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Initial experience with near-infrared spectroscopy in the treatment of coronary atherosclerotic disease in Mexico

Experiencia inicial con espectroscopia de infrarrojo cercano en el tratamiento de la enfermedad aterosclerótica coronaria en México

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Palabras clave: *espectroscopia de infrarrojo cercano, ultrasonido intravascular, placa vulnerable, índice de carga del núcleo lipídico, imagenología de aterosclerosis coronaria.*

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ABSTRACT

Atherosclerotic coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide. In recent years, the emergence of intravascular imaging technologies has enabled more precise characterization of vulnerable plaques-those with a high lipid core burden and increased risk of rupture. Near-infrared spectroscopy (NIRS), when integrated with intravascular ultrasound (IVUS), constitutes an advanced diagnostic modality capable of identifying high-risk lesions even in the absence of non-ischemia inducing stenosis. This combined IVUS-NIRS platform enables real-time chemical characterization of atherosclerotic plaques through the lipid core burden index (LCBI), while simultaneously providing detailed structural assessment via IVUS. Recently adopted in interventional cardiology practices across Mexico and Latin America, this technology enhances risk stratification and supports more informed decision-making during percutaneous coronary intervention (PCI). In this article, we present an updated review of the technical fundamentals, clinical utility, and key evidence supporting the use of IVUS-NIRS in coronary artery disease, including pivotal findings from the LRP, PROSPECT II, and PREVENT trials. These studies highlight the predictive value and therapeutic potential of IVUS-NIRS in guiding PCI beyond conventional angiographic or physiological parameters. Additionally, we share the initial clinical experience in Mexico, including representative case images that illustrate the practical application of IVUS-NIRS in daily practice. This imaging modality provides

RESUMEN

La enfermedad coronaria ateroesclerótica (EAC) continúa siendo una de las principales causas de morbilidad y mortalidad a nivel mundial. En los últimos años, la aparición de tecnologías de imagen intravascular ha permitido una caracterización más precisa de las placas vulnerables, aquellas con una alta carga de núcleo lipídico y mayor riesgo de ruptura. La espectroscopia cercana al infrarrojo (NIRS), cuando se integra con el ultrasonido intravascular (IVUS), constituye una modalidad diagnóstica avanzada capaz de identificar lesiones de alto riesgo incluso en ausencia de estenosis inductoras de isquemia. Esta plataforma combinada IVUS-NIRS proporciona una evaluación química en tiempo real de la placa ateroesclerótica a través del índice de carga lipídica (LCBI), al tiempo que ofrece una valoración estructural detallada mediante IVUS. Recientemente incorporada a la práctica de la cardiología intervencionista en México y América Latina, esta tecnología mejora la estratificación del riesgo y facilita la toma de decisiones más informadas durante la intervención coronaria percutánea (ICP). En este artículo, presentamos una revisión actualizada sobre los fundamentos técnicos, la utilidad clínica y la evidencia clave que respalda el uso de IVUS-NIRS en la enfermedad arterial coronaria, incluyendo hallazgos fundamentales de los ensayos clínicos LRP, PROSPECT II y PREVENT. Estos estudios destacan el valor predictivo y el potencial terapéutico de IVUS-NIRS para guiar la ICP más allá de los parámetros angiográficos o fisiológicos convencionales. Asimismo, compartimos la experiencia clínica inicial en México, incluyendo imágenes representativas de casos que ilustran la aplicación práctica de

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an additional diagnostic layer that supports optimized lesion selection, guides intensification of lipid-lowering and antithrombotic therapy, and contributes to a more personalized, evidence-based approach in contemporary interventional cardiology.

IVUS-NIRS en la práctica diaria. Esta modalidad de imagen proporciona una capa diagnóstica adicional que permite optimizar la selección de lesiones, orientar la intensificación de la terapia hipolipemiante y antitrombótica, y contribuir a un enfoque más personalizado y basado en evidencia en la cardiología intervencionista contemporánea.

Abbreviations:

ACS = acute coronary syndromes
CAD = coronary artery disease
iFR = Instantaneous Wave-Free Ratio
IVUS = intravascular ultrasound
LCBI = lipid core burden index
LCP = lipid core plaque
LRP = lipid-rich plaque
NIRS = near-infrared spectroscopy
OMT = optimal medical therapy.
PCI = percutaneous coronary intervention

INTRODUCTION

The rupture of lipid-rich plaques is the principal mechanism responsible for the onset of acute coronary syndromes (ACS), including myocardial infarction and sudden cardiac death. Nevertheless, the management of coronary artery disease (CAD) has focused primarily on hemodynamically significant lesions, as assessed by either hyperemic or non-hyperemic physiological indices. In spite of that, recent evidence has demonstrated that a considerable proportion of vulnerable plaques are non-obstructive and do not induce myocardial ischemia.[1-3] The combined use of intravascular ultrasound (IVUS) and near-infrared spectroscopy (NIRS) enables accurate in vivo characterization of the chemical composition of atherosclerotic plaques and facilitates the identification of lesions that meet criteria for high rupture risk.[4-8]

For the first time, this dual-modality technology is available in Mexico. In this context, we present a review of the IVUS-NIRS platform, an overview of its clinical utility, and representative imaging cases derived from our initial experience in the country.

NIRS employs near-infrared light to interrogate the chemical properties of arterial tissue. It capitalizes on the fact that various substances absorb and scatter NIR light (wavelengths from 800 to 2,500 nm) differently across the spectrum. A NIRS spectrometer emits light into the tissue and measures the fraction of reflected light over a broad range of optical wavelengths. The output is plotted as an absorbance spectrum, with wavelength on the x-axis, allowing characterization of lipid-specific signatures.[9,10]

Lipids exhibit a characteristic absorption pattern due to the presence of carbon-hydrogen bonds in their molecular structure. This enables the generation of chemical maps, or chemograms, that highlight regions with high lipid content, quantified by the lipid core burden index (LCBI).[11] When combined with IVUS, this technology provides structural insights into plaque architecture and thickness, offering high specificity for lipid detection while producing interpretable, color-coded chemograms.[12] As with other IVUS platforms, the IVUS-NIRS system can be used *in vivo* with whole blood, without requiring contrast or saline flushes for image acquisition.[13]

Clinical evidence

There is a growing body of evidence supporting the utility of structural characterization of coronary atherosclerotic plaques.[14] Among the most pivotal studies is the prospective Lipid-Rich Plaque (LRP) trial,[15] which demonstrated that NIRS can safely and effectively identify vulnerable plaques and patients at increased risk of future coronary events. Specifically, plaques with a maxLCBI4mm ≥ 400 (cut-off value obtained from previous observational studies that found that atherosclerotic plaques causing acute coronary syndromes exhibited significantly elevated values of maxLCBI4mm ≥ 400) were associated with nearly double the risk of major adverse

cardiovascular events (MACE) compared to plaques with values < 400 (adjusted HR: 1.89; p = 0.0021) over a two-year follow-up period[16] *(Figure 1)*.

Subsequently, the PROSPECT II study evaluated the combined use of intravascular ultrasound (IVUS) and near-infrared spectroscopy (NIRS) in non-culprit arteries following a recent myocardial infarction, enrolling 898 patients with a median follow-up of four years.[8] The investigators identified three major plaque-level characteristics as predictors of adverse cardiovascular events during follow-up: high lipid burden defined by a maxLCBI4mm ≥ 324.7 (OR:7.8), plaque burden ≥ 70% (OR:12.9), and minimum lumen area (MLA) ≤ 4 mm^2 (OR:4.97). Lesions exhibiting both high lipid content and large plaque burden were associated with a 7% rate of adverse events at four years, while lesions without these features had an event rate of only 0.2%[17] *(Figure 2)*, suggesting that the combination of these two factors are the major contributors to the likelihood of atherosclerotic plaque rupture, even without taking into account the minimum luminal area.

Most recently, the PREVENT randomized controlled trial assessed the safety and efficacy of preventive PCI in non-ischemia-inducing vulnerable plaques (defined as fractional flow reserve > 0.80), compared with optimal medical therapy (OMT) alone.[18] The trial included 1,606 patients with stable CAD or acute coronary syndromes. The target lesions were not responsible for the index event, and patients were randomized to preventive PCI plus OMT (n = 803) or OMT alone (n = 803), with a two-year follow-up. Vulnerable plaques were identified based on at least two of the following criteria: MLA < 4.0 mm^2, plaque burden > 70%, maxLCBI4mm > 315, or thin-cap fibroatheroma (identified via optical coherence tomography). The incidence of the primary endpoint was significantly lower in the PCI group (0.4%) compared to the OMT group (3.4%), yielding an absolute risk reduction of 3.0% (p = 0.0003). At seven-year follow-up, the cumulative MACE rate remained lower in the PCI group (6.5%) versus the OMT group (9.4%)[19] *(Figure 3)*.

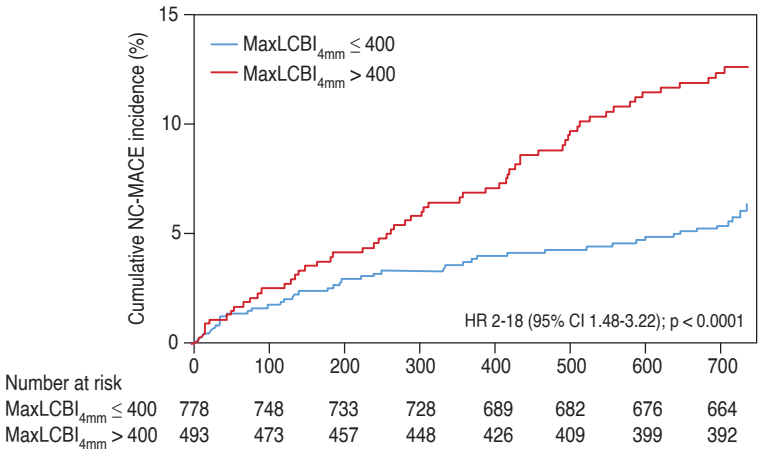

Figure 1: LRP study 24-month patient-level cumulative incidence of non-culprit MACE. Patients with maxLCBI$_{4mm}$ > 400 had an unadjusted HR of 2.18 (95% CI 1.48-3.22; p < 0.0001) and an adjusted HR of 1. 89 (1.26-2.83; p = 0. 0021) to have non-culprit MACE relative to patients with maxLCBI$_{4mm}$ of 400 or less.[15]

Technical aspects

The IVUS-NIRS catheter currently available in Mexico (DUALPRO-MAKOTO, Nippro, Japan) is compatible with 6 French or larger guide catheters and integrates both IVUS and NIRS sensors *(Figure 4)*, allowing simultaneous acquisition of structural and chemical imaging. The IVUS component operates within a frequency range of 35 to 65 MHz, which can be adjusted based on the required depth of penetration to generate high-resolution intravascular images. Automated pullback (up to 150 mm) is required for IVUS-NIRS image acquisition, with user-selectable speeds of 0.5, 1.0, or 2 mm/s. Manual IVUS image acquisition is also possible.

Once the pullback is completed, the main screen displays three key panels *(Figure 5)*. On the left, cross-sectional IVUS images are shown, with a surrounding halo indicating axial lipid distribution-red representing lipid-negative areas and yellow denoting lipid-rich zones. The upper-right panel shows the chemogram, a two-dimensional visual map that represents the probability of the presence of a lipid core plaque (LCP) within specific scan regions. High probabilities are represented in yellow, while lower probabilities gradually transition to red.

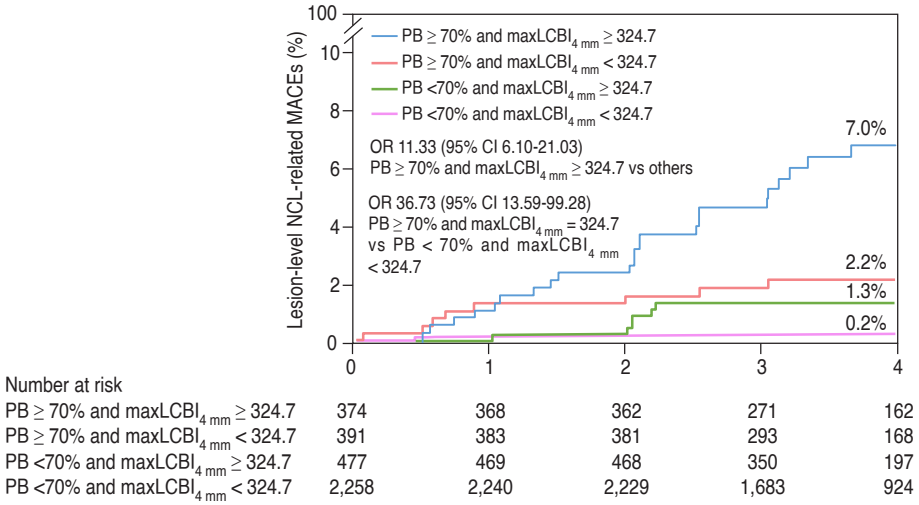

Figure 2:

Non-culprit lesion level MACEs at four years in the PROSPECT II study. The combination of high lipid content (maxLCBI4mm ≥ 324.7) and large plaque burden (≥ 70%) conferred the highest risk of MACEs (OR of 11.33) versus not having one of these plaque characteristics. Furthermore, not having both of them adjudged a very low probability of MACEs (0.2% of MACEs at four years).[8]

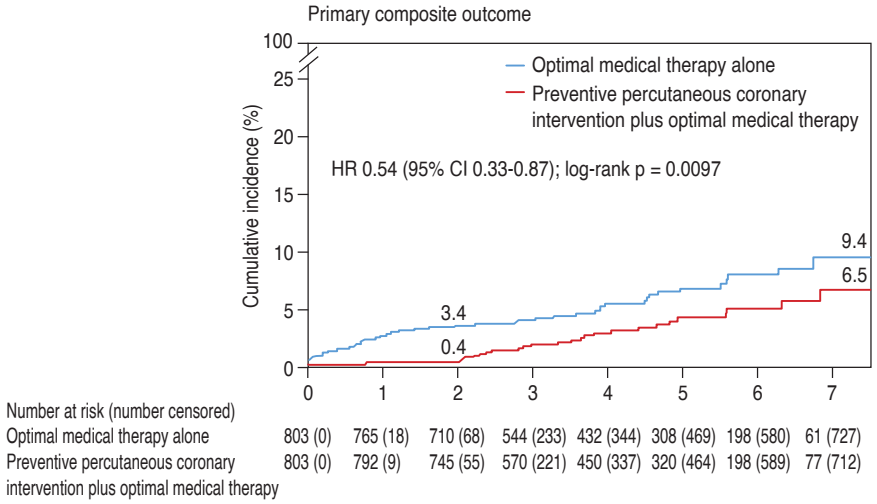

Figure 3:

Cumulative incidence of the primary composite outcome at seven years in the PREVENT trial. Although the frequency of events was low, PCI of non-ischemia-inducing lesions (plus optimal medical therapy) with high-risk characteristics resulted in fewer adverse events than optimal medical therapy alone.[18]

Yellow highlights are displayed when the lipid probability exceeds 0.6 at any point. To the left of the chemogram, the lipid core burden index (LCBI) is automatically calculated and presented. This index is derived from the ratio of positive lipid probability scores (> 0.6) to all valid lipid data points within the selected segment and is expressed on a 0-1,000 scale, reflecting low to high lipid burden. The system also displays the maximum LCBI in any predefined 4 mm segment (maxLCBI4mm), along with its exact location. The use of the 4 mm segment stems primarily from its practical implementation in early NIRS systems. Its length represents a compromise between spatial resolution and clinical relevance, allowing detection of focally dangerous areas without diluting them into longer segments. This 4 mm section of the assessed artery is quite narrow but sufficient to consider a surrogate for the circumferential extension of a lipid core, becoming the standard in clinical and validation studies, as it provides a focal and reproducible metric. The bottom-right panel provides a longitudinal IVUS image, overlaid with a block-level chemogram. This view is divided into 2 mm segments and uses a four-color scale (yellow, brown, orange, red) to summarize lipid probability from highest to lowest within each block.

Initial experience and utility in daily practice

Although the IVUS-NIRS platform has been available in Mexico for less than one year, it has rapidly proven valuable in both the diagnostic and interventional phases of coronary evaluation. During diagnostic procedures, IVUS offers high-resolution assessment of plaque morphology and vessel architecture, while NIRS provides chemical insight into intraplaque composition. During PCI, this technology allows intraprocedural assessment of stent results and identification of high-risk residual plaques.[20]

In our initial experience, in over 50 cases in an «all comers» fashion for either stable disease or acute coronary syndromes, the Makoto IVUS-NIRS system has been complication-free (0% of catheter-induced complications) and has identified multiple examples of lipid-rich atherosclerotic plaques. These findings have been used in clinical decision-making, allowing individualized treatment strategies.[21-23] Of these 54 initial cases in our experience, the information provided by IVUS-NIRS, in addition to the conventional use of IVUS for technical guidance of our PCIs, resulted in stenting of two non-culprit (two different patients) non-ischemia-inducing atherosclerotic plaques *(Figures 6 and 7)* that had been previously assessed by Instantaneous Wave-Free Ratio (iFR) but with very high risk characteristics by IVUS-NIRS, high-risk location (proximal coronary segments), and concomitant high clinical risk factors (both acute coronary syndrome context). In addition, lesions with a fibrotic appearance on IVUS were frequently observed, but with

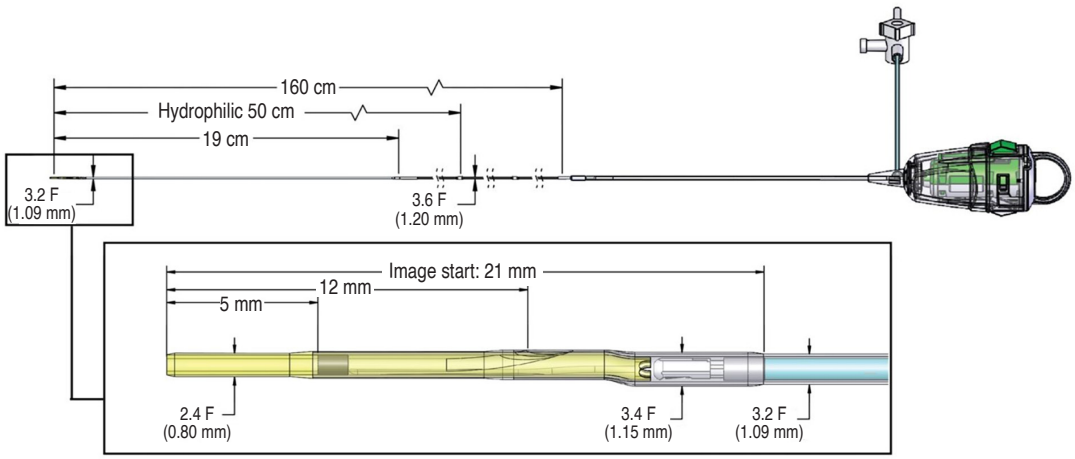

Figure 4:

Dual-Pro Makoto Catheter.[25]

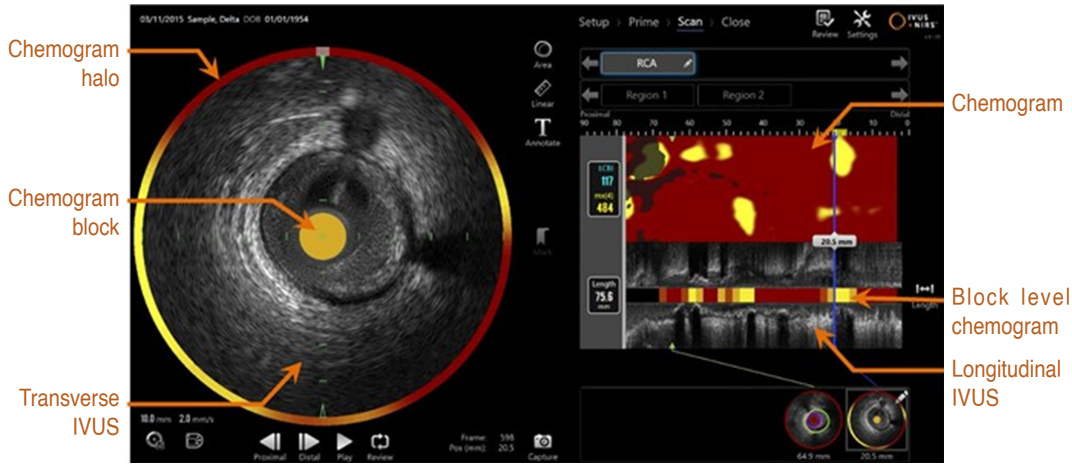

Figure 5:

Main working display of the Makoto IVUS-NIRS console.
IVUS = integrated with intravascular ultrasound. NIRS = near-infrared spectroscopy.

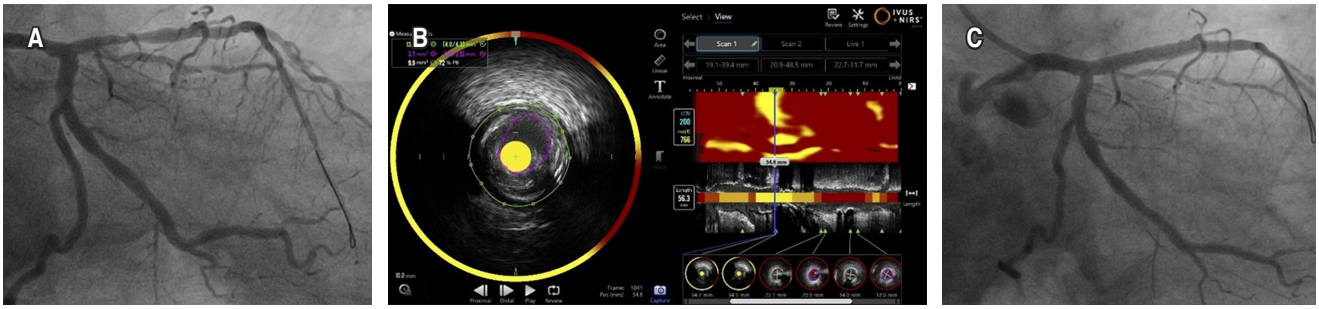

Figure 6: A) Non-ischemia inducing stenosis in the proximal Left anterior descending by Instantaneous Wave-Free Ratio (iFR 0.92). **B)** High-risk features identified by IVUS-NIRS: on the left, the axial IVUS image reveals a mixed-content atherosclerotic lesion with heterogeneous appearance and multiple intraplaque hypoechoic zones. In the upper left, measurements show a minimum lumen area (MLA) of 3.7 mm^2 and a plaque burden (PB) of 72%. The circumferential halo highlights the axial distribution of lipid content. On the right, the longitudinal chemogram demonstrates a high lipid burden with a maxLCBI$_{4mm}$ of 766. In the bottom-right, the longitudinal IVUS image combined with a block-level chemogram shows intense yellow areas representing regions of maximal lipid concentration. **C)** Angiographic result after IVUS-guided stent implantation.
IVUS = integrated with intravascular ultrasound. NIRS = near-infrared spectroscopy.

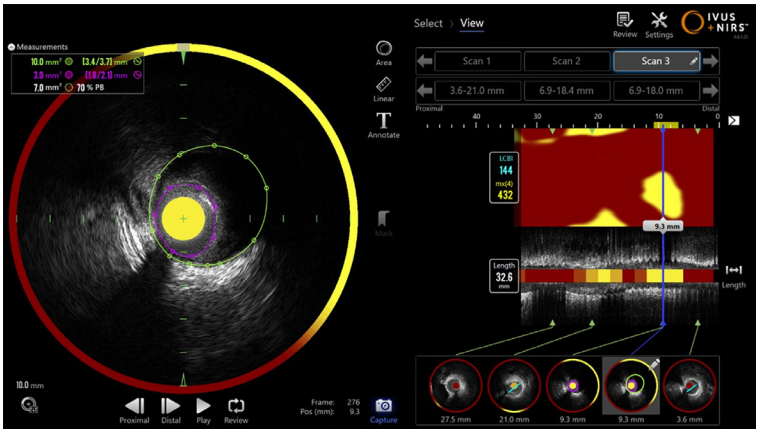

Figure 7: Atherosclerotic plaque at the right coronary artery, predominantly composed of lipid-rich content, evidenced by a maxLCBI$_{4mm}$ of 432. This finding is consistent with predominantly hypoechoic regions in the axial IVUS image. The circumferential yellow halo confirms the axial localization of intraplaque lipid. Considered a high-risk plaque by high lipid core burden, high plaque burden (70%), and a minimum lumen area of less than 4 mm^2.
IVUS = integrated with intravascular ultrasound.

considerable amount of intraplaque lipids by NIRS *(Figure 8)*. Also, the other nine non-ischemia-inducing atherosclerotic plaques with high lipid burden by IVUS-NIRS were found (maxLCBI4mm > 315) at distal coronary segments but without other characteristics associated with plaque vulnerability (MLA > 4 mm or plaque burden < 70%). Nevertheless, that discovery led to an intensification of their lipid-lowering treatment beyond that originally intended, specifically the addition of PCSK9 inhibitors to the usual statin plus ezetimibe regimen.

While a uniform consensus has yet to be established, current data suggest that a vulnerable atherosclerotic plaque-prone to rupture or erosion-is currently defined by a combination of a maxLCBI4mm > 315 on NIRS (324 in the PROSPECT trial), a minimum lumen area < 4.0 mm^2, and a plaque burden > 70% on IVUS (or a fibrous cap thickness < 65 µm on optical coherence tomography).[17] This additional diagnostic layer provided by IVUS-NIRS may, in highly selected cases, support a decision to intervene on a non-ischemia-inducing lesion with high rupture potential. Conversely, it may justify a conservative approach in borderline functional lesions that lack vulnerability features. Furthermore, identifying plaques with high lipid content should prompt intensification of lipid-lowering therapy, aggressive modification of cardiovascular risk factors (e.g., smoking cessation, treatment of hypertension or diabetes), and closer clinical follow-up.[24]

The implementation of this technology in Mexico is still associated with several challenges. There is limited availability of IVUS-NIRS consoles nationwide, and the system carries

a higher cost compared to basic intravascular ultrasound platforms. Although the acquisition of NIRS-derived images requires only a short learning curve, proper interpretation across various clinical scenarios necessitates specific training and experience.

CONCLUSION

The incorporation of IVUS-NIRS technology into interventional cardiology practice in Mexico represents a significant advancement in the structural and functional characterization of coronary atherosclerotic plaques. Historically, therapeutic decision-making has been guided primarily by angiographic and physiological criteria, which, although effective for evaluating hemodynamically significant stenoses, are limited in their ability to detect biologically vulnerable lesions at high risk of rupture. IVUS-NIRS bridges this gap by integrating two complementary modalities: near-infrared spectroscopy for direct detection of intraplaque lipid content, and intravascular ultrasound for high-resolution assessment of plaque morphology, burden, luminal dimensions, and post-PCI outcomes.

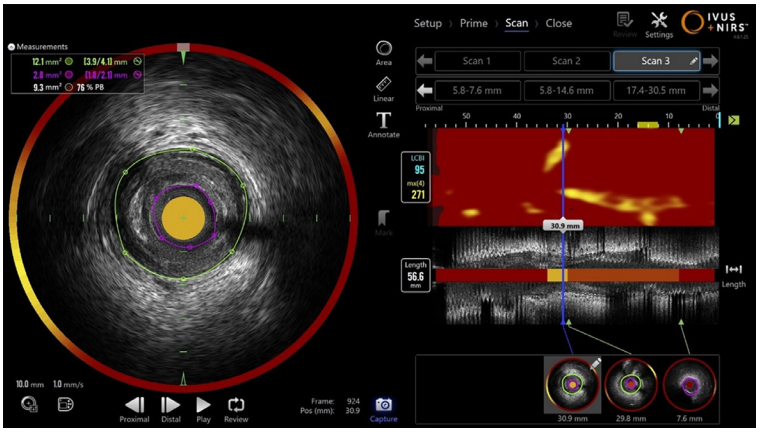

Figure 8: Image of a mixed atherosclerotic plaque at the right coronary artery. The axial IVUS image displays hypoechoic regions interspersed with isoechoic and hyperechoic areas. Evaluation of the corresponding chemogram revealed a moderate lipid burden with a $maxLCBI_{4mm}$ of 271, consistent with the mixed nature of the plaque. Notice the high plaque burden (76%) and the minim lumen area of 2.8 mm^2. The iFr of this lesion resulted in 0.82, so it was treated with stenting.
IVUS = integrated with intravascular ultrasound.

This combined imaging strategy enables more refined risk stratification, supporting percutaneous interventions tailored to the biological vulnerability of each lesion. The availability of IVUS-NIRS in Mexico and across Latin America opens the door to a new paradigm in precision cardiovascular medicine. Its integration into routine cath lab workflows has the potential not only to optimize immediate clinical outcomes but also to establish preventive strategies for high-risk patients, enabling more precise decisions regarding when to intervene and whom to target for intensified medical therapy.

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