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Multi-modality diagnostic assessment in interventional cardiology

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Chapter 1

Introduction and Outline of the Thesis

Introduction and Outline of the Thesis

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).

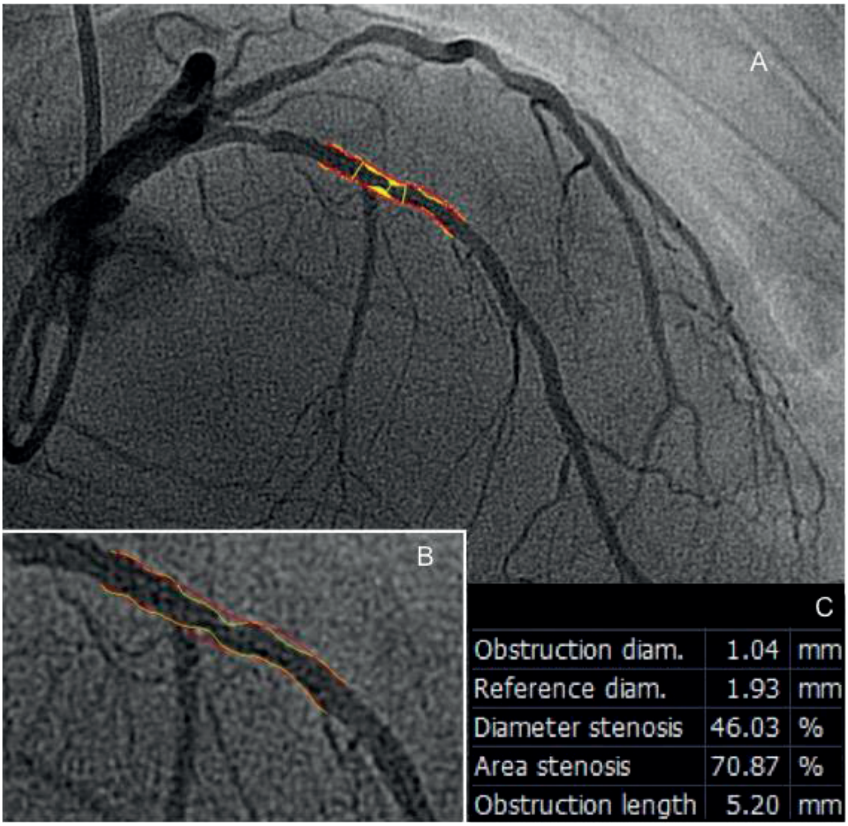

Figure 1. Quantitative coronary angiography (QCA) analysis of a proximal left anterior descending (LAD) artery lesion. Panel A shows the coronary segment of interest; Panel B is a zoomed image of the same coronary segment; in both cases with yellow is highlighted the actual lumen of the vessel and with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

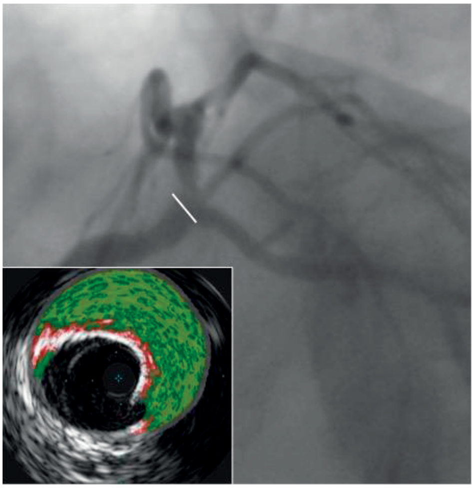

Figure 2. Virtual histology intravascular ultrasound (VH-IVUS) of a distal left-main (LM) lesion. The VH-IVUS cross-section demonstrates superficial calcium (white color) with some necrotic tissue (red) with a large fibrofatty pool (mixed dark and light green).

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.

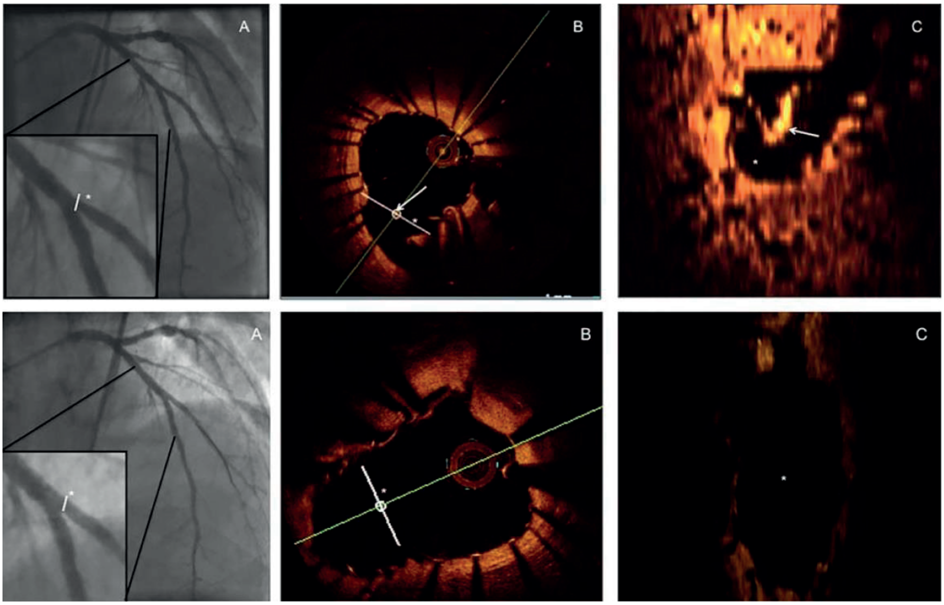

Figure 3. A left anterior descending (LAD) bifurcation treated with Tryton side-branch stent, before (first line) and after (second line) final kissing-balloon inflation (FKBI).

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.

REFERENCES

1. De Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth Z, Jagic N, Mobius-Winkler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engstrom T, Oldroyd KG, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Juni P, Fearon WF and Investigators FT. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med*. 2012;367:991-1001.
2. Mehta SR, Cannon CP, Fox KA, Wallentin L, Boden WE, Spacek R, Widimsky P, McCullough PA, Hunt D, Braunwald E and Yusuf S. Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. *JAMA*. 2005;293:2908-17.
3. Pijls NH, van Son JA, Kirkeeide RL, De Bruyne B and Gould KL. Experimental basis of determining maximum coronary, myocardial, and collateral blood flow by pressure measurements for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty. *Circulation*. 1993;87:1354-67.
4. Mintz GS. Clinical utility of intravascular imaging and physiology in coronary artery disease. *J Am Coll Cardiol*. 2014;64:207-22.
5. Sinclair H, Bourantas C, Bagnall A, Mintz GS and Kunadian V. OCT for the identification of vulnerable plaque in acute coronary syndrome. *JACC Cardiovasc Imaging*. 2015;8:198-209.
6. Stone GW, Maehara A, Lansky AJ, de Bruyne B, Cristea E, Mintz GS, Mehran R, McPherson J, Farhat N, Marso SP, Parise H, Templin B, White R, Zhang Z, Serruys PW and Investigators P. A prospective natural-history study of coronary atherosclerosis. *N Engl J Med*. 2011;364:226-35.
7. Kolh P, Windecker S, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Juni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A, European Society of Cardiology Committee for Practice G, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Committee ECG, Sousa Uva M, Achenbach S, Pepper J, Anyanwu A, Badimon L, Bauersachs J, Baumbach A, Beygui F, Bonaros N, De Carlo M, Deaton C, Dobrev D, Dunning J, Eeckhout E, Gielen S, Hasdai D, Kirchhof P, Luckraz H, Mahrholdt H, Montalescot G, Paparella D, Rastan AJ, Sanmartin M, Sergeant P, Silber S, Tamargo J, ten Berg J, Thiele H, van Geuns RJ, Wagner HO, Wassmann S, Wendler O, Zamorano JL, Task Force on Myocardial Revascularization of the European Society of C, the European Association for Cardio-Thoracic S and European Association of Percutaneous Cardiovascular I. 2014 ESC/EACTS Guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur J Cardiothorac Surg*. 2014;46:517-92.
8. Reiber JH, Serruys PW, Kooijman CJ, Wijns W, Slager CJ, Gerbrands JJ, Schuurbiers JC, den Boer A and Hugenholtz PG. Assessment of short-, medium-, and long-term variations in arterial dimensions from computer-assisted quantitation of coronary cineangiograms. *Circulation*. 1985;71:280-8.
9. Tu S, Huang Z, Koning G, Cui K and Reiber JH. A novel three-dimensional quantitative coronary angiography system: In-vivo comparison with intravascular ultrasound for assessing arterial segment length. *Catheter Cardiovasc Interv*. 2010;76:291-8.

10. Pyxaras SA, Tu S, Barbato E, Barbati G, Di Serafino L, De Vroey F, Toth G, Mangiacapra F, Sinagra G, De Bruyne B, Reiber JH and Wijns W. Quantitative angiography and optical coherence tomography for the functional assessment of nonobstructive coronary stenoses: comparison with fractional flow reserve. *Am Heart J*. 2013;166:1010-1018 e1.
11. Yong AS, Ng AC, Brieger D, Lowe HC, Ng MK and Kritharides L. Three-dimensional and two-dimensional quantitative coronary angiography, and their prediction of reduced fractional flow reserve. *Eur Heart J*. 2011;32:345-53.
12. McDaniel MC, Eshtehardi P, Sawaya FJ, Douglas JS, Jr. and Samady H. Contemporary clinical applications of coronary intravascular ultrasound. *JACC Cardiovasc Interv*. 2011;4:1155-67.
13. Choi SY, Maehara A, Cristea E, Witzenbichler B, Guagliumi G, Brodie B, Kellett MA, Jr., Dressler O, Lansky AJ, Parise H, Mehran R, Mintz GS and Stone GW. Usefulness of minimum stent cross sectional area as a predictor of angiographic restenosis after primary percutaneous coronary intervention in acute myocardial infarction (from the HORIZONS-AMI Trial IVUS substudy). *Am J Cardiol*. 2012;109:455-60.
14. Choi SY, Witzenbichler B, Maehara A, Lansky AJ, Guagliumi G, Brodie B, Kellett MA, Jr., Dressler O, Parise H, Mehran R, Dangas GD, Mintz GS and Stone GW. Intravascular ultrasound findings of early stent thrombosis after primary percutaneous intervention in acute myocardial infarction: a Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) substudy. *Circ Cardiovasc Interv*. 2011;4:239-47.
15. Fujii K, Carlier SG, Mintz GS, Yang YM, Moussa I, Weisz G, Dangas G, Mehran R, Lansky AJ, Kreps EM, Collins M, Stone GW, Moses JW and Leon MB. Stent underexpansion and residual reference segment stenosis are related to stent thrombosis after sirolimus-eluting stent implantation: an intravascular ultrasound study. *J Am Coll Cardiol*. 2005;45:995-8.
16. Claessen BE, Mehran R, Mintz GS, Weisz G, Leon MB, Dogan O, de Ribamar Costa J, Jr., Stone GW, Apostolidou I, Morales A, Chantziara V, Syros G, Sanidas E, Xu K, Tijssen JG, Henriques JP, Piek JJ, Moses JW, Maehara A and Dangas GD. Impact of intravascular ultrasound imaging on early and late clinical outcomes following percutaneous coronary intervention with drug-eluting stents. *JACC Cardiovasc Interv*. 2011;4:974-81.
17. Oviedo C, Maehara A, Mintz GS, Araki H, Choi SY, Tsujita K, Kubo T, Doi H, Templin B, Lansky AJ, Dangas G, Leon MB, Mehran R, Tahk SJ, Stone GW, Ochiai M and Moses JW. Intravascular ultrasound classification of plaque distribution in left main coronary artery bifurcations: where is the plaque really located? *Circ Cardiovasc Interv*. 2010;3:105-12.
18. de la Torre Hernandez JM, Hernandez Hernandez F, Alfonso F, Rumoroso JR, Lopez-Palop R, Sadaba M, Carrillo P, Rondan J, Lozano I, Ruiz Nodar JM, Baz JA, Fernandez Nofrerias E, Pajin F, Garcia Camarero T, Gutierrez H and Group LS. Prospective application of pre-defined intravascular ultrasound criteria for assessment of intermediate left main coronary artery lesions results from the multicenter LITRO study. *J Am Coll Cardiol*. 2011;58:351-8.
19. Park SJ, Kim YH, Park DW, Lee SW, Kim WJ, Suh J, Yun SC, Lee CW, Hong MK, Lee JH, Park SW and Investigators M-C. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. *Circ Cardiovasc Interv*. 2009;2:167-77.
20. Jang JS, Song YJ, Kang W, Jin HY, Seo JS, Yang TH, Kim DK, Cho KI, Kim BH, Park YH, Je HG and Kim DS. Intravascular ultrasound-guided implantation of drug-eluting stents to improve outcome: a meta-analysis. *JACC Cardiovasc Interv*. 2014;7:233-43.

21. Sanidas E and Dangas G. Evolution of intravascular assessment of coronary anatomy and physiology: from ultrasound imaging to optical and flow assessment. *Eur J Clin Invest*. 2013;43:996-1008.
22. Prati F, Guagliumi G, Mintz GS, Costa M, Regar E, Akasaka T, Barlis P, Tearney GJ, Jang IK, Arbustini E, Bezerra HG, Ozaki Y, Bruining N, Dudek D, Radu M, Erglis A, Motreff P, Alfonso F, Toutouzas K, Gonzalo N, Tamburino C, Adriaenssens T, Pinto F, Serruys PW, Di Mario C and Expert's OCTRD. Expert review document part 2: methodology, terminology and clinical applications of optical coherence tomography for the assessment of interventional procedures. *Eur Heart J*. 2012;33:2513-20.
23. Wijns W, Shite J, Jones MR, Lee SW, Price MJ, Fabbiocchi F, Barbato E, Akasaka T, Bezerra H and Holmes D. Optical coherence tomography imaging during percutaneous coronary intervention impacts physician decision-making: ILUMIEN I study. *Eur Heart J*. 2015;36:3346-55.
24. Prati F, Di Vito L, Biondi-Zoccai G, Occhipinti M, La Manna A, Tamburino C, Burzotta F, Trani C, Porto I, Ramazzotti V, Imola F, Manzoli A, Materia L, Cremonesi A and Albertucci M. Angiography alone versus angiography plus optical coherence tomography to guide decision-making during percutaneous coronary intervention: the Centro per la Lotta contro l'Infarto-Optimisation of Percutaneous Coronary Intervention (CLI-OPCI) study. *EuroIntervention*. 2012;8:823-9.
25. Meneveau N, Souteyrand G, Motreff P, Caussin C, Amabile N, Ohlmann P, Morel O, Lefrancois Y, Descotes-Genon V, Silvain J, Braik N, Chopard R, Chatot M, Ecarnot F, Tauzin H, Van Belle E, Belle L and Schiele F. Optical Coherence Tomography to Optimize Results of Percutaneous Coronary Intervention in Patients with Non-ST-Elevation Acute Coronary Syndrome: Results of the Multicenter, Randomized DOCTORS (Does Optical Coherence Tomography Optimize Results of Stenting) Study. *Circulation*. 2016.
26. Tonino PA, De Bruyne B, Pijls NH, Siebert U, Ikeno F, van' t Veer M, Klauss V, Manoharan G, Engstrom T, Oldroyd KG, Ver Lee PN, MacCarthy PA, Fearon WF and Investigators FS. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2009;360:213-24.
27. Tu S, Holm NR, Koning G, Huang Z and Reiber JH. Fusion of 3D QCA and IVUS/OCT. *Int J Cardiovasc Imaging*. 2011;27:197-207.
28. Pyxaras SA, Toth GG, Di Gioia G, Ughi GJ, Tu S, Rusinaru D, Adriaenssens T, Reiber JH, Leon MB, Bax JJ and Wijns W. Anatomical and functional assessment of Tryton bifurcation stent before and after final kissing balloon dilatation: Evaluations by three-dimensional coronary angiography, optical coherence tomography imaging and fractional flow reserve. *Catheter Cardiovasc Interv*. 2016.
29. Pyxaras SA, Tu S, Barbato E, Reiber JH and Wijns W. Optimization of Tryton dedicated coronary bifurcation system with coregistration of optical coherence tomography and fractional flow reserve. *JACC Cardiovasc Interv*. 2013;6:e39-40.
30. Pyxaras SA, Adriaenssens T, Barbato E, Ughi GJ, Di Serafino L, De Vroey F, Toth G, Tu S, Reiber JHC, Bax JJ, Wijns W. In-stent fractional flow reserve variations and related optical coherence tomography findings: the FFR-OCT co-registration study. Int J Cardiovasc Imaging 2017. doi: 10.1007/s10554-017-1262-4. [Epub ahead of print]