Second-Generation Optical Coherence Tomography in Clinical Practice. High-Speed Data Acquisition Is Highly Reproducible in Patients Undergoing Percutaneous Coronary Intervention

Nieves Gonzalo, a Guillermo J. Tearney, b Patrick W. Serruys, a Gijs van Soest, a Takayuki Okamura, a Héctor M. García-García, a Robert Jan van Geuns, a Martin van der Ent, a Jurgen Ligthart, a Brett E. Bouma, b and Evelyn Regar a

aThoraxcenter, Erasmus MC, Rotterdam, The Netherlands
bWellman Center for Photomedicine, Massachusetts General Hospital, Boston, Massachusetts USA

This study was partially financed by Ligthlab Imaging, Inc., and Wellman Center of Photomedicine.

Correspondence: E. Regar, MD, PhD, Thoraxcenter, Bld 585, ‘s-Gravenjkkwal 230, 3015-CE Rotterdam, The Netherlands E-mail: e.regar@erasmusmc.nl

Received December 11, 2009. Accepted for publication February 19, 2010.

Introduction and objectives. The development of second-generation optical coherence tomography (i.e. Fourier domain optical coherence tomography, FD-OCT) has made it possible to perform high speed pull-backs during image acquisition without the need for transient occlusion of the coronary artery. The objective of this study was to assess the reproducibility of FD-OCT systems for characterizing plaque and evaluating stent implantation in patients undergoing a percutaneous coronary intervention.

Methods. The study included 45 patients scheduled for percutaneous coronary intervention who were enrolled between May and December 2008. Image acquisition was performed by FD-OCT using a non-occlusive technique and employing pull-back speeds ranging from 5 to 20 mm/s. Interstudy, interobserver and intraobserver reproducibility of plaque characterization and stent analysis were assessed.

Results. Fourier domain imaging was successfully performed in all patients (n=45). The average flush rate was 3±0.4 mL/s and the contrast volume per pull-back was 16.1±3.5 mL. The mean pull-back duration and length were 3.2±1.2 s and 53.3±12.4 mm, respectively. The interstudy reproducibility for visualizing edge dissection, tissue prolapse, intrastent dissection and malapposition was excellent (κ=1). The kappa values for interstudy, interobserver and intraobserver agreement on plaque characterization were 0.92, 0.82 and 0.95, respectively.

Conclusions. A second-generation OCT system (i.e. FD-OCT) involving high-speed data acquisition demonstrated good interstudy, interobserver and intraobserver reproducibility for characterizing plaque and evaluating stent implantation in patients undergoing a percutaneous coronary intervention.

Key words: Optical coherence tomography. Reproducibility. Stent assessment. Atherosclerotic plaque.

Tomografía de coherencia óptica de segunda generación en la práctica clínica. La adquisición de datos de alta velocidad muestra una reproducibilidad excelente en pacientes tratados con intervenciones coronarias percutáneas

Introducción y objetivos. Se ha desarrollado una segunda generación de sistemas de tomografía de coherencia óptica (OCT) (dominio de Fourier, OCT-DF) que permiten las retiradas a alta velocidad sin necesidad de ocluir transitoriamente la arteria coronaria durante la obtención de imágenes. El objetivo de este estudio es evaluar la reproducibilidad de los sistemas de OCT-DF para la caracterización de la placa y la evaluación de la implantación del stent en pacientes a los que se practican intervenciones coronarias percutáneas.

Métodos. Entre mayo y diciembre de 2008, se incluyó en el estudio a 45 pacientes para los que se había programado una intervención coronaria percutánea. La adquisición de la OCT-DF se realizó con una técnica no oclusiva con velocidades de retirada de entre 5 y 20 mm/s. Se evaluó la reproducibilidad entre estudios, entre observadores y en el observador para la caracterización de la placa y el análisis de los stents.

Resultados. La obtención de imágenes de dominio de Fourier se realizó satisfactoriamente en todos los pacientes (n = 45). El ritmo de infusión medio fue de 3 ± 0.4 ml/s y el volumen de contraste por retirada, 16.1 ± 3.5 ml. La media de duración y longitud de la retirada fue de 3.2 ± 1.2 s y 53.3 ± 12.4 mm. La reproducibilidad entre estudios, en cuanto a la visualización de la disección del borde, el prolapso tisular, la disección en el stent y la mala aposición, fue excelente (κ = 1). Los valores de kappa para la coincidencia entre estudios, entre observadores y en el observador para la caracterización de la placa fueron 0.92, 0.82 y 0.95 respectivamente.
INTRODUCTION

Optical coherence tomography (OCT) has emerged in recent years as one of the most promising intracoronary diagnostic tools.\(^1\)\(^2\) This light based imaging technique is able to generate images of the coronary artery with a level of resolution (10 µm) never reached before in vivo. This has offered new insights into atherosclerotic plaque pathology as well as into acute and long-term vessel wall response to stent implantation.\(^3\)\(^4\)

Up to now, the main challenge for a widespread clinical application of intracoronary OCT was a rather complex imaging procedure. Blood causes multiple light scattering and substantial signal attenuation, and needs to be cleared from the vessel during OCT image acquisition. The first generation commercially available time domain (TD) OCT systems employed proximal occlusion of the vessel with a low-pressure balloon (0.5 atm), similar to angioscopy, and simultaneous, distal flush delivery during pull-back of the OCT imaging probe.\(^9\) This protocol limited the coronary segment that could be imaged, and intrinsically created myocardial ischemia during imaging, restricting OCT to selected patient cohorts.\(^10\)\(^13\)

The new generation OCT systems (other monikers for the same technology are Fourier domain [FD] OCT, optical frequency domain imaging [OFDI], spectral domain imaging or swept source OCT) were developed to overcome this limitation. Most distinctively, these second generation OCT systems do not require transient balloon occlusion. Unprecedented capacity for data acquisition and pull-back speeds (20 mm/s) allow for the visualization of long coronary segments within a few seconds while blood is temporally displaced by the injection of flush through the guiding catheter.\(^14\)

While this concept is attractive, there has been no systematic research investigating the impact of such high pull-back speeds on the reproducibility of data obtained in the clinical setting. On theoretical grounds, the rapid acquisition reduces the motion of artifacts during the heart cycle, and thus, potentially, sources of error, whereas an increased pitch between consecutive, cross-sectional images could add sources of error. The FD-OCT frame rate is typically 100 frames per second, which at a pull-back speed of 20 mm per second, results in 5 frames per mm or a frame pitch of 200 micron. A typical TD-OCT frame rate is 20 frames per second, with a pull-back speed of 3 mm per second, resulting in 7 frames per mm or a pitch of 142 microns.

The objective of the present study was to assess the reproducibility of the new generation, intracoronary FD-OCT systems for plaque and stent assessment in vivo. We investigated therefore the reproducibility of morphologic features that have been described in the past to be of potential clinical relevance in patients undergoing percutaneous coronary intervention (PCI).

METHODS

Study Population

Non-consecutive patients scheduled for elective PCI were enrolled between May and December 2008. The study protocol was approved by the Ethics Committee of Erasmus Medical Center. All the patients gave written informed consent. Exclusion criteria for FD-OCT imaging were: \(a\) TIMI 0 flow at target lesion site; \(b\) lesion beyond acute bends or in a location within the coronary anatomy where the catheter cannot reach.

Technical Principles of New Generation Optical Coherence Tomography

OCT uses reflected light to create high-resolution cross-sectional images of the vessel. An interferometer splits the light source into 2 “arms” – a reference arm and a sample arm, which is directed into the tissue. The images are created based on the comparison of the back-reflected optical intensity from the 2 arms (interference signal).

The first clinically available OCT systems used TD technology, while new generation systems are based on FD technology.
Both TD-OCT and FD-OCT use low-coherent near-infrared light. A wavelength around 1300 nm is selected because it minimizes the energy absorption in the light beam caused by protein, water, haemoglobin and lipids. TD-OCT uses a broadband light source and the reference arm contains a moving mirror that allows scanning of each depth position in the image pixel by pixel. This mechanical scanning process limits the rate at which images can be acquired. FD-OCT uses a wavelength-swept laser as a light source and the reference mirror is fixed. This change in technology results in a better signal-to-noise ratio and faster sweeps, allowing a dramatically higher A-line rate, and hence a faster image acquisition and pull-back speed than TD-OCT.\textsuperscript{16,17}

**Fourier Domain-Optical Coherence Tomography Systems**

Two different FD-OCT prototypes were used (LightLab Imaging, Inc, Westford, MA and Wellman Center for Photomedicine, MGH, Boston, MA). All systems use a wavelength-swept laser as a light source. Table 1 summarizes the specifications of the second generation systems compared to TD-OCT (LightLab Imaging, Inc, Westford, MA). All FD-OCT imaging catheters had a short monorail design, with catheter profiles ranging from 2.4 Fr to 3.2 Fr, but all of them were compatible with 6F guiding catheters. FD-OCT imaging catheters contained a fiber-optic imaging core covered by and withdrawn within a translucent sheath. The optical imaging core rotated at approximately 100 revolutions per second and the pull-back speed ranged from 5 to 20 mm/s using a dedicated pull-back device. Data were processed in real time and digitally stored.

**Optical Coherence Tomography Data Acquisition**

We used a standard femoral approach in all patients. Weight adapted, unfractionated heparin was given to maintain an activated clotting time >300 s. After placement of the guiding catheter (6 F) into the coronary ostium, a standard PCI guide wire was advanced into the coronary artery in conventional manner. FD-OCT imaging was performed before stenting (cohort A) and after stent implantation (Cohort B). After administration of nitrates (0.2 mg NTG ic), the FD-OCT imaging catheter was advanced into the coronary artery in rapid exchange technique.

Radiopaque markers at the distal catheter tip and at the imaging core allowed positioning of the optical probe distal to the region of interest. (Figure 1). After FD-OCT catheter placement, blood was cleared by injection of iso-osmolar contrast (Iodixanol 370, Visipaque\textsuperscript{TM}, GE Health Care, Ireland) at 37\degree Celsius with an injection pump (Mark-V ProVis, Medrad, Inc. Indianola, PA, US; flow rate 3 mL/s) through the guiding catheter. The FD-OCT pull-back was started as soon as the artery was cleared from blood and stopped when the imaging core reached the guiding catheter.

**Assessment of Interstudy and Interobserver Reproducibility**

Pull-backs in native coronaries as well as after stent implantation were analyzed as follows. To evaluate the interstudy reproducibility, a FD-OCT pull-back through the region of interest was repeated using the same catheter twice under identical conditions of pull-back speed, frame rate and flush rate. The catheter was not removed from the artery between the 2 acquisitions. These 2 pull-backs were then analyzed independently. To evaluate the interobserver variability, 2 experienced OCT analysts reviewed the first FD-OCT pull-backs independently. To evaluate intraobserver variability, one observer repeated the analysis of the same pull-back one week later.

**Stent Assessment**

After stent implantation, study and observer agreement for the following parameters was evaluated according to the following definition\textsuperscript{18}: a) edge dissection: disruption of the endoluminal
vessel surface at the stent edges (5 mm prox and distal); b) tissue prolapse: protrusion of tissue between the stent struts without disruption of the continuity of the endoluminal vessel surface; c) intra-stent dissection: disruption of the vessel endoluminal vessel surface in the stent segment; and d) malapposition: presence of at least one strut separated from the vessel wall (Figure 2). Incidence of these phenomena was assessed on a per vessel basis.

**Plaque Type Assessment**

Native coronary segments were evaluated as follows: 60 corresponding atherosclerotic plaques were selected in both pull-backs, using landmarks such as side branches or stent edges. The 2 observers assessed these pre-selected plaques according to the following definitions: a) fibrous plaque: homogeneous, highly backscattering regions, b) fibrocalcific plaque: low scattering regions with sharply delineated borders; and c) lipid-rich plaque: diffusely bordered low scattering regions (Figure 3).

**Statistical Analysis**

Continuous variables are expressed as mean (standard deviation) and categorical variables are expressed as percentages. The kappa coefficient (κ) was used to test the inter-study, interobserver and intraobserver agreement for plaque characterization and stent assessment.

**RESULTS**

**Patient Characteristics and Fourier Domain-Optical Coherence Tomography Imaging Success**

Forty-five patients (49 vessels) were enrolled in the study. The average age was 63 (10) years and 80%
Gonzalo N et al. Reproducibility of Second-Generation OCT

Rev Esp Cardiol. 2010;63(8):893-903

897

Figure 2. Stent implantation assessment. Clinical examples of edge dissection (A, A'), intrastent dissection (B, B'), tissue prolapse (C, C') and malapposition (D, D') obtained with different Fourier Domain-OCT systems in different patients (upper panel Wellman Center for Photomedicine, MGH; lower panel Lightlab Imaging Inc).

TABLE 2. Fourier Domain-Optical Coherence Tomography Imaging Characteristics

<table>
<thead>
<tr>
<th>Vessel</th>
<th>LAD</th>
<th>21/49 (42.8%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCX</td>
<td>14/49 (28.6%)</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>13/49 (26.6%)</td>
<td></td>
</tr>
<tr>
<td>LIMA</td>
<td>1/49 (2.0%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indication for FD-OCT</th>
<th>Neuroradiology (2 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque assessment</td>
<td>2 (4.5%)</td>
</tr>
<tr>
<td>Post stent implantation</td>
<td>24 (53.3%)</td>
</tr>
<tr>
<td>Pre and post stent implantation</td>
<td>10 (22.2%)</td>
</tr>
<tr>
<td>Follow-up stent</td>
<td>9 (20%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pull-back Speed, mm/s</th>
<th>20</th>
<th>32/49 (65.3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10</td>
<td>10/49 (20.4%)</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>1/49 (2.0%)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>6/49 (12.3%)</td>
</tr>
</tbody>
</table>

| Flush rate, mL/s   | 3 | 0.4 |
| Pull-back duration, s | 3.2 | 1.2 |
| Pull-back length, mm | 53.3 | 12.4 |
| Contrast volume per pull-back, mL | 16.1 | 3.5 |

FD-OCT indicates Fourier Domain- optical coherence tomography; LAD, lateral anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; LIMA, left internal mammary artery.

were males. The incidence of cardiovascular risk factors was as follows: 23/45 (51%) hypertension, 12/45 (27%) diabetics, 29/45 (64%) dyslipidemia, and 13/45 (29%) current smoking. Nineteen patients (42%) had suffered a previous myocardial infarction, 7/45 (16%) had coronary artery bypass surgery and 22/45 (49%) had previous PCI. The indication for the elective PCI was stable angina in 31/45 (69%), unstable angina in 10/45 (22%) and acute myocardial infarction in 4/45 (9%).

The imaging probe could be positioned successfully in the coronary artery in all patients. Ninety-seven pull-backs showed excellent image quality. Artifacts that did not allow a proper image assessment were observed in 12 pull-backs and 2 pull-backs were not evaluable due to incomplete blood clearance. The procedural characteristics are summarized in Table 2. The implanted stent type was at the operator discretion. In 10 patients, FD-OCT was performed before and after stent implantation at the discretion of the operator. After treatment of the culprit lesion, a second vessel was selected for plaque assessment in 2 patients (4.5%) and for follow-up of a previously implanted stent in 9 patients (20%).

During FD-OCT imaging, transient chest pain and ECG changes were observed in 8% and 10% of the patients respectively. The ECG changes consisted of ST depression or T wave changes. ST elevation was not observed in any case. No coronary dissection, perforation spasm, embolization, arrhythmia, or other adverse event occurred.
Stent Assessment Reproducibility

OCT analysis after stent implantation was performed in 27 patients (28 vessels). Edge dissection was observed in 14 vessels (50%). Twenty-five (89%) showed evidence of tissue prolapse and 26 (93%) showed intrastent dissection. Malapposition of at least one strut was visible in 23 vessels (82%). The interstudy reproducibility (n=17 vessels) for the visualization of edge dissection, tissue prolapse, intrastent dissection and malapposition was excellent ($\kappa=1; P<.001$). The kappa values for inter and intraobserver reproducibility are shown in Table 3.

Plaque Characterization Reproducibility

A total of 60 plaques were identified in both pull-backs. Figure 4 summarizes the classification results. There was agreement between the 2 pull-
The main findings are: the new generation, FD-OCT technology with high-speed pull-back a) has excellent inter-study reproducibility in vivo; b) allows for reproducible plaque classification; and c) allows assessment of periprocedural vessel trauma associated with coronary stent implantation with low interobserver, intraobserver and interstudy variability.

The present study also confirms that the new OCT systems allow visualization longer coronary segments (average, 54.4 [12.5] mm) in less time (average, 3.5 [1.4] sec) and with less flush volume as compared to previously reported data for TD-OCT. This is in agreement with a recently published study by Takarada et al comparing TD-OCT and FD-OCT in patients treated with stents.

OCT has rapidly evolved to an attractive intracoronary imaging tool for the interventional cardiologists, as it offers the potential to address clinically relevant issues that may improve routine stent implantation and consequently long-term outcome. Its high in-vivo resolution allows for an accurate assessment of the mechanical stent vessel wall interaction, including strut apposition and periprocedural dissections. In the drug-eluting stent era, reasons for failure, including restenosis

<table>
<thead>
<tr>
<th>TABLE 3. Inter and Intraobserver Reproducibility for Stent Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Malapposition</td>
</tr>
<tr>
<td>Edge dissection</td>
</tr>
<tr>
<td>Tissue prolapse</td>
</tr>
<tr>
<td>Infrastent dissection</td>
</tr>
</tbody>
</table>

The values indicate the kappa coefficients for each parameter.

backs for plaque classification in 57 out of the 60 plaques (κ=0.92; P<.001) (Figure 5). Interobserver variability showed agreement for 2 observers in the classification of 53 out of 60 plaques (κ=0.82; P<.001). The intraobserver variability showed agreement in the classification of 58 out of 60 plaques (κ=0.95; P<.001).

DISCUSSION

To our knowledge, this is the first study assessing the interstudy, interobserver and intraobserver reproducibility of FD-OCT systems for stent assessment and plaque characterization in vivo.
OCT has proven useful for the evaluation of the acute effects of stent implantation on the vessel wall. In the present study, a high proportion of the patients showed evidence of tissue prolapse between the stent struts or intra-stent dissections, likewise edge dissections were visible in half of the cases. Even more pronounced, malapposition of at least one individual strut was observed in the majority of the cases. The inter- and intraobserver reproducibility of TD-OCT for stent assessment after implantation was evaluated by Kubo et al. They showed an acceptable intraobserver concordance for inadequate stent apposition ($\kappa=0.90$), tissue protrusion ($\kappa=0.92$), stent edge dissection ($\kappa=0.96$), and residual ruptured plaque ($\kappa=0.92$). Relatively lower interobserver concordance for inadequate stent apposition ($\kappa=0.75$), tissue protrusion ($\kappa=0.86$), stent edge dissection ($\kappa=0.89$), and residual ruptured plaque ($\kappa=0.86$) was found. In our data, the inter-study reproducibility for the identification of edge dissection, tissue prolapse, intrastent dissection, and late stent thrombosis are poorly understood.

In this particular clinical scenario, detailed assessment of the vascular microstructure might be helpful to prevent potentially life threatening events, such as stent thrombosis, as it has been linked to incomplete healing, mechanical stent failure and incomplete coverage of lipid rich or necrotic core lesions. The relatively complex imaging procedure hampered the use of the first generation, TD-OCT in patients undergoing PCI. In the present study, we evaluated the new FD-OCT systems that simplify the acquisition procedure and can contribute to spread the clinical application of this imaging technology.

The data presented in the article corresponds to the first cases performed in our center with the FD-OCT systems and also reflects the learning curve of the operators. Optimization of the acquisition technique can reduce the number of cases with incomplete blood clearance. A recent study showed that FD-OCT allows a clear visualization of 99.4% of the segments imaged (as compared with 80.8% with TD-OCT).
and malapposition was excellent. The inter- and intraobserver reproducibility showed a certain degree of variability, especially for malapposition assessment. In the present study, malapposition was evaluated by visual assessment. This qualitative analysis can be affected by the artifact of the shadow produced by the struts. Furthermore, in drug-eluting stents, the presence of polymer must be taken into account when evaluating malapposition and a correction for the strut thickness of each individual stent type should be applied. The use of a quantitative method to define malapposition could help to improve the inter- and intraobserver reproducibility.

The assessment of stent malapposition is of clinical relevance as there is IVUS data suggesting a possible relationship between this phenomenon and stent thrombosis. Previous studies have suggested increased malapposition at overlap areas and in closed cell designs. This could represent a potential link to stent fracture and restenosis.

A previous OCT study by our group reported that after stent implantation tissue prolapse was visible in 97.5%, intra-stent dissection in 86.3% and edge dissection in 25% of the cases. Furthermore, 63.8% of the patients showed at least one malapposed strut. This study showed also that those findings were not associated with clinical events during the hospitalization. However, the long-term implications are not known and should be the objective of future studies. Second-generation OCT has made this information much more accessible due to a simplified acquisition procedure. This greatly facilitates studies to understand the clinical relevance of these findings in large patient populations, especially with quantitative assessment methods for malapposition.

Plaque Characterization Reproducibility

The present study demonstrates also an excellent interstudy reproducibility for plaque characterization. Fifty-seven out of the 60 plaques were classified congruently in both pull-backs. There were only 3 cases of misclassification between fibrous and lipid-rich plaques. The observed inter and intraobserver variability for plaque characterization is in line with reported with TD-OCT in-vitro data ($\kappa=0.88$ and 0.91 for inter- and intraobserver, respectively). In vivo, Jang et al reported acceptable intraobserver concordance for lipid-rich plaque ($\kappa=0.86$) and calcification ($\kappa=0.88$), with a higher interobserver variability (lipid-rich plaque $\kappa=0.47$, calcification $\kappa=0.57$). In contrast to earlier reported data, that have highlighted the risk of misclassification between lipid pools and calcium deposits, in our series the most frequent disagreement between observers concerned the classification of fibrous and lipid-rich plaques. This might be related with the presence of artifacts derived from the catheter position or its optical efficiency during rotation. These artifacts can create false low scattering regions that can be misinterpreted as lipid-rich plaques. Quantitative plaque characterization methods under development could help to overcome the limitations of observer-dependent, visual evaluation.

Three-dimensional reconstructions of human coronary stented arteries with plaque characterization and macrophages detection derived from optical frequency domain imaging have been reported. This opens new possibilities for the in vivo evaluation of coronary atherosclerosis and the effect of coronary stenting.

The assessment of plaque characteristics in the catheterization laboratory can be helpful to guide PCI (eg, to recognize the lower distensibility of heavily calcified lesions) and has potential value for the detection of plaques with high risk of rupture. Compared to histology, OCT has proven to have high sensitivity and specificity to detect some of the features associated with rupture-prone lesions such as necrotic core, presence of macrophages and thin fibrous cap.

Limitations

The present study is observational and has a limited sample size. To assess the interstudy reproducibility the pull-back was repeated twice under identical conditions. We acknowledge that the change in the acquisition conditions might affect the inter-study reproducibility. Even when we tried to include a variety of atherosclerotic plaques with different morphology and composition, the pre-selection of the plaques might have influenced the reproducibility. We acknowledge that some of the findings defined as tissue prolapse may correspond to thrombus, as the differentiation between those 2 entities after stent implantation can be difficult.

CONCLUSIONS

The second generation OCT technology (FD-OCT) with high speed data acquisition shows good inter-study, interobserver and intraobserver reproducibility for plaque characterization and stent implantation assessment in patients undergoing PCI.

ACKNOWLEDGMENTS

This study was supported in part by Lightlab Imaging Inc and the Wellman Center of Photomedicine. We would like to thank Robert Beurskens for invaluable technical assistance with the imaging systems.

Gonzalo N et al. Reproducibility of Second-Generation OCT

Rev Esp Cardiol. 2010;63(8):893-903 901
REFERENCES


33. Kubo T, Imanishi T, Takarada S, Kuroi A, Ueno S, Yamano
T, et al. Assessment of culprit lesion morphology in acute
myocardial infarction: ability of optical coherence tomography
compared with intravascular ultrasound and coronary

34. Kume T, Akasaka T, Kawamoto T, Okura H, Watanabe
N, Toyota E, et al. Measurement of the thickness of the
fibrous cap by optical coherence tomography. Am Heart J.