Understanding Why and When Optical Coherence Tomography Does Not Detect Vulnerable Plaques
Is It Important?

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The goal of research into the in vivo detection of vulnerable plaques is to provide a clinician with a diagnostic tool that identifies vulnerable plaques prospectively to prevent acute events. This tool must have both a high positive predictive value and a high negative predictive value in the clinical setting (not just against histopathology) and cannot require specific expertise or core-laboratory analysis to determine whether a plaque should be treated pre-emptively—in other words, a yes/no, red light/green light, treat/don’t treat tool. Optical coherence tomography (OCT) has been proposed to be that tool. OCT criteria for a thin-cap fibroatheroma (TCFA), the most common type of vulnerable plaque, include the presence of lipid with an overlying, macrophage-containing thin fibrous cap.

See Article by Phipps et al

However, early enthusiasm is often followed by skepticism as critical analyses appear. In a core-laboratory study by Kim et al in which the intraobserver reproducibility was high, the interobserver intraclass correlation coefficient among 4 highly trained individuals (a better, but still idealized representation of what would happen clinically) was 0.49 for OCT fibrous cap thickness and 0.77 (95% confidence interval, 0.53–0.97) and 0.71 (95% confidence interval, 0.55–0.86) for maximum and average arc of OCT lipid, respectively. In a study by Fujii et al, the sensitivity, specificity, positive predictive value, and diagnostic accuracy for the OCT detection of a TCFA were 100%, 97%, 41%, 100%, and 98%, respectively. In a similar study by Brown et al, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy for the OCT detection of a TCFA were 72.7%, 79.8%, 30.8%, and 95.9%, respectively. In a fourth study by Nakano et al, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of OCT were 77.8%, 97.4%, 60.9%, 98.8%, and 96.4%. In addition to being discordant with these studies, Phipps et al, in this issue of Circulation: Cardiovascular Interventions, identified reasons for the discrepancy between OCT and histopathologic lipid detection; they showed that foam cell infiltration was responsible for 70% of false TCFA diagnoses causing both thick-capped fibroatheromas to appear as TCFAs and the appearance of TCFAs when no lipid core was present. Other limitations to the accurate OCT assessment of lipid include artifacts caused by shallow or tangential beam angulation and drop-out and confounders such as the presence of fibrous cap microcalcifications or hemosiderin that can affect the appearance of lipid, cause difficulties distinguishing between lipid and calcium, and affect serial studies looking at pharmacological interventions, such as impact of statins on TCFA fibrous cap thickness. (Of note, there is no difference between optical frequency domain imaging and frequency-domain-OCT; they merely represent different implementations of the same fundamental technology.) Finally, the number of TCFAs in each of these studies was small; and there can be disagreement among pathologists as to whether specific lesions are or are not TCFAs.

More recently, it has been suggested that the use of 2 imaging technologies may improve on the diagnostic accuracy of any single technology and overcome limitations, such as the ones identified by Phipps et al. While once a fantasy, combined imaging devices are now a reality. However, when comparing different imaging modalities, there is rarely agreement among them about the diagnosis of individual TCFAs whether assessed in vivo or in vitro although agreement is generally worse in vivo adding to the issues about clinical vulnerable plaque detection. Infraredx (Burlington, MA) has developed a combined intravascular ultrasound (IVUS) and near-infrared spectroscopic catheter that is available commercially. Prototype combined IVUS and OCT catheters have been used in animal models. OCT has been combined with near-infrared autofluorescence to produce clinical images and, potentially, remove much of the ambiguity in the identification of lipid from OCT alone. If combined imaging technologies are the answer, then the question becomes which ones. Grayscale IVUS+near-infrared spectroscopy? Grayscale IVUS+OCT? Radiofrequency IVUS+OCT? OCT+near-infrared spectroscopy or autofluorescence? IVUS or OCT+assessment of endothelial shear stress? The many potential combinations have been summarized in a review article by Bourantas et al. Many of these combinations are technically possible although some are more practical than others; and issues of intellectual property, financing, ease-of-use, and adoption may limit the commercialization of certain combinations. Although Phipps et al are to be commended on their study and although pathological correlations and understanding...
reasons for limitations are important, at some point, it is necessary to move beyond correlations to clinical outcomes studies—first as prospective registries, but ultimately as multicenter outcomes trials in which events are actually reduced. Imaging findings that reliably predict (or exclude) events are more important than studies showing that one or another technology (or any combination of technologies) correlate (or do not correlate) with histopathology with a greater (or lesser) degree of accuracy. This has been done in PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree), \(^3\) VIVA (VH-IVUS in Vulnerable Atherosclerosis), \(^2\) and ATHEROREMO-IVUS (European Collaborative Project on Inflammation and Vascular Wall Remodeling in Atherosclerosis-IVUS)\(^3\) despite the highly critical animal study by Thim et al\(^4\) questioning the validity of VH-IVUS; and it is being replicated in PROSPECT-II that includes both a prospective registry and an embedded, randomized outcomes substudy called PROSPECT-Absorb.

Disclosures
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References


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