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STATE-OF-THE-ART PAPER

Hybrid Intravascular Imaging

Current Applications and Prospective Potential in the Study of Coronary Atherosclerosis

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The miniaturization of medical devices and the progress in image processing have allowed the development of a multitude of intravascular imaging modalities that permit more meticulous examination of coronary pathology. However, these techniques have significant inherent limitations that do not allow a complete and thorough assessment of coronary anatomy. To overcome these drawbacks, fusion of different invasive and noninvasive imaging modalities has been proposed. This integration has provided models that give a more detailed understanding of coronary artery pathology and have proved useful in the study of the atherosclerotic process. In this review, the authors describe the currently available hybrid imaging approaches, discuss the technological innovations and efficient algorithms that have been developed to integrate information provided by different invasive techniques, and stress the advantages of the obtained models and their potential in the study of coronary atherosclerosis. (J Am Coll Cardiol 2013;61:1369–78) © 2013 by the American College of Cardiology Foundation

Coronary artery disease is the leading cause of death in the developed world (1). Its prevalence has been attributed to population aging and sedentary lifestyles and is expected to rise in the coming years. During the past decades, there has been considerable progress in understanding the pathophysiology of coronary artery disease, while devices, imaging techniques, and therapeutic strategies have been developed aiming to optimize the treatment of patients with ischemic heart disease. These advances have made feasible the treatment of complex lesions and high-risk patients, improving their prognosis and quality of life.

However, these developments have also created the need for more detailed imaging of coronary anatomy and pathology. It is apparent that contrast coronary angiography, which is the traditional method for the visualization of coronary artery disease, has significant limitations in assessing the extent and severity of atherosclerosis, as it permits only a 2-dimensional evaluation of luminal dimensions and is unable to provide information regarding vessel walls. Atheroma burden and its composition seem to affect prognosis, as there is evidence that cardiovascular outcomes and the occurrence of acute coronary events depend not only on the severity of luminal narrowing but also on plaque characteristics and inflammation (2). To address these limitations and study in more detail the natural evolution of atherosclerosis, considerable effort has been made in developing new imaging modalities that would permit the precise evaluation of coronary pathology. Advances in signal processing and the miniaturization of medical devices have allowed numerous intravascular imaging techniques to emerge (e.g., intravascular ultrasound [IVUS], optical coherence tomography [OCT], near-infrared spectroscopic [NIRS] imaging, intravascular magnetic spectroscopy, intravascular magnetic resonance imaging, Raman spectroscopy, intravascular photoacoustic [IVPA] imaging, near-infrared fluorescence [NIRF] imaging, and time resolved fluorescence spectroscopic [TRFS] imaging), which have enriched our knowledge of coronary atherosclerosis by providing detailed visualization of luminal and plaque morphology and reliable quantification of the atheroma burden and its composition (Online Fig. 1) (3,4). Although these modalities offer a plethora of new data, each also has inherent limitations that do not allow complete evaluation of the coronary arteries (Online Appendix). To address this drawback, hybrid imaging has been proposed. Hybrid imaging is the combination of different imaging techniques with complementary strengths into advanced images and

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Abbreviations and Acronyms

CTCA = computed tomographic coronary angiography

IVPA = intravascular photoacoustic

IVUS = intravascular ultrasound

NIRF = near-infrared fluorescence

NIRS = near-infrared spectroscopic

OCT = optical coherence tomography

QCA = quantitative coronary angiography

3D = 3-dimensional

TRFS = time-resolved fluorescence spectroscopic

models that allow more detailed and comprehensive coronary visualization.

The aims of this review are to describe the currently available intravascular-based hybrid imaging modalities, cite the advantages of the provided images and models, stress the methodological limitations of each approach, and discuss their potential value in the study of coronary atherosclerosis.

Hybrid Intravascular Imaging: Current Status

Fusion of IVUS and coronary angiography. The fusion of IVUS and x-ray angiography was performed for the first time in 1992 and was the first intravascular-based hybrid imaging technique (5). Although the proposed approach had significant methodological limitations, it opened new horizons in coronary representation, as it combined information regarding vessel geometry (given by coronary angiography) and vessel wall pathology (provided by IVUS). In recent years, several more efficient methodologies have been introduced that have managed to overcome the limitations of this approach (e.g., unreliable extraction of the catheter path and orientation of the IVUS frames) and achieve reliable and complete coronary representation (6–8).

The obtained 3-dimensional (3D) models allow comprehensive visualization of vessel geometry and plaque distribution and have been extensively used in research to study the association between local hemodynamic factors and the progression of atherosclerosis. Thus, today it is known that low and oscillatory shear stress have both atheropromoting and neointimal formation effects and contribute to the development of high-risk plaques (9–11). Recently, the PREDICTION (Prediction of Progression of Coronary Artery Disease and Clinical Outcome Using Vascular Profiling of Shear Stress and Wall Morphology) study was reported, in which serial IVUS examinations were used to investigate the effect of blood flow on the natural evolution of atherosclerosis. In that study, the acquired IVUS data were fused with angiographic data to reconstruct the coronary arteries of 502 patients at baseline and at 6-month to 10-month follow-up. Blood flow simulation was performed in the baseline models, and endothelial shear stress was estimated. It was found that low endothelial shear stress was associated with plaque progression and expansive remodeling and was an independent predictor of luminal narrowing and of future culprit lesions (12).

Currently, 3 systems are available that can integrate IVUS and x-ray angiography in a user-friendly environment and include advanced visualization modules for comprehensive 3D coronary representation (Fig. 1) (13–15). Although these provide holistic and detailed coronary visualization, they have applications only in research. This controversy has been attributed to the facts that coronary reconstruction is time consuming and requires specific expertise and that the additional information it provides cannot affect medical management.

Fusion of IVUS and computed tomography. The integration of IVUS and x-ray may allow the evaluation of plaque distribution in a vessel, but it cannot include coronary bifurcations and portray side branches. Two approaches have been proposed for this purpose, but both appear tedious and time consuming (16,17). This limitation was addressed by the method developed by van der Giessen et al. (18), who fused IVUS and computed tomographic coronary angiographic data. The proposed method used computed tomographic coronary angiography (CTCA) to define the centerline of the lumen and anatomical landmarks seen on both IVUS and CTCA to identify the position and the orientation of IVUS images onto the extracted centerline. Similar approaches have been recently proposed by Boogers et al. (19) and Voros et al. (20) (Online Fig. 2).

Although these methods are restricted only to patients who have undergone CTCA, coronary angiography, and IVUS, they have attracted attention because they permit direct comparison of the estimations of IVUS and CTCA. This erratic combination of invasive and noninvasive techniques has broken the boundaries of conventional imaging and allowed the detailed evaluation of the capabilities and limitations of CTCA in characterizing coronary atheroma. Thus, these techniques have already been used to demonstrate that CTCA provides reliable identification of plaque and accurate evaluation of the luminal, outer vessel wall, and plaque dimensions, but it has moderate capability in assessing the proportions of different plaque types in its composition (19,21).

Combination of IVUS and NIRS imaging. IVUS has limited capability in detecting the composition of the plaque, while the radiofrequency backscatter analysis of the IVUS signal, which seems to provide more reliable plaque characterization, results in erroneous estimations about the lipid tissue in stented segments and in areas behind calcified plaques (22). To address this drawback, a fusion of IVUS and NIRS imaging has been proposed. A new intravascular imaging catheter has recently been developed, the TVC Imaging System (MC 7 system, InfraReDx, Burlington, Massachusetts), which has both an NIRS light source and an IVUS probe on its tip, allowing the simultaneous acquisition of NIRS and IVUS data (Fig. 2). The feasibility of combined IVUS and NIRS imaging has already been tested, and currently this hybrid catheter is being used in the IBIS-3 (Integrated Biomarker and Imaging Study 3), which is examining the effect of rosuvastatin on lipid-rich coronary atherosclerotic plaques (23).