AsiaIntervention 2018;4:110-116

# Feasibility and safety of non-occlusive coronary angioscopic observation using a 4 Fr guiding catheter

**Masato Matsushita**[1], MD; Masamichi Takano[1]*, MD, PhD; Ryo Munakata[1], MD, PhD; Tomofumi Sawatani[1], MD; Osamu Kurihara[1], MD, PhD; Hidenori Komiyama[1], MD, PhD; Daisuke Murakami[1], MD, PhD; Akihiro Shirakabe[2], MD, PhD; Nobuaki Kobayashi[2], MD, PhD; Noritake Hata[2], MD, PhD; Yasushi Miyauchi[1], MD, PhD; Yoshihiko Seino[1], MD, PhD; Wataru Shimizu[3], MD, PhD

*1. Department of Cardiovascular Medicine, Nippon Medical School Chiba Hokusoh Hospital, Chiba, Japan; 2. Division of Intensive Care Unit, Nippon Medical School Chiba Hokusoh Hospital, Chiba, Japan; 3. Department of Cardiovascular Medicine, Nippon Medical School, Tokyo, Japan*

**KEYWORDS**

- miscellaneous
- other imaging modalities
- radial

## Abstract

**Aims:** Coronary angioscopy (CAS) is a robust imaging methodology for evaluation of vascular healing response after stenting. However, the procedure requires a guiding catheter with a diameter of more than 6 Fr, which is rather invasive at follow-up angiography. Recently, coronary angioscopes of a smaller diameter have been able to pass through a 4 Fr guiding catheter. This study aimed to investigate the feasibility and safety of slender CAS observation using a 4 Fr guiding catheter.

**Methods and results:** Thirty-three consecutive patients who underwent follow-up angiography were evaluated. Following usual angiography via the radial artery, the stent segment was observed by non-occlusive CAS through a 4 Fr guiding catheter. Low molecular weight dextran-L (4 mL/sec) was flushed from a guiding catheter to replace coronary blood. The success rate, anatomical or procedural factors related to the success, and incidence of adverse events were examined. The success rate was 84.8% (n=28/33). The luminal diameter at the orifice of the target vessel was larger in the successful than in the failed group (4.03±0.61 mm vs. 3.39±0.61 mm, respectively; p=0.009). The presence of deep engagement of the guiding catheter into the target vessel was a key factor for sufficient observation (100% in the successful group vs. 0% in the failed group; p<0.0001). No adverse events, such as dissection or acute coronary syndrome, were reported.

**Conclusions:** The new method of CAS through a 4 Fr guiding catheter demonstrated high feasibility and safety. This less invasive observation via CAS may be useful for stent follow-up.

**Corresponding author: Division of Cardiovascular Medicine, Nippon Medical School Chiba Hokusoh Hospital, 1715 Kamagari, Inzai, Chiba 270-1694, Japan. E-mail: takanom@nms.ac.jp*



SUBMITTED ON 28/12/2017 - REVISION RECEIVED ON 02/04/2018 - ACCEPTED ON 09/05/2018

DOI: 10.4244/AIJ-D-18-00003

## Abbreviations

**BVS** bioresorbable vascular scaffold
**CAG** coronary angiography
**CAS** coronary angioscopy
**ECG** electrocardiogram
**LMT** left main trunk
**LAD** left anterior descending artery
**LCx** left circumflex
**QCA** quantitative coronary angiography
**RCA** right coronary artery
**VLST** very late stent thrombosis

## Introduction

Although thrombotic events have decreased markedly since the introduction of second-generation drug-eluting stents in daily practice, life-threatening very late stent thrombosis (VLST) will never vanish. VLST originates from delayed arterial healing (or a persistent uncovered stent), stent malapposition, hypersensitivity reaction to the stent polymer, and neoatherosclerosis[1]. Furthermore, the bioresorbable vascular scaffold (BVS) is becoming common as a new device for the treatment of coronary artery diseases. At present, scaffold thrombosis is the main ongoing limitation of BVS, attributed to the large strut thickness[2,3].

In order to understand the pathogenesis of VLST or scaffold thrombosis in human beings, intravascular imaging is essential. Moreover, comprehending the vascular healing response in a stented segment provides helpful information about patient treatment and is therefore clinically significant.

Coronary angioscopy (CAS) is a unique intravascular imaging modality because the vessel lumen can be directly visualised. As shown in previous reports, growth of neointima and uncovered struts in the stented segment can be sufficiently evaluated by CAS[4]. In addition, CAS is capable of detecting intracoronary thrombi with high sensitivity. CAS is therefore one of the valuable tools for follow-up examination after coronary stenting. However, conventional CAS requires a guiding catheter with a diameter of more than 6 Fr which is rather invasive, because a 4 or 5 Fr sheath and a catheter of the same diameter are commonly used at the angiographic procedure for stent follow-up. CAS using a smaller diameter has recently become available, and an angioscope can pass through the lumen of a 4 Fr guiding catheter. Although the first-in-man case of CAS observation with a 4 Fr guiding catheter was reported previously, systematic data about this procedure are absent[5].

The aim of this study was to investigate the feasibility and safety of a new procedure using CAS through a 4 Fr small diameter guiding catheter for clinical use at stent follow-up.

## Methods

### SUBJECTS

The present study prospectively investigated 58 consecutive patients who underwent coronary angiography (CAG) for stent follow-up at Nippon Medical School Chiba Hokusoh Hospital between September 2016 and December 2016. Twenty-five patients were eliminated because of exclusion criteria, which were 1) an aorto-ostial stent segment such as the left main trunk (LMT) or right coronary artery (RCA) less than 10 mm from the orifice (n=7), 2) chronic renal failure (serum creatinine >2.0 mg/dL) (n=0), 3) decompensated heart failure (n=0), 4) history of anaphylactic shock caused by contrast media (n=0), 5) no consent to undergoing CAS examination (n=6), 6) in-stent restenosis (diameter stenosis >50%) (n=3), 7) *de novo* stenosis in a stented branch (n=9), and 8) stent segment in a bypass graft (n=0). Thirty-three patients underwent CAS to observe the condition of deployed stents. The study flow chart is shown in **Figure 1**. The study protocol was approved by the Ethics Committee of our institute and an informed consent was obtained from all patients participating in this study.

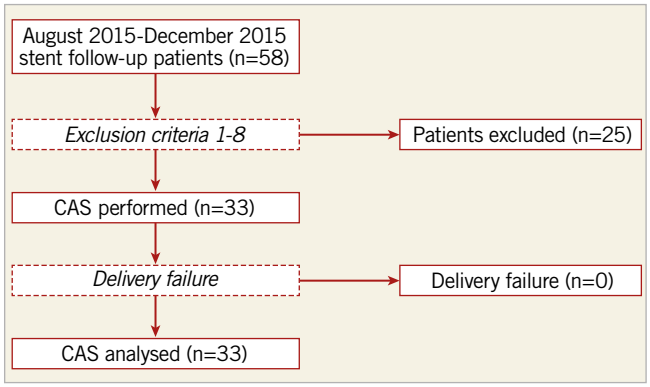


**Figure 1.** *Study flow chart. Twenty-five out of 58 stent follow-up patients were excluded according to the exclusion criteria. No cases of angioscope delivery failure were reported.*

### PROCEDURES

All procedures were performed through the transradial approach using a 4 Fr sheath. Four thousand units of unfractionated heparin were administered before the procedure and 50 µg of nitroglycerine were administered to each coronary artery immediately before CAG. After ordinary CAG for stent follow-up, the stent segment was observed by CAS. A non-occlusive and short monorail type of coronary angioscope (Smart-*i*™ type S11; iHeart Medical Co. Ltd., Tokyo, Japan) **(Figure 2)** and a 4 Fr guiding catheter (Kiwami; Terumo Corp., Tokyo, Japan) were used. The diameters of the coronary angioscope were 1.2 mm at the tip and 0.6 mm at the shaft. The guiding catheter had a diameter of 0.055 inches (1.27 mm), enabling the angioscope to pass inside the catheter lumen. The appropriate shape of the guiding catheter was selected according to the anatomy of the coronary arteries, such as Judkins left (JL), Judkins right (JR), Amplatz left (AL), and Backup left (BL). After engagement of the guiding catheter into the target vessel, a 0.014-inch guidewire was crossed over the stent segment. The angioscope was advanced along the guidewire distal to the stent through the guiding catheter. For removal of coronary blood, low molecular weight dextran-L at a flow rate of 4 mL/sec (total

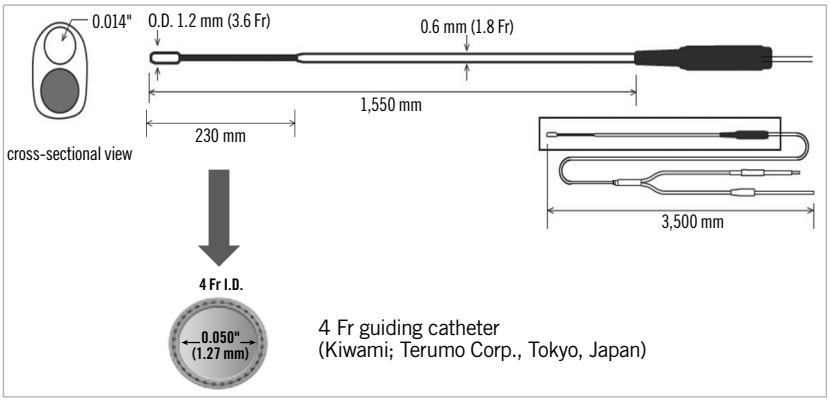


**Figure 2.** *Profile of Smart-i™ (type S11) and guiding catheter. The tip of the angioscope was 1.2 mm and the inner diameter of the 4 Fr guidewire was 1.27 mm.*

volume of 36 mL) was flushed from the guiding catheter using the auto-injector. In the target stent segment, the angioscope was pushed and/or pulled back slowly and gently during the flush.

### ENDPOINT

The primary endpoint was the success rate of CAS observation. Image quality was used to divide the obtained images into two groups: the successful group in which the quality was sufficient for evaluation of the stent segment due to continuously clear images with complete replacement of the blood, and the failed group in which observation was insufficient due to discontinuous images or no image acquisition owing to residual blood.

In addition, we analysed lesion characteristics contributing to successful observation of CAS as follows: location of the target vessel (left anterior descending artery [LAD], left circumflex artery [LCx], or RCA) and the stent segment (just proximal, proximal, mid, or distal), ostial diameter of the target vessel, reference diameter in the stent segment, lumen diameter at the tip of the guiding catheter, deployed stent diameter, deployed stent length, and achievement of deep engagement of the guiding catheter into the target vessel. The just proximal segment was defined as the LAD or LCx ≤10 mm from the bifurcation. Vessel diameter and distance were analysed by quantitative coronary angiography (QCA) using QAngio XA, Version 7.2.34.0 (Medis medical imaging systems bv, Leiden, the Netherlands). Deep engagement of the left coronary artery was defined as selective insertion into the LAD or LCx, and that of the RCA was defined as adaptation more than 10 mm from the orifice.

The secondary endpoint was estimation of the safety of the 4 Fr coronary angioscope. Procedure-related adverse events, such as changes in the electrocardiogram (ECG) during the observation, and the occurrence of coronary dissection and acute coronary syndrome were checked.

### STATISTICAL ANALYSIS

All data were analysed using Statistical Package for Social Sciences (SPSS) software, Version 22.0 (IBM Corp., Armonk, NY, USA). All numerical data were expressed as the mean±standard deviation or the median (25-75% interquartile range), depending on normality. If the data were normally distributed, the values were expressed as the mean±standard deviation. If the data were not normally distributed, the values were expressed as the median (25-75% interquartile range). The t-test was used to compare quantitative variables between groups, and chi-square analysis was used to compare qualitative data between groups. A p-value of <0.05 was considered to be statistically significant.

## Results

### PATIENT CHARACTERISTICS

Patient and lesion characteristics are shown in **Table 1**. The right radial approach accounted for 84.8% (n=28) of cases and the left side was chosen in the others. Delivery failure to the stent segment was not reported. Types of guiding catheter used were JL in 14, BL in four, AL in four cases for the LAD; JL in two, BL in two cases for the LCx; and JR in five, AL in one, BL in one case(s) for the RCA.

The location of the stent segments is also shown in **Table 1**. Among 33 cases, four cases had LMT lesions and one case had an aorto-ostial RCA; these segments were excluded from the analysis because engagement of the guiding catheter conceals the stents in the aortic ostium. Finally, 60 segments of 33 vessels were analysed in this study.

### SUCCESS RATE AND FACTORS OF SUCCESSFUL OBSERVATION

Among 33 patients, 28 patients (84.8%) were categorised as the successful group and five (15.2%) were placed in the failed group. Mean time of clear imaging in the successful group was 5.7±2.5 sec. The proportion of cases in which the whole targeted stent was evaluated in the successful group was 42.9% (n=12/28). The ratio of observed length to whole targeted stent in the successful group was 85.4% (77.0-100%). Haemodynamics, including blood pressure and heart rate, laboratory data, and ejection fraction, were similar in both groups **(Table 2)**. The success

**Table 1. Patient and lesion characteristics.**

| | | n=33 |
|---|---|---|
| Age (years) | | 67.8±9.4 |
| Gender, male (%) | | 24 (72.4%) |
| Body weight (kg) | | 64.1±10.0 |
| Height (cm) | | 162.4±7.5 |
| BMI (kg/m$^2$) | | 24.3±2.7 |
| Diagnosis before stenting | Acute coronary syndrome | 13 (39.4%) |
| | Stable angina | 12 (36.4%) |
| | Silent myocardial ischaemia | 8 (24.2%) |
| Diseased vessel | 1-vessel disease | 14 (42.4%) |
| | 2-vessel disease | 13 (39.4%) |
| | 3-vessel disease | 6 (18.2%) |
| AHA/ACC type | A | 3 (9.1%) |
| | B1 | 9 (27.3%) |
| | B2 | 17 (51.5%) |
| | C | 4 (12.1%) |
| Previous CABG | | 1 (3.0%) |
| Previous myocardial infarction | | 17 (51.5%) |
| Coronary risk factor | Hypertension | 25 (73.6%) |
| | Diabetes mellitus | 20 (60.6%) |
| | Dyslipidaemia | 28 (84.8%) |
| | Current smoking | 21 (63.6%) |
| Stent follow-up period (months) | | 17.8±18.2 |
| Ejection fraction on echocardiogram (%) | | 61.7±10.9 |
| Targeted vessel | LAD | 22 (66.7%) |
| | LCx | 4 (12.1%) |
| | RCA | 7 (21.2%) |
| Location of stent segment (60 total segments) | Just proximal | 17 (51.5%) |
| | Proximal | 20 (60.6%) |
| | Mid | 18 (54.5%) |
| | Distal | 5 (15.2%) |

Data are presented as mean±SD or number (%). AHA/ACC: American Heart Association/American College of Cardiology; BMI: body mass index; CABG: coronary artery bypass grafting

**Table 2. Comparison of clinical factors between successful and failed groups.**

| | | Successful group n=28 | Failed group n=5 | *p*-value |
|---|---|---|---|---|
| Haemo-dynamics | Systolic blood pressure (mmHg) | 127.1±17.9 | 140.2±16.9 | 0.141 |
| | Diastolic blood pressure (mmHg) | 66.2±11.7 | 68.4±11.5 | 0.698 |
| | Heart rate (/min) | 67.0±14.3 | 65.8±10.4 | 0.860 |
| Labora-tory data | Haemoglobin (mg/dl) | 13.5±1.3 | 13.3±1.1 | 0.784 |
| | eGFR (ml/min) | 67.0±17.1 | 64.8±21.2 | 0.802 |
| | BNP (pg/ml) | 60.8±78.7 | 50.7±56.9 | 0.787 |
| Ejection fraction on echocardiogram (%) | | 61.8±10.8 | 61.4±12.5 | 0.951 |

Data are presented as mean±SD. The *p*-values between groups were determined using t-test. BNP: brain natriuretic peptide; eGFR: estimated glomerular filtration rate

rate did not differ between the LAD, LCx, and RCA (86.4%, 75.0%, and 85.7%, respectively; p=0.877). The segment-by-segment success rate was 70.0% (n=42/60) and the rate per location was 17.6% (n=3/17) for the just proximal site, 85.0% (n=17/20) for the proximal site, 94.4% (n=17/18) for the middle site, and 100% (n=5/5) for the distal site. Just proximal segments showed a lower success rate than the other segments (just proximal segments 17.6% [n=3/17] vs. the other segments 90.7% [n=39/43]; p<0.001) **(Figure 3)**. **Table 3** shows the results of QCA analysis. The reference diameter in the stent segment, lumen diameter at the tip of the guiding catheter, deployed stent diameter, and deployed stent length were not different between the successful and the failed groups. The ostial diameter of the target vessel was greater in the successful group than in the failed group (successful group: 4.14±0.55 mm vs. failed group: 3.39±0.61 mm; p=0.009). The success rate was significantly higher in patients with deep engagement of the guiding catheter than in patients

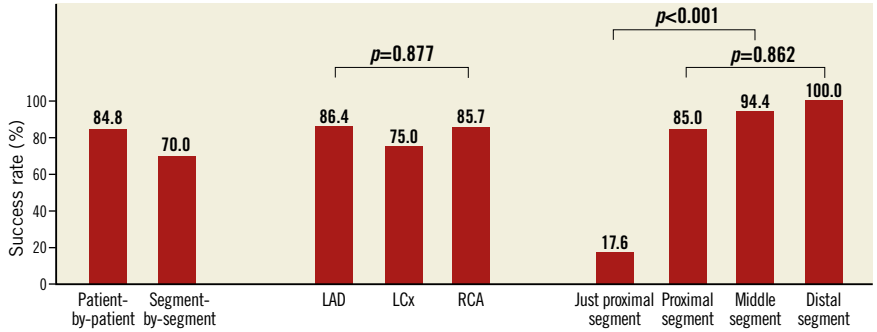


**Figure 3.** *Success rate of 4 Fr CAS. Patient-by-patient success rate was 84.8% and segment-by-segment success rate was 70.0%. Just proximal segments showed a lower success rate than the other segments. p-values between groups were determined using the chi² test. LAD: left anterior descending; LCx: left circumflex; RCA: right coronary artery*

**Table 3. Findings of quantitative coronary angiography.**

| | Successful group n=28 | Failed group n=5 | *p*-value |
|---|---|---|---|
| Ostial diameter of target vessel, mm | 4.14±0.55 | 3.39±0.61 | 0.009 |
| Reference diameter in stent segment, mm | 2.83±0.41 | 2.53±0.53 | 0.161 |
| Lumen diameter at tip of guiding catheter, mm | 3.09±0.43 | 2.75±0.54 | 0.124 |
| Deployed stent diameter, mm | 3.10±0.44 | 3.30±0.27 | 0.240 |
| Deployed stent length, mm | 30.6±15.2 | 25.2±17.8 | 0.678 |

Data are presented as mean±SD. The *p*-values between groups were determined using t-test.

without. As shown in **Figure 4**, the successful group achieved 100% deep engagement of the guiding catheter, while the failed group achieved 0% (p<0.001).

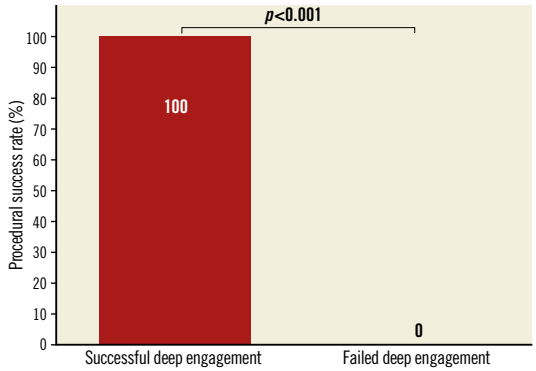


**Figure 4.** *Association between procedural success and deep engagement of the guiding catheter. Deep engagement of the guiding catheter was the most important factor of the procedural success. p-values between groups were determined using the chi² test.*

Representative cases are shown in **Figure 5**. These included the successful case and the failed case of 4 Fr CAS carried out for the LCx. The guiding catheter in the successful case achieved selective insertion to the LCx, while that in the failed case did not.

### ADVERSE EVENTS RELATED TO CAS PROCEDURES

In all cases, no transient ST-T changes on the ECG were found during the observation. No serious adverse events, such as coronary dissection and acute coronary syndrome, were observed.

## Discussion

The present investigation demonstrated that more than 80% of stent segments were sufficiently observed by slender CAS through a 4 Fr small diameter guiding catheter. The procedures were less invasive and quite safe.

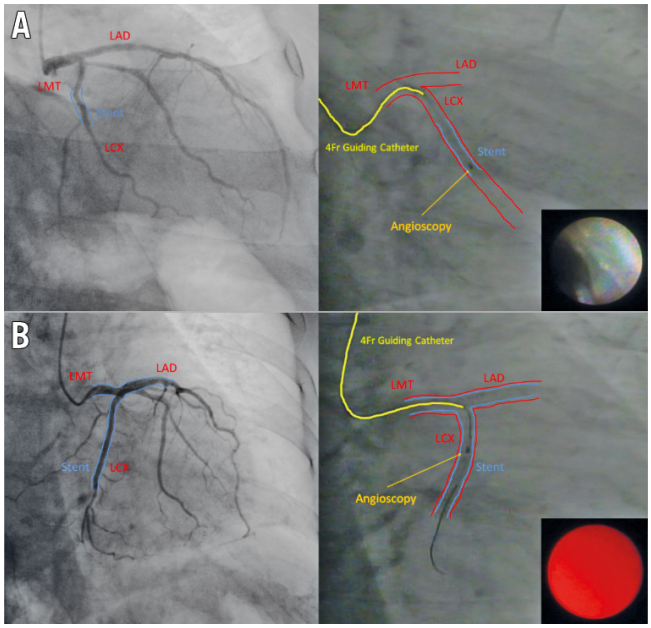


**Figure 5.** *Representative cases of 4 Fr CAS for the LCx. Successful (A) and failed (B) cases are shown. The guiding catheter achieved a deep engagement position in the successful case (enabling the observation of neointimal stent coverage), while it did not in the failed case. The neointimal stent coverage of the successful case was Grade 1. Stent coverage could not be evaluated in the failed case due to the residual blood flow.*

The innovation of fibre optics and laser technologies in the early 1980s helped the development of CAS[6-9]. As fibrescopes became flexible and thin, CAS was utilised for observation of coronary lumens in clinical practice. Two types of CAS catheters have been used, each of which has its advantages and disadvantages: balloon-occlusion (FULLVIEW NEO™; FiberTech Co., Ltd., Chiba, Japan) and non-occlusion (Visible™; FiberTech Co., Ltd.). The monorail type of balloon-occlusion angioscope provides continuous images without residual blood. However, this invites transient myocardial ischaemia during the observation and has low delivery performance due to its large diameter and high rigidity. In contrast, the non-occlusion angioscope is easily deliverable, but with inferior image quality as compared to the occlusion angioscope. Moreover, a guidewire inside a microcatheter (over-the-wire catheter) is replaced by a fibrescope, and the wire is lost for the observation. Both types require a guiding catheter of more than 6 Fr in diameter. The systems and procedures of CAS have changed little since the beginning of their development.

To the best of our knowledge, our study was the first to evaluate novel procedures using a slender CAS catheter. The current investigation was performed by a non-occlusive and 4 Fr-compatible system, which has the advantage of simplicity and less invasiveness over conventional procedures. In addition, a guidewire was left in the target vessel because of the monorail system of the

catheter. The guidewire is helpful for bail-out in case of unexpected complications including dissection, and this may help to guarantee procedural safety.

In our series, 84.8% of cases were sufficiently evaluated by the 4 Fr CAS system. Previous studies have reported that the success rate using an 8 Fr guiding catheter and the occlusion type of angioscope resulted in a success rate of 82-83%[4,10]. The occlusion type of angioscope cannot be delivered in the presence of severe tortuosity or calcification proximal to the target lesion. No cases of delivery failure were reported in the present study, suggesting that the current CAS catheter produced a delivery capability under back-up force by a 4 Fr guiding catheter. Although the definition of procedural success and the exclusion criteria were different from the previous reports, our observation showed a similar success rate regardless of the small size of the 4 Fr guiding catheter. The first-in-man case of a 4 Fr CAS system was accomplished with flushing of iodine contrast media[5]. The current procedure, using low molecular weight dextran-L, was less invasive compared to the previous procedure.

According to our results, deep engagement of the guiding catheter into the target vessel and its diameter at the ostium were related to the success rate. In particular, deep engagement of the guiding catheter was a key factor of the procedural success. Deep engagement of the guiding catheter and consequent selective injection of low molecular weight dextran-L was able to wash out coronary blood efficiently, and this provided clear images without residual blood. The ostial diameter of the target vessel was another factor of the procedural success. In general, a large vessel makes CAS observation difficult because of the large amount of coronary blood that needs to be washed out. However, a large vessel diameter was a favourable condition for the observation. Although the precise reasons were unclear, large vessels may facilitate deep engagement of the guiding catheter and enable good washout of blood. The tip of the guiding catheter with a small diameter is flexible, and a 4 Fr guiding catheter may allow deep engagement easily and safely. This is the one of the most important advantages of a small diameter system when performing CAS. The 4 Fr system provides sufficient observation even when the mother-and-child catheter system is necessary if performing CAS with a larger diameter guiding catheter. No major complications were reported in this study. From the viewpoint of safety, our procedures were acceptable for clinical use.

## Limitations

Several limitations in the present study must be noted. First, our report is a single-centre trial with a relatively small population and is limited to patients evaluated for neointimal stent coverage with no restenosis. In addition, the selection of the guiding catheter depended on each operator. Operators selected the tip shape of the guiding catheter according to the anatomy of each vessel. These biases may have affected the procedural success and occurrence of adverse events using 4 Fr CAS. Second, aorto-ostial lesions were excluded from the analysis. We excluded these lesions on the grounds that the tip of the guiding catheter disturbs observation of the ostial RCA or LMT. Given the low success rate even in the just proximal segment of the LAD or LCx, 4 Fr CAS would be unsuitable to observe ostial lesions. However, this disadvantage might also be applicable to CAS with the larger diameter system. Actually, in balloon-occlusion type CAS, the ostium including the LMT is invisible because of the approximately 2 cm distance between the catheter tip and the occlusion balloon. Third, the present study categorised several cases into the successful group in which the neointimal coverage was only partially observed. We need to recognise the difficulty of observing just proximal segments, as shown above. Nevertheless, the average consecutive observation time of 5.7 sec and the observed length ratio of 85.4% against the whole targeted stent length in our successful group are considered to be relatively adequate to evaluate neointimal coverage after stent deployment. Fourth, the present study evaluated only procedure-related adverse events during the CAS procedure; it did not assess the events after the procedure such as 1-day, 7-day, or 30-day events. Nevertheless, no complications during the CAS procedure occurred in the present study. We consider that this result substantially endorses its safety.

Historically, CAS contributed towards the illumination of the pathogenesis of acute coronary syndrome[4] and the identification of vulnerable plaques as its origin[11]. Although we focused on implanted stents in this study, 4 Fr CAS could contribute considerably to every situation in daily practice, including stent follow-up and plaque evaluation. Moreover, it has the potential to become an important technique for follow-up of new devices (such as BVS) in the near future.

## Conclusions

In conclusion, the present study is the first-in-man report showing the feasibility, safety, and lesser invasiveness of CAS with a 4 Fr slender system.

## Impact on daily practice

CAS is a robust imaging methodology for evaluating vascular healing response after stenting. Conventional CAS generally requires a 6 Fr guiding catheter and is rather invasive for stent follow-up. This study demonstrated a high success rate and the safety of CAS with a slender 4 Fr system. It could contribute to every situation in daily practice, including stent follow-up and plaque evaluation.

## Acknowledgements

We are grateful to the staff of the Division of Cardiovascular Medicine and to the staff of the Angiographic Laboratory at Nippon Medical School Chiba Hokusoh Hospital for their valuable support in collecting the data.

## Conflict of interest statement

The authors have no conflicts of interest to declare.

## References


1. Taniwaki M, Radu MD, Zaugg S, Amabile N, Garcia-Garcia HM, Yamaji K, Jørgensen E, Kelbæk H, Pilgrim T, Caussin C, Zanchin T, Veugeois A, Abildgaard U, Jüni P, Cook S, Koskinas KC, Windecker S, Räber L. Mechanisms of Very Late Drug-Eluting Stent Thrombosis Assessed by Optical Coherence Tomography. *Circulation.* 2016;133:650-60.

2. Serruys PW, Chevalier B, Dudek D, Cequier A, Carrié D, Iniguez A, Dominici M, van der Schaaf RJ, Haude M, Wasungu L, Veldhof S, Peng L, Staehr P, Grundeken MJ, Ishibashi Y, Garcia-Garcia HM, Onuma Y. A bioresorbable everolimus-eluting scaffold versus a metallic everolimus-eluting stent for ischaemic heart disease caused by de-novo native coronary artery lesions (ABSORB II): an interim 1-year analysis of clinical and procedural secondary outcomes from a randomised controlled trial. *Lancet.* 2015;385:43-54.

3. Ellis SG, Kereiakes DJ, Metzger DC, Caputo RP, Rizik DG, Teirstein PS, Litt MR, Kini A, Kabour A, Marx SO, Popma JJ, McGreevy R, Zhang Z, Simonton C, Stone GW; ABSORB III Investigators. Everolimus-Eluting Bioresorbable Scaffolds for Coronary Artery Disease. *N Engl J Med.* 2015;373:1905-15.

4. Mizuno K, Satomura K, Miyamoto A, Arakawa K, Shibuya T, Arai T, Kurita A, Nakamura H, Ambrose JA. Angioscopic evaluation of coronary-artery thrombi in acute coronary syndromes. *N Engl J Med.* 1992;326:287-91.

5. Takano M, Imaizumi T, Tabata A, Hata N, Seino Y, Shimizu W, Mizuno K. Minimally invasive coronary angioscopy: observation using a new non-occlusive fibrescope through a 4 Fr guiding catheter. *AsiaIntervention.* 2015;1:126-8.

6. Litvack F, Grundfest WS, Lee ME, Carroll RM, Foran R, Chaux A, Berci G, Rose HB, Matloff JM, Forrester JS. Angioscopic visualization of blood vessel interior in animals and humans. *Clin Cardiol.* 1985;8:65-70.

7. Spears JR, Marais HJ, Serur J, Pomerantzeff O, Geyer RP, Sipzener RS, Weintraub R, Thurer R, Paulin S, Gerstin R, Grossman W. In vivo coronary angioscopy. *J Am Coll Cardiol.* 1983;1:1311-4.

8. Mizuno K, Arai T, Satomura K, Shibuya T, Arakawa K, Okamoto Y, Miyamoto A, Kurita A, Kikuchi M, Nakamura H, et al. New percutaneous transluminal coronary angioscope. *J Am Coll Cardiol.* 1989;13:363-8.

9. Hombach V, Höher M, Hannekum A, Hügel W, Buran B, Höpp HW, Hirche H. [First clinical experience with coronary endoscopy]. [Article in German]. *Dtsch Med Wochenschr.* 1986;111:1135-40.

10. Ramee SR, White CJ, Collins TJ, Mesa JE, Murgo JP. Percutaneous angioscopy during coronary angioplasty using a steerable microangioscope. *J Am Coll Cardiol.* 1991;17:100-5.

11. Uchida Y, Nakamura F, Tomaru T, Morita T, Oshima T, Sasaki T, Morizuki S, Hirose J. Prediction of acute coronary syndromes by percutaneous coronary angioscopy in patients with stable angina. *Am Heart J.* 1995;130:195-203.