

# Serial optical coherence tomography and angioscopic assessments of 10-year in-stent restenosis of Cypher sirolimus-eluting stent treated with drug-coated balloon angioplasty

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## Abstract

The drug-coated balloon (DCB) angioplasty is considered a standard therapeutic option for in-stent restenosis. In the present case, we observed high-intensity spots on optical coherence tomography (OCT) and bright spots on coronary angioplasty (CAS) immediately after DCB angioplasty. The superficial high-intensity area on OCT presumably corresponded with the bright spots on CAS. The high-intensity superficial regions were thought to represent an iopropamide/paclitaxel mixture. The present serial observation demonstrated that the eluted drugs remained for at least 2 months but disappeared within 6 months. At the site where we observed the drugs, neointimal growth was successfully inhibited and stabilized at the 6-month follow-up. The association of eluted drugs after DCB angioplasty with consequent neointimal growth is of scientific interest. Further prospective imaging studies with a large sample size are warranted to clarify this association.

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## Keywords

Drug-coated balloon, optical coherence tomography, angiography, coronary angioplasty, in-stent restenosis, neointimal growth

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## Introduction

The drug-coated balloon (DCB) angioplasty is considered a standard therapeutic option for in-stent restenosis (ISR). Recent case reports have provided optical coherence tomography (OCT) and coronary angiography (CAS) findings immediately after DCB angioplasty.<sup>1,2</sup> However, longitudinal observations with OCT and CAS after DCB angioplasty have not been reported to date. In the present case report, we evaluated the longitudinal change of neointima after DCB angioplasty for a 10-year ISR of a first-generation drug-eluting stent with OCT and CAS.

## Case report

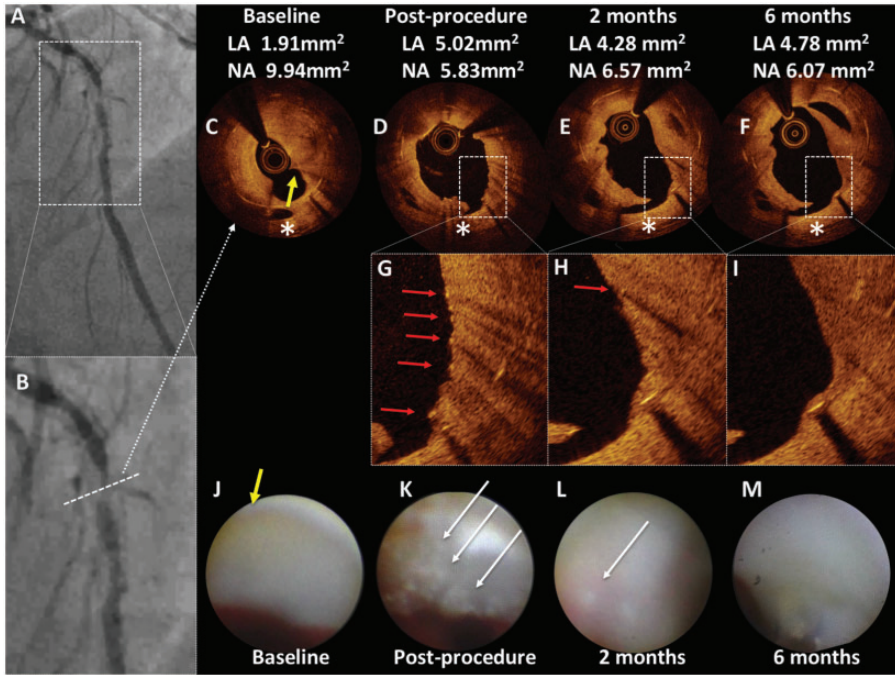
A 71-year-old man underwent primary percutaneous coronary intervention in the proximal left anterior descending artery with  $3.5 \times 18$  mm and  $3.0 \times 28$  mm Cypher sirolimus-eluting stents (Cypher SES, Cordis, Miami, FL, USA) 10 years ago. In 2016, coronary angiography performed because of his recurrent effort angina showed an ISR of the stents (Figure 1a, b). OCT (Dragonfly Optis imaging catheter, Abbott Vascular, Santa Clara, CA, USA) demonstrated a heterogeneous pattern of neointimal hyperplasia with a minimum lumen area of  $1.91 \text{ mm}^2$  (Figure 1c). The ISR was pre-dilated with a  $3.0 \times 13$  mm scoring balloon at 14 atm (NSE, Goodman, Japan), followed by  $3.0 \times 20$  mm and  $3.5 \times 26$  mm DCB at 14 atm (SeQuent Please, B Braun, Melsungen, Germany). Post-procedural OCT showed high-intensity

spots with and without shadows (Figure 1d, g), which appeared to correspond with the bright spots in the CAS images (Visible, FiberTech Co. Ltd., Tokyo, Japan) (Figure 1k, Movie 1). We performed both OCT and CAS under angiographic record, and angio-OCT and angio-CAS co-registration enabled matching of the OCT and CAS images. Serial imaging assessments of the ISR lesion with OCT and CAS at the 2- and 6-month follow-ups were performed. On OCT at the 2-month follow-up, a small high-intensity area with shadows was demonstrated (Figure 1e, h), whereas at the 6-month follow-up, the superficial high-intensity area had disappeared without incremental neointimal hyperplasia (Figure 1f, i). On CAS, bright spots and intimal hemorrhage remained at the 2-month follow-up (Figure 1l, Movie 2) but had disappeared at 6 months, and smooth neointimal coverage (yellow color grade 1, neointimal coverage grade 2) was observed (Figure 1m, Movie 3).<sup>3</sup> Although the neointimal area increased slightly at 2 months (from  $5.83$  to  $6.57 \text{ mm}^2$ ), it had decreased at the 6-month follow-up (from  $6.57$  to  $6.07 \text{ mm}^2$ ).

The patient provided informed consent for the procedures and for publication of this case report.

## Discussion

We observed high-intensity spots on OCT and bright spots on CAS following the procedure. The superficial high-intensity area on OCT presumably corresponded with the bright spots on CAS.<sup>1,2,4</sup>



**Figure 1.** In-stent restenosis of the Cypher sirolimus-eluting stent at 10-year follow-up (a, b) was treated by drug-coated balloon angioplasty. Matched OCT cross-sections at baseline MLA site (c to i) with corresponding angiographic images (j to m) are presented. The yellow arrows show heterogeneous and light-attenuating neointima on OCT (c) and the yellow plaque on coronary angiography (j); the red arrows show high-intensity spots (g, h); and the white arrows show bright spots (k, l). OCT, optical coherence tomography; MLA, minimum lumen area; LA, lumen area; NA, neointimal area; \* indicates side branch.

The high-intensity superficial regions are thought to represent an iopromide/paclitaxel mixture.<sup>4</sup> At the 2-month follow-up, the spots remained but were fewer in number. At 6 months, we no longer observed any spots on OCT or CAS. This serial observation demonstrated that the eluted drugs remained for at least 2 months and disappeared within 6 months. Previous pathological data from an animal study support these findings.<sup>5</sup>

Demonstrating an association between the spots on CAS or OCT and consequent neointimal growth would be of scientific interest. In the present case, the vessel surface covered by the antiproliferative drugs appeared to be stabilized because the

neointimal area did not significantly change or slightly decreased from the post-procedure assessment to the 6-month follow-up (post-procedure: 5.83 mm<sup>2</sup>; 2 months: 6.57 mm<sup>2</sup>; 6 months: 6.07 mm<sup>2</sup>). Homogeneous intima on OCT and the white intimal surface on CAS at 6 months also support this finding.<sup>6,7</sup> Effective DCB angioplasty might not only inhibit proliferation of neointima but also stabilize neointimal morphology. Further prospective imaging studies using a large sample size are warranted to investigate the association between drug elution and neointimal growth after DCB angioplasty. The combined use of OCT and CAS could play an important role in clarifying this association.

### Declaration of conflicting interest

S. Nakatani, Y. Sotomi, and Y. Higuchi received speaker honoraria from Bayer, Daiichi-Sankyo, Amgen, Astellas, BioPharma, Boehringer Ingelheim, Bristol-Myers Squibb, Abbott Vascular Japan, Boston Scientific Japan, Terumo, Cardinal Health, and Medtronic. Y. Sakata reports grants and personal fees from Daiichi-Sankyo, Bayer, Boehringer Ingelheim, and Bristol-Myers Squibb. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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