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Application of an enhanced device to transluminal retrieval of malappositioned coronary stents: An experimental study

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Objectives: This study investigated the application of a novel enhanced device to retrieval of deployed stents in a porcine coronary model.

Background: Recurrence of in-stent restenosis and stent thrombosis still remains to be resolved. Under these conditions, it is sometimes necessary to retrieve malfunctional stents responsible for thrombosis. However, few data exist regarding the feasibility and safety of retrieval device use in previously deployed coronary stents.

Methods: We have developed an enhanced device consisting of an asymmetric forceps, conducting shaft (1.6 mm diameter, 150 cm length), and control handle. Bare-metal stents (3 mm diameter) were implanted in four pigs to create a malapposition model. Coronary artery injury was evaluated by intravascular ultrasound (IVUS) and histological imaging on the first and 14th days.

Results: The device was delivered to the coronary artery using the existing catheter (7 Fr). After opening the forceps, the blade was forced into the space between the vessel wall and the stent, and the stent struts were then grasped with the forceps. This was then pulled back into the catheter, still grasping the stent struts with the forceps. All stents were successfully retrieved by this method ($n = 4$). On the first day, no apparent vessel wall injury was detectable by IVUS, although histological findings revealed damage to endothelial monolayer on retrieval of deployed stent. On the 14th day, mild intimal thickening was observed by IVUS and histology.

Conclusions: These results demonstrate that the present device can be applied to transluminal retrieval of acquired malappositioned coronary stents.

KEYWORDS
in-stent restenosis, stent retrieval, stent thrombosis

1 | INTRODUCTION

Drug-eluting stents (DES) have been developed to inhibit the response to vessel wall injury, mainly responsible for restenosis after stent implantation. As a result, restenosis and target-vessel revascularization after DES implantation have been reduced compared with bare-metal stents (BMS).[1] However, late strut malapposition with positive remodeling after stent implantation is associated with increased risk

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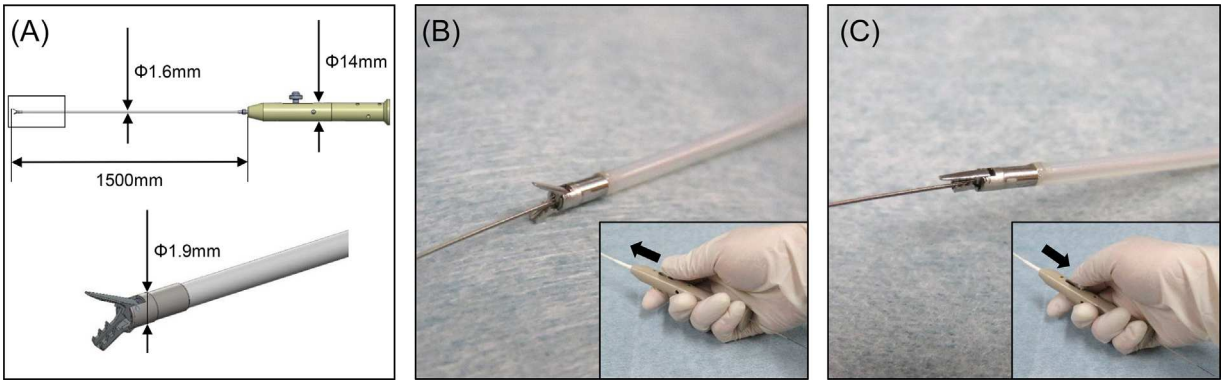

FIGURE 1 Device for retrieval of coronary stents. The device incorporates an asymmetric forceps which can be slipped into the space between the vessel wall and the stent (A). The forceps can be opened (B) and closed (C) with button operation of control handle. Note that the guidewire can be freely accessed through the center of the forceps (C)

of in-stent restenosis and very late stent thrombosis (VLST) leading to myocardial infarction and death,[2,3] although malapposition due to under sizing dose not likely replicate a clinical setting.

In some cases, such inappropriately positioned stents should be retrieved because of high risk of occurrence of regional thrombosis and blood-flow restriction.[4–8] Although several nonsurgical techniques for retrieval of intravascular foreign bodies have been investigated,[8–13] retrieval using such procedures has been difficult, and surgical techniques have still been required in some cases.[6,14,15]

There are several devices that enable to retrieve entrapped stents from dislodgment for fracture. However, at the time retrieving malapposed stents, we need different type of device such as that with forceps. For this purpose, we previously developed a prototype of device.[16] However, the device size and flexibility were not suitable for retrieving stents from coronary artery. Therefore, we developed an enhanced type of device with smaller forceps. The device shaft became more flexible than that of previous one. In this study, we have investigated the application of this enhanced device in a porcine coronary artery model.

2 | METHODS

2.1 | Device design

Our device consists of a forceps, a conducting shaft 1.6 mm in diameter and 150 cm in length, and a control handle (Figure 1A). The device incorporates an asymmetric forceps which can be slipped into the space between the vessel wall and the stent. The grip force of the

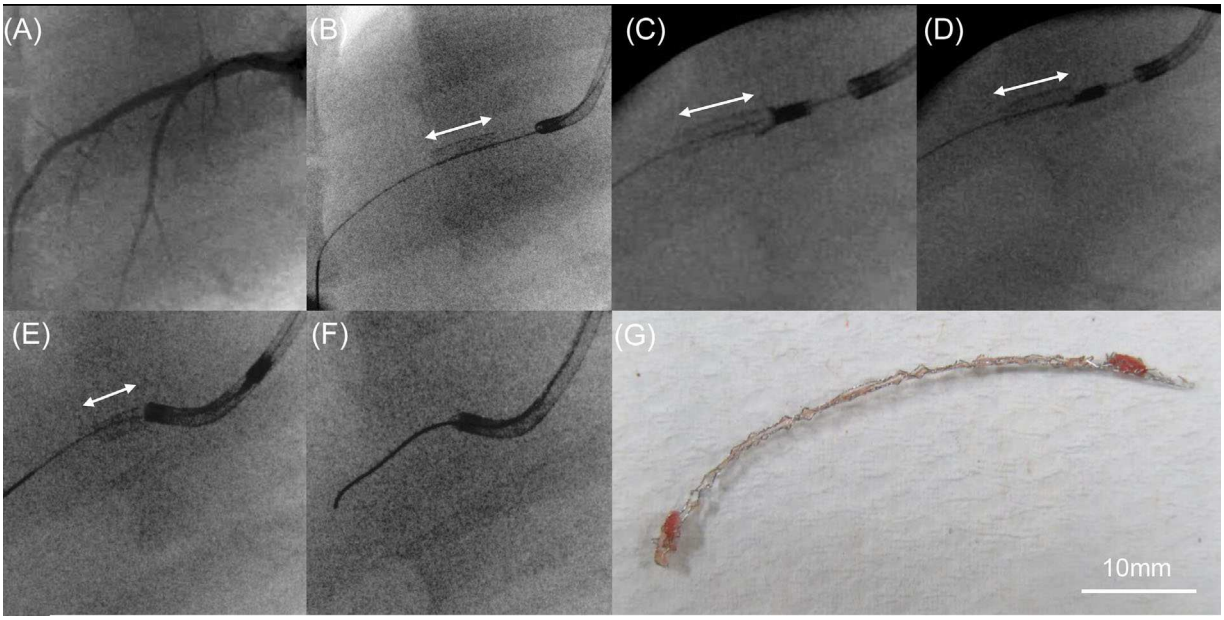

FIGURE 2 Procedure for retrieving a coronary stent. We implanted a bare-metal stent in left anterior descending artery (LAD) with malapposition (A, B). The device was delivered from the catheter to LAD and the blade of the forceps was forced to slip into the space between the vessel wall and the stent (C). The forceps successfully grasped the stent edge (D) and pulled the stent back into the catheter (E, F). Note that the stent was stretched parallel to its long axis and shortened in the short axis (G)

device is 19.6 N, which is sufficient to retrieve the deployed stent. The forceps can be opened and closed with button operation of the control handle (Figures 1B and 1C).

The device was designed to operate safely in the coronary artery which is more than 2.5 mm in diameter. To advance the device into the coronary artery, the device has a lumen in the center of the shaft to allow passage of a 0.014-in guidewire. Thus, the device can be advanced into the coronary artery as an over-the-wire system. Importantly, even in the closed position, the forceps have sufficient space for the guidewire to freely pass through (Figure 1C). The 7 Fr guiding catheter system was used to deliver the device and retrieve the deployed coronary stent.

2.2 | Animal study protocol

The animal study was approved by the Animal Care and Use Committee of Kanazawa University, and experiments were conducted according to the "Basic Guidelines for Conduct of Animal Experiments" published by the Ministry of Health, Labor, and Welfare, Japan.

BMS (Multi Link 8, Abbott, Chicago, IL) with 3 mm in diameter were implanted in four pigs (mean weight 34.8 kg); investigations were carried out on the first day of the procedure, or 14 days (n = 2, each time point) after stent retrieval. All pigs were treated with aspirin (200 mg, Bayer, Land Nordrheine-Westfalen, Germany) and clopidogrel (300 mg, Sanofi Aventis, Gouda, The Netherlands) pre-procedure. In the 14th day model, aspirin (200 mg) was administered daily until the end of the study. After anesthesia with ketamine (20 mg/kg intramuscularly), pigs were maintained under general anesthesia with sevoflurane and oxygen. During the experimental procedure, we carefully monitored level of anesthesia to maintain appropriate sedation. ECG, and heart rate were continuously monitored with a polygraph recording system (OptiPlex755, Nihon-Kohden, Tokyo, Japan) throughout the entire procedure. Heparin (5000 IU) was administered via the left carotid artery through a 7 Fr sheath, and 2000 IU were injected per hour.

Stent deployment was performed by the method previously described.[17] All stents were deployed to the left anterior descending artery (LAD). Briefly, stent delivery catheters (7 Fr Heartrail II, JR-4.0, TERUMO, Tokyo, Japan) were inserted through the sheath and were advanced over the 0.035-in guidewire to the orifice of the left coronary artery. After coronary angiography (Figure 2A), a 0.014-inch guidewire was inserted into LAD and intravascular ultrasound (IVUS) was performed to measure lumen diameter. To generate the malapposition stent model, BMS 3.0 mm in diameter were delivered with nominal or low pressure (less than nominal) to the artery which was 3.0-3.5 mm in diameter (Figure 2B). Inappropriate expansion of the stents at the proximal site was confirmed by IVUS. Stents were then retrieved by the device. After stent retrieval, IVUS and angiography were repeatedly performed to evaluate injury of the artery. In the 14th day model, IVUS was again performed to evaluate injury and healing responses before

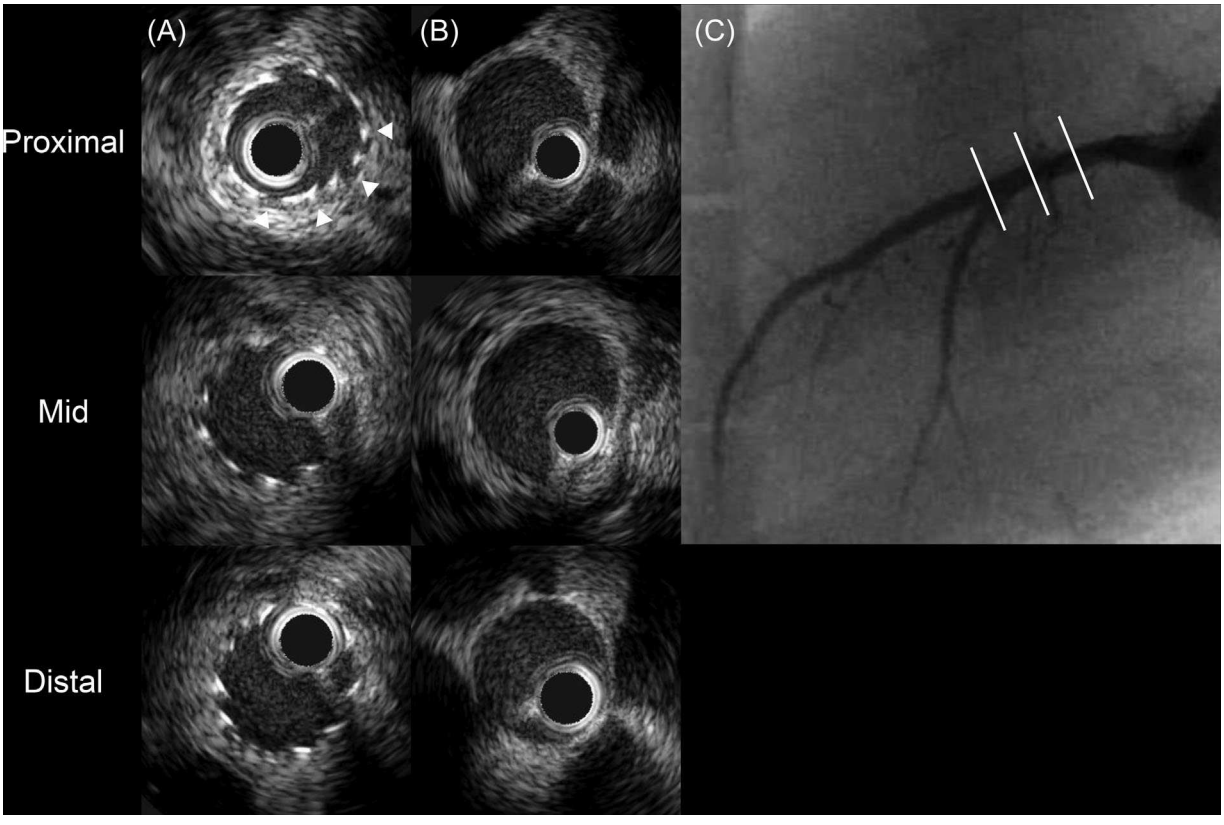

FIGURE 3 Representative IVUS findings after stent retrieval on the first day. Inappropriate expansion of the stents at the proximal site was confirmed by intravascular ultrasound (IVUS) (A, white arrow heads). We could not detect coronary dissection by IVUS after stent retrieval (B). Final angiography revealed absence of vessel rupture or occlusion (C)

euthanasia. At the end of the study, hearts were harvested and processed for histological evaluation. Under these conditions, anesthesia was controlled to render animals unresponsive to pain.

2.3 | Tissue preparation

Coronary arteries were perfused with saline, perfusion-fixed with 4% formaldehyde, and embedded in paraffin. Sections (5-6 μm thick, total of three sections) were cut and stained with hematoxylin and eosin (New Histology Science Laboratory Corporation, Tokyo, Japan) and evaluated using an optical microscope (BZ-9000, KEYENCE, Osaka, Japan).

3 | RESULTS

3.1 | Procedure of stent retrieval

The device was delivered to LAD through the catheter. After the forceps was opened, its blade was forced to slip into the space between the vessel wall and the stent (Figure 2C). The forceps was then closed and successfully grasped the stent edge (Figure 2D). The stent struts were grasped by the forceps, and the stent was pulled back into the catheter (Figures 2E, 2F, and Video). The retrieved stent was stretched parallel to its long axis and shortened in the short axis. This stent deformation might have occurred physically when the stent was caught by the device and stretched during the covering procedure by the guide catheter. The stent struts were surrounded by intima-like tissue (Figure 2G). Angiography revealed an absence of vessel rupture or occlusion. We successfully retrieved all stents and all pigs survived following the procedure.

3.2 | IVUS and histological findings

On the first day, no critical coronary dissection was detected by IVUS after stent retrieval (Figure 3). On the 14th day, the proliferation of tissue resembling neointima was observed by IVUS, although lumen area was preserved (Figure 4). Under these conditions, on the first day, histological findings revealed that the intimal structure was preserved, although the endothelial monolayer was damaged by stent retrieval (Figure 5A). This suggests that the cells adherent to retrieved stent struts (Figure 2G) are endothelial cells and sub-endothelial cell tissue which represent a part of the vessel wall. On the 14th day, we observed spindle-shaped and rounded cell types in the thickening intima by histology (Figure 5B).

4 | DISCUSSION

In the present study, we have developed an enhanced device designed to retrieve a deployed coronary stent without need for a surgical

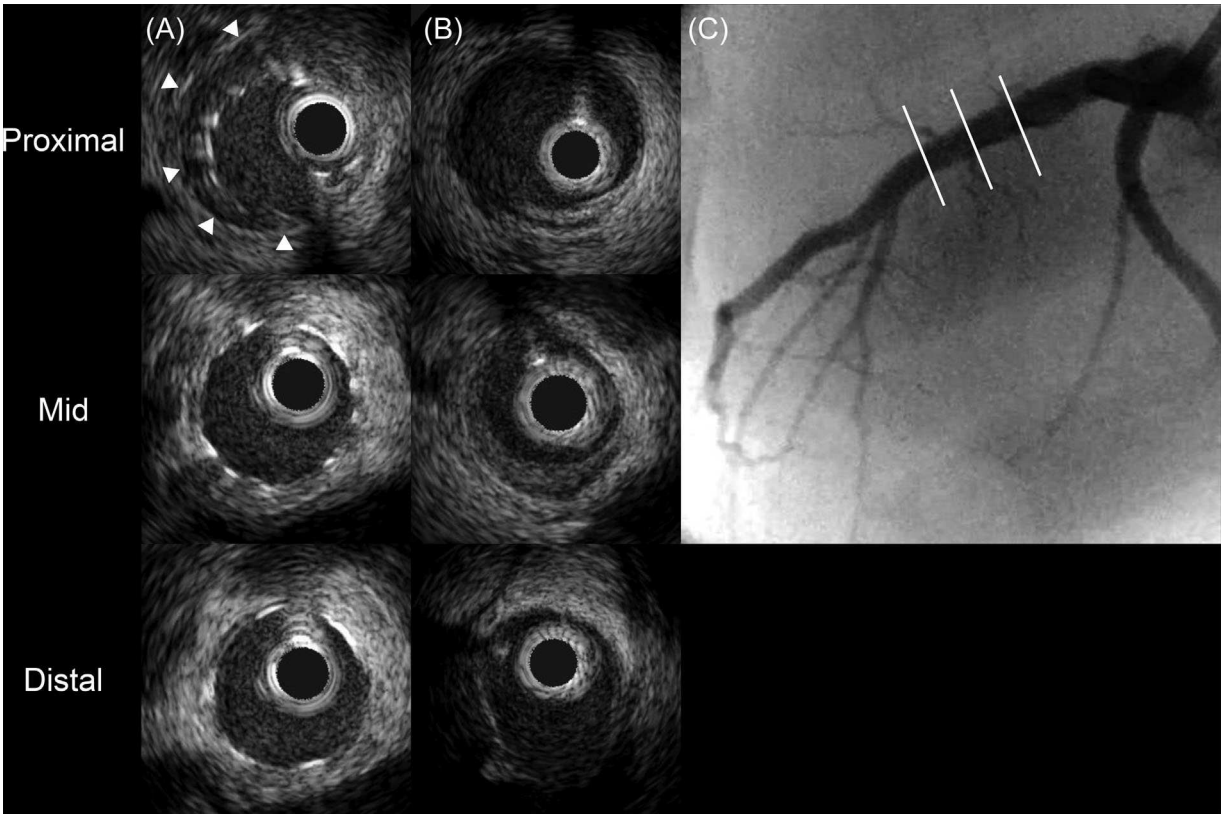

FIGURE 4 Representative IVUS findings after stent retrieval on the 14th day. Inappropriate expansion of stents at the proximal site was confirmed by intravascular ultrasound (IVUS) (A, white arrow heads). IVUS findings showed that proliferation of tissue resembling neointima was observed, but lumen area was preserved (B). Final angiography revealed an absence of vessel rupture or occlusion (C)

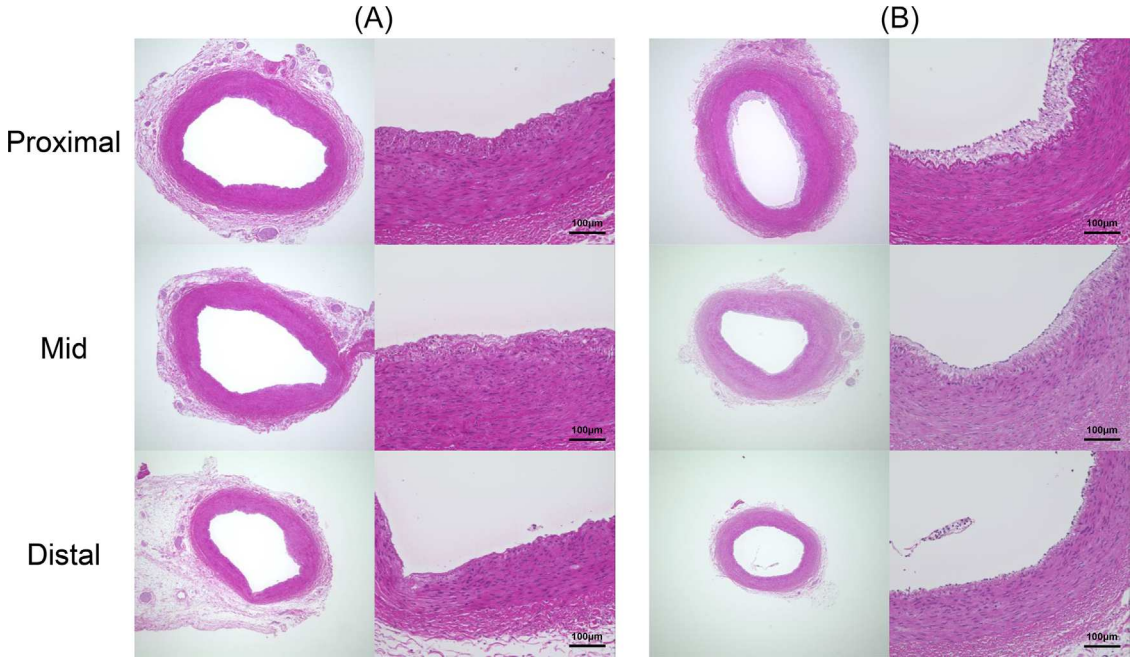

FIGURE 5 Representative histological findings on the first and 14th day. On the first day, the endothelial monolayer was damaged by stent retrieval (A). On the 14th day, intimal thickening with incorporated spindle-shaped and rounded cells was observed. These findings suggested that an inflammatory response had occurred (B). We could not detect coronary artery injury either on the first or 14th day

procedure. One of most important advantages of the present device was that it could be introduced into the targeted coronary artery along the 0.014-in guidewire by an over-the-wire system. This allows the interventional operator manipulating the guidewire to quickly approach the targeted deployed coronary stent. In addition, the existing guide catheter can be used for retrieving the stents grasped by the forceps in safety. Fortunately, coronary artery dissection did not occur and coronary flow was preserved during and after the procedure, although damaged endothelial monolayer was observed after stent retrieval.

Acute incomplete stent apposition may be left untreated by interventions such as high pressure post-dilation using a large-diameter balloon,[18] because acute incomplete stent apposition is resolved by growth of neointimal filling the space between the incomplete stent apposition struts and the vessel wall.[19] However, a recent report demonstrated that malapposition of stent was the leading potential cause of stent thrombosis in both first and second generation DES.[20] Acute incomplete stent apposition is mostly technique-dependent and can occur after implantation of any type of stent. Studies have shown that late-persistent and late-acquired incomplete stent apposition were more frequent in patients with VLST and malapposition of stent was closely related to thrombus formation.[21,22] However, there is no effective treatment for VLST which is caused by late-persistent and late-acquired incomplete stent apposition.

A previous study has demonstrated successful retrieval of unexpanded stent in left main coronary artery with an initial goose-neck snare[23]; however, no effective device currently exists which can retrieve expanded stents from coronary artery. We therefore developed an enhanced device designed to retrieve malappositioned stent from the coronary artery by modifying the structure of the forceps to allow it grasp the stent firmly. In the present study, we succeeded in retrieving malappositioned stent from the coronary artery without critical coronary injury. However, the endothelial monolayer was damaged by stent retrieval, and intimal thickening with incorporated spindle-shaped and rounded cells was observed, probably due to an inflammatory response. Experimental studies demonstrate that the response to healing in a porcine coronary artery is six times faster than that in a human coronary artery.[24] Our experimental time course of the 14th day after stent retrieval in swine may be equivalent to that of 3 months in humans.

Several methods have been reported for retrieval not only of stent, but also of fractured balloon in coronary angioplasty.[9,25] In addition, our previous device was helpful for retrieval of stents and fragmented guidewires.[16] Since our device could be advanced into the coronary artery and stents could be grasped firmly, it enabled retrieval of other intravascular foreign bodies such as fractured central venous catheters.

4.1 | Study limitations

Our study had some limitations. First, we only studied healthy pigs without evidence of arteriosclerosis. We speculate that malapposi-tioned stents would be retrievable in an arteriosclerosis model, although vessel response after stent retrieval might be greater than that in normal vessel. Additionally, it is unclear that the dissection and perforation will be occur in severe atherosclerotic disease. The

further study with atherosclerotic swine model[26,27] will demonstrate the vessel response after stent retrieval in the presence of atherosclerosis. Second, this study was performed only in the acute phase. Retrieved stents were not covered with neointima, so the forceps was able to grasp the stent edge. Therefore, it is not clear whether our device could be safely used in the chronic phase after stent deployment. We previously demonstrated that neointimal proliferation starts 2 days after BMS implantation, and that stent struts were completely covered with neointima within 14 days in a porcine coronary model.[28] Under these conditions, the stent edge covered with neointima could be grasped by the forceps, because the asymmetric nature of the improved forceps allowed it to slip under the stent easily. Third, we performed retrieval of deployed coronary stent only at the proximal site in LAD, because our device shaft was considered too soft to advance the forceps to the distal site in the coronary artery. We will need to modify the shaft to allow penetration of the forceps to a more distal site in the coronary artery.

5 | CONCLUSIONS

We have developed a novel enhanced device for effective retrieval of malappositioned coronary stent. Further modification of the device structure will be necessary to fully optimize its potential. Nonetheless, the present study clearly demonstrates that the device can be applicable for transluminal retrieval of stents.

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SUPPORTING INFORMATION

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