Multi-modality diagnostic assessment in interventional cardiology

Pyxaras, S.

Author: Pyxaras, S.
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Chapter 1

Introduction and Outline of the Thesis

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During the past decades percutaneous coronary intervention (PCI) contributed to a significant improvement of the prognosis of patients with coronary artery disease (CAD)[1, 2]. Invasive diagnostic assessment has an important role on PCI-guidance, allowing the functional evaluation of epicardial artery stenoses[3] and offering invaluable insights of the structure and metrics of coronary vessels affected by atherosclerosis[4-6].

The "golden-standard" of invasive diagnostic assessment in CAD remains coronary angiography[7]. Selective injection of contrast medium in the coronary arteries through dedicated catheters allows not only an initial, qualitative evaluation of possible vessel stenoses, but offers also a roadmap for PCI. Bi-dimensional angiographic images can – on their turn – be used as source information for quantitative coronary angiography (QCA) assessment, by the use of dedicated software[8]. This latter allows the precise reconstruction of the vessel's lumen-contour and the quantification of focal coronary stenoses due to atherosclerotic disease (Figure 1).

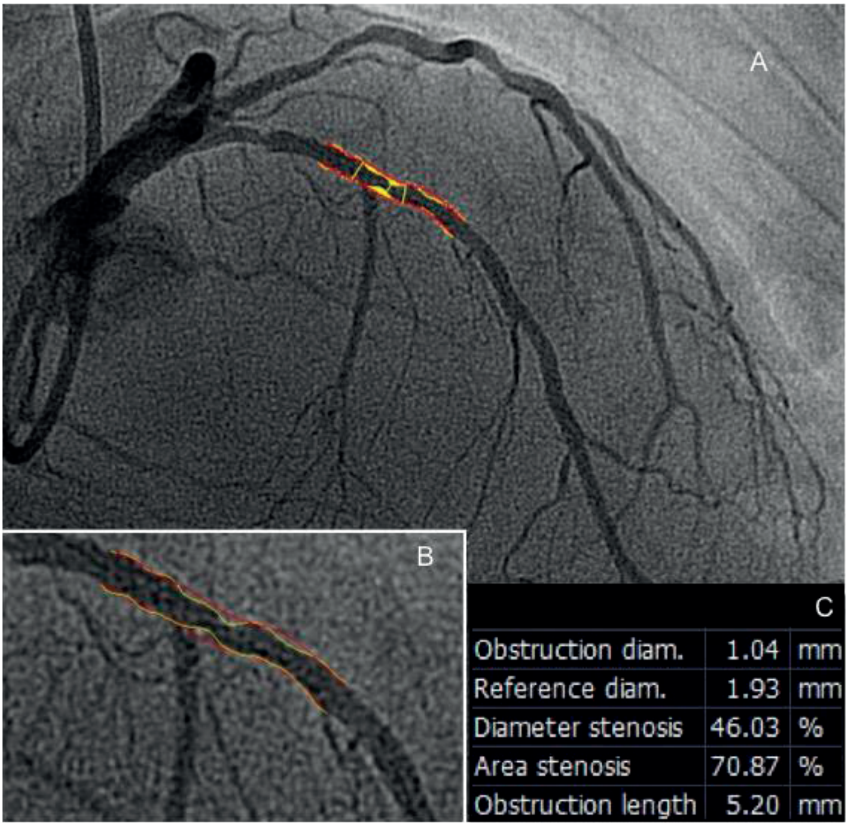

Figure 1. Quantitative coronary angiography (QCA) analysis of a proximal left anterior descending (LAD) artery lesion. Panel A shows the coronary segment of interest; Panel B is a zoomed image of the same coronary segment; in both cases with yellow is highlighted the actual lumen of the vessel and with red the interpolated reference vessel contour. Panel C shows the output of the QCA analysis.

Three-dimensional quantitative coronary angiography (3D-QCA) has been recently developed to overcome inherent limits of conventional QCA, related with the assessment of a three-dimensional structure (coronary vessel) using a bi-dimensional angiographic projection. By means of 3D-QCA-software a volumetric reconstruction of the coronary segment of interest is being performed from two different angiographic projections at least 25° apart[9]. As a result of this integrated anatomic reconstruction, 3D-QCA – derived metrics such as minimum luminal diameter (MLD) and minimum luminal area (MLA) can better identify haemodynamically significant lesions as compared to QCA[10, 11].

Intravascular-ultrasound (IVUS) has been the first widely available intracoronary-imaging tool that was used on-line in the catheterization laboratory for PCI-guidance. Two different types are currently available, the solid-state electronic phased array transducer, that has 64 stationary transducer elements around the tip that image at 20 MHz, and the mechanical single-element rotating transducer, that offers greater resolution due to the higher ultrasound frequency (40 MHz)[12]. Post-PCI IVUS assessment can detect stent underexpansion, stent edge-dissection and malapposition, all pathophysiological entities that have been associated to worse clinical outcomes[13-16]. Likewise, IVUS has been used to guide therapeutic options in the setting of left main disease[17-19] and coronary chronic total occlusions (CTO)[20].

Virtual histology intravascular ultrasound (VH-IVUS) is based on spectral analysis of primary raw backscattered ultrasound waves of the IVUS catheter and allows tissue characterization of coronary lesions by detecting four tissue types: fibrous tissue, fibrofatty tissue, necrotic core and dense calcium[21] (Figure 2). VH-IVUS-detected thin-cap fibroatheromas have been proposed as independent predictors of future cardiovascular events[6].

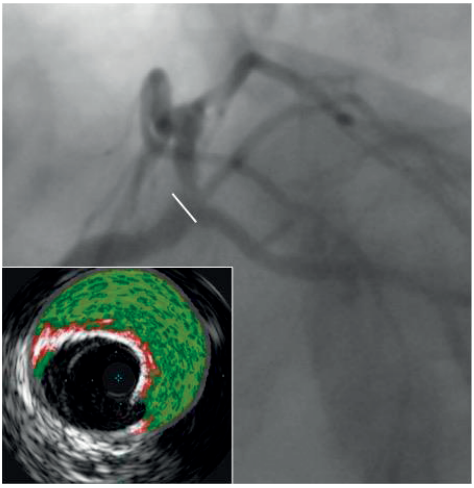

Figure 2. Virtual histology intravascular ultrasound (VH-IVUS) of a distal left-main (LM) lesion. The VH-IVUS cross-section demonstrates superficial calcium (white color) with some necrotic tissue (red) with a large fibrofatty pool (mixed dark and light green).

Optical coherence tomography (OCT) is an alternative to IVUS intravascular imaging modality that uses the back-reflection of near-infrared light from optical interfaces in tissue, resulting in cross-sectional and longitudinal images of the investigated coronary segment. The extremely high resolution of 10 μm allows in–vivo histologic characterization of epicardial vessels, with possibility of assessment of neointimal proliferation, tissue characterization, macrophage accumulation, presence of intracoronary thrombus and vulnerable plaque detection[5, 22]. In parallel, OCT-imaging performed after stent deployment allows PCI-guidance, by assessing stent expansion, stent-strut apposition, edge-dissection, minimal stent area and stent-strut endothelialization[22, 23]. Optical coherence tomography – guidance has been associated to improved clinical outcome both in patients with stable CAD as well as in patients with acute coronary syndrome[24, 25].

Fractional flow reserve (FFR) consists in assessing the functional relevance of a given epicardial vessel stenosis by using a guiding wire with a pressure sensor and positioning it distally to the assessed stenosis. Fractional flow reserve is defined as the ratio between intracoronary pressure (Pd) and aortic pressure (Pa) under conditions of maximal hyperemia, induced by intravenous administration of adenosine[3]. Values of FFR < 0.80 are indicative of ischemia and were associated to poor prognosis in patients with stable CAD[1, 26]. Currently, FFR is used as "gatekeeper" in the catheterization laboratory to guide decision-making (PCI vs. medical treatment) in patients with coronary lesions of uncertain angiographic severity[7].

The implementation of anatomical and functional information during cardiac catheterization is today feasible using dedicated software[27]. Fractional flow reserve values along the coronary vessel can be co-registered with OCT and angiography and this information can be useful to optimize PCI, particularly in the setting of bifurcation lesions, the latter being characterized by increased complexity[28, 29] (Figure 3). Co-registration of FFR and OCT revealed that in-stent pressure-drops are associated to neointimal hyperplasia[30].

Objective and Outline of the Thesis

The objective of the thesis was to evaluate the current role of intracoronary imaging and hemodynamic assessment in PCI optimization. A brief overview of currently available intracoronary imaging techniques and functional assessment methods is presented in **Chapter 1**.

Chapter 2 presents the optimization of a dedicated bifurcation stent-system using co-registration of FFR with OCT. Comparison of 3D-QCA with OCT for the functional assessment of coronary stenosis is presented in **Chapter 3** which shows that 3D-QCA-derived metrics have a better correlation with FFR of non-obstructive coronary stenoses as compared to OCT-derived anatomic parameters.

Chapter 4 presents the co-registration modality of FFR and OCT using a three-dimensional angiographic roadmap. In **Chapter 5**, the impact of the fusion of anatomical and functional assessment using 3D-QCA, OCT and FFR on a series of patients with coronary bifurcation lesions treated with dedicated stents is presented. In this setting, the use of contemporary balloon-inflation after stent deployment was associated to an improved anatomical and functional result.

Chapter 6 highlights the association between in-stent variations in fractional flow reserve and optical coherence tomography findings. The proposed co-registration approach demonstrates that suboptimal FFR values after PCI are associated to an increased rate of neointimal proliferation as shown by OCT-imaging. Finally, **Chapter 7** reviews extensively each intracoronary imaging tool, as well as all available techniques of hemodynamic assessment of coronary stenoses. The theoretical basis of every method is presented and the role on guiding decision-making and PCI-optimization during cardiac catheterization procedures is highlighted.

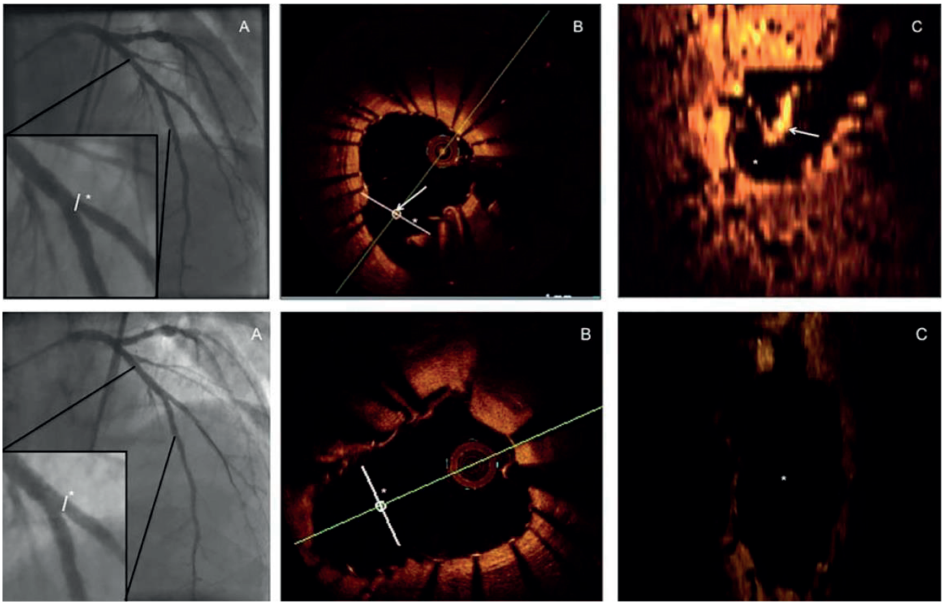

Figure 3. A left anterior descending (LAD) bifurcation treated with Tryton side-branch stent, before (first line) and after (second line) final kissing-balloon inflation (FKBI).

Panel A: angio with zoom on the bifurcation. Panel B: Optical coherence tomography (OCT) short axis view on the site of the LAD bifurcation as seen in panel A. Panel C: Visualization of the ostium of the side branch before FKBI, with "cut-plane" visualization technique. The asterisk indicates the correspondence of the bifurcation between panels A, B and C. The white line indicates the correspondence of the "cut-plane" between panels A, B and C. The white arrow indicates stent struts, as visualized in OCT short axis (panel B) and "cut-plane" modality.

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