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An invited review following *the Soujinkai Fujiu Memorial Award*: Development of Stent-enhanced 3D Optical Coherence Tomography and its Clinical Application for Coronary Bifurcation Lesions

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Abstract Three-dimensional optical coherence tomography (3D-OCT) has been introduced as guidance for percutaneous coronary intervention. It facilitates understanding of the device's interaction with the coronary arteries, particularly in bifurcation lesions. This review describes the development and recent advances in 3D-OCT and its clinical applications.

Key words: three-dimensional, optical coherence tomography, coronary artery disease, bifurcation lesion, coronary intervention

Introduction

Optical coherence tomography (OCT) is an imaging modality that acquires high-resolution coronary tomographic images by sweeping the inside of coronary arteries using near infrared as a light source. This modality allows for visualization of the vascular luminal surface with approximately 10 times greater resolution than that of intravascular ultrasound.[1] Utilizing a swept-source laser that can change its frequency at high speed, frequency-domain OCT enables high-speed pullback and can acquire continuous tomographic images that are less affected by the heartbeat.[2] Tearney et al. reported that the inside of blood vessels can be observed three-dimensionally by reconstructing these continuous tomographic images.[3] Following this report, the function of three-dimensional (3D) visualization was installed on the console of St. Jude's ILUMIEN FD-OCT system, but stents implanted in coronary arteries were not visualized on the screen. We newly developed a stent-enhanced 3D OCT that realizes unique stent visualization and observed the interaction between the coronary arterial wall and stents placed by percutaneous coronary intervention (PCI).

Principle

Stents placed in the coronary artery cannot be clearly depicted only by 3D construction of continuous OCT cross-sectional images. Metallic stent struts present as a thin bright line that casts a shadow because the metal completely reflects near-infrared beams from the OCT catheter. The shadow of the stent is drawn on surrounding tissue in the 3D image. In the portion where the stent is separated from the blood vessel wall (i.e., side branch [SB] orifice), the stent cannot be confirmed (Fig. 1E).

On the A-line, a peak-intensity signal is exhibited on the surface of the luminal side of the stent and there is a shadow with low signal intensity behind the strut (Fig. 1C). We developed in-house software that automatically detects these characteristic signals, emphasizes the stents, and then exports cross-sectional images to bitmap sequence files frame by frame (Fig. 1D). By reconstructing continuous cross-sectional images with commercially available volume-rendering software (INTAGE Realia, Cybernet, Tokyo, Japan), we succeeded in displaying a 3D OCT with a clearly depicted stent (Fig. 1F). The resolution in the long axis direction depends on the pullback speed. The slower the sweep, the better the resolution in the long axis, but there is an increase in heartbeat artifacts. On the contrary, the faster the sweep, the thicker the frame in the long axis, resulting in less stent continuity on the 3D image. There is a trade-off between the resolution in the long axis direction and the heartbeat artifact, and a pullback with a frame thickness of 0.1 - 0.125 mm is appropriate to precisely identify the strut configuration.[4]

To create a 3D OCT image off-line, 3 steps are necessary. First, raw OCT data are needed to output from the console to the hard drive, then the stent is detected with dedicated software, and finally, the 3D image is created with volume-rendering software. By improving the work process, it became possible to show a 3D OCT image in approximately 5 min. We reported successful observation of the stent during a PCI procedure.[5] After that, the same function was installed on the OCT / OFDI console, and now stent-enhanced 3D OCT images can be observed on the console immediately after the OCT image acquisition.[6]

Clinical usefulness

Using the stent-enhanced 3D-OCT, we evaluated various cases of stents placed in coronary arteries. The thrombus formed in the stent was clearly visible as an irregular surface mass and disappeared after administration of the IIb/IIIa inhibitor followed by post-dilation.[7] In addition, the absorption process of the bioabsorbable scaffold crossing over the SB was clearly observed.[8] Stent fracture causing re-stenosis in the remote phase was demonstrated by 3D OCT.[9] In a case in which the proximal part of the implanted stent was deformed by the Filtrap™ catheter during PCI, 3D OCT clearly showed how the stent was deformed and the guide wire could be successfully reinserted by the appropriate route with the deformed stent restored by ballooning.[10] We reported cases in which the

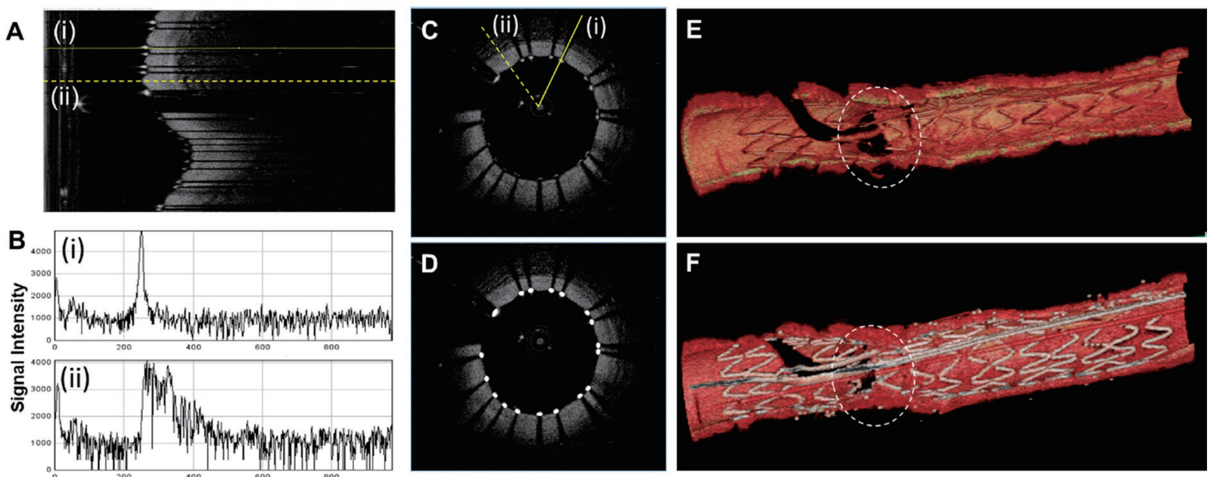

Fig. 1 Principle of stent-enhanced 3D optical coherence tomography

A. Multiframe TIFF image, B. Signal intensity profile, C. Conventional cross-sectional OCT image, D. Stent-enhanced OCT image. E. 3D reconstruction, F. Stent-enhanced 3D reconstruction. (i) and (ii) in panels A − C indicate stent strut and fibrous tissue, respectively. Dotted circles in panels E and F indicate the side branch orifice.

guide wire passed through the stent struts in front of the ostium into a jailed SB was observed by 3D OCT during bifurcation PCI.[5] Stent-enhanced 3D OCT facilitated understanding of the interaction between stents and the coronary arterial wall or PCI guide wires.

Clinical application for coronary bifurcation lesions

During coronary bifurcation PCI, 23 consecutive cases were observed using stent-enhanced 3D OCT. This study showed that not only the recrossing location of the guide wire into the jailed SB, but also the positional relationship between the bifurcation carina and the longitudinal stent-link are strongly associated with the frequency of the residual jailed struts after SB dilation (Fig. 2).[11] Because the treatment of bifurcation lesions may be influenced by the operator's preference, a multicenter prospective registry was conducted to examine the factors affecting SB dilation.[12] One hundred sixty-eight cases were enrolled from 11 institutions in Japan. Of these, 115 cases underwent a standard single stent procedure with final kissing balloon inflation (FKBI). Incomplete stent apposition (ISA), including residual jailed struts at the ostium of the SB after FKBI, could thus be analyzed. Multivariate analysis revealed that the bifurcation angle between the distal main vessel (MV) and SB, the stent configuration covering the SB (presence of the longitudinal stent-link), and the guide wire recrossing position were strongly associated with the residual ISA at the SB ostium after FKBI. The incidence of ISA in the group in which the guide wire was passed through the distal cell without the link at the ostium of the SB (optimal kissing balloon inflation [KBI] group) was significantly smaller than that in other groups. The larger the BA, the greater the increase in the ISA, but the tendency was stronger in left main (LM) bifurcation than in non-LM bifurcation. The presence of the stent-link at the carina is a random factor. If there is no longitudinal stent-link at the carina, guide wire recrossing through the distal side is definitely better, in contrast to cases in which there is a link at the carina, where there was no significant difference regarding with incidence of ISA at the SB ostium after FKBI between the proximal and distal recrossing groups. No clear answer for this situation could be found due to the relatively small registration. Subsequent analysis using computational fluid dynamics revealed that the accumulation of struts in the carina

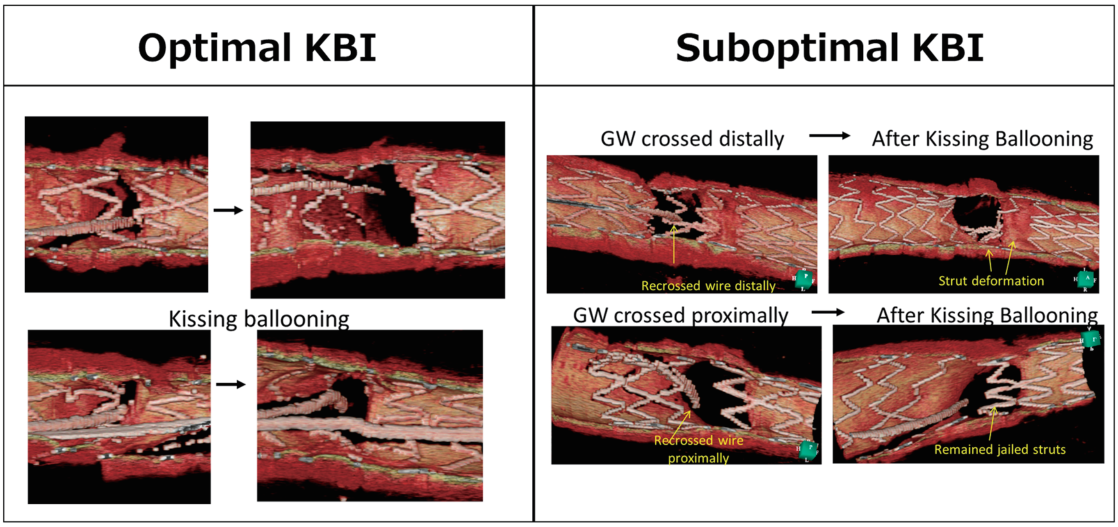

Fig. 2 Optimal and suboptimal final kissing balloon inflation
The recrossing location of the guide wire (GW) into the jailed side branch and the jailing configuration (positional relationship between bifurcation carina and the longitudinal stent-link) are strongly associated with the side branch opening after final kissing balloon inflation (KBI).

portion (called "metallic carina") created a low shear stress area around the struts, potentially leading to thrombus formation (Fig. 3). Although there was no difference in cardiovascular events 1 year after the index PCI, the rate of restenosis at the SB orifice tended to be lower in the optimal KBI group than in others. Furthermore, serial changes in the SB ostial area after FKBI were investigated. We retrospectively analyzed the cases of 37 consecutive patients who underwent provisional MV stenting with FKBI for coronary bifurcation lesions under OCT guidance and follow-up OCT at 6 to 12 months. We divided the patients into 2 groups (optimal KBI group vs others). Serial changes in the SB ostial area in the optimal KBI group significantly increased from baseline to follow-up, whereas in the other group, they tended to decrease (0.43mm^2 [-0.29 to 0.91] vs. -0.65mm^2 [-1.33 to 0.34]; P=0.0136 and 9.47% [-8.37 to 27.33] vs. -13.77% [-31.64 to 10.88]; P=0.0182).[13] This investigation suggested that optimal KBI was important to prevent SB ostial narrowing after provisional MV stenting with FKBI. The recrossing position of the guide wire is only a factor that can be controlled intentionally under 3D OCT guidance. The recrossing position in one-third of the cases was not at the optimal distal cell at the first attempt, resulting in the need for more attempts when the recrossing position of the guide wire into the jailed SB was confirmed by stent-enhanced 3D OCT after the operator's manipulation in attempt to insert the guide wire into the distal cell. In addition, the success rate of distal recrossing in the first attempt in LM cases was relatively low (56%) compared with non-LM cases (88%). Without confirmation of the recrossing position by 3D OCT, the SB would be expanded in an inappropriate cell, suggesting the importance of confirming the position by 3D OCT. To investigate this hypothesis, we conducted a multicenter, randomized controlled trial of 3D optical frequency domain imaging (OFDI; Terumo, Tokyo)-guided vs angio-guided bifurcation PCI. The primary endpoint was the frequency

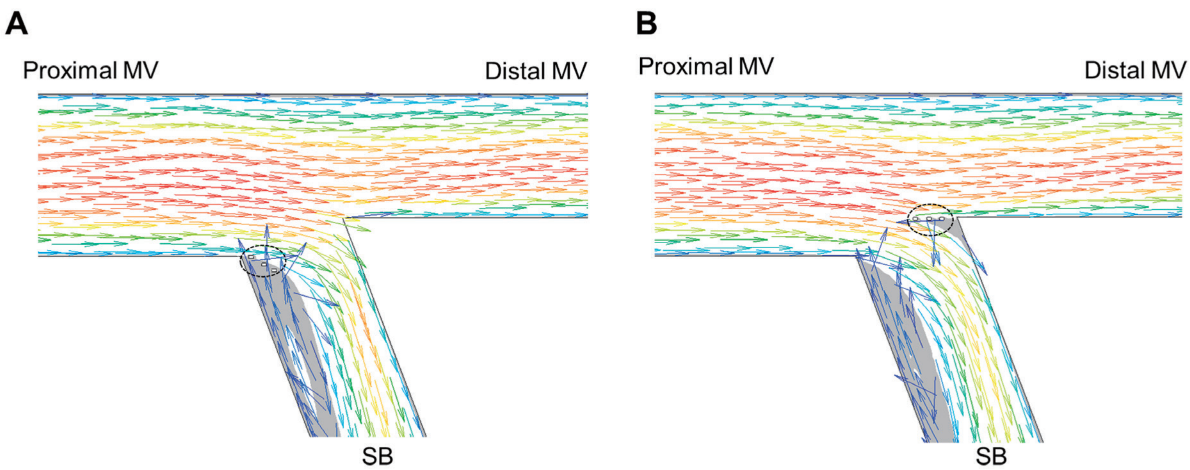

Fig. 3 Computational fluid dynamics
Effect of the accumulation of struts after final kissing balloon inflation (FKBI) on blood flow was demonstrated by computational fluid dynamics. An experimental bifurcation model was created with a proximal main vessel (MV) diameter of 5.25 mm, distal MV diameter of 4 mm, and side branch (SB) of 3.5 mm, and the branch angles were set to 70 degrees. The blood flow distribution of the distal MV:SB was set to 7:3 as the inflow condition and 0.02 m/s as the outflow condition, and the analysis was performed. A. Struts accumulate at the opposite side of the carina after FKBI with the distal recrossing. B. Struts accumulate at the carina after FKBI with the proximal recrossing. The dotted circle indicates the accumulation of struts. Although the blood flow line was affected by the remaining struts, a low velocity region (less than 0.2 cm/s, gray zone) was formed from the periphery of the struts to the downstream side.

of ISA at the entrance of the SB after FKBI. A total of 105 cases were entered. Feasibility of online 3D OFDI for assessing the wire recrossing point was 98.2%. Optimal wire recrossing was achieved in all lesions guided by the online 3D OFDI (56/56 lesions, 100%). The frequency of ISA after FKBI was significantly lower in the 3D OFDI-guided group than in the angio-guided group. Three-dimensional OFDI imaging guidance may therefore be preferable in bifurcation PCI.[14]

To date, it is unconfirmed whether stenting at bifurcation PCI under 3D OCT/OFDI guidance improves a patient's long-term clinical outcome. A registry is currently underway to enroll 600 bifurcation PCI cases at multiple centers and to investigate the long-term outcome.

Conclusion

Development and clinical usefulness of stent-emphasized 3D OCT/OFDI, particularly for guidance in bifurcation PCI, is described. The 3D reconstructed image of OCT/OFDI is expected to help visually clarify the relationship between the stent and blood vessel, and contribute to improving the outcome of PCI.

Conflict of Interest

The authors declare no conflict of interest.

Reference

1. Jang, I-K., Bouma, B.E., Kang, D-H., Park, S-J., Park, S-W., Seung, K-B., Choi, K-B., Shishkov, M., Schlendorf, K., Pomerantsev, E., Houser, S.L., Aretz, H.T. and Tearney, G.J.: Visualization of coronary atherosclerotic plaques in patients using optical coherence tomography: comparison with intravascular ultrasound. *J. Am. Coll. Cardiol.*, **39**(4): 604-609, 2002.
2. Gonzalo, N., Tearney, G.J., Serruys, P.W., van Soest, G., Okamura, T., Garcia-Garcia, H.M., Jan van Geuns, R., van der Ent, M., Ligthart, J., Bouma, B.E. and Regar, E.: Second-generation optical coherence tomography in clinical practice. High-speed data acquisition is highly reproducible in patients undergoing percutaneous coronary intervention. *Rev. Esp. Cardiol.*, **63**(8): 893-903, 2010.
3. Tearney, G.J., Waxman, S., Shishkov, M., Vakoc, B.J., Suter, M.J., Freilich, M.I., Desjardins, A.E., Oh, W-Y., Bartlett, L.A., Rosenberg, M. and Bouma, B.E.: Three-Dimensional Coronary Artery Microscopy by Intracoronary Optical Frequency Domain Imaging. *JACC Cardiovasc. Imaging*, **1**(6): 752-761, 2008.
4. Okamura, T., Onuma, Y., Garcia-Garcia, H.M., Bruining, N. and Serruys, P.W.: High-speed intracoronary optical frequency domain imaging: implications for three-dimensional reconstruction and quantitative analysis. *EuroIntervention*, **7**(10): 1216-1226, 2012.
5. Okamura, T., Yamada, J., Nao, T., Suetomi, T., Maeda, T., Shiraishi, K., Miura, T. and Matsuzaki, M.: Three-dimensional optical coherence tomography assessment of coronary wire re-crossing position during bifurcation stenting. *EuroIntervention*, **7**(7): 886-887, 2011.
6. Kume, T. and Uemura, S.: Current clinical applications of coronary optical coherence tomography. *Cardiovasc. Interv. Ther.*, **33**(1): 1-10, 2018.
7. Okamura, T., Serruys, P.W. and Regar, E.: Three-dimensional visualization of intracoronary thrombus during stent implantation using the second generation, Fourier domain optical coherence tomography. *Eur. Heart J.*, **31**(5): 625, 2010.
8. Okamura, T., Serruys, P.W. and Regar, E.: Cardiovascular flashlight. The fate of bioresorbable struts located at a side branch ostium: serial three-dimensional optical coherence tomography assessment. *Eur. Heart J.*, **31**(17): 2179, 2010.
9. Okamura, T. and Matsuzaki, M.: Sirolimus-eluting stent fracture detection by three-dimensional optical coherence tomography. *Catheter. Cardiovasc. Interv.*, **79**(4): 628-632, 2012.
10. Sugawara, Y., Uemura, S., Okamura, T., Ueda, T., Watanabe, M., Okayama, S. and Saito, Y.: Three-dimensional optical coherence tomography: Precise diagnosis of stent deformation. *IJC Heart Vessels*, **4**: 211-212, 2014.

11. Okamura, T., Onuma, Y., Yamada, J., Iqbal, J., Tateishi, H., Nao, T., Oda, T., Maeda, T., Nakamura, T., Miura, T., Yano, M. and Serruys, P.W.: 3D optical coherence tomography: new insights into the process of optimal rewiring of side branches during bifurcational stenting. *EuroIntervention*, **10**(8): 907-915, 2014.
12. Okamura, T., Nagoshi, R., Fujimura, T., Murasato, Y., Yamawaki, M., Ono, S., Serikawa, T., Hikichi, Y., Norita, H., Nakao, F., Sakamoto, T., Shinke, T. and Shite, J.: Impact of guidewire recrossing point into stent jailed side branch for optimal kissing balloon dilatation: core lab 3D optical coherence tomography analysis. *EuroIntervention*, **13**(15): e1785-e1793, 2018.
13. Fujimura, T., Okamura, T., Tateishi, H., Nakamura, T., Yamada, J., Oda, T., Mochizuki, M., Nishimura, S., Nishimura, T. and Yano, M.: Serial changes in the side-branch ostial area after main-vessel stenting with kissing balloon inflation for coronary bifurcation lesions, assessed by 3D optical coherence tomography. *Eur. Heart J. Cardiovasc. Imaging*, **19**(10): 1117-1125, 2018.
14. Onuma, Y., Kogame, N., Sotomi, Y., Miyazaki, Y., Asano, T., Takahashi, K., Kawashima, H., Ono, M., Katagiri, Y., Kyono, H., Nakatani, S., Muramatsu, T., Sharif, F., Ozaki, Y., Serruys, P.W. and Okamura, T.: A Randomized Trial Evaluating Online 3-Dimensional Optical Frequency Domain Imaging-Guided Percutaneous Coronary Intervention in Bifurcation Lesions. *Circ. Cardiovasc. Interv.*, **13**(12): e009183, 2020.