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EDITORIAL

Ultrasound and light: friend or foe? On the role of intravascular ultrasound in the era of optical coherence tomography

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Abstract More than 20 years after its introduction, intravascular ultrasound (IVUS) has outlived many other intracoronary techniques. IVUS was useful to solve many interventional problems and assisted us in understanding the dynamics of atherosclerosis. It serves as an established imaging endpoint in large progression-regression trial and as an important workhorse in many catheterization laboratories. Nowadays, increasingly complex lesions are treated with drug-eluting stents. The application of IVUS during such interventions can be very useful. Recently, optical coherence tomography (OCT), a light-based imaging technique, has entered the clinical arena. The "omnipresence" of OCT during scientific sessions and live courses with PCI may raise in many the question: Does IVUS have a future in the "era of OCT"? Three review articles, highlighted by this editorial, demonstrate the broad spectrum of current IVUS applications and underline the significant role of IVUS during the last two decades. OCT, the much younger technique, still has to prove its value. Yet OCT is likely to take over some of the current indications of IVUS as a research tool. In addition, OCT is currently gaining clinical significance for stent optimization during complex interventional procedures. Nevertheless, there is little doubt that IVUS still has a major role in studies on coronary atherosclerosis and for guidance of coronary stenting. Thus, ultrasound and light—are they friend or foe? In fact, both methods are good in their own rights. They are complementary rather than competitive. Moreover, in combination, at least for certain indications, they could be even better.

Keywords Intravascular ultrasound · Optical coherence tomography · Coronary atherosclerosis · Progression-regression · Arterial remodeling · Vulnerable plaque · Drug-eluting stent · Biodegradable vascular scaffolds

Abbreviations

IVUS	Intravascular ultrasound
RF	Radiofrequency
OCT	Optical coherence tomography
TCFA	Thin-cap fibroatheromas
PCI	Percutaneous coronary intervention
DES	Drug eluting stent

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Introduction

More than twenty years after its introduction, *intravascular ultrasound* (IVUS) is still alive and has outlived many other intracoronary techniques that have disappeared from the clinical arena. IVUS has been an "eye-opener" that has helped to solve many interventional problems and assisted us in understanding the dynamics of atherosclerosis, which involves the entire vascular wall during lesion development. IVUS not only serves as an established imaging endpoint in large progression-regression trials, but is also an important workhorse in many catheterization laboratories around the globe. Nowadays, increasingly complex lesions are treated with drug-eluting stents (DES), and the application of IVUS during such percutaneous coronary interventions (PCI) can be very useful. Recently, *optical coherence tomography* (OCT), a novel light-based invasive imaging technique, has entered the clinical arena. The "omnipresence" of OCT during scientific sessions, during live courses with PCI, and on the front pages of renowned cardiology journals may raise in many the question: *Does IVUS—the established technique—have a future in the "era of OCT"?*

To answer this question and to fully understand the role of IVUS in the past and at present, it is worthwhile to make a brief step back in time. The introduction of gray-scale IVUS in the late 1980s, stimulated meticulous validation studies [1–5]. Further improvement in IVUS image quality and device miniaturization increased the safety and clinical applicability of this technique. The addition of the third dimension and the possibility to acquire images in an ECG-gated fashion permitted highly reproducible volumetric measurements of plaque and vessel dimensions [6–8]. Subsequently, the development of novel techniques for the analysis of IVUS radiofrequency data provided quantitative information on plaque composition [9–12] that could not be obtained with conventional gray-scale IVUS [13]. In the current issue of the journal, Garcia-Garcia et al. [9] present an interesting overview on the development of gray-scale IVUS and discuss technical similarities and differences between the radiofrequency-based IVUS imaging modalities.

In fact, IVUS allowed for the first time a direct visualization of "the enemy" in vivo by depicting the burden of atherosclerotic changes in the coronary vessel wall. The hypothesis of arterial remodeling, which introduced by Glagov et al. [14] based on their work in vitro, was proven and extended by IVUS research in vivo [15–18]. IVUS demonstrated positive vessel remodeling to be an important feature of both vulnerable and ruptured coronary plaques [16]. Serial examination of the coronary vessel dimensions with IVUS permitted the assessment of true vascular remodeling in vivo [15, 17]. In these serial studies, a broad spectrum of remodeling behavior was demonstrated; in particular, lumen size of mildly diseased left main coronary arteries depended more on the direction of vessel remodeling than on plaque growth [15, 17]. Such insight into the dynamic nature of coronary remodeling has had an impact on how interventional cardiologists estimate true vessel size in the context of coronary stenting [19, 20].

In addition, IVUS was instrumental in the understanding of the dynamic nature of atherosclerosis progression-regression [18, 21–24]. For the first time, serial IVUS demonstrated in vivo the direct relation between serum cholesterol and the progression of plaque size [22]. Subsequently, large-scale multicenter trials with serial IVUS confirmed the aforementioned observations, and demonstrated the ability of statins to stop disease progression and to induce plaque regression at high doses [18, 21]. Serial IVUS studies provide established surrogate endpoints; this allows the testing of novel drugs with smaller study sample sizes and shorter study durations, which is likely to expedite the process of drug development and testing [21]. Moreover, there is evidence that coronary plaque progression as assessed with serial IVUS is linked with adverse cardiovascular events [23, 24]. In the current issue of the journal, Gogas et al. [18] shed light on various aspects of coronary remodeling and progression-regression studies with IVUS.

As briefly mentioned above, radiofrequency-based (RF) IVUS techniques were developed to characterize and quantify coronary plaque composition [9–12]. Both technical details and current insights from RF-IVUS studies are highlighted in the two review articles by Gracia-Garcia et al. and Gogas et al. [9, 18]. For instance, RF-IVUS derived thin-caped fibroatheromas (TCFA) are thought to be IVUS-equivalents of vulnerable plaques based on histopathological criteria [18]. Observations from the PROSPECT study showed a significant association between non-culprit RF-IVUS derived TCFA, assessed at a single point in time, and future coronary event risk [25]. But in fact there is only limited knowledge about the fate of RF-IVUS derived TCFA, and therefore, the treatment of non-obstructive lesions with RF-IVUS derived features of plaque vulnerability is still unclear. Recently, a serial study by Kubo et al. [26] suggested quite dynamic changes in RF-IVUS derived plaque phenotypes, which questions the value of single-point observations of plaque phenotypes. On the other hand, volumetric assessment of necrotic core volume is highly reproducible and its reduction may reflect plaque stabilization, making this parameter an interesting target for pharmacological intervention trials [27].

OCT—the "new kid on the block"—provides coronary imaging in vivo with a high near field resolution, which results in a superior lumen border detection compared to IVUS. However, OCT has a limited penetration depth, which is an evident shortcoming for the assessment of total vessel size and vascular remodeling, and implies the inferiority of OCT in progression-regression trials compared to IVUS. Yet in the context of vulnerable plaque detection, only OCT is able to depict and measure fibrous caps; this may help to identify plaques prone to rupture [28, 29]. On the other hand, the relatively user-friendly RF-IVUS analysis method provides quantification of different plaque components (e.g. necrotic core volume) which are displayed in simplified color-coded images. The interpretation of the "pseudo-microscopic" OCT images is more difficult; moreover, the discrimination between lipidic and calcified plaque components can be quite challenging as both can have low image intensities [29]. Considering the advantages and limitations of IVUS and OCT for the assessment of vulnerable plaques, the combined use of RF-IVUS and OCT may improve its detection as recently suggested [28, 29].

Also in target lesions of percutaneous coronary interventions (PCI), careful assessment of plaque composition may be useful, as a large necrotic core recently predicted cardiac marker release after stenting—most likely due to microembolization and/or induction of a no-reflow phenomenon [30]. For that reason, IVUS assessment before PCI may have the potential to identify lesions at risk of complications and may help to tailor interventional procedures (e.g. use of embolic protection devices and/or direct stenting) [29, 31].

Conventional grayscale IVUS has already proven its particular value in the early 1990s. It demonstrated to the interventional community the shortcomings of that time and was instrumental in developing the concept of optimizing stent expansion by use of balloon catheters with a larger size and higher inflation pressures [32]. In fact, IVUS guidance helped to improve the acute procedural result which greatly prevented (sub)acute stent thrombosis—the main problem in the early days of bare metal stenting [32, 33]. While various studies suggested that the use of IVUS can result in larger stent dimensions, less restenosis, and reduced need for repeat revascularization procedures, the results of various randomized multicenter studies were not unequivocal with regards to the routine use of IVUS guidance [34, 35]. Nevertheless, many experts agree that IVUS guidance can be very useful during stenting of bifurcations, left main stems, long lesions, small vessels, and in diabetics [20]. Moreover, the forward-looking IVUS catheter, which is currently under clinical evaluation, may facilitate the recanalization of chronic total occlusions of coronary arteries. In addition, IVUS can be extremely helpful in the prevention, detection, and management of various complications such as spiral dissections or stent-related problems.

The introduction of drug-eluting stents (DES) during the first decade of this century virtually abolished the need for repeat PCI to treat instent restenosis. The enthusiasm associated with the early DES results let us believe that IVUS optimization of stenting became much less important [36]. Then, the observation of late and very late stent thromboses in DES represented a "wake-up call" to carefully study the mechanisms involved. Therefore, various IVUS studies were performed and suggested that, besides other factors, DES underexpansion may be particularly important [37–39]. IVUS insights into the failure of DES as well as other stent-related issues are discussed in a review by Brugaletta et al. [40] in the present issue of the journal. IVUS guidance of DES implantation was recently shown to reduce late stent thrombosis and other major adverse cardiac events as well as the need for repeat revascularization [41].

New intracoronary devices, such as bioresorbable vascular scaffolds (BVS), are made of non-metallic materials that are classified by RF-IVUS as being "calcified and necrotic tissue" [42, 43]. Although this classification is obviously incorrect (RF-IVUS is not validated for characterization of such material), this technique may help to track the process of bioresorption and integration of biodegradable stent material into the vessel wall [42–46]. Recent data suggest that after bioresorption the "normal" structures of the arterial wall may be partially restored [42]. In the current issue of the journal, Brugaletta et al. [40] present an interesting overview of the IVUS guidance of DES and BVS implantation.

Compared to IVUS, the high-resolution technique OCT provides more detailed information on stent struts and their interaction with the vessel wall. OCT permits, for instance, a more accurate assessment of stent strut apposition to the vessel wall and allows the identification of even very thin neointimal layers during follow-up of DES [47, 48]. In addition, as previously discussed, OCT may complement RF-IVUS when identifying vulnerable high-risk lesions before stent implantation [29]. In fact, OCT may also be an interesting tool to study various mechanistical concepts in the clinical setting—concepts that can otherwise only be examined with bench-top research such as micro-computed tomography [49]. Guidance of coronary stenting with OCT has recently been shown to be feasible and safe [46].

However, OCT also has some shortcomings in this particular setting, such as (1) limited assessment of true vessel size, (2) suboptimal clearance of blood by flushing large proximal coronary segments, and (3) lack of computerized plaque tissue detection [47, 48]. Moreover, while we (greatly) know how to interpret IVUS, the enormous amount of detail depicted by OCT requires considerable effort before we will be able to make full use of all the information provided by OCT.

The three review articles, highlighted by this editorial comment, demonstrate the broad spectrum of current IVUS applications and underline the significant role of IVUS during the last two decades. OCT is a much younger technique which still has to prove its value. Yet OCT is likely to take over some of the current indications of IVUS as a research tool. In addition, OCT is currently gaining clinical significance in the field of stent optimization during complex PCI procedures. Nevertheless, there is little doubt that IVUS still has a major role in studies on progression-regression and composition of atherosclerotic plaques as well as for guidance of coronary stenting.

Thus, *ultrasound and light—are they friend or foe?* In fact, both methods are good in their own rights. They are complementary rather than competitive. Moreover, in combination, at least for certain indications, they could be even better.

Conflict of interest None.

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