Clinical Feasibility of a Fully Automated 3D Reconstruction of Rotational Coronary X-Ray Angiograms

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Background—Although fixed view x-ray angiography remains the primary technique for anatomic imaging of coronary artery disease, the known shortcomings of 2D projection imaging may limit accurate 3D vessel and lesion definition and characterization. A recently developed method to create 3D images of the coronary arteries uses x-ray projection images acquired during a 180° C-arm rotation and continuous contrast injection followed by ECG-gated iterative reconstruction. This method shows promise for providing high-quality 3D reconstructions of the coronary arteries with no user interaction but requires clinical evaluation.

Methods and Results—The reconstruction strategy was evaluated by comparing the reconstructed 3D volumetric images with the 2D angiographic projection images from the same 23 patients to ascertain overall image quality, lesion visibility, and a comparison of 3D quantitative coronary analysis with 2D quantitative coronary analysis. The majority of the resulting 3D volume images were rated as having high image quality (66%) and provided the physician with additional clinical information such as complete visualization of bifurcations and unobtainable views of the coronary tree. True-positive lesion detection rates were high (90 to 100%), whereas false-positive detection rates were low (0 to 8.1%). Finally, 3D quantitative coronary analysis showed significant similarity with 2D quantitative coronary analysis in terms of lumen diameters and provided vessel segment length free from the errors of foreshortening.

Conclusions—Fully automated reconstruction of rotational coronary x-ray angiograms is feasible, produces 3D volumetric images that overcome some of the limitations of standard 2D angiography, and is ready for further implementation and study in the clinical environment. (Circ Cardiovasc Interv, 2010;3:71-79.)

Key Words: angiography ■ imaging ■ coronary disease ■ reconstruction ■ rotational angiography

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One technique that reduces the operator dependence for acquiring optimal angiographic views is rotational angiography (RA), where the C-arm is programmed to rotate during continuous contrast injection, acquiring many views of the coronary tree during a single acquisition.6 RA still requires that the operator mentally fuses the multiple 2D images to generate a 3D impression. Removal of this operator-dependent step through automated or semiautomated generation of a full 3D representation from the rotational 2D angiography images has become the subject of much recent work.7–12 For instance, semiautomated 3D coronary segment modeling can be completed using 2 or more projection images acquired during the same cardiac phase from different viewing angles.5,13 Such an approach can be used to model the vessel centerlines and borders of a given segment, but it is limited to only these basic features and requires time, experience, and user interaction.
Alternatively, fully automatic 3D reconstruction can be used to generate a true computed tomography-like volume of the entire coronary tree. This strategy entails acquiring a rotational sequence spanning a wide angular range (≥180°) during continuous contrast injection followed by 3D reconstruction using methods such as filtered back-projection or iterative reconstruction, similar to standard computed tomography reconstruction. Overcoming the motion of the coronary arterial tree has required further developments, such as gating, optimal cardiac phase selection, and motion compensation, to produce high-quality 3D reconstructions. In this study, we sought to demonstrate the feasibility of the 2-step process of 3D QCA acquisition followed by automatic 3D reconstruction in the interventional suite and to assess the accuracy and potential clinical value of the derived 3D volume reconstructions.

Methods

Patient Enrollment and Image Acquisition

A flow diagram showing the different phases of this study is shown in Figure 1. The Colorado Multiple Institutional Review Board approved the feasibility study described in this article. The study comprised 23 patients who underwent coronary angiography and gave informed consent to participate between March 2007 and September 2008. Those patients with clinical indication for a coronary angiogram and who were older than 18 years and possessed an ability and willingness to consent were approached for inclusion in the study. Exclusion criteria included known allergy to iodinated contrast, renal insufficiency (creatinine >1.5 mg/dL), acute myocardial infarction, or previous coronary artery bypass graft. Women who were pregnant or breast-feeding and patients who had received iodinated contrast material within the past week also were excluded. As safety was still being established during this time period, patients with a low likelihood of disease were specifically sought.

Iodixanol (Visipaque 320) contrast agent was used in conjunction with the Acist Voyager automated injector system to deliver a flow rate of 1 to 2 cc/s of contrast for a volume that did not exceed 18 mL for each coronary system. The Allura Xper FD20 system was placed in the head propeller position for image acquisition, and the patients’ arms were positioned above their head. The 180° rotational protocol (start at left anterior oblique, 120°, and end at right anterior oblique, 60°) was initiated by isocentering the heart in the posteroanterior and lateral positions as previously described. After requesting the patients to hold their breath at end-inspiration (with attention given to avoid Valsalva), the operator simultaneously triggered the Voyager contrast injection system and depressed the cineangiography pedal. Additional acquisitions, such as left ventriculography and other standard coronary angiography views for the left coronary artery (LCA) and right coronary artery (RCA), were performed as needed by the attending cardiologist. Although the delivered x-ray dose to the patient was not recorded during this study, other published studies have addressed this.  

3D Reconstruction

The images were reconstructed off line using the following procedure: (1) automatic cardiac gating based on the recorded ECG signal and (2) reconstruction with integrated 2D motion compensation. The optimal cardiac phase for reconstruction was calculated using a projection-based method for determining the least motion state of the heart. Projection images were then selected from the acquisition for reconstruction using retrospective ECG gating, as previously described. The gating window width chosen for this study was 20% of the R-R interval. Higher heart rates result in more frequent spacing of the selected images throughout the 180° angular range of the rotation and therefore can theoretically produce better reconstructions.

Reconstruction at the specified cardiac phase was completed with a technique termed simultaneous thresholded algebraic reconstruction in combination with projection-image-based 2D motion compensation at an isotropic resolution of 0.36 mm. This reconstruction algorithm has previously been evaluated for accuracy using a software phantom and shows <4% error in vessel radius measurement.

Phantom Experiment

A phantom composed of aluminum alloy and machined with cylindrical sections of different known diameters (1, 2, 3, 4, and 5 mm) was used to estimate the accuracy of the software used for reconstruction and 3D quantitative analysis. This phantom was imaged using the same 180° delayed x-ray acquisition and reconstructed by simulated ECG signals with heart rates of 50, 60, 70, and 80 bpm. The same reconstruction parameters were used as for the patient data. Quantitative analysis was performed on the final reconstructions using the semiautomated tool described later (see Quantitative Evaluation section). To correct for the influence of different visualization settings (window or level) on the measurements, a ratio was calculated using a known diameter (for instance, 2 mm): ratio = measured diameter/known diameter. This ratio could then be used to correct all subsequent measurements: corrected measurement = measured diameter/ratio.

Qualitative Evaluation of Clinical Images

The 3D reconstructions from clinical studies were loaded into a prototype viewing system (Philips Healthcare) for evaluation. The data sets were displayed using a predefined automated method based on the image histogram. This technique establishes a minimum and maximum threshold for display that seeks to maximize visualization of high-contrast vessels. A variety of visualization tools, such as volume renderings, maximum intensity projections, gradient-based measures, and inverted sum renderings, were available for the reviewer to analyze, with the latter being used the most frequently (Figures 2a through 2d).

Two interventional cardiologists were presented with the 3D reconstructions in parallel with the 2D rotational angiograms from the same patient and asked to evaluate the 2 data sets based on a 2-part questionnaire. The first part rated the overall image quality of the 3D reconstruction based on a Likert scale (1 = low, 5 = high). Sample reconstructions (Figures 3a through 3c) with prespecified quality ratings were displayed concurrently with the goal of aligning the scores between the 2 reviewers. Clinical utility of the 3D reconstruction was assessed using a series of 5 yes-or-no questions, which are listed in the Results section. Each yes answer was assigned scores between the 2 reviewers. Clinical utility of the 3D reconstruction was assessed using a series of 5 yes-or-no questions, which are listed in the Results section. Each yes answer was assigned
a score of 1 point and each no answer a score of 0 points, which were summed for each reconstruction.

The second portion of the questionnaire comprised a segment-by-segment comparison in which the reviewer was asked to note the presence and degree of any stenoses (by visual estimation) on both the reconstructed 3D vessels and the 2D rotational angiograms. Segments were defined according to the modified American Heart Association coronary classification. A lesion was defined as any substantial and visually evident (>20%) reduction in vessel diameter as judged by the reviewer. Each vessel was then categorized as a true-negative (no lesion visualized on 2D angiograms or on 3D reconstruction), a false-negative (no lesion in 3D but 1 in 2D), a true-positive (lesion present in both 2D and 3D), or a false-positive (lesion present in 3D but not 2D). For each segment that involved a bifurcation, the reviewers also were asked whether the bifurcation was fully visualized on the rotational 2D angiograms or on the 3D reconstruction.

Quantitative Evaluation
Two-dimensional and 3D quantitative coronary analyses (QCAs) were performed on the first 5 patients with both an LCA and an RCA acquisition by 1 experienced reviewer. For each patient, the reviewer selected 2 different coronary segments from 1 of the 257 images acquired during the rotational acquisition of both the LCA and the RCA and determined the 2D lengths and diameters using the 2D QCA software available in the Xcelera package after catheter-based calibration. If a stenosis was visible, it was selected as one of the segments. Otherwise, normal vessel segments were chosen for analysis in the 2D image in which it was most clearly visualized with little or no overlap with other vessels (primary criterion) and in which foreshortening was visually minimized (secondary criterion). Three-dimensional QCA was performed on the 3D images from the same patients, using an experimental, semiautomated tool (Philips Healthcare) that computes a surface rendering based on the chosen window or level settings. The user then selects the beginning and end points of the vessel segment or catheter that correspond to the same locations used for 2D QCA, and the 3D length and diameter are automatically determined. Additionally, the software calculates the amount of vessel segment foreshortening that would be present in any 2D gantry view. This foreshortening value (%) was recorded for the gantry view chosen for 2D analysis and was used to compare the 2D and 3D measurements.

Statistical Analysis
Variables are expressed as either percentages or as mean±SD. Linear correlations were calculated with standard least squares linear regression using the formula 3D value=(a+b)×2D value. Bland-Altman plots are displayed as the difference versus the mean of the 2D and 3D measurements, with bias calculated as the mean of the differences. Calculations were performed using MATLAB and Microsoft Excel. The authors had full access to the data and take responsibility for its integrity. All authors have read and agreed to the manuscript as written.
Results

Phantom Experiment Results
A 2D image of the phantom that was used to estimate the accuracy of the reconstruction software (diameters indicated on the image) is depicted in Figure 4a. After reconstruction using simulated heart rates of 50 to 80 bpm, the measurements obtained indicate good agreement (<2% average error) with the expected values for both length and diameters >1 mm (Figure 4b, Table 1). These measurements were corrected using the known 2-mm diameter segment to mimic the use of a catheter for diameter calibration on clinical data sets. The error for the 1-mm sample is somewhat higher (average 5.6%) than for the other diameters.

Study Population
Twenty-three LCAs and 17 RCAs were acquired for evaluation from the 23 patients in this study. A summary of the study population characteristics is included in Table 2. No adverse events were noted in these patients because of the prolonged contrast injection. Additional angiographic views were required in 82.6% of the LCA acquisitions and 41.1% of the RCA acquisitions after the 180° RA acquisition to complete the diagnostic examination. These additional views were typically needed to compensate for the lack of cranial or caudal angulation in the RA protocol or to image at higher magnification.

Qualitative Evaluation Results
Offline reconstruction was successful for all cases with no algorithm failures. The optimal phase selection chose diastole for the majority of reconstructions (95%), with an average chosen phase of 73.8±11.4% of the R-R interval. Two of the 50 bpm
<table>
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<tr>
<th>Diameter (mm)</th>
<th>60 bpm</th>
<th>70 bpm</th>
<th>80 bpm</th>
<th>Average</th>
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<tr>
<td>1 mm</td>
<td>0.81 (18.8)</td>
<td>1.10 (9.7)</td>
<td>1.01 (0.6)</td>
<td>0.87 (12.5)</td>
</tr>
<tr>
<td>2 mm*</td>
<td>2.00</td>
<td>2.00</td>
<td>2.00</td>
<td>2.00</td>
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<tr>
<td>3 mm</td>
<td>3.04 (1.4)</td>
<td>2.93 (2.4)</td>
<td>2.95 (1.7)</td>
<td>3.02 (0.8)</td>
</tr>
<tr>
<td>4 mm</td>
<td>4.12 (3.0)</td>
<td>3.98 (0.5)</td>
<td>4.11 (2.7)</td>
<td>3.99 (0.3)</td>
</tr>
<tr>
<td>5 mm</td>
<td>5.15 (3.0)</td>
<td>4.98 (0.4)</td>
<td>5.03 (0.6)</td>
<td>4.90 (1.9)</td>
</tr>
<tr>
<td>Length, mm†</td>
<td>9.97 (0.3)</td>
<td>10.13 (1.4)</td>
<td>10.12 (1.2)</td>
<td>10.03 (0.3)</td>
</tr>
</tbody>
</table>

Diameter measurements were first corrected using the 2-mm diameter section as a calibration object. The data are expressed as both the average measurement along the section and the percent error from the known value (in parentheses).

*This sample was used to correct the other diameter measurements.
†True length was 10 mm.
reconstructions (5%) were performed at end systole (30% of the R-R interval). The average number of heart beats acquired during the rotation was $7.4 \pm 1.3$. Figures 3d through 3f show examples of reconstructions that were given quality ratings of high, average, and low. The scores assigned by the reviewers indicate that the reconstructions predominantly exceeded the intermediate quality score (Table 3). Those reconstructions that received a quality rating of $<3$ represented a minority of the data (17.4% of LCAs and 11.8% of RCAs), and for this subset, we evaluated the likely causes (Figure 5). Of the 5 LCAs that received a low rating (1 or 2) by 1 or both reviewers, the most prominent finding was severe foreshortening of vessel segments throughout the duration of the acquisition (3 of the 5 cases), which resulted in less-than-optimal reconstruction of those segments. The remaining 2 LCAs and 2 RCAs, which were rated as low quality, were the result of patient and acquisition-specific problems, such as arrhythmia (1 LCA) and delayed beginning or early termination of contrast injection (1 LCA and 2 RCAs), which led to reduced opacification during the run. These reconstructions were removed from the subsequent vessel segment comparison.

The clinical utility scores indicated that both reviewers often found that the 3D reconstructions supplemented rather than replaced the value of the 2D projection images (Tables 3 and 4). For example, in most patients, both reviewers found that the 3D data provided information that permits evaluation of more segments than 2D alone, allowed better visualization of at least 2 ostia, and provided unobtainable gantry views that could aid in diagnosis. Although there was good agreement between the 2 reviewers on most questions, they did differ on question 5, which asked whether the 3D images would encourage the reviewer to obtain additional angiographic views.

For the segment-by-segment comparison (Figure 6), the results from both reviewers show that the rates of both false-positives and false-negatives are low (Table 5). However, there is a discrepancy in the rate of false-positives detected between the 2 reviewers, especially for the LCAs. The true-positive rates ranged from 90 to 100%, and the false-positive rates ranged from 0 to 8.1%, although the overall number of lesions was low (33 to 34 total, with approximately half $>50$%). Of the 22 total discrepancies between the 3D volumetric and 2D angiographic images detected by both reviewers, 73% (16) were located in the proximal or mid portion of the main vessels, such as left anterior descending branch, left circumflex branch, and the main right stem. Of the total bifurcations analyzed (122 and 124 for the 2 reviewers), they noted that 45.9% and 29.8% were only fully depicted on the 3D reconstruction, indicating that the 2D rotational images were not sufficient by themselves for this purpose (Figure 7). However, when using both the 2D and the 3D data together for evaluation, only 1 to 2
bifurcations, depending on the reviewer, were not fully depicted.

Quantitative Evaluation Results
QCA also was performed on a subset of patients by 1 reviewer. A comparison of the segment lengths (n=20) as measured using standard 2D QCA, and the 3D measurements performed on the reconstructions show excellent agreement (3D length=1.02×2D length+4.2, \( r^2=0.9 \)), although 3D demonstrated a tendency toward longer length measurements, as expected (Figure 8a, squares). The amount of foreshortening predicted from the 3D data that would result from the fixed gantry view of the vessel segment chosen for 2D QCA varied substantially, with an average of 14.6% (range, 0.6 to 50.6%). This percentage is comparable with the amount of foreshortening calculated by comparing the measured 2D and 3D lengths for all segments (15.2%). Therefore, correction of the measured 2D length for the predicted foreshortening determined by the 3D QCA software improved the correlation between the length measurements (\( r^2=0.94 \)) and reduced the apparent bias from 4.8 to 0.6 mm (Figure 8a, circles).

Three-dimensional diameter measurements were corrected for the potential effect of modified histogram settings using the catheter for normalization (average ratio of measured to actual catheter diameter, 1.19±0.08). The highest correlation with the 2D data was found for the mean vessel segment diameter (3D diameter=0.89×2D diameter+0.21, \( r^2=0.9 \)), with the 3D measurements exhibiting a small negative bias (Figure 8b). Maximum and minimum diameter measurements showed a slightly less robust correlation (\( r^2=0.82 \) and 0.72, respectively).

Discussion
This study presents the results of the first in-depth clinical and quantitative analysis of a fully automatic 3D coronary reconstruction algorithm that produces volumetric computed tomography-like images as opposed to a centerline-based model with estimated diameters as we have previously reported.\(^1\,^8\) The safety and feasibility of the 180° selective coronary rotational angiographic acquisition technique was documented, and the frequency of successful, automatic reconstructions yielding high-quality 3D images that displayed clinical value was encouraging. Most reconstructions were designated as high quality, even though the algorithm was not modified to account for suboptimal acquisitions from delayed injection or early termination of contrast that accounted for several low-quality ratings. Severe foreshortening and overlap throughout the rotational acquisition were also influential factors in both the 2D rotation and the reconstruc-
tion quality and could potentially be alleviated by modified acquisition trajectories that incorporate cranial and caudal angulation.

The development of 3D reconstruction of coronary arteries should not be judged as a replacement for 2D angiographic images but, instead, as a means to expand the clinical utility of the acquired images and to provide complementary quantitative analysis and a patient-specific 3D coronary tree for in-room uses. A segment-by-segment comparison indicated that the 3D reconstructions generated in this study accurately depict lesions, though further algorithm improvements to reduce the false-positives may be needed. However, the physician always will have the option of referring to the 2D angiograms to validate or refute the 3D data such that a low incidence of false-positives should not outweigh the benefits provided by having the 3D reconstruction available in room.

Several specific potential clinical uses of the 3D reconstruction were identified in this study, and additional potential benefits of in-room use are now apparent. Two independent reviewers often believed that the 3D reconstruction permitted evaluation of more segments than 2D alone, allowed better visualization of at least 2 ostia, and provided unobtainable gantry views that could aid in diagnosis. Rotation of 3D reconstructions to find an optimal working view for PCI, examination of vessels from gantry angles that are impractical to obtain, and calculation of foreshortening maps are tools currently available for 3D models of selected coronary segments that now could be applied to 3D reconstructions of the entire coronary tree. In addition, there is a clear workflow advantage to the fully automatic generation of the 3D reconstruction, especially for PCI guidance.

Length and diameter measurements obtained from 3D QCA measurements of defined coronary segments were correlated with and had a low level of bias when compared to the 2D analysis, and it is expected that further studies will reveal the advantages of 3D-based measurements. As shown in this and other studies, 2D length measurements are often biased from variable degrees of foreshortening, and this can only be accurately corrected by using 3D information. A high correlation between the 2D and 3D diameter measurements was found, which is attributable to using normal vessel segments for the majority of the measurements. Further investigations are needed to dem-

Figure 7. Bifurcation analysis. Angiograms acquired at the beginning (left), middle (center left), and end (center right) of the C-arm rotation and the resulting 3D reconstruction (right image, volume-rendered axial view) are shown for 2 examples of bifurcation analysis. a, Both reviewers indicated that the first and second obtuse marginal bifurcations were clearly visible on both the 2D images and 3D volume, whereas the left main bifurcation was only clear on the 3D data. b, Both reviewers were able to see the left main, proximal left circumflex, and first and second OM bifurcations on both 2D and 3D, whereas the first diagonal bifurcation was only visualized on the 3D data. LAO indicates left anterior oblique and RAO, right anterior oblique.

Figure 8. Bland-Altman plots comparing 2D and 3D QCA determinations of vessel lengths (a) and vessel diameters (b). a, The square symbols are absolute measurements, and the circles are measurements after correction for foreshortening. The uncorrected bias = 4.77 mm (14.7% of the mean) is shown with a black solid line with a 95% CI of −6.6 to 16.1 (shown by 2 black dotted lines). The corrected bias = 0.55 mm (1.6% of the mean) is shown by a light gray solid line with a 95% CI of −4.1 to 5.2 (shown by 2 light gray dotted lines). b, Bias = −0.12 mm is shown with a black solid line, with a 95% CI of −0.62 to 0.39 (shown by 2 black dotted lines).
onstrate that 2D and 3D QCA diameter measurements of eccentric lesions could differ, depending on the chosen gantry view for 2D QCA.

This initial study of 3D coronary reconstruction has several limitations. The first is the relatively small number of patients and that all the data were acquired and analyzed in a laboratory that has significant experience with RA and 3D reconstruction, which may have increased the number of good acquisitions (ideal isocentering, breath-hold coaching, experience with injection rate and timing, etc). Second, the reviewers were not blinded to the 2D data when evaluating the 3D data; in fact, they were presented simultaneously to more closely mimic the clinical situation, even though it is a potential source of bias. We also chose to only compare the 3D data with the rotational 2D data and not to include any additional fixed angiographic views that might have been acquired subsequently. Finally, 2D angiography, although often used as the only diagnostic imaging modality for lesion detection and characterization, is not an ideal gold standard for comparison to a 3D data set.

In summary, the results of this study highlight the potential of a fully automatic, gated, iterative reconstruction approach for providing clinically useful and accurate 3D volumetric images of the coronary arteries for use in PCI. These results justify the further development of this technique for in-room use and testing on a larger group of patients likely to need PCI. Because the 3D reconstructions were not available in-room for this study, it was not possible to assess additional aspects of potential clinical value. For example, it is unclear whether having the 3D reconstructions available for review and analysis during the case would have either mitigated the need for additional imaging or helped in optimizing the gantry position for additional acquisitions. Further studies incorporating in-room evaluation of the reconstructed 3D data are needed to answer questions that affect contrast volume, radiation dose, workflow, PCI performance, and other clinical outcome measures. Finally, it will be important to perform a formal validation study for 3D QCA using 3D reconstructions based on RA.

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Disclosures
John D. Carroll, MD, is coinventor of patented 3D vascular modeling software assigned to the University of Colorado and University of Chicago that has been licensed to Philips Healthcare but was not used in this study. Dr. Carroll is a consultant and speaker for Philips Healthcare. Four of the authors are employed by Philips Healthcare or Philips Research.

References


### CLINICAL PERSPECTIVE

The purpose of coronary imaging is to accurately visualize coronary anatomy, detect disease, and guide intervention. Though catheter-based coronary angiography has been a revolutionary tool for patient care, the 2D format of projection images is fundamentally unrealistic and has been shown to lead to misrepresentation of clinically relevant features of the coronary tree and lesions. Technology advancements, while allowing the transition from film to digital images, have not changed the 2D image format during the past 50 years. This article describes the next evolution in this imaging modality: a rotational C-arm acquisition during extended contrast injection that is followed by fully automated reconstruction to provide 3D images of the coronaries. Specifically, this article characterizes for the first time the image quality and potential clinical utility of this new method developed for use in the catheterization laboratory. In this offline study, the volumetric images obtained from a cohort of patients were compared with the acquired 2D images in terms of overall image quality, stenosis detection, potential clinical advantages and disadvantages, and 3D quantitative coronary analysis. After demonstrating the feasibility and reasonable quality of the 3D reconstructions, additional studies are needed to further validate accuracy and to study the added clinical value this technology brings to the care of patients undergoing both diagnostic coronary angiography and subsequent coronary intervention.
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