Percutaneous coronary interventions of bifurcation lesions

Grundeken, M.J.D.

Citation for published version (APA):
Chapter 12

In vitro validation and comparison of different software packages or algorithms for coronary bifurcation analysis using calibrated phantoms: implications for clinical practice and research of bifurcation stenting

Yuki Ishibashi
Maik J. Grundeken
Shimpei Nakatani
Javaid Iqbal
Marie-Angele Morel
Philippe Généreux
Chrysaftos Girasis
Jolanda J. Wentzel
Hector M. Garcia-Garcia
Yoshinobu Onuma
Patrick W.J.C. Serruys

Catheterization and Cardiovascular Interventions. 2015;85:554–563
ABSTRACT

Background
The accuracy and precision of quantitative coronary angiography (QCA) software dedicated for bifurcation lesions compared with conventional single-vessel analysis remains unknown. Furthermore, comparison of different bifurcation analysis algorithms has not been performed.

Methods
Six plexiglas phantoms with 18 bifurcations were manufactured with a tolerance <10 µm. The bifurcation angiograms were analyzed using Cardiovascular Angiography Analysis System (CAAS; Version 5.10, Pie Medical Imaging, Maastricht, The Netherlands) and QAngio XA (Version 7.3, Medis Medical Imaging System BV, Leiden, The Netherlands) software packages.

Results
Conventional single-vessel analysis underestimated the reference vessel diameter and percent diameter stenosis in the proximal main vessel while it overestimated these parameters in the distal main vessel and side branch. CAAS software showed better overall accuracy and precision than QAngio XA (with automatic Y- or T-shape bifurcation algorithm selection) for various phantom diameters including minimum lumen diameter (0.012±0.103 mm vs. 0.041±0.322 mm, P=0.003), reference vessel diameter (-0.050±0.043 mm vs. 0.116±0.610 mm, P=0.026), and % diameter stenosis (-0.94±4.07 % vs. 1.74±7.49 %, P=0.041). QAngio XA demonstrated higher minimal lumen diameter, reference vessel diameter, and % diameter stenosis when compared to the actual phantom diameters; however, the accuracy of these parameters improved to a similar level as CAAS when T-shape algorithm in the QAnxio XA was solely used.

Conclusion
The use of the single-vessel QCA method is inaccurate in bifurcation lesions. Both CAAS and QAngio XA (when the T shape is systematically used) bifurcation software packages are suitable for quantitative assessment of bifurcations.
INTRODUCTION

Two-dimensional quantitative coronary angiography (QCA) analysis in bifurcation remains technically challenging. When a conventional single-vessel analysis is used in a bifurcated lesion, two analyses should be performed: one from the proximal main to the distal main branch and the other from the proximal main to the side branch (SB) \(^1,^2\). In the so-called polygon of confluence \(^3\), the edge detection of single-vessel algorithms are not able to define the vessel contours crossing the bifurcation, which frequently requires manual corrections of contour and may introduce subjectivity or bias. Due to natural tapering after the bifurcation, the interpolated reference diameter calculated for the proximal main vessel (PMV) and tapered distal branches underestimates the % diameter stenosis (DS) of the PMV and overestimate %DS in the distal main vessel (DMV) or SB \(^4,^5\). To overcome these limitations, the dedicated bifurcation algorithms have been developed. Currently, two software packages are commercially available: the Cardiovascular Angiography Analysis System (CAAS; Pie Medical Imaging, Maastricht, The Netherlands) and QAngio XA software (Medis Medical Imaging Systems BV, Leiden, The Netherlands). CAAS has been validated in a phantom model with quantification of minimum lumen diameter (MLD) measurements showing a highly accurate and precise performance across a wide range of diameter values \(^6,^7\), whereas bifurcation algorithm of QAngio XA with segments was shown in vivo to be robust and reproducible in two clinical studies \(^8,^9\). However, it remains to be investigated whether the bifurcation algorithms, compared to a single-vessel analysis, significantly improve the accuracy of the analysis. Furthermore, the difference in accuracy between bifurcation analysis algorithms remains unknown. We, therefore, aimed to compare single-vessel analysis and bifurcation QCA analysis using CAAS and QAngio XA in calibrated phantoms.

MATERIALS AND METHODS

 Phantom Models

Six plexiglas phantoms, each of them mimicking a vessel with three successive bifurcations, were designed in 3D and manufactured with a tolerance <10 µm \(^10\). Every individual bifurcation had a lesion, wherein at least one vessel segment had a DS of >60% with the MLD being located within 3-6 mm from the point of bifurcation. The range of diameters, lesion length, angulation, and Medina class \(^5\) used in the design of these 18 bifurcations reflected the anatomic variation and the fractal nature of bifurcations in the human coronary tree as derived from relevant literature \(^6,^7,^{11,12}\).
**Acquisition and Calibration of Phantom Models**

The digital angiograms were acquired on a biplane angiographic system (Axiom Artis™; Siemens, Forchheim, Germany)\(^9\). All phantoms were filled with 100% Iodixanol 320 (Visipaque™; GE Healthcare, Cork, Ireland) and imaged at 30 frames per second, in a 20 cm field of view, with the center of the phantom placed precisely at the isocenter. For validation purposes, images acquired in anteroposterior (AP) direction by either C-arm were analyzed. Images acquired at 30 rotation, once in right and once in left anterior oblique projection, were also analyzed, to investigate the impact of gantry angulation on the accuracy and precision of the measurements.

**Quantitative Angiographic Analysis**

QCA was performed off-line by an experienced observer using a single-vessel analysis and a bifurcation segmental analysis. As the bifurcation phantom was made in a flat plane, our analysis was performed in AP view, to minimize errors resulting from foreshortening and/or overlap. Calibration was performed on a 10-mm grid board and the recording geometry of the x-ray system obtained from the Digital Imaging and Communications in Medicine (DICOM) (National Electrical Manufacturers’ Association, DICOM, Rosslyn, VA) header and the phantom thickness were taken into account to determine the true pixel size in the phantom plane, separately for each C-arm\(^9\). Radiographic system settings, phantom position, table height, and distance from source to the image intensifier distance were kept constant throughout each phantom and centimeter grid acquisition and were identical for all phantoms. Then, the same pixel size was manually entered in each analysis.

MLD, reference vessel diameter (RVD), %DS of PMV, DMV, and SB segments were compared with the phantom diameters (PDs) for vessel segments.

**Single-vessel analysis**

Angiographic images of the 18 bifurcations were analyzed using single-vessel analysis of the CAAS. The middle frame out of the total frame count of a given acquisition was consistently analyzed to avoid frame selection bias. To obtain the angiographic parameters separately in PMV, DMV, and SB, two analyses were performed per bifurcation: (1) MV analysis; PMV to DMV and (2) SB analysis; PMV to SB. Subsequently the QCA was manually segmented. To allow a comparison with the bifurcation analyses, the MV was divided into two segments (PMV and DMV) at the site of the carinal point. For the SB analysis, the start point of the SB was set at the carina.

**Bifurcation segmental analysis**

The angiography of the bifurcations was analyzed using the CAAS version 5.10 and QA-angio XA version 7.3 for 2D bifurcation segmental analyses including the edge segments
In vitro validation of (bifurcation) QCA using calibrated bifurcation phantoms

analysis. Standard procedure for bifurcation analysis has been previously described ⁹. Briefly, it consisted of the following steps: (1) the middle frame out of the total frame count of a given acquisition was consistently analyzed to avoid frame selection bias; (2) the same pixel size with single-vessel analysis was manually entered; (3) the bifurcation segmentation was initialized by placing one proximal and two distal delimiter points at the largest possible distance from the bifurcation to be analyzed, however, not touching the adjacent bifurcation lesions or the phantom borders; (4) contours were detected using the lumen detection algorithm and MLD was determined using previously described methodology ⁶,⁷. In QAngio XA software, the two bifurcation models (T shape; a main vessel being a proximal vessel that continues in the same direction into a distal vessel, and a SB at an acute angle and Y shape; a proximal vessel with two distal branches that are approximately equal in size and split off at similar angles) are available ⁹. Initially, software was allowed to automatically select the analysis algorithm. Subsequently, all bifurcation analyses with QAngio XA were repeated using both the Y- and the T-shape algorithms.

Statistics

Statistical analysis was performed using JMPVR 10 for Windows (SAS Institute, Cary, NC). Continuous variables were presented as mean±standard deviation and paired values were compared by Wilcoxon signed rank test. The individual signed differences were averaged; the mean of these signed differences (bias) is a measure of accuracy; the standard deviation is a measure of precision. The agreement for MLD between the CAAS bifurcation analysis and the PDs, QAngio XA using default Y- or T-shape bifurcation analysis and the PDs or QAngio XA using solely the T shape and the PDs were also performed using the Bland-Altman analysis. The accuracy between the measurements and the PDs and its precision were calculated; the repeatability coefficient (equal to 1.96 * standard deviation of the bias) was determined as the measure of variability. All statistical tests were two sided and a P-value < 0.05 was considered statistically significant.

RESULTS

Accuracy and precision of tested software packages for MLD, RVD, and %DS value are presented in Table 1 including measurements obtained exclusively with the T-shape program.
Table 1. The Respective Comparison Between Accuracy Measures Relative to the Calibrated Phantom Values Using the Conventional Single Vessel Analysis and Two Bifurcation Algorithms

<table>
<thead>
<tr>
<th>Lesions</th>
<th>parameters</th>
<th>Single vessel analysis by CAAS</th>
<th>Bifurcation segment analysis by CAAS</th>
<th>Bifurcation segment analysis by QAngio XA (auto)</th>
<th>Bifurcation segment analysis by QAngio XA (T-shape)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Accuracy 1</td>
<td>Precision</td>
<td>Limits of agreement</td>
<td>Accuracy 2</td>
<td>Precision</td>
</tr>
<tr>
<td>All (n=54)</td>
<td>RVD</td>
<td>0.108</td>
<td>0.352</td>
<td>±0.690</td>
<td>-0.050</td>
<td>0.043</td>
</tr>
<tr>
<td>All (n=54)</td>
<td>MLD</td>
<td>-0.015</td>
<td>0.146</td>
<td>±0.286</td>
<td>0.012</td>
<td>0.103</td>
</tr>
<tr>
<td>All (n=54)</td>
<td>%DS</td>
<td>5.69</td>
<td>11.28</td>
<td>±22.11</td>
<td>-0.94</td>
<td>4.07</td>
</tr>
<tr>
<td>PMV (n=18)</td>
<td>RVD</td>
<td>-0.263</td>
<td>0.102</td>
<td>±0.200</td>
<td>-0.051</td>
<td>0.035</td>
</tr>
<tr>
<td>PMV (n=18)</td>
<td>MLD</td>
<td>-0.039</td>
<td>0.130</td>
<td>±0.255</td>
<td>0.031</td>
<td>0.086</td>
</tr>
<tr>
<td>PMV (n=18)</td>
<td>%DS</td>
<td>-3.29</td>
<td>3.61</td>
<td>±7.08</td>
<td>-1.71</td>
<td>2.38</td>
</tr>
<tr>
<td>DMV (n=18)</td>
<td>RVD</td>
<td>0.183</td>
<td>0.138</td>
<td>±0.270</td>
<td>-0.066</td>
<td>0.036</td>
</tr>
<tr>
<td>DMV (n=18)</td>
<td>MLD</td>
<td>-0.008</td>
<td>0.112</td>
<td>±0.220</td>
<td>0.024</td>
<td>0.097</td>
</tr>
<tr>
<td>DMV (n=18)</td>
<td>%DS</td>
<td>3.16</td>
<td>4.88</td>
<td>±9.56</td>
<td>-1.95</td>
<td>3.48</td>
</tr>
<tr>
<td>SB (n=18)</td>
<td>RVD</td>
<td>0.405</td>
<td>0.334</td>
<td>±0.655</td>
<td>-0.032</td>
<td>0.075</td>
</tr>
<tr>
<td>SB (n=18)</td>
<td>MLD</td>
<td>0.008</td>
<td>0.045</td>
<td>±0.088</td>
<td>-0.017</td>
<td>0.123</td>
</tr>
<tr>
<td>SB (n=18)</td>
<td>%DS</td>
<td>17.23</td>
<td>11.26</td>
<td>±22.07</td>
<td>0.88</td>
<td>5.35</td>
</tr>
</tbody>
</table>
Comparison Between Angiographic Measurements by Single-Vessel Analyses and PDs

The conventional single-vessel method measured a significantly smaller RVD in the PMV and a larger RVD in the DMV and SB (Figure 1). Consequently, all the %DS and RVD were overestimated significantly compared to the PDs when using the conventional single-vessel method (p=0.003, p=0.014, respectively). Using single-vessel analyses, MLD values for each segment had an accuracy and precision of -0.039 ± 0.130 mm, -0.008 ± 0.112 mm, and 0.008 ± 0.045 mm for PMV, DMV, and SB, respectively. The values of
<table>
<thead>
<tr>
<th>Year</th>
<th>No. patients</th>
<th>Primary endpoint</th>
<th>Planned repeat angiography, Yes or No</th>
<th>Angiographic endpoint</th>
<th>QCA software</th>
<th>algorithm</th>
<th>Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>85</td>
<td>Angiographic restenosis (either branch) 6 months</td>
<td>Yes</td>
<td>Binary in-segment restenosis of both the MB and SB at 6 months</td>
<td>QCA-CMS</td>
<td>Single</td>
<td>Provisional vs systematic (crush, T, culotte)</td>
</tr>
<tr>
<td>Pan et al 2004</td>
<td>91</td>
<td>Composite of cardiac death, MI, and the need for TVR at 6 months</td>
<td>Yes</td>
<td>Angiographic restenosis (either branch) 6 months</td>
<td>CAAS II</td>
<td>single</td>
<td>Provisional vs systematic (T)</td>
</tr>
<tr>
<td>2006</td>
<td>413</td>
<td>Death, MI (nonprocedural), TVR, or stent thrombosis at 6 months</td>
<td>Yes</td>
<td>Significant restenosis (50% diameter stenosis) of the MV and/or occlusion of the SB</td>
<td>QAngio XA 7.0</td>
<td>Bifurcation</td>
<td>Provisional vs systematic (crush, culotte, T)</td>
</tr>
<tr>
<td>Ferenc et al 2008</td>
<td>202</td>
<td>Angiographic restenosis of the SB at 9 months</td>
<td>Yes</td>
<td>in-segment per cent diameter stenosis of the SB at 9 months</td>
<td>QAngio XA 7.0</td>
<td>Bifurcation</td>
<td>Provisional vs systematic (T)</td>
</tr>
<tr>
<td>NORDIC 2009</td>
<td>424</td>
<td>Death, MI (nonprocedural), TVR, or stent thrombosis at 6 months</td>
<td>Yes</td>
<td>in-segment and in-stent restenosis of MV and/or SB after 8 months</td>
<td>QAngio XA 7.0</td>
<td>Bifurcation</td>
<td>Systematic (crush vs culotte)</td>
</tr>
<tr>
<td>The DIVERGE 2009</td>
<td>302</td>
<td>Composite of death, MI, and TLR at 9 months</td>
<td>Yes</td>
<td>Binary angiographic restenosis at 9 months</td>
<td>QAngioXA 7.1</td>
<td>Bifurcation</td>
<td>No, a prospective multicenter registry. (Axxess stent) Double Kissing Crush versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions Provisional vs systematic crush</td>
</tr>
<tr>
<td>DKCRUSH-II 2009</td>
<td>370</td>
<td>Cardiac death, MI, or TVR at 12 months</td>
<td>Yes</td>
<td>Restenosis in the MV and SB at 8 months</td>
<td>CAAS 5.7</td>
<td>Bifurcation</td>
<td>Provisional vs systematic crush</td>
</tr>
<tr>
<td>CACTUS 2009</td>
<td>350</td>
<td>Death, MI, TVR at 6 months</td>
<td>Yes</td>
<td>In-segment restenosis rate at 6 months</td>
<td>QCA-CMS</td>
<td>single</td>
<td>Provisional vs systematic crush</td>
</tr>
</tbody>
</table>
### Table 2. Angiographic endpoints and used QCA algorithms in randomized studies, multicenter study or ongoing study (continued)

<table>
<thead>
<tr>
<th>Year</th>
<th>No. patients</th>
<th>Primary endpoint</th>
<th>Planned repeat angiography, Yes or No</th>
<th>Angiographic endpoint</th>
<th>QCA software</th>
<th>algorithm</th>
<th>Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thueinger Bifurcation Study</td>
<td>2009</td>
<td>110</td>
<td>Death, MI, stent thrombosis, CABG, or TLR at 6 months</td>
<td>Yes</td>
<td>Restenosis in the MV and SB at 6 months</td>
<td>Quantcor QCA V2.0</td>
<td>single</td>
</tr>
<tr>
<td>BBC ONE</td>
<td>2010</td>
<td>500</td>
<td>All cause of death, MI, TVF at 9 months, cardiac death, non-procedure-related index lesion MI, stent thrombosis, or TLR by PCI or CABG within 6 months.</td>
<td>No</td>
<td>No</td>
<td>Not described</td>
<td>single</td>
</tr>
<tr>
<td>NORDIC 3</td>
<td>2011</td>
<td>477</td>
<td>Cardiac death, MI, or TLR by PCI or CABG within 6 months.</td>
<td>Yes</td>
<td>in-segment and in-stent restenosis (50% diameter stenosis) of the MV and/or SB at 8 months</td>
<td>QAngio XA 7.2</td>
<td>Bifurcation</td>
</tr>
<tr>
<td>The TRYTON trial</td>
<td>2013†</td>
<td>704</td>
<td>Cardiac death, MI, or TVR at 9 months</td>
<td>Yes</td>
<td>In-segment % DS of the Tryton SB compared to SB balloon angioplasty at 9 months</td>
<td>QAngio XA 7.2 CAAS 5.9 or 5.11*</td>
<td>Single Bifurcation*</td>
</tr>
</tbody>
</table>

CABG: coronary artery bypass graft; MB main branch; MI, myocardial infarction; MV, main vessel; PCI: percutaneous coronary intervention; SB, side branch; TLR: target vessel revascularisation; TVF: target vessel failure; TVR: target vessel revascularisation. * The nine-month follow-up angiograms were re-analysed in both core labs (Cardiovascular Research Foundation, New York, NY, USA; Cardialysis B.V., Rotterdam, The Netherlands) using the bifurcation software.
MLD for all segments did not significantly differ between the conventional single vessel analysis and the PDs.

### Figure 2.

The agreement for minimum lumen diameter (MLD) between the CAAS and the phantom diameters (PDs), QAngio XA using default Y- or T-shape bifurcation, and the PDs or QAngio XA using solely the T shape were also performed using the Bland–Altman analysis; (A) MLD all, (B) MLD proximal main vessel (PMV), (C) MLD distal main vessel (DMV), (D) MLD side branch (SB). Solid lines represent the mean difference (bias), dotted lines represent the 95% limits of agreement (bias ±1.96 SD).
CAAS and QAngio XA Bifurcation Algorithms in Reference to PDs

Agreement between the two bifurcation software packages in MLD assessment is presented in Figure 2. Bland–Altman plots comparing MLD for 54 vessel segments analyzed by CAAS or QAngio XA compared to the PDs showed that the limit of agreement between CAAS and the PDs, QAngio XA using default Y- or T-shape algorithm and the PDs, or QAngio XA using solely the T shape and the PDs were -0.179 to 0.214, -0.618 to 0.648 mm, and -0.194 to 0.170, respectively (Figure 2). The values of MLD did not significantly differ between the QAngio XA using the default Y- or T-shape program and the PDs. Moreover, RVD and %DS in the QAngio XA using the default Y- or T-shape program were overestimated significantly compared to the PDs (p=0.002, p=0.047, respectively). With the CAAS software, MLD and %DS were not significantly different from the PDs. Accu-

**Figure 3.** The respective comparison between accuracy measures relative to the calibrated phantom values using the two bifurcation methods and two bifurcation algorithms were shown for minimum lumen diameter (MLD; panel A), reference vessel diameter (RVD; panel B), and percent diameter stenosis (%DS; panel C).
<table>
<thead>
<tr>
<th>Year</th>
<th>No. patients</th>
<th>Primary endpoint</th>
<th>Planned repeat angiography, Yes or No</th>
<th>Angiographic endpoint</th>
<th>QCA software</th>
<th>algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>105</td>
<td>Death, MI, and TLR at 6 months</td>
<td>Yes</td>
<td>Angiographic restenosis (either branch) 6 months</td>
<td>CAAS II</td>
<td>single</td>
</tr>
<tr>
<td>2007</td>
<td>139</td>
<td>Death, MI, CABG and ischemia driven TLR at 6 months</td>
<td>Yes</td>
<td>Angiographic late loss at 6 months</td>
<td>Not described</td>
<td>single</td>
</tr>
<tr>
<td>2008</td>
<td>30</td>
<td>in-hospital Cardiac death, MI, CABG, TLR and TVR</td>
<td>Yes</td>
<td>TLR and TVR at 6 months</td>
<td>CAAS 5.4</td>
<td>bifurcation</td>
</tr>
<tr>
<td>2010</td>
<td>28</td>
<td>Death, MI and TVR at 1 month</td>
<td>Yes</td>
<td>Angiographic restenosis (either branch) 6 months</td>
<td>Medis (not described in detail)</td>
<td>bifurcation</td>
</tr>
<tr>
<td>2011</td>
<td>63</td>
<td>Cardiac death, stroke, MI, CABG, TLR and TVR at 6 months</td>
<td>Yes</td>
<td>Vessel patency, late lumen loss and binary restenosis rate at 6 months</td>
<td>CAAS 5</td>
<td>bifurcation</td>
</tr>
<tr>
<td>2011</td>
<td>63</td>
<td>Cardiac death, stroke, MI, CABG, TLR and TVR at 12 months</td>
<td>Yes</td>
<td>late lumen loss, percent diameter stenosis and binary restenosis rate at 12 months</td>
<td>QCA-CMS 5.0</td>
<td>single</td>
</tr>
<tr>
<td>2011</td>
<td>151</td>
<td>the acute device success and angiographic success</td>
<td>No</td>
<td>No</td>
<td>Not described</td>
<td>Not described</td>
</tr>
<tr>
<td>2012</td>
<td>20</td>
<td>stroke, MI, stent thrombosis and TLR / TVR at 6 months</td>
<td>Yes</td>
<td>TVR at 6 months</td>
<td>QAngio XA</td>
<td>bifurcation</td>
</tr>
</tbody>
</table>

CABG: coronary artery bypass graft; MI: myocardial infarction; TLR: target lesion revascularisation; TVR: target vessel revascularisation
In vitro validation of (bifurcation) QCA using calibrated bifurcation phantoms

racy of CAAS and QAngio XA using the default Y- or T-shape program for MLD, RVD, and %DS were 0.012±0.103 mm versus 0.041±0.322 mm (p=0.003), -0.050±0.043 mm versus 0.116±0.610 mm (p=0.026), and -0.94±4.07% versus 1.74±7.49% (p=0.041), respectively (Table 1). CAAS software provided more precise values than QAngio XA software using the default Y- or T-shape program for MLD, RVD, and %DS measurements. QAngio XA software using the default Y- or T-shape program, accuracy values for RVD and %DS were quite large in three cases (1.70 mm vs. 0.08 mm and 43.07% vs. 0.66%, 3.23 mm vs. -0.03 mm and 5.32% vs. -0.32%, 2.62 mm vs. -0.09 mm and 18.51% vs. 2.86%) when Y-shape algorithms were applied as default for Medina class (0,1,0) bifurcation (Figures 1 and 3). As a result, the Y-shape algorithm over-diagnosed binary restenosis in two cases, yielding a positive predictive value of 93%. When the T-shape algorithm was used in all cases, the accuracy of %DS and RVD improved considerably up to 0.24±3.80% and -0.025±0.064 mm, respectively (Figure 3). The MLD, RVD, and %DS of the T shape was no longer statistically different from the CAAS bifurcation method. Conversely, when the Y shape algorithm was consistently applied for all bifurcations, the accuracy of precision for RVD in reference to the PDs became worse (Figure 3).

DISCUSSION

The main findings of this study are: (1) with conventional single-vessel QCA, the RVD, and %DS were significantly larger than the PDs. (2) CAAS and T shape in the QAngio XA are highly accurate and precise for MLD, RVD, and %DS when compared in vitro with a series of custom-made, precision manufactured Plexiglas phantoms. (3) When algorithms either T shape or Y shape were selected by default mode, QAngio XA demonstrated a higher RVD and %DS than CAAS and the PDs; however, accuracy improved and became comparable to the CAAS algorithm when the T shape was systematically used.

Percutaneous treatment of coronary artery bifurcation lesions is a recognized challenge in interventional cardiology. Dedicated software packages for bifurcation assessment can provide angiographic parameters; however, it is important to validate precision and accuracy of available software packages.

The value of MLD in the conventional single-vessel analysis was similar to the PDs; however, our results demonstrated that %DS of DMV and SB is overestimated by the conventional single-vessel analysis. Overestimation of %DS in the DMV and SB has potentially clinical implications. First, when the single-vessel analysis is applied in preprocedural assessment of a bifurcation lesion, the lesion severity would be over exaggerated and may result in the overtreatment of insignificant stenosis. The major bifurcation trials such as BBC ONE, CACTUS, and Thueringer bifurcation study have used the single-vessel analysis (Table 2). Inclusion based on the single-vessel analysis may result
in biased selection of target lesions. The use of dedicated bifurcation software has been recommended by the European Bifurcation Club Angiographic Sub-Committee to overcome the numerous limitations of standard QCA when applied on bifurcation lesions. Second, in the first-in-man/registry studies testing a dedicated bifurcation stent with a planned repeat angiography (Table 3), overestimation of SB %DS at follow up would result in increased rates of ischemia driven target lesion revascularization. According to the Academic Research Consortium definition, at repeat angiography, revascularization for a lesions with >70% stenosis (by corelab QCA) or >50% stenosis with evidence of ischemia are considered as ischemia driven. In the trial with planned repeat angiography, the use of single-vessel analysis might influence the event adjudication.

Percentage DS has been less reliable than the MLD in the evaluation of the functional significance of ostial SB stenosis and RVD of a given vessel segment gets interpolated from the diameter outside the obstruction boundaries. Compared to single-vessel analysis, accuracy of %DS assessment significantly improved with the two bifurcation software packages (Table 1, P-values; single-vessel analysis by CAAS vs. bifurcation segment analysis by CAAS: p<0.001, single-vessel analysis by CAAS vs. bifurcation segment analysis by QAngio XA with a default setting: p<0.001). However, the accuracy of %DS was better in CAAS than QAngio XA with a default setting (p=0.041). When the analysis was stratified according to the location of stenosis (Table 1), the variance of %DS was prominent in SB. This is due to an obvious error of measurement when Y-shape algorithms is by default applied for Medina class (0,1,0). When the T-shape algorithm was forced for all analyses, the accuracy improved and becomes comparable with CAAS. It could be, therefore, recommended to systematically use T-shape algorithm when QAngio XA is used for bifurcation studies. Indeed, in the third Nordic bifurcation study, the T-shape model was chosen for all bifurcation analyses. This approach should give the best measurements of bifurcation lesions with a high accuracy and precision. Y-shape could be considered when the specific Y-shape device (e.g., Axxess plus™ stent) is being evaluated (Table 3).

Limitations
The phantom design naturally has the inherent limitations of an artificial construction trying to mimic real life. The smooth and static walls of the phantoms neither resemble the jagged irregular appearance of the coronary vessel walls, especially after balloon dilation, nor they reflect movement with each cardiac cycle.
CONCLUSION

The conventional single-vessel QCA method is inaccurate in bifurcation lesions, underestimating RVD and %DS in the PMV with overestimation of these parameters in the DMV and SB. CAAS bifurcation software accurately measured MLD, RVD, and %DS when compared to the PDs. When the default bifurcation algorithms (T-shape, Y-shape) of the QAngio XA system was automatically selected, QAngio XA demonstrated a higher MLD, RVD, and %DS than CAAS and the PDs. However, if the T-shape algorithm is consistently used in the QAngio XA bifurcation method, the accuracy in measuring RVD and %DS improved and became comparable to the CAAS bifurcation method. Therefore, CAAS bifurcation software and QAngio XA bifurcation software (when the T shape is systematically used) are both suitable for quantitative assessment of bifurcation lesion.
REFERENCES


