Optical Coherence Tomography in Coronary Atherosclerosis

Abstract
Despite developments in therapeutic and diagnostic technologies, the global burden of atherosclerotic coronary artery disease is increasing. Intravascular imaging has become an invaluable adjunct to percutaneous coronary intervention. Optical coherence tomography (OCT) is a catheter based invasive imaging system that uses light instead of ultrasound to produce high resolution in vivo images of coronary arteries and deployed stents. The technical aspects of intracoronary image acquisition, advantages, disadvantages of use and current applications of OCT in coronary atherosclerosis are discussed.

Keywords: Optical coherence tomography; Atherosclerosis; Coronary artery disease

Abbreviations: IVUS: Intravascular Ultrasound; OCT: Optical Coherence Tomography; FFR: Fractional Flow Reserve; TD-OCT: Tissue-Domain Optical Coherence Tomography; FD-OCT: Frequency-Domain Optical Coherence Tomography; PCI: Percutaneous Coronary Intervention; TCFA: Thin-Capped Fibroatheroma; MACE: Major Adverse Cardiovascular Event

Introduction
Despite advances in therapeutic and diagnostic technologies, ischaemic heart disease remains a global leading cause of death [1]. Most cases result from atherosclerosis, an inflammatory and fibro-proliferative process resulting in activation of growth factors, vasoregulatory mechanisms and cytokines resulting in intimal thickening and subsequent endoluminal obstruction [2]. More sophisticated interventional techniques have been adopted to combat the increasing burden of atherosclerosis, including intravascular ultrasound (IVUS), fractional flow reserve (FFR) and more recently, optical coherence tomography (OCT). This paper provides an overview of the principles and current uses of OCT in diagnosing and guiding the treatment of atherosclerotic coronary artery disease.

Principles of optical coherence tomography
Intravascular OCT provides a method of obtaining cross-sectional tomographic vascular imaging with definition that is superior to other currently available modalities. It acts as an optical analogue of IVUS, where ultrasound is replaced by light that is reflected or back-scattered from internal structures within tissue. This ‘echo time delay’ produces a measurable signal intensity or magnitude. As the speed of light does not allow direct measurement of the echo time delay, interferometric techniques are employed to analyse the reflected light signal. Two main technologies exist to create OCT images, time domain (TD-OCT) and Fourier or frequency domain (FD-OCT). While TD-OCT uses a moving mirror as its reference arm and a broadband light source, FD-OCT uses a fixed mirror with a variable frequency light source allowing simultaneous detection of reflections from all echo time delays [3]. This allows faster image acquisition rates, improved signal-to-noise ratio with subsequent higher quality imaging, making FD-OCT the imaging mode of preference [4]. By utilising this ultrafast frequency swept near-infrared light source to image the vessel, FD-OCT is able to gain axial resolutions in the region of 10 to 15µm and lateral resolutions of 20 to 90µm. The rotating fibre-optic system creates a detailed tissue image with a ten-fold greater resolution than that achieved with IVUS [5-7], due to the shorter wavelength (1280-1350nm range) of the imaging light compared with ultrasound. However, the shorter wavelength limits tissue penetration to 1 to 3 mm as compared with 4 to 8mm achieved with IVUS, with the exception of calcified lesions in which ultrasound has a limited penetration [8].

Due to the high attenuation of light by red blood cells, effective OCT requires the clearing or flushing of blood from the lumen prior to imaging the desired segment of vessel. The slow acquisition speed of TD-OCT requires proximal balloon occlusion of the coronary of interest, with subsequent flushing of the artery to remove blood from the field of view. This limits its widespread adoption because of prolonged intravascular occlusion potentiating the risk of coronary damage and myocardial ischaemia. In FD-OCT, a greater frame rate is achieved because the swept source laser can be focussed quicker than the reference mirror can be moved in TD-OCT. Therefore, comprehensive volumetric microscopy of the vessel can be safely performed with the intra-arterial flushing of blood with a 10-15ml bolus of crystalloid solution, usually radio contrast, obviating the need for balloon occlusion of the vessel [9].

OCT in coronary atherosclerosis, percutaneous coronary intervention and plaque characterisation
Both TD and FD-OCT are deemed safe in assessing atherosclerotic plaque characteristics, as well as guiding percutaneous coronary intervention (PCI) [10-13]. The high definition of OCT imaging allows all aspects of plaque morphology to be accurately delineated including fibrous tissue, lipid accumulation and calcific deposition [6,14].

A large proportion of acute coronary events arise from sudden luminal obstruction caused by thrombosis as a result of plaque rupture or erosion. Our current understanding of
vulnerable plaque biology suggests that approximately 80% of significant plaque rupture occurs within inflamed thin-capped fibroatheromas (TCFA) [15]. It is accepted that TCFA comprise of a thin fibrous cap less than 65µm in diameter, overlying a large necrotic lipid pool (>2 quadrants of the cross-sectional image), with associated inflammatory cell cap infiltration [16]. Studies using virtual histology IVUS have previously determined TCFA as a predictor of major adverse cardiovascular events (MACE) [17,18]. As OCT provides superior in vivo characterisation of plaque morphology, identifying TCFA may prospectively identify the most vulnerable lesions and therefore influence prognosis. This has been validated in clinical studies comparing OCT with IVUS in acute coronary cohorts [16,19], particularly as a rupture-prone fibrous cap less than 65 microns is well under the resolution capacity of IVUS. In vivo and post mortem studies have also corroborated the ability of OCT to accurately detect TCFA, especially in identifying its increased incidence in myocardial infarction [20-22]. Furthermore, OCT has been successfully used to examine the role of pharmacological interventions on plaque anatomy and stability [23-25].

In normal vessels, the coronary artery appears as a three layered structure with OCT. A dark band denotes the low signal anatomy and stability [23-25].

In addition to plaque characterisation, OCT has been used to optimise and guide PCI by providing a clear depiction of the boundaries between vessel, lumen and metallic stent struts. The near infra-red OCT light does not penetrate metal, hence stent struts are visualized as linear structures with strong surface reflection and typical dorsal shadowing [28]. Earlier papers allude to OCT outperforming IVUS in detecting spontaneous and PCI-induced dissection, tissue prolapse and incomplete stent apposition, all of which have been implicated in acute as well as late stent thrombosis [12,29,30]. Limited outcome data also exists to show OCT-guided PCI as superior to angiography alone [31]. This unrivalled endovascular resolution has allowed assessment of the

**Table 1:** Image characteristics of optical coherence tomography with different plaque morphologies.

| Tissue Characteristics | OCT characteristics |
|------------------------|----------------------|
| Fibrous                | Homogenous           |
|                        | High reflectivity    |
|                        | Low attenuation      |
| Lipid                  | Diffuse edges        |
|                        | High reflectivity    |
|                        | High attenuation     |
| Calcific               | Low reflectivity (compared to IVUS) |
|                        | Low attenuation      |
| Red thrombus           | Mass protruding into vessel lumen |
|                        | Medium reflectivity  |
|                        | High attenuation     |
| White thrombus         | Luminal protrusion   |
|                        | Medium reflectivity  |
|                        | Low attenuation      |
| Stents: Metallic       | High reflectivity    |
|                        | High attenuation     |
| Biodegradable          | Low reflectivity (if residual polymer present) |
|                        | Low attenuation      |

(IVUS - intravascular ultrasound)

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vascular response at individual stent strut level following device deployment. Hence, numerous in-vivo OCT studies have exploited its capability to study factors related to the prognosis of stent-implanted lesions, including neointimal hyperplasia, stent strut coverage, stent malaposition and in-stent neatherosclerosis [32-34].

Technical drawbacks to OCT, in addition to limited tissue depth penetration, include inability to image plaques located at the very ostium of the coronaries, particularly with TD-OCT where balloon occlusion is required. Moreover, distinguishing different plaque morphology relies on operator experience and is subject to an element of inter-observer variability, analogous to grey-scale with IVUS [35].

Conclusion

Intracoronary OCT currently provides unparalleled high resolution anatomical data which the Interventional cardiologist can use to optimise treatment. It allows detailed structural analysis of atherosclerotic plaques and helps characterise the vascular healing process post PCI. However, there are still limitations with this technique and alternative imaging modalities such as IVUS still have a role in plaque delineation and PCI optimisation. Future developments such as micro-OCT will offer spatial resolution that is ten times that of FD-OCT, permitting sub-cellular analysis of the atherosclerotic process and improved diagnostic capabilities for the prospective prevention of coronary artery disease. Potential research combining doppler-like signal detection with OCT will allow integration of physiological and anatomical assessment using a single device.

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References

1. Global status report on non-communicable diseases 2014. Geneva, World Health Organization, 2015.
2. Ross R (1993) The pathogenesis of atherosclerosis: a perspective for the 1990s. Nature 362(6423): 801-809.
3. Bezerra HG, Costa MA, Guagliumi G, Rolls AM, Simon DI (2009) Intracoronary Optical Coherence Tomography: A Comprehensive Review: Clinical and Research Applications. JACC Cardiovasc Interv 2(11): 1035-1046.
4. Takarada S, Imanishi T, Liu Y, Ikejima H, Tsujioka H, et al. (2010) Advantage of next-generation frequency-domain optical coherence tomography compared with conventional time-domain system in the assessment of coronary lesion. Catheter Cardiovasc Interv 75(2): 202-206.
5. Yamagushi M, Tenshima M, Akasaka T, Hayashi T, Mizuno K, et al. (2008) Safety and feasibility of an intravascular optical coherence tomograph image wire system in the clinical setting. Am J Cardiol 101(5): 562-567.
6. Jang IK, Bouma BE, Kang DH, Park SJ, Park SW, et al. (2002) Visualization of coronary atherosclerotic plaques in patients using optical coherence tomography: comparison with intravascular ultrasound. J Am Coll Cardiol 39(4): 604-609.
7. Kawase Y, Hoshino K, Yoneyama R, McGregor J, Hajjar RJ, et al. (2005) In vivo volumetric analysis of coronary stent using optical coherence tomography with a novel balloon occlusion-flushing catheter: a comparison with intravascular ultrasound. Ultrasound Med Biol 31(10): 1343-1349.
8. Prati F, Regar E, Mintz GS, Arbustini E, Di Mario C, et al. (2010) Expert review document on methodology, terminology, and clinical applications of optical coherence tomography: physical principles, methodology of image acquisition, and clinical application for assessment of coronary arteries and atherosclerosis. Eur Heart J 31(4): 401-415.
9. McCabe JM, Croce KJ (2012) Optical coherence tomography. Circulation 126(17): 2140-2143.
10. Imola F, Mallus MT, Ramazzotti V, Manzoli A, Papalardo A, et al. (2010) Safety and feasibility of frequency domain optical coherence tomography to guide decision making in percutaneous coronary intervention. EuroIntervention 6(5): 575-581.
11. Barlis P, Gonzalo N, Di Mario C, Prati F, Buellfeldt L, et al. (2009) A multicentre evaluation of the safety of intracoronary optical coherence tomography. EuroIntervention 5(1): 90-95.
12. Gonzalez N, Barlis P, Serruys PW, Garcia-Garcia HM, Onuma Y, et al. (2009) 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 2(5): 445-452.
13. Gonzalez N, Serruys PW, Okamura T, Shen ZJ, Onuma Y, et al. (2009) Optical coherence tomography assessment of the acute effects of stent implantation on the vessel wall: A systematic quantitative approach. Heart 95(23): 1913-1919.
14. Yabushita H, Bouma B, Houser S, Aretz T, Jang I, et al. (2002) Characterization of human atherosclerosis by optical coherence tomography. Circulation 106(13): 1640-1645.
15. Schaar JA, Muller JR, Fulk E, Virmani R, Fuster V, et al. (2004) Terminology for high-risk and vulnerable coronary artery plaques. Report of a meeting on the vulnerable plaque. Eur Heart J 25(12): 1077-1082.
16. Miyamoto Y, Okura H, Kume T, Kawamato T, Neishi Y, et al. (2011) Plaque characteristics of thin-cap fibroatheroma evaluated by OCT and IVUS. JACC Cardiovasc Imaging 4(6): 638-646.
17. Stone GW, Maehma A, Lansky AJ, de Bruyne B, Criseta R, et al. (2011) A prospective natural-history study of coronary atherosclerosis. N Engl J Med 364(3): 226-235.
18. Calvert PA, Obaid DR, O’Sullivan M, Shapiro LM, McNab D, et al. (2011) Association between IVUS findings and adverse outcomes in patients with coronary artery disease: the VIVA (VIUS in Vulnerable Plaque) study. JACC Cardiovasc Imaging 4(8): 894-901.
19. Kubo T, Imanishi T, Takarada S, Kuroi A, Ueno S, et al. (2007) 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 50(10): 933-939.
20. Kume T, Akasaka T, Kawamoto T, Okura H, Watanabe N, et al. (2006) Measurement of the thickness of the fibrous cap by optical coherence tomography. Am Heart J 152(4): 755 e1-4.
21. Kume T, Okura H, Kawamoto T, Akasaka T, Toyota E, et al. (2008) Relationship between coronary remodeling and plaque characterization in patients without clinical evidence of coronary artery disease. Atherosclerosis 197(2): 799-805.
22. Kubo T, Imanishi T, Kashiwagi M, Ikejima H, Tsujioka H, et al. (2010)
Multiple coronary lesion instability in patients with acute myocardial infarction as determined by optical coherence tomography. Am J Cardiol 105(3): 318-322.

23. Takarada S, Imanishi T, Kubo T, Tanimoto T, Kitabata H, et al. (2009) Effect of statin therapy on coronary fibrous-cap thickness in patients with acute coronary syndrome: assessment by optical coherence tomography study. Atherosclerosis 202(2): 491-497.

24. Kataoka Y, Puri R, Hammadah M, Duggal B, Uno K, et al. (2014) Frequency-domain optical coherence tomographic analysis of plaque microstructures at non-culprit narrowings in patients receiving potent statin therapy. Am J Cardiol 114(4): 549-554.

25. Komukai K, Kubo T, Kitabata H, Matsu Y, Ozaki Y, et al. (2014) Effect of atorvastatin therapy on fibrous cap thickness in coronary atherosclerotic plaque as assessed by optical coherence tomography: the EASY-FIT study. J Am Coll Cardiol 64(21): 2207-2217.

26. Kume T, Akasaka T, Kawamoto T, Ogasawara Y, Watanabe N, et al. (2006) Assessment of coronary arterial thrombus by optical coherence tomography. Am J Cardiol 97: 1713-1717.

27. Wang L, Parodi G, Maehara A, Valenti R, Migliorini A, et al. (2015) Variable underlying morphology of culprit plaques associated with ST-elevation myocardial infarction: an optical coherence tomography analysis from the SMART trial. Eur Heart J Cardiovasc Imaging 17: 513-522.

28. Terashima M, Rathore S, Suzuki Y, Nakayama Y, Kaneda H, et al. (2009) Accuracy and reproducibility of stent-strut thickness determined by optical coherence tomography. J Invasive Cardiol 21(11): 602-605.

29. Bouma BE, Tearney GJ, Yabushita H, Shishkov M, Kamm CR, et al. (2003) Evaluation of intracoronary stenting by intravascular optical coherence tomography. Heart 89(3): 317-320.

30. Bezerra HG, Attizzani GF, Sirbu V, Musumeci G, Lortkipanidze N, et al. (2013) Optical coherence tomography versus intravascular ultrasound to evaluate coronary artery disease and percutaneous coronary intervention. JACC Cardiovasc Interv 6(3): 228-236.

31. Prati F, Di Vito L, Biondi-Zoccai G, Occhipinti M, La Manna A, et al. (2012) Angiography alone versus angiography plus optical coherence tomography to guide decision-making during percutaneous coronary intervention: the Centro per la Lotta contro l’Infarto-Optimisation of Percutaneous Coronary Intervention (CLI-OPCI) study. EuroIntervention 8(7): 823-829.

32. Guagliumi G, Costa MA, Sirbu V, Musumeci G, Bezerra HG, et al. (2011) Strut coverage and late malapposition with paclitaxel-eluting stents compared with bare metal stents in acute myocardial infarction: optical coherence tomography study of the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial. JACC Cardiovasc Interv 4(5): 317-324.

33. Guagliumi G, Musumeci G, Sirbu V, Bezerra HG, Suzuki N, et al. (2010) Optical coherence tomography assessment of in vivo vascular response after implantation of overlapping bare-metal and drug-eluting stents. JACC Cardiovasc Interv 3(5): 531-539.

34. Kang SJ, Mintz GS, Akasaka T, Park DW, Lee JY, et al. (2011) Optical coherence tomographic analysis of in-stent neointimal hyperplasia after drug-eluting stent implantation. Circulation 123(2): 2954-2963.

35. Manfrini O, Mont E, Leone O, Arbustini E, Eusebi V, et al. (2006) Sources of error and interpretation of plaque morphology by optical coherence tomography. Am J Cardiol 99(2): 156-159.