

# Etude de l'angioplastie guidée par tomographie en cohérence optique

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Médecine - Pathologie cardiorespiratoire et vasculaire

## ÉTUDE DE L'ANGIOPLASTIE GUIDEE PAR TOMOGRAPHIE

## **EN COHERENCE OPTIQUE**

### OPTICAL COHERENCE TOMOGRAPHY-GUIDED ANGIOPLASTY AS A NEW TOOL TO IMPROVE CORONARY EVALUATION AND GUIDE PERCUTANEOUS CORONARY INTERVENTION PROCEDURES

## THÈSE présentée et soutenue publiquement

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Optical coherence tomography-guided angioplasty as a new tool to improve coronary evaluation and guide percutaneous coronary intervention procedures

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### Abbreviations

- ACS, acute coronary syndrome
- AMI, acute myocardial infarction
- CAD, coronary artery disease
- CAG, coronary angiography
- FD-OCT, Fourier domain optical coherence tomography
- FFR, fractional flow reserve
- IVUS, intravascular ultrasonography
- LSI, lumen symmetry index
- NSTE-ACS, non-ST-segment elevation acute coronary syndrome
- OCT, optical coherence tomography
- PCI, percutaneous coronary intervention
- RVSI, reference vessel symmetry index
- STEMI, ST-segment elevation myocardial infarction
- TCFA, thin-capped fibroatheroma
- TD-OCT, time domain optical coherence tomography

1. Introduction: Optical coherence tomography in cardiology

Recent advances made in imaging techniques have greatly improved the understanding of coronary physiology, luminal morphology and plaque vulnerability as well as stent deployment. With these progress, even complex coronary lesions and restenosis can be safely treated by interventionalists [1]. OCT with great sensitivity are capable of detecting the detailed characteristics within vessels, making it increasingly becoming an ideal imaging tool for assessment of lumen dimensions and lesion characteristics, facilitating the application of coronary interventions [2, 3]. We briefly review the features of OCT as well as its potential application in coronary artery disease.

#### 1.1 Limitations of coronary angiography

Coronary angiography (CAG) has been introduced into clinical practice for more than 40 years, and is one of the most commonly performed diagnostic procedures worldwide. However, CAG has well-known limitations in the detection of coronary atherosclerosis. Coronary angiogram is a twodimensional silhouette of the three-dimensional coronary artery lumen. Also, it has limited reliability in assessing plaque composition and dimensions, and distribution of atherosclerosis and low sensitivity in detecting calcium [4]. CAG may underestimate severe coronary lesions when diffuse atherosclerosis results in uniform narrowing of the lumen [5]. Moreover, the segment of the artery with atherosclerotic plaque tends to grow outwards during remodeling, which is also a reason why a significant atherosclerotic plaque is easily missed on the angiogram [6]. Another limitation of CAG is the intra- and inter-observer variability [7]. Given CAG has obvious drawbacks and offers no direct information on the coronary lesion characteristics, even the most experienced interventionalist, confronted with lesion and patient complexity, may face challenges in decisions based only on the angiographic lumen profile alone. There is a urgent need to develop advanced intra-coronary imaging techniques to overcome these limitations of angiographic assessment.

#### **1.2 Features of intravascular OCT**

Intravascular OCT is able to provide clear, reliable images of vessel structure of normal and diseased coronary arteries. In an *ex vivo* study, Brezinski *et al.* firstly demonstrated the ability of OCT to detect the thin intimal cap layers associated with unstable plaques in 1997 [8]. Jang *et al.* were the first to conduct *in vivo* study of OCT in 2005, in which OCT clearly presented the morphology of culprit lesions in patients with stable or unstable angina and acute myocardial infarction (AMI) [9]. Important applications for intravascular OCT include evaluation of angiographically intermediate coronary artery, guidance of coronary stent implantation, and assessment of the mechanism of stent thrombosis or restenosis.

OCT employs near infra-red light rays and depends on interferometric principles [10, 11]. There are two types of OCT systems, namely first generation time domain (TD)-OCT system and second generation Fourier domain (FD)-OCT system [12]. The latter is a key milestone toward clinical feasibility, since it enables to image orders of magnitude faster and significantly decreases the time for image acquisition [13]. In addition, FD-OCT system do not require the occlusion of the vessel as the TD-OCT did, which may significantly reduce the risk of life-threatening arrhythmias [14].

In contrast to intravascular ultrasonography (IVUS), OCT systems have a higher sensitivity, with 10–20 µm of axial resolution, 20–30 µm of lateral resolution. But light emitted by OCT has a lower depth penetration [15]. A comparison of physical characteristics of OCT versus IVUS and CAG is made in Table 1 [16, 17]. However, for both TD and FD-OCT systems, intracoronary contrast injection is required during image acquisition, which is common limitation of OCT application.

	CAG	TD-OCT <sup>a</sup>	FD-OCT <sup>b</sup>	IVUS <sup>c</sup>
Energy source	X-radiation	Near-infrared light	Near-infrared light	Ultrasound (20–45 MHz)
Wave length, µm	10 <sup>-5</sup> -10 <sup>-2</sup>	1.3	1.3	35–80
Resolution				
Axial, µm	59–137	15	15	100–200
Lateral, µm	NA	40		200–300
Frame rate, frames/s	NA	15–20	100	30
Pull-back rate, mm/s	NA	1–3	20	0.5–1
Maximum scan diameter, mm	NA	7	10	15
Tissue penetration, mm	200–450	1.5–2	2	10

#### Table 1 Physical characteristics of OCT vs. IVUS, CAG [18, 19]

#### 1.3 Measurement of vessel dimensions

A number of studies have been conducted to assess the ability of OCT in quantifying luminal dimensions, but yielding conflicting results. In an *ex vivo* study of eight specimens, OCT overestimated luminal area by up to 0.8 mm<sup>2</sup> [20]. However, the results may be influenced by tissue shrinkage since they used histomorphometry as the reference standard. In phantom models, the mean cross-sectional luminal area detected by OCT was equal to phantom true luminal area, with high reproducibility in OCT measurements [21, 22]. In recent years, OCT has been frequently compared against IVUS, in order to test its ability for quantifying luminal dimensions *in vivo* [20, 23]. In the OPUS-CLASS study, strong correlations were established between luminal dimensions measured by IVUS and OCT, and both modalities presented good inter-observer variability [21]. However, IVUS showed significantly higher root-mean-squared deviation, revealing a better agreement for OCT measurements. Importantly, comparing to OCT, luminal area appears to be approximately 5–10% larger when measured using IVUS [21, 23, 24]. It is not easy to differentiate whether OCT underestimates or IVUS overestimates the luminal dimensions. Thus, concerns have been raised that OCT-based parameters of luminal dimensions may possibly lead to the implantation of smaller diameter stents. Since OCT acquires smaller measurement values of luminal dimensions, caution must be given when assessing lesions and stent size using literaturevalidated IVUS parameters [25].

#### 1.4 Detection of atherosclerotic plaque characterization and plaque rupture

Visualization of atherosclerotic plaques by OCT was initially validated in a large post-mortem specimen [26], and then *in vivo* human studies were carried out to testify the ability of OCT to characterize different plaques: fibrous plaques appear to be a homogeneous rich signal; fibrocalcific plaques are characterized by signal-poor regions with sharply delineated borders; lipid-rich plaques are presented as diffusely bordered signal-poor regions. OCT systems allow operators to identify coronary plaques and lesions, based on their own characterization, much clear and easier compared to other imaging modalities, with great intra- and inter-observer reliabilities and high sensitivity and specificity [27, 28]. Thus, OCT also enable to discriminate the changes in plaque morphology/phenotype and vascular response in response to pharmacological therapy, such as statin [29, 30].

Autopsy studies have showed that thin-capped fibroatheroma (TCFA) is closely linked to plaque rupture in ACS and is considered a vulnerable plaque [31]. A TCFC is visualized as a signal-rich band (indicating vascular smooth muscle cell and extracellular matrix in and around fibrous cap), overlying a signal-poor region (indicating the necrotic core) on OCT. Although OCT is unable to quantify large lipid cores due to limited tissue penetration ability, its high resolution allows precise visualization and quantification of the thin fibrous cap (< 100 µm)[32].

Nonculprit plaque ruptures were observed in 20% of patients with coronary artery disease [33]. OCT allows visualization of the detailed morphological changes during plaque rupture, which are typically characterized by a large lipid core that appears as signal poor region with poorly defined border and rapid signal drop off. Additionally, ruptured plaques can be classified into two categories based on the site of rupture: rupture occurring at the mid-portion of the plaque or at shoulders [34]. The longitudinal appearances of ruptured plaques are also useful for evaluating their morphology and differentiating their nature. Toutouzas *et al.* pointed out that ruptured plaques, among culprit lesions in ACS, tend to be predominantly located in the first 30 mm of coronary arteries [35]. By contrast, plaque rupture is found more frequent at the shoulders of the plaque in patients with ST-segment elevation myocardial infarction (STEMI), in particular a site with open-wide aperture against the blood flow [36, 37]. In addition, OCT findings enable the identification of cardiovascular risk factors according to coronary atherosclerotic plaque characteristics [38, 39]. It can be used to find the relationship between plaque morphological findings and the adverse cardiac events, such as post-percutaneous coronary interventions (PCI) cTn elevations in non-ST-segment elevation ACS patients [40]. However, the current OCT systems have a low tissue penetration capacity, which makes it difficult to distinguish tissue behind a thick cap, lipid core, or calcification.

### 1.5 Guidance of stent implantation during PCI

Lesion preparation guided by OCT prior to PCI/ stent implantation has two main steps, including (1) obtain precise and detailed information about lesion characteristics and plaque distribution across the vessel; and (2) selection of the appropriate device on the basis of parameter values provided by OCT. After intervention, unfavorable stent deployment and vessel injury may occur. OCT can be utilized to disclose the morphology of stent edges and to assess procedural complications [41, 42]. Although OCT is unable to visualize the whole stent strut, its images can provide a clear depiction of the boundaries within lumen and vessel.

#### 1.5.1. Calcification

The presence of calcified and rigid lesions makes PCI challenging, and adjuvant techniques are often required to achieve satisfactory stent outcomes [43, 44]. Angiography has been reported to detect calcified lesions with low sensitivity (48%), except for severe calcification [45]. Conversely, calcium is precisely and easily detected by OCT, characterized by a poor or

heterogeneous signal region with sharply delineated borders. Based on pathological study, given the light penetrates calcium without shadowing, OCT can more accurately estimate the area of calcification than IVUS does [46]. In addition, OCT allows the operator to distinguish superficial and deep calcification, for instance, to identify a calcified lesion located at the intima-lumen interface or at the media-adventitia border. It can quantify the thickness of the calcified plate, the distance from the lumen and the circumferential arc distribution [47]. Therefore, OCT may be useful as a clinical tool for quantifying calcified plaques.

#### 1.5.2. Assessment of stent-related vascular injury

High-pressure deployment is necessary for adequate stent expansion, but it also induces procedural vessel injury. With high resolution, OCT is able to visualize details of stent and distinguish different types of injury after implantation. Acute effects of stent implantation on the vessel wall have been recognized as intra-stent or edge dissection, tissue prolapse, and intrastent thrombus. Intra-stent dissection is a disruption of the luminal surface within the stent segment. It can appear in two forms, one as a linear rim of tissue with a clear separation from the vessel wall, plaque, or stent struts, or another as an empty cavity behind the struts. In contrast, edge dissection is defined as the presence of a linear rim of tissue with a width of  $\geq$  200 µm and a clear separation from the vessel wall of plaque that is adjacent (< 5 mm) to a stent edge [48]. A dissection can be described by measuring the length, angle, or width of the vessel flap. Data on IVUS revealed a link between significant stent edge dissection and early stent thrombosis [49]. The incidence of OCT-detected edge dissections has been reported to be as high as 21% to 39.2%, compared with 9.2% to 21.3% of IVUS-detected dissections [50-54]. Bouma et al. showing that the frequency of stent edge dissection detection was 4.8% by IVUS versus 19% by OCT [55]. Plague type at the stent edges has been reported as fibrotic 55.6% and 31.1%, fibrocalcific 22.2% and 33.3%, fibroatheroma 15.3% and 28.9%, and TCFA 6.9% and 6.7% at distal and proximal edge, respectively [56].

Tissue prolapse is a convex-shaped protrusion of tissue between adjacent stent struts toward the lumen, without disruption of the continuity of the luminal vessel surface. The distance from the arc connecting adjacent stent struts to the greatest extent protrusion is more than 50 µm. Tissue protrusion includes plaque protrusion and thrombus protrusion. On OCT images, plaque protrusion is characterized by a smooth surface and no signal attenuation, and thrombus protrusion by an irregular surface and significant signal attenuation. Since unstable lesions contain soft lipid tissue and thrombi, tissue protrusion is more commonly observed in the culprit lesions of ACS. Gonzalo *et al.* reported tissue prolapse in 97.5% of 73 consecutive patients [41 with stable coronary artery disease (CAD) and 32 with ACS and more extensive tissue prolapse was observed in unstable patients than stable ones [57].

Strut coverage may be a predictor for adverse cardiovascular events. The length of an uncovered stent strut segment has been found to contribute to stent thrombosis. OCT allows an accurate assessment *in vivo* of strut tissue coverage and neointimal hyperplasia at follow-up, providing quantitative measurements of minimal lumen area, minimal stent cross section area, percentage lumen obstruction and percent neointimal hyperplasia, due to its ability to characterize lumen-vessel/stent interface [15, 58]. Currently, OCT has been applied to evaluate short- and midterm healing properties (neointimal coverage of struts) following stent implantation [59].

1.5.3. Assessment of stent deployment

Suboptimal stent deployment, using specific quantitative OCT criteria, has been confirmed as a independent outcome predictor for device-oriented cardiovascular events [60].

Incomplete stent apposition is defined the measured distance from the stent surface to the lumen contour being greater than the total thickness of the stent strut and polymer. Incomplete stent apposition has been found as a potential detrimental factor for the development of late stent thrombosis [61, 62]. Incomplete stent apposition may occur either acutely at the time of stent deployment or later as a consequence of vessel remodeling. Also, incomplete stent apposition is often seen in calcified lesions, because the calcified lesion is not expanded uniformly by PCI. The

frequency of malapposed struts, particularly in complex coronary lesions, can be as high as 9.1% to 17% following PCI [63]. Angiography often fails to recognize incomplete stent apposition. Owing to its superior intraluminal resolution, OCT can detect struts with incomplete stent apposition. One of the limitations of OCT in the diagnosis of stent malapposition is its low depth of light penetration, which limits the application of OCT for examining the mechanisms or consequences of stent malapposition [64].

Stent under-expansion is defined by the in-stent minimal lumen area  $\geq$  90% of the average lumen area, and  $\geq$ 100% of lumen area of the reference segment with the lowest lumen area. There is a general agreement that gross stent underexpansion is related to a higher incidence of in-stent restenosis and thrombosis [65]. In a mixed population containing stable CAD patients and ACS patients, Prati *et al.* found stent under-expansion in 11.4% and incomplete stent apposition in 29.7% on OCT imaging [66].

#### 1.6 OCT-guided angioplasty for coronary imaging—Lessons from clinical studies

Given the novelty of the technique, there are currently no well-established indications for the clinical use of intracoronary OCT. Some studies recommended OCT imaging particularly used for high-risk patients, for instance, those with ACS, stent thrombosis or in-stent, restensis, or for high-risk lesions, for instance bifurcations, distal left main disease, long or diffuse lesions [67-69].

### 1.6.1. Safety

OCT imaging technique has gained considerable attention in many centers worldwide, and our work was performed within this context. Recent clinical studies have demonstrated its safety in routine clinical practice, with low rate of major complications reported [70, 71]. Energy applied during an intravascular OCT scan is relatively low, with output power in a 5.0-8.0 mW range. Such low energy is unable to cause functional or structural damage to the tissue. Thus, the safety of OCT depends mainly on the mechanical injury of a catheter and the extent of ischemia caused by blood flow occlusion or the amount of contrast injected when a non-occlusive OCT system is

employed. Preliminary studies have showed that OCT image acquisition is safe when using both occlusive and non-occlusive systems. Several studies have been conducted to investigate the safety of intracoronary OCT imaging [14, 72, 73]. In a single-center study, Imola *et al.* evaluate the safety and feasibility of FD-OCT for guiding PCI procedures. The results showed that FD-OCT was a safe and feasible technique during PCI [73]. All but one (99.1%) procedures were successful. No patients experienced death or any major complications. In another study, OCT was successful in 93.7% (60/64) of studied patients using the non-occlusive technique, with a mean amount of contrast injection of  $30.5 \pm 3.3$  mL (range 22–35 mL) for OCT assessment. No major complications were observed even though a large number of these patients had ACS [72]. All mild adverse events were rapidly resolved. A multi-centre study reported on the safety of the occlusive OCT technique in 76 patients with CAD [14]. Vessel occlusion time averaged 48.3  $\pm$  13.5 s; and no death and severe procedural complications were observed. In addition, no impairment in renal function or increased serum creatinine level up to 48 h after the procedure was occurred.

#### 1.6.2. Efficacy

Several early clinical trials had been conducted to evaluate the feasibility and effectiveness of OCT imaging. In a recent clinical study involving experimental animals, Suzuki *et al.* found a strong correlation between histological parameters and OCT measurements of the luminal area (r=0.98; P<.001). This correlation was stronger than that observed between IVUS measurements and histological parameters (r=0.803; P<.001) [74]. Also, the study found a lower variation among OCT measurements than that of IVUS (3.7% for OCT *vs.* 4.3% for IVUS). In another study with the non-occlusive technique in 64 patients [72], OCT was found to provided accurate measurements of luminal area with higher reproducibility for two serial pull-backs. Similarly, in another study OCT was used to analyze more than 2000 cross-sections, and it accurately depicted the whole circumference of vessels and yielded good image quality in 96% of cases [75]. Even in the study with the occlusive technique, a 100% imaging success rate was achieved [14]. Based on these

encouraging preliminary findings, OCT seems to be successful to acquire good quality in at least 90% of the image cross-sections, irrespective of acquisition technique applied.

Currently, more and more clinical studies are performed to define the clinical value of the OCT guidance in PCI [76]. OCT findings enables clinicians to differentiate the patients with ACS caused by plaque erosion from those caused by plaque rupture, facilitating personalized therapy [77]. With OCT findings, the relationships of culprit plaque lesion features and subsequent coronary artery remodeling as well as the outcomes of patients can be precisely assessed [78, 79]. In this-year study, Kuku *et al.* found that OCT-guided PCI in comparison with angiography-guided was associated with reduction in adverse events for the composite of cardiac deaths, myocardial infarction and repeat revascularizations [80].

Fractional flow reserve (FFR) is widely used for the assessment of myocardial ischemia. In a study by Seike F *et al.*, OCT-derived FFR showed a stronger linear correlation with FFR measurements (r = 0.89) than quantitative coronary angiography % diameter stenosis (r = -0.65), suggesting it as an alternative method for the assessment of functional myocardial ischemia [81]. In another study, OCT-guided PCI offered a reduction in target lesion revascularization (4.1% vs. 14.2% p<0.01) compared with FFR-guided group, without impact on major adverse cardiovascular events or all cause death [82].

In very recent years, several clinical studies have been conducted to compared the performance of different imaging modalities (OCT, angiography, IVUS) for PCI guidance [83, 84]. Although OCT can add value to angiography as a diagnostic and/or intervention tool for PCI guidance, some findings are conflicting. In the study by Ali *et al.*, 450 patients were randomly allocated to IVUS, angiography and OCT during PCI. The final median minimum stent area was 5.79 mm<sup>2</sup>, 5.89 mm<sup>2</sup> and 5.49 mm<sup>2</sup> for OCT, IVUS and angiography guidance, respectively. OCT guidance was non-inferior but not superior IVUS guidance. Also, OCT guidance was also not superior to angiography guidance [84]. However, investigations are still ongoing and have yielded no conclusive results based on comprehensive parameters.

### Conclusion

OCT has the potential to become the most reliable imaging modality for assessment of coronary plaques and stent implantation. However, the impact of intracoronary clinical significance to date has been limited to observations. Further investigation on the role of OCT guidance to lesion treatment is needed.

## 2. Working hypothesis, questions and objectives

Coronary angiography is an invasive imaging technique for diagnostic and interventional procedures. With injection of radiopaque contrast, it indeed provides real-time luminogram, which can translate into accurate and highly reproducible measurements for clinical decision-making and for research applications. Although CAG has long been considered the gold-standard diagnostic method for CAD and is widely accepted as a firm basis for determining treatment strategies for PCI, it sometimes fails to acquire accurate images that reflect critical characteristics of atherosclerotic lesions or vessel–stent relationships [85, 86]. In particular, angiography lacks accuracy in the presence of overlapping vessels, foreshortening, or calcium in the vessel wall. Furthermore, angiography has limited ability to characterize atherosclerotic plaques, beyond the detection of calcium and grossly ulcerated plaques or dissections. Thus, there are some scenarios in which even an experienced interventional cardiologist requires complementary information in addition to measurements obtained by angiography. At the end of the 20<sup>th</sup> century, novel techniques that are capable of fully reflecting lesion and stent features were urgently needed for interventional cardiology.

Intravascular ultrasound is widely used for improving the accuracy of the coronary luminogram in cases of overlapping, foreshortened or calcified vessels, and for giving information about the plaque burden, plaque morphology, or calcium distribution. OCT uses near-infrared light to generate cross-sectional images of the coronary arteries. Near-infrared light has shorter wavelength and higher frequency than ultrasound has; therefore, OCT images have 10-fold higher resolution than IVUS images, at the expense of lower penetration into the tissue [87]. The higher resolution of OCT enables the visualization and measurement of lesion details that angiography and IVUS cannot achieve. Although OCT started in cardiology as a research tool, it had the potential to become a routine tool for diagnostic application and guidance of therapeutic interventions.

Intravascular OCT has advantages in terms of high spatial resolution, precise plaque assessment, and real-time image processing [88, 89]. OCT thus rapidly appeared to be a new tool

that could reliably visualize coronary artery morphology in normal and diseased arteries, enabling to identify a variety of plaque components. It was also shown to also provide highly reproducible measurements of lesion length and reference vessel lumen diameter, which might guide stent selection and deployment. In addition, OCT presented as a valuable tool to evaluate the outcomes of coronary interventions, for example to precisely evaluate stent expansion and strut apposition. Finally, OCT had been used to depict the stent-related vascular injury and healing and the underlying mechanisms of stent failure, such as in-stent restenosis. Such additional information might facilitate clinical decision-making process and eventually improve clinical outcomes.

As described above, the capability of intravascular OCT seemed superior to other imaging modalities, such as angiography, in examining plaque features and stent implantation during PCI. Although the application of OCT during PCI seemed logical and promising, the assessment of OCT when our thesis work began had been limited to observations and its clinical significance had yet not been fully validated. Furthermore, OCT had several inherent drawbacks, including the relatively shallow depth of light penetration into the arterial wall, particularly for assessing calcium, thrombotic and lipid components, compared with ultrasound examination. Additionally, first-generation TD-OCT also required blood removal with balloon occlusion method during image acquisition, making the PCI procedure more complex and precluding the use of this technique for ostial lesions, including the left main coronary artery or lesions. As the newly developed FD-OCT system did not require coronary artery occlusion and had a faster pullback speed [90, 91], it might be more suitable for PCI. Thus, the clinical significance of OCT for PCI needed to be established through prospective, well-designed large clinical trials.

#### 2.1 Working hypothesis:

At the beginning of our thesis work, the working hypothesis was as follows: The increasing level of patient/lesion complexity being treated by interventional cardiologists today requires a much higher standard of procedural precision and safety compared with the past. Angiography

alone may be inadequate in detecting all clinically relevant pathological events. Given unique advantages of OCT, OCT-guided PCI may lead to superior stent measurements versus angiography alone and to subsequent modifications of therapeutic strategies by physicians. Prospective studies or observational registries are now required.

Then we speculated that OCT could more accurately assess coronary artery plaque rupture before stenting and edge dissection after stenting, compared with CAG alone. It might provide more detailed information in stent implantation in practical application.

### 2.2 Objectives:

1) To evaluate whether OCT-guided angioplasty would provide useful clinical information beyond that obtained by angiography and whether this information would subsequently modify physicians' behaviors and treatment choices.

2) To investigate whether OCT can provide an accurate assessment of the coronary artery plaque rupture before stenting, or edge dissection after stenting, and may subsequently provide guidance for optimizing the stenting procedure.

3) To evaluate the vascular pathophysiology and morphological features and predict stent edge dissections detected by OCT in patients with non-ST-segment elevation (NSTE)-ACS.

3. OCT-guided angioplasty yield useful clinical information and modify

## physicians' strategies

#### 3.1 Background and objectives

With the combination of sophisticated cardiac catheterization technique, modern medication and experienced operators, PCI has evolved into a most effective nonsurgical modality for successfully treating patients with CAD[92]. Recent advances made in imaging techniques have greatly improved the understanding of coronary physiology, luminal morphology and plaque vulnerability as well as stent deployment [1]. However, the complexity of PCI has increased significantly over time, from the original simple, isolated target lesion in the proximal coronary segment of coronary arteries to the unclear disease scenarios such as ACS, in presence of distal left main bifurcation, diffuse or multivessel disease, bioabsorbable scaffolds. Although CAG is a widely accepted imaging technique, it has limited accuracy in assessing plaque composition, dimensions and distribution, low sensitivity in detecting calcifications, and unclear reliability in guiding stent deployment [4]. For even the most experienced interventional cardiologist, angiography alone has major limitations for decision making and procedural guidance.

OCT has become the current state-of-the-art intracoronary imaging modality that allows visualization of detailed morphological characteristics of both atherosclerotic plaque and stent [93]. Because of the high frame rate in acquisition and the high-speed pullback, OCT automatically displays a pristine longitudinal lumen contour that is easier to measure and interpret. The high spatial resolution of OCT offers precise examination details, including more specific determination of tissue characteristics (e.g., calcification, thrombus, neointimal tissue) and more accurate assessment of stent parameters such as vessel wall apposition, strut coverage, tissue prolapse, and edge dissection[94]. Although OCT is unable to visualize the whole stent strut, its images can provide a clear depiction of the boundaries within lumen and vessel [42]. Factors such as stent diameter and length, landing zones, lesion characteristics requiring special preparation are among the parameters that can be readily identified by OCT [10]. From a technical perspective, OCT can be very helpful in detailed planning of interventional strategies and optimizing PCI results, particularly with complex lesions [95].

In this context, OCT may have potential to become a critical tool that enables physicians to deliver more precise and optimal treatment during PCI, especially in a complex setting, thereby providing superior clinical outcomes. Unfortunately, the safety and feasibility of OCT-guided procedures during PCI, in which OCT revealed lesion characteristics and pathological events that were not disclosed by angiography, have rarely been reported. Therefore, a comparative prospective study between CAG and OCT evaluation before and after PCI is needed.

We hypothesized that OCT had potential clinical benefit in planning and mapping PCI procedures to optimize the results of stent implantation. In this study, we investigated whether and how OCT actually provided additional information for CAD diagnosis and guidance of PCI procedures.

### Clinical significance of optical coherence tomography-guided angioplasty on treatment selection

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Abstract. The present study aimed to observe whether optical 2 coherence tomography (OCT)-guided angioplasty is able to provide useful clinical information beyond that obtained by 3 4 angiography as well as provide recommendations for physicians 5 that may improve treatment selection. This prospective study 6 included 83 patients with coronary artery disease (>18 years) undergoing coronary angiography (CAG) for ST-elevation 7 myocardial infarction (n=13), non-ST-elevation myocardial 8 infarction (n=19), stable angina (n=22), unstable angina (n=10), 9 10 silent ischemia (n=11), or elective percutaneous coronary intervention (n=8). Following the initial CAG (CAG-pre), 11 the patients underwent OCT before angioplasty (OCT-pre, 12 24 patients), after angioplasty (OCT-post, 22 patients), or both 13 14 (37 patients). The thrombus burden, calcification and plaque 15 dissection or rupture were compared between the OCT-pre and CAG-pre recordings. Following angioplasty, stent malap-16 17 position, suboptimal stent deployment, suboptimal stent 18 lesion coverage, and edge dissection were compared between OCT-post and CAG-post alone. Among the 83 patients, 45.7% 19 had single-vessel and 54.3% had multiple-vessel disease. 20 21 OCT pre- and post-angioplasty revealed significantly more 22 information on the procedure than CAG alone. This clinical information changed the clinical strategies in 41/83 (49.4%) 23 24 patients, including 58 modifications of therapeutic strategy (69.9%, 58/83): Thrombus aspiration in 2 cases (2.4%), admin-25 26 istration of glycoprotein IIb/IIIa inhibitors in 8 cases (9.6%), 27 additional balloon inflation in 23 cases (27.7%), additional stent implantation in 17 cases (20.5%), avoiding stent implantation 28 29 in 4 cases (4.8%), collateral intervention in 2 cases (2.4%), and 30 guidewire reposition in 2 cases (2.4%). In conclusion, OCT-pre

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Key words: coronary artery disease, coronary angiography, percutaneous coronary intervention, optical coherence tomography

and OCT-post provided additional clinical information beyond 31 that obtained by angiography alone, which resulted in modification of the treatment strategies in half of the included 33 patients. 34

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#### Introduction

Coronary artery disease (CAD) is one of the most common 38 cardiovascular diseases in the elderly population world-39 wide (1). Percutaneous coronary intervention (PCI) has 40 become the mainstay invasive therapy for CAD patients (2). 41 Recent advances in interventional cardiology have highlighted 42 the importance of a detailed understanding of the tissue 43 characteristics of coronary atherosclerotic lesions, including 44 the identification of plaque stability, estimation of lesion 45 covering, and tearing degree pre- and post-PCI (3,4). Coronary 46 angiography (CAG) has been considered to be the gold stan-47 dard diagnostic method for CAD and is widely accepted as 48 a firm basis for determining treatment strategies for PCI (5). 49 50 However, previous evidence indicated that CAG may not provide accurate images in certain cases and may fail to reflect 51 specific critical characteristics of atherosclerotic lesions or 52 vessel-stent associations in high-risk cases (5-7). Therefore, 53 novel techniques that fully reflect lesion and stent features 54 have been developed in interventional cardiology. 55

Optical coherence tomography (OCT) is a novel technique 56 that can provide cross-sectional and three-dimensional imaging 57 in vivo with ultra-high resolution (10-20  $\mu$ m) (8-12). It is a 58 59 particularly attractive technique because it provides real-time images and microstructural information on the tissues (13,14). 60 Furthermore, it can be used to provide a detailed analysis of 61 the coronary artery wall, including plaque characterization, 62 thin-cap fibroatheroma (TCFA) and vulnerable plaque identifi-63 cation, and assessments of the vascular response to PCI, which 64 may be responsible for acute coronary events (11,12,15-17). 65 Considerable evidence currently indicates that the early use 66 of OCT reveals various abnormal vessel reactions associated 67 with stent implantation, such as stent malapposition, subop-68 timal stent deployment, thrombus, tissue prolapse, and edge 69 dissection (18,19). Finally, OCT is also helpful for guiding 70 coronary management and interventions, including stent 71 apposition and the early identification of procedure-associated 72

complications (17,20). However, the evaluation of OCT clinical usefulness requires a prospective comparison of the two tech-2 niques in a significant number of patients.

The present study, a comparative prospective study of the CAG and OCT findings prior to and/or following PCI, was designed and conducted to investigate whether OCT may provide further information in addition to the traditional CAG and lead to substantial changes in PCI treatment strategies.

#### 10 Materials and methods

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Study population. In the present study, 83 consecutive patients 12 (>18 years old) with CAD scheduled to undergo PCI were 13 recruited prospectively at the Department of Cardiology, 14 15 University Hospital Jean-Minjoz (Besançon, France) between January 2011 and December 2012. The study was designed 16 to separately analyze the treatment strategy changes that were 17 respectively achieved by OCT performance when performed 18 before or after angioplasty and to determine the possible advan-19 tages and inconveniences of performing both. OCT was run 20 before angioplasty, subsequent to the initial CAG in 24 patients 21 22 (OCT-pre group); or it was run after angioplasty following 23 angiography in 22 patients (OCT-post group); 37 patients 24 underwent OCT both before and after angioplasty (Fig. 1). The protocol was approved by the Ethics Committee of the 25 26 Regional Health Agency Bourgogne/Franche-Comté (Comité 27 de Protection des Personnes EST II), and all patients provided written informed consent for the OCT-guided and CAG-guided 28 29 PCI and the follow-up. 30 31 Outcomes. The primary study objective was to determine the percentage of patients in whom an alteration in the procedural 32 33 treatment strategy was decided based on the information obtained from OCT imaging. This was defined as a change in 34

35 one or more of the following parameters: i) Additional balloon 36 inflation; ii) implantation of Additional stent(s); iii) use of 37 glycoprotein (GP) IIb/IIIa inhibitors; iv) use of thrombus aspi-38 ration; v) use of rotational atherectomy; vi) avoiding stenting. 39 The secondary objective was to compare the percentages of 40 patients in whom OCT revealed the presence of one or more of

41 the following parameters: Thrombus burden, plaque rupture, spontaneous dissection, and identified calcification (11). 42 43 These parameters identified respectively by OCT-pre and 44 CAG-pre recordings were compared. Following angioplasty, 45 the incidences of stent malapposition, suboptimal stent deployment, suboptimal lesion coverage, and edge dissection were 46 47 also compared as recorded by OCT-post vs. post-angioplasty

fluoroscopy. 48 Safety outcomes were assessed according to the proce-49

dural duration and perioperative outcomes of OCT, including 50 51 coronary no-reflow phenomenon as described by Berg and

52 Buhari (21), coronary perforation, occlusive dissection, coronary spasm, stent occlusion, and PCI-associated myocardial

- 53 54 infarction (MI).
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CAG procedure. CAG was performed via femoral or radial 56

artery access in all patients. Unfractionated heparin (2,500 U; 57

58 Pharmacia & Upjohn, London, UK) was administered prior

59 to CAG, and a 6F guiding catheter was inserted toward the

coronary ostium. Adequate views of the region of interest 60

Characteristics	n	%
Sex		
Male	38	45.8
Female	45	54.2
Hypertension	49	59.04
Dyslipidemia	48	57.83
Diabetes mellitus	13	15.66
Smoker	37	44.58
Obesity	21	25.3
Family history of CVD	20	24.10
Prior history		
Myocardial infarction	38	45.8
Heart failure	4	4.82
Stroke	3	3.61
Renal insufficiency	11	13.25
Valvular heart disease	9	10.84
Angioplasty	38	45.8
CABG	2	2.41
Indication for coronary angiography		
STEMI	13	15.7
NSTEMI	19	22.9
Stable angina	22	26.5
Unstable angina	10	12.0
Silent ischemia	11	13.3
Elective PCI	8	9.6
Extent of disease		
Single-vessel disease	38	45.7
Two-vessel disease	33	39.8
Three-vessel disease	12	14.5

CVD, cardiovascular diseases; CABG, coronary artery bypass grafting; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-STEMI; PCI, percutaneous coronary intervention.

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that avoided vessel foreshortening and side-branch overlap 102 were obtained subsequent to the administration of an intra- 103 coronary bolus of nitroglycerin (200 µg; Nitronal Injection, 104 Pohl-Boskamp GmbH & Co., Hohenlockstedt, Germany). 105 Classical qualitative angiographic criteria (11) were used, and 106 the quantitative CAG procedure was performed by experi- 107 enced personnel using standard methodology (22,23). 108 109

OCT evaluation. OCT and CAG examinations were consecu- 110 tively performed during PCI when a patient fulfilled the 111 following criteria: i) Suitable coronary artery anatomy for 112 OCT evaluation as instructed by the international consensus 113 of clinicians (9,24,25); ii) stable hemodynamics; iii) absence 114 of severe co-morbid conditions, including severe renal or liver 115 dysfunction, or other co-morbidities, such as cancer; iv) no 116 contraindications to iodinated contrast media, aspirin, and/or 117 clopidogrel. However, the OCT was not examined if CAG 118 quality was sufficient for the physician to make a suitable treat- 119 ment decision. OCT images were acquired using the FD-OCT 120

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Figure 1. Flow chart of OCT-guided angioplasty and treatment strategy alterations based on the OCT data. OCT, optical coherence tomography; OCT-pre, 80 OCT performed following the initial coronary angiography; OCT-post, OCT performed following angioplasty. 81

Optis system (Lightlab Imaging Incorporated, Westford, MA, USA) and 6F guide catheter compatible Dragonfly Duo and Dragonfly Optis catheter (Lightlab Imaging Incorporated). The catheter was introduced into the coronary artery via a standard 0.014-inch angioplasty wire, after prior injection of an intracoronary bolus of nitroglycerin. To remove all blood adequately from the imaging site, nonocclusive flushing was performed using continuously injected contrast medium via an automated power injector, and the OCT catheter was pulled back at a speed of 18 mm/sec to guarantee sufficient time to acquire images of a 54-mm long segment (frame density: 10 frames/mm). When poor image quality was obtained, the pullback was repeated subsequent to modification of the flushing intensity or probe position. The data were then digitally stored for offline analysis (25,26). OCT images were analyzed online and offline using Lightlab software (V1.13, Lightlab Imaging Incorporated). All OCT images were analyzed in University Hospital of Besancon by 2 independent operators blinded to the angiographic findings and procedural strategy. Discordant OCT analyses were resolved by consensus. Definitions and recommendations for modifying treatment

strategies. Various features were determined during the OCT examination according to previously published consensus opinions and studies (9,23-25). Any inner-layer plaque profile discontinuity was considered a plaque rupture. A thrombus was defined as any intraluminal mass of  $\geq 200 \ \mu m$  without vessel wall surface continuity or a highly backscattered luminal protrusion in continuity with the vessel wall resulting in signal-free shadowing. Dissection was confirmed as the presence of a linear rim of tissue with a width of  $\geq 200 \ \mu m$ that was evidently separated from the vessel wall or plaque. Stent malapposition was identified as a distance between the stent and lumen that was greater than the sum of strut thick-ness plus abluminal polymer thickness; this was considered to be significant if the stent-lumen distance was >200  $\mu$ m. Suboptimal stent expansion was deemed to be present when 

the ratio of in-stent minimal lumen area (MLA) to average 84 reference area was <80%. 85

In accordance with previously published studies (24,26), the following actions and decision changes were recommended when the OCT examination detected abnormalities that were not originally recognized by the angiography results: Edge dissection and narrowing of the referenced lumen required additional stent implantation; stent under-expansion and malapposition required further dilation of the previously implanted stent with a non- or semi-compliant balloon; stent implantation was not indicated in patients with confirmed stenosis of <50% at the thrombosis site without dissection or plaque rupture; platelet GP IIb/IIIa receptor antagonist administered to patients with OCT-detected thrombosis who did not originally receive this medication; thrombus aspiration was indicated in patients with major thrombosis burdens; or guidewire relocation was conducted when the original 100 guidewire was inserted into the false lumen of the dissection 101 or out of the struts of the stent. The clinician decided whether 102 to perform additional interventions. 

Statistical analysis. Continuous variables are presented as 105 mean  $\pm$  standard deviation, whereas categorical variables 106 are expressed as absolute number and percentage. Intergroup 107 differences were assessed using Fisher's exact test or Student's 108 t-test when appropriate. All calculations were performed using 109 SPSS software (version 11.5; SPSS Inc., Chicago, IL, USA), 110 and values of P<0.05 were considered to indicate a statistical analysignificant difference.

#### Results

Clinical baseline characteristics. The baseline characteristics of all patients are listed in Table I. All patients (38 men, 117 45 women; mean age,  $65.8\pm11.3$  years old) were diagnosed 118 with CAD. The comorbidities, concurrent medications and 119 potential numbers of affected coronary arteries are shown in 120

radie fr. freatment of the menuced patients pre- and/or post-angloplasty (n=0.)	Table II.	Treatment of	f the included	patients pre-	- and/or post-	angioplasty	(n=83)
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	Prior to procedure, n (%)	Following procedure, n (%)	P-value
Aspirin	83 (100)	83 (100)	NS
Thienopyridines			
Clopidogrel	71 (85.5)	71 (85.5)	NS
Prasugrel	10 (12.1)	10 (12.1)	NS
Ticagrelor	2 (2.4)	2 (2.4)	NS
Anticoagulant			
Unfractionated heparin	77 (92.8)	77 (92.8)	NS
Enoxaparin	2 (2.4)	2 (2.4)	NS
Bivalirudin	4 (4.8)	4 (4.8)	NS
Glycoprotein IIb/IIa inhibitor			
Tirofiban	1 (1.2)	3 (3.6)	0.37
Abciximab	2 (2.4)	10 (12.0)	0.036
Eptifibatide	2 (2.4)	11 (13.3)	0.018



Figure 2. Comparisons of CAG and OCT findings in a patient with variant angina. (A) CAG image showing vascular stenosis (arrow) in the middle segment of 102 the left anterior descending artery. (B) OCT image showing vascular stenosis with a thrombus along the vessel wall *in situ* without significant atherosclerotic 103 lesions. The patient's symptoms were relieved by the administration of nitroglycerin. Therefore, coronary thrombosis with occasional coronary spasms was 104 considered in this patient following the OCT examination. Accordingly, stent implantation was not conducted and the clinical treatment strategy was changed 105 to the administration of glycoprotein IIb/IIIa receptor inhibitor and antispasmodic medications. Follow-up demonstrated treatment efficacy. CAG, coronary angiography; OCT, optical coherence tomography 

Tables I and II. Among the 83 patients, 13 with ST-segment elevation myocardial infarction (STEMI) (15.7%), 19 with non-STEMI (22.9%), 22 with stable angina (26.5%), 10 with unstable angina (12.0%), 11 with silent ischemia (13.3%), and 8 with elective percutaneous coronary intervention (9.6%) underwent coronary angiography. More than 50% of the patients had multi-vessel disease (54.3%), including 33 with two-vessel disease (39.8%) and 12 with three-vessel disease (14.5%); only 38 had single-vessel disease (45.7%). Three typical cases demonstrating the advantages of the OCT examination compared with CAG are shown in detail in Figs. 2-4.

Qualitative data provided by OCT and CAG prior to and 110 following angioplasty. The qualitative analysis results of 111 the CAG and OCT images pre- and post-PCI are shown in 112 Table III. A flowchart of the OCT-guided angioplasty and 113 OCT-based changes in treatment strategy is also provided in 114 Fig. 1. Among the 83 patients, a total of 61 patients under- 115 went OCT before angioplasty (24 patients received only 116 OCT pre-guided angioplasty and 37 patients received OCT 117 pre- and post-guided angioplasty) and 59 patients under- 118 went OCT following angioplasty (22 patients received only 119 OCT post-guided angioplasty and 37 patients received OCT 120





pre- and post-guided angioplasty). Prior to PCI, compared with CAG, OCT was more sensitive for plaque rupture (0 vs. 10 cases; P=0.007), diagnosing thrombus (9 vs. 20 cases; P=0.0162), dissection (4 vs. 12 cases; P=0.0289), and calcification (15 vs. 49 cases; P<0.001). Subsequent to PCI, compared with CAG, OCT was again more sensitive for the diagnosis of thrombus (1 vs. 24 cases; P<0.001), stent edge dissection (5 vs. 32 cases; P<0.001), stent malapposition (1 vs. 42 cases; P<0.001), intimal tissue protrusion (8 vs. 49 cases; P<0.001), suboptimal stent expansion (15 vs. 29 cases; P=0.0065), stent incomplete lesion coverage (11 vs. 20 cases; P=0.0467) and stent struts coverage bifurcation (0 vs. 35 cases; P<0.001). 

Quantitative characteristics provided by OCT and CAG prior to and following angioplasty. The target vessel and lesion characteristics detected pre- and post-PCI are shown in Table IV. Prior to PCI, the lesion diameter and ratio of diameter stenosis identified by OCT were significantly different from those measured by CAG (1.7±0.6 mm vs. 1.3±0.6 mm and 47.1±0.4% vs. 57.0±16.9%, respectively; P<0.001); after PCI, the stent diameter and ratio of diameter stenosis on OCT were significantly different from those measured by CAG (3.0±0.6 mm vs. 2.6±0.5 mm and 10.0±8.3% vs. 14.3.0±8.0%, 

respectively; P<0.001). The reference vessel diameter measured by OCT was not significantly different from that measured by CAG (3.3±1.7 vs. 3.0±0.9 mm and 3.3±1.5 vs. 3.0±0.6 mm, 100 respectively; P>0.050) both before and after PCI. All vessel 101 cross-sectional areas that could not be measured directly by 102 CAG were also obtained by OCT. 

Treatment strategy changes based on OCT. Alterations in the 105 treatments provided the patients due to the additional infor- 106 mation obtained by OCT images are listed in Table V. The 107 reason for the changes in treatment strategies based on the 108 OCT findings were as follows: Thrombus detection, for which 109 2 patients were treated with thrombus aspiration and 8 with GP 110 IIb/IIIa inhibitors, while 4 patients avoided stent implantations; 111 dissection detection, for which 11 patients received additional 112 stent implantation; stent malapposition observation, for which 113 1 patient received additional stent implantation and 11 received 114 additional balloon inflation; suboptimal stent expansion, for 115 which 12 patients were treated with additional balloon inflation: 116 plaque rupture, for which 2 patients were treated with additional 117 stent implantation; stent incomplete coverage lesion detection, 118 for which 3 patients received additional stent implantation; stent 119 coverage bifurcation, for which 2 patients received bifurcation 120

A, Pre-angioplasty (n=61)			
Variable	CAG, n (%)	OCT, n (%)	P-value
Plaque rupture	0 (0.0)	10 (16.4)	0.0007
Thrombus	9 (14.8)	20 (32.8)	0.0162
Dissection	4 (6.6)	12 (19.7)	0.0289
Calcification	15 (24.6)	49 (80.3)	< 0.0001
Guidewire into the false lumen	0 (0.0)	1 (1.7)	NS
Guidewire through outside of stent	0 (0.0)	1 (1.7)	NS
3, Post-angioplasty (n=59)			
Variable	CAG, n (%)	OCT, n (%)	P-value
Thrombus	1 (1.7)	24 (40.7)	<0.0001
Dissection	5 (8.5)	32 (54.2)	< 0.0001
Stent malapposition	1 e(1.7)	42 (71.19)	< 0.0001
ntimal tissue protruding	8 (13.6)	49 (83.1)	< 0.0001
Suboptimal stent expansion	15 (25.4)	29 (49.2)	0.0065
ncomplete Lesion coverage	11 (18.6)	20 (33.9)	0.0467
Stent coverage bifurcation	40 (67.8)	40 (67.8)	NS
Stent strut coverage bifurcation	0 (0.0)	35 (59.3)	< 0.0001
CAG, coronary angiography; OCT, optical coherer	nce tomography; NS, not significan	t.	



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 Figure 4. OCT image obtained at 6 months of follow-up in a patient with stent malapposition in the left anterior descending artery. Coronary angiography
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 revealed stenosis distal to the stent; however, OCT identified stent malapposition, endothelial uncovering on the struts of the stent, and that the guidewire
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 (arrow) was protruding beyond the stent. The treatment strategy consisted of guidewire repositioning. OCT, optical coherence tomography.
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57 intervention; and guidewire translocation, for which 2 patients 58 were treated by guidewire repositioning. Therefore, there were

59 58 modifications of the therapeutic strategy in total. Because, in

60 some cases, several types of changes of strategy intervened in a

single patient treatment changes occurred in 41 patients among 117 the 83 patients included in the study (i.e., 49.4% of patients). 118 The 41 patients with the treatment strategy changes included 8 119 (9.6%, 8/83) whose therapy modification was based on OCT-pre 120

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 Table IV. Quantitative characteristics of potentially affected vessels and lesions as provided by CAG and OCT pre- and
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 post-angioplasty.
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Variable	CAG	OCT	P-value
Lesion diameter (mm)	1.3±0.6	1.7±0.6	<0.0001
Reference vessel diameter (mm)	3.0±0.9	3.3±1.7	NS
Ratio of diameter stenosis (%)	57.0±16.9	47.1±0.4	< 0.0001
Lesion area (mm <sup>2</sup> )	-	2.8±0.6	-
Reference vessel area (mm <sup>2</sup> )	-	8.7±2.9	-
Ratio of area stenosis (%)	-	67.4±0.2	-
3, Post-angioplasty results (n=59) Variable	CAG	OCT	P-value
Stent diameter (mm)	2.6±0.5	3.0±0.6	0.0002
Reference vessel diameter (mm)	3.0±0.6	3.3±1.5	NS
Ratio of diameter stenosis (%)	14.3±8.0	$10.0 \pm 8.3$	0.0052
Stent area (mm <sup>2</sup> )	-	7.2±2.6	-
Reference vessel area (mm <sup>2</sup> )		9.0±4.6	171
(initi)			

data only, 26 (31.3%, 26/83) whose therapy modification was
based on OCT-post data only, and 7 (8.4%, 7/83) whose therapy
modification was based on both (Fig. 1).

Safety outcomes. The mean procedural duration was
 48.5±23.5 min for OCT and 12.5±8.1 min for CAG. One
 patient experienced a coronary spasm during the OCT
 examination that was relieved following the administration of
 coronary dilative medication. No perioperative complications
 of no-reflow, coronary perforation, occlusive dissection, stent
 occlusion, or PCI-associated MI were observed.

#### 43 Discussion

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45 Although CAG is widely considered the gold standard for 46 the diagnosis of CAD as well as a primary examination for 47 guiding PCI procedures and judging coronary intervention success (5,27,28), studies have suggested that its use alone may 48 miss important information. Such studies have claimed that treat-49 ment strategies would be modified if the OCT examination was 50 51 used with or instead of CAG (27,29). A previous study demon-52 strated that OCT use may lead to a change in procedural strategy in 50% of patients in the patients with non-ST-segment elevation 53 acute coronary syndromes (11). Therefore, the present study 54 55 prospectively compared CAG- and OCT-guided interventional therapies for CAD performed before and/or after the angio-56 plasty procedure and confirmed that evaluating CAD patients 57 58 with OCT compared with CAG provided additional clinical 59 information for the diagnosis and guiding of PCI therapy. This

60 finding highly suggests that OCT may be necessary for complex

lesions in which the correlation between vascular lesions, vessel91walls, and stents is not accurately detected by CAG. Thus, the92current study findings support the results of the previous studies93and indicate that the use of OCT provides crucial information94that may modify the treatment strategies in CAD.95

However, the present study had certain limitations. 96 Firstly, the number of included cases is relatively small since 97 it was a pilot observational prospective study whose design 98 included data form only 37 patients with both OCT-pre and 99 post-angioplasty; the other patient data was for either OCT-pre 100 or post-angioplasty only. The potential middle- and long-term 101 clinical benefits of OCT-guided PCI compared with the 102 CAG-guided PCI should be confirmed in a large randomized 103 controlled trial. The patients included in the current study 104 were followed up for a limited duration; therefore, the study 105 is currently unable to evaluate the effect of OCT-guided 106 PCI on clinical outcomes. To the best of our knowledge, 107 there is no study comparing the effect of OCT-guided PCI 108 with angiography-guided PCI on the clinical outcome of 109 patients with CAD. A recently published trial identified that 110 OCT-guided PCI was safe and resulted in similar minimum 111 stent area to that of angiography-guided PCI (16). 112

Previous studies suggested that, despite the limitation of 113 OCT images to a depth of 2-3 mm (29), the high resolution 114 of OCT results in higher sensitivity compared with CAG for 115 identifying lesion characteristics (30,31); thus, it may be a 116 potentially powerful tool to guide PCI. The present prospec-117 tive study confirmed that OCT was more sensitive for detecting 118 small thrombi along the vessel walls that are difficult to detect 119 by CAG, particularly when the thrombus was crushed by 120

V. Treatment

balloons following PCI (29,30). In the present study, 2.4% of patients required thrombus aspiration, 9.6% required administration of a GP IIb/IIIa receptor antagonist, and 4.8% avoided stent implantation when a thrombus with <50% stenosis was identified by OCT, which would be neglected and be consid-ered stenosis by angiography. In addition, OCT appeared to be helpful in patients with vascular dissection (30,32). The current results revealed that OCT compared with CAG indi-cated a higher prevalence of dissection as was suggested in previous studies (33,34).

OCT performed after angioplasty is better able to demonstrate the stent-vessel wall association as well as visualize individual stent struts and their distance from the vessel wall (10,17,27,35). The present study results indicated that dissections were not identified by CAG; however, they were detected by OCT. Considering that stent malapposi-tion is an important reason for late stent thrombosis (33,34), OCT-guided PCI may reduce the risk of late thrombosis, although this finding requires further confirmation in large randomized controlled trials. OCT is also capable of detecting plaque rupture and intracoronary thrombus (36). Although CAG and OCT can both be used to locate lesions and estimate their pre- and post-PCI severity, OCT is more accurate in comparison with CAG for these purposes (33,34). The present study observed that the reference vessel diameter measured by OCT was larger compared with that measured by CAG. Therefore, the data provided by OCT may assist physicians to select a larger stent than when guided by CAG, thus avoiding stent malapposition.

In the current study, the use of OCT enabled the detection of guidewire translocation in two patients. The guidewire had entered the false lumen of the dissection in one patient, while it had passed through the stent mesh and became positioned between the struts and vascular intima in the other case. Evidently, OCT-guided PCI may reduce these risks by the early detection of guidewire translocation. However, whether these advantages actually translate into clinical benefits has yet to be determined by long-term studies.

A previous study indicated that OCT may not increase periprocedural complications, including coronary no-reflow, coronary perforation, occlusive dissection, and stent occlusion (37). However, those complications were not observed in the current study when either imaging procedure was performed.

In conclusion, the evaluation of CAD patients with OCT compared with CAG provided additional clinical information for the diagnosis and guidance of PCI therapy. Therefore, for cases with unclear images prior to and following angioplasty, it is suggested that an OCT examination should be conducted to further clarify the correlation between vascular lesions, vessel walls, and stents. However, future prospective long-term studies are required to confirm whether the systematic application of OCT, which significantly increases the procedure time as it is currently performed, would improve the long-term prognosis of these patients. 

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Number of person-times	Thrombus aspiration	Use of GP IIb/IIIa inhibitors	Additional balloon inflation	Additional stent implantation	Avoiding stent implantation	Guidewire repositioning	Bifurcation intervention	Total
Thrombus, n	2	8			4			14
Dissection, n				11				Π
Malapposition, n			11	1				12
Suboptimal stent expansion, n			12					12
Plaque rupture, n				2				5
Stent incomplete coverage lesions, n				3				З
Stent coverage bifurcation, n							7	2
Guidewire translocation, n						2		7
Total strategy modification, n	2	8	23	17	4	2	2	58
Strategy modification percentage, %	2.4	9.6	27.7	20.5	4.8	2.4	2.4	6.69
GP, glycoprotein.								

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#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Authors' contributions

JH was involved in the acquisition and analysis of data and in the preparation and revision of the manuscript at all stages; KB, MC and RC were involved in performing the coronary angiography, including optical coherence tomography in the patients included in the study and in recording the data; MW and XC were involved in the analysis of data and preparation of the manuscript; FE was involved in the coordination of the study and in the preparation and revision of the manuscript; FS and NM were involved in the design of the study, in the submission of the study to the ethical committee, in performing the coronary angiography in the patients and in the revision of the manuscript.

#### Ethics approval and consent to participate

The protocol was approved by the Ethics Committee of the Regional Health Agency Bourgogne/Franche-Comté (Comité

de Protection des Personnes EST II), and all patients provided written informed consent for the OCT-guided and CAG-guided PCI and the follow-up.

#### **Consent for publication**

Not applicable. 

#### **Competing interests**

The authors declare that they have no competing interests.

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### 3.2 Main conclusions and remarks

- Among 83 patients included, 46% had single-vessel and 54% had multiple-vessel disease.
- OCT-pre and post-angioplasty revealed significantly more procedural information than angiography alone.
- Information provided by OCT detection changed the clinical strategies in 41/83 (49.40%) patients, including thrombus aspiration in 2 (2.41%), administration of GP IIb/IIIa inhibitors in 8 (9.64%), additional balloon inflations in 23 (27.71%), additional stent implantations in 17 (20.48%), avoiding stent implantation in 4 (4.84%), collateral intervention in 2 (2.41%), and guidewire repositioning in 2 patients (2.41%).
- Conclusion: OCT-pre and -post procedure provided additional clinical information beyond that obtained by angiography alone and modified treatment strategies in approximately half of patients. However, it remains to be determined whether this translates into improved longerterm outcomes.

4. OCT optimizes the detection of coronary artery plaque rupture and stent edge dissection during PCI
### 4.1 Background and objectives

Previous evidence from postmortem studies has shown that atherosclerotic plaque rupture with a broken or eroded capsule is closely linked to acute coronary thrombotic accidents [96]. Thus, it is of great importance to detect accurately. The task of early identification of plaque types as well as plaque rupture, therefore, of great importance. Unfortunately, accurate diagnosis of plaque stability and a more accurate assessment of plaque rupture is lacking.

CAG is an established technique for the diagnosis of CAD. CAG, however, is only able to vaguely evaluate the lumen but unable to directly assess coronary atherosclerosis; it thus has inherent limitations when applied to atherosclerosis volume or plaque burden. CAG is not suitable for precise detection of ruptured coronary plaques, as it probably identifies only the largest lesions [97]; in some cases, atypical coronary plaque ruptures can easily be misdiagnosed or overlooked through CAG examination. Qualitative angiographic analysis showed that coronary ruptures distinct from the culprit lesion were identified by intravascular ultrasound in only 41.5% of cases [98].

During stent implantation, unexpected vessel tearing may occur at the transition between the rigid stent struts and the adjacent arterial wall, which may be a trigger of thrombosis or major adverse cardiac events. CAG and IVUS have traditionally been used for the diagnosis of dissections at stent edges[50]. IVUS has substantially contributed to reducing the incidence of stent thrombosis by enabling appropriate stent sizing and management of stent underexpansion. Compared with grayscale IVUS, image acquisition by OCT is much faster with higher resolution[99]. It is a 10–20 µm light-based intravascular imaging modality that immediately provides after acquisition automatic detection metrics of the coronary lumen and stents across the entire explored vessel. OCT is mainly limited by its penetration depth. Within its penetration depth OCT has much high sensitivity and specificity for characterizing stent morphology and vascular injury after stent implantation in the catheterization laboratory. Also, OCT is able to provide more detailed information on acute findings immediately after stent implantation [100]. Therefore, it was

reasonable to assume that OCT could visualize these unfavorable findings (e.g. stent edge dissection) which are not detectable by angiography or IVUS. Preliminary studies provided early insights on the incidence and characteristics of stent edge dissections by OCT, which showed higher sensitivity compared to angiography for the detection of edge dissections [56, 100].

However, the role of OCT in the quantitative detection of plaque rupture before angioplasty and stent edge dissection during PCI, in comparison with CAG, had not been established. The objectives of the our study were i) to evaluate the frequency of coronary artery plaque rupture before stenting and edge dissections after stenting visible by intracoronary OCT in comparison with angiography. ii) to assess the location of plaque dissection and stent edge dissection with OCT, and iii) to verify whether the information provided by OCT might contribute to the optimization of PCI procedures.

# Original Article Identification of coronary artery plaque rupture before stenting and stent edge dissection after stenting by optical coherence tomography and their management

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**Abstract:** Background: Optical coherence tomography (OCT) is a high-resolution imaging modality that can provide an accurate assessment of the coronary artery plaque rupture before stenting, or edge dissection after stenting, and may subsequently provide guidance for optimizing the stenting procedure. Methods: A total of 112 patients with coronary artery disease, who underwent OCT before and after percutaneous coronary intervention (PCI), were enrolled into the study. Interventional procedures were performed with the ameliorated deployment of stents according to OCT. Results: Before PCI, 101 coronary lesion sites were examined, in which 12 plaque ruptures involved in intima (11.9%) were detected by OCT and only four ruptures involved in intima (4.0%) were detected by CAG (P =0.0327). All 12 OCT-detected plaque ruptures were limited to the intima. After PCI, 180 stent edges (89 proximal and 91 distal edges) were examined, in which 48 were OCT-detected edge dissections (26.7%, 48/180) and five were CAG-detected dissections (2.8%, 5/180) (P<0.0001). Among these 48 OCT-detected dissections, 23 lesions were involved in the adventitia. including 10 lesions at the proximal edge (35.7%, 10/28) and 13 lesions at the distal edge (65.0%, 13/20, P = 0.0433). Finally, four stents were deployed over the plaque ruptures due to OCT, and 13 stents were implanted over the OCT-detected edge dissections. Conclusion: OCT may detect plaque rupture missed by CAG, allow the thorough examination of stent edge dissections after PCI, and may subsequently provide guidance for optimizing the PCI procedure.

Keywords: Optical coherence tomography (OCT), coronary angiography (CAG), coronary artery, dissection

### Introduction

Coronary artery dissection is a common complication of percutaneous coronary intervention (PCI), which may induce thrombus formation. In severe cases, it can lead to acute coronary occlusion and become life-threatening. Therefore, the timely detection and treatment of coronary artery dissections is vital to improve the success rate of PCI and patient prognosis. Coronary angiography (CAG) is widely used to guide PCI and evaluate the efficacy of coronary intervention, and is the gold standard for diagnosing coronary artery disease (CAD) with poor resolution for plaque dissection or rupture.

Optical coherence tomography (OCT) is a novel technology that provides cross-sectional and

three-dimensional imaging in vivo with ultrahigh resolution (approximately 10-20 µm) [1, 2]. DOCTORS Study, a randomized-multicenter trial, suggested that OCT guidance during PCI provided useful information beyond that obtained by angiography alone in patients with acute coronary syndrome and the OCT findings affected physician decision-making directly, leading to a change in procedural strategy in half of cases with higher postprocedure fractional flow reserve [3]. In another previous study, Wijns W et al. [4] considered that physician decision-making was affected by OCT imaging prior to PCI in 55% of all cases and at post-PCI in 25% of all cases. Hence, OCT information might modify the treatment strategy in approximately half of the patients studied.

Table 1.	Baseline	characteristics	of	patients
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	Overall
	(n = 112)
Age, yrs	64.7±10.4
Male, n (%)	51 (45.5)
Female, n (%)	61 (54.5)
Hypertension, n (%)	64 (57.1)
Dyslipidemia, n (%)	63 (56.3)
Diabetes mellitus, n (%)	19 (17.0)
Smoker, n (%)	41 (36.6)
Obesity, n (%)	29 (25.9)
With family history of CVD, n (%)	25 (22.3)
Myocardial infarction, n (%)	43 (38.4)
Heart failure, n (%)	6 (5.4)
Stroke, n (%)	4 (3.6)
Renal insufficiency, n (%)	14 (12.5)
Valvular heart disease, n (%)	12 (10.7)
Angioplasty, n (%)	39 (34.8)
Indication for coronary angiogram	
STEMI, n (%)	12 (10.7)
Non STEMI, n (%)	26 (23.2)
Stable angina, n (%)	24 (21.4)
Unstable angina, n (%)	39 (34.8)
Silent ischemia, n (%)	11 (9.8)
No. vessels diseased	
One, n (%)	48 (42.9)
Two, n (%)	43 (38.4)
Three, n (%)	21 (18.7)
Target vessel	
Left main coronary artery, n (%)	3 (2.7)
Left anterior descending artery, n (%)	52 (46.4)
Left circumflex artery, n (%)	19 (17.0)
Right coronary artery, n (%)	38 (33.9)

CVD, cardiovascular diseases; STEMI, ST-segment elevation myocardial infarction.

However, this did not refer to the nature of the dissections including depth and location, and the evaluation of the necessity of stent implantation according to OCT results. In our study, we aimed to determine whether OCT may provide a timely and accurate diagnosis of plaque rupture or dissection before PCI or the degree of immediate dissection at the stent edge after PCI, and verify whether the information provided by OCT may contribute to PCI procedures and ameliorate the implantation of the stent.

#### Methods

This prospective study was approved by the local ethics committee, and all patients provid-

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ed written informed consent. A total of 112 adult patients with CAD (51 male and 61 female patients, average age: 64.7±10.4 years) in a single center (Department of Cardiology, University Jean Minjoz Hospital, Franche-Comté University, Besançon, France) from March 2011 to September 2014 were recruited into this study. Baseline characteristics of patients are presented in Table 1. Among these 112 patients, 12 patients had ST-segment elevation myocardial infarction, 26 patients had non-ST-segment elevation myocardial infarction, 24 patients had stable angina, 39 patients had unstable angina, and 11 patients had silent ischemia. Furthermore, among these 112 patients, 42.9% of these patients were diagnosed with single-vessel disease, 38.4% of these patients were diagnosed with doublevessel disease, and 18.7% of these patients were diagnosed with multivessel disease. Exclusion criteria were as follows: (1) patients with contraindications for PCI; (2) patients with interventional failure caused by difficulty in passing the OCT catheter through the lesions; (3) patients the stent edges after PCI that could not to be completely displayed, or the distance between the vessel wall and edge of the stent was <5 mm on the OCT image. Because 15 patients did not underwent OCT before PCI, and another 13 patients did not underwent OCT after PCI, only 97 patients with OCT images before PCI and 99 patients with OCT images after PCI were included for further analysis. During each OCT procedure, no serious complication was observed in all the patients studied; except for one patient who experienced temporary coronary spasm, which was relieved several minutes after the administration of nitroglycerin, and two patients who presented with transient reduction of blood flow in the investigated coronary artery.

### CAG and OCT procedures

CAG and OCT were performed in all patients to identify potential coronary artery plaque ruptures or dissections before and after PCI. CAG was performed via the femoral or radial artery access using the Seldinger method, while OCT was performed using the FD-OCT Optis system (Lightlab Imaging Incorporated, Westford, MA, USA) [3-6] using non-blocking blood flow technology. After the guidewire was inserted into the target blood vessel, the OCT catheter was pushed into the distal lesion along the guide-

<b>Table 2.</b> Qualitative findings of Plaque rupture before angiop	lasty
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	CAG	OCT	Dualua
	(n = 101)	(n = 101)	P value
Plaque intimal rupture, n (%)	4 (4.0)	29 (28.7)	< 0.0001
Involved in intimal dissection, n (%)	4 (4.0)	12 (11.9)	0.0327
Non-involved in intimal dissection, n (%)	0 (0.0)	17 (16.8)	<0.0001
CAG coronary angiography: OCT optical cohere	ance tomogr	anhy	

CAG coronary angiography; OCT optical coherence tomography.

wire. The automated pullback was performed at 20 mm/s, while blood signals were removed by continuous injection of the iso-osmotic contrast medium via the guiding catheter. If the obtained image was of poor quality, the pullback was repeated after modifying the probe position or flushing intensity of the contrast medium. The data were digitally stored for offline analysis [7-9]. All OCT and CAG images were analyzed using the previously validated criteria by two independent investigators who were blinded to the clinical presentation and lesion characteristics [8].

### Modification of standard treatment strategy

The CAG images were screened for the following typical manifestations of coronary artery dissection: (1) a separate intima within the lumen of the coronary artery, displaying a thin and bright linear structure parallel to the lumen or spiral; (2) the contrast agent filled a false lumen with delayed clearance or retention of the contrast agent, and the true lumen was compressed or revealed no changes; (3) isolated intimal fragment fluttering with blood flow within the lumen of the coronary artery; or (4) irregular lumen of the coronary artery with segmental broadening [1].

The OCT images were analyzed according to previously established definitions of plaque ruptures and edge dissections [5, 6, 9]. Briefly, plaque ruptures were identified as rims of tissue protruding into the lumen in this study [5, 10-11]. Edge dissection was defined as the presence of a linear rim of tissue, with a width  $\geq$  200 µm and a clear separation from the vessel wall, or a plaque that was adjacent (<5 mm) to the stent edge [4, 6, 11]. A dissection was classified as either intimal, if it was limited to the intima or atheroma and did not extend to the media, or adventitial, if it extended through the media [10].

Based on these OCT results, the following standards were determined for stent implantation(s) [9]: (a) plague rupture associated with stenosis of >50%; (b) plaque rupture exceeding 10 mm in length; (c) dissections combined with thrombosis; (d) dissections that

show false lumen with entrance; (e) dissections that cause coronary artery occlusion or are on the brink of occlusion.

### Statistical analysis

The successive quantitative data were reported as means ± standard deviation (SD). All qualitative data were assessed using Fisher's exact test. A two tailed P-value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS 13.0 for Windows release 13:0 (Copyright Spss Inc., 1989-2004 Armonk, NY, USA).

#### Results

Detection of plaque rupture and stent edge dissection by optical coherence tomography

Before PCI, a total of 101 coronary arteries were evaluated in 97 patients, including three left main coronary arteries (LM), 46 left anterior descending (LAD) branches, 17 left circumflex branches (LCX) and 35 right coronary arteries (RCA). A significantly higher number of plaque ruptures or spontaneous dissections was detected by OCT than by CAG. That is, 12 plaque ruptures involved in intima (11.9%, 12/101) in 12 patients (12.4%, 12/97) were detected by OCT (Table 2), while 4 plaque ruptures involved in intima (4.0%, 4/101) in four patients (4.1%, 4/97) were detected by CAG. [11.9% (OCT) vs. 4.0% (CAG), P = 0.03 for the lesions; and 12.4% (OCT) vs. 4.1% (CAG), P = 0.03) for the patients].

After PCI, a total of 103 coronary arteries with 103 stents and 180 stent edges were analyzed (89 proximal and 91 distal edges) in 99 patients, including three LMs, 48 LAD branches, 16 LCXs and 36 RCAs. A significantly higher number of dissections at the stent edges were detected by OCT than by CAG; that is, 48 OCTdetected dissections (26.7%, 48/180) were



**Figure 1.** (A) Coronary angiography (CAG) showing thrombus (arrows) in the middle of the left anterior descending (LAD) artery. (B-E) Optical coherence tomography (OCT) showing the thrombus in the middle of the LAD (B), atherosclerotic lesion associated with 76.5% stenosis at the proximal edge of thrombus (C), and a dissection nearly 7.9-mm long due to plaque rupture involving the intima (C, D, E). OCT revealed the entrance of the dissection (D), providing the rationale for the interventional cardiologist to implant a stent at the dissection lesion site instead of performing a single thrombus aspiration.

found at the stent edges and five CAG-detected dissections (2.8%, 5/180) were found at stent edges (*P*<0.0001).

# Location of plaque dissection and stent edge dissection

Before PCI, 10 OCT-detected plaque ruptures were found at the proximal shoulder of plaques, and two OCT-detected plaque ruptures were found at the distal shoulder (P = 0.0165). All OCT-detected dissections were limited to the intima.

After PCI, 28 stent edge dissections at 89 proximal edges of stents and 20 stent edge dissections at 91 distal edges of stents were found by OCT. It appears that there was a trend of higher occurrence for dissections at the proximal edge (31.5%, 28/89) than at the distal edge (22.0%, 20/91) in these stents, although the difference did not reach statistical significance (P =

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0.1776). Twenty-three lesions involved the adventitia in the 48 stent edge dissections, including 13 lesions at the distal edge (65.0%, 13/20) and 10 lesions (35.7%, 10/28) at the proximal edge of the stent; and the difference was statistically significant (P = 0.0433).

# Supplementary stent implantation based on optical coherence tomography

A total of 17 patients (15.2%) benefited from supplementary stent implantation after diagnostic CAG or after PCI due to the higher resolution of OCT compared to that of CAG in all 112 patients with CAD, in which four patients with plaque rupture before PCI were implanted with a stent (**Figure 1**) and 13 patients with stent edge dissection after PCI were implanted with a second stent (**Figures 2** and **3**), including eight stents in 20 distal edge dissections and five stents in 28 proximal edge dissections (P =0.401).

### Optical coherence tomography for coronary artery dissection



**Figure 2.** (A) Coronary angiography (CAG) showing no abnormalities (arrow) at the proximal of the right coronary artery (pRCA); (B) Optical coherence tomography (OCT) showing no stent-associated stenosis in the middle of the RCA; (C-E) OCT images showing a nearly 13.8-mm long dissection at the proximal edge of stent in the pRCA that appeared normal by CAG. The exit of the dissection (C), the true and false lumens (D), the intimal tear (D) and the entrance (E) of the dissection were clearly revealed. Accordingly, the interventional cardiologist decided to implant a stent at the proximal edge of the stent.



**Figure 3.** (A) Coronary angiography (CAG) revealed a blurred lesion (arrows) at the distal edge of the stent on the left anterior descending (LAD) artery. (B, C) Optical coherence tomography (OCT) demonstrated a dissection with a length of 5.6 mm at the distal edge of the stent involving the intima. The skeleton of the stent and the entrance of the dissection were clearly displayed (B). The true and false lumens of the dissection were also revealed (C), which were treated with another stent implantation at the position of the dissection at the distal edge of the stent.

#### Discussion

Coronary artery dissection is a rare and lifethreatening cause of acute coronary syndrome (ACS) [12]. With the development of new imag-

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ing modalities and interventional techniques, the detection rate of coronary artery plaque rupture and dissection has been significantly increased. CAG remains the main routine examination used for diagnosing coronary plaque

rupture and guiding the coronary intervention procedure. However, CAG can only vaguely display the outlines of the vessel walls through comparing images with and without contrast medium, and it cannot clearly show the details of the intramural lesions of coronary arteries. Therefore, atypical coronary plaque ruptures can easily be misdiagnosed or overlooked through CAG examination. OCT is a new intravascular imaging technology, and is currently the only technology that can clearly display the microscopic structures of blood vessels in vivo nearly at the histologic level [13]. It may thereby be used for the prompt detection of plaque rupture and edge dissections, since it can distinctly display the position of the entrance and exit, length, true and false lumens, and thickness of the tearing intima; leading to the accurate assessment of the characteristics of plaque ruptures and dissections and their severity.

Our results indicate that OCT can detect a significantly higher number of lesions, including both plaque rupture before PCI and stent edge dissection after PCI, compared to CAG. Percutaneous coronary angioplasty or direct stent implantation is the preferred method for the treatment of coronary plaque rupture. In our study, 33.3% (4/12) of the plaque rupture lesions were treated with stents, according to the plaque rupture characteristics displayed by OCT before PCI. In addition, approximately 27.1% (13/48) of lesions required implantation of another stent to block the edge dissection. prevent the dissection from expanding, or increase the stability of a vessel. OCT not only identified the plaque rupture promptly, but also guided the choice of clinical intervention strategy [14].

The increased density of nourishing blood vessels within the coronary atherosclerotic plaque can result in hemorrhage and rupture of plaques. The breakdown of the thin fibrous caps of these unstable plaques is the main cause of atherosclerosis-induced plaque rupture. Vasospasm and the increased shear force of blood flow are also high risk factors for atherosclerosis-induced rupture. Our results demonstrate that most rupture lesions were located at the proximal shoulder of unstable atheromatous plaques, and involved the intima. This is possibly caused by the large mechanical force associated with the blood flow at the proximal shoulder of the plaques. The tearing of the coronary intima caused by the balloon dilatation of vessel(s) with stenosis during the PCI process is the most common reason for secondary dissection [2] Severe tearing and separation of the intima or media of the coronary artery manifests as coronary artery dissection [2, 15]. In this study, 26.7% (48/180) of dissections occurred at the stent edges after stent implantation. Furthermore, stent proximal edge dissections were more frequent than distal edge dissections (31.5% vs. 22.0%), but the P-value was not statistically significant (P = 0.1776). Moreover, the distal dissections revealed a higher rate of adventitia involvement than the proximal dissections (65.0% vs. 37.5%, P = 0.04). It remains equivocal whether the high incidence of dissections at the proximal edge of stents is associated with the instability of the proximal shoulder of plaques that are prone to tear, or related to the incomplete coverage of the plaque dissection by stents at the proximal shoulder. In-depth studies with a larger sample size would be desirable in the future to elucidate these mechanisms. However, the distal diameter of the coronary artery is smaller than proximal diameter. Vessels at the distal edge bear greater pressure during balloon dilatation. This would cause dissections to be deeper at the distal end of the stent than at the proximal end of the stent.

### Conclusions

In conclusion, the results of this study suggest that OCT can clearly display coronary artery plaque rupture lesions before PCI, and edge dissections after PCI, and provide guidance in optimizing coronary interventional procedures. For patients with suspicious ruptures or dissections before or after PCI, an OCT examination may be recommended. Further long-term studies are needed to confirm whether the generalized application of OCT can help improve longterm prognosis in a larger population of patients.

### Disclosure of conflict of interest

None.

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### 4.2 Main conclusions and remarks

- Before PCI, 12 plaque ruptures involved in the intima (11.9%) were detected by OCT and only 4 ruptures involved in the intima (4.0%) were detected by CAG (P = 0.0327). All 12 OCT-detected plaque ruptures were limited to the intima.
- After PCI, there were 48 OCT-detected edge dissections (26.7%, 48/180) and 5 CAG-detected dissections (2.8%, 5/180) (P<0.0001). Among these 48 OCT-detected dissections, 23 lesions were involved in the adventitia, including 10 lesions at the proximal edge (35.7%, 10/28) and 13 lesions at the distal edge (65.0%, 13/20, P = 0.0433).</li>
- Four stents were deployed over the plaque ruptures due to OCT detection, and 13 stents were implanted over the OCT-detected edge dissections.
- Conclusion: OCT may detect plaque rupture missed by CAG, and allow the thorough examination of stent edge dissections after PCI. The additional information may subsequently provide guidance for optimizing the PCI procedure.

# 5. Utilization of OCT in the evaluation and risk factor identification of

# stent edge dissection

### 5.1 Background and objectives

Percutaneous coronary intervention (PCI) is a common and established therapy for coronary artery disease. Coronary dissections after PCI are associated with an increased risk of major adverse cardiovascular events. Stent edge dissection occurs at the transition point between the rigid stent and the unstented reference segment—in other words, at the stent edge. Persistent dissections after stenting, especially large flow limiting stent edge dissections, have an enhanced short-term risk of major adverse cardiovascular events due to sudden vessel obstruction with consecutive myocardial ischemia[101].

Reports about the frequency of stent edge dissections depend on the imaging technique used and range from 1.7 % in an angiographic investigation to 7.8–19.3 % per lesion in several IVUS observations[102, 103]. However, angiography underestimates the true incidence of stent edge dissections and even with IVUS a relevant amount of stent edge dissections is missed [100].

OCT is a high-resolution (10–20 µm) intravascular imaging technique that uses near-infrared light to create images. An excellent contrast between lumen and vessel wall in OCT allows accurate lumen measurements. It has been used to visualize and quantify intraluminal dimensions as well as the composition of the vessel wall including the assessment of the plaque morphology and different degrees of vessel injuries after stent implantation. With the emerging use of OCT and due to its high resolution and its ability to identify even small vessel injuries which are undetected by other imaging modalities, a much higher incidence of stent edge dissections has been reported (26–40%)[56, 104-106].

Given that stent edge dissections have been suggested to be associated with clinical complications, it is of paramount importance to identify predictors of stent edge dissections for distinguishing high-risk population. Angiography data have shown that the predictors of coronary artery dissection after balloon angioplasty were greater balloon-to-artery ratio, the presence of calcium, longer lesion length, and greater number of balloon inflations[107]. Detection with IVUS, greater stent expansion and the presence of large calcified and/or attenuated plaques at the edge

of the stent were identified as independent predictors for stent edge dissection[108]. However, to date the true incidence and predictors of stent edge dissections remains unsolved by OCT.

The aims of the current study were to evaluate the morphological features of stent edge dissection and to identify the predictors for untreated stent edge dissections detected by OCT after PCI in patients with non-ST-elevation ACS (NSTE-ACS). Patients in this study were a subgroup of the DOCTORS study, a randomized, prospective, multicenter, open-label clinical trial to evaluate the utility of OCT in optimizing results of angioplasty in patients with NSTE-ACS [109].

# Dissections des bords de stent chez les patients avec NSTEMI ayant bénéficié

# d'une angioplastie avec stenting guidée par l'OCT

# Données de l'essai DOCTORS

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### I. Introduction

La découverte du stent est considérée comme l'une des dix inventions ayant -permis de changer le monde au siècle dernier. Son impact était exceptionnel et d'autant plus remarquable dans le domaine de la cardiologie interventionnelle. En effet, l'une des complications majeure de l'angioplastie conventionnelle, au ballon, était la dissection coronaire. Cependant, les dissections de petite taille ont été souvent observées, mais leur évolution était favorable sans conséquences cliniques, et cela était parfois valable aussi pour les dissections de grande taille en cas de conservation du flux coronaire sans sténose résiduelle <sup>(1)</sup>. Dans le cas contraire, l'implantation de stent a permis de réduire efficacement l'aspect de sténose intra-luminale résiduelle en angiographie <sup>(2)</sup>.

Le mécanisme de l'élargissement de la lumière après le stenting peut impliquer (a) une redistribution axiale importante de la plaque athéromateuse de la lésion vers les segments de référence, (b) une dilatation vasculaire, et (c) une embolisation ou (d) une compression de la plaque <sup>(3)</sup>. Lors de l'implantation de stent, l'expansion du vaisseau peut être accompagnée par une dissection imprévue, au niveau de la zone de transition entre les mailles rigides d'un stent actif (DES) et les parois artérielles adjacentes <sup>(4)</sup>. Cette dissection entraine un risque élevé–de thrombose de stent qui est à l'origine des événements cardiovasculaires majeurs (MACE).<sup>(5-9).</sup>

L'échographie endocoronaire coronaire (IVUS) permet de détecter les dissections des bords des DES, qui ne sont pas vues à l'angiographie, dans 6.6-9.2% des cas. Les volumineuses plaques calcifiées et la plaque résiduelle excentrique aux bords de DES, l'asymétrie des bords de DES, et la ratio entre la surface de la lumière et la surface du stent ont été identifiés comme facteurs prédictifs indépendants de dissection des bords de DES. Les dissections des bords de DES, au niveau des zones saines de l'artère évoluent le plus souvent vers un hématome intra-mural <sup>(10-11)</sup>

La tomographie par cohérence optique (OCT) possède une meilleure résolution spatiale, de l'ordre de 10-20  $\mu$ m, que l'IVUS, et permet une analyse plus fine de la morphologie de la plaque et l'identification des dissections des bords après implantation de stent <sup>(12)</sup>. L'incidence des dissections des bords des stents révélée par l'OCT est de 21 -37,8%, dont plus de 84%-n'étaient pas visibles à l'angiographie.

L'athérosclérose des bords et la technique de angioplastie percutanée (PCI) semblent avoir un lien de causalité avec les dissections des bords des DES. L'évaluation détaillée de ces dissections par OCT conditionne leur éventuelle prise en charge<sup>(13-14)</sup>.

La majorité des syndromes coronariens aigus (SCA) est due à une occlusion ou rétrécissement de la lumière de l'artère avec une thrombose complète ou partielle, qui provient, sur le plan physiopathologique, par ordre de fréquence, (a) de la rupture de plaque (55-60%), (b) l'érosion de la plaque (30-35%), et (c) le nodule calcifié superficiel (2-7%)<sup>(15-18)</sup>. L'OCT a été utilisée dans l'évaluation morphologique de la plaque constituant la lésion responsable du SCA; la rupture d'une plaque fibro-athéromateuse à chape fine avec formation de thrombus a été fréquemment retrouvée au niveau de l'artère coupable <sup>(19)</sup>. L'OCT est également utilisable comme technique d'imagerie endo-coronaire à la phase aigüe d'un SCA avec ou sans élévation du segment ST. Cette analyse retrouve les mêmes données morphologiques au niveau des lésions coupables : l'érosion de plaque, le thrombus intra-coronaire, la rupture de plaque fibro-athéromateuse à chape fine <sup>(20)</sup>.

L'étude DOCTORS est un essai clinique randomisé, prospectif, multicentrique, en ouvert, visant à évaluer l'utilité de l'OCT pour optimiser les résultats de l'angioplastie d'une lésion responsable du syndrome coronarien aigu sans sus-décalage du segment ST.

Dans ce travail nous avons analysé le sous-groupe des patients victimes de NSTEMI, randomisés dans le bras angioplastie guidée par l'OCT<sup>(21)</sup>.

L'objectif de notre étude était d'évaluer, dans cette sous-population de l'essai DOCTORS, les caractéristiques morphologiques et les facteurs prédictifs de dissection des bords de stent diagnostiquée par OCT.

## II. Patients et méthodes

### A. Sélection des patients, design de l'étude et procédures

Tous les patients du groupe « angioplastie guidée par l'OCT »,-soit 120 patients, ont été inclus à partir de l'essai clinique DOCTORS. Les critères d'inclusion et d'exclusion, les détails de la conception, le design de l'étude ; et les procédures interventionnelles de l'étude DOCTORS ont été décrits dans le l'article de référence DOCTORS <sup>(21)</sup> (Annexe 1).

### B. Analyse quantitative de l'angiographie coronarienne

Toutes les angiographies coronaires ont été analysées en salle d'angiographie au centre coordinateur du CHU de Besançon, à l'aide d'un algorithme automatisé d'analyse coronarienne quantitative (QAngio XA 7.3, Medis Medical Imaging Systems BV, Leiden, Pays-Bas). Les mesures moyennées ont été effectuées dans deux incidences orthogonales.

### C. Tomographie par Cohérence optique : technique d'acquisition et analyse d'images.

Les images OCT ont été acquises en utilisant le système Optis FD-OCT (Lightlab Imaging Incorporated, Westford, MA) et le cathéter 6F compatible Dragonfly Duo et Dragonfly Optis (Lightlab Imaging Incorporated, Westford, MA). Le cathéter de l'OCT a été introduit au niveau de l'artère coronaire à l'aide d'un guide d'angioplastie conventionnel de 0.014F (système monorail). L'examen a été réalisé après une préparation par antithrombotiques (déjà obtenue dans le cadre de la prise en charge du syndrome coronairen aigu) associée à une injection intra-coronaire de dérivés nitrés. Le cathéter OCT (C7 Dragonfly, St. Jude Medical) a été avancé d'au moins de 10 mm en aval de la lésion ou de l'extrémité distale du stent. Le milieu transparent est obtenu grâce à l'injection automatisée de produit de contraste concomitante du retrait de la sonde (15 à 20 ml à 4 ml/s) et un retrait automatique (18 mm/seconde) permet d'étudier le vaisseau sur une longueur donnée. Une fois l'acquisition (densité de frame : 10 images/seconde) réalisée, la sonde est retirée. Les images obtenues sont présentées sous 2 formes : coupe axiale et coupe longitudinale dite *« long view »*. Les logiciels intégrés aux consoles permettent une analyse semi-automatique des acquisitions (surface de la lumière, surface du stent, reconstruction tridimensionnelle).

Toutes les images OCT ont été analysées à l'aide du logiciel Lightlab® au centre coordinateur (CHU de Besançon) par deux opérateurs indépendants en aveugle par rapport aux données de l'angiographie et la stratégie procédurale. Les analyses discordantes ont été résolues par consensus <sup>(21-23)</sup>. Les valeurs retenues pour l'analyse finale étaient celles résultant de l'analyse du laboratoire central.

### D. Définitions de lésions et segments de référence.

Les critères OCT pour la définition des objectifs principaux ont été établis selon des documents de consensus récents, l'ensemble de ces définitions ont été précédemment décrites (24) (22). Les principales définitions ainsi que des images représentatives du prolapsus tissulaire, de la malposition des stents, de la sous-expansion et de la dissection des bords figurent dans l'article de référence (21) [Annexe 2]. Les définitions de la lésion et du segment de référence du document de l'IVUS consensus, modifiés, publié dans le Journal of American College of Cardiology (JACC) ont été adoptées pour la tomographie par cohérence optique endovasculaire (IVOCT).<sup>(22)</sup>

### Définitions des segments de référence :

<u>Référence proximale</u>: le site ayant la plus grande lumière en amont de la sténose mais dans le même segment (généralement à 10 mm de la sténose, sans branche de division majeure), de préférence dans une zone sans extension de la plaque.

<u>Référence distale</u>: le site ayant la plus grande lumière en aval de la sténose mais dans le même segment (généralement à 10 mm de la sténose, sans branche de division majeure), de préférence dans une zone sans extension de la plaque.

<u>Taille moyenne de la lumière de référence</u>: la valeur moyenne de la taille (diamètre et surface) de la lumière aux sites de référence proximaux et distaux.

### E. Dissection des bords de stent : définitions et paramètres analysés

Les extrémités (bordures) de stent ont été définies comme la première et la dernière coupe transversale du segment stenté où les mailles pouvaient être vues dans les quatre quadrants de l'image.

La zone peristent a été définie comme étant le premier cadre suivant immédiatement la bordure de stent (de 0,2 mm d'environ).

Les bords de stent ont été définis comme les zones se trouvant jusqu'à 5 mm immédiatement en amont et en aval des extrémités (proximale et distale) du stent.

La dissection des bords de stent a été définie en OCT comme la zone avec interruption ou rupture de la continuité de la surface endoluminale du vaisseau à l'extrémité du stent (5 mm proximal et distal) avec visualisation des flaps ou des cavités.

**Quantification de la dissection des bords** : afin de mesurer les dimensions de la dissection des bords, l'extension longitudinale de la dissection le long du vaisseau et la longueur du flap de dissection (de sa pointe au point de jonction avec la paroi du vaisseau) ont été mesurées.<sup>(14,12)</sup>

La sévérité de chaque dissection a été estimée morphologiquement de manière plus approfondie à l'aide d'une évaluation qualitative de la profondeur de la zone disséquée du vaisseau comme:

• Intimale : limité à la couche intima ou à l'athérome

• Médiale : s'étendant dans la couche de médias

• Adventicielle: s'étendant à la membrane élastique externe.

La présence d'un **hématome intramural** a été définie comme une accumulation de produit de contraste ou liquide de flush (ou de sang) dans l'espace médial, déplaçant la membrane élastique interne vers l'intérieur et la membrane élastique externe vers l'extérieur.<sup>(14,21)</sup>

Au niveau de l'extrémité (**la bordure du stent**), **l'indice de symétrie du vaisseau** a été calculé comme étant le rapport entre le diamètre minimal et le diamètre maximal de l'artère<sup>.(14)</sup>

Les sites de référence du bord de stent étaient les coupes transversales au niveau de la zone qui paraissait la plus saine (lumière maximale avec plaque minimale), cela jusqu'à 5 mm de la bordure proximale et distale du stent <sup>(10,25,26)</sup>.

L'indice de symétrie du vaisseau de référence a été calculé comme étant le rapport entre diamètre minimal et le diamètre maximal au niveau du site de référence.

L'Indice de symétrie du vaisseau de référence du bord distal du stent (IRSV distal) a été défini comme le rapport entre le diamètre minimal du vaisseau de référence et le diamètre maximal au bord distal du stent.

L'indice de symétrie du vaisseau de référence du bord proximal du stent (IRSV proximal) a été défini comme le rapport entre le diamètre minimal du vaisseau de référence et le diamètre maximal au bord proximal du stent.

L'indice de symétrie de la lumière distale avant le stenting (ISL distal) a été défini comme le rapport entre le diamètre minimal de la lumière distale et le diamètre maximal avant le stenting au bord distal du stent.

L'indice de symétrie de la lumière proximale avant le stenting (ISL proximal) a été défini comme le rapport entre le diamètre minimum de la lumière proximale et le diamètre maximal avant le stenting au bord proximal du stent.

### F. Analyses statistiques

Les variables quantitatives sont exprimées en valeur moyenne +/- écart-type pour les variables normalement distribuées et médianes (intervalle interquartiles) pour les variables non-normalement distribuées. La normalité des variables continues a été vérifiée en utilisant le test de Kolmogorov-Smirnov. Les variables catégoriques sont décrites en nombre (pourcentage). Les données quantitatives ont été comparées à l'aide des tests t-Student ou Mann-Whitney et les variables qualitatives à l'aide du test de Fisher. Une analyse multivariée par régression logistique a été réalisée pour déterminer les facteurs prédictifs indépendants de la dissection du bord de stent à l'aide de la méthode progressive par étapes (Wald). Une valeur p <0,05 était considérée comme statistiquement significative. Toutes les analyses ont été effectuées en utilisant SPSS 15 pour Windows, SPSS Inc.

# III. Résultats

A. Données cliniques, angiographiques, et des procedures.

Les 120 patients inclus ont bénéficiés d'une angioplastie guidée par l'OCT. Ils étaient majoritairement de sexe masculin (79,2%) et avaient un âge moyen de  $60.8 \pm 11.5$ ans. Les facteurs de risque cardiovasculaire le plus souvent rencontrés étaient : l'hypertension artérielle (56%), l'hypercholestérolémie (49%) et le tabagisme (39%). Une minorité avait un angor instable (8%). La lésion cible stentée était une lésion unique au niveau de l'artère coupable sans atteinte diffuse au sein de cette même artère. Cette artère a été définie comme étant l'artère responsable de SCA-NSTEMI. Les données cliniques, angiographiques sont résumées dans la Tableau 1 et ont été déjà décrites dans l'article de référence <sup>(24,21)</sup>.

La troponine à l'admission était à 0.54  $[0.2; 1.7] \mu g/L$ . L'artère interventriculaire antérieure était le plus fréquemment atteinte (46%). La plupart des patients avaient une atteinte monotronculaire (65.0%), avec une lésion de type B1 ou B2 (66.7%) selon la classification de l'Amerian Heart Association.

La population totale a été répartie en deux groupes selon la présence/absence à l'OCT d'une dissection en bordure du stent. Les caractéristiques des deux groupes figurent dans le tableau 2.

Caractéristique	Total N =120	Р
	N(%)/m±DS/médiane (min-	
	max)	
Age (ans)	60.8 ±11.5	
Sexe masculin	95 (79.2)	
Diabète	26 (21.7)	
Surpoids	75 (62.5)	
Hypercholestérolémie	59 (49.2)	
Hypertension artérielle	67 (55.8)	
Tabagisme actif	47 (39.2)	
Hérédité coronarienne	39 (32.5)	
Angor instable	10 (8.3)	
Troponine à l'admission (µg/L)	0.54 (0.2, 1.7)	
DFG ml/min/1,73m2	93.9 (72.1. 116.8)	
Nombres d'artères atteintes		p< 0.01
Monotronculaire	78 (65.0)	
Bi ou tritronculaire	42 (35.0)	
Artère coupable		p< 0.01
Artère coronaire droite	38 (31.6)	
Artère circonflexe	26 (21.7)	
Artère interventriculaire antérieure	56 (46.7)	
Type de lésion selon la classification		P<
ACC/AHA		0.01
А	30 (25.0)	
B1 ou B2	79 (66.7)	
С	10 (8.3)	

Tableau 1 Caractéristiques des patients à l'inclusion : données cliniques et angiographiques

DS: déviation standard, MLA : surface minimale de la lumière, MLD : diamètre minimal de la lumière.

La troponine à l'admission était à 0.54 [0.2; 1.7] µg/L. L'artère interventriculaire antérieure était le plus fréquemment atteinte (46%). La plupart des patients avaient une atteinte monotronculaire (65.0%), avec une lésion de type B1 ou B2 (66.7%) selon la classification de l'Amerian Heart Association.

La population totale a été répartie en deux groupes selon la présence/absence à l'OCT d'une dissection en bordure du stent. Les caractéristiques des deux groupes figurent dans le tableau 2.

### B. Analyse qualitative et quantitative par l'OCT des bords de stent

La population totale a été répartie en deux groupes selon la présence/absence à l'OCT d'une dissection en bordure du stent. Les caractéristiques des deux groupes figurent dans le tableau 2. Au total, quarante et quatre (44/36.7%) dans le groupe avec dissection versus (76/63%) sans dissection. Il n'y avait pas de différence significative de taux de dissection en fonction de l'âge ou de sexe des patients.

	Groupe avec	Groupe sans	Р.
	dissection (N=44)	dissection (N=76)	
	N(%)/m±DS/	N(%)/m±DS/	
	Médiane (min-max)	Médiane (min-max)	
Age	59.8 ± 11. 3	60.7±11.4	0.461
Sexe masculin (%)	36 (81.8)	59 (77.6)	0.219
Thrombose (%)	34 (77.27)	50 (65.79)	0.219
Score de thrombose	7.50 (3.22, 15.58)	7.50 (3.00, 14.11)	0.687
Rupture intimale(%)	29 (69.91)	34 (44.73)	0.0365
Erosion	35 (79.55)	38 (50.00)	0.0018
Type de plaque			
Lipidique(%)	41 (93.18)	66 (86.84)	0.369
Fibreuse (%)	26 (59.09)	37 (48.68)	0.343
Calcique (%)	31 (70.45)	42 (55.26)	0.122
Longueur (mm)	$15.65 \pm 5.14$	16.16 ±6.96	0.671
MLD (mm)	$1.20\pm0.31$	1.26 ±0.29	0.273
Diamètre de référence (mm)	$3.05 \pm 0.42$	$3.02\pm0.42$	0.755
% de sténose de diamètre	60.93±10.83	58.16 ±9.97	0.158
Surface de référence (mm)	$7.49 \pm 2.16$	$7.30 \pm 2.07$	0.641
MLA (mm <sup>2</sup> )	$1.23 \pm 0.73$	$1.29 \pm 0.71$	0.666
% de sténose de surface	$81.83 \pm 9.90$	81.63 ±9.47	0.911
Epaisseur de la chape	67.62 (42.50, 89.99)	60.00 (49.63, 80.00)	0.240
fibreuse (µm)			

Tableau 2.	Données	pré-procédur	ales de l'OCT sten	ting
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DS: déviation standard, MLA : surface minimale de la lumière, MLD : diamètre minimal de la lumière.

*Au niveau de l'extrémité proximale* de stent, nous avons observé 22 dissections soit 50%. Parmi ces 22 dissections proximales, vingt (90.90%), siégeaient au niveau de l'adventice.

*Au niveau de l'extrémité distale* de stent, nous avons également identifié 22 dissections, dont dix (45.45%, 10/22 ; P =0.0042).de type adventitiel.

Au total, un geste d'angioplastie avec pose de stent a été réalisé chez 32 patients dans le groupe d'angioplastie guidée par l'OCT. Pour 24 d'entre eux, ce geste a été réalisé en raison d'une couverture incomplète de la lésion, alors que la dissection adventitielle était le motif d'une geste complémentaire chez 8 patients.

# C. Les données OCT avant l'angioplastie des 2 groupes, groupe avec dissection et sans dissections. Tableau 2.

Il n'y avait pas de différence significative entre les deux groupes en termes de :(1) lésions avec thrombose et (2) le type de plaque (lipidique, fibreuse et calcique). Cependant, les patients avec dissections des bords avaient significativement plus d'érosion de plaque que ceux du groupe sans dissection (79.55% vs 50.00%, P= 0.0018). De même, il y'avait significativement plus de rupture intimale dans le groupe avec dissection (65.91% vs 44.74 %, P=0.0365) en comparaison avec le groupe sans dissection. Concernant les paramètres quantitatifs tels la longueur de lésion, MLD, le degré de sténose exprimé en pourcentage et l'épaisseur de la chape fibreuse, il n'y avait de différence significative entre les deux groupes.

### D. Les données OCT post-stenting.

La protrusion des tissus (plaque ou thrombus) après le stenting a été retrouvée de manière similaire dans les deux groupes ; néanmoins, on notait une légère tendance à l'augmentation du taux de rupture intimale dans le groupe avec dissection (86.42% vs 68.42%, P=0.057). Le taux de couverture de la branche fille était similaire dans les deux groupes ; une couverture optimale des lésions a été retrouvée plus fréquemment dans le groupe sans dissection et cette différence était statistiquement significative (89.47 % vs 75%, P=0.0351).Tableau 3

	Groupe avec	Group sans	Р
	dissection	dissection	
	(n=44)	(n=76)	
	N(%)/m, DS	N(%)/m, DS	
	Min-max	Min-max	
Protrusions tissulaires (plaque/thrombus)	42 (95.45)	65 (85.53)	0.129
Plaque lisse	30 (68.18)	46 (60.52)	0.718
Plaque rompue	38 (86.42)	52 (86.42)	0.057
Plaque irrégulière	34 (77.27)	55 (72.37)	0.790
Thrombus	33 (75.00)	55 (72.37)	0.937
Couverture de la branche fille	33 (75.00)	57 (75.00)	1.000
Couverture optimale de la lésion	33 (75.00)	68 (89.47)	0.0351
Stent malapposition	24 (54.55)	39 (51.32)	0.850
Distance maximale entre les mailles et la	0.20 (0.00, 0.35)	0.18 (0.00, 0.39)	0.999
paroi de vaisseau (mm)			
Longueur maximale des mailles (mm)	2.30 (0.91, 4.16)	1.78 (0.80, 4.80)	0.865
Surface des mailles/surface de lumière	21.28 (8.31, 43.59)	30.65 (22.48, 56.19)	0.0158
Stent sous déployé (%)	8 (18.18)	40 (52.63)	0.0003
Surface Minimale intra-stent (mm <sup>2</sup> )	$6.34 \pm 2.14$	$5.70 \pm 1.64$	0.128
Surface de référence (mm <sup>2</sup> )	$7.37 \pm 2.69$	$7.96 \pm 2.39$	0.626
Surface Intra-stent moyenne / surface de	$81.58 \pm 12.50$	$73.85 \pm 12.50$	0.0086
référence			
Longueur de stent	$22.07\pm8.44$	$21.47 \pm 8.30$	0.704
Diamètre minimal du stent (mm)	$2.76\pm0.49$	$2\ .70\pm0.42$	0.546
Diamètre de référence (mm)	$3.12\pm0.58$	$3.53\pm0.89$	0.490
Diamètre de sténose résiduelle	$11.66 \pm 7.89$	$11.63 \pm 8.22$	0.993
Surface minimale intra stent (mm <sup>2</sup> )	$6.20 \pm 2.23$	$6.04 \pm 1.93$	0.687
Surface minimale de référence (mm <sup>2</sup> )	$8.01 \pm 3.12$	8.01 ±2.45	0.999
Surface de sténose résiduelle	$21.48 \pm 13.73$	$22.97 \pm 14.23$	0.576

Tableau 3 Les données OCT procédurale après l'angioplastie (le premier OCT-Run après le stenting).

Sous deployment de stent : surface de sténose résiduelle > ou = 30 %.

Bien que le taux de la malappostion de stent n'ait pas été différente entre les deux groupes, le rapport entre la surface des mailles et la surface de la lumière était apparemmenplus élevé-dans le groupe sans dissection (30.75% vs 21 .28%, P= 0.0158). La même observation a été faite pour le sous déploiement de stent, nous avons noté un plus grand nombre de stents sous déployés dans le groupe sans dissection et cela de manière significative (52.63% vs 18.18%, P=0.0003). Le rapport entre la surface moyenne Intra-stent / et la surface de référence était significativement plus bas dans le groupe sans dissection comparé au groupe avec dissection (73.85+12.50% vs 81.58 + 12.50, P= 0.0086).

Quant aux autres paramètres quantitatifs comme la longueur de stent, MLD et MLA, le diamètre de sténose résiduel, la surface de sténose résiduelle, il n'a y avait pas de différence significative entre les deux groupes au dernier OCT-Run, réalisé en post angioplastie avec stenting.

### E. L'analyse de la symétrie des vaisseaux de référence au niveau des bords de stent.

Les données de l'analyse OCT du rapport entre la dissection des bords et la symétrie du vaisseau de référence sont représentées dans le Tableau 7.

### 1. Au niveau de l'extrémité distale

Au niveau de l'extrémité distale de stent, il n'y avait pas de différence significative de taux de dissections des bords entre les deux groupes pour les données quantitatifs comme le diamètre distal de stent, la surface du bord distal du stent, le diamètre de référence distal, la surface de référence distale, le diamètre de référence distal minimal, le diamètre de référence distal maximal, la surface distale de la lumière du vaisseau. Toutefois, dans le groupe sans dissection, les patients avaient une valeur plus élevée du diamètre distal de la lumière (2.60 + 2.20 vs 2.39 + 2.41 mm, P= 0.0418), du diamètre de référence distal minimal (2.39 + 0.46 vs 2.16 + 0.60 mm, P= 0.0220), et de l'ISL [0.88 (0.82, 0.91) vs 0.84 (0.77, 0.90), P= 0.0125]. A noter également, une tendance pour le diamètre de référence distal maximal (2.83 + -0.57 vs 2.63 + -0.65 mm, P =

0.080), et l'IRSV [0.87 (0.83, 0.92) vs 0.86 (0.80, 0.90), P= 0.063] en faveur de groupe sans dissection, sans atteindre la significativité statistique.

### 2. Au niveau de l'extrémité proximale

Au niveau de l'extrémité proximale, il n'y avait pas de différence significative de diamètre de stent, surface de stent, diamètre de référence, surface de référence, diamètre de référence maximal, diamètre de la lumière, surface de la lumière, diamètre minimal et maximal de la lumière entre les deux groupes. On notait une tendance vers des valeurs plus-élevées pour le diamètre de référence minimal en faveur de groupe sans dissection  $(3.15\pm 0.57 \text{ vs } 2.96 \pm 0.60, P= 0.084)$ . L'IRSV [0.87 (0.82, 0.90) vs 0.81 (0.81, 0.89), P=0.0212] et de l'ISL [0.86 (0.81, 0.89 vs 0.83 (0.78, 0.88), P=0.0259] étaient significativement plus élevés dans le groupe sans dissection comparés au groupe avec dissection.

Tableau 4 Analyse de la symétrie du vaisseau au niveau des extrémités (premier OCT-Run).

	Groupe avec	Groupe sans	Р
	dissection	dissection	
	(n=44)	(n=76)	
Diamètre distal de stent (moyenne, mm)	3.04±0.54	2.98±0.43	0.565
Surface du bord distal de stent (mm <sup>2</sup> )	7.51±2.59	7.32±1.96	0.635
Extrémité distale de stent/valeurs de référence			
Diamètre de référence distal (moyenne, mm)	2.95±0.69	3.09±0.49	0.203
Surface de référence distale (mm <sup>2</sup> )	7.19±3.29	7.69±2.57	0.351
Diamètre de référence distal minimal (mm)	2.70±0.61	2.87±0.45	0.100
Diamètre de référence distal maximal (mm)	3.21±0.77	3.30±0.56	0.473
IRSV Distal	0.86 (0.80, 0.90)	0.87 (0.83, 0.92)	0.063
Extrémité distale du vaisseau			
Diamètre distale de la lumière $(M, mm)$	2.39±2.41	2.60±2.20	0.0418
Surface distale de la lumière (mm <sup>2</sup> )	4.86±0.62	5.51±0.48	0133
Diamètre distale minimal de la lumière (mm)	2.16±0.60	2.39±0.46	0.0220
Diamètre distale maximal de la lumière (mm)	2.63±0.65	2.83±0.57	0.080
Distal ISL	0.84 (0.77, 0.90)	0.88 (0.82, 0.91)	0.0125
Diamètre proximal de stent ( <i>M</i> , mm)	3.18±0.51	3.09±0.43	0.317
Surface proximal de stent (mm <sup>2</sup> )	8.22±2.65	7.76±2.46	0.314
Extrémité (bord) proximale de stent			
Diamètre de référence proximal (M, mm)	3.28±0.63	3.37±0.62	0.435
Surface de référence proximale (mm <sup>2</sup> )	8.77±3.48	9.34±3.35	0.379
Diamètre de référence proximal minimal (mm)	2.96±0.60	3.15±0.57	0.084
Diamètre de référence proximal maximal (mm)	3.66±0.66	3.65±0.67	0.938
IRSV Proximal	0.81 (0.81, 0.89)	0.87 (0.82, 0.90°	0.0212
Extrémité proximale du vaisseau			
Diamètre proximal de la lumière $(M, mm)$	2.86±0.66	3.02±0.66	0.185
Surface proximale de la lumière (mm <sup>2</sup> )	6.70±3.08	7.32±3.04	0.286
Diamètre proximale minimal de la lumière (mm)	2.60±0.69	2.74±0.59	0.252
Diamètre proximale maximal de la lumière (mm)	3.12±0.66	3.26±6 0.73	0.277
ISL Proximal	0.83 (0.78, 0.88)	0.86 (0.81, 0.86)	0.0259

L'Indice de symétrie du vaisseau de référence du bord distal de stent (IRSV distal) : diamètre minimal du vaisseau de référence / diamètre maximal au bord distal du stent.

Indice de symétrie du vaisseau de référence du bord proximal de stent (IRSV proximal): diamètre minimal du vaisseau de référence / diamètre maximal au bord proximal de stent.

Indice de symétrie de la lumière distale avant le stenting (distal ISL): diamètre minimal de la lumière distale / diamètre maximal avant le stenting au bord distal de stent.

Indice de symétrie de la lumière proximale avant le stenting : (ISL proximal): Diamètre minimum de la lumière proximale / diamètre maximal avant le stenting au bord proximal de stent.

M (valeur moyenne)

## F. Facteur prédictifs de dissection des bords de stent. Tableau 5

L'analyse multivariée par régression logistique (Wald forward stepwise) a montré que l'érosion (Odds ratio [OR] : 1.4, 95%, l'intervalle de confiance [CI] : 1.30 to 15.43, P= 0.0179), le sous déploiement de stent (OR : 0.21, 95% CI : 0.06 to 0.71, P= 0.0122), la couverture non-optimale de la lésion (OR : 1.4, 95% CI : 0.03 to 0.55, P= 0.0051), l'IRSV proximal (OR :0.002, 95% CI :0.00 to 0.76, P=0.0406) et distal (OR : 0.001, 95% CI : 0.00 to 0.50, P= 0.0305) étaient des facteurs de risque indépendants de dissection de bords de stent.

**Tableau 5** Facteurs prédictifs de dissections des bords de stent analysés selon le modèle de régression logistique (Forward Wald Stepwise).

			95.0% CI for EXP (B)	
	Р	OR	Minimal	maximal
Erosion	0.0179	1.51	1.30	15.43
Sous déploiement de stent	0.0122	0.21	0.06	0.71
Couverture optimale de la lésion	0.0051	0.14	0.03	0.55
IRSV Distal	0.0305	0.001	0.00	0.50
IRSV Proximal	0.0406	0.002	0.00	0.76
Constant	0.0031	204587.1		

L'Indice de symétrie du vaisseau de référence du bord distal du stent (IRSV distal) a été défini comme le rapport entre le diamètre minimal du vaisseau de référence et le diamètre maximal au bord distal du stent.

L'indice de symétrie du vaisseau de référence du bord proximal du stent (IRSV proximal) a été défini comme le rapport entre le diamètre minimal du vaisseau de référence et le diamètre maximal au bord proximal du stent.
#### IV. Discussion

L'étude DOCTORS a montré que l'OCT fournissait des informations supplémentaires utiles, outres celles qui sont obtenues par l'angiographie seule chez les patients avec SCA-NSTEMI, et était associée à un meilleur résultat fonctionnel évalué par la FFR <sup>(21)</sup>. Tous les patients de notre étude provenaient du groupe d'angioplastie guidée par l'OCT. Nous avons effectué une analyse morphologique des données de l'OCT concernant les dissections des bords, et essayé d'identifier les facteurs prédictifs de dissection de bords des DES chez les patients avec SCA-NSTEMI après angioplastie avec implantation d'un stent.

# A. Sous-déploiement de stent, optimisation de l'expansion du stent et dissection du bord du stent.

L'optimisation des résultats de l'angioplastie, guidée par l'imagerie endo-coronaire, l'OCT, était l'apport principal de l'étude DOCTORS. Cette optimisation était au prix d'une procédure prolongée, un volume plus important de produits de contraste, sans ajouter un risque d'infarctus de myocarde per procédural ou une insuffisante rénale<sup>(21)</sup>. Les résultats de notre étude montrent l'existence d'un rapport entre la dissection des bords de stent et le sous déploiement de stent. En effet, le sous déploiement est apparu comme étant un facteur de risque indépendant de dissection des bords. Le sous déploiement de stent est par ailleurs considéré comme un facteur de risque d'évènements cardiovasculaires majeurs lors du suivi par l'OCT <sup>(27)</sup>. Dans le registre français PESTO, les auteurs ont retrouvé une anomalie morphologique à l'OCT chez 97% des patients, le sous déploiement de stent et la malapposition constituaient la moitié de ces anomalies (45%)<sup>(28)</sup>. Ces résultats renforcent le concept d'une optimisation du résultat de l'angioplastie par une post dilatation en cas de résultat intermédiaire. Toutefois, l'optimisation des résultats par la post dilatation n'est pas sans risque, puisqu'elle est associée parfois à un risque de dissection des bords de stent<sup>(29)</sup>.

Le lien de causalité entre les dissections, profondes (médianes et adventitielles) et le risque de revascularisation itérative de site cible d'une part et l'infarctus de myocarde type 4 d'autre part s'est avéré positif.<sup>(30, 28,9)</sup>.

## **B.** Érosion de plaque, couverture optimale de la lésion par le stent, et dissections de bords de stent

La majorité des syndromes coronarien aigus sont dus à une occlusion ou rétrécissement de la lumière de l'artère avec une thrombose complète ou partielle, qui provient, sur le plan physiopathologique, par ordre de fréquence, de la rupture de plaque (55-60%), l'érosion de la plaque (30-35%), et le nodule calcifié superficiel (2-7%).<sup>(15-18)</sup> L'érosion de plaques se traduit par un thrombus intra-luminal sans discontinuité de l'épaisse chape fibreuse, et cela est valable même dans les cas avec noyau nécrotique, bien qu'elle en soit le plus souvent dépourvue <sup>(31)</sup>. De plus, par rapport à l'IVUS et à l'angiographie, la supériorité de l'OCT a été démontrée dans la détection de rupture ou érosion de plaque <sup>(14)</sup>

L'érosion de plaque est une anomalie fréquemment retrouvée à l'l'OCT chez des patients atteints de SCA, en particulier chez ceux qui présentent un SCA-NSTEMI et chez les patients plus jeunes.<sup>(32)</sup>. La sévérité de la sténose au niveau de l'artère coupable à la phase aigüe d'un SCA est moindre en cas d'érosion de plaque comparée à la rupture de plaque.<sup>(31)</sup>

D'un point de vue histopathologique, le précurseur de l'érosion est souvent une plaque lipidique modérée avec remodelage négatif, une plaque fibroathéromateuse et cette érosion donne souvent un aspect presque normal à l'angiographie coronaire <sup>(33)</sup>. Dans une étude menée chez cent vingt patients en phase aigüe de STEMI, bénéficiant d'une imagerie endocoronaire en phase aigüe, les auteurs ont rapporté que l'érosion de plaque a été retrouvée chez un quart des patients avait l'aspect d'une plaque fibreuse excentrique <sup>(34)</sup>.

Les résultats de notre étude corroborent ces données de la littérature. En effet, les résultats de notre étude montrent que l'érosion de plaque pourrait être considérée comme étant un facteur de risque de dissection de bords de stent, secondaire à son aspect excentrique ou au remodelage négatif de la paroi de l'artère lors de l'expansion et aux forces d'étirement au moment de l'angioplastie avec implantation de stent chez les patients présentant un SCA-NSTEMI.

Notre étude a également montré qu'une couverture non optimale de la lésion était un facteur de risque de dissection des bords de stent après le premier run d'OCT. Un geste d'angioplastie complémentaire avec pose

de stent a été réalisé ayant permis une couverture complète des dissections, confirmée au contrôle OCT final <sup>(21)</sup>. Cette donnée est certainement en accord avec le raisonnement logique qui veut que la couverture optimale de lésion puisse réduire le risque de dissection des bords. Ce résultat est en accord avec les études précédentes <sup>(35,36,14)</sup>, ces études avait montré un effet protecteur liée la couverture optimale de lésion.

C. Asymétrie de l'artère coupable et dissection des bords de stent.

Dans une étude précédente précédent, l'IVUS a pu identifier la dissection des bords dans 9,2% des implantations de DES et a montré que l'excentricité résiduelle des plaques et la symétrie des bords des stents prédisent les dissections des bords des stents coronaires <sup>(10)</sup>.Dans une étude sur une cohorte à faible effectif bénéficiant d'OCT, il y avait une tendance d'une valeur supérieure de l'asymétrie axiale de stent (symétrie axiale de stent/ surface maximale de stent) chez les patients ayant une dissection du bord de stent (P = 0,0727), mais il n'y avait pas de différence significative de symétrie de stent) (symétrie de stent= diamètre minimal de stent/diamètre maximal de stent aux deux extrémités de stent) <sup>(13)</sup>. Dans une autre étude, à plus grand effectif bénéficiant d'OCT, l'excentricité de lumière (la différence entre le diamètre maximal et le diamètre minimal de stent) et l'excentricité de prédicteurs indépendants pour les dissections détectées par l'OCT. Les patients avec dissection avaient un indice d'excentricité (de stent et de lumière), plus élevé après l'angioplastie avec implantation d'un stent<sup>(14)</sup>.

Dans notre étude chez les patients atteints de NST-ACS, nous avons constaté que les patients présentant une dissection du bord de stent pourraient avoir un indice de symétrie vasculaire plus élevé des deux extrémités (bords) de stent et un indice de symétrie de la lumière aux deux extrémités du vaisseau plus élevé avant l'implantation de stent. Un indice de symétrie de la lumière plus élevé pourrait être considéré comme un facteur de risque indépendant de dissection du bord de stent.

## V. Conclusion

La dissection des bords de stent est une complication fréquente et parfois grave de l'angioplastie coronaire. Elle est sous-estimée à l'angiographie coronaire et les nouvelles techniques de l'imagerie endocoronaire, l'OCT et l'IVUS, permettent une meilleure identification. Plusieurs facteurs prédictifs ont été identifiés comme : l'indice de la symétrie vasculaire, l'indice de symétrie de la lumière aux deux extrémités du vaisseau plus élevé avant l'implantation de stent.

L'évolution au long terme est favorable dans la majorité des cas.

## Iconographies

Angiographie de la coronaire droite avec sténose subtotale au niveau de CD2 distale Avant l'angioplastie

<6-47@> E D Sten

A Image OCT avant l'angioplastie, vaisseau de référence, extrémité distale



## Image OCT : Rupture de plaque



## Image OCT, l'asymétrie du vaisseau



## Image OCT asymétrie du vaisseau de référence



E Image OCT, érosion de plaque à proximité de dissection du bord au niveau de l'extrémité distale



## Angiographie de l'artère coronaire droite après stenting







## Image OCT, dissection de bord de stent







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### 5.2 Main conclusion and remarks

- OCT findings before stenting showed that the group with dissection had significantly more intimal rupture (65.91% vs. 44.74%, P = 0.0365) and plaque erosion (79.55% vs. 50.00%, P = 0.0018) than those in the group without dissection.
- After stenting, the frequency of optimal covering of lesion was significantly higher in the group without dissection as compared to the group with dissection (89.47% vs.75%, P=0.0351). On the contrary, patients in the group with dissection presented a lower percentage of stent underexpansion (18.18% vs. 52.63, P = 0.0003).
- Target vessels for stenting were more symmetric in the group without dissection than in the group with dissection.
- Multivariate logistic regression analysis revealed that during OCT-guided PCI, plaque erosion, vessel asymmetry, non-optimal lesion coverage were risk factors for stent edge dissection in patients with non-ST-segment elevation ACS.
- Conclusion: Utilization of OCT identifies predictors for patients with non-ST-segment elevation ACS, enabling risk stratification of patients who are at a higher risk of adverse outcomes.

6. General Discussion and Conclusion

According to the 2013 Guidelines from the European Society of Cardiology on the management of stable CAD, OCT can be used to further characterize the vessel lesions and improve stent deployment [121]. The 2014 European Society of Cardiology/ European Association for Cardiothoracic Surgery Guidelines on myocardial revascularization recommend the use of OCT to optimize stent implantation and assess the mechanisms of stent failure in selected patients [122]. Recently, according to the Society of Cardiovascular Angiography and Interventions Consensus Statement, OCT is "probably beneficial" for determination of optimal stent placement (sizing, apposition, and lack of edge dissection) and "possibly beneficial" for assessment of plaque morphology [123].

Learning from previous randomized clinical studies, it may be stated that OCT can be used at different time points for different purposes during cardiac catheterization: (1) before PCI intervention to confirm the diagnosis of CAD and to identify the need for subsequent PCI; this technique appears particularly useful when the culprit lesion is unclear or the diagnosis is uncertain on CAG images, for example, angiographically intermediate lesions [124]; (2) during the PCI procedure to guide the intervention step by step; and (3) after PCI, to assess stent outcomes and to optimize the stent implantation if needed. As we mentioned before, PCI as an invasive procedure is associated with significant rates of post-procedural complications. Therefore, stent implantation should be optimized in the AMI setting to as much as possible improve short- and long-term clinical outcomes. OCT is considered to assist stent implantation by (1) identifying appropriate landing zones for stent placement; (2) providing accurate measurement of the detailed parameters of target vessels, such as length, width and tapering, lesion severity (particularly in NSTEMI); and (3) assessing stent deployment, such stent expansion, apposition, and residual stenosis [67, 125].

#### OCT-guided angioplasty yield useful clinical information and modify physicians' strategies

There is currently no consensus on specific OCT criteria for optimal stent deployment. In the Centro per la Lotta contro l'Infarto-Optimisatio of Percutaneous Coronary Intervention (CLI-OPCI) study, several definitions were put forward for the assessment of stent deployment: (1) minimal stent area (MSA) >90% mean reference lumen area, (2) stent malapposition with a distance >200  $\mu$ m, (3) edge dissections with a width >200  $\mu$ m, and (4) edge lumen narrowing with a lumen area <4 mm<sup>2</sup> [66]. In the CLI-OPCI study, promising results were achieved with OCT guidance as compared with CAG. OCT disclosed unfavorable stent/lumen outcomes, including stent malapposition or underexpansion, edge dissection, lumen narrowing, thrombus, which resulted in the need of further stenting or additional balloon dilation in 35% of patients. At 1 year of follow-up, compared to the CAG guidance group, OCT guidance group had a significant lower incidence of cardiac death or myocardial infarction than the group without OCT guidance, (13.0% vs. 7%, P = 0.01) as well as a lower adjusted risk of death and adverse cardiac events (OR 0.49, 95% CI 0.96 vs. 0.25).

To date, there are only few prospective, randomized trials assessing the role of OCT for guiding PCI. However, several reports have shown the potential of OCT to support its role in clinical decision-making in PCI, from which we can learn valuable lessons [66, 73, 111, 126, 127]. In previous studies, the feasibility of OCT to detect thrombus burden in selected ACS patients without stent placement had been examined. OCT was able to display lesion characteristics that were not disclosed by CAG and thus facilitated treatment decisions [128, 129]. In a pilot study of 90 patients who undergone PCI, OCT findings led to additional interventions (balloon dilatation and stenting) in 32% of patients [73]. The short-term outcomes showed that the 6-month event-free survival rate was 98%. In another study of 108 patients undergoing OCT-guided coronary stenting, OCT findings resulted in deferral of treatment in 19% of cases and further interventions in 34% of patients [126]. In a series of 150 consecutive patients, pre-PCI OCT findings resulted in the modification of angiography-guided strategy in 82% of the patients, including one-half for the

angiographically planned stent length, one-quarter for stent diameters, and more than one-half for post-dilation balloon diameters [127]. Moreover, after PCI, OCT measurements also led to further interventions in 55% of the target vessels, mostly with additional balloon dilations or stent implantation to correct stent malapposition or dissections. In the ILUMIEN I study which enrolled 418 patients, pre-PCI OCT images altered the procedure strategy in 55% of cases [130]. On completion of PCI, based on OCT imaging, further intervention was performed in 25% of cases, including 14.5% for malapposition, 7.6% for stent under-expansion and 2.7% for stent edge dissection. The DOCTORS study is a randomized, prospective, multicenter clinical trial, evaluating the utility of OCT for optimization of the stent and clinical results in patients with NSTE-ACS, beyond angiography alone [109]. This study randomized 240 NSTE-ACS patients to OCT-guided versus angiography-guided PCI intervention (n=120 each group). Post-procedure OCT imaging revealed higher sensitive for detection of under-expansion (42% vs. 11%), stent malapposition (32% vs. 0) and stent edge dissection (37.5% vs. 4%) in comparison to CAG alone. OCT findings altered procedural strategies in half of cases in the OCT group, leading to a significantly lower diameter stenosis at the end of PCI [111]. Post procedural FFR values were significantly higher in the OCT-guided group than in that with CAG alone (0.94±0.04 vs. 0.92±0.05, p=0.005). Although the OCT technique was associated with the use of more contrast and longer procedural time, there were no significant differences in the rates of acute kidney injury and overall procedural complications between both groups, suggesting that OCT did not increase periprocedural complications. In our study, we found that OCT performed before PCI was more sensitive than CAG for diagnosing thrombus, dissection, and calcification. After PCI, OCT was more sensitive than CAG for the diagnosis of thrombus, dissection, stent malapposition, intimal tissue protrusion, poor stent expansion, lesion coverage, and stent skeleton coverage bifurcation. OCT provided quantitative parameters of lesion and stent diameter, which were significantly different from those measured by CAG. Information provided by OCT detection indeed altered clinical strategies deemed necessary by the operators in nearly half of the patients, including thrombus aspiration,

administration of GP IIb/IIIa inhibitors, additional balloon inflations, additional stent implantations, avoiding stent implantation, collateral intervention, and guide-wire repositioning. These data suggested that OCT, both before and after PCI, may provide additional procedural information than angiography alone, possibly facilitating the optimization of stent implantation during PCI procedures.

Taken together, preliminary data indicate that OCT can alter the operator's intention-to-treat and modify the overall revascularization strategy, potentially avoiding unnecessary interventional procedures. However, data supporting the clinical utility of OCT-guided PCI remain scant, although the overall goal of the use of a new technique should aim at improving the outcome, at mid- and long-term. We will discuss this important point below.

# OCT optimizes the detection of coronary artery plaque rupture and stent edge dissection during PCI

OCT has been increasingly used for identifying key morphology of plaque components that predict vulnerability and rupture, such as thin fibrous caps, high density of macrophages, and large necrotic cores [131]. A previous study explored the correlations between culprit plaque morphology and clinical outcomes, which showed that ruptured plaques more frequently caused STEMI than eroded or calcified plaques did [115]. Vergallo *et al.* carried out three-vessel OCT in 38 patients with ACS because of either plaque rupture or plaque erosion [132]. They found that patients with ruptured culprit plaques might be at a higher risk of stent failure due to a higher burden and severity of atherosclerosis. However, the long-term incidence of adverse events remains undetermined. Thus, the identification of culprit lesion morphology by OCT detection facilitates risk stratification of patients and improve medical management of coronary disease.

Although CAG remains the main routine examination used for identifying coronary plaque rupture and guiding the coronary intervention procedure, CAG can only vaguely display the outlines of the vessel walls through comparing images with and without contrast medium, and it cannot clearly visualize the details of the intramural lesions of coronary arteries. Therefore, atypical coronary plaque ruptures can easily be misdiagnosed or overlooked through CAG examination. One of the main advantages of OCT is its unprecedented resolution, which enables accurate detection of plaque cap rupture and precise differentiation between ruptured plaques and those with intact fibrous caps [133, 134]. In a study, Kubo et al. compared the capacity of OCT, IVUS and coronary angioscopy in the assessment of culprit lesions in patients with AMI [117]. The results showed that OCT had a highest accuracy (73%, 23% and 100%, respectively) for detecting plaque rupture, plaque erosion and coronary thrombi in comparison to IVUS (40%, 0%, 33%, respectively) and coronary angioscopy (43%, 3%, 100%, respectively). In a cross-sectional study with patients treated with statins who had good lipid control, plague rupture was detected by OCT in 39.6% of the patients with STEMI, among whom 35.4% with stable angina and 25% with unstable angina [135]. In our study, before PCI, a total of 101 coronary arteries were evaluated in 97 patients. A significantly higher number of plaque ruptures or spontaneous dissections was detected by OCT than by CAG (12 %, vs. 4.0%). Ten OCT-detected plague ruptures were found at the proximal shoulder of plaques, and 2 OCT-detected plaque ruptures were found at the distal shoulder, a difference that was significant. All OCT-detected plague ruptures were limited to the intima. Among these patients, four patients with plague rupture before PCI were implanted with a stent. These results suggest that OCT can clearly display coronary artery plaque rupture lesions before PCI, and guide the coronary intervention procedure.

Most OCT studies define edge dissection if it occurs within the 5 mm regions adjacent to the stent borders. OCT is currently the only technology that can clearly display the microscopic structures of blood vessels *in vivo* nearly at the histological level. It may thereby be used for the accurate detection of edge dissection, since it can distinctly distinguish the position of the entrance and exit, quantify the length and thickness of the tearing intima; leading to the accurate assessment of the characteristics of edge dissection. On the basis of OCT appearance, Chamie *et al.* put forward the classification of edge dissection according to morphology (flap or cavity) and

depth of penetration (intimal, medial, or adventitial) [104]. Rates of edge dissection greatly vary depending on the imaging modality used for detection. Ann *et al.* compared the rates of stent edge dissection by using CAG, IVUS and OCT in 58 consecutive patients after stent implantation, and found that OCT had a highest sensitivity for detection of edge dissection (24%), compared to IVUS (4%) and CAG (3%) [136]. Another OCT study showed that the incidence of OCT-detected stent edge dissections was 37.8% in 249 treated lesions, although most of them (84%) were invisible on CAG. These dissections were located much more frequently at distal edges (67.9%) than at proximal edges [104]. Moreover, they found that vessel overstretching plays a significant role in distal edge dissection and that every 1% increase in the ratio of stent/lumen diameter resulted in a 22% increase in its risk. In our study, we found that OCT could identify stent-related edge dissections at the stent edges were detected by OCT (48/180) than by CAG (5/180). On OCT imaging, 28 stent edge dissections at 89 proximal edges of stents and 20 stent edge dissections at 91 distal edges of stents were identified. There seemed to a trend of higher occurrence of dissections at the proximal edge (32%) than at the distal edge (22.0%) of these stents.

### Utilization of OCT in the evaluation and risk factor identification of stent edge dissection

Stent edge dissection may be associated with an increased risk of target lesion revascularization, type IVa myocardial infarction as well as short- and mid-term incidence of stent thrombosis [49, 120, 137, 138]. It is important to identify risk factors of stent edge dissection and avoid them as much as possible during PCI procedures.

Several studies have been conducted to assess incidence, predictors, morphology, and angiographic findings of edge dissections after stent implantation using different imaging techniques. Liu *et al.* used IVUS to assess incidence and predictors of edge dissections after drug-eluting stent implantation in 887 patients with 1,045 non–in-stent restenosis lesions in 977 native arteries. IVUS identified edge dissections after 9.2% of drug-eluting stent implantations, among

which 51.2% involved the proximal and 48.8% the distal stent edge. Residual plaque eccentricity, lumen-to-stent-edge-area ratio, and stent edge symmetry predicted coronary stent edge dissections [51]. Another IVUS study showed that greater stent expansion and the presence of large, calcified, and/or attenuated plagues were independent predictors of stent edge dissection after drug-eluting stent implantation[108]. Recently, OCT has increasingly become a useful imaging modality for guiding PCI procedures. Chamie et al. identified several independent predictors of OCT-detected edge dissections, including presence of atherosclerotic plaque at stent edges, calcification angle, minimum fibrous cap thickness, thin-cap fibroatheromas, stent/lumen eccentricity, and vessel overstretching [104]. In another OCT study, the lumen eccentricity of the stent at its edges, the stent-edge-to-lumen-area-ratio and diseased vessel wall morphology of the reference segment adjacent to the stent edge were found to be independent risk factors for the presence of stent edge dissections in cardiovascular high-risk patients with type 2 diabetes, suggesting the importance of avoidance of longitudinal and transverse mismatch between stent and vessel in reducing the occurrence of stent edge dissections[103]. Similarly in our study, we found plaque erosion, vessel asymmetry, non-optimal lesion coverage might be risks of stent edge dissection in patients with non-ST-segment elevation ACS. Further study is required to confirm and extend these results.

#### **Unsolved questions**

Although OCT can clearly detect stent malapposition, stent edge dissection, and tissue protrusion inside a stent which may be undetectable by CAG alone, such findings detected only by OCT may not have apparent clinical significance. Surprisingly, a number of early studies based on angiographic evidence support minimal influence of small dissections on adverse outcomes [139, 140]. Small stent edge dissections after stenting which are detectable only on OCT tend to be smaller during the follow-up, and most of them will resolve completely. Also, the rate of incomplete stent apposition spontaneously decreases with time when the stent-lumen gap is gradually filled

with neointima. Gutierrez-Chico et al. investigated the outcomes of incomplete stent apposition diagnosed by OCT throughout a 12-month follow-up [141]. Incomplete stent apposition resolved in all cases with strut-lumen distances < 270 µm and in 93% of cases with strut-lumen distances < 400 µm. Similar outcomes were found in another clinical study involving 395 stent edges in 230 patients. The results showed that small dissections, disclosed by OCT imaging, even left untreated, have a minimal impact on major adverse cardiac events at 12-month follow-up, if their longitudinal length  $\leq$ 1.75 mm, flap depth  $\leq$ 0.52 mm, flap opening  $\leq$ 0.33 mm, without extending to the media [104]. De Cock et al. assessed the incidence of acute vessel injury after drug-eluting stent implantation in 62 lesions [142]. They used OCT to determine the healing response at 9 months. After PCI, OCT detected more edge dissections than angiography did, and only a proportion of these lesions were concomitantly visible on both CAG and OCT. Although acute edge dissections were found in 56% of patients, residual flap was visible only in one-third at follow-up. Among those acute findings after stenting only visible on OCT, most of them being superficial, small, and nonflow-limiting, if left untreated, are benign [100, 142, 143]. Therefore, we may reasonably ask whether all post-procedural OCT findings, especially those invisible angiographically, necessarily require additional interventions. Currently, there is a lack of specific OCT criteria to be used for optimization of stent deployment and refinement of the decision-making process.

#### Novel applications and future investigations

A potential use of OCT regarding PCI planning is risk stratification. Previous OCT studies have linked lesion morphology with peri-procedural microvascular damage or myocardial infarction. OCT-derived TCFA is a predictor of peri-PCI complications. The presence of OCT-determined large lipid burden and TCFA was associated with microvascular obstruction or no-reflow after PCI in patients with ACS [144, 145] Lee *et al.* applied OCT to explore the relationship between pre-PCI plaque morphology and post-PCI cardiac troponin I elevation [146]. Based on OCT measurements, presence of TCFA was associated with post-PCI cardiac troponin I elevation, and it was found as an independent predictor of post-PCI myocardial infarction (OR, 10.47). In addition, in-stent thrombus or dissection detected by OCT after PCI also predicted periprocedural myocardial infarction. In a study of Gutiérrez-Chico *et al.*, incomplete stent appositions were categorized according to distinct morphological patterns of endothelial coverage, namely homogeneous, layered, crenellated, bridged, partially bridged, and bare [141]. They hypothesized that each pattern, appearing as different OCT images, was related to different pathological mechanisms, thereby stratifying risks according to the different patterns of incomplete stent apposition. These data clearly support the role of OCT imaging as a useful tool for risk stratification of PCI results.

The intervention on complex coronary lesions demands special attention since they are related to high rates of acute and late stent failure. The usefulness of OCT in the guidance of complex coronary interventions, such as bifurcation, overlap, positioning of multiple scaffolds in diffuse disease, has been preliminarily evaluated [147-149]. Alegri'a-Barrero *et al.* have analyzed the feasibility and effectiveness of OCT-guided stent re-crossing versus angiographic guidance [148]. The OCT-guided group showed a significantly lower incidence of malapposed stent struts, especially in the quadrants towards the side branch ostium (9.5 *vs.* 42%). However, further investigation of OCT versus other modalities in complex situations is needed.

Despite clear advantages of OCT, OCT has its own disadvantages: the additional contrast injection, the lack of ostial lesion imaging, and low tissue penetration that impedes the quantification of plaque burden [16]. Future trends in intravascular OCT will include a combination or fusion of OCT with other modalities, for instance IVIU, into a common catheter to improve stent deployment. In a study conducted by Huang *et al.*, the use of ultrasound was attempted to enhance the penetration depth of OCT [150]. In addition, to reduce misjudgment of the operator, a real-time point-to-point correspondence between the angiographic and OCT images has been developed [47, 151]. Integration of OCT into the PCI workflow provided better control of image acquisition and analysis, enabling the operator to reduce the risk of geographic mismatch and map optimal stent deployment [47, 152].

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Currently, the utilization of OCT allows us a better understanding of the pathophysiology of CAD, an accurate identification of vulnerable plaques, and facilitation of stent implantation, thereby improving our ability to more precisely treat our patients in a timely manner [27, 41]. But still, data linking the images and clinical outcomes are lacking. Whether OCT-guided PCI and subsequent treatment modification would translate into better moderate- and long-term outcomes compared with angiography alone or other modalities, especially in the contemporary era of new generation drug-eluting stents and bioresorbable vascular scaffold stents, as well as potent adjunct pharmacological treatment, remains to be proven with large, prospective, randomized clinical trials with hard clinical endpoints [153].

#### Limitation of the study

Our studies have limitation. The study at the origin of the 1<sup>st</sup> 2 papers published on our results was conducted in a single-center with a relatively small sample size, despite of a prospective design. Further large-scale prospective, randomized studies are needed to reveal the clinical superiority of OCT-guided PCI against angiography alone. This was among the aim of the 3<sup>rd</sup> study, a prospective randomized trial. Whether OCT-guided PCI may actually improve the prognosis of CAD patients should be extensively investigated in the future on a large number of patients, i.e. multicenter in their design. Our studies did not encompass the mid-term/long-term follow-up of patients, and are thus unable to answer the crucial question of the clinical usefulness of the OCT procedure. Further studies should assess whether OCT-related changes in treatment strategies would actually be associated with improved clinical outcomes during long-term follow-up.

#### Conclusion

OCT imaging with its high resolution and ease of use seems promising in decision making during PCI procedures for the interventional cardiologist, including evaluating controversial plaque lesions, assessing stent implantation, and surveying stent-related vascular injury. OCT may detect plaque rupture missed by CAG and thoroughly examine stent edge dissections after PCI. OCT

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also provided quantitative parameters of lesion and stent diameter, which were significantly different from those were measured by CAG alone. Thus, OCT has potential to assist clinicians throughout the stent implantation procedure, impacting on planned interventional strategy. In addition, during OCT-guided PCI, plaque erosion, vessel asymmetry, non-optimal lesion coverage might be risks of stent edge dissection in patients with non-ST-segment elevation ACS. Utilization of OCT enables risk stratification of patients who are at a higher risk of adverse outcomes by identification of risk predictors. However, routine clinical use of OCT will require establishment of standard definitions/criteria. Moreover, randomized trials are now warranted to assess whether OCT-guided PCI results in improved long-term clinical outcomes.

Summary in French

#### Résumé en français

L'angiographie coronaire (CAG) est considérée comme la méthode diagnostique de référence pour la maladie coronarienne (CAD) et pour déterminer les stratégies thérapeutiques interventionnelles coronariennes (PCI) ; cependant, elle peut s'avérer impuissante à détecter certaines caractéristiques des lésions athéromateuses ou des relations vaisseau-stent. La tomographie en cohérence optique (OCT) possède des avantages en termes de résolution spatiale et de traitement des images en temps réel. Elle pourrait devenir un précieux outil pour une application de routine au diagnostic et à la stratégie thérapeutique.

Dans une première étude, nous avons réalisé une étude comparative prospective chez 83 patients, l'OCT était réalisée avant stenting (OCT-pré) et/ou après stenting (OCT-post). Avant la PCI, l'OCT était plus sensible que la CAG pour diagnostiquer la présence de thrombus, de dissection et de calcification. Après PCI, l'OCT était plus sensible que la CAG pour diagnostiquer thrombus, dissection, malapposition du stent, protrusion de l'intima artérielle, sous-déploiement du stent, couverture de la lésion, et couverture de la bifucation par les mailles du stent. L'OCT apportait aussi des paramètres quantitatifs significativement différents de ceux mesurés par CAG. L'information apportée par l'OCT modifiait la prise en charge clinique chez 49% des patients, avec, au total 58 modifications de stratégie thérapeutique. L'OCT, avant et après la PCI, apporte donc à la procédure interventionnelle des données additionnelles par rapport à l'angiographie seule, et change les stratégies thérapeutiques chez environ la moitié des patients.

Dans notre deuxième étude, nous avons recherché si l'OCT pouvait évaluer avec précision la rupture de plaque coronarienne avant stenting ou la dissection du bord de stent après stenting. Un

total de 112 patients avec CAD ont été inclus dans cette étude. Avant PCI, 12 ruptures de plaque ont pu être détectées par l'OCT alors que la CAG n'en détectait que 4. Après PCI, une dissection du bord de stent a pu être détectée dans 48 cas par OCT et seulement 5 cas par CAG. Du fait de l'utilisation de l'OCT, 4 stents ont été déployés par-dessus la rupture de plaque et 13 stents implantés par-dessus les dissections du bord. L'OCT peut donc détecter des ruptures ignorées par la CAG et diagnostiquer avec précision les dissections du bord de stent après PCI, améliorant donc la procédure de stenting.

Dans notre troisième étude, nous avons analysé les paramètres cliniques de 120 patients avec syndrome coronaire aigu (ACS) sans élévation du segment ST inclus dans l'Etude DOCTORS (un essai clinique randomisé, prospective, multicentrique, ouvert) et chez qui était réalisée une PCI quidée par l'OCT. Les patients étaient répartis entre un groupe avec dissection (n=46) et un groupe sans dissection (n=76). Les facteurs de risque de dissection du bord de stent ont été identifiés en utilisant une analyse en régression logistique multivariée, selon la méthode pas-à-pas ascendante de Wald. Les observations apportées par l'OCT avant le stenting ont montré que les patients avec dissection avaient plus souvent des ruptures intimales et des érosions de la plaque. Après stenting, la couverture optimale de la plaque et un déploiement correct du stent était plus fréquents dans le groupe sans dissection. La dissection de bord du stent était quant à elle significativement associée à l'érosion de la plaque, au sous-déploiement du stent, à une couverture non optimale de la plaque, et à des anomalies du 'reference vessel symmetry index' (RVSI) distal et proximal. Au cours du stenting, l'érosion de la plaque et l'asymétrie vasculaire, et une couverture non optimale de la plaque, sont donc, dans notre étude, des facteurs prédictifs du risque de dissection du bord de stent chez les patients avec ACS sans élévation du segment ST.

En conclusion, l'imagerie par OCT est prometteuse comme support de la prise de décision au cours des procédures de PCI, pour évaluer les lésions athéromateuses, juger de la bonne implantation du stent, et dépister les lésions vasculaires dues au stent. L'OCT représente donc bien une aide potentielle pour le cardiologue interventionnel tout au long de la procédure de stenting, avec un impact certain sur la stratégie interventionnelle initialement programmée. De plus, l'OCT se révèle comme un nouvel outil pour prédire la dissection des bords de stent chez les patient avec ACS sans élévation du segment ST, rendant possible une stratification des patients quant à ce risque. Des essais cliniques randomisés sont maintenant nécessaires pour savoir si l'assistance par l'OCT pendant la procédure améliore le pronostic à long terme des patients après PCI.

Summary in English
### Summary in English

Although coronary angiography (CAG) has been considered the gold-standard diagnostic method for coronary artery disease (CAD) and is the basis for determining treatment strategies for percutaneous coronary intervention (PCI), it may fail to reflect some critical characteristics of atherosclerotic lesions or vessel-stent relationships. Intravascular optical coherence tomography (OCT) has advantages in terms of higher spatial resolution and real-time image processing. OCT can reliably visualize coronary artery morphology and microstructure, thereby presenting the potential to become a routine tool for diagnostic application and guidance of therapeutic interventions.

In a first clinical research, we performed a comparative prospective study in 83 patients between CAG and OCT findings, after initial coronary angiography and before angioplasty (OCT-pre) and/or after angioplasty (OCT-post). Compared with CAG, OCT was more sensitive for diagnosing thrombus, dissection, and calcification before PCI. After PCI, compared with CAG, OCT was more sensitive for diagnosing thrombus, dissection, stent malapposition, intimal tissue protrusion, suboptimal stent expansion, lesion coverage, and stent struts coverage bifurcation. OCT provided quantitative parameters of lesion and stent diameter, which were significantly different from those measured by CAG. This piece of information provided by OCT detection changed the clinical strategies in 49% of patients; in total there were 58 modifications of therapeutic strategy. These data showed that OCT, before and after PCI, provided additional procedural information to angiography alone and changed treatment strategies in approximately half of patients.

In our second clinical study, we investigated whether OCT can provide an accurate assessment of the coronary artery plaque rupture before stenting or edge dissection after stenting, and may subsequently provide guidance for optimizing the stenting procedure. A total of 112 patients with CAD, who underwent OCT and CAG before and after PCI, were enrolled into the study. Before PCI, 12 plaque ruptures were detected by OCT and only 4 were detected by CAG. After PCI, edge dissections were OCT-detected in 48 cases and CAG-detected in 5. Because of OCT, 4 stents were deployed over the plaque ruptures, and 13 stents were implanted over edge dissections. Therefore, OCT may detect plaque ruptures missed by CAG and thoroughly examine stent edge dissections after PCI, which subsequently provides guidance for optimizing the PCI procedure.

In our third clinical study, clinical parameters of 120 patients with non-ST-segment elevation acute coronary syndrome (ACS) undergoing OCT-guided PCI and included in the DOCTORS Study (a randomized, prospective, multicenter, open-label clinical trial) were analyzed. The patients were divided in a group with dissection (n = 46) and a group without dissection (n = 76). Risk factors for stent edge dissection under OCT-guided PCI were identified by multivariable logistic regression analysis using forward stepwise (Wald) method. OCT findings before stenting showed that the group with dissection had significantly more intimal rupture and plaque erosion than the group without dissection. After stenting, the frequency of optimal lesion coverage was significantly higher in the group without dissection. Patients in the group without dissection presented a lower percentage of stent underexpansion. Stent edge dissection was significantly correlated with plaque erosion, stent underexpansion, non-optimal lesion coverage, and RVSI abnormalities both at distal edge and at proximal edge. Therefore, during OCT-guided PCI, plaque

erosion, vessel asymmetry, and non-optimal lesion coverage, might be risks of stent edge dissection in patients with non-ST-segment elevation ACS.

In conclusion, OCT imaging is promising in decision making during PCI procedures, including evaluating controversial plaque lesions, assessing stent implantation, and surveying stent-related vascular injury. Thus, OCT has potential to guide interventional cardiologists throughout the stent implantation procedure, impacting on planned interventional strategy. In addition, OCT is the most novel image technology to predict stent edge dissection for patients with non-ST-segment elevation ACS, enabling risk stratification of patients who are at a higher risk of this complication. Large-scale randomized trials are now warranted to assess whether OCT results and guidance during de procedure improve long-term clinical outcomes of PCIs.

# List of personal publications on the subject

of the thesis

## List of publications related to the University thesis.

- Jianfeng HUANG, Salah NOURI, MD, Romain Chopard, MD, PhD, Geraud Souteyrand, MD, Pascal Motreff, MD, PhD, Christophe Caussin, MD, Nicolas Amabile, MD, Patrick Ohlmann, MD, PhD, Olivier Morel, MD, PhD, Yoann Lefrançois, MD, Vincent Descotes-Genon, MD, Johanne Silvain, MD, PhD, Eric Van Belle, MD, PhD, Loïc Belle, MD, François Schiele, MD, PhD, Nicolas MENEVEAU, Incidence of stent edge dissection under Optical Coherence Tomography in patients with Non–ST-Elevation Acute Coronary Syndrome (being prepared for publication).
- Jianfeng HUANG, Kamal BELMADANI, Marion CHATOT, Fiona ECARNOT, Romain CHOPARD, Manhong WANG, Xu CAI, Francois SCHIELE, Nicolas MENEVEAU, Identification of coronary artery dissection and guidance of treatment strategies by optical coherence tomography. International Journal of Clinical and Experimental Medicine 2017;10(8):12150-12157
- Jianfeng HUANG, Kamal BELMADANI, Marion CHATOT, Fiona ECARNOT, Romain CHOPARD, Manhong WANG, Xu CAI, Francois SCHIELE, Nicolas MENEVEAU, Clinical significance of optical coherence tomography–guided angioplasty on treatment selection. Experimental and Therapeutic Medicine (in press, accepted for publication on November 17, 2016).
- B BONNET, Philoctimon PLASTARAS, Jianfeng HUANG, Marie France SÉRONDE, Romain CHOPARD, Prognostic impact of tissue protrusion after stenting in patients with acute coronary syndrome: an optical coherence tomography study, Archives of Cardiovascular Diseases Supplements, 2015, 7(1):8

List of the communications, with Huang JF as co-author, at scientific congresses and meetings, related to the University thesis:

- Does Optical Coherence Tomography-Guided Angioplasty Yield Useful Clinical Information and Modify Physician Strategy? TCT international congress 2012; October 22-26, 2012 in Miami, USA.
- Does Optical Coherence Tomography-Guided Angioplasty Yield Useful Clinical Information and Modify Physician Strategy? ACC congress 2013; March 9-11, 2013; San Francisco, USA.
- Does Optical Coherence Tomography-Guided Angioplasty Yield Useful Clinical Information and Modify Physician Strategy? ESC congress 2013; Aug 31 - Sep 04, 2013; Amsterdam, The Netherlands.
- Prognostic impact of tissue prolapse after stent implantation in patients with non-ST elevation acute coronary syndromes: an optical coherence tomography study. ESC, 2014; 30 Aug 30 -03 Sep 03 2014; Barcelona, Spain.

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#### Résumé en français

L'imagerie par Imagerie en Cohérence Optique (OCT) est prometteuse comme support de la prise de décision au cours des procédures d'interventions coronariennes percutanées (PCI), pour évaluer les lésions athéromateuses, juger de la bonne implantation du stent, et dépister les lésions vasculaires dues au stent. L'OCT représente donc bien une aide potentielle pour le cardiologue interventionnel tout au long de la procédure de stenting, avec un impact certain sur la stratégie interventionnelle initialement programmée. De plus, l'OCT se révèle comme un nouvel outil pour prédire la dissection des bords de stent chez les patient avec syndrome aigu coronarien sans élévation du segment ST, rendant possible une stratification des patients quant à ce risque. Des essais cliniques randomisés sont maintenant nécessaires pour savoir si l'assistance par l'OCT pendant la procédure améliore le pronostic à long terme des patients après PCI.

#### Summary in English

Optical Cohenrence Tomography (OCT) imaging is promising in decision making during Percutaneous Coronary Intervention (PCI) procedures, for evaluating controversial plaque lesions, assessing stent implantation, and surveying stent-related vascular injury. Thus, OCT has potential to guide interventional cardiologists throughout the stent implantation procedure, impacting on planned interventional strategy. In addition, OCT is the most novel image technology to predict stent edge dissection for patients with non-ST-segment elevation acute coronary syndrome, enabling risk stratification of patients who are at a higher risk of this complication. Large-scale randomized trials are now warranted to assess whether OCT results and guidance during de procedure improve long-term clinical outcomes of PCIs.