

OCT Guidance During Stent Implantation in Primary PCI: A Randomized Multicenter Study With Nine Months of Optical Coherence Tomography Follow-up

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Abstract

Aims: To assess the possible merits of optical coherence tomography (OCT) guidance in primary percutaneous coronary intervention (pPCI).

Methods and results: 201 patients with ST-elevation myocardial infarction (STEMI) were enrolled in this study. Patients were randomized either to pPCI alone (angio-guided group, n=96) or to pPCI with OCT guidance (OCT-guided group, n=105) and also either to biolimus A9 or to everolimus-eluting stent implantation. All patients were scheduled for nine months of follow-up angiography and OCT study. OCT guidance led to post-pPCI optimization in 29% of cases (59% malapposition and 41% dissections). No complications were found related to the OCT study. OCT analysis at nine months showed significantly less in-segment area of stenosis (6% [-11, 19] versus 18% [3, 33]; p=0.0002) in favor of the OCT-guided group. The rate major adverse cardiovascular events was comparable at nine months in both groups (3% in the OCT group versus 2% in the angio-guided group; p=0.87).

Conclusions: This study demonstrates the safety of OCT guidance during pPCI. The use of OCT optimized stent deployment in 1/3 of patients in this clinical scenario and significantly reduced in-segment area of stenosis at nine months of follow-up. Whether such improvements in OCT endpoints will have a positive impact on late clinical outcomes demands both a larger and longer-term follow-up study.

Keywords: optical coherence tomography, OCT, primary PCI, ST-segment elevation myocardial infarction, drug-eluting stents.

Introduction

Drug-eluting stents (DES) represent a breakthrough technology in interventional cardiology due to their reduction of restenosis, but concerns have recently been raised regarding a possible increase in late stent thrombosis in patients with ST-segment elevation myocardial infarction (STEMI) treated with DES, especially when a large thrombus burden is present (1, 2). Stent underexpansion, malapposition, incomplete lesion coverage and residual plaque burden are well-recognized as major contributors of late-stent thrombosis (3, 4, 5, 6, 7, 8). Intravascular imaging, namely intravascular ultrasound (IVUS), has played a pivotal role in identifying the sub-optimal results of percutaneous coronary intervention (PCI) and further refine stent implantation techniques with reduction of adverse clinical outcomes compared with angiography-guided PCI (9).

Optical coherence tomography (OCT) is the latest imaging technique available for clinical use with the highest resolution (~10 μm , i.e., 10-fold greater than IVUS) enables an unprecedented level of detail in the assessment of vessel morphology (10, 11, 12, 13, 14). While some observational data support the role of OCT guidance during primary PCI (15, 16, 17), a randomized study is lacking. The objective of this randomized study was, therefore, to assess the safety and efficacy of OCT- versus angio-guided primary PCI with second-generation DES implantation at nine months.

Methods

Study population, study design and PCI procedures. The present study was a subanalysis of the ROBUST trial (NCT 00888758), a multicenter, randomized interventional trial comparing biolimus A9-eluting and everolimus-eluting stents with OCT-guided stent implantation in STEMI with nine months of angiographic and OCT follow-up. A two-stage randomization scheme (angio-guided versus OCT-guided pPCI and everolimus versus biolimus A9 drug eluting stent) was applied in this trial. Between February 2011 and October

2012, 201 STEMI patients treated with primary PCI were enrolled. The study design and treatment flow of this subanalysis are shown in *Figure 1*. The study design was approved by the appropriate national and institutional regulatory authorities and ethics committees, and all patients provided written informed consent. STEMI was defined as chest pain with a duration of >20 minutes and <12 hours and ST-segment elevation >0.1 mV in ≥ 2 contiguous leads on a 12-lead electrocardiogram. Patients between 18-85 years of age admitted with STEMI (without cardiogenic shock, left main disease and ostial lesion) in a native coronary artery (diameter range 2.5-3.75 mm) with a lesion suitable for stenting were included. Interventions were carried out by the radial approach using a 6-French sheath and guiding catheters. All patients were pre-treated with aspirin, heparin and clopidogrel. The activated clotting time (ACT) was kept within 250-300 seconds during the entire procedure. After diagnostic angiography with quantitative coronary analysis (QCA) employing Quantcore software (Pie Medical, The Netherlands), patients were randomly assigned (using a sealed envelope) to either angiography-guided primary PCI (angio-guided group, N=96) or to primary PCI with adjunctive OCT guidance (OCT-guided group, N=105). Patient enrolment was stopped prematurely because of budget restrictions and did not reach the originally calculated sample of 400 patients powered for the clinical comparison. However, the sample size was adequate for OCT and QCA analysis. While the use of glycoprotein IIb/IIIa receptor antagonists and manual thrombus aspiration were left to the discretion of the operator, they were strongly recommended. Either biolimus A9- (BioMatrix[®], Biosensors International, Biosensors Europe, Morges, Switzerland) or everolimus-eluting (Promus, Boston Scientific, Natick, MA, USA) stents were used. Dual antiplatelet therapy (aspirin plus clopidogrel) post-procedure was recommended for 12 months in both groups. Primary PCI was performed according to standard practice with stent implantation at low pressure (≤ 10 atm) with high-pressure (HP) (≥ 15 atm) non-compliant (NC) balloon post-dilatation inside the stent. After stent

implantation was considered optimal, final angiography was performed, using at least at two orthogonal projections.

OCT image acquisition and analysis. In the OCT-guided group, OCT (C7-XR™ intravascular imaging system, LightLab® Imaging, St. Jude Medical Company, St. Paul, Minnesota, USA with a C7 Dragonfly™ intravascular imaging catheter) was performed after stent deployment with “optimal angiographic results”. A non-occlusive technique was used in all patients, with continuous flushing of the artery with contrast dye (total amount of 15 cc) using an injector with a speed of 4 cc/s. Automated pullback was performed at a rate of 20 mm/s for a length of 54 mm. The images were recorded in the OCT system console and analyzed on-line in the cathlab and off-line in CoreLab. All cross-sectional images (frames) were initially screened for quality assessment and excluded from analysis if any portion of the stent was off the screen or if the image was of poor quality due to residual blood, artifacts, or reverberation. A second and/or third image was obtained to obtain an image of good quality. Qualitative imaging assessment of every frame was also performed to detect the presence of an intraluminal thrombus. Optimal OCT criteria for stent deployment were as follows: 1) minimal lumen area (MLA) >80% of the mean proximal and distal vessel lumen references (i.e., most “normal-looking” cross-sections); 2) in cases without proximal vessel references, MLA was >90% of the distal reference lumen area; 3) no significant malapposition; and 4) no dissection at the edges of the stented segment. Strut/stent malapposition was determined when the negative value of the strut-level intimal thickness (SIT) was greater than the strut thickness, according to the stent manufacturer’s specifications corrected for strut blooming thickness. Because the luminal surface of the strut is expected to be found in the middle of the blooming, half of the blooming value was used as a standard for calculation. The final cut-off value for malapposition was 144 μm for BioMatrix® and 106 μm for Promus Element™. The therapeutic decision was based on acute online OCT imaging in the cathlab and was left to the

discretion of pPCI operators. To determine the reproducibility of OCT analysis, a quantitative analysis of 100 struts were performed by these two operators. The interobserver difference for SIT was $0.01 \pm 0.03 \mu m$ ($r = 0.0897$). Final OCT pullback was mandatory and was performed after final procedure optimization. After the final OCT study, final angiography was performed. All the images were digitally stored and independently analyzed by blinded analysts at the Cardiovascular Imaging Core Lab, Harrington Heart & Vascular Institute, University Hospitals, Case Medical Center, Cleveland, OH, USA.

Patient follow-up, clinical outcomes, endpoints, and definitions. All patients were scheduled for 30 days of clinical and nine months of clinical, angiographic, and OCT follow-up. Major adverse cardiovascular events (MACE; including death, myocardial infarction [MI], and target lesion revascularization [TLR]) were assessed. Death was reported as cardiac or non-cardiac. Q-wave MI was defined as the development of new, pathologic Q waves in two or more ECG leads, with post-procedural creatine kinase (CK) levels three times higher than the upper limit of normal ($<2.9 \mu\text{katal/l}$) and CK-MB $>10\%$ of CK levels. Non-Q-wave MI was defined as an elevation of post-procedural CK levels three times higher than the upper limit of normal, with CK-MB above normal and no-Q-wave. TLR was defined as revascularization within 5 mm to the stent edges (in-segment) on angiography. All TLR required significant stenosis and objective evidence of ischemia related to the restenotic artery before treatment. The following features were captured in the QCA analysis at nine months of follow-up: binary restenosis (BR), in-segment and in-stent late loss (LL), diameter of stenosis (DS), and minimal lumen diameter (MLD). OCT analysis provided the mean and MLD, mean and MLA, in-segment area of stenosis (AS) and number of uncovered and malapposed stent struts. The reference area was defined as the average of 5 mm (25 frames) proximal and distal to the stent edge, except for slices of bad quality, with image distorting side branches, or severe dissection. The inter-slice distance was $200 \mu m$ along the entire target segment (*Figure*

2 online). Dedicated semiautomated software developed at the Cardiovascular Imaging Core Lab, Harrington Heart & Vascular Institute, University Hospitals, Case Medical Center, Cleveland, OH, USA was used for the OCT analysis (OCTivat-Stent) (**Figure 3 online**) in this study to delineate the lumen contours of each cross-sectional image. Lumen, stent, and neointimal hyperplasia (NH) mean areas were calculated. Quantitative strut analysis was also performed using this dedicated software, which takes into account characteristics of both stents (thickness of struts and polymer) used in this study. The software has been validated and proved to have less interobserver variability and higher sample rate than conventional pure manual analysis. It has 94% sensitivity and 90% specificity for identifying uncovered struts. Struts were considered uncovered, if at least part of stent blooming was not separated from vessel contour by tissue layer. For a more detailed description, we refer to the original paper (18). OCT endpoints were the percentage of uncovered stent struts, the percentage of malapposed stent struts, in-stent AS and in-stent MLD at nine months.

Statistical analysis. Categorical variables were described as group counts and relative frequencies (percentages), while continuous variables were described as group means, standard deviations (SDs), and totals (N). Tests of statistical hypotheses in contingency tables were performed using the Fisher Exact Test based on a hypergeometric distribution. Since most of the continuous variables subject to statistical testing showed significant departures from normality (as expressed by e.g. the Shapiro-Wilk normality test), the non-parametric Wilcoxon Rank-Sum Test was used to compare continuous outcomes across different groups defined by either of the treatment arms (OCT- versus angio-guided pPCI, stent type Biomatrix versus Promus). McNemar's test was applied for comparisons of binary categorical variables between the individual stages of follow-up (e.g. baseline vs. 30 days of follow-up). The level of statistical significance was set to $\alpha=0.05$ for all tests. In multiple testing scenarios (e.g. a battery of tests performed in a certain table), Bonferroni corrections of the nominal level of

statistical significance were applied in individual tests in order to keep the family-wise Type I error rate alpha at 0.05. The statistical analysis was conducted using dedicated software (R version 3.0.2; R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline demographic and procedural characteristics. Baseline demographic and procedural characteristics were well-balanced in both groups (*Table 1*). We did not observe any complications related to the OCT studies, either during the index procedure or at follow-up. More stents and higher mean implantation pressures were used in the OCT-guided group. Interestingly, suboptimal results not fulfilling at least one of the four defined criteria were found on-line in almost one-third of the patients (29/105) randomized to the OCT-guided group. Malapposition was found in 17 (59%) and any dissection in 12 (41%) out of 29 patients. In the case of malapposition, a larger balloon and/or higher pressure had been used to optimize the result. Any dissection had been managed with the implantation of an additional stent. However, the detailed core lab analysis showed that suboptimal results was even more frequent (34%; 36/105). Physicians missed malapposition in 7 out of 11 patients, and the suboptimal area of stenosis was not corrected in 16 out of 20 patients. On the other hand, significant dissections were treated correctly in all patients (5/5 patients). Some degree of thrombus formation was found in all patients in the OCT-guided group. The fluoroscopy time was significantly shorter in the angio-guided group compared to the OCT-guided group (10 [7-14] min versus 7 [5-10] min; $p=0.0001$). On the other hand, more contrast medium were used in the OCT guided group (230ml [193-270] versus 168ml [130-190]; $p<0.0001$). However, the level of creatinine after procedure was within the normal limits and did not differ between groups (75 μ mol/l [69-84] in the OCT-guided group versus 76 μ mol/l [69-89]

in the Angio-guided PCI; $p=0.177$). Other post -procedure angiographic and biomarkers values were comparable in both groups (*Table 2 online*).

MACE and angiographic analysis at nine months of follow-up. MACE rates were comparable between both groups at 30 days and nine months of follow-up (2% versus 0%, $p=0.499$ and 3% versus 1%, $p=0.623$, respectively). One stent thrombosis was found in each group (both were deemed early and definite) (*Table 3 online*). Angiographic data were available for 90% (95/105) patients of the OCT-guided group and 95% (91/95) of the angio-guided pPCI group. BR was very low and comparable in both groups (2% versus 3%; $p=0.671$). Furthermore, in-stent and in-segment angiographic late LL at nine months did not differ significantly between the groups, although there was a trend towards both smaller in-stent and in-segment late LL in the OCT-guided group (0.06 ± 0.49 mm vs. 0.18 ± 0.32 mm respectively; $p=0.055$) (*Tables 4, Figure 4 online*).

OCT analysis at nine months of follow-up. At nine months of follow-up, appropriate OCT data were available for 88% (92/105) of patients in the OCT-guided group and 90% (86/96) of the angio-guided pPCI group. (*Table 5*). A significantly smaller in-segment AS was revealed in the OCT-guided group compared with the angio-guided group (6% [-11, 19] versus 18% [3, 33]; $p=0.0002$). The number of either uncovered or malapposed struts, in-segment MLD, and in-segment MLA did not differ significantly between groups (13% [5, 18] versus 17% [4, 27]; 1% [0, 1] versus 1% [0, 1]; 2.9 mm [2.6, 3.0] versus 2.8 mm [2, 3] and 6.7 mm² [5.0, 8.0] versus 6 mm² [5.0, 8.0] respectively). Furthermore, the value of mean in-stent NH was comparable in both groups (1.2 mm² \pm 0.6 versus 1.3 mm² \pm 0.7; $p=0.6$). No residual thrombi were found in the target segment in both groups. Interestingly, 15% (out of 84,882 struts) late-acquired stent malapposition was found in OCT-guided pPCI at nine months. On the other hand, the rate of malapposed struts using the index procedure decreased by 44% at nine month in this group.

Discussion

This is the first randomized study comparing both the safety and efficacy of OCT guidance during primary PCI for STEMI with second-generation DES implantation. Furthermore, 90% of patients in both groups underwent OCT assessments at nine months of follow-up. Routine use of OCT guidance during primary PCI was associated with reduced in-segment AS at nine months of follow-up. The rate of malapposed struts was very low and did not differ between the groups. During the acute phase of STEMI and based on the OCT imaging, the operators decided more often (in 30% of cases) to perform further procedure optimization despite the optimal angiographic result. However, this approach was associated with a higher number of implanted stents with no difference in the rate of MACE during follow-up.

Our data are in concordance with the results of recently presented non-randomized observational studies. In pioneering work, Imola et al. first demonstrated that OCT guidance during PCI is feasible and safe, even in patients with complex lesions (20). Undoubtedly, the progress in OCT instrumentation and the non-occlusive technique have played major roles in reducing the OCT-related complications (20). Although the limitations of angiography, either as a diagnostic procedure or as an intervention, are well-established, it still represents the workhorse imaging approach. However, in the pooled analysis of non-randomized trials, IVUS-guided DES implantation was associated with significantly lower rates of MACE compared with angiography guidance (OR: 0.79;95% CI:0.69 to 0.91; p=0.001), including a reduction in all-cause mortality, MI, TLR, and stent thrombosis (9). Since OCT enables strut-level assessment and clearly depicts dissections, thrombi, and plaque composition; we

hypothesized that compared with angio-guided pPCI, OCT-guided pPCI would optimize the results and improve outcomes related to DES implantation during STEMI. In the present study, the use of OCT resulted in further post-OCT interventions in 28% of patients randomized to the OCT-guided group. In the majority of cases (59%), additional post-dilatation was performed for malapposed struts. Dissections were found in 41% of cases and, according to the protocol, all significant dissections were treated with the implantation of another stent. This therapeutic decision was left to the pPCI operator's discretion and led to a significantly higher number of stents being used in the OCT-guided group (1.4 versus 1.2; $p=0.03$). Prati et al. reported additional post-OCT interventions in 34% of patients receiving OCT (11). Stefano et al. demonstrated stent malapposition in 39% of cases despite the routine use of HP NC post-dilatation; additional balloon dilatation was performed in 90% of these cases. In this study, HP NC post-dilatation was mandatory as part of the protocol. Despite this, the difference between the MLD and the MSA doubt the optimal circular shape at the end of pPCI. Very recently, Im et al. (21) in their observational study demonstrated acute stent malapposition in 62% of lesions with a favorable clinical outcome. Acute stent malapposition with a volume $>2.56 \text{ mm}^3$ differentiated late-persistent stent malapposition from resolved acute stent malapposition. Late-acquired stent malapposition was detected in 15% of all lesions. Whether such findings from the elective procedures would correspond with a completely different pathomorphology of STEMI remains unclear (22), especially in the era of novel potent antiplatelet drugs. Moreover, as mentioned above, OCT is more sensitive than other imaging modalities in detecting dissections, but it remains controversial as to whether all dissections have to be treated. In the present trial, all dissections evaluated by the operator as significant were treated with the implantation of an additional stent. Recently, in a study by Stefano et al., among 29% of dissections, 76% were deemed benign and only 24% (4/17) were treated. There were no complications associated with untreated

edge dissections. It seems that dissection with a longitudinal length <1.75 mm, with <2 concomitant flaps, flap depth <0.52 mm, flap opening <0.33 mm, and not extending deeper than the media layer have favorable outcomes and can be left untreated (23).

So far, there is no clear evidence that OCT-guided PCI improves outcomes. However, some observational studies have reported better clinical outcomes with OCT guidance compared to angiography-guided interventions (16). Low and comparable MACE rates were observed in our study; however, it is important to consider that our sample size was not powered to detect differences in clinical outcomes. Therefore, further investigations in larger populations are required to confirm these findings. In-stent late LL reported in present study was one of the lowest reported ever (24).

OCT assessment and clinical implications. The endpoints of the present study were those assessed by OCT at nine months of follow-up. The only difference found in this study was a significantly smaller in-segment AS in the OCT-guided group compared with the angio-guided group (6% [-11, 19] versus 18% [3, 33]; $p=0.0002$). Whether these findings will be translated into better clinical outcomes has to be confirmed in future larger randomized trials with long-term follow-up. The number of either uncovered or malapposed struts, in-segment MLD, in-segment MLA and the value of mean in-stent NH did not differ significantly between groups (13% [5, 18] versus 17% [4, 27]; 1% [0, 1] versus 1% [0, 1]; 2.9 mm [2.6, 3.0] versus 2.8 mm [2, 3] and 6.7 mm^2 [5.0, 8.0] versus 6 mm^2 [5.0, 8.0]; $1.2 \text{ mm}^2 \pm 0.6$ versus $1.3 \text{ mm}^2 \pm 0.7$; $p=0.6$), respectively). Unfortunately, in our study only follow-up comparison of whole groups of guided vs. unguided is eligible for analysis. Patients were not randomized to assure equal baseline values of reference diameter of infarct related artery, what results in possible bias and lower sensitivity of MLA/MLD comparison. On the other side, the AS assess the stenosis using reference segment of unaffected part of vessel, thus it is less sensitive to baseline diameter of native vessel. Therefore the AS seems to be the most sensitive tool for comparison of focal restenosis. "Though the in-segment area of stenosis was significantly less in the OCT-guided group, the in stent parameters like the in-stent binary restenosis, in-stent hyperplasia and in-stent minimal lumen area did not significantly differ"

Furthermore, because of the lack of baseline OCT data in the Angio-guided group, we may only hypothesize the potential role of small and untreated edge dissections on the follow-up OCT in-segment results.

While OCT may refine PCI precision by means of identifying stent underexpansion and malapposition, not depicted by angiography, it is still unclear as to what the thresholds are regarding OCT findings. Interestingly, in this study, the rate of malapposed struts at the index procedure decreased by 44% at nine months in OCT-guided pPCI at nine months this group. On the other hand, 15% of new (clinically silent) late-acquired stent malappositions were found in this group, probably as a result of positive vessel remodeling. This finding will be further analyzed in the upcoming comprehensive stent strut analysis.

Although we did not evaluate the role of pre-intervention OCT in our study, a customized approach, such as appropriate stent selection based on OCT findings concerning the plaque distribution and lumen dimensions, performing additional thrombus aspiration, or selective infusion of anti-platelet drugs in the case of a large thrombus burden and vasoconstriction shown by OCT could help further refine the results and eventually reduce the adverse outcomes of primary PCI (12). Recently, Wijns et al. published the results of the ILUMIEN 1 study which enrolled patients with stable angina, unstable angina, or non-ST-elevation MI (25). In this study, physician decision-making was affected by OCT imaging prior to PCI in 57% and after PCI in 27% of all cases. Further investigation is required in this setting. Currently, by using HP NC post-dilatation, the benefit of the routine OCT guidance for primary PCI provided by experienced operators is very limited. However, we proved the feasibility of the OCT guidance, with no safety issues raised in the trial. Net clinical benefit of the OCT guidance has not been proved in any population, however in this study we present the first STEMI-only randomized patients' population. We believe that in-depth understanding

of vessel morphology pre, during and post-stent implantation during primary PCI might influence the later clinical outcome.

Study limitations. There are limitations to our study. First, this study was underpowered for the clinical endpoints. Nonetheless, it is the first randomized study to compare angio- vs. OCT-guided primary PCI. Second, only mid-term follow-up was available for the patients involved in this study. Third, one has to take into account the low-risk profile of our cohort of patients because of the majority of patients were Killip I; patients with left main coronary artery disease and cardiogenic shock were excluded from the study. Fourth, the inability of OCT to image ostial lesions and large vessels with a reference diameter >5mm is another limitation of this work. On the other hand, the design of the protocol represents real-life practice in high-volume 24/7 primary PCI cathlabs, where the site or individual issue was part of the study. Finally, two different types of DESs were used in this study that has to be taken into account.

Conclusions

The present study demonstrates the safety and possible merit of OCT guidance during second-generation DES deployment in patients who present with STEMI and undergo primary PCI. OCT analysis post-primary PCI affected physician decision-making in about 30% of cases. At nine months, OCT guidance led to a significantly reduced in-segment AS. Larger randomized trials with longer-term follow-up are warranted.

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References

1. Sianos G, Papafaklis MI, Daemen J, et al. Angiographic stent thrombosis after routine use of drug eluting stents in ST-segment myocardial infarction: The importance of thrombus burden. *J Am Coll Cardiol.* 2007;50:573-583.
2. Steg PG, Fox KAA, Eagle KA, et al. Mortality following placement of drug-eluting and bare-metal stents for ST-segment elevation acute myocardial infarction in the Global Registry of Acute Coronary Events. *Eur Heart J.* 2009;30:321-329.
3. Kuchulakanti PK, Chu WW, Torguson R, et al. Correlates and long-term outcomes of angiographically proven stent thrombosis with sirolimus- and paclitaxel-eluting stents. *Circulation* 2006;113:1108-1113.
4. Takano M, Ohba T, Inami S, Seimiya K, Sakai S, Mizuno K. Angioscopic differences in neointimal overage and in persistence of thrombus between sirolimus-eluting stents and bare metal stents after a 6-month implantation. *EHI* 2006;27:2189-2195.
5. Virmani R, Gaugliumi G, Farb A, et al. Localized hypersensitivity and late coronary thrombosis secondary to a sirolimus-eluting stent: Should we be cautious? *Circulation* 2004;109:701-705.
6. Joner M, Finn AV, Farb A, et al. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol.* 2006;48:193-202.
7. Cook S, Wenaweser P, Togni M, et al. Incomplete stent apposition and very late stent thrombosis after drug-eluting stent implantation. *Circulation* 2007;115:2426-34.
8. Fuji K, Carlier SG, Mintz GS, et al. 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.

9. Jang JS, Song YJ, Kang W, et al. Intravascular ultrasound-guided implantation of drug eluting stents to improve outcome. A meta-analysis. *J Am Coll Cardiol Intervent* 2014;7:233-43.
10. Kume T, Akasaka T, Kawamoto T, et al. Assessment of coronary arterial thrombus by optical coherence tomography. *Am J Cardiol* 2006;97(12):1713-7.
11. Bezerra HG, Attizzani GF, Sirbu V, et al. Optical coherence tomography versus intravascular ultrasound to evaluate coronary artery disease and percutaneous coronary interventions. *JACC Cardiovasc Interv.* 2013;3:228-36.
12. Bezerra HG, Attizzani GF, Costa MA, et al. Three-dimensional imaging of fibrous cap by frequency-domain optical coherence tomography. *Catheter Cardiovasc Interv.* 2013;81:547-9.
13. Kume T, Akasaka T, Kawamoto T, et al. Measurement of the thickness of the fibrous cap by optical coherence tomography. *Am Heart J.* 2006;152:e1-e4.
14. Sawada T, Shite J, Garcia-Garcia HM, et al. Feasibility of combined use of intravascular ultrasound radiofrequency data analysis and optical coherence tomography for detecting thin-cap fibroatheroma. *Eur Heart J.* 2008;29:1136-1146.
15. Stefano GT, Bezerra HG, Mehanna E, et al. Unrestricted utilization of frequency domain optical coherence tomography in coronary interventions. *Int J Cardiovasc Imaging* 2013;29(4):741-52.
16. Prati F, Di Vito L, Biondi-Zoccai G, et al. 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;8:823-829.

17. Cervinka P, Spacek R, Bystron M, et al. Optical coherence tomography-guided primary percutaneous coronary intervention in ST-segment elevation myocardial infarction patients. A pilot study. *Can J Cardiol* 2014;30:420-427.
18. Lu H, Gargasha M, Wang Z, et al. Automatic stent detection in intravascular OCT images using bagged decision trees. *Biomed Opt Express*. 2012;3(11):2809-24
19. Lu H, Gargasha M, Wang Z, et al. Evaluation of Highly Automated Software for Analyzing Intravascular Optical Coherence Tomography Pullbacks of Stents. *J Am Coll Cardiol*. 2014;64(11 S).
20. Imola F, Mallus MT, Ramozzotti V, et al. Safety and feasibility of frequency domain optical coherence tomography to guide decision making in percutaneous coronary intervention. *Eurointervention* 2010;6:575-81.
21. Im E, Kim BK, Ko YG, Shin DH, Kim JS et al. Incidences, predictors, and clinical outcomes of acute and late stent malapposition detected by optical coherence tomography after drug-eluting stent implantation. *Circ Cardiovasc Interv*. 2014;7:88-96
22. Attizzani GH, Capodanno D, Ohno Y, et al. Mechanism, pathophysiology and clinical aspects of incomplete stent apposition. *J Am Coll Cardiol*. 2014;63(14):1355-67.
23. Chamié D, Bezerra HG, Attizzani GF, et al. Incidence, predictors, morphological characteristics, and clinical outcomes of stent edge dissections detected by optical coherence tomography. *J Am Coll Cardiol Intv* 2013;6:800-13.
24. Mauri L, Orav J, Kuntz RE. Late loss in lumen diameter and binary restenosis for drug-eluting stent comparison. *Circulation* 2005;111:3435-3442.
25. Wijns W, Shite J, Jones MR, et al. Optical coherence tomography imaging during percutaneous coronary intervention impacts physician decision-making: ILUMIEN I study. *EHI* 2015;36:3346-3355.

Legends

Figure 1: Patient flow and treatment flow

PCI=percutaneous coronary interventions, OCT=optical coherence tomography

Figure 2: Scheme of stenosis area calculation (online)

MLA=minimal lumen area, AS=area of stenosis

Figure 3. Stent analysis output of OCTivat-Stent (online)

A. Automatic lumen detection result, lumen tracing, major and minor axes are shown in cyan. **B.** Detected stent struts are automatically classified as covered (green) versus uncovered (red). Stent contour (blue) is estimated using detected strut locations. **C.** Strut-level tissue coverage thickness measurement (magenta). **D.** Frame-level NIH area (yellow) quantification for the cross section in panel C. **E.** Strut-level malapposition distance measurement. **F.** Frame-level malapposition area (red) quantification for the cross section in panel E.

Figure 4: Cumulative distribution of mean in-stent late lumen loss at nine months of follow-up (online)

OCT=optical coherence tomography; FU= follow-up

Table 1: Baseline demographic and procedural characteristics

OCT=optical coherence tomography; pPCI=primary percutaneous coronary intervention; CAD=coronary artery disease; MI=myocardial infarction; CABG=coronary artery bypass graft; LAD=left anterior descending; RCA=right coronary artery; LCx=left circumflex; values in square brackets represent quartiles 1-3; pPCI=primary percutaneous coronary intervention; MLD=minimal lumen diameter; GPIIb/IIIa i=glycoprotein IIb/IIIa inhibitors; DS=diameter stenosis; DAPT=dual antiplatelet treatment.

Table 2: Post-procedural angiographic and biomarker characteristics (online)

OCT=optical coherence tomography; pPCI=primary percutaneous coronary intervention; Min. in stent D.=minimal in-stent diameter; Min. in seg. D.=minimal in-segment diameter; DS stent=diameter stenosis in-stent; DS in-segment=diameter stenosis in-segment; CK max=creatinine kinase peak; values in square brackets represent quartiles 1-3.

Table 3: MACE at 30 days and nine months of follow-up (online)

MACE=major adverse cardiovascular events; IdTLR=ischemia-driven target lesion revascularization; MI=myocardial infarction; OCT=optical coherence tomography.

Table 4: Angiographic data at nine months of follow-up

OCT=optical coherence tomography; pPCI=primary percutaneous coronary intervention.

Table 5:

OCT data at nine months of follow-up

OCT=optical coherence tomography; pPCI=primary percutaneous coronary intervention;

Mean, (STD), Median (Q1, Q3)