Intracoronary imaging techniques for the diagnosis of calcified lesions

NATALIA PINILLA, JOSÉ GILDARDO PAREDES-VÁZQUEZ, ÁNGELA MARÍA HERRERA PEÑA, FERNANDO GUERRERO PINEDO, NIEVES GONZALO

Intracoronary imaging techniques currently play a crucial role in the evaluation of calcified lesions, which are present in over 30% of lesions requiring revascularization. These lesions are associated with a higher rate of both short- and long-term cardiovascular events compared to noncalcified lesions(1,2). Furthermore, coronary calcification is more prevalent in patients of advanced age, those with a history of smoking, hypertension, diabetes, and chronic kidney disease. Calcification is also associated with greater plaque burden and anatomical complexity, including long lesions, vessel tortuosity, bifurcations, and chronic total occlusions(3-5).

Percutaneous coronary intervention (PCI) of calcified lesions is associated with reduced stent expansion and increased risk of peri-procedural complications(5,6). After adjustment for clinical and anatomic factors, coronary calcification is an independent predictor of cardiovascular events, stent failure, need for revascularization of the treated lesion, myocardial infarction, and death(4,7,8). For these reasons, intracoronary imaging for plaque assessment is recommended to detect significant calcification, which may require plaque modification to prevent complications and stent underexpansion.

The use of intracoronary imaging techniques such as intravascular ultrasound (IVUS) or optical coherence tomography (OCT) is valuable for detecting, evaluating, and selecting plaque modification strategies. These imaging modalities contribute to achieve better results in terms of stent expansion, which is a key predictor of stent failure(9). International guidelines currently recommend the use of intracoronary imaging in the management of complex lesions(9-12).

CORONARY CALCIFICATION DETECTION AND EVALUATION

Angiography has limited sensitivity for calcium detection and does not reliably identify the key features to decide the need and type of plaque modification techniques(2). The sensitivity of angiography ranges from 40% in mild calcifications to 85% in calcifications distributed across all four quadrants of the artery's circumference. At least 100 degrees of circumference are

TABLE 1. Comparison of imaging techniques for the detection, characterization and quantification of calcium

Type of lesion	Angiography	IVUS	OCT
Lesion with moderate calcium content	★	★★	★★★
Lesion with high calcium content	★★★	★★★	★★★
Plaque with necrotic core	🛇	★★★	★
Depth	🛇	🛇	★★★
Length	🛇	★	★★★
Calcium arc	🛇	★★★	★★★
Deep calcium	★	★★★	★★

IVUS: Intravascular Ultrasound; OCT: Optical Coherence Tomography.

necessary to reliably observe calcium with angiography(1,2). Both IVUS and OCT have a high sensitivity and specificity for calcium detection; they also allow the evaluation of the type of calcification and its extension, important features to determine treatment options(1,2,13). IVUS exhibits a sensitivity of 86.7% and a specificity of 93.3%, whereas OCT typically demonstrates a lower sensitivity of 77%, with variability depending on the operator's experience with the imaging technique(14). *Table 1* shows the differences between angiography, IVUS and OCT with respect to calcium detection.

TYPES OF CALCIFICATION

According to the *calcification pattern*, calcium plaques can be divided into:

1. Nodular pattern

When calcium protrudes into the lumen with nodular morphology and posterior shadow (*Fig. 1*).

2. Parietal pattern

The parietal pattern allows the identification of the following characteristics:

- According to *circumferential extent*:
  a. **Eccentric:** when calcium covers <180° of vessel circumference.
  b. **Concentric:** when calcium covers >180° of vessel circumference.
- According to *depth*:
  a. **Superficial calcium:** when calcium is closer to the lumen than to the media. The fibrous cap is <0.5 mm (*Fig. 2*).
  b. **Deep calcium:** when calcium is closer to the adventitia than to the lumen. The fibrous cap is >0.5 mm. If the calcium is very deep, the internal border, but not the external border, can be identified (*Fig. 3*).
- According to the *longitudinal extent*: which can be measured in the longitudinal projection of both intracoronary imaging techniques. Plaques with calcium extent >5.0 mm in length are prone to stent underexpansion.

Calcium produces posterior acoustic shadowing in IVUS, making it difficult to assess its thickness directly. As a surrogate marker, the presence of reverberations in IVUS has been linked to the presence of superficial thin calcium (<0.5 mm). However, this association is controversial. In contrast,

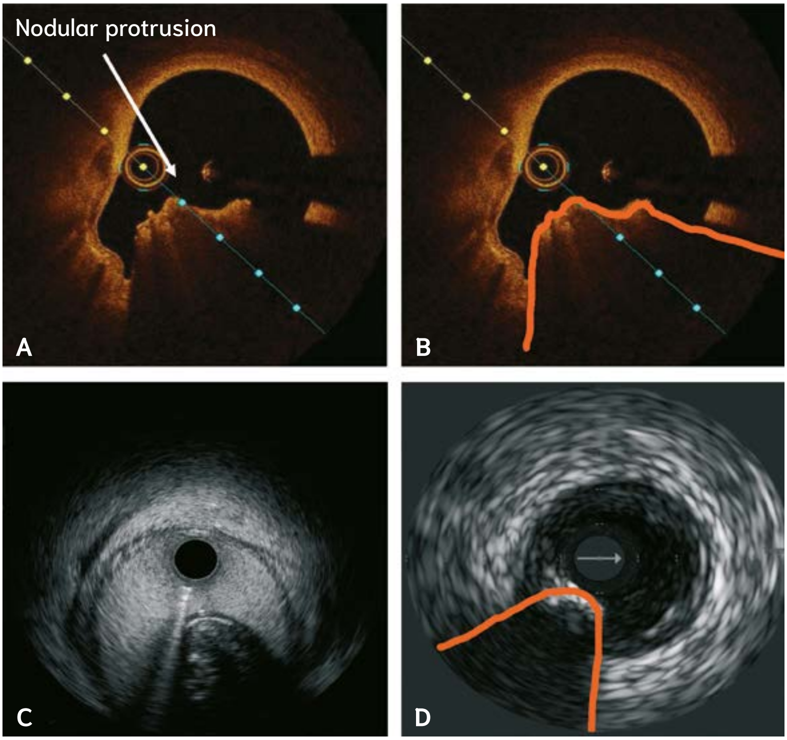

Figure 1. Nodular pattern. A and B) OCT. C and D) IVUS.

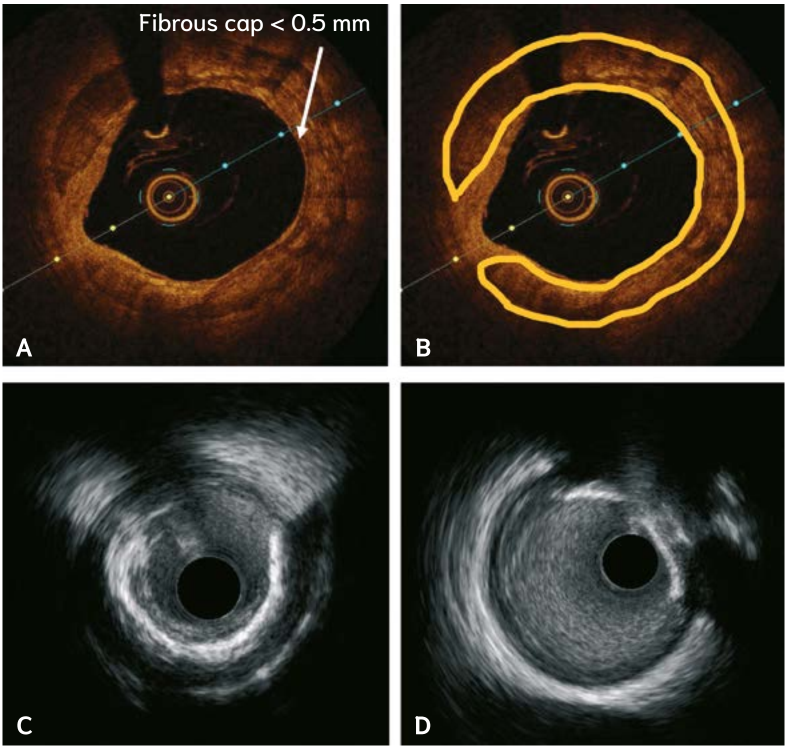

Figure 2. Parietal pattern – superficial calcium. A and B) OCT. C and D) IVUS.

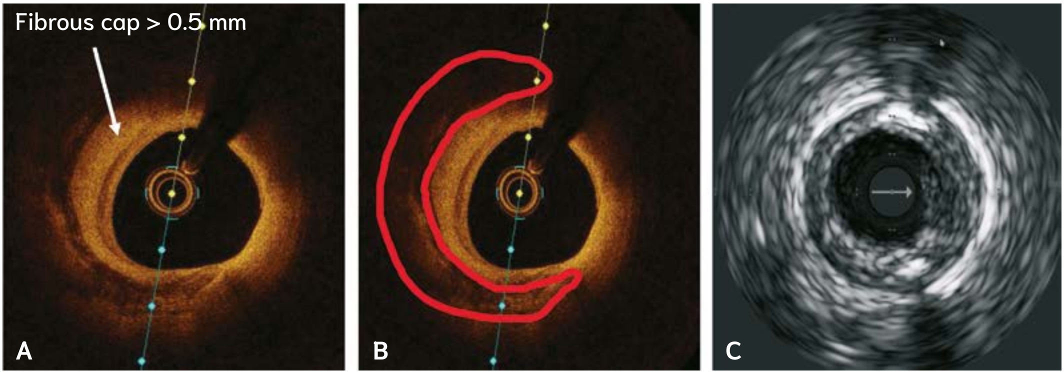

Figure 3. Parietal pattern – deep calcium. A and B) OCT. C) IVUS.

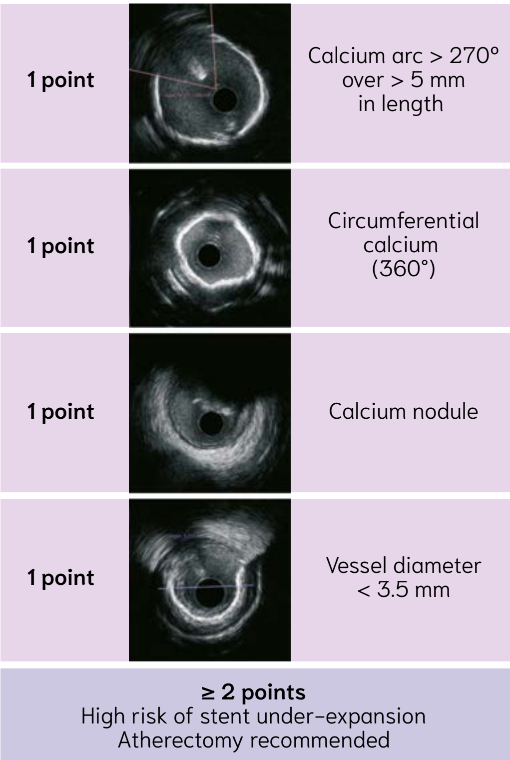

Figure 4. IVUS calcium quantification score.

parietal calcium in OCT does not produce posterior shadowing, allowing for more accurate thickness assessment[13]. Nodular calcium however produces shadowing with both techniques (IVUS and OCT).

Calcium quantification scores have been developed, both for IVUS and OCT, to predict the risk of stent underexpansion. The IVUS-based score of calcium quantification includes 4 parameters (*Fig. 4*): >5 mm in length with calcium arc >270° (1 point), calcium arc >360° (1 point), presence of calcified nodule (1 point), and adjacent vessel smaller than 3.5 mm (1 point). A score ≥2 suggests the need to perform a plaque modification technique prior to stenting[15].

The OCT-based score includes 3 parameters (*Fig. 5*): calcium arc > 180° (2 points), calcium length > 5 mm (1 point) and calcium thickness > 0.5 mm (1 point). Lesions with a score > 2 are at risk of stent underexpansion if adequate plaque preparation is not performed[3].

SELECTION OF PLAQUE MODIFICATION TECHNIQUE BASED ON INTRACORONARY IMAGING

Evaluating the morphological characteristics and calcium thickness through intracoronary imaging enables the selection of the most efficient technique and the assessment of plaque modification outcomes before stent implantation, ensuring adequate expansion. Several algorithms to assist in guiding the

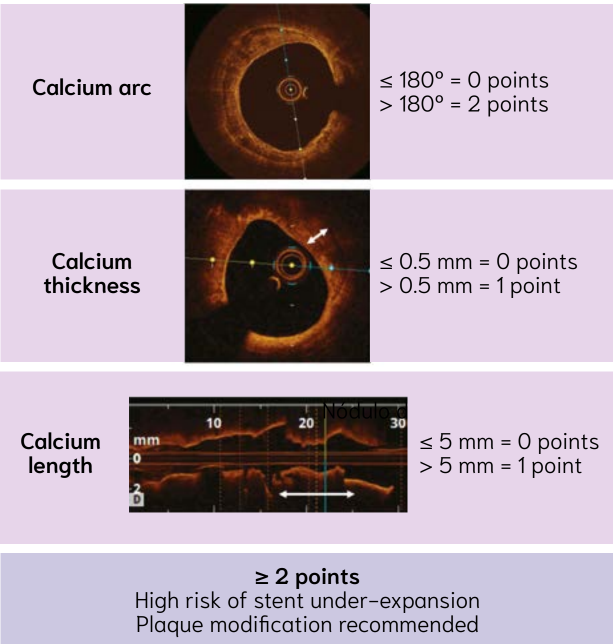

Figure 5. **OCT calcium quantification score.**

modification of calcified plaque have been published. However, evidence from comparative studies on these algorithms remains very limited[8,16]. What coincides among these algorithms is the use of techniques such as rotational atherectomy and excimer laser for lesions in which it is not possible to cross a device.

In general, those lesions in which the calcium does not have risk criteria for underexpansion (arc <180°, longitudinally extending <5 mm and thickness <0.5 mm) can be adequately modified using high-pressure balloons or modified balloons (scoring or cutting). When the plaque calcification has risk criteria for stent underexpansion or a calcium nodule exists, more advanced plaque modification techniques such as atherectomy (rotational or orbital), intravascular lithotripsy, laser or double-layer balloons (OPN) will be necessary.

Calcium depth is a crucial factor in selecting the appropriate technique for plaque modification. This is especially significant as certain techniques, like atherectomy, primarily target superficial rather than deep plaque portions. Currently, several ongoing studies are investigating the efficacy of each technique in treating different patterns of calcium, which will provide more robust evidence for selecting image-based preparation methods for calcified plaques.

An essential aspect of employing imaging in calcified lesions is evaluating the effectiveness of the chosen technique to ensure sufficient calcium modification before stent implantation.

The effect of the different plaque modification techniques (dissection, fracture, filing) depends on their mechanism of action:

a. **Non-compliant balloons (NC)**[17]: NC balloons enhance arterial compliance by creating fractures in thin superficial calcium, inducing dissections in the transition zones between calcified

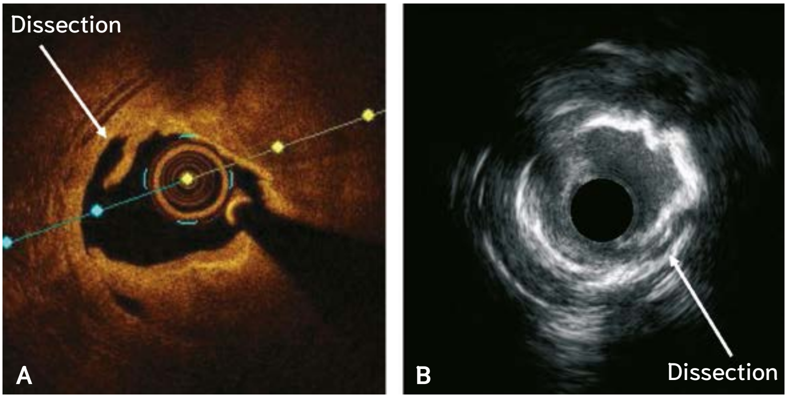

Figure 6. Non-compliant balloon. A) OCT. B) IVUS.

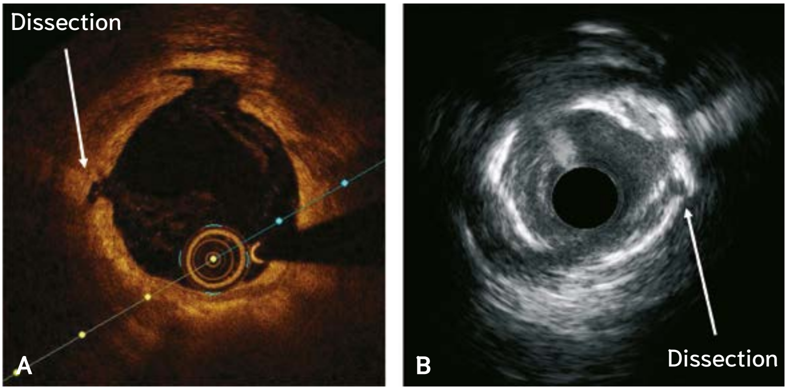

Figure 7. Cutting balloon. A) OCT. B) IVUS.

lesions and fibrotic tissue, and promoting extension of the media and adventitia. This ultimately leads to an increase in arterial lumen size[18] (*Fig. 6*).

b. **Cutting/scoring balloons:** these balloons are equipped with spiral nitinol atherotomes or strings, which create longitudinal plaque incisions. This promotes the controlled creation of dissections rather than uncontrolled plaque disruption. They are used as a plaque modification technique, particularly effective for calcium with a superficial pattern, and exhibit greater modification power when calcium is concentric[19,20] (*Fig. 7*).
c. **Rotational atherectomy:** produces uniform tissue modification, generating a concavity with polished edges[21]. Rotational atherectomy primarily reduces the thickness of calcified plaque through filing, rather than creating fractures directly. This process prepares the plaque for subsequent fracture using balloons. It could be beneficial in cases of calcium with a thick superficial pattern and nodular pattern[22] (*Fig. 8*).
d. **Intravascular Coronary Lithotripsy (IVL):** uses pressurized sonic waves to break up calcific deposits within the coronary artery, with minimal impact on other structures of the arterial wall. Its primary mechanism involves creating fractures in the calcified plaque. IVL is particularly useful for modifying a thick calcium pattern that may be resistant to other plaque modification technologies[23-26] (*Fig. 9*).

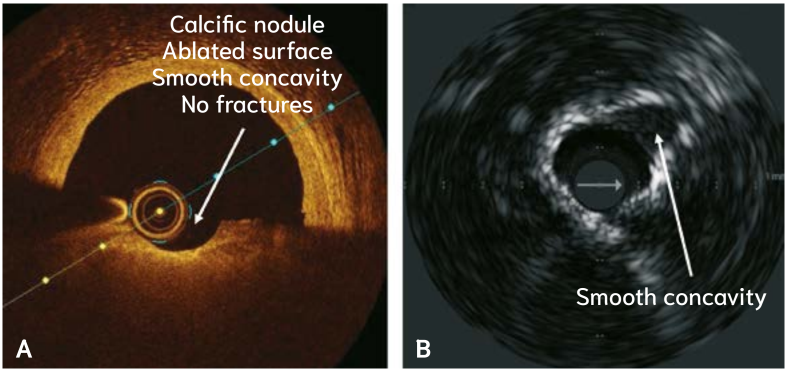

Figure 8. Rotational atherectomy. A) OCT. B) IVUS.

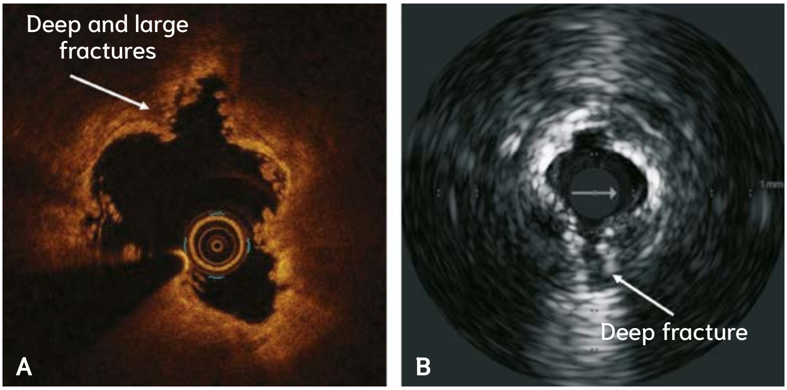

Figure 9. Intravascular lithotripsy. A) OCT. B) IVUS.

e. **NC OPN balloons:** these are non-compliant balloons with a double coating that allows them to reach pressures over 35 atmospheres. Their mechanism of action is similar to NC balloons, but the double layer gives them resistance to rupture, which can cause fractures in thick calcified plaques, expansion of the vascular lumen and tissue dissection. They represent a useful tool in calcium with a thick concentric pattern[27-29] (*Fig. 10*).

OPTIMIZATION OF STENT IMPLANTATION BASED ON INTRACORONARY IMAGING

Intracoronary imaging enables the assessment of the outcome of calcium plaque modification, considering factors such as the presence of calcium fractures, their depth, and arrangement in the plaque

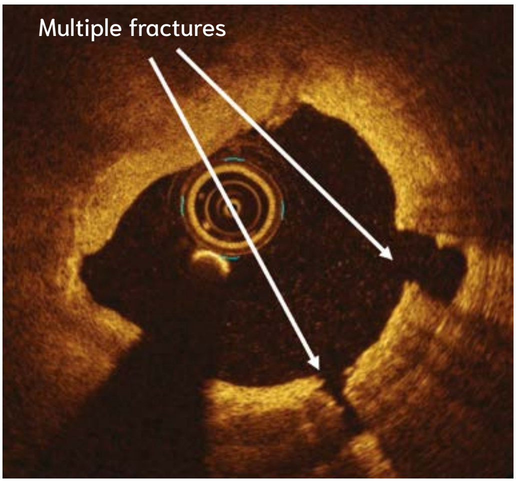

Figure 10. NC Balloon OPN. OCT.

[TABLE OF CONTENTS]

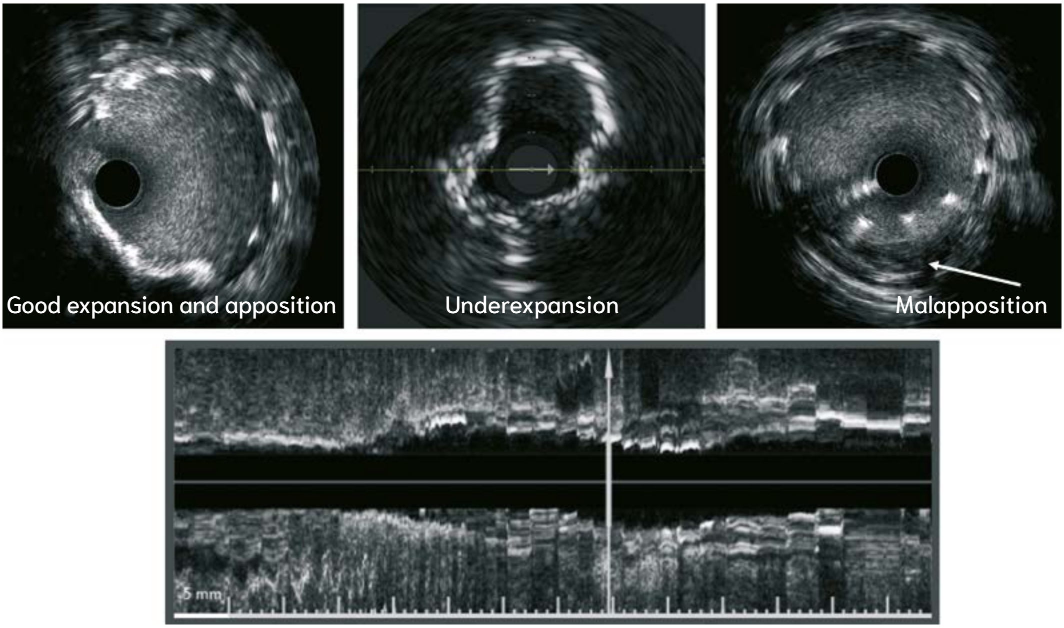

Figure 11. IVUS-guided stent optimization.

circumference. Evaluating the outcome before stent implantation enables the assessment of the need to employ a plaque modification strategy that may require the use of other available devices mentioned in this chapter.

Similar to non-calcified plaques, intracoronary imaging is invaluable for accurately selecting the appropriate stent based on vessel diameter and the length of the lesion. It also aids in assessing stent apposition and expansion, as well as identifying and addressing any dissections or residual disease at the proximal and distal edges. Stent expansion, the parameter most strongly related to stent failure, is especially relevant in calcified lesions with expansion-resistant plaques[9].

It is crucial to recognize that PCI in plaques with severe calcification are complex procedures. The use of plaque modification devices can lead to long dissections and deep fractures, thereby increasing the likelihood of residual minor dissections. Evidence of malapposition of the stent struts in segments with fractures may also occur, along with difficulties in achieving expansion within the acceptable range (80-90%) (*Figs. 11 and 12*).

REFERENCES

1. Mintz GS, Popma JJ, Pichard AD, Kent KM, Satler LF, Chuang YC, et al. Patterns of calcification in coronary artery disease. A statistical analysis of intravascular ultrasound and coronary angiography in 1155 lesions. Circulation. 1995; 91(7): 1959-65.
2. Wang X, Matsumura M, Mintz GS, Lee T, Zhang W, Cao Y, et al. In Vivo Calcium detection by comparing optical coherence tomography, intravascular ultrasound, and angiography. JACC Cardiovasc Imaging. 2017; 10(8): 869-79.
3. Fujino A, Mintz GS, Matsumura M, Lee T, Kim SY, Hoshino M, et al. A new optical coherence tomography-based calcium scoring system to predict stent underexpansion. EuroIntervention. 2018; 13(18): e2182-e9.

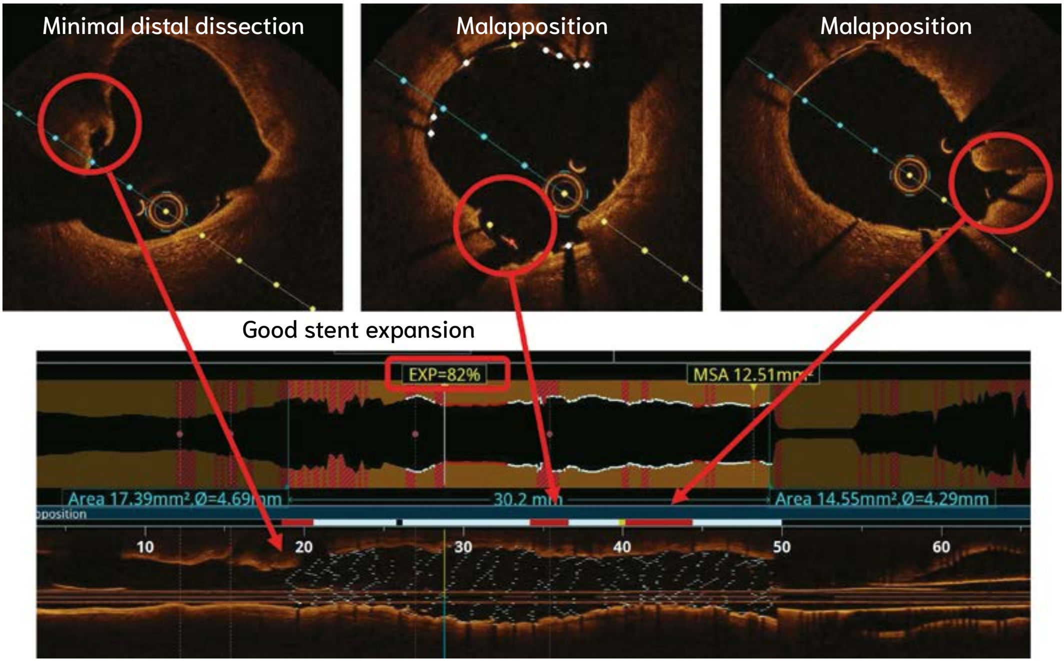

Figure 12. OCT-guided stent optimization.

4. Huisman J, van der Heijden LC, Kok MM, Danse PW, Jessurun GA, Stoel MG, et al. Impact of severe lesion calcification on clinical outcome of patients with stable angina, treated with newer generation permanent polymer-coated drug-eluting stents: A patient-level pooled analysis from TWENTE and DUTCH PEERS (TWENTE II). Am Heart J. 2016; 175: 121-9.
5. Mori H, Torii S, Kutyna M, Sakamoto A, Finn AV, Virmani R. Coronary artery calcification and its progression: What does it really mean? JACC Cardiovasc Imaging. 2018; 11(1): 127-42.
6. Secco GG, Foin N, Viceconte N, Borgia F, De Luca G, Di Mario C. Optical coherence tomography for guidance of treatment of in-stent restenosis with cutting balloons. EuroIntervention. 2011; 7(7): 828-34.
7. Bourantas CV, Zhang YJ, Garg S, Iqbal J, Valgimigli M, Windecker S, et al. Prognostic implications of coronary calcification in patients with obstructive coronary artery disease treated by percutaneous coronary intervention: a patient-level pooled analysis of 7 contemporary stent trials. Heart. 2014; 100(15): 1158-64.
8. Karimi Galougahi K, Shlofmitz E, Jeremias A, Gogia S, Kirtane AJ, Hill JM, et al. Therapeutic approach to calcified coronary lesions: Disruptive technologies. Curr Cardiol Rep. 2021; 23(4): 33.
9. Raber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y, et al. Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions. EuroIntervention. 2018; 14(6): 656-77.
10. Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, Bischoff JM, et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: Executive summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022; 145(3): e4-e17.
11. Lawton JS, Tamis-Holland JE, Bangalore S, Bates ER, Beckie TM, Bischoff JM, et al.

2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022; 145(3): e18-e114.

12. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. EuroIntervention. 2019; 14(14): 1435-534.
13. De Maria GL, Scarsini R, Banning AP. Management of calcific coronary artery lesions: Is it time to change our interventional therapeutic approach? JACC Cardiovasc Interv. 2019; 12(15): 1465-78.
14. McInerney A, Escaned J, Gonzalo N. Online coregistration of intravascular ultrasound and optical coherence tomography. Minerva Cardiol Angiol. 2021; 69(6): 641-54.
15. Zhang M, Matsumura M, Usui E, Noguchi M, Fujimura T, Fall KN, et al. Intravascular ultrasound-derived calcium score to predict stent expansion in severely calcified lesions. Circ Cardiovasc Interv. 2021; 14(10): e010296.
16. Bulluck H, McEntegart M. Contemporary tools and devices for coronary calcium modification. JRSM Cardiovasc Dis. 2022; 11: 20480040221089760.
17. Seyithanoglu BY, Zaki Masud AR, Ergene O, Morris WM, Kozan O, Corbelli JC, et al. Compliant vs non-compliant balloons. A prospective randomized study. Jpn Heart J. 1998; 39(1): 45-54.
18. Block PC. The mechanism of transluminal angioplasty. Int Angiol. 1985; 4(1): 77-9.
19. Almeda FQ, Klein LW. Cutting balloon angioplasty: to cut is to cure? J Invasive Cardiol. 2002; 14(12): 725-7.
20. de Ribamar Costa J, Jr., Mintz GS, Carlier SG, Mehran R, Teirstein P, Sano K, et al. Nonrandomized comparison of coronary stenting under intravascular ultrasound guidance of direct stenting without predilation versus conventional predilation with a semi-compliant balloon versus predilation with a new scoring balloon. Am J Cardiol. 2007; 100(5): 812-7.
21. Kobayashi N, Ito Y, Yamawaki M, Araki M, Sakai T, Sakamoto Y, et al. Optical frequency-domain imaging findings to predict good stent expansion after rotational atherectomy for severely calcified coronary lesions. Int J Cardiovasc Imaging. 2018; 34(6): 867-74.
22. Amemiya K, Yamamoto MH, Maehara A, Oyama Y, Igawa W, Ono M, et al. Effect of cutting balloon after rotational atherectomy in severely calcified coronary artery lesions as assessed by optical coherence tomography. Catheter Cardiovasc Interv. 2019; 94(7): 936-44.
23. Ali ZA, Nef H, Escaned J, Werner N, Banning AP, Hill JM, et al. Safety and effectiveness of coronary intravascular lithotripsy for treatment of severely calcified coronary stenoses: The Disrupt CAD II Study. Circ Cardiovasc Interv. 2019; 12(10): e008434.
24. Hill JM, Kereiakes DJ, Shlofmitz RA, Klein AJ, Riley RF, Price MJ, et al. Intravascular lithotripsy for treatment of severely calcified coronary artery disease. J Am Coll Cardiol. 2020; 76(22): 2635-46.
25. Kereiakes DJ, Hill JM, Ben-Yehuda O, Maehara A, Alexander B, Stone GW. Evaluation of safety and efficacy of coronary intravascular lithotripsy for treatment of severely calcified coronary stenoses: Design and rationale for the Disrupt CAD III trial. Am Heart J. 2020; 225: 10-8.
26. Yeoh J, Hill J. Intracoronary lithotripsy for the treatment of calcified plaque. Interv Cardiol Clin. 2019; 8(4): 411-24.
27. Secco GG, Ghione M, Mattesini A, Dall'Ara G, Ghilencea L, Kilickesmez K, et al. Very high-pressure dilatation for undilatable coronary lesions: indications and results with a new dedicated balloon. EuroIntervention. 2016; 12(3): 359-65.
28. Secco GG, Buettner A, Parisi R, Pistis G, Vercellino M, Audo A, et al. Clinical experience with very high-pressure dilatation for resistant coronary lesions. Cardiovasc Revasc Med. 2019; 20(12): 1083-7.
29. Rheude T, Rai H, Richardt G, Allali A, Abdel-Wahab M, Sulimov DS, et al. Super high-pressure balloon versus scoring balloon to prepare severely calcified coronary lesions: the ISAR-CALC randomised trial. EuroIntervention. 2021; 17(6): 481-8.