



Wolverine cutting balloon in the treatment of stent underexpansion in heavy coronary calcification: bench test using a three-dimensional printer and computer simulation with the finite-element method

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Abstract

Heavy coronary calcification hinders successful stent implantation, and cutting balloons can be used for post-dilation after stent deployment. However, evidence regarding its use is limited to case reports. Therefore, this study aimed to investigate in-stent dilation in circumferential coronary calcifications using Wolverine cutting balloons, compared with conventional non-compliance (NC) balloons. Circumferential coronary calcification models were designed based on the patient's intravascular ultrasound images. Three-dimensional printed models were subjected to bench tests and software analysis was performed using the finite-element method (FEM). As a result, the bench test showed that higher balloon pressure was needed to dilate the models with stent implantation, either using Wolverine (17.1 ± 2.7 atm) or NC Emerge (18.9 ± 1.8 atm), while lower pressure was needed in models without stents using Wolverine [11.7 ± 2.9 atm, analysis of variance (ANOVA) $p < 0.001$]. Furthermore, models without stents were all successfully cracked by Wolverine at the first dilation, while models with stent implantation needed more dilations (ANOVA $p = 0.0132$). The FEM showed similar results that the first principal stress was the highest in Wolverine-dilated models without stents. In conclusion, implanted stents significantly increase the difficulty of balloon dilation and adequate pretreatment is critical for successful coronary stenting.

Keywords Calcification · Cutting balloon · 3D printer · Finite-element analysis

Abbreviations

NC	Non-compliance
FEM	Finite-element method
PCI	Percutaneous coronary intervention
ANOVA	Analysis of variance

Introduction

Highly calcified lesions are important contributing factors for stent underexpansion in percutaneous coronary intervention (PCI) [1, 2]. Stent underexpansion results in abnormal shear stress and leads to local hemodynamic changes [3],

which increase the risk of restenosis and stent thrombosis. Additional post-dilation, which means the dilation after stent deployment, is required for stent underexpansion. However, in-stent dilation becomes more difficult in a heavily calcified lesion, even with a high balloon pressure. Techniques such as rotational atherectomy and excimer laser could be a solution, but they are not available in every facility and may even lead to serious complications [4, 5]. Cutting balloons are catheter balloons with metallic blades on the surface, and by concentrating pressure on the blade edge, these balloons have shown potential in dealing with undilatable calcifications [6–8]. In our previous study [9], we discovered that the expansion of circumferential coronary calcification can be achieved using a Wolverine cutting balloon with a low pressure. However, studies on treatments after stent underexpansion are scarce, and the use of a cutting balloon and its mechanism of in-stent dilation have not been investigated. Therefore, we conducted this study to evaluate the utility of the Wolverine cutting balloon for the treatment of stent underexpansion in heavy coronary calcification.

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Methods

Experiment 1: bench test

Similar to our previous studies [9, 10], intravascular ultrasound data from a patient with circumferential coronary calcification in the left ascending artery were obtained, and the engineering software Autodesk Fusion 360 (Autodesk Inc., CA, USA) was used to build coronary calcification models (Fig. 1). This study was approved and overseen by the Ethics Committee of Kyoto University, and the requirement of informed consent was waived because we only used imaging data. A 3D printer was employed to create calcification models, using clear resin as printing material. Non-compliant balloons (NC Emerge; 2.5/12 mm; Boston Scientific, MA, USA) and Wolverine cutting balloons (henceforth: Wolverine; 2.5/10 mm; Boston Scientific, MA, USA) were used to expand calcification models. According to the balloon type and the existence of the stent, four groups were identified; models in Groups A and B were dilated by NC emerge (Group A: without stents; Group B: with stents) and models in Groups C and D were dilated by Wolverine (Group C: without stents; Group D:

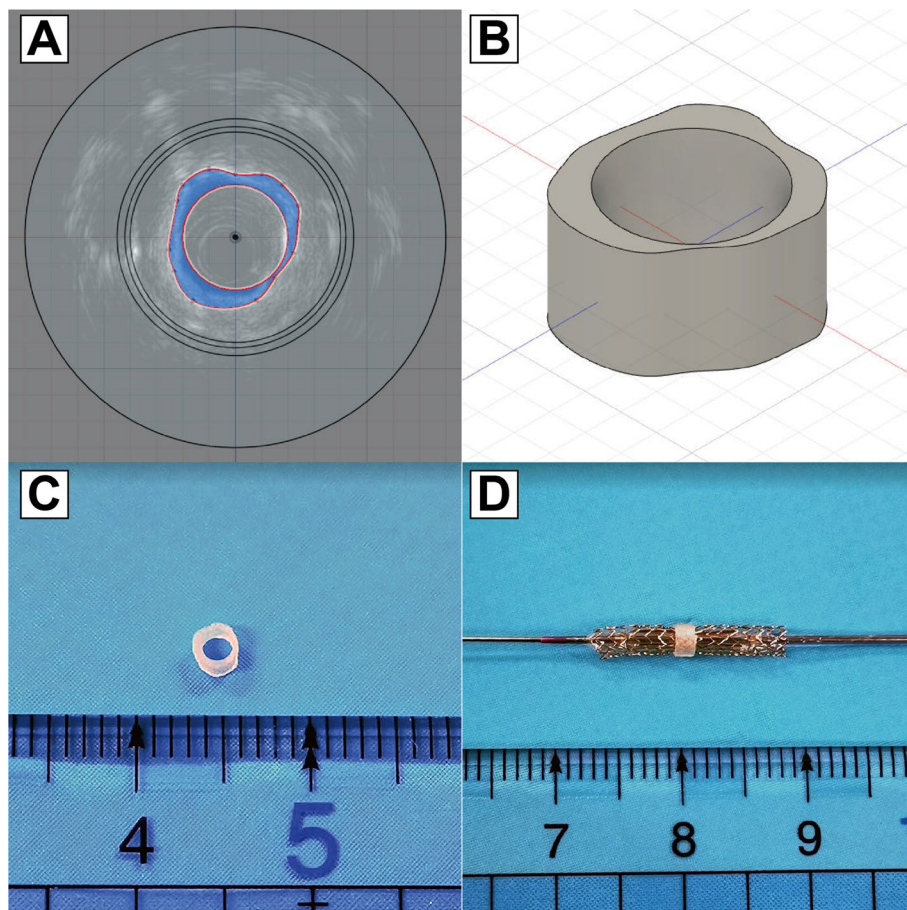
with stents). There were 15 calcification models in each group; each model was dilated up to three times, and dilating pressure was added up to 20 atm each time.

We primarily compared the maximum balloon pressure, success rate, and number of dilations among the groups. The success rate of expansion was defined as the rate of successfully dilated models (dilation up to 3 times), and maximum balloon pressure was defined as the highest dilating pressure added to the balloon.

Experiment 2: structural analysis

We developed calcification models by Autodesk Fusion 360, using the same blueprint as that in Experiment 1. Balloons and stents were designed as well (Fig. 2). The first principal stress was the maximum tensile stress due to the loading conditions, we analyzed the maximum first principal stress of the calcification model in response to the balloon pressure, with the same settings as those in Experiment 1—Wolverine and NC emerge were used to dilate the calcification with or without stent implantation. The properties of platinum chromium stents, such as Young's modulus and Poisson's ratio, are listed in Table 1. The finite-element method (FEM) was performed in the analysis.

Fig. 1 Calcification models developed by intravascular ultrasound (IVUS) imaging data from a real patient. **A** The cross-section of the patient's IVUS image; **B** the model designed in engineering software; **C, D** the actual models printed by a three-dimensional printer



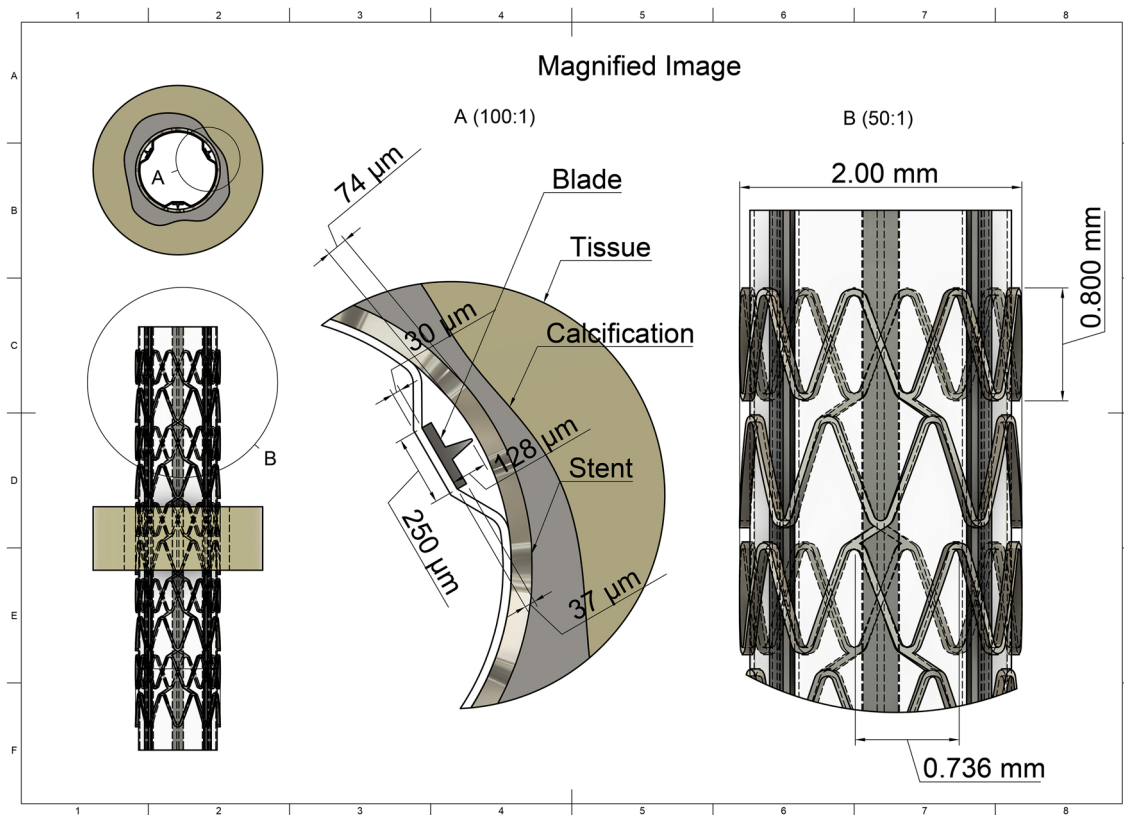


Fig. 2 Design of the stent, coronary calcification, and surrounding tissue. Soft connective tissue was set up around the calcification

Table 1 Properties of materials used in simulation

	Young's modulus (GPa)	Poisson's ratio
Calcified plaque	20	0.17
Stent	250	0.30
Cutting blade	210	0.30
Balloon	0.6	0.40
Surrounding tissue	0.001	0.49

Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation (SD), if normally distributed, categorical variables are presented as numbers and percentages. Continuous and categorical variables were compared using analysis of variance (ANOVA) and the Chi-square test, respectively. Further analysis using Tukey's test after ANOVA was also performed. JMP 15.0 (Statistical Analysis System, Institute Inc., NC, USA) was used for statistical analysis.

Results

Experiment 1: bench test

The calcification model was traced from the intravascular ultrasound image of a patient, and the length of the calcification was set to 1.5 mm. The maximum balloon pressures were 16.8 ± 3.8 atm for Group A, 18.9 ± 1.8 atm for Group B, 11.7 ± 2.9 atm for Group C, and 17.1 ± 2.7 atm for Group D (ANOVA $p < 0.0001$). The Tukey's test was applied to further compare each group, and significant differences were observed between Groups A and C ($p < 0.0001$) and between Groups B and C ($p < 0.0001$). The results indicated that the balloon pressure was significantly higher after stent implantation, even when a cutting balloon was used (Fig. 3). There were significant differences in the number of dilations among the four groups— 1.7 ± 0.9 times in Group A, 1.7 ± 0.9 times in Group B, 1 ± 0 times in Group C, and 1.1 ± 0.5 times in Group D (ANOVA $p = 0.0132$). No significant difference was observed in the success rate between the groups (Group A, 93.3%; Group B, 86.7%; Group C, 100%; and Group D 100%, $p = 0.28$).

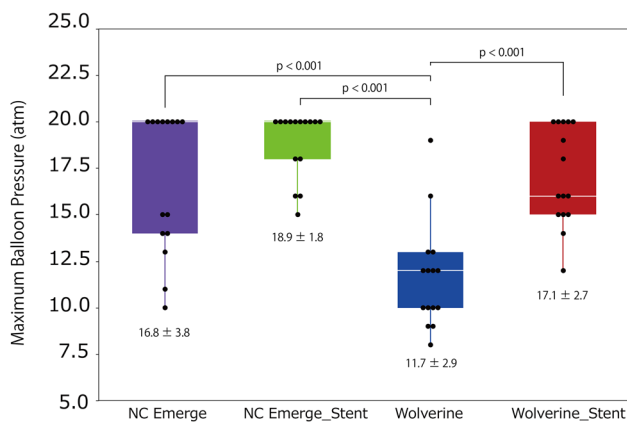


Fig. 3 Maximum balloon pressure. The Wolverine cutting balloon achieved expansion at a significantly lower maximum balloon pressure

Experiment 2: structural analysis by the FEM

We developed stent models using Autodesk Fusion 360 based on Synergy's design (8 crowns, 2 links, inner diameter 2 mm, strut 74 μ m, Fig. 2). Similar to our previous studies, we traced and extruded the model based on a patient, the calcification was surrounded by connective tissue, and the length of the calcification was set to 1.5 mm. The properties of the balloon catheters were the same as those in our previous study [9].

The first principal stress of the calcified lesion in response to a balloon pressure of 20 atm was calculated using FEM. As a result, it was 61.2 MPa for NC Emerge without stent implantation, 47.2 MPa for NC Emerge with stent implantation, 461.0 MPa for Wolverine without stent implantation, and 151.6 MPa for Wolverine with stent implantation (Figs. 4 and 5).

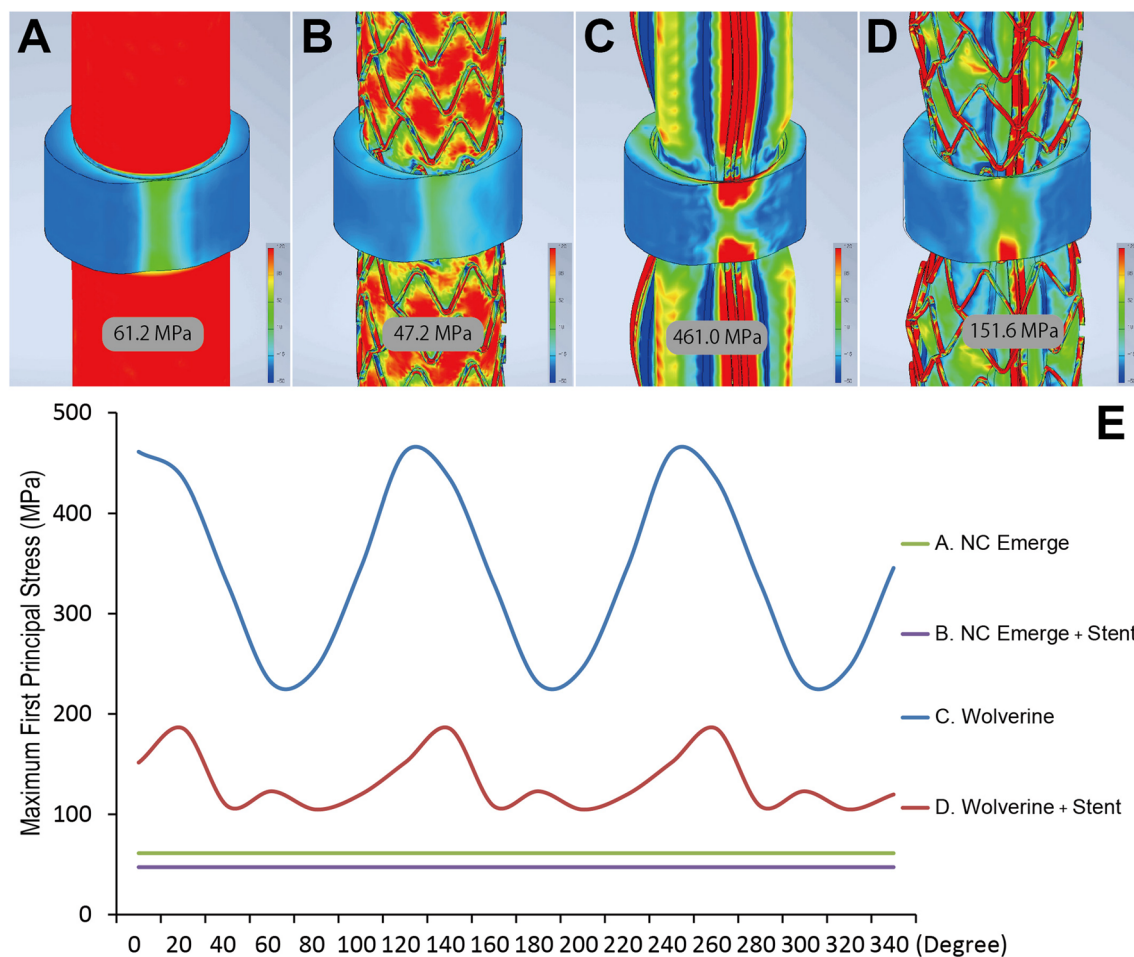


Fig. 4 Structure analysis by the finite-element method. The first principal stress was calculated. **A** First principal stress by NC Emerge without stent implantation; **B** first principal stress by NC Emerge with stent implantation; **C** first principal stress by Wolverine without stent implantation; **D** first principal stress by Wolverine with stent implantation. **E** The maximum first principal stress obtained by balloon rota-

tion from 0 to 350° in 10° increments; the first principal stress was significantly decreased after stent implantation. When the Wolverine was rotated, the maximum first principal stress was found at the thinnest part of the calcification and the blade hit the thinnest part in all cases

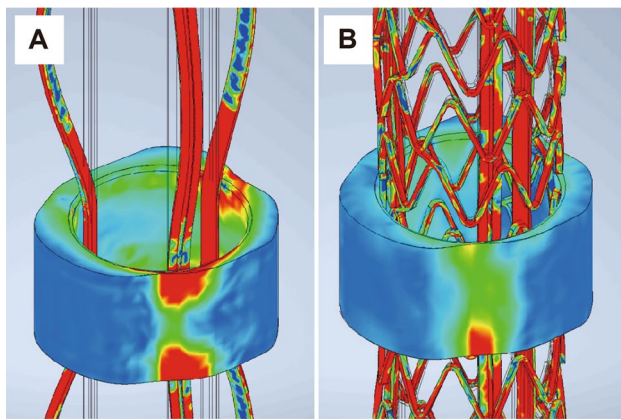


Fig. 5 Separation of pressure by the implanted stent can be observed if the balloon was set as invisible. **A** Dilation by Wolverine in the calcification model without stent implantation. **B** Dilation by Wolverine in calcification model with stent implantation

Discussion

In this study, we found that the maximum balloon pressure for heavy coronary calcification was significantly higher, and first principal stress in response to balloon pressure was lower after stent implantation. In-stent dilation became more difficult, even with subsequent procedures using a cutting balloon. Hence, adequate pretreatment of coronary calcification is a prerequisite for successful stent implantation. In addition, the current study elucidated the mechanism of subsequent dilation by cutting balloons after stent underexpansion through bench tests and software analysis.

Wolverine for stent underexpansion

Coronary calcification can lead to stent underexpansion. It is difficult to manage and is an important trigger of in-stent restenosis or thrombosis if left untreated [2, 11]. Conventional NC Emerge angioplasty might fail to dilate the heavy circumferential calcification, while shockwave lithoplasty or excimer laser may not be available in every facility [12]. A cutting balloon is indicated for resistant lesions, and studies have described its successful application for calcifications that are undilatable with NC Emerge [6, 8]; it was also more accessible and less complicated than other alternatives [13]. However, studies that demonstrated the use of cutting balloons for stent underexpansion in coronary calcifications are limited to case reports. In this study, we compared the efficacy of balloons in the dilation of heavy coronary calcifications with or without stent implantation. The results of the bench test showed that a significantly higher balloon pressure was required after stent implantation in both the NC Emerge and Wolverine groups, and that the maximum balloon pressure was the lowest in the Wolverine group

without stent implantation. Similar to our previous study [9], in models without stents, the Wolverine balloons achieved successful expansion with a lower balloon pressure than NC Emerge, however, no significant difference was observed between the Wolverine and NC Emerge groups with stent implantation, and the maximum balloon pressure and number of dilations were comparable between these groups, with an insignificant *p* value. The results were consistent with those of structural analysis as the FEM showed that the first principal stress in response to balloon dilation was lower in calcification models with stent implantation. Evidence on in-stent dilation by cutting balloons is limited, and this study provided insights into the mechanism of in-stent dilation by Wolverine through both bench tests and software analysis.

Pretreatment is critical

In a highly calcified lesion, insufficient pretreatment leads to stent underexpansion, which exposes the patient to the risk of restenosis or stent thrombosis [1, 3]. In addition, stents hinder medial expansion, making post-dilation more difficult. This study showed that after stent implantation, in-stent dilation turned out to be more difficult since the dilating pressure was separated by the implanted stent strut; it acts as a “chain armor” that protects calcification from the damage of blades. Such a “stent-chain armor” effect impedes the expansion procedures after stent implantation.

There are several studies on the treatment of stent underexpansion, such as a rotational atherectomy system [14–16] or excimer laser [5, 17], but these techniques might be associated with undesirable complications during in-stent procedures. Luca et al. [12] evaluated 16 patient samples with underexpanded stents in coronary calcifications; one coronary dissection and one burr entrapment occurred during the procedure and two revascularizations and one death occurred during the 1-year follow-up. Saroji et al. [18] evaluated the safety of orbital atherectomy in 41 patients with in-stent restenosis secondary to stent underexpansion; 2 patients had periprocedural myocardial infarction and 2 had coronary perforation. Julian et al. [19] investigated the outcomes of intravascular lithotripsy in 13 patients with resistant stent underexpansion; no adverse events were observed perioperatively. However, the sample size of the abovementioned studies was small, and the safety is questionable. In this study, higher pressure was required after stent implantation, and some models required a pressure > 20 atm to crack. The risk of rupture increased once the pressure was > 20 atm because it was the rated burst pressure of the balloon. This is the reason why studies have emphasized the importance of predilation [6, 15, 20] and Farman et al. [6] suggested that every effort should be made to crack the calcification and prepare the vessel before stent deployment. This study

indicates that adequate pretreatment of coronary calcifications is easier and more efficient than post-dilation.

Three-dimensional printing and the FEM

This study was possible because of the increasing capability of general-purpose computers and the widespread use of 3D printers. It is expected that more studies will be possible in the future that combine theoretical structural analysis and empirical experiments using 3D printers. Although there have been reports on the expansion mechanism of cutting balloons using the FEM [21], the results of the FEM vary greatly depending on the settings of the initial conditions, material properties, and the existence of stress singularities.

We considered that the FEM results alone were weak and needed to be supported by 3D-printed models. In this study, the results of the FEM and the bench test were consistent, which bolstered the validity of this study.

Limitations

This study has several limitations. First, the properties of 3D-printed calcification models were not the same as the circumferential calcification in the coronary artery, and variation may exist among the 3D-printed models. Second, the balloon pressure added to Wolverine was up to 20 atm, while the rated burst pressure was 12 atm for Wolverine. However, since the Wolverine used the same material as NC Emerge, it was mostly safe during the study. Third, only Wolverine and NC Emerge were used as study materials, and no comparison was made between different designs of cutting balloons or different materials of balloon catheters.

Conclusion

Dilation after stent delivery becomes more difficult, even with cutting balloons. The cutting balloon cannot act directly on the calcified lesion, and the implanted stent significantly separates the pressure. Therefore, proper pretreatment of calcified lesions is a prerequisite for successful stent implantation.

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Declarations

Conflict of interest The authors have no conflicts of interest to declare.

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