

**Novel 3D-CT evaluation of carotid stent volume: greater chronological expansion
of stents in patients with vulnerable plaques**

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Abstract

Purpose: Although self-expanding carotid stents may dilate gradually, the degrees of residual stenosis have been quantified by the NASCET criteria, which is too simple to reflect the configuration of the stented artery. We measured the volumes of the stent lumens chronologically by 3D-CT in patients after carotid artery stenting (CAS), and analyzed the correlations between the volume change and medical factors.

Methods: Fourteen patients with carotid artery stenosis were treated using self-expanding, open-cell stents. All patients underwent preoperative plaque MRI (magnetization-prepared rapid acquisition gradient-echo, MPRAGE) and chronological 3D-CT examinations of their stents immediately after their placement and 1 day, 1 week, and 1 month after the procedure. The volume of the stent lumen was measured using a 3D workstation. The correlations between stent volume and various factors including the presence of underlying diseases, plaque characteristics, and the results of the CAS procedure were analyzed.

Results: Stent volume gradually increased in each case and had increased by 1.04-1.55 (mean, 1.25)-fold at 1 postoperative month. The presence of underlying medical diseases, plaque length, the degree of residual stenosis immediately after CAS, and plaque calcification did not have an impact on the change in stent volume. On the other hand, the stent volume increase was significantly larger in the patients with vulnerable plaques that demonstrated high MPRAGE signal intensity ($P < 0.05$).

Conclusions: A 3D-CT examination is useful for precisely measuring stent volume.

Self-expanding stents in carotid arteries containing vulnerable plaques expand significantly more than those without such plaques in a follow-up period.

Key words: carotid artery stenting, carotid stenosis, plaque MRI, 3D-CT

List of Abbreviations: CAS = carotid artery stenting; CI = confidence interval; HU = Hounsfield unit; ICC = intraclass correlation coefficients; MPRAGE = magnetization-prepared rapid acquisition gradient-echo; NASCET = the North American Symptomatic Carotid Endarterectomy Trial; WW/WL = window width and window level

Introduction

CAS is performed as an alternative treatment for carotid artery stenosis in patients for whom endarterectomy is considered to be high-risk. Today, self-expanding stents are widely used because of their flexibility and conformability. Previous authors have reported that self-expanding stents gradually dilate, even after placement in biliary tracts [1], coronary [2, 3] or carotid arteries [4-8]. However, they evaluated stent dilatation using plain radiography, angiography, or ultrasound imaging and quantified the degree of stenosis using the NASCET criteria [9]. We agree that the NASCET method is quite useful because of its simplicity and good interobserver reproducibility, but it is a one-dimensional evaluation method and does not reflect the overall configuration of the stented artery. In the recent studies examining the flow dynamics of carotid arteries [10, 11], it was difficult to elucidate the hemodynamic conditions within the arteries from the degree of stenosis determined using the NASCET method alone. Carotid arteries and deployed stents are three-dimensional structures, and stents dilate not only at the most stenotic point but also in other regions after they have been deployed. Additionally, if we can clarify the special conditions under which chronological expansion of self-expanding stents is observed more significantly, CAS procedures for the patients with such conditions may be tailored. Postoperative 3D-CT images can clearly depict the deployed stent that demarcates the lesion of carotid stenosis. In this study, we measured stent volumes based on 3D-CT images to more precisely evaluate the time course of stent dilatation and attempt to find factors that impact on the changes of stent volume.

Methods

This study was approved by the institutional ethical committee of Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences.

Patient population

From January 2009 to December 2010, 34 CAS procedures were performed at our hospital on 31 consecutive patients with symptomatic or asymptomatic carotid artery stenosis of >60% degree on the NASCET criteria confirmed by digital subtraction angiography. A Precise stent (Cordis endovascular, Miami Lakes, FL) was used in 27 cases, and a Wallstent (Boston Scientific, Natick, MA) was used in 7 cases. We excluded a small group of the patients treated using a Wallstent that has different natures of the device. This study included the patients in whom the follow-up radiological 3D-CT imaging studies as mentioned below were completed. Clinical data regarding the patients' medical background were obtained from their medical records.

Finally, 14 patients who were successfully treated with Precise stents and completely followed-up with 3D-CT imaging were included. A Precise stent was appropriately deployed to the target lesion in each case, and there were no complications. The patients' background and plaque characteristics are summarized on Table 1. Eleven patients had a history of transient ischemic attack or stroke within 90 days before CAS, and 3 patients were asymptomatic despite displaying carotid stenosis of >60% on

angiography. Twelve patients were hypertensive, 7 had dyslipidemia, and 6 had diabetes mellitus.

CAS procedure

The administration of both aspirin (100 mg/day) and clopidogrel (75 mg/day) was initiated 7-10 days before the CAS procedure and was continued for at least 3 months after the procedure. CAS was performed by two educators certified by Japanese Society for Neuroendovascular Therapy (K.T. and K.S.) using a distal protection device, such as an AngioGuard EX (Cordis endovascular), FilterWire EZ (Boston Scientific) or PercuSurge GuardWire (Medtronic, Santa Rosa, CA). The lesion was pre-dilated with a 3.0 mm diameter angioplasty balloon, and an 8, 9, or 10 mm diameter, open-cell, self-expanding stent (Precise stent, Cordis endovascular) was deployed. The size of the deployed stent was 1.0-1.5 mm larger than the estimated diameter of the common carotid artery. All stents were post-dilated using 3.0-5.0 mm balloons, which were 0.5-1.0 mm smaller than the diameter of the distal internal carotid artery.

Postoperative chronological 3D-CT exams

Postoperative 3D-CT images were obtained with a 16-channel multidetector row CT scanner (Aquilion 16, Toshiba, Tokyo, Japan) using the following settings: section thickness: 1.0 mm, table feed: 30 mm/s, gantry rotation time: 0.5 s, pitch factor: 0.94, tube voltage: 120 kV, tube current: 150 mA. The 3D-CT examinations were performed immediately after the stent placement, and at 1 day, 1 week, and 1 month

after the procedure. No contrast agent was used for the 3D-CT as it was only necessary to visualize the frame of the stent. The examination performed at 1 week after the CAS included both plain 3D-CT and enhanced 3D-CT angiography using a contrast agent so as to allow the detection of in-stent thrombosis.

Measurement of stent volume

The volume of the stent was measured using a 3D workstation (ZIO station, Amin Co., Ltd., Tokyo, Japan) (Fig.1). We constructed a 3D volume rendering image of the stent from the DICOM data, and the stent was segmented using the threshold technique. By setting WW/WL at appropriate levels for delineating the boundaries of the stent (WW/WL=500/1500 HU; values obtained from a phantom study), the stent was successfully separated from the surrounding tissue. The stent border was outlined manually, and the non-stent area was removed. Finally, the volume of the stent was automatically calculated by the workstation.

CT of plaque calcification

Plaque calcification was evaluated based on axial CT images preoperatively. The cut-off point between calcified tissue and other tissues was set at 130 HU, as documented in previous studies [12]. A calcification arc involving more than 50% of the vessel circumference was defined as heavy calcification, that involving 25% to 50% of the vessel circumference was classified as moderate calcification, and that involving less than 25% of the vessel circumference was defined as light calcification.

MRI for assessing plaque vulnerability

The preoperative MRI evaluation of plaque characteristics was performed with 3D inversion-recovery-based T1-weighted MR imaging (MPRAGE) using axial sections, a black-blood sequence (inversion time: 650 msec, TR: 1300msec), and fat suppression (water excitation technique) [13, 14]. We used standard neck array and spine array coils and a Magnetom Verio 3.0-T system (Siemens Medical Solution, Erlangen, Germany). The scan covered the stenotic lesion and the carotid artery bifurcation, and the other scanning parameters were as follows: TE: 3.23 msec, FOV: 260 × 260 mm, matrix: 256 × 256, section thickness: 1.0 mm, flip angle: 10°, and data acquisition time: 310 seconds.

The MR images were reviewed by an experienced neurosurgeon (T.H.). The signal intensity of the carotid plaque was assessed on MPRAGE MRI relative to that in the adjacent sternocleidomastoid muscle measured by placing a round region of interest 5-8 mm in diameter in the area with homogenous signal intensity. A plaque displaying signal intensity of greater than 200% relative to that of the muscle was categorized as a MPRAGE high intensity plaque (Fig. 2A, B).

Inter-/intraobserver variability

To determine the levels of intraobserver and interobserver variability, ICC with 95% CI were calculated. Two observers independently reviewed the CT images and measured the volume of the stent lumen (first, H.I.; second, Y.O.). Each observer was

blinded to the other's assessment. The first observer repeated the volume measurement after a >6-month interval.

Statistical analysis

We analyzed the relationships between the rate of change in stent volume and various factors, including underlying medical conditions (hypertension, dyslipidemia, diabetes mellitus), residual rate of stenosis immediately after CAS, and plaque characteristics (calcification, lesion length, and signal intensity on MPRAGE MRI). The Mann-Whitney U test was used to assess the changes in stent volume and the correlations between stent volume and various factors. Residual stenosis after stent placement and lesion length were treated as continuous variables and assessed through nonparametric analysis using Spearman's rank correlation coefficient. Statistical analysis was performed with JMP ver. 9.0.0 (SAS Institute Inc., Cary, NC). Differences were considered significant at P values of <0.05.

Results

3D-CT data were obtained immediately after the CAS procedure, and follow-up CT examinations were performed at 1 day, 1 week (mean \pm SD; 5.9 ± 0.9 days), and 1 month after the procedure (34.5 ± 8.3 days) (Fig. 2C). The ICC for the intraobserver and interobserver variability in the stent volume measurements were 0.92 and 0.86, respectively, both of which indicated excellent correlations. The devices used and the stent volume measurements are shown in Table 2. The mean ratios of the volume

recorded at each time point to that observed immediately after the CAS were 1.06 at 1 day, 1.13 at 1 week, and 1.25 at 1 month (Fig. 3). There were statistically significant increases between each time point (day 0 to day 1: $P=0.0018$, day 1 to 1 week: $P=0.0077$, 1 week to 1 month: $P=0.0063$, and $P<0.0001$: day 0 to 1 month; Mann-Whitney U test; Fig 3). Case 14 displayed the smallest change in stent volume at 1 month after the procedure (1.04 fold increase), whereas Case 3 demonstrated the largest increase (1.55 fold).

The relationships between the rate of change in stent volume and various factors are demonstrated in Fig. 4. There were no significant relationships between the volume changes observed at 1 month after the procedure and any of the medical conditions (hypertension: $P=0.784$, dyslipidemia: $P=0.798$, diabetes mellitus: $P=1.000$; Mann-Whitney U test). Neither the postoperative residual rate of stenosis or lesion length had a significant impact on the degree of stent expansion (residual stenotic rate: Spearman $\rho=0.0515$, $P=0.861$; lesion length: $\rho=0.195$, $P=0.377$). Although the patients with smaller stent volume immediately after CAS demonstrated the larger rate of the volume change in one month (Spearman $\rho=-0.552$, $P=0.046$), their absolute values of the stent volume one month later were still smaller (Spearman $\rho=0.858$, $P=0.002$). There were no significant differences in the volume change ratios among the 8 mm, 9 mm, and 10 mm diameter stents, nor did the presence or absence of calcification involving $>50\%$ or $>25\%$ of the vessel circumference have a significant effect on stent volume ($P=1.000$, 0.894 , respectively). On the other hand, in the patients with plaques displaying high signal intensity on MPRAGE, the rate of volume

change in the month after the procedure was significantly greater than that in the patients with low intensity plaques ($P=0.0332$).

Discussion

Chronological measurement of stent volume

The degree of carotid artery stenosis is usually expressed by NASCET method or as the cross-sectional area of the region displaying the greatest stenosis. However, these indices do not reflect the overall configuration of the stent. We adopted the stent lumen volume as an index for evaluating ongoing stent dilatation. This is the first paper to report the chronological changes in carotid stent volume based on 3D-CT images. For aortic aneurysms, difficulty in assessing the three-dimensional structures with one-dimensional measurement systems and superiority of volumetric measurement were reported [15, 16]. Yao et al [17] measured the segmental vessel volume of the carotid artery before and after carotid endarterectomy in a 3D ultrasound study. We used 3D-CT data to measure stent volume because 3D-CT allows clearer visualization of the artery and the stent than other techniques such as MR angiography and duplex sonography. 3D-CT also has a good resolution, making it easy to eliminate the structures surrounding the stent.

Various authors have reported that self-expanding stents enlarge over time after deployment [1, 4-7], and previous coronary IVUS studies found that self-expanding stents continued to enlarge over the 6 month study period [18]. Bussière et al [6] detected the enlargement of self-expanding carotid stents and concluded that additional

balloon angioplasty might not be required. Clark et al [5] reported that the cross-sectional areas of the carotid stents in their population had increased by 48.9% at the 6 months follow-up. Our results demonstrated a 25% increase in the mean stent volume at the 1 month follow-up examination. The volume of the stent lumen might increase more over a longer follow-up period, although it is not easy to directly compare our results with those of previous reports because of the different measuring methods employed.

MPRAGE MRI and stent dilatation

In our study, the stents deployed in carotid arteries containing atherosclerotic plaques that displayed high signal intensity on MPRAGE MRI were dilated more than those in arteries containing low intensity plaques. This suggests that plaque characteristics impact on the time course of stent dilatation. Willfort-Ehringer et al [7] reported that the expansion of the central diameter of carotid stents was most pronounced in areas containing echo-lucent “soft” plaques. MPRAGE MRI has been reported to be useful for evaluating plaque characteristics [14, 19]. Hishikawa et al [13] found that plaques that displayed high signal intensity on MPRAGE consisted of a large necrotic core and intraplaque hemorrhaging. The plaques that displayed low signal intensity on MPRAGE were found to contain fibrous components, and hence, were more rigid.

The necrotic core inside lipid-rich soft plaques can protrude through the stent struts during CAS procedures [20]. This deformation leads to in-stent thrombus and embolic complications [21]. Given the expectation of delayed expansion, it may be reasonable

to avoid an immediate large increase in the lumen in order to prevent plaque protrusion in patients with vulnerable plaques. The Precise stent has a strong radial force, which contributes to its delayed expansion, but plaque protrusion might occur more easily. Fortunately, we did not encounter the cases with early plaque protrusion or in-stent thrombosis in our series. In the future, it will be necessary to design stents in consideration of both the prevention of plaque protrusion and the desired degree of postoperative stent dilatation.

Impacts of underlying medical factors and calcification on stent dilatation

Bussière et al demonstrated that the absence of dyslipidemia was predictive of an increased risk of unsuccessful treatment with stenting alone; i.e., without angioplasty [6]. In our study, most of the patients with a history of dyslipidemia had already received cholesterol-lowering drugs, so no significant correlation between a history of dyslipidemia and chronological stent dilatation was detected.

Severe calcification in coronary and carotid lesions is also considered to be a predictor of incomplete expansion [22-24]. In our study, plaque calcification did not have a significant influence on the time course of stent dilatation. Even “heavy calcification”; i.e., that involving more than 50% of the vessel circumference, had no significant impact. Tsutsumi et al [25] revealed fragmentation of a calcified lesion after CAS in patients with highly calcified plaques, and similar findings were observed in some of our cases. Post-dilatation was performed in all of our cases, so the calcified lesions might have been fragmented, and hence, only had a small effect on stent

dilatation. However, as patients with extremely thick calcifications are not eligible for CAS at our institution, the effects of calcification might have been underestimated.

Study limitations

First, this was a retrospective study with a small sample size and a short observation period. In future studies consisting of a larger number of patients and a longer follow-up period, we might be able to clarify an acceptable degree of residual stenosis after CAS based on patient-specific radiological and medical conditions. Second, we only measured the volume of the stent lumen and ignored possible neointimal hyperplasia or thrombosis inside the stent because it was difficult to set appropriate WW/WL thresholds for delineating the boundaries of the vessel lumen. Accordingly, changes in stent volume do not directly reflect the actual change in the size of the vessel lumen, although Watarai et al detected chronological increases in the size of the vessel lumen that were proportional to the dilatation of the stent diameter until 12 weeks after CAS [8]. In future studies, the vessel lumen should be measured in order to evaluate the relationship between the changes in stent lumen and those of the vessel lumen. Third, the measurement of stent volume was mostly performed using a time-consuming manual process in this study. It took around one hour to measure the volume of one stent. The development of new software for automatically measuring the volume of the stent lumen would contribute toward advancing this kind of study.

Conclusions

A 3D-CT examination is useful for precisely measuring stent volume and evaluating the time course of its expansion. Self-expanding stents in carotid arteries containing vulnerable plaques expand significantly more than those without such plaques in a follow-up period. For patients with vulnerable plaques in whom delayed large expansion of the stent can be expected, it may be reasonable to avoid an immediate large increase in the lumen during CAS in order to prevent production of a large amount of debris or plaque protrusion.

Disclosures

The authors have no personal or institutional interest in any of the drugs, materials, or devices described in this article.

Acknowledgements

Financial support: This research was supported by SENSHIN Medical Research Foundation, 2010 (no applicable grant number).

Portions of this work were presented in abstract form at the 10th Meeting of Asian Australasian Federation of Interventional and Therapeutic Neuroradiology, Nagoya, Japan, June 14, 2012.

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Figure legends

Fig 1. Measurement of stent volume based on 3D-CT images

A: A volume-rendering image of a carotid stent and the surrounding bones. B: An MIP image obtained before adjusting the window width and window level (WW/WL). C: The border of the stent could be clearly visualized from the same angle by using appropriate WW/WL settings (500/1500). D: The border of the stent was manually outlined, and the non-stent area was removed. The volume of the stent was automatically calculated.

Fig. 2. Time course of the increase in stent volume in Case 3, which involved a vulnerable plaque.

A: A left common carotid arteriogram showing severe stenosis in the left internal carotid artery. B: MPRAGE MRI demonstrating a carotid plaque (arrow) displaying a signal intensity that was 2.58 fold higher than that of the adjacent muscle (arrowhead). C: MIP images showing a stent with a volume of 1.19 cm³ immediately after stent placement (left), 1.26 cm³ 1 week later (center), and 1.85 cm³ 1 month later (right).

Fig 3. Graphs demonstrating the time course of the change in the mean ratio of the stent volume at each time point to that observed immediately after CAS.

The dashed line represents the mean values for each period, which significantly increased between each period.

Fig 4. Graphs showing the rate of volume change at 1 month after CAS in the patients with or without various medical factors and radiological findings.

The stents deployed in carotid arteries with plaques that displayed high intensity on MPRAGE MRI expanded more significantly than those deployed in arteries that demonstrated low intensity on MPRAGE MRI at the 1-month follow-up ($P=0.0332$).

Fig. 1

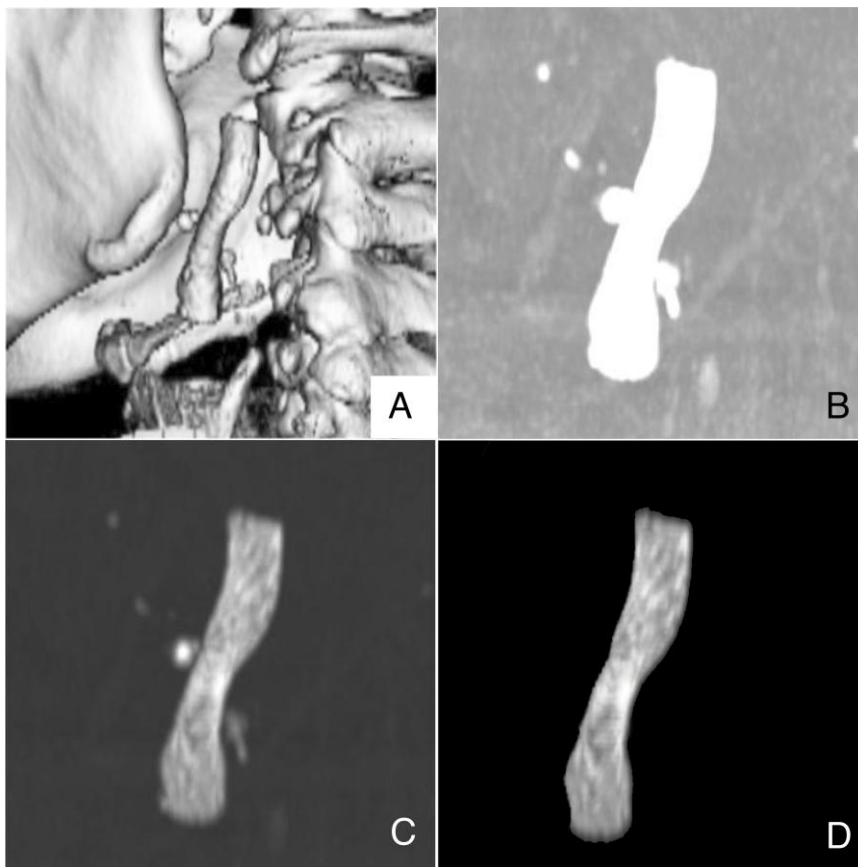


Fig. 2

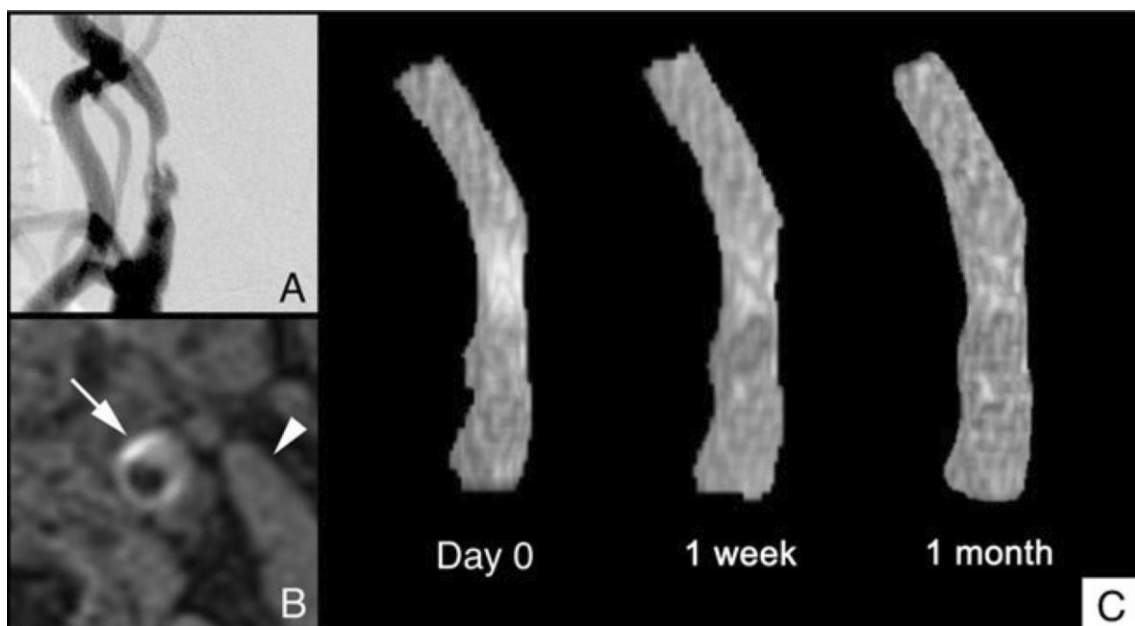


Fig. 3

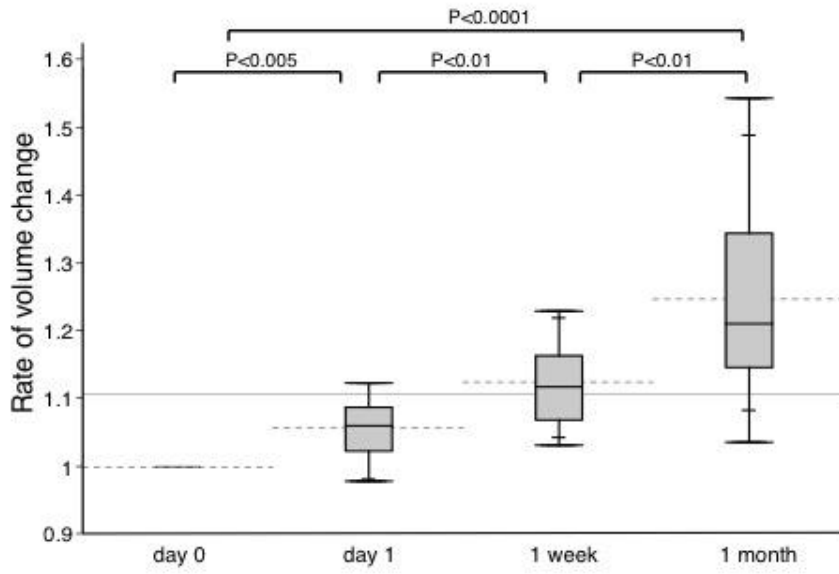


Fig. 4

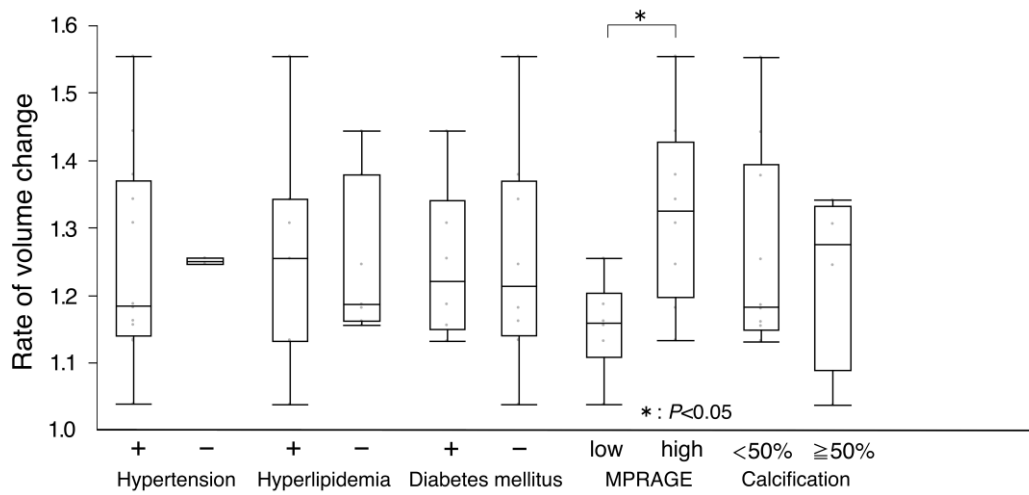


Table 1: Patient summary – background and plaque characteristics

No.	Age(y)/		lesion	HT	HL	DM	calcification	MPRAGE	lesion		stenosis(%)	
	Sex								length(mm)	pre	post	
1	71M	Lt Sx	+	-	-	light	high	21	90	20		
2	77M	Rt Sx	-	+	+	-	low	8	80	0		
3	71M	Lt Sx	+	+	-	-	high	18	85	20		
4	67M	Rt Sx	+	-	+	-	high	16	95	25		
5	77M	Rt Sx	-	-	-	heavy	low	17	80	10		
6	66M	Rt ASx	+	+	-	heavy	high	25	60	30		
7	77M	Rt ASx	+	-	-	light	high	17	60	20		
8	72M	Lt Sx	+	-	+	light	high	21	95	25		
9	74M	Rt Sx	+	+	+	heavy	high	15	95	20		
10	80M	Rt Sx	+	+	-	light	low	15	70	30		
11	81M	Rt Sx	+	+	+	light	low	11	90	0		
12	76M	Rt Sx	+	-	+	light	low	30	90	5		
13	78M	Lt Sx	+	-	-	moderate	high	29	80	40		
14	75M	Lt ASx	+	+	-	heavy	low	8	85	40		

Rt/Lt: right/left, Sx: symptomatic, Asx: asymptomatic, M: man, HT: hypertension,
HL: hyperlipidemia, DM: diabetes mellitus,

Table 2: Patient summary – devices and stent volume

No.	stent	EPD	devices		volume of the stent lumen (cm ³)			
			pre dilatation	post dilatation	day 0	day 1	1 week	1 month
1	Precise 9/40	GW	Sterling 3.0/40	Sterling 4.0/30	1.45	1.55	1.67	2.00
2	Precise 10/40	AG	N/A	Submarine 4.0/20	2.39	2.39	2.89	3.00
3	Precise 8/40	AG	Sterling 3.0/40	Submarine 4.0/40	1.19	1.26	1.26	1.85
4	Precise 10/40	GW	Submarine 3.0/40	Aviator 4.0/30	1.78	2.00	2.20	2.57
5	Precise 10/40	AG	Submarine 3.0/40	Sterling 5.0/30	2.19	2.36	2.50	2.73
6	Precise 8/40	AG	Sterling 3.0/40	Aviator 4.0/30	1.40	1.50	1.70	1.88
7	Precise9 /40	AG	Submarine 3.0/40	Sterling 4.0/30	2.03	2.10	2.30	2.36
8	Precise 8/40	AG	Sterling 3.0/40	Aviator 4.0/30	1.92	1.99	2.11	2.28
9	Precise 8/40	GW	Submarine 3.0/40	Sterling 4.0/40	1.43	1.61	1.65	1.87
10	Precise 10/40	GW	Submarine 3.0/40	Sterling 4.5/20	2.38	2.38	2.54	2.70
11	Precise 8/40	GW	Sterling 3.0/40	Sterling 3.0/40	1.88	1.97	2.02	2.13
12	Precise 10/40	GW	Sterling 3.0/40	Sterling 4.5/30	2.11	2.28	2.34	2.44
13	Precise 8/40	GW	Sterling 3.0/40	Aviator 4.0/30	2.03	2.29	2.24	2.40
14	Precise 8/40	FW	Sterling 3.0/40	Jackal 4.0/30	1.79	1.75	1.85	1.86

EPD: embolic protection device, GW: PercuSurge GuardWire,

AG: Angioguard EX, FW: FilterWire EZ, N/A: not applied