

Optical Coherence Tomography Is Now Ready: Sharpening the Tool

Francesco Prati^{a,b} and Maria Teresa Mallus^a

^aInterventional Cardiology, San Giovanni Hospital, Rome, Italy

^bCLI Foundation, Rome, Italy

There is a general consensus that optical coherence tomography (OCT) is a breakthrough technology that will increase our understanding for the mechanism of stent failure and will provide new insights on the pathophysiology of acute coronary syndromes.^{1,2}

The inability of infrared light to penetrate red blood cells posed technical problems in the search of an optimal modality of acquisition for the previous time domain OCT. Two modalities were set up to displace blood, the first requiring the occlusion of the studied artery by means of a gentle balloon dilatation, and the second based on the intracoronary injection of iso-osmolar contrast.^{3,4} However, there are few validation studies on the reproducibility of qualitative and quantitative analysis obtained with time domain OCT, because some pioneers alerted the interventional cardiology community that this innovative imaging technique was about to be replaced by the second generation frequency domain OCT (FD-OCT).⁵ This novel technology represents a true step forward for OCT as it provides a higher number of lines per cross-section and therefore has a better resolution. Furthermore, the acquisition process is markedly improved. The fact that the catheter goes over a regular wire, exactly like intravascular ultrasound (IVUS) probes, simplifies acquisition and makes images more stable than they used to be. The surprising pull-back speed that can reach 25 mm/s in the LightLab system enables the acquisition of long coronary segments in a few seconds: for example, at a speed of 20 mm/s a segment length of 50 mm can be imaged in less than 3 s with 100 frames/s.

However, these surprising features can pose some problems. An obvious question is whether at such a superb speed morphological details can be obtained with high reproducibility.

The paper by Gonzalo et al⁶ published in this issue of *Revista Española de Cardiología* represents the first attempt to verify OCT reproducibility for detection of atherosclerotic plaques and stented segments.

The authors studied 45 patients (45 coronary segments) with FD-OCT, using different acquisition speeds, with the 20 mm/s pull-back being the most used (65% of cases). A high reproducibility in the visualization of stent features (edge and intra-stent dissection, tissue prolapse, and malapposition) and plaque composition was obtained. Furthermore, FD-OCT allowed the visualization of long coronary segments (average 54.4 mm) in about 3 s and required less “flush” volume than time domain OCT.

The authors should be congratulated for having reported for the first time on the reproducibility of OCT findings. Obviously, there is much to do in this field and the paper itself raises some burning questions. A first issue is which acquisition speed should be applied: the light speed (20 mm/s) seems to be a reasonable compromise between the image quality and the need to acquire long segments with little contrast but it may reduce the reproducibility of OCT findings. It would be of interest to compare the variability in OCT interpretations of pull-backs obtained at different speeds.

The reproducibility demonstrated for FD-OCT in the identification of coronary plaques composition is obviously good news. The morphology of an atherosclerotic lesion can affect coronary interventions and an accurate study of plaque components is a prerequisite for the identification of lesions prone to coronary events, the so-called vulnerable lesions.

Surprisingly, Gonzalo et al⁶ reported a higher level of disagreement for fibrous and lipid-rich plaques, while previous studies showed some degree of misclassification for lipid pools and calcium deposits.⁷ This latter is an important issue that should be kept in mind. On one hand, the appearance on OCT results of lipid and calcific components is not very different, with the necrotic lipid pools being less well delineated than calcifications and having diffusely bordered, signal-poor regions (lipid pools) with overlying signal-rich bands, corresponding to fibrous caps. On the other hand, the distinction

SEE ARTICLE ON PAGES 893-903

Correspondence: Dr F. Prati,
Via Appia Nuova, 52. 00183 Rome, Italy
E-mail: fprati@hsangiovanni.roma.it

between plaque components having just one of the two characteristics (calcium vs lipid pool) is often artificial, as plaque may reveal both features. There is a need for post-processing software that can address specific region of interest of the plaque, detailing the inherent composition and providing measurements of specific elements to accomplish this goal. These dedicated softwares should be developed to identify the presence and location of necrotic lipid cores and reveal local inflammation by showing and quantifying inflammatory cells such as macrophages.

OCT is the most promising imaging modality to study plaque vulnerability, a burning issue in the search for morphological information that reveals the propensity of coronary lesions toward instability and development of acute coronary syndromes. As a second ambitious project, OCT may become the tool to investigate, with serial studies, the variation of atherosclerosis in response to specific treatments. To accomplish this task, further work is needed and we expect that in the near future other papers will provide new quantitative data on the reproducibility of OCT findings for assessment and quantification of plaque components. However, the maximal acquisition speed of 25 mm/s that can be achieved with the LightLab technology conveys marked advantages during the pull-back but may pose some problems for the accuracy of the images obtained in serial studies. At such a speed it is not possible to apply post-processing labeling modalities to select, for instance, late diastolic frames; furthermore, unlike for IVUS, the acquisition is so fast that a certain segment (for a length greater than 10 mm) will be obtained only in one of the 2 cycle phases. This could be a reason for concern if we consider that luminal areas exhibit marked variations between systole and diastole.

Moving to the field of coronary intervention, the history of stent advent nicely exemplifies the concept that the possibility to address the vessel architecture from the inside using intra-coronary probes provides a huge amount of knowledge to improve interventional procedures. The introduction of stents in clinical practice was initially burdened by an unacceptably high incidence of sub-acute thrombosis but the use of IVUS opened the way to understanding the reasons for stent failure. IVUS clarified that after optimal angiographic results many first generation stents were still having a marked under-expansion with irregular eccentric lumen and incomplete apposition of the stent struts to the vessel wall.⁸ These findings led to a new strategy for stent deployment based on high-pressure balloon dilatation inside the stent, to be done with angiographic guidance.⁹ In other words, IVUS taught us how to implant a stent.

More recently, IVUS showed that the presence of a large plaque burden tended to increase the amount of neointima at follow-up,¹⁰ and therefore the risk of restenosis. Interventional cardiology is in continuous progress: about 10 years ago we welcomed the introduction of drug eluting stents, an innovative concept where the stent is not simply a scaffold but a structure to elute drugs. However, even today the development of stents that are able to reduce restenosis in the most difficult clinical and anatomical scenarios remains a challenge for the device companies and a hope for interventional cardiologists.¹¹ Furthermore, and even more important, there is a need for drug eluting stents with no risk of late thrombosis.^{1,12}

For the first time there is an imaging modality that, due to a superb resolution, can visualize and, at the same time, quantify tiny elements that may be related to stent failure: plaque prolapse, edge and intra-stent dissection and malapposition.¹³⁻¹⁶

The fact that all these features can be visualized with low intra- and inter-observer variability is very good news. The clinical role of these findings is still unknown but it is reasonable to think of them as morphological details that can have an impact on interventional procedures.

OCT is now on the stage and promises to act as a protagonist. Next, OCT needs to be sharpened; the most exciting coronary imaging modality must also become a reliable one.

REFERENCES

1. Prati F, Regar E, Mintz GS, Arbustini E, Di Mario C, Jang IK, et al for the Expert's OCT Review Document. Expert review document on methodology and clinical applications of OCT. Physical principles, methodology of image acquisition and clinical application for assessment of coronary arteries and atherosclerosis. *Eur Heart J*. 2010;31:401-15.
2. Kubo T, Imanishi T, Takarada S, Kuroi A, Ueno S, Yamano T, et al. Assessment of culprit lesion morphology in acute myocardial infarction: ability of optical coherence tomography compared with intravascular ultrasound and coronary angiography. *J Am Coll Cardiol*. 2007;50:933-9.
3. Prati F, Cera M, Ramazzotti V, Imola F, Giudice R, Albertucci M. Safety and feasibility of a new non-occlusive technique for facilitated intracoronary optical coherence tomography (OCT) acquisition in various clinical and anatomical scenarios. *EuroIntervention*. 2007;3:365-70.
4. Prati F, Cera M, Ramazzotti V, Imola F, Giudice R, Giudice M, et al. From bench to bed side: A novel technique to acquire OCT images. *Circ J*. 2008;72:839-43.
5. Takarada S, Imanishi T, Liu Y, Ikejima H, Tsujioka H, Kuroi A, et al. Advantage of next-generation frequency-domain optical coherence tomography compared with conventional time-domain system in the assessment of coronary lesion. *Catheter Cardiovasc Interv*. 2010;75:202-6.
6. Gonzalo N, Tearney GJ, Serruys PW, van Soest G, Okamura T, García-García HM, et al. Tomografía de coherencia óptica de segunda generación en la práctica clínica. La adquisición de datos de alta velocidad muestra

- una reproducibilidad excelente en pacientes tratados con intervenciones coronarias percutáneas. *Rev Esp Cardiol*. 2010;63:893-903.
7. Manfrini O, Mont E, Leone O, Arbustini E, Eusebi V, Virmani R, et al. Sources of error and interpretation of plaque morphology by Optical Coherence Tomography. *Am J Cardiol*. 2006;98:156-9.
 8. Colombo A, Hall P, Nakamura S, Almagor Y, Maiello L, Martini G, et al. Intracoronary stenting without anticoagulation accomplished with intravascular ultrasound guidance. *Circulation*. 1995;91:1676-88.
 9. Nakamura S, Hall P, Gaglione A, Tiecco F, Di Maggio M, Maiello L, et al. High pressure assisted coronary stent implantation accomplished without intravascular ultrasound guidance and subsequent anticoagulation. *J Am Coll Cardiol*. 1997;29:21-7.
 10. Prati F, Di Mario C, Moussa I, Reimers B, Mallus MT, Parma A, et al. In-stent neointimal proliferation correlates with the amount of residual plaque burden outside the stent: an intravascular ultrasound study. *Circulation*. 1999;99:1011-4.
 11. Wijns W. Late stent thrombosis after drug eluting stent: seeing is understanding. *Circulation*. 2009;129:364-5.
 12. Tanigawa J, Barlis P, Di Mario C. Intravascular optical coherence tomography: optimisation of image acquisition and quantitative assessment of stent strut apposition. *EuroIntervention*. 2007;3:128-36.
 13. Otake H, Shite J, Ako J, Shinke T, Tanino Y, Ogasawara D, et al. Local determinants of thrombus formation following sirolimus-eluting stent implantation assessed by Optical Coherence Tomography. *JACC Cardiovasc Interv*. 2009;2:459-66.
 14. Ozaki Y, Okumura M, Ismail TF, Naruse H, Hattori K, Kan S, et al. The fate of incomplete stent apposition with drug-eluting stents: an optical coherence tomography-based natural history study. *Eur Heart J*. 2010;31:1470-6.
 15. Gonzalo N, Barlis P, Serruys PW, García-García HM, Onuma Y, Ligthart J, et al. 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. Capodanno D, Prati F, Pawlowsky T, Cera M, La Manna A, Albertucci M, et al. Comparison of optical coherence tomography and intravascular ultrasound for the assessment of in-stent tissue coverage after stent implantation. *EuroIntervention*. 2009;5:538-43.