Hybrid intravascular imaging: the key for a holistic evaluation of plaque pathology

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Even from the beginning of this century it was apparent that plaque composition and characteristics determine the final act of atherosclerosis and affect clinical outcomes[1]. However, recent reported medium-scale natural history of atherosclerosis studies have shown that plaque burden, composition and phenotype as determined by intravascular ultrasound (IVUS) have a limited capability in identifying lesions that are likely to progress and cause events[2,3]. Potential explanations for these findings are the intrinsic limitations of IVUS (i.e., fundamental sensitivity only to gradients of density/ echogenicity, limited resolution, and the increased noise and artefacts that are often seen in IVUS images) and the fact that the methodologies developed for the analysis of the backscatter IVUS signal and the characterisation of the composition of the plaque (i.e., virtual histology or integrated backscatter analysis) are likely to provide inaccurate estimations, especially in complex and calcified lesions[4,5]. To overcome these drawbacks, efforts have been made to develop new intravascular imaging techniques, such as optical coherence tomography (OCT), which permits higher resolution imaging of plaque pathology, and near-infrared spectroscopy (NIRS) which allows reliable characterisation of the composition of the plaque, and design hybrid catheters such as the combined OCT-IVUS and the NIRS-IVUS catheters which allow simultaneous OCT-IVUS and NIRS-IVUS imaging, respectively[6].

Several reports which compared different intravascular techniques (i.e., IVUS, NIRS, angioscopy or OCT) have shown discrepancies between the estimations of these modalities for the composition and phenotypic characteristics of the studied plaques[7-9]. These diversities are clearly due to the fact that each of the imaging techniques operates on different basic principles, with each technique only measuring a small and different subset of the histopathological characteristics defining the target plaque phenotype. None of the existing imaging techniques appears capable of portraying all of the structural, compositional, and pathophysiological characteristics of complex lesions, a fact that highlights the value of hybrid intravascular imaging in the study of atherosclerosis. In this issue of EuroIntervention, Roleder et al examine for the first time the ability of a hybrid NIRS-IVUS imaging modality to detect plaques with a thin-cap fibroatheroma phenotype (TCFA)[10]. Sixty patients (76 arterial segments) were included in the present analysis. The

authors confirmed the findings of pathology studies showing that lesions with a TCFA phenotype were more likely to exhibit positive remodelling, to have an increased plaque burden, a smaller minimal cross-sectional area, longer length and an increased lipid component. NIRS-IVUS-determined plaque characteristics (i.e., the presence of positive remodelling and an increased lipid component) allowed detection of TCFA with a high sensitivity, specificity, positive and negative predictive value (range: 78-100%).

However, OCT, with its high axial resolution, may appear to be the best modality for the identification of TCFA, but it should not be regarded as the gold standard. Reports have shown that OCT can often provide erroneous estimations about the composition of the

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plaque and thus Sawada et al proposed the combination of IVUS and OCT for the identification of high-risk plaques[9,11]. Moreover, a TCFA phenotype does not always indicate plaque vulnerability. Numerous studies have demonstrated that TCFA are often seen in patients with coronary artery disease and are likely to progress, regress and stay quiescent without leading to coronary events[12,13]. In the PROSPECT study, only 5% of the detected TCFA caused events, a percentage that was considerably higher in TCFA with an increased plaque burden and a minimal lumen area <4 mm[2][2]. In addition, the PREDICTION study demonstrated that, irrespective of their phenotype, 40% of the plaques with a >70% plaque burden which are exposed to low endothelial shear stress are likely to progress causing a significant luminal obstruction[3].

From the above it is apparent that our objective should not be the detection of a specific plaque morphology that has been associated with an increased risk of future events (i.e., TCFA or fibroatheroma) but rather the identification of plaques with multiple features indicating increased vulnerability. Therefore, it would have been more appropriate if Roleder et al had used the information provided by both imaging techniques to detect plaques with high-risk characteristics (i.e., plaques with macrophage infiltration, an increased necrotic core component, an increased plaque burden, a TCFA phenotype, and minimum lumen area <4 mm^2) and then to examine the efficacy of each modality in detecting these lesions.

There is a rapid evolution in hybrid intravascular imaging, where it appears that technology often advances faster than clinical research. A typical example is the YELLOW study that involved separate NIRS and IVUS imaging and reported a significant reduction of the lipid component in stenotic lesions after intensive treatment with rosuvastatin for seven weeks[14]. Interestingly, in this study there was an increase in the external elastic membrane volume at follow-up in the intensive care group despite the reduction in the lipid component, a finding that raises concerns about the accurate co-registration of IVUS and NIRS data. This limitation would have been overcome if imaging had been performed with the combined TVC catheter (MC 7 system; Infraredx, Inc., Burlington, MA, USA) which was introduced in the clinical setting before the completion of the YELLOW trial. Similarly, Roleder et al in this report evaluated the ability of NIRS-IVUS-derived characteristics to detect OCT-defined TCFA when the recent advances in the spectral processing of the reflected NIRS signal have already permitted the direct detection of thin fibrous caps with a high accuracy (area under the curve: 0.76)[14]. In addition, Fard et al designed a hybrid NIRS-OCT catheter which allows evaluation of luminal dimensions, identification of vessel wall microstructures (given by OCT) and characterisation of plaque composition (provided by NIRS)[15]. These developments are anticipated to be incorporated in future software and to enhance the role of hybrid NIRS-based imaging in the study of atherosclerosis.

There is no doubt that hybrid intravascular imaging provides unique opportunities for a more complete evaluation of plaque pathology. Therefore, there has been a trend in recent years towards the development of multimodality catheters that will permit simultaneous, complementary imaging of the atheroma. Validation of these advances using histological data and in clinical studies that will compare the new hybrid modalities with a single or another hybrid imaging technique is anticipated in the near future. The focus of these studies, however, should not be restricted to the assessment of the accuracy of the new approaches in the visualisation of specific features that are seen in high-risk plaques, but it should also be in line with the concept of multimodality imaging and should examine the ability of these techniques to provide a holistic evaluation of plaque morphology, physiology and vulnerability.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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