Methods

Study Population

We retrospectively enrolled 51 consecutive de novo native coronary artery lesions from 44 angina patients who were treated using a single 2nd-generation DES (Xience Prime, Promus Element, or Nobori) under OCT guidance. Exclusion criteria were as follows: coronary artery bypass graft, post-stent dilation using 2 balloons (kissing balloon inflation and hugging balloon inflation), in-stent restenosis, uninterpretable OCT image, and inability to cross the lesion with the OCT catheter. This study was approved by the Kawasaki Medical School Internal Review Board. Because of the retrospective study design, written informed consent for the interventional procedures, including OCT imaging, was obtained from the patients.

Study Protocols

Cardiac Catheterization and OCT

After intravenous heparin (100U/kg) and intracoronary nitroglycerin (200 μg) were...
administered, conventional diagnostic coronary angiography was performed. A 6 or 7Fr coronary guide catheter was used to engage the target coronary artery. Before the percutaneous coronary intervention (PCI) procedure, a commercially available Time-domain OCT wire (ImageWire; LightLab Imaging Inc, MA, USA) or Fourier-domain OCT catheter (C7; St. Jude Medical, MN, USA) was used to record the imaging of the culprit lesion. As previously described, OCT recording was performed to acquire image sequence using an automated pullback, which started at least 10 mm distal to the target lesion. Thereafter, PCI was performed using a single 2nd-generation DES. All PCI procedures, including stent selection, usage of Rotablator (Boston Scientific, MA, USA), and post dilatation other than stent balloon, were at the operator’s discretion. After successful stent implantation, OCT imaging was repeated to acquire postprocedural imaging.

OCT Analysis  OCT imaging was analyzed by dedicated interventional cardiologists using a commercially available offline review workstation (St. Jude Medical). By OCT, calcification is defined as well-delineated, signal-poor regions with sharp borders by which the lipid plaque can be differentiated. Arc, area, and maximal thickness of the calcium were measured at the target lesion with the greatest extent of calcification. The longitudinal extension of the calcification was also assessed. Minimal stent diameter (MSD) and minimal stent area (MSA) as well as maximal stent diameter at the MSA site were detected and measured on the postprocedural OCT imaging. Stent eccentricity was defined as (maximal stent diameter minus MSD) divided by maximal stent diameter. The final maximal deployment pressure was obtained from the physician’s procedural report, and the predicted stent or balloon diameters were derived from the manufacturers’ compliance charts. If the stent was postdilated, the predicted stent diameters were derived from the balloon used for postdilation. Stent expansion was defined as MSD (or MSA) divided by the values predicted by the manufacturers’ compliance charts.

Statistical Analysis  Analyses were performed using SPSS 21 software (SPSS Inc, Chicago, IL, USA). Categorical variables are presented as number and percentage. Continuous variables are presented as mean±standard deviation, regardless of the distribution, to facilitate visualization of the tables. Among the 2nd-generation DES groups, Pearson’s chi-square test was used for comparisons of categorical variables, and 1-way ANOVA or Kruskal-Wallis test was used for comparisons of continuous variables, depending on the results of normality test (Shapiro-Wilk test). Pearson’s correlation coefficients between stent eccentricity and quantity of calcium were calculated and represented using scatter plot graphics. In addition, Pearson’s correlation coefficients between stent eccentricity and quantity of calcium were calculated. Because of the skewed distribution of quantity of calcium (arc, area, and length of calcium) and stent eccentricity, data were normalized by logarithmic transformation for statistical analysis. Patients were divided into 4 groups according to the median values of the arc and area of calcium. Data were analyzed by 2-way factorial ANOVA after testing the normality of the data, and then differences among means were analyzed using Tukey-HSD multiple comparison tests. A 2-sided P value <0.05 was
considered significant.

**Results**

In this study, 3 types of 2nd-generation DES (Xience Prime; Abbott Vascular, CA, USA, n=17. Promus Element; Boston Scientific, MA, USA, n=15. Nobori; Terumo Corporation, Kanagawa, Japan, n=19) were used to treat 51 de novo native coronary artery lesions. Overall patient, lesion, and procedural characteristics are summarized in Table 1. In this study, 3 types of 2nd-generation DES (Xience Prime; Abbott Vascular, CA, USA, n=17. Promus Element; Boston Scientific, MA, USA, n=15. Nobori; Terumo Corporation, Kanagawa, Japan, n=19) were used to treat 51 de novo native coronary artery lesions. Overall patient, lesion, and procedural characteristics are summarized in Table 1. In addition, the arc of calcium showed weak but significant correlation with stent expansion defined by MSA, and the area of calcium showed signifi-

Correlations between stent expansion and the amount of coronary calcium (arc/area of calcium) are presented in Figures 2A-D. The arc and area of calcium showed weak but significant correlation with stent expansion defined by MSA (arc of calcium, r=−0.53, P<0.01; area of calcium, r=−0.48, P=0.01, respectively) (Figures 2A,B). In addition, the arc of calcium showed significant correlation with stent expansion defined by MSA (r=−0.33, P<0.02) (Figure 2C). On the other hand, the area of calcium did not show a significant correlation with stent expansion defined by MSA (r=−0.26, P=0.07) (Figure 2D). Maximal thickness of calcium did not show significant correlation with either stent expansion defined by MSA (r=−0.23, P=0.11) or MSA (r=−0.07, P=0.61). Also, the length of calcium did not show significant correlation with either stent expansion defined by MSA (r=−0.16, P=0.26) or MSA (r=−0.15, P=0.30).

Furthermore, there was a significant positive correlation between stent eccentricity and the area of calcium (r=0.42, P<0.01), whereas the arc of calcium did not correlate significantly (r=0.22, P=0.13). There was also a significant positive correlation between stent eccentricity and maximal thickness of calcium (r=0.37, P<0.01).

Correlations between stent expansion and the amount of coronary calcium were similar after exclusion of the 6 lesions modified by pre-interventional rotational atherectomy (MSD and arc of calcium, r=−0.36, P=0.01; MSA and area of calcium, r=−0.39, P<0.01; MSA and arc of calcium, r=−0.33, P=0.03; MSA and area of calcium, r=−0.28, P=0.07, respectively).

To further investigate if a combination of the arc and area of calcium predicts stent expansion, patients were divided into 4 groups according to the median values of the arc (=90°) and area (=1.58 mm²) of calcium: group 1 (smaller arc and smaller area of calcium); group 2 (larger arc and smaller area of calcium); group 3 (smaller arc and larger area of calcium); and group 4 (larger arc and larger area of calcium). Stent expansion defined by MSA was significantly different among the 4 groups (P=0.02) and post-hoc analysis showed significant difference between groups 1 and 4 (P=0.01) (Figure 3A). Stent expansion defined by MSA showed a similar trend (P=0.16) (Figure 3B).

### Table 2. Patient, Lesion, and Procedural Characteristics by Stent Type

<table>
<thead>
<tr>
<th>Variable</th>
<th>Xience Prime</th>
<th>Promus Element</th>
<th>Nobori</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70±10</td>
<td>67±11</td>
<td>67±14</td>
<td>0.69</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>8 (62)</td>
<td>8 (57)</td>
<td>12 (71)</td>
<td>0.72</td>
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<tr>
<td>Diabetes mellitus, n (%)</td>
<td>2 (15)</td>
<td>7 (50)</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>11 (85)</td>
<td>14 (100)</td>
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<td>Dyslipidemia, n (%)</td>
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<td>Smoking, n (%)</td>
<td>3 (23)</td>
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<tr>
<td>Family history, n (%)</td>
<td>4 (31)</td>
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</table>

Lesion and procedural characteristics (n=51)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diagnosis (stable angina/ACS)</th>
<th>Target coronary artery (LAD/LCX/RCA)</th>
<th>Type of target lesion (A/B1/B2/C)</th>
<th>Stent diameter (mm)</th>
<th>Stent length (mm)</th>
<th>Rotablator, n (%)</th>
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<th>Post dilatation balloon, n (%)</th>
<th>Inflation time (s)</th>
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</table>
| Values are mean ± SD or number and percentage. Abbreviations as in Table 1.

### Table 3. OCT Data and Stent Expansion (n=51)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Arc of calcium (°)</th>
<th>Area of calcium (mm²)</th>
<th>Length of calcium (mm)</th>
<th>Thickness of calcium (mm)</th>
<th>MSD (mm)</th>
<th>MSA (mm²)</th>
<th>Stent expansion defined by MSD (%)</th>
<th>Stent expansion defined by MSA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Values are presented as mean ± SD. MSA, minimal stent area; MSD, minimal stent diameter; OCT, optical coherence tomography.</td>
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Discussion

The main findings of this study were: (1) stent expansion of 2nd-generation DES was generally smaller than expected from the manufacturer’s compliance charts in the clinical setting, and (2) the amount and extent of coronary calcification as assessed by OCT were associated with stent expansion and stent eccentricity. To the best of our knowledge, this is the first report to demonstrate a relationship between stent expansion and coronary calcification as assessed by OCT.

Stent underexpansion was an important predictor for in-stent restenosis following bare-metal stent implantation, and even in the era of DES, stent underexpansion still plays an important role as a cause of stent restenosis and thrombosis. Although stent expansion should be predicted by the manufacturers’ compliance charts, actual stent expansion at the stenotic coronary lesions in vivo is usually smaller than expected.

Table 4. OCT Data and Stent Expansion by Stent Type (n=51)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Xience Prime</th>
<th>Promus Element</th>
<th>Nobori</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arc of calcium (°)</td>
<td>94.5±28.8</td>
<td>87.5±38.7</td>
<td>101.0±49.2</td>
<td>0.50</td>
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<tr>
<td>Area of calcium (mm²)</td>
<td>2.25±1.17</td>
<td>1.55±1.32</td>
<td>2.13±1.65</td>
<td>0.14</td>
</tr>
<tr>
<td>Length of calcification (mm)</td>
<td>5.95±4.15</td>
<td>5.71±2.86</td>
<td>5.94±3.56</td>
<td>0.92</td>
</tr>
<tr>
<td>Thickness of calcium (mm)</td>
<td>1.00±0.39</td>
<td>0.87±0.32</td>
<td>0.98±0.38</td>
<td>0.55</td>
</tr>
<tr>
<td>MSD (mm)</td>
<td>2.20±0.40</td>
<td>2.06±0.37</td>
<td>2.41±0.44</td>
<td>0.05</td>
</tr>
<tr>
<td>MSA (mm²)</td>
<td>4.97±1.86</td>
<td>3.92±1.46</td>
<td>5.76±2.33</td>
<td>0.02</td>
</tr>
<tr>
<td>Stent expansion defined by MSD (%)</td>
<td>71.3±8.0</td>
<td>73.6±8.4</td>
<td>74.7±9.6</td>
<td>0.51</td>
</tr>
<tr>
<td>Stent expansion defined by MSA (%)</td>
<td>64.2±10.7</td>
<td>62.4±10.7</td>
<td>68.2±13.9</td>
<td>0.36</td>
</tr>
</tbody>
</table>

Values are mean±SD. Abbreviations as in Table 3.

Figure 2. Correlation between stent expansion and the quantity of coronary calcium. Correlation between stent expansion defined by MSD and the arc of calcium (A) or area of calcium (B). Correlation between stent expansion defined by MSA and the arc of calcium (C) or area of calcium (D). MSA, minimal stent area; MSD, minimal stent diameter.
Stent Expansion and Coronary Calcification

and extent of coronary calcification were associated with stent expansion, which is discordant with results from previous IVUS studies. These discordant results may relate to the enhanced resolution of OCT for delineating and quantifying coronary calcification compared with IVUS. The ultrasound signal cannot penetrate thick deposits of calcium and therefore only visualizes the surface of the calcified plaque. Moreover, acoustic shadowing caused by ultrasound obscures the external part of the calcium. In fact, IVUS poorly quantifies the area of calcification compared with OCT as referenced to histology. Kume et al compared the calcium arc and calcium area measured by OCT and IVUS with those obtained by histology. Calcium arc and area measured by OCT correlated better with histology than the IVUS values. In addition, measurement of the arc of calcium might not be accurate because of side lobe artifact, so the arc of calcium values in previous studies have usually been semiquantitatively categorized as <90°, 90–180°, 180–270°, and >270°. In contrast, OCT clearly delineates coronary calcification without artifact and therefore offers better quantitative assessment of calcified plaque.

In the present study, the area of calcium measured by OCT correlated significantly with stent expansion defined by MSD and not with stent expansion defined by MSA. This result possibly arose, because the degree of stent expansion was limited by large, thick areas of calcium with subsequent expansion laterally toward the vessel wall with minimal or no calcium content. The significant correlation between stent eccentricity and area/maximal thickness of calcium may support this hypothesis. A combination of relatively simple cutoff values for the arc (90°) and area (1.58 mm²) of calcium could predict stent expansion defined by MSD. Although a similar trend was observed for stent expansion defined by MSA, it was not statistically significant, perhaps because of the small sample size. Another possible explanation is that eccentric stent expansion possibly compensated for small MSD and weakened the effect of calcium on stent expansion defined by MSA.

Although the longitudinal length of calcium may also affect stent expansion, the results of our study did not show any relationship between the length of calcium and stent expansion. This may suggest that MSA is affected by the calcium burden of a single cross-section rather than the total amount of calcium. Furthermore, maximal thickness (axial extension) of calcium did not show a significant effect on stent expansion, though there was a trend of negative correlation between maximal thickness of calcium and stent expansion defined by MSD.

Recently, volumetric OCT analysis of coronary calcium content was proposed to be accurate. The effect of calcium volume on total stent expansion (ie, actual stent volume/expected stent volume) needs to be investigated. Stent expansion may be affected by the difference in the stent platform (size, material, and thickness). As shown in Table 2 and Table 4, differences in the diameter of the 3 types of DES used in the procedures seemed to affect the final MSD and MSA. On the other hand, there was no significant difference in stent expansion among the 3 different DES with different platforms. Owing to the small sample size for each stent, this study is underpowered to assess differences in stent expansion among the different 2nd-generation DES.

Our present study has an important clinical implication: an interventional strategy may be modified using the arc and area of calcium as assessed by OCT. Aggressive calcium ablation by rotational atherectomy, predilatation using a scoring balloon, and prolonged inflation of the delivery or postdilatation balloon may be warranted to achieve better stent expansion for lesions with a high likelihood of stent underexpansion. Although the superiority of OCT for postprocedural assessment compared with IVUS is well recognized, our present study suggests the superiority of OCT for preprocedural lesion assessment as well. In addition, preprocedural lesion assessment with OCT may have a potential to predict long-term stent me-

![Figure 3](image) Differences in stent expansion defined by MSD (A) and MSA (B). Patients were divided into 4 groups according to median values of the arc (90°) and area of calcium (1.58 mm²). *Difference between Group 1 and Group 2 (A). MSA, minimal stent area; MSD, minimal stent diameter.
Study Limitations

First, this was a retrospective observational study, although consecutive patients meeting the inclusion and exclusion criteria were enrolled. Second, to assess the relation of stent expansion and coronary calcification in vivo, we enrolled only de novo lesions and excluded complex lesions. Therefore, our results cannot be generalized to complex lesions such as in-stent restenosis, chronic total occlusion, and acute coronary syndrome. Third, the analyzed cross-sections using OCT could be inconsistent between pre- and post-PCI. Fourth, 6 lesions modified with rotational atherectomy were included in this study, though we confirmed similar results after the exclusion of these lesions. Finally, operators were not blinded to the OCT results. Because the treatment strategy was left to the operators’ discretion, this could have affected the final result of stent expansion. However, we believe that this study reflects real-world PCI and patient backgrounds, and therefore has pertinent clinical implications.

Conclusions

Expansion of 2nd-generation DES was smaller than expected from the manufacturers’ compliance charts, similar to that previously reported with bare-metal stents and 1st-generation DES. The amount of target lesion coronary calcium as assessed by OCT may be an important determinant of stent expansion.

Acknowledgment

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Disclosures

Conflict of Interest: None.

References