EuroIntervention

Is refined OCT guidance of stent implantation needed?

Nieves Gonzalo*, MD, PhD; Javier Escaned, MD, PhD; Fernando Alfonso, MD, PhD; Pilar Jiménez-Quevedo, MD, PhD; Brian Zakhem, MBBS, FRACP; Camino Bañuelos, MD; Rosana Hernández-Antolín, MD, PhD; Carlos Macaya, MD, PhD

Interventional Cardiology, Hospital Clínico Universitario San Carlos, Madrid, Spain

The authors have are no conflicts of interest to declare.

KEYWORDS
Optical coherence tomography, stent, restenosis, stent thrombosis

Abstract

The development of optical coherence tomography (OCT) provides new opportunities for the evaluation of coronary stents. Having a much higher spatial resolution than intravascular ultrasound (IVUS), OCT is currently used for long-term assessment of stent implantation. In the immediate future, however, it is quite likely that OCT will be used synergically with IVUS to optimise stent deployment; the criteria for optimising stent implantation using OCT will be clearly indebted to the evidence gathered with IVUS, with an added value in contexts like ambiguous images presenting after stenting, or in complex percutaneous coronary interventions (PCI) procedures like bifurcation stenting. However, since OCT is capable of identifying, during PCI, findings of potential relevance beyond the resolution IVUS, such as thrombus or tissue protrusion, intra-stent or edge dissections, or specific patterns of hyperplasia in restenotic lesions, it is foreseeable that new OCT-specific recommendations for optimal stent implantation will be made in the near future.

** Corresponding author: Interventional Cardiology, Hospital Clínico San Carlos, C/ Martín Lagos s/n, 28040 Madrid, Spain*
E-mail: nieves_gonzalo@yahoo.es

Introduction

Angiography is the most frequent imaging modality used in assessing the results of percutaneous coronary intervention (PCI). In spite of the readiness and simplicity of the technique, the information obtained is derived from a planar projection of the luminal silhouette, being therefore fraught with multiple shortcomings: it does not provide information on the interaction between the stent and the vessel wall, and can only be interpreted in the absence of overlapping shadows from other coronary branches. Furthermore, its prognostic relevance to predict subsequent cardiac events or stent failure (stent restenosis or thrombosis) is limited.

Intracoronary imaging techniques were developed to complement coronary angiography thus allowing a more detailed evaluation of stent implantation. Intravascular ultrasound (IVUS), the first of the intracoronary imaging techniques developed, was instrumental in understanding the pitfalls of the archaic stent deployment technique, which was associated with an unacceptably high rate of stent thrombosis. In the bare-metal stent (BMS) era, multiple studies were performed using IVUS guidance to optimise stent deployment by ensuring adequate stent expansion, apposition and luminal dimensions had been achieved. Some studies suggested that, by using IVUS, the target vessel revascularisation rate could be decreased when compared with angiographic guidance[1,2] and a relevant role for IVUS in the prevention of restenosis was anticipated. However, the dramatic decrease in restenosis rate brought by the introduction of drug-eluting stents (DES) made these considerations obsolete thus leading to a relative loss of interest in IVUS guidance of DES implantation. This was the case until it became clear that restenosis also occurs in DES, and that IVUS shows potential in predicting the likelihood of long-term DES failure[3].

Optical coherence tomography (OCT) is a light-based intracoronary imaging technique that is being increasingly used in catheterisation laboratories worldwide. Its ability to provide high-resolution (axial 10 µm) images of the coronary artery *in vivo* has opened new possibilities for the assessment of the acute and long-term effects of stent implantation. The development of new systems (Fourier-domain OCT, FD-OCT) able to image long coronary segments in a few seconds using only small amounts of contrast has made this technique widely applicable. In this paper we will discuss the value and potential clinical implications of OCT guidance for stent implantation.

Stenosis evaluation with OCT prior to stenting

OCT can contribute to pre-stenting evaluation of the target stenosis by providing information on lumen dimensions and plaque composition. Regarding the quantification of lumen area, a very clear delineation of the lumen-intima interface can be obtained allowing automatic area measurements with a very good reproducibility[4]. Luminal area can thus be used to characterise stenosis severity. However, while optimal cut-off luminal area values have been established for IVUS, for the time being no dedicated studies using OCT for this purpose have been published. This may be important, since differences in luminal areas measured with IVUS and OCT have been reported[5], a fact that, therefore, makes advisable not to take for granted that cut-off values for both intracoronary techniques are identical. Atherosclerotic plaque appearance on OCT depends on its composition (Figure 1). This information about plaque type can influence the procedure strategy (e.g., heavily calcified lesions that have lower distensibility may require specific strategies for an adequate stent expansion). Furthermore, it can have prognostic implications, for example, it has been demonstrated that the frequency of no-reflow phenomenon increases according to the lipid content of the plaque as assessed by OCT[6]. In acute coronary syndromes, OCT can visualise features related to the culprit plaque such as plaque rupture and subsequent thrombosis (Figure 2).

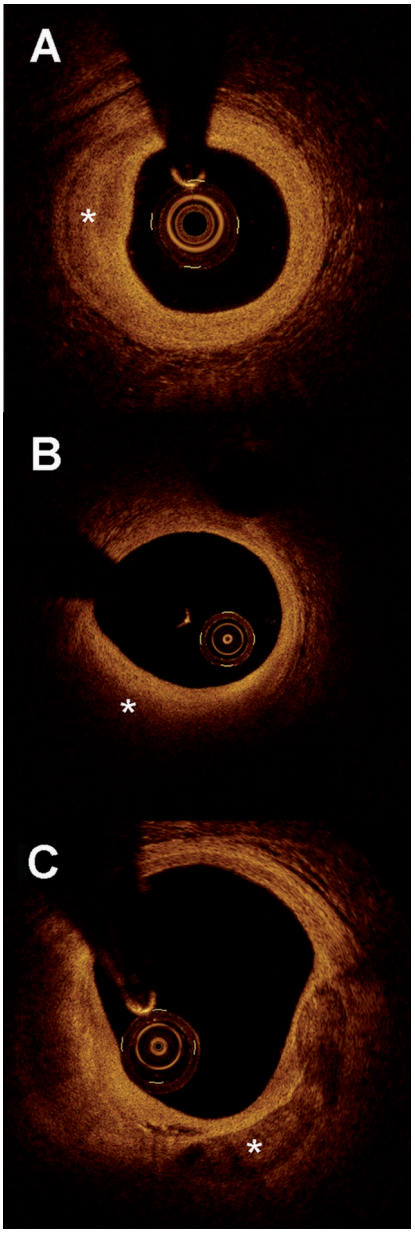

Figure 1. Plaque composition as assessed by optical coherence tomography. A) Fibrous plaque: homogeneous, highly backscattering (i.e., signal-rich) region (*). B) Lipid-rich plaque: diffusely bordered signal poor region (*). C) Fibrocalcific plaque: signal poor region with sharply defined borders (*).

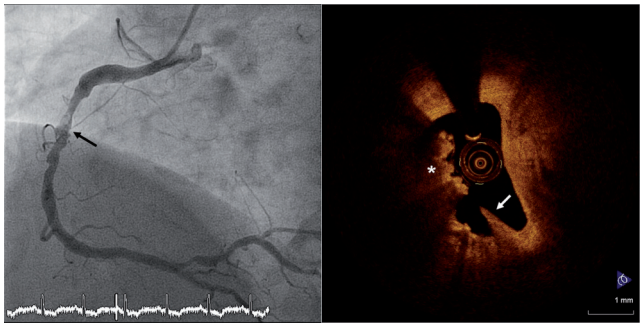

Figure 2. Plaque rupture and thrombus. The figure corresponds to a patient who suffered an inferior ST elevation myocardial infarction treated successfully with thrombolysis. An angiogram was performed the day after (left panel) showing an irregular lesion with filling defect suggestive of thrombus in the right coronary artery (arrow). The optical coherence tomography examination (right panel) demonstrated the presence of a plaque rupture (arrow indicates the ruptured fibrous cap) with abundant thrombus (irregular material protruding in the lumen with shadow).

OCT and stent failure

OCT can identify several morphological findings that have been related with stent restenosis and thrombosis in IVUS studies. Furthermore, its unique resolution allows the detection of certain features (i.e., tissue coverage in DES, small degree of malapposition, small intra-stent or edge dissections) that are not visible with IVUS. Even when there is a lack of data in this field, the detection and correction of the predictors of stent failure could potentially yield a clinical benefit in patients undergoing PCI. However, this needs to be confirmed in specifically designed clinical trials with long-term follow-up.

Restenosis

As discussed previously, the arrival of DES has dramatically reduced the incidence of stent restenosis but it has not abolished this important clinical problem. Several predictors of restenosis can be identified with OCT after stent deployment thus facilitating its correction with the aim of preventing this complication. The identification of the underlying mechanisms leading to the restenosis (that can vary depending on the stent type) is also pivotal for an adequate treatment of these lesions. In this paper, we shall emphasise three types of potentially relevant observations that can be obtained during periprocedural OCT assessment of coronary segments treated with stents: 1) evidence of inadequate stent expansion, strut apposition or scaffolding; 2) evidence of associated extensive vessel damage; and 3) evidence on the characteristics of neointimal hyperplasia in previously implanted stents.

Stent under expansion, gaps between stents (Figure 3) and incomplete lesion coverage are potential mechanisms leading to stent restenosis that can be readily detected with OCT. The irregular distribution of the drug delivery has been postulated as a cause of restenosis in DES. This could be related to i) stent fracture or ii) non-uniform distribution of the stent struts. These two features can be studied with OCT. Stent fracture is identified on OCT by the lack of circumferential struts and the distortion of the stent geometry and has been shown to be more frequent in first generation sirolimus-eluting stents[7]. Strut distribution can vary depending on the stent type and can be assessed *in vivo* with OCT.

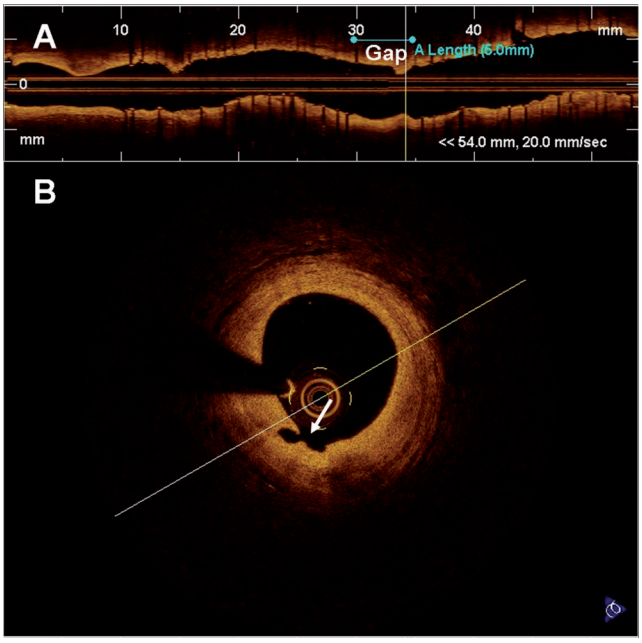

Figure 3. Gap between stents. A) longitudinal optical coherence tomography (OCT) image showing a gap between the two implanted stents. B) OCT cross-section in the gap region showing the absence of stent struts and the presence of a small dissection (indicated by the arrow).

High-pressure deployment is necessary for an adequate stent expansion but it can induce periprocedural vessel damage. Experimental data have related the vessel response to injury after implantation with stent restenosis. Given its high-resolution, OCT allows a detailed visualisation of vessel damage after stent implantation and can distinguish different types of injury: i) tissue prolapse: convex-shaped, protrusion of tissue between adjacent stent struts towards the lumen, without disruption of the continuity of the luminal vessel surface; ii) intra-stent dissection: disruption of the luminal vessel surface in the stent segment (Figure 4); iii) edge dissection: disruption of the luminal vessel surface in the edge

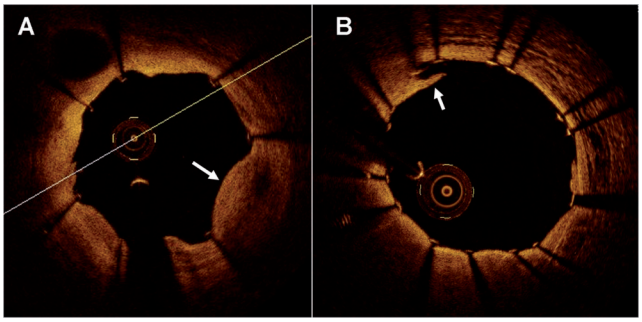

Figure 4. Tissue prolapse and intra-stent dissection by optical coherence tomography A) tissue prolapse: convex-shaped, protrusion of tissue between adjacent stent struts towards the lumen, without disruption of the continuity of the luminal vessel surface (arrow) B) intra-stent dissection: disruption of the luminal vessel surface in the stent segment (arrow).

segments (within 5 mm proximal and distal to the stent, no struts are visible) (Figure 5). Furthermore, this technique allows the quantification of these findings[8]. A recent study showed that the frequency of tissue prolapse or intra-stent dissections after stenting was high, irrespective of the clinical presentation of the patients. IVUS data have suggested that non-flow-limiting edge dissections are not necessarily associated with an increase in acute or long-term events or development of restenosis[9]. However, there is lack of data regarding the clinical relevance and the relation of tissue prolapse, intra-stent dissections or edge dissections as assessed by OCT with restenosis. Studies including serial OCT examinations would be needed to establish the potential link between vessel injury and restenosis.

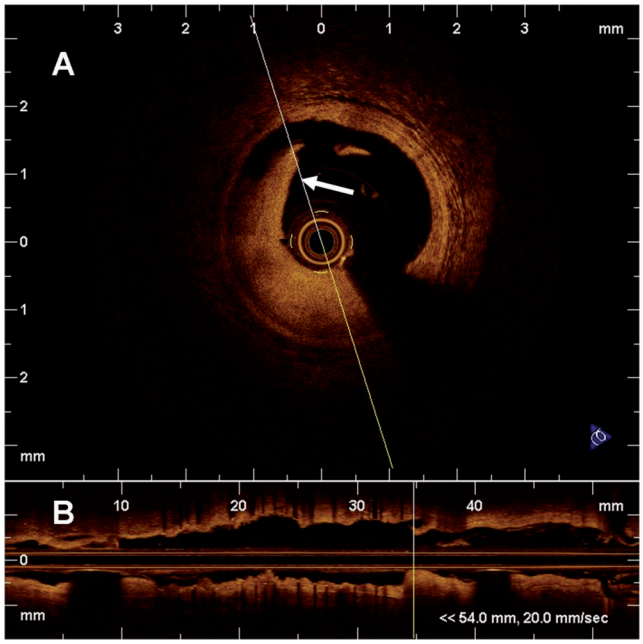

Figure 5. Edge dissection. A) Optical coherence tomography (OCT) cross section showing a disruption of the luminal vessel surface (flap is indicated by the arrow). B) The longitudinal OCT reconstruction shows the location of the dissection in the proximal edge of the stent.

OCT is able to provide a detailed assessment of the restenotic tissue. We have demonstrated that there are differential patterns of restenotic tissue that can be distinguished with OCT[10]. A recent study has shown that late restenosis in BMS show features suggestive of the development of new atherosclerotic lesions in the neointima[11]. The clinical or prognostic implications of those findings are not well established and will require further investigation.

Through the identification of the mechanism of stent restenosis, OCT can be useful to guide the correct treatment of this problem. While in BMS restenosis is usually related to excessive neointimal proliferation, in DES there is frequently an underlying mechanical cause (i.e., stent under expansion) that needs to be corrected in order to prevent a new restenosis. Furthermore, OCT can also be used to assess the success of different devices used to treat restenosis (Figure 6).

Stent thrombosis

Even though it is an infrequent event, stent thrombosis is a potentially life-threatening complication after stent implantation and it is one of the major concerns for the interventional cardiologist. While subacute stent thrombosis mechanisms are predominantly mechanical, late stent thrombosis seems to be more related with other causes such as delayed endothelialisation. OCT can accurately evaluate mechanical problems such as stent under expansion or malapposition and currently it seems to be the best available tool for *in vivo* study of vascular healing after stenting.

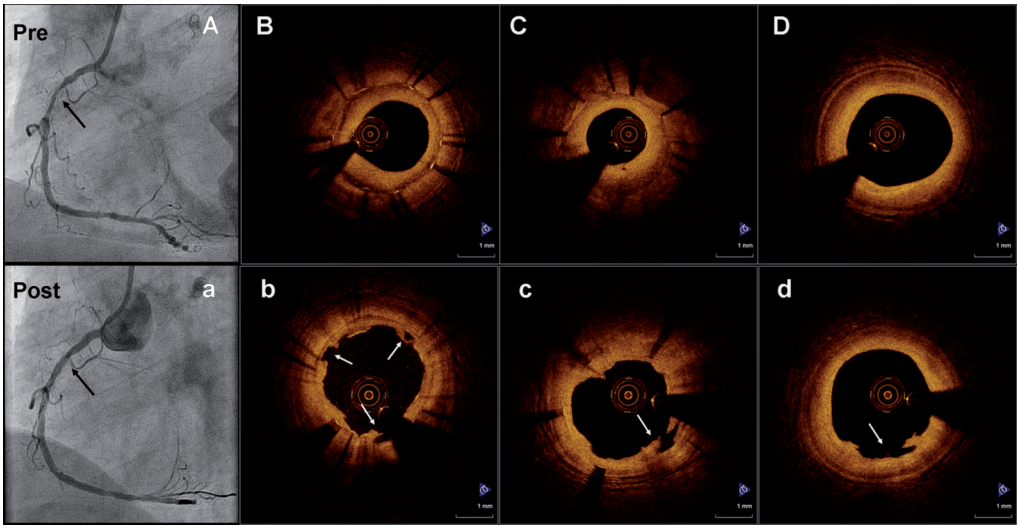

Figure 6. Stent restenosis treated with paclitaxel eluting balloon. A: angiogram showing a diffuse restenosis of a bare-metal stent implanted in the right coronary artery. B and C are optical coherence tomography (OCT) cross-sections in the restenosis region showing a layered appearance (inner signal rich region and outer low signal region around the struts). D shows the proximal edge of the stent where fibrous plaque is visible. a: angiogram after treatment of the restenosis with a paclitaxel eluting balloon. b and c: OCT cross-sections in the region treated showing the dissections created by the balloon in the neointimal tissue. d: shows a proximal edge dissection induced by the balloon not visible by angiography.

TISSUE COVERAGE ASSESSMENT

Pathological series have identified delayed endothelialisation as the most powerful histological predictor of stent thrombosis. In order to prevent restenosis, DES inhibit neointimal proliferation. The inhibition is so intense that the struts are often covered by tiny layers of tissue not visible with conventional IVUS. The high resolution images provided by OCT allow the visualisation and measurement of the very thin layers of tissue with a very good correlation with pathology (Figure 7). Several OCT studies published in the last years have shown differences in tissue coverage between BMS and DES and between different types of DES[12,13]. OCT studies have also shed light on the temporal course of struts coverage and have demonstrated that a high proportion of patients (80%) can have uncovered struts two years after DES implantation[14]. Furthermore, there is data relating the presence or absence of tissue coverage with the clinical presentation. We showed that patients treated with DES for ST elevation myocardial infarction had more frequently uncovered struts at follow-up than patients treated for stable or unstable angina[15]. This might reflect the differences in the plaque type leading to the event and underlying stent implantation.

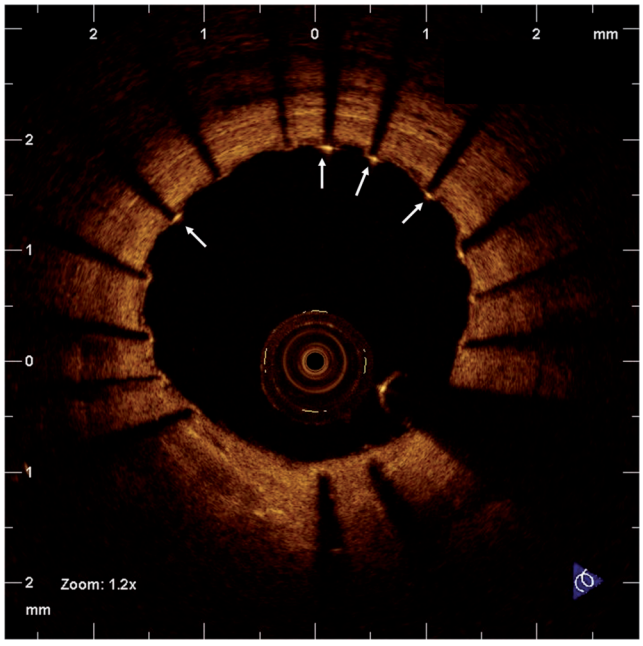

Figure 7. Uncovered struts as assessed by optical coherence tomography (OCT). Drug-eluting stent imaged with OCT nine months after implantation. The arrows indicate several struts where no tissue coverage is visible by OCT. The rest of the struts are covered by a very thin layer of tissue.

The ability of OCT to provide information about stent coverage could potentially be useful for clinical decision making, particularly the duration of the dual antiplatelet therapy in certain patients. However, it is important to realise that the link between absence of struts coverage by OCT and clinical events has not been established yet[16]. The resolution of the technique is high but it can not visualise a single cell layer, meaning that absence of coverage by OCT is not synonymous with absence of endothelialisation. Furthermore, OCT can not distinguish the type of tissue covering the struts (i.e., normal neointima vs. fibrin) and it can not evaluate whether the vessel has recovered its normal endothelial function. Therefore, even when OCT can provide very useful insights about vascular healing after stent implantation, caution should be taken in the interpretation of the results. Specifically designed studies with long-term follow-up are warranted to establish the clinical significance of the absence of strut coverage by OCT.

STENT APPOSITION

Incomplete stent apposition is defined as separation of at least one stent strut from the vessel wall. Given its higher resolution, OCT is more sensitive than IVUS for the detection of incomplete stent apposition (Figure 8). Consequently, OCT studies have demonstrated a relatively high proportion of malapposed struts after stent deployment with this phenomenon being particularly evident in regions of stent overlap and in severely calcified lesions[17]. Device design (strut thickness, closed cell design), lesion characteristics (calcification, long lesion) and procedural technique (stent

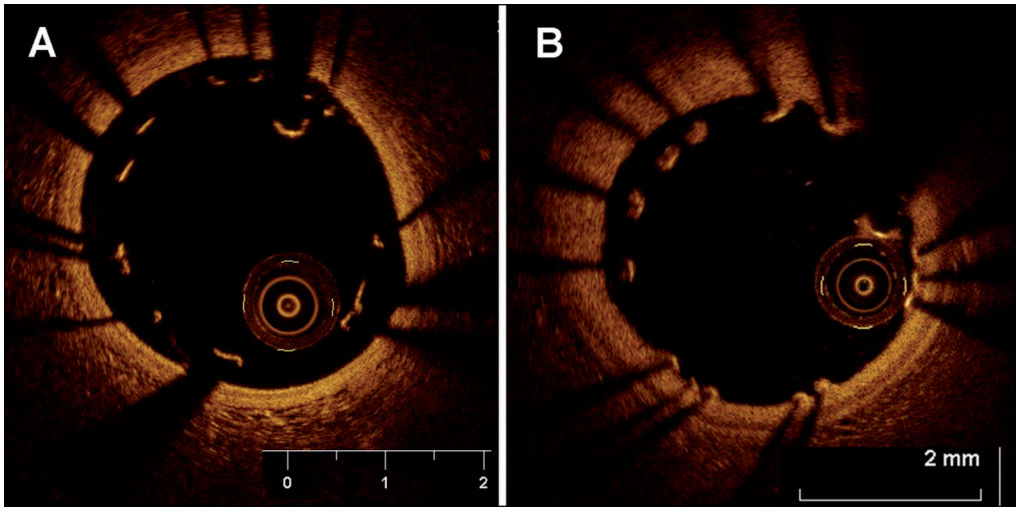

Figure 8. Malapposition evaluated with optical coherence tomography. A: Malapposition after stent implantation; B: Malapposition at follow-up: some of the struts (from 9 to 12 o'clock) are covered by tissue but not apposed to the vessel wall.

deployment pressure, non-compliant balloon) are likely to influence the presence of incomplete stent apposition. In complex lesions with a high risk of malapposition, OCT can be useful to assess plaque characteristics in order to guide treatment strategy (i.e., use of rotational atherectomy in heavily calcified lesions) and optimise the final result. At follow-up, OCT can also assess the presence of late acquired malapposition and can provide insights into its mechanisms (such as the dissolution of thrombus jailed between the stent and the vessel wall or the presence of chronic stent recoil). IVUS studies have suggested a potential relationship between incomplete stent apposition and stent thrombosis but the clinical relevance of small degrees of malapposition detected by OCT remains unknown. Prospective long term data will be required to establish whether there is a link between malapposition and clinical events.

INTRACORONARY THROMBUS

Thrombus can be visualised by OCT as an irregular structure, protruding into the lumen with associated shadow. The technique resolution, allows the visualisation of small thrombus attached to stent struts after implantation or at follow-up[15,18] (Figure 9). The stent length, the presence of uncovered struts and an asymmetric stent expansion have been postulated as local determinants of intracoronary thrombus formation in SES[18]. In this setting, OCT could be useful to guide stent deployment in order to achieve an adequate and symmetric expansion. However the clinical significance of the presence of intracoronary thrombus visualised with OCT is unknown. The described frequency of this phenomenon is much higher than the reported incidence of clinical stent thrombosis. Furthermore, in several OCT studies, the presence of intracoronary thrombus has not been associated with thrombotic clinical events[18]. Not only local but also systemic factors may play an important role in the development of clinical thrombosis. Large scale studies would be needed to understand the relationship between small intracoronary thrombus visualised by OCT and clinical stent thrombosis.

VESSEL DAMAGE AFTER STENT IMPLANTATION

The disruption of the vessel integrity with prolapse of necrotic core between the stent struts after stent deployment has been associated with stent thrombosis in pathological studies. In the clinical practice, the implications of the prolapsed tissue between the stent struts are not well established. IVUS studies have not demonstrated differences in the rate of stent thrombosis between patients with and without plaque prolapse[9]. The high-resolution of OCT allows the identification of small amounts of tissue prolapse not visible with IVUS. The presence of tissue prolapse in OCT is a very common finding but its long-term implications are poorly understood. The technique is also able to identify small intra-stent dissections[8]. While the vessel integrity is an important factor in the prevention of thrombus formation, there is lack of data regarding the potential relation between this OCT finding and stent thrombosis.

RESIDUAL REFERENCE SEGMENT STENOSIS

Residual reference segment stenosis has been associated with stent thrombosis in IVUS studies. The presence of residual lumen stenosis and incomplete lesion coverage can be readily identified by OCT. Furthermore, the technique can provide additional information about the plaque type left at the edges after stent implantation that may potentially have clinical implications[19]

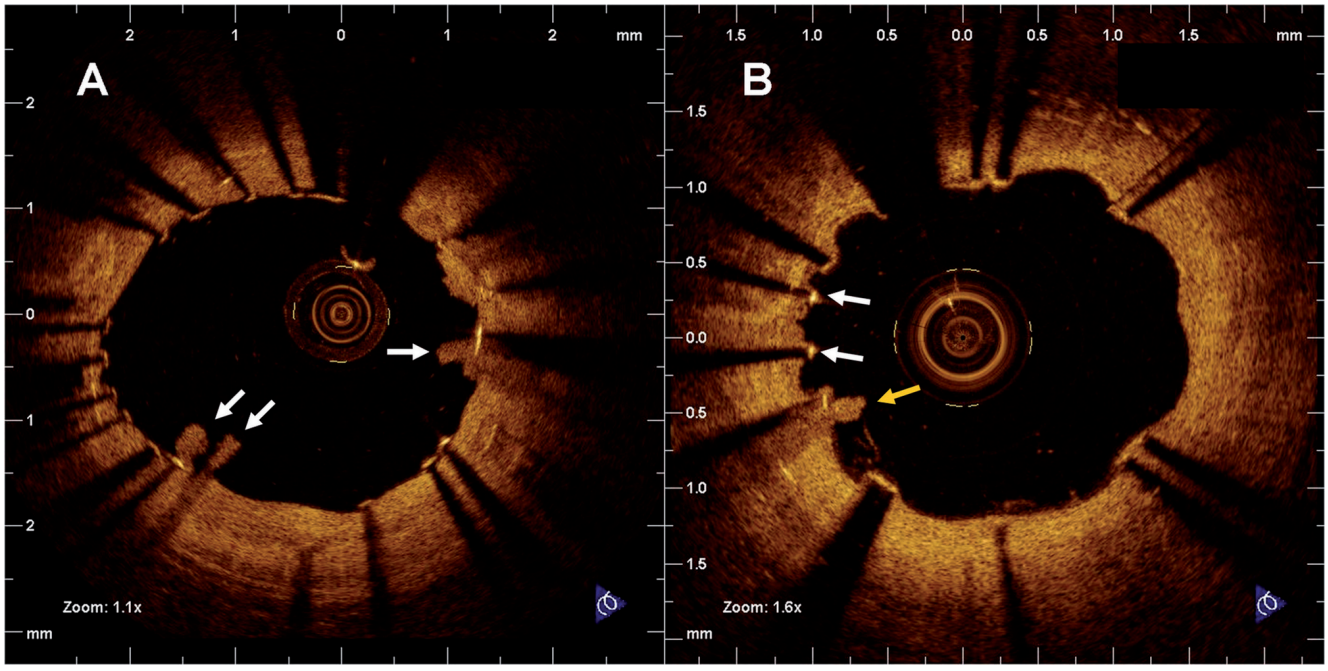

Figure 9. Intracoronary thrombus imaged with optical coherence tomography (OCT). A: Intracoronary thrombus after stent implantation. An irregular material with dorsal shadowing (suggestive of thrombus) attached to some of the struts can be observed (arrows) in this OCT cross-section. B: Intracoronary thrombus at follow-up. The figure shows a drug-eluting stent imaged with OCT nine months after implantation. In some struts, no tissue coverage is visible by OCT (white arrows). The yellow arrow indicates the presence of intracoronary thrombus (irregular mass with dorsal shadow) attached to one of the struts.

OCT for the evaluation of ambiguous images after stent implantation

Occasionally, ambiguous angiographic images can be observed after stent implantation and they can create doubts about the need of further interventions. OCT may be helpful to clarify the origin of these images. Hazy regions at the borders of the stent can correspond to edge dissections, thrombus or residual uncovered plaque. When they are located inside the stent, they can be associated with the presence of intracoronary thrombus or intra-stent dissections. While OCT is a much more sensitive technique than angiography for the detection of these phenomena, there is no data regarding their clinical implications. Therefore, caution should be taken when interpreting these images in order to avoid unnecessary interventions.

OCT to guide stent implantation in complex lesions

Bifurcations represent a complex subset of coronary lesions with higher rates of stent failure. Even when several techniques and dedicated devices have been developed, there is no general consensus about the optimal treatment strategy for these lesions. DES have reduced the incidence of restenosis in coronary bifurcations but the concern remains about the risk of stent thrombosis. Malapposition is a common phenomenon in the ostium of the side branch in bifurcations stenting. A potential delayed endothelialisation in the malapposed struts or in overlapping struts in two stents techniques has been also suggested. These two factors together could contribute for the higher risk of stent thrombosis in bifurcations and both can be analysed in detail with OCT[20] (Figure 10). Further, this imaging technique can provide new insights about the characteristics of the atherosclerotic plaque in bifurcations, another important factor that could potentially contribute to the higher risk of stent failure in these lesions[21]. Regarding the guidance during bifurcation stenting, OCT can identify the extension and composition of the plaque along the main branch and in the ostium of the side branch. This additional information could potentially be useful to guide the procedure.

Great advances have been achieved in the last few years in the treatment of chronic total occlusions (CTO) through the development of specific guidewires and devices. Still, CTOs are the subgroup of lesions with a lower procedural success rate and its treatment remains challenging. In this complex scenario, OCT can provide useful additional information that may potentially be useful to safely guide the procedure. Preliminary ex vivo experience with forward-looking OCT systems that use multiple longitudinal OCT slices to generate cross-sectional images of occluded arteries have been reported[22]. OCT was able to differentiate between occluded lumen and different layers of the arterial wall and showed potential to identify micro channels. This information could be used to direct the guidewire in order to cross the cap of the occlusion. Once the guidewire has been advanced into the lesion, OCT can provide useful information about the composition of the plaque causing the occlusion. Further, when a dissection occurs, OCT can be used to differentiate true from false lumen[23]. Future developments such as OCT-based Doppler techniques could potentially be used to assess the presence of microchannels[24].

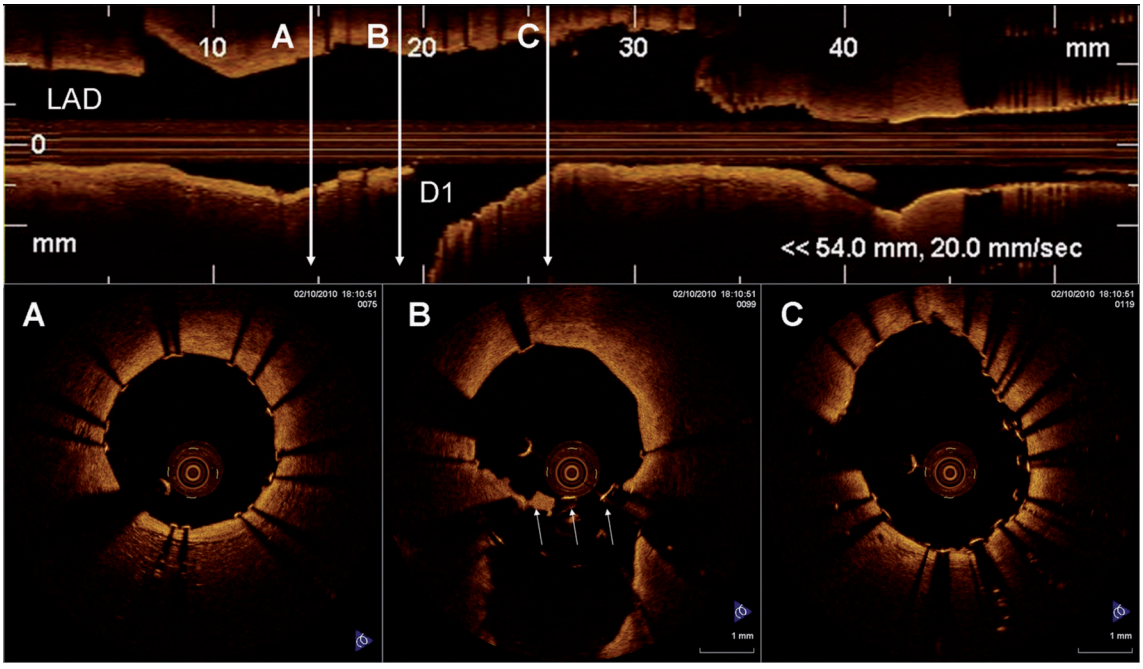

Figure 10. Bifurcation stenting assessed by optical coherence tomography. The upper panel shows the longitudinal OCT reconstruction of a bifurcation lesion (LAD-diagonal) treated with a mini-crush technique. A: OCT cross-section in the LAD distal to the diagonal. Good stent expansion and apposition can be observed. B: OCT cross-section in the bifurcation region, showing malapposed struts in the ostium of the side-branch (arrows). C: OCT cross-section in the LAD proximal to the bifurcation. Two layers of stent struts can be observed (from 2 to 6 o'clock). LAD: left anterior descendent; D1: diagonal

Conclusions

The high resolution images provided by OCT have opened a new era in the evaluation of coronary stents. It can be a useful tool in the pre-stenting lesion assessment through its ability to provide information on lumen dimensions and plaque composition. The unique capabilities of the technique to identify several morphological findings associated with stent restenosis and thrombosis offer new opportunities to improve stent deployment technique with the aim of preventing these complications. Further, OCT may have an added value in contexts like ambiguous images presenting after stenting, or in complex settings such as bifurcation stenting or CTOs.

References

1. Fitzgerald PJ, Oshima A, Hayase M, Metz JA, Bailey SR, Baim DS, Cleman MW, Deutsch E, Diver DJ, Leon MB, Moses JW, Oesterle SN, Overlie PA, Pepine CJ, Safian RD, Shani J, Simonton CA, Smalling RW, Teirstein PS, Zidar JP, Yeung AC, Kuntz RE, Yock PG. Final results of the Can Routine Ultrasound Influence Stent Expansion (CRUISE) study. *Circulation* 2000;102:523-30.

2. Oemrawsingh PV, Mintz GS, Schalij MJ, Zwinderman AH, Jukema JW, van der Wall EE. Intravascular ultrasound guidance improves angiographic and clinical outcome of stent implantation for long coronary artery stenoses: final results of a randomized comparison with angiographic guidance (TULIP Study). *Circulation* 2003;107:62-7.

3. Roy P, Steinberg DH, Sushinsky SJ, Okabe T, Pinto Slottow TL, Kaneshige K, Xue Z, Satler LF, Kent KM, Suddath WO, Pichard AD, Weissman NJ, Lindsay J, Waksman R. The potential clinical utility of intravascular ultrasound guidance in patients undergoing percutaneous coronary intervention with drug-eluting stents. *Eur Heart J* 2008;29:1851-7.

4. Gonzalo N, Garcia-Garcia HM, Serruys PW, Commissaris KH, Bezerra H, Gobbens P, Costa M, Regar E. Reproducibility of quantitative optical coherence tomography for stent analysis. *EuroIntervention* 2009;5:224-32.

5. Gonzalo N, Serruys PW, Garcia-Garcia HM, van Soest G, Okamura T, Ligthart J, Knaapen M, Verheye S, Bruining N, Regar E. Quantitative ex vivo and in vivo comparison of lumen dimensions measured by optical coherence tomography and intravascular ultrasound in human coronary arteries. *Rev Esp Cardiol* 2009;62:615-24.

6. Tanaka A, Imanishi T, Kitabata H, Kubo T, Takarada S, Tanimoto T, Kuroi A, Tsujioka H, Ikejima H, Komukai K, Kataiwa H, Okouchi K, Kashiwaghi M, Ishibashi K, Matsumoto H, Takemoto K, Nakamura N, Hirata K, Mizukoshi M, Akasaka T. Lipid-rich plaque and myocardial perfusion after successful stenting in patients with non-ST-segment elevation acute coronary syndrome: an optical coherence tomography study. *Eur Heart J* 2009;30:1348-55.

7. Barlis P, Sianos G, Ferrante G, Del Furia F, D'Souza S, Di Mario C. The use of intra-coronary optical coherence tomography for the assessment of sirolimus-eluting stent fracture. *Int J Cardiol* 2009;136:e16-20.

8. Gonzalo N, Serruys PW, Okamura T, Shen ZJ, Onuma Y, Garcia-Garcia HM, Sarno G, Schultz C, van Geuns RJ, Ligthart J, Regar E. Optical coherence tomography assessment of the acute effects of stent implantation on the vessel wall: a systematic quantitative approach. *Heart* 2009;95:1913-9.

9. Futamatsu H, Sabate M, Angiolillo DJ, Jimenez-Quevedo P, Corros C, Morikawa-Futamatsu K, Alfonso F, Jiang J, Cervinka P, Hernandez-Antolin R, Macaya C, Bass TA, Costa MA. Characterization of plaque prolapse after drug-eluting stent implantation in diabetic patients: a three-dimensional volumetric intravascular ultrasound outcome study. *J Am Coll Cardiol* 2006;48:1139-45.

10. Gonzalo N, Serruys PW, Okamura T, van Beusekom HM, Garcia-Garcia HM, van Soest G, van der Giessen W, Regar E. Optical coherence tomography patterns of stent restenosis. *Am Heart J* 2009;158:284-93.

11. Takano M, Yamamoto M, Inami S, Murakami D, Ohba T, Seino Y, Mizuno K. Appearance of lipid-laden intima and neovascularization after implantation of bare-metal stents extended late-phase observation by intracoronary optical coherence tomography. *J Am Coll Cardiol* 2009;55:26-32.

12. Xie Y, Takano M, Murakami D, Yamamoto M, Okamatsu K, Inami S, Seimiya K, Ohba T, Seino Y, Mizuno K. Comparison of neointimal coverage by optical coherence tomography of a sirolimus-eluting stent versus a bare-metal stent three months after implantation. *Am J Cardiol* 2008;102:27-31.

13. Barlis P, Regar E, Serruys PW, Dimopoulos K, van der Giessen WJ, van Geuns RJ, Ferrante G, Wandel S, Windecker S, van Es GA, Eerdmans P, Juni P, di Mario C. An optical coherence tomography study of a biodegradable vs. durable polymer-coated limus-eluting stent: a LEADERS trial substudy. *Eur Heart J* 2010;31:165-76.

14. Takano M, Yamamoto M, Inami S, Murakami D, Seimiya K, Ohba T, Seino Y, Mizuno K. Long-term follow-up evaluation after sirolimus-eluting stent implantation by optical coherence tomography: do uncovered struts persist? *J Am Coll Cardiol* 2008;51:968-9.

15. Gonzalo N, Barlis P, Serruys PW, Garcia-Garcia HM, Onuma Y, Ligthart J, Regar E. Incomplete stent apposition and delayed tissue coverage are more frequent in drug-eluting stents implanted during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction than in drug-eluting stents implanted for stable/unstable angina: insights from optical coherence tomography. *JACC Cardiovasc Interv* 2009;2:445-52.

16. Kubo T, Imanishi T, Kitabata H, Kuroi A, Ueno S, Yamano T, Tanimoto T, Matsuo Y, Masho T, Takarada S, Tanaka A, Nakamura N, Mizukoshi M, Tomobuchi Y, Akasaka T. Comparison of vascular response after sirolimus-eluting stent implantation between patients with unstable and stable angina pectoris: a serial optical coherence tomography study. *JACC Cardiovasc Imaging* 2008;1:475-84.

17. Tanigawa J BP, Dimopoulos K, Di Mario C. Optical coherence tomography to assess malapposition in overlapping drug-eluting stents. *EuroIntervention* 2008;3:580-583.

18. Otake H, Shite J, Ako J, Shinke T, Tanino Y, Ogasawara D, Sawada T, Miyoshi N, Kato H, Koo BK, Honda Y, Fitzgerald PJ, Hirata K. Local determinants of thrombus formation following sirolimus-eluting stent implantation assessed by optical coherence tomography. *JACC Cardiovasc Interv* 2009;2:459-66.

19. Gonzalo N SP, Okamura T, Shen ZJ, Garcia-Garcia HM, Onuma Y, van Geuns RJ, Ligthart J, Regar E. Relation between plaque type and dissections at the edges after stent implantation: an optical coherence tomography study. *Int J Cardiol* 2010;In press.

20. Tyczynski P, Ferrante G, Kukreja N, Moreno-Ambroj C, Barlis P, Ramasami N, De Silva R, Beatt K, Di Mario C. Optical coherence tomography assessment of a new dedicated bifurcation stent. *EuroIntervention* 2009;5:544-51.

21. Gonzalo N, Garcia-Garcia HM, Regar E, Barlis P, Wentzel J, Onuma Y, Ligthart J, Serruys PW. In vivo assessment of high-risk coronary plaques at bifurcations with combined intravascular ultrasound and optical coherence tomography. *JACC Cardiovasc Imaging* 2009;2:473-82.

22. Munce NR, Yang VX, Standish BA, Qiang B, Butany J, Courtney BK, Graham JJ, Dick AJ, Strauss BH, Wright GA, Vitkin IA. Ex vivo imaging of chronic total occlusions using forward-looking optical coherence tomography. *Lasers Surg Med* 2007;39:28-35.

23. Schultz C, van der Ent M, Serruys PW, Regar E. Optical coherence tomography to guide treatment of chronic occlusions? *JACC Cardiovasc Interv* 2009;2:366-7.

24. Munce NR, Wright GA, Mariampillai A, Standish BA, Leung MK, Tan L, Lee K, Courtney BK, Teitelbaum AA, Strauss BH, Vitkin IA, Yang VX. Doppler optical coherence tomography for interventional cardiovascular guidance: in vivo feasibility and forward-viewing probe flow phantom demonstration. *J Biomed Opt* 2010;15:011103.