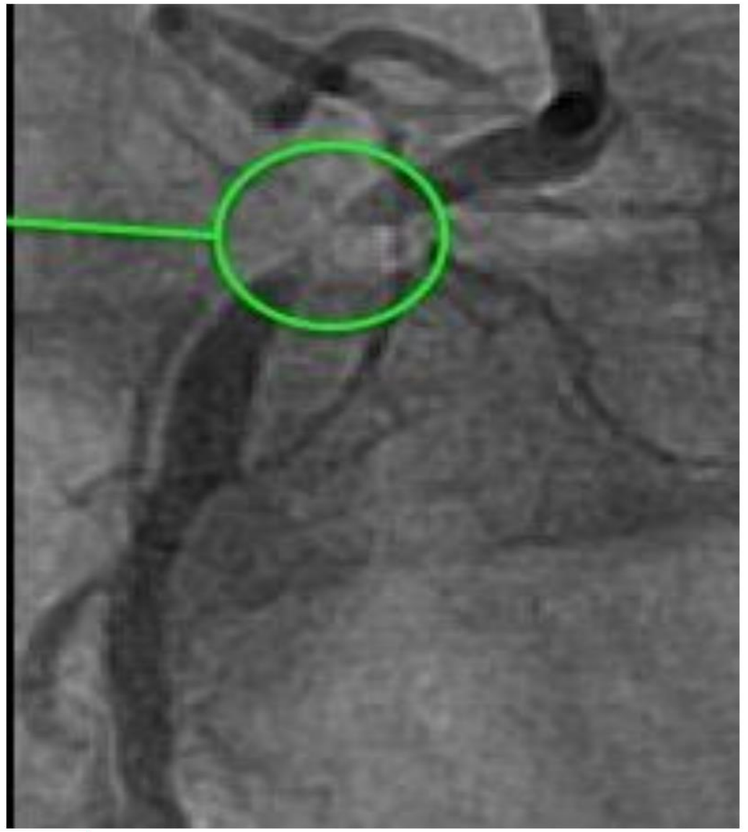
All images were obtained from the same lesion in the same patient and matched for the 2 time points of intracoronary imaging investigation. For intravascular ultrasonography (IVUS), external elastic lamina borders (green line) and lumen borders (red line) are superimposed and a reduction in percent atheroma volume from 62% to 50% is indicated. Note the calcification (solid white linear structure) extending between 3 and 5 hours in this matched IVUS cross section in panels A and D. For near-infrared spectroscopy, a reduction in maximum lipid core burden index (4 mm) was measured; the dotted lines in panels B and E indicate the 4-mm region with greatest lipid accumulation. For optical coherence tomography, an increase in minimal fibrous cap thickness (noted by white arrows in panels C and F) from 56 µm to 158 µm was measured.

Key to Predicting Acute Events

FFR Negative

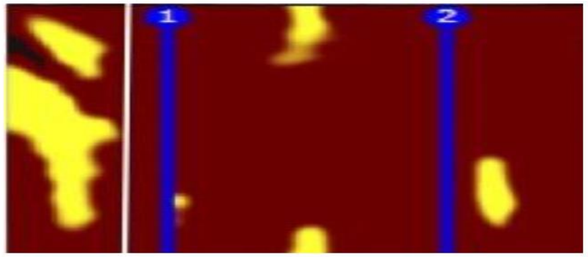


Unstable Angina at 7 months



NEW culprit at Vulnerable Plaque

Case Study Courtesy of :
Dr. Ryan Madder
Spectrum Hospital
Grand Rapids, MI



BẰNG CHỨNG LÂM SÀNG

Preventive percutaneous coronary intervention versus optimal medical therapy alone for the treatment of vulnerable atherosclerotic coronary plaques (PREVENT): a multicentre, open-label, randomised controlled trial

Seung-Jung Park, Jung-Min Ahn*, Do-Yoon Kang, Sung-Cheol Yun, Young-Keun Ahn, Won-Jang Kim, Chang-Wook Nam, Jin-Ok Jeong, In-Ho Chae, Hiroki Shiomi, Hsien-Li Kao, Joo-Yong Hahn, Sung-Ho Her, Bong-Ki Lee, Tae Hoon Ahn, Ki-Yuk Chang, Jei Keon Chae, David Smyth, Gary S Mintz, Gregg W Stone, Duk-Woo Park, for the PREVENT Investigators†*

Summary

Background Acute coronary syndrome and sudden cardiac death are often caused by rupture and thrombosis of lipid-rich atherosclerotic coronary plaques (known as vulnerable plaques), many of which are non-flow-limiting. The safety and effectiveness of focal preventive therapy with percutaneous coronary intervention of vulnerable plaques in reducing adverse cardiac events are unknown. We aimed to assess whether preventive percutaneous coronary intervention of non-flow-limiting vulnerable plaques improves clinical outcomes compared with optimal medical therapy alone.

Methods PREVENT was a multicentre, open-label, randomised controlled trial done at 15 research hospitals in four countries (South Korea, Japan, Taiwan, and New Zealand). Patients aged 18 years or older with non-flow-limiting (fractional flow reserve >0·80) vulnerable coronary plaques identified by intracoronary imaging were randomly assigned (1:1) to either percutaneous coronary intervention plus optimal medical therapy or optimal medical therapy alone, in block sizes of 4 or 6, stratified by diabetes status and the performance of percutaneous coronary intervention in a non-study target vessel. Follow-up continued annually in all enrolled patients until the last enrolled patient reached 2 years after randomisation. The primary outcome was a composite of death from cardiac causes, target-vessel myocardial infarction, ischaemia-driven target-vessel revascularisation, or hospitalisation for unstable or progressive angina, assessed in the intention-to-treat population at 2 years. Time-to-first-event estimates were calculated with the Kaplan–Meier method and were compared with the log-rank test. This report is the principal analysis from the trial and includes all long-term analysed data. The trial is registered at ClinicalTrials.gov, NCT02316886, and is complete.

Findings Between Sept 23, 2015, and Sept 29, 2021, 5627 patients were screened for eligibility, 1606 of whom were enrolled and randomly assigned to percutaneous coronary intervention (n=803) or optimal medical therapy alone (n=803). 1177 (73%) patients were men and 429 (27%) were women. 2-year follow-up for the primary outcome

Published Online
April 8, 2024
https://doi.org/10.1016/S0140-6736(24)00413-6

See Online/Comment
https://doi.org/10.1016/S0140-6736(24)00488-4

*Contributed equally

†A full list of the investigators in the PREVENT trial is in the appendix (pp 3–4)

Division of Cardiology (Prof S-J Park MD, J-M Ahn MD, D-Y Kang MD, Prof D-W Park MD) **and Division of Biostatistics** (S-C Yun PhD), **Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; Division of Cardiology, Chonnam National University Hospital, Gwangju, South Korea** (Prof Y-K Ahn MD); **Division of Cardiology, CHA University School of Medicine, CHA Ilsan Medical Center, Goyang, South Korea** (W-J Kim MD); **Division of**

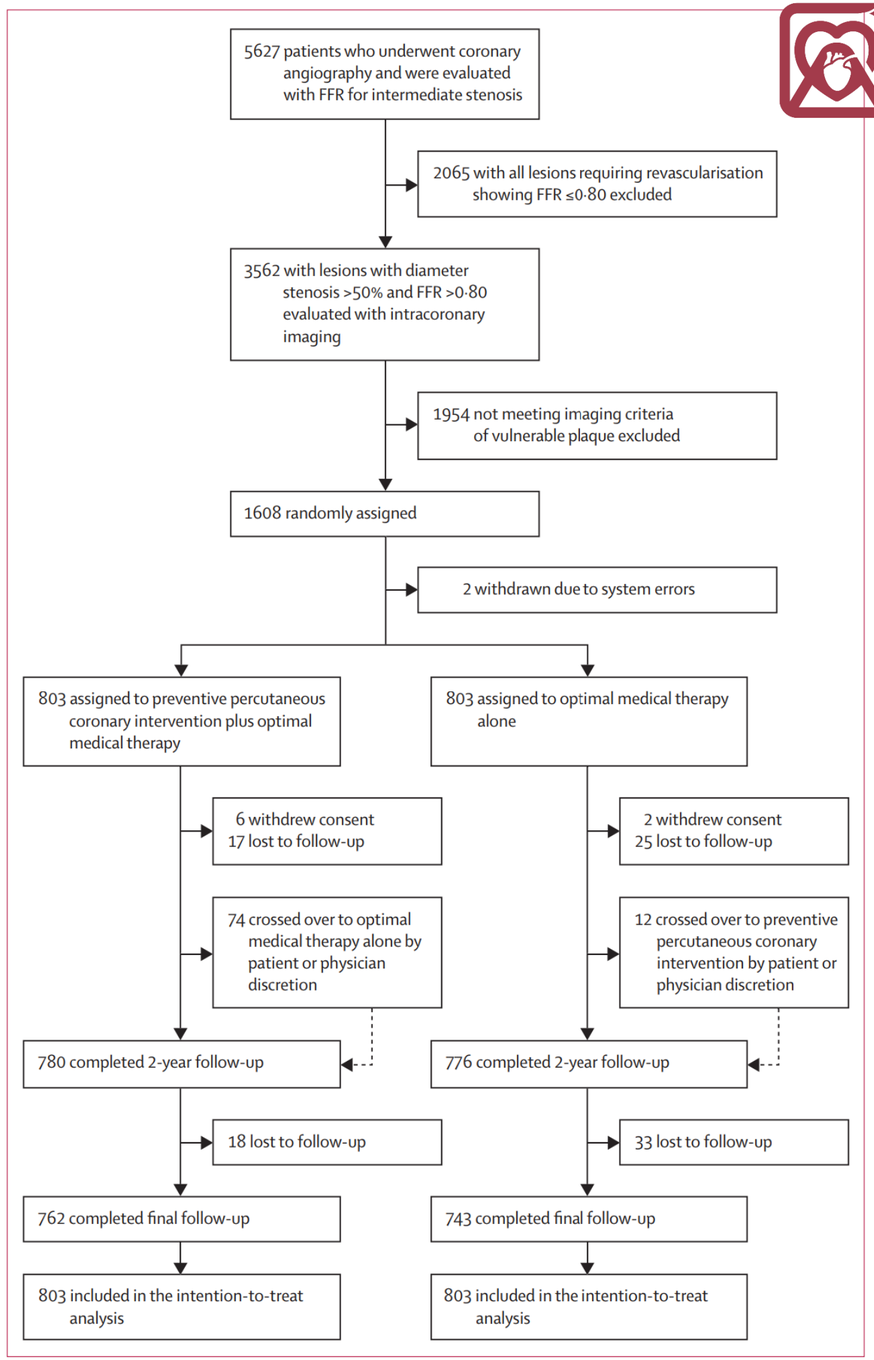


Figure 1: **Trial profile**
FFR=fractional flow reserve.

Two Large Independent Studies. Same Result.

MaxLCBI$_{4mm}$ ≥400

With the help of IVUS+NIRS imaging, results from both the Prospect II and LRP clinical studies identify non-obstructive high-risk plaques and conclude that the most vulnerable plaque contains both high PB and high lipid content.

39x
more likely to have an event within 4 years.[2,5]

PACMAN-AMI POSITIVE IVUS AND NIRS ENDPOINTS[1]	
Change Percent Atheroma Volume (PAV) by IVUS	-1.2% PAV
Change Total Atheroma Volume (TAV) by IVUS	-11.3mm
Change maxLCBI$_{4mm}$ by NIRS	-41.2 maxLCBI$_{4mm}$

PACMAN-AMI, PROSPECT II, LRP Study and many more studies show that patients remain at risk of MACE after their interventions when on statin therapy alone; more can be done.

NIRS has succeeded in observing the process of change to a more stable plaque composition[1] where other techniques were unable[4].

~70%
of the patients exhibited a vulnerable plaque substrate in the non-culprit vessel.[1]

A significant reduction in ischemia-driven revascularization (non-TLR) in the treatment group.

We have the abillity to identify non-obstructive high-risk plaque, allowing physicians to be more **proactive** with their method of care.

VULNERABLE PATIENT LEVEL ENDPOINT - RESULTS

	HR (95%CI)	p Value	Conclusion
Primary Endpoint: maxLCBI$_{4mm}$ as a continuous variable	1.18 (1.05-1.32)	0.004	For each 100 unit increase of maxLCBI$_{4mm}$ the risk of NC-MACE increases by 18%
Secondary Endpoint: maxLCBI$_{4mm}$ >400	1.89 (1.26-2.83)	0.002	A patient with maxLCBI$_{4mm}$ greater than 400 is at 89% higher risk of NC-MACE

VULNERABLE PLAQUE LEVEL ENDPOINT - RESULTS

	HR (95%CI)	p Value	Conclusion
Primary Endpoint: maxLCBI$_{4mm}$ as a continuous variable	1.45 (1.30-1.60)	<0.0001	For each 100 unit increase of maxLCBI$_{4mm}$ the risk of NC-MACE increases by 45%
Secondary Endpoint: maxLCBI$_{4mm}$ >400	4.22 (2.39-7.45)	<0.0001	A coronary segment with maxLCBI$_{4mm}$ greater than 400 is at 322% higher risk of NC-MACE

What is the LRP study?

- **PI: Ron Waksman**
- 1563 Patients enrolled in 44 Hospital Centers
- Multi-Center & Multi-National Study
- Patients with known or suspected coronary artery disease undergoing cardiac catheterization with possible ad hoc PCI for an index event in whom it also was feasible to image additional non-culprit territories were enrolled.
- A minimum of 50mm of non-culprit artery had to be imaged with LCBI in this artery blinded to the Interventional Cardiologist.
- All enrolled patients with LRP max4mmLCBI ≥ 250 and half of enrolled patients with LRP max4mmLCBI ≤ 250 were followed for 2 years.
- All MACE events were reported and adjudicated by an independent clinical events committee. MACE comprised of cardiac death, cardiac arrest, non-fatal myocardial infarction, acute coronary syndrome, revascularisation by coronary artery bypass grafting or PCI, and readmission to hospital for angina with more than 20% diameter stenosis progression related and unrelated to the treatment at index procedure.

VULNERABLE PATIENT LEVEL ENDPOINT - RESULTS

	HR (95%CI)	p Value	Conclusion
Primary Endpoint: $maxLCBI_{4mm}$ as a continuous variable	1.18 (1.05-1.32)	0.004	For each 100 unit increase of $maxLCBI_{4mm}$ the risk of NC-MACE increases by 18%
Secondary Endpoint: $maxLCBI_{4mm}$ >400	1.89 (1.26-2.83)	0.002	A patient with $maxLCBI_{4mm}$ greater than 400 is at 89% higher risk of NC-MACE

VULNERABLE PLAQUE LEVEL ENDPOINT - RESULTS

	HR (95%CI)	p Value	Conclusion
Primary Endpoint: $maxLCBI_{4mm}$ as a continuous variable	1.45 (1.30-1.60)	<0.0001	For each 100 unit increase of $maxLCBI_{4mm}$ the risk of NC-MACE increases by 45%
Secondary Endpoint: $maxLCBI_{4mm}$ >400	4.22 (2.39-7.45)	<0.0001	A coronary segment with $maxLCBI_{4mm}$ greater than 400 is at 322% higher risk of NC-MACE

What is the PROSPECT II study?

- **PI: David Erlinge**
- 902 pts with troponin + ACS after successful PCI enrolled at 16 centers
- Median follow-up 3.7 years
- After successful treatment of all flow-limiting lesions in pts with recent MI (STEMI or troponin + NSTEMI), intravascular imaging was performed in the proximal 6-10 cm of all 3 coronary arteries with a combination NIRS-IVUS catheter
- Study looked at high risk plaque characterization such as: mx(4)LCBI of 324.7, Plaque Burden ≥70% and Minimum Lumen Area < 4mm2

- Following treatment of flow-limiting lesions in AMI with contemporary DES, Mace occurred in 14.4% of patients at median 3.7 year follow up.
- 8.0% were caused by unanticipated events arising from untreated non-flowlimiting plaques vs. 4.6% from recurrent events at treated culprit lesions
- The combination of lipid-rich plaque and large plaque burden identified vulnerable plaques that placed patients at especially high risk for future MACE

What is the PACMAN-AMI study?

- **PI: Professor Lorenz Räber**
- 300 Patients enrolled
- Multi-Center & Multi- National Study
- Understand the impact of Statins and alirocumab (PCSK9i) on coronary plaque
- PACMAN-AMI reveals that Alirocumab is able to achieve this MACE rate reduction by reducing the size of LRP as detected by NIRS[1,3].
- Early intervention on LRP found by NIRS to reduce risk of MACE in ACS patients[1].

- PACMAN-AMI demonstrated the mechanism of MACE rate reduction from lowering LDL that starts with NIRS LRP.
- This allows for patients to be identified by LRP for greatest benefit from PCSK9i administration.

Endpoints, all met with statistical significance:

Change Percent Atheroma Volume(PAV) by IVUS..... **-1.2% PAV**

Change Total Atheroma Volume (TAV) by IVUS..... **-11.3 mm^3**

Change $mxLCBI_{4mm}$ by NIRS..... **-41.2 $mxLCBI_{4mm}$**

Change in min Fibrous Cap Thickness by OCT..... **+29.7 um**

JSCAI
The official journal of the Society for Cardiovascular Angiography & Interventions

Imaging and Physiology in Focus

Near-Infrared Spectroscopy Detects Lipid-Rich Plaque Preceding ST-Segment Elevation Myocardial Infarction

Shazil Mahmood, MD *, Samia Mazumder, MD, Ryan D. Madder, MD

Department of Cardiovascular Medicine, William Beaumont University Hospital, Corewell Health East, Royal Oak, Michigan

Case report

A 57-year-old woman with unstable angina underwent invasive coronary angiography demonstrating a culprit lesion in the midsegment of the right coronary artery (RCA) (Figure 1A). Combined near-infrared spectroscopy (NIRS) and intravascular ultrasound (IVUS) imaging of the culprit lesion before stent placement demonstrated a plaque burden (PB) of 84% by IVUS and a large lipid-rich plaque (LRP) by NIRS characterized by a maximum lipid core burden index in 4 mm ($maxLCBI_{4mm}$) of 668 (Figure 1B). NIRS also demonstrated LRP extending beyond the distal angiographic margin of the culprit lesion at the site of mild angiographic stenosis (Figure 1C). The patient underwent successful percutaneous coronary intervention (PCI) using a stent of sufficient length to cover both the culprit lesion and the adjacent LRP. Post-PCI NIRS-IVUS demonstrated an optimal stent result. Final angiography showed a moderate severity nonculprit lesion in the distal RCA just proximal to the bifurcation (Figure 1D). Review of the post-PCI NIRS-IVUS images revealed this nonculprit lesion had a minimum luminal area (MLA) of 5.3 mm^2, a PB of 55%, and a large lipid burden with a $maxLCBI_{4mm}$ of 679 (Figure 1E, F). Owing to an MLA of 5.3 mm^2 by IVUS and only moderate stenosis severity by angiography, PCI was not performed on this nonculprit lesion. The patient was discharged home on dual antiplatelet therapy and a high-intensity statin.

Approximately 5 years later, the patient presented to the emergency room with acute chest pain and was found to have an inferior ST-segment elevation myocardial infarction (STEMI). She was taken emergently to the catheterization laboratory and found to have a de novo culprit lesion in the distal RCA just proximal to the bifurcation at the site of the large LRP detected by NIRS 5 years earlier (Figure 1G, H). The patient underwent successful primary PCI of the culprit lesion in the distal RCA.

Discussion

This case emphasizes multiple known facts about NIRS findings at culprit and nonculprit lesions and highlights several knowledge gaps that exist with respect to NIRS-detected LRP. Among the known facts, multiple previous studies among patients with acute coronary syndromes (ACS) have shown NIRS frequently identifies large LRP having a $maxLCBI_{4mm}$ >400 at culprit lesion sites. Consistent with these studies, the culprit lesion triggering the index ACS in the present case had a NIRS $maxLCBI_{4mm}$ of 668. In addition to its consistency with previous NIRS studies, this finding is also congruent with histopathologic studies demonstrating the rupture of large LRP to be responsible for the majority of ACS events. In the present case, NIRS also detected LRP extending beyond the angiographic culprit lesion margins, a finding previously reported to be commonplace. This observation emphasizes the importance of using intracoronary imaging to identify the optimal landing zones for stent deployment, as landing a stent edge within an LRP has been associated with an increased risk of subsequent stent-related events.[1] Based on this premise, a longer stent was used during the baseline PCI to cover both the culprit lesion and adjacent LRP.

Perhaps, the most interesting aspect of this case relates to the imaging findings of the nonculprit lesion in the distal RCA at the conclusion of the baseline procedure. Neither the moderate stenosis severity by angiography at the nonculprit site nor the IVUS MLA of 5.3 mm^2, which is well above IVUS MLA thresholds known to be associated with hemodynamic significance, would represent indications for PCI at the time the baseline case was performed. Furthermore, the PB of 55% is not in excess of the 70% PB associated with vulnerability. In contrast to the lower-risk IVUS findings, the NIRS finding of a $maxLCBI_{4mm}$ of 679 at the nonculprit site is indicative of both increased patient-level and lesion-level risk. As shown in the Lipid-Rich Plaque study, plaques having a $maxLCBI_{4mm}$ >400 carry a 4-fold increase of site-specific coronary events.[2] Similarly, in the PROSPECT II study, plaques having a $maxLCBI_{4mm}$ >325 were associated with a 7-fold increased risk of site-specific major adverse cardiovascular events.[3]

While consistent with the findings of the Lipid-Rich Plaque and PROSPECT II studies, this case also highlights several uncertainties regarding NIRS-detected LRP. First, the follow-up periods in the Lipid-Rich Plaque and PROSPECT II studies were 2 and 3.7 years,

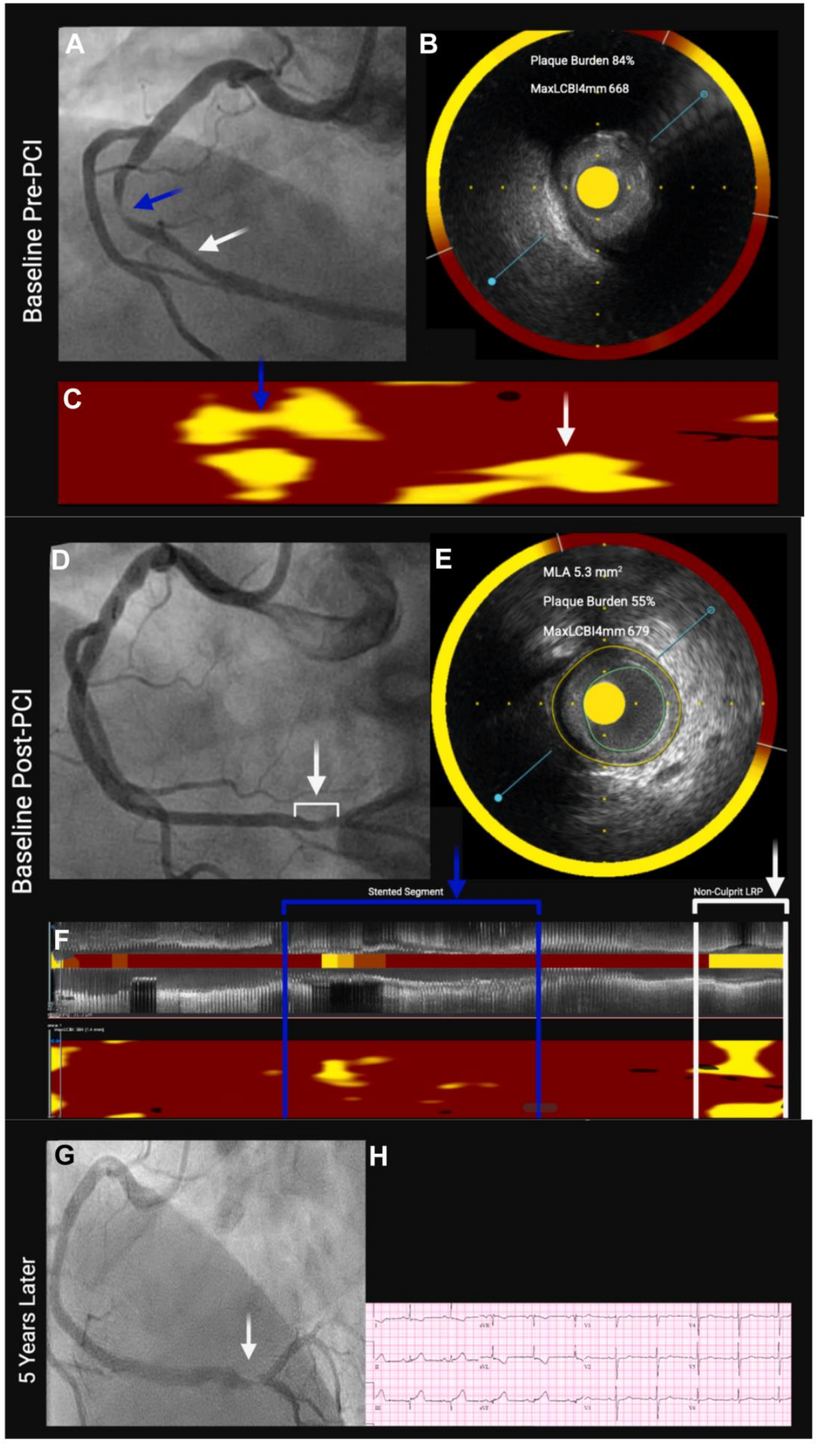
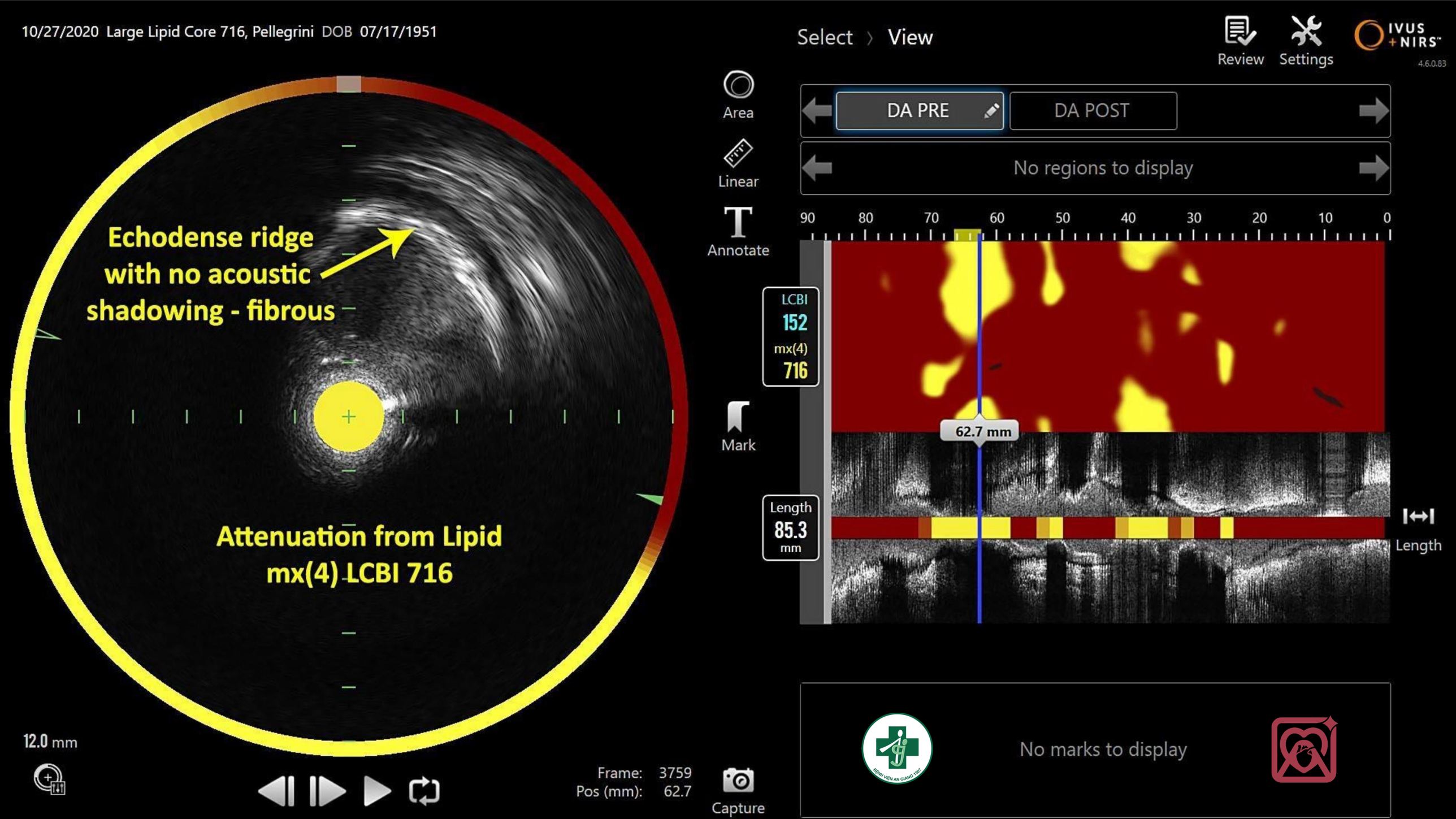


Figure 1.
Near-infrared spectroscopy (NIRS) lipid-rich plaque (LRP) at baseline followed by ST-segment elevation myocardial infarction (STEMI) 5 years later. (**A**) Baseline angiogram—blue arrow shows culprit lesion and white arrow shows mild angiographic stenosis. (**B**) Cross-sectional NIRS-intravenous ultrasound (IVUS) image of culprit lesion showing large plaque burden (PB) and large LRP. (**C**) NIRS chemogram showing culprit lesion LRP (blue arrow) and lipid corresponding to site of mild angiographic stenosis (white arrow). (**D**) Final angiogram at conclusion of baseline percutaneous coronary intervention (PCI). White bracket and arrow show nonculprit lesion with moderate angiographic stenosis. (**E**) Cross-sectional NIRS-IVUS image of nonculprit lesion in distal right coronary artery (RCA) showing adequate minimum luminal area (MLA) and moderate PB by IVUS and a high $maxLCBI_{4mm}$ by NIRS. (**F**) NIRS chemogram showing stenting segment (blue brackets) and large LRP at nonculprit site in distal RCA (white brackets). (**G**) Angiogram at time of STEMI presentation 5 years later showing a culprit lesion in the distal RCA. (**H**) Electrocardiogram showing inferior STEMI.


10/27/2020 Large Lipid Core 716, Pellegrini DOB 07/17/1951
Select › View
Review
Settings
IVUS + NIRS
4.6.0.83
Area
Linear
Annotate
Mark
Capture
DA PRE
DA POST
No regions to display
90 80 70 60 50 40 30 20 10 0
LCBI
152
mx(4)
716
62.7 mm
Length
85.3
mm
Length
Echodense ridge with no acoustic shadowing - fibrous
Attenuation from Lipid mx(4) LCBI 716
12.0 mm
Frame: 3759
Pos (mm): 62.7
No marks to display

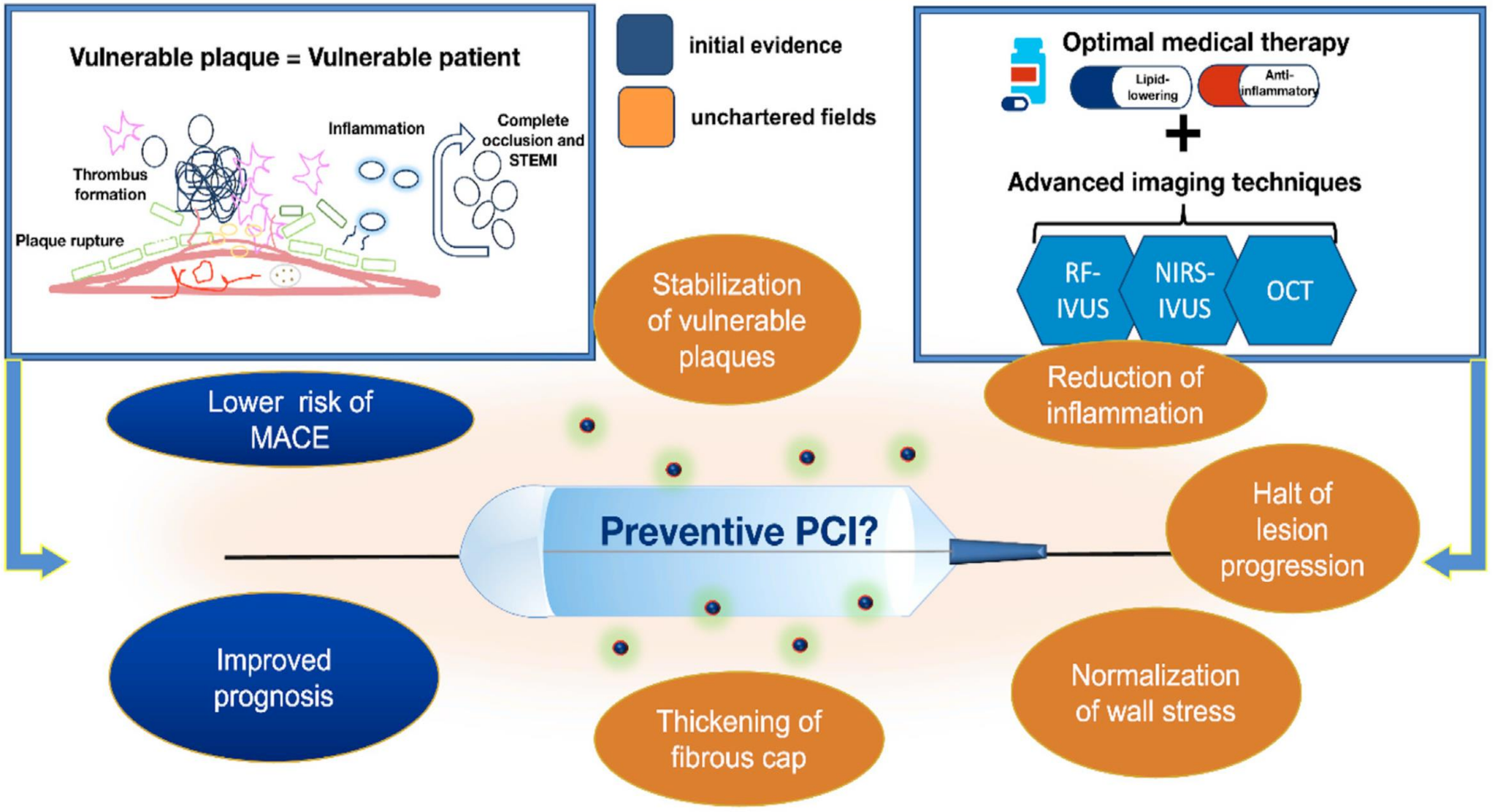
Imaging Technology Comparison

IVUS+NIRS™

ONLY the Makoto Imaging System and Dualpro IVUS+NIRS catheter offer **complete vessel characterization** for better clinical decision-making.

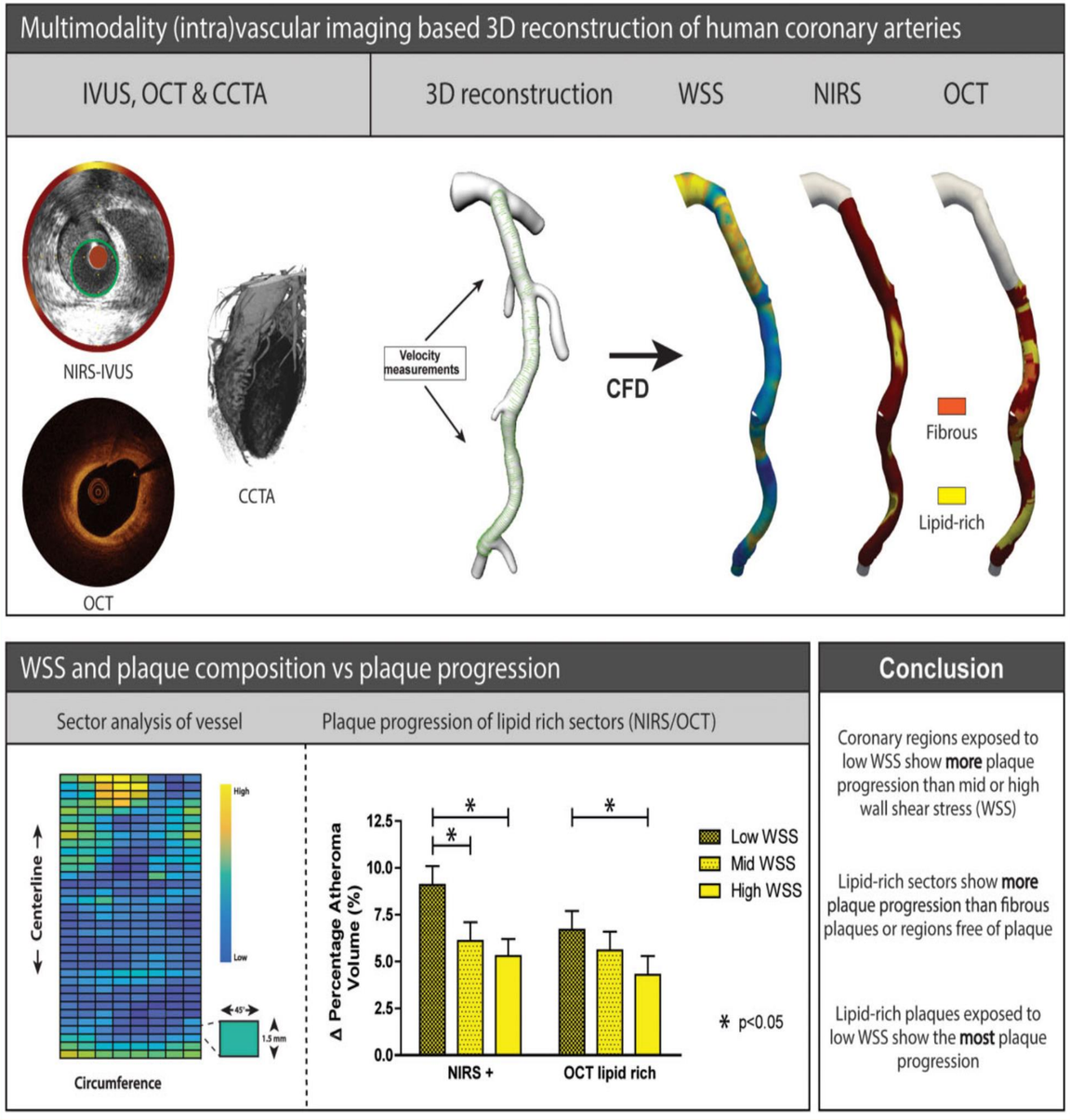
	Angiography	Angioscopy	OCT	IVUS	NIRS	Dualpro IVUS+NIRS
Lipid Core		○	○	○	●	●
Expansive Remodeling				●		●
Plaque Burden				●		●
Calcification	○			●		●
Lumen Dimension	○		●	●		●
Stent Apposition Expansion	○		●	●		●
Thin Cap			●			○
Thrombus	○	●	●	○		○

Goals, initial evidence and unmet needs of vulnerable plaques



Central Illustration. Role of preventive percutaneous coronary intervention (PCI) in vulnerable plaque. IVUS = intravascular ultrasound; MACE = major adverse cardiovascular event; NIRS-IVUS = near-infrared spectroscopy-IVUS; OCT = optical coherence tomography; RF = radiofrequency.

Graphical Abstract



Keywords Coronary artery disease • Near-infrared spectroscopy • Intravascular ultrasound • Optical coherence tomography Wall shear stress

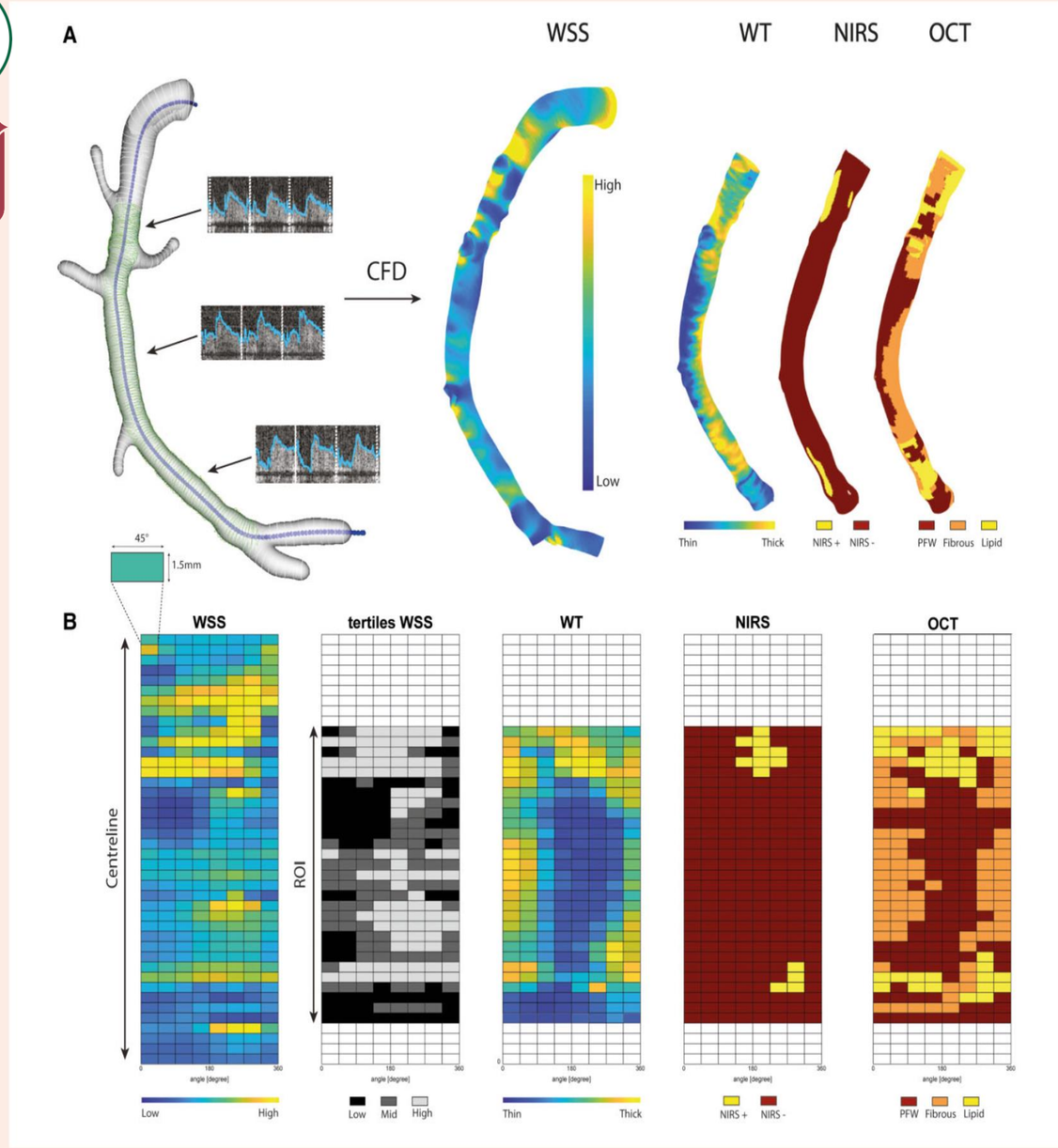


Figure 1 Methodology overview of 3D reconstruction, WSS, and data analysis matching plaque components. (*A*) Example of a 3D-reconstructed RCA. IVUS-derived lumen contours (green) were fused with the CT-derived vessel centreline (blue) and CT-derived side branch contours (white). By adding local flow measurements and using CFD, WSS was calculated in these reconstructed models. NIRS- and OCT-derived plaque phenotypes were matched and plotted on the IVUS-derived 3D reconstruction, the ROI. (*B*) From the 3D-reconstructed vessels, 2D maps were created by cutting the vessel open in the longitudinal direction. For statistical analysis, the 2D maps were divided into sectors of 1.5 mm/45°. Examples of 2D maps in this overview are as follows: the continuous WSS, the WSS tertiles (low, mid, high), wall thickness (WT), NIRS-derived plaque phenotype, and OCT-derived phenotype.