Intravascular ultrasound, optical coherence tomography and near infrared spectroscopy

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Abstract

Intravascular ultrasound (IVUS), optical coherence tomography (OCT) and near infrared spectroscopy (NIRS) allow for a thorough analysis of the atheroma's morphology in vivo. Moreover, it helps to guide coronary intervention and assess the results of stenting. IVUS, OCT and NIRS provide unique data about the analyzed tissue and thus all of them complement each other. Their application in daily clinical practice helps to understand the underlying pathology of disease and may contribute to the improvement of outcomes in coronary interventions.

Keywords:
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Introduction

The introduction of intravascular imaging opened new horizons for the presentation of coronary atherosclerosis in vivo. It became possible to follow the development of atherosclerosis and to detect atheromas that are prone to rupture (vulnerable plaques) known as thin fibrous cap atheromas (TCFA). Moreover, intravascular imaging helps to guide coronary interventions and to assess their results. Nowadays, available intravascular imaging modalities utilize ultrasound and near infrared light (nIR). Due to their intrinsic properties, both ultrasound and nIR deliver unique information about the analyzed tissue and thus complement each other. The following review presents the basics of intravascular ultrasound (IVUS), optical coherence tomography (OCT) and nIR spectroscopy (NIRS) in terms of plaque description, percutaneous coronary intervention (PCI) guidance and clinical application.

Intravascular ultrasound

The intravascular ultrasound (IVUS) is an invasive imaging modality that utilizes ultrasound (20–40 MHz) to present the vessel wall [1]. The dedicated IVUS catheter is advanced into the coronary vessel over a guidewire. The procedure is
More precise analysis of soft plaque composition by IVUS is derived by spectral analysis of its signal, known as Virtual Histology (VH-IVUS). VH-IVUS identifies 4 different types of plaque components: fibrous (green), fibro-fatty (yellow), dense calcium (white) and necrotic core (red) [5] (Fig. 1). Its accuracy has been documented by in vivo and in vitro studies. Moreover, VH-IVUS is able to detect thin fibrous cap atheroma (TCFA). TCFA is covered with fibrous cap less than 65 μm thick and IVUS resolution does not allow for direct measurement of cap thickness. Hence, the plaque is recognized as TCFA by VH-IVUS if the necrotic core (red color) has a direct contact with the lumen and occupies more than 40% of the plaque in 3 consecutive cross-sectional images. The PROSPECT study showed that the presence of such recognized TCFA increases the risk of future coronary events [6]. However, the results of the PROSPECT study should be discussed in light of controversies around precision of VH-IVUS. The histology data suggested poor accuracy of VH-IVUS in the necrotic core detection [7].

For many years IVUS imaging also served as a tool to estimate the significance of the intermediate coronary artery stenosis. The cut-off value of lumen area for non-left main (LM) stenosis was 4 mm² [8]. However, reports comparing the results of FFR and IVUS suggested that such cut-off value should be less than 3.07 mm² in non-LM stenosis, and less than 5.5 mm² in LM stenosis [9]. Nowadays, it is only appropriate to assess the significance of LM stenosis by IVUS, and despite the results of FFR studies clinical observations suggest that 6 mm² lumen area is the most appropriate cut-off value [10].

IVUS also helps to guide coronary interventions. Obtained measurements of the treated plaque facilitate the choice of appropriate stent diameter and length, and to assess the results of stenting (Fig. 1). IVUS easily presents stent under-expansion, stent malapposition and vessel dissection – three main risk factors for the acute stent thrombosis [11]. It is suggested that the optimal minimal DES area should be more than 8 mm² in LM, more than 6 mm² in proximal segment of LAD, and more than 5 mm² in proximal segment of Cx post procedure [12]. IVUS guided PCI significantly decreases all-cause mortality in both left main and non-left main stenting [13–15].

**Optical coherence tomography**

Similarly to IVUS, OCT provides cross-sectional images of the vessel. Instead of ultrasound OCT utilizes niR to present the morphology of the vessel; niR wavelength ranges between 1250 and 1350 nm. niR is split in two paths (red) [5] (Fig. 1). Its accuracy has been documented by in vitro studies. Moreover, VH-IVUS is able to detect thin fibrous cap atheroma (TCFA). TCFA is covered with fibrous cap less than 65 μm thick and IVUS resolution does not allow for direct measurement of cap thickness. Hence, the plaque is recognized as TCFA by VH-IVUS if the necrotic core (red color) has a direct contact with the lumen and occupies more than 40% of the plaque in 3 consecutive cross-sectional images. The PROSPECT study showed that the presence of such recognized TCFA increases the risk of future coronary events [6]. However, the results of the PROSPECT study should be discussed in light of controversies around precision of VH-IVUS. The histology data suggested poor accuracy of VH-IVUS in the necrotic core detection [7].

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As opposed to the IVUS imaging, the utilization of niR for OCT imaging requires blood removal from the vessel at the time of imaging, as the wavelength of niR does not penetrate through red blood cells. First TD OCT systems
Intravascular ultrasound, optical coherence tomography and near infrared spectroscopy required coronary artery occlusion at the time of imaging, which increased the risk of life threatening arrhythmias. The now-available FD-OCT imaging systems are so fast that the procedure may be performed at the time of a 3 s long injection of the contrast agent [18], which makes the procedure much safer [19].

OCT system is composed of the workstation and intravascular catheters with the OCT probe. The catheters are monorail systems and are advanced over a guidewire to the coronary artery. At the time of imaging the contrast is injected to flush the blood away and the probe is pulled back from distal segment to proximal segment of the artery. OCT imaging lasts 2.7 s and presents from 54 (10 μm step) to 72 mm (13 μm step) of the vessel length during the single pullback of the probe.

The use of light significantly improved the resolution of intravascular imaging. It ranges between 10 and 20 μm. However, the improved resolution is at the cost of beam penetration into the vessel wall. It obtains a signal only from 1 to 3 mm of the vessel wall, and thus does not allow to present plaque burden, and consequently plaque volume and vessel remodeling [17].

Nevertheless, similarly to IVUS, OCT provides quantitative analysis of the vessel lumen and OCT automated contour detection is very accurate and allows a very precise measurement of lumen area, lumen diameter and length of region of interest. Moreover, a novel OCT system (Ilumien Optis, St Jude Medical) provides an automated three-dimensional reconstruction of the analyzed segment (Fig. 2), which is overlaid on the angiography image to precisely guide PCI [20].

In healthy segments of coronary artery OCT presents four layers of the arterial wall: inter-elastic lamina, media, external elastic lamina and adventitia (Fig. 2). At the site of atheroma OCT is able to distinguish lipid, fibrotic and calcified components of the analyzed tissue. The lipid is characterized by high signal attenuation with the diffuse edges, calcium – by signal-poor area with sharp borders, and fibrotic components are presented as homogenous tissue with high reflectivity [21]. The high accuracy of plaque composition delivered by OCT was confirmed by histology [22] (Fig. 2). OCT is also able to present thrombus (and differentiate white thrombus from red one), intimal tear, intramural hematoma, micro vessels, and macrophage [17].

Thanks to high resolution of OCT imaging it became possible to directly measure the thickness of the fibrotic cap covering the lipid core and thus to detect TCFA. It makes OCT the gold standard to detect vulnerable plaques [23] (Fig. 2).

High resolution of OCT imaging enables to present the results of coronary intervention with the unprecedented precision. The stent strut malapposition, stent under-expansion and vessel dissection are very clearly presented by OCT. Due to light properties, metallic struts are only visible at their adluminal edge, and the knowledge about the strut thickness is necessary for stent apposition assessment. If the distance between the middle of the blooming struts and the vessel contour is more than the strut thickness, the malapposition is detected [24] (Fig. 2). Contrary to metallic stents, the whole polymeric struts of bioresorbable vascular scaffolds (BVS) are presented by OCT and malapposition

Fig. 2 – Representative images of intravascular optical coherence imaging (OCT). (A) Cross-sectional OCT image of healthy segment of coronary vessel presenting the internal elastic lamina (IEL), the media (M), external elastic lamina (EEL) and adventitia (Ad). (B) Cross-sectional OCT image of fibrotic lesions. (C) Cross-sectional OCT image of lipid-rich lesion covered with thin fibrous cap atheroma (TCFA – white arrows). The image presents also small red thrombi. (D) Cross-sectional OCT image of calcification (white arrow). (E) Cross-sectional OCT image after the implantation of the everolimus eluting stent with visible stent struts in malapposition (white arrows). (F) Cross-sectional OCT image post implantation of bioabsorbable vascular scaffold with visible polymeric struts. (G) Three-dimensional reconstruction of coronary artery at the site of stent implantation.
is easily detected as a gap between the scaffold and the vessel contour. BVS imaging by OCT is also able to present a scaffold disruption, which is not possible to detect by fluoroscopy [25]. Notably, OCT is the only method that can appropriately assess the expansion of BVS.

In addition to the stent apposition, OCT presents plaque protrusion through stent struts and thrombus formation. OCT has been broadly applied in the assessment of vessel healing after stent implantation. It perfectly presents stent struts coverage by neointima and provides neointima characteristic [26]. The heterogenous, layered, homogenous and lipid rich neointima may be described by OCT within implanted stent and at follow-up. The lack of homogenous neointima is associated with poorer clinical outcome [27]. Lipid-rich neointima indicates the presence of neoatherosclerosis within the stent, the heterogenous neointima is associated with high amount of fibrin, and layered neointima with persistent peri-struts inflammation [28].

OCT imaging also provides new approach in the treatment of myocardial infarction. It distinguishes between plaque rupture and plaque erosion as a cause of vascular thrombosis. Initial clinical observations suggest that eroded plaque may be subjected only to thrombectomy and left unstented without any major adverse cardiac events observed during the long-term follow-up [29].

**Near infrared spectroscopy**

NIRS utilizes nir in a range between 780 and 2500 μm to analyze the molar absorptivity of the tissue. Since light is absorbed with a different degree for every single particle, NIRS is able to present the chemical composition of the analyzed object. NIRS has been introduced into coronary imaging as modality focused on the detection of lipid deposition within the vessel [30]. As opposed to OCT, the applied wavelength of niR does not require blood removal from the vessel lumen to perform the analysis. Moreover, the intravascular NIRS is the only tool to assess tissue composition through the eyes of the implanted stent struts [31].

Similar to OCT and IVUS, the NIRS system is composed of an off-line station and intravascular catheters, which contain NIRS probe. NIRS probe is advanced into region of interest and pulled back with a speed 0.5 mm/s. NIRS penetration into the vessel wall is about 1 mm. Raw spectra of NIRS are decoded into a 7-digit color map and a 7-digit color block chemogram. A lipid distribution over the vessel is presented as yellow, tan and orange pixels whereas red pixels indicate its absence. If a pixel does not contain enough data (e.g. as caused by a guidewire), it appears black. The X-axis on the NIRS map presents the length of the pullback and the Y-axis on the map presents vessel circumference in degrees (0–360°) (Fig. 3).

NIRS mapping allows calculation of lipid core burden index (LCBI). It is a rate of all yellow pixels within the analyzed segment and is expressed per mille. LCBI is calculated for the total length of the region of interest, and the 4 mm segment with the highest LCBI (LCBI⁴mm) is emphasized. The NIRS block chemogram presents the probability of lipid deposition within 2 mm segments. For both NIRS map and NIRS chemogram the yellow indicates >0.97, tan indicates 0.84–0.97, orange indicates 0.57–0.83 and red indicates < 0.57 probability of lipid deposition. In summary, NIRS map is a very simple picture with lipids presented as yellow pixels on the red background. The presentation of lipid deposition by NIRS map and block chemogram has been validated by the histology [32] (Fig. 3).

In current practice NIRS has been only applied for research purposes and does not have any clinical applica-

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**Fig. 3 – Representative image of intravascular near infrared spectroscopy (NIRS) combined with IVUS image.** The figure presents NIRS map with detected lipids (yellow color) and the NIRS block chemogram. Black pixels present the region with not enough data to analysis. Green dashed arrows present the segment of the vessel with the highest lipid-core burden index = 283. The white dashed line corresponds to the cross-sectional image of IVUS with overlaid NIRS map as a colourful ring.
IVUS vs. OCT vs. NIRS

As opposed to IVUS, OCT requires blood removal from the vessel at the time of imaging. It does not allow for ostial lesion assessment. Moreover, OCT requires additional contrast injection and should be used with caution in patients with renal insufficiency. Smaller diameters and lumen areas are also provided by OCT as compared to IVUS measurements. The difference falls between 10% and 20%; thus IVUS cut-off values of lumen area cannot be used in OCT imaging to assess significance of coronary stenosis [38].

In terms of lipid detection, NIRS and OCT correlate moderately [39] and NIRS and VH-IVUS correlate poorly [40]. The correlation between NIRS and VH-IVUS is also poor in calcified lesions [38]. On the other hand, the comparison of TCFA detection by IVUS with OCT showed that OCT overestimates the number of vulnerable plaques [41].

Finally, the analysis from multimodality imaging (OCT, IVUS, NIRS) suggests that OCT derived TCFA is the strongest predictor of distal embolization as compared to LCBI values and plaque burden [42].

Conclusion

Every intravascular imaging modality offers quantitative analysis of the lesion and implanted stent, and provides unique information about the plaque composition and vessel healing. The use of IVUS, OCT and NIRS helps to clarify clinical problems and to guide coronary intervention. It seems that modern invasive cardiology should exploit more intravascular imaging techniques on a daily clinical basis to improve patients’ outcomes.

Conflict of interest

No conflict of interest.

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Ethical statement

Authors state that the research was conducted according to ethical standards.

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