

In Vivo Validation of CAAS QCA-3D Coronary Reconstruction Using Fusion of Angiography and Intravascular Ultrasound (ANGUS)

Johan C.H. Schuurbiers,¹ BSC, Nieves Gonzalo Lopez,² MD, Jurgen Ligthart,² BSC, Frank J.H. Gijssen,¹ PHD, Jouke Dijkstra,³ PHD, Patrick W. Serruys,² MD, PHD, FACC, Antonius F. Van der Steen,^{1,4} PHD, and Jolanda J. Wentzel,^{1,4*} PHD

Objectives: The CAAS QCA-3D system (Pie Medical Imaging BV, the Netherlands) was validated against 3D reconstructions based on fusion of angiography and intravascular ultrasound (ANGUS), allowing slice by slice validation of the lumen areas and 3D geometric values. **Background:** Accurate online 3D reconstruction of human coronary arteries is of outmost importance during clinical practice in the catheterization laboratory. The CAAS QCA-3D system provides technology to 3D reconstruct human coronary arteries based on two or more angiographic images, but was not validated in realistic arteries before. **Methods:** Ten patients were imaged using biplane angiography and an ECG gated (TomTec) intravascular ultrasound (IVUS) pullback (stepsize 0.5 mm, Boston Scientific). The coronary arteries were 3D reconstructed based on (a) fusion of biplane angiography and IVUS (ANGUS) and (b) CAAS QCA-3D using the biplane angiography images. For both systems the length, the curvature and the lumen areas at 0.5 mm spacing were calculated and compared. **Results:** Bland-Altman analysis indicated that the CAAS QCA-3D system underestimated the lumen areas systematically by $0.45 \pm 1.49 \text{ mm}^2$. The segment length was slightly underestimated by the CAAS QCA-3D system (62.1 ± 11.3 vs. $63.2 \pm 11.4 \text{ mm}$; $P < 0.05$), while the curvature of the analyzed segments were not statistically different. **Conclusions:** The CAAS QCA-3D system allows 3D reconstruction of human coronary arteries based on biplane angiography. Validation against the ANGUS system showed that both the 3D geometry and lumen areas are highly correlated which makes the CAAS QCA-3D system a promising tool for applications in the catheterization laboratory and opens possibilities for computational fluid dynamics.

© 2009 Wiley-Liss, Inc.

Key words: angiography; IVUS; 3D-reconstruction; validation

INTRODUCTION

Conventional coronary angiography displays the complex three-dimensional (3D) geometry of the coronary arterial tree as two-dimensional (2D) images. The interpretation of these 2D views can be affected by vessel tortuosity, foreshortening, overlap, and individual anatomic variation, leading to an imprecise estimation of the vessel dimensions [1]. This inaccuracy is important in the daily practice in the catheterization laboratory because it may influence the selection of the correct size of the devices and therefore could have an impact on the clinical result of percutaneous coronary interventions (PCI) [2]. Recently, 3D reconstructions techniques based on routine biplane 2D projections have been developed to overcome the limitations of conventional 2D angiography [3–6]. Studies

¹Biomedical Engineering, ErasmusMC, Rotterdam, The Netherlands

²Interventional Cardiology, ErasmusMC, Rotterdam, The Netherlands

³LKEB, Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands

⁴Inter Cardiologisch Institute The Netherlands, Utrecht, The Netherlands

Conflict of interest: This study was in part supported by a grant from Pie Medical Imaging BV.

*Correspondence to: Dr. J.J. Wentzel, Biomechanics Laboratory, Biomedical Engineering, EE2322, ErasmusMC, P.O. box 2040, 3000 CA Rotterdam, The Netherlands. E-mail: j.wentzel@erasmusmc.nl

Received 27 August 2008; Revision accepted 15 October 2008

DOI 10.1002/ccd.21872

Published online 23 March 2009 in Wiley InterScience (www.interscience.wiley.com).

on the accuracy of 3D reconstruction techniques based on biplane angiography showed that known phantom or stent dimensions could be reconstructed with small errors [3,7,8]. However, those studies suffered from two limitations (1) the cross-sections were circular, not accounting for the irregular shape resulting from lumen intruding plaques and (2) only a small region of interest was studied for which the viewing angles were optimized, so that foreshortening only minimally affected their results. In this study, we validated the dimensions and the shape of 3D reconstructed full segments of human coronary arteries obtained with the CAAS QCA-3D technology against the 3D reconstructions achieved by the well established, validated ANGUS reconstruction technique based on a combination of Angiography and Intravascular Ultrasound (IVUS) [9].

MATERIALS AND METHODS

Patient Population

Eleven patients selected for PCI were imaged using biplane angiography and IVUS in one of the coronary arteries. One patient was excluded from further analysis because of poor angiographic image quality. Cross-sections at bifurcations were excluded from the analysis, because the IVUS lumen contours cannot be reliably determined at bifurcation sites.

So in total data of 10 coronary segments (LCA $n = 2$, RCA $n = 5$, LCX $n = 3$) accounting for 1157 IVUS cross-sections were examined. The medical ethics committee approved the study and all patients gave a written informed consent.

Biplane Angiography

The biplane angiograms (512×512) were recorded at 25 frames/sec using diluted contrast agent (Visipaque, GEHealthcare BV, Eindhoven, vol/vol 2:1 with saline) to allow simultaneous visualization of the IVUS catheter and lumen. For each recording the x-ray beams were positioned such as to optimally visualize the studied segment without excessive foreshortening which might affect the reconstruction accuracy and with an angle between both x-ray beams of more than 30 degrees. From the x-ray recordings, a single biplane set of end-diastolic frames was selected, optimally showing the catheter and the contrast-filled lumen. In each single biplane image set two clearly identifiable reference points were defined to match the two reconstruction techniques (CAAS QCA-3D and ANGUS): a proximal reference point corresponding to the distal end of the guiding catheter and a distal reference point

corresponding to the echo transducer (at the start of the IVUS pullback).

CAAS QCA-3D

With the CAAS QCA-3D system (Pie Medical Imaging BV, The Netherlands) the selected set of biplane angiographic images were used to reconstruct coronary arteries in 3D space assuming an elliptical cross-sectional shape. After indicating a so called common image point, which should unambiguously be visible in both projections, a path through the lumen covering the segment to be analyzed had to be entered. The luminal borders at both projections are found by automatic contour detection [10]. Because the ANGUS reconstruction technique demands the use of diluted contrast to simultaneously visualize the artery lumen and IVUS catheter-imaging core, the image quality of the biplane angiogram was slightly reduced. This might affect the CAAS QCA-3D automated contour detection. Therefore, we allowed manual corrections were needed. On a subset of patients, the contour detection was repeated to obtain a measure for intra-observer variability. In addition, for the same subset of patients and the same region of interest biplane angiograms with full contrast and the same x-ray geometry were selected and analyzed twice. These analyses were repeated by a second observer, so that intra- and inter-observer variability for full contrast angiograms could be derived.

From the detected luminal borders a centerline was determined. The 3D reconstruction algorithm reconstructs the vessel lumen in 3D assuming an elliptical cross-sectional shape by using (1) the recording geometry as obtained from the Dicom-header of the x-ray images, (2) the centerlines, and (3) the lumen borders. The 3D reconstruction takes a few seconds on a fast PC (3GHz Intel Xeon). The 3D reconstructed vessel geometry in between the earlier defined reference points was exported. The exported 3D geometry containing approximately 12 cross-sectional contours per mm and 64 points on each cross-sectional contour was used for comparison with the ANGUS reconstructed segment.

Intravascular Ultrasound

For the acquisition of the IVUS data an R-wave gated motorized stepped pullback was performed using a 2.9 Fr sheath-based catheter (Atlantis SR Pro, 40MHz or Ultra Cross 30MHz, Boston Scientific). The transducer was withdrawn with a step size of 0.5 mm and the RF images were stored on a computer system (Tomtec Imaging Systems, Germany). To obtain the lumen borders from the IVUS images a semiautomatic contour detection program QCU analytical software package (LKEB, Dept of Radiology, Leiden University

Medical Center LUMC, Leiden, The Netherlands) was used.

ANGUS

The ANGUS technique, applying biplane angiography and the IVUS contours described extensively in Slager et al. [9], was used to derive the true 3D lumen reconstruction of the vessel. Briefly, the selected single set of biplane angiographic images made with diluted contrast was used to reconstruct the catheter path in 3D. Therefore, in both angiographic images, the imaging core of the sheath-based catheter was indicated. Because a sheath-based catheter is used the imaging core position (core-line) corresponds to the pullback path of the echo transducer. A 3D coordinate system is defined by recording a calibration cube with the same x-ray geometry. Application of home made software written in Matlab (Mathworks, Natick, USA) using the coreline positions and the calibration cube resulted in a 3D catheter path reconstruction. Passage of the contrast agent front, also visible in the IVUS images, was used to synchronize both imaging modalities in time. Subsequently, the vessel was reconstructed by combining the 3D reconstructed core-line with the IVUS contours positioned perpendicular to the coreline.

Matching of CAAS QCA-3D and ANGUS

The 3D proximal and distal reference points were used to determine the corresponding segments in 3D for both the CAAS QCA-3D and the ANGUS reconstruction. Because for the ANGUS reconstruction the IVUS catheter was not always pulled back the full length between the distal and proximal reference points, we determined the overlapping segment which was reconstructed by both techniques. The positions of the cross-sections in the segment reconstructed by CAAS QCA-3D that corresponded to the cross-sections in the segment reconstructed by ANGUS were determined by linear interpolation. Consequently, the cross-sectional dimensions of both techniques could be compared on a slice by slice basis. Subsequently, for the matched 3D reconstructions of the coronary arteries obtained with the CAAS QCA-3D and ANGUS technique, a number of geometrical values were determined. For each cross-section, the lumen area, maximal and minimal diameters were calculated. The 3D length of the centerline of the matching segments was calculated. The curvature ($1/\text{radius}$) of the centerline was determined by the best fit of a circle through the centerline points. Furthermore, the shape of the CAAS QCA-3D centerline was compared with the ANGUS centerline by calculating the distance between corresponding centerline points.

Statistics

The cross-sectional geometric values were compared using regression analysis and Bland-Altman statistics. Bland-Altman is a statistical method to compare two measurements techniques. The differences between the two techniques are plotted against the averages of the two techniques. The average difference of the lumen area, presented as a horizontal line in this plot represents the systematic error in lumen area, while the regression line represents the proportional error between the two methods, i.e., the error dependent on the average size of lumen area. The inter- and intra-observer variability for lumen areas obtained with CAAS QCA-3D are reported as average differences \pm standard deviation. The curvature, length, and distance were compared using a paired *t*-test (SPSS, 11.0.1, SPSS, Chicago, IL, USA).

RESULTS

Ten coronary segments out of 10 patients were successfully 3D reconstructed using both the ANGUS and the CAAS QCA-3D system (Fig. 1). The diameter stenosis based on IVUS of the analyzed segments ranged from 30.6 to 61.9% ($44.9 \pm 9.8\%$). The length of the 3D reconstructed segments measured by CAAS QCA-3D ranged from 46 mm to 78 mm, with an average length of 62.1 ± 11.3 mm. The length was slightly underestimated compared to the ANGUS system (63.2 ± 11.4 mm, paired *t*-test, $P < 0.05$). The average distance between the centerlines was 1.0 ± 0.4 mm ($P < 0.05$). The curvature of the 3D reconstructed coronary segments was not statistically different for the ANGUS and CAAS QCA-3D system being respectively $0.038 \pm 0.011 \text{ mm}^{-1}$ (radius = 29.8 ± 12.5 mm; range, 19.6–59.4 mm) and $0.036 \pm 0.012 \text{ mm}^{-1}$ (radius = 31.2 ± 13.4 mm; range, 19.1–62.8 mm).

The values of the cross-sectional lumen area, minimal lumen diameter, and maximal lumen diameter obtained with the ANGUS system and CAAS QCA-3D were compared on a slice by slice basis. Figure 1 (lower right panel) shows an example of the correspondence between the lumen areas obtained with CAAS QCA-3D system and the ANGUS system when comparing them with respect to the position on the centerline. Pooling the data of all patients, in total 1157 cross-sections were included in the analysis. Linear regression analysis showed a correlation of 0.87 between the luminal areas of the ANGUS versus the CAAS QCA-3D system (Fig. 2). Figure 3 shows the Bland-Altman plot of the lumen cross-sectional areas. Bland-Altman analysis indicated that the CAAS QCA-3D system underestimated the luminal cross-sectional

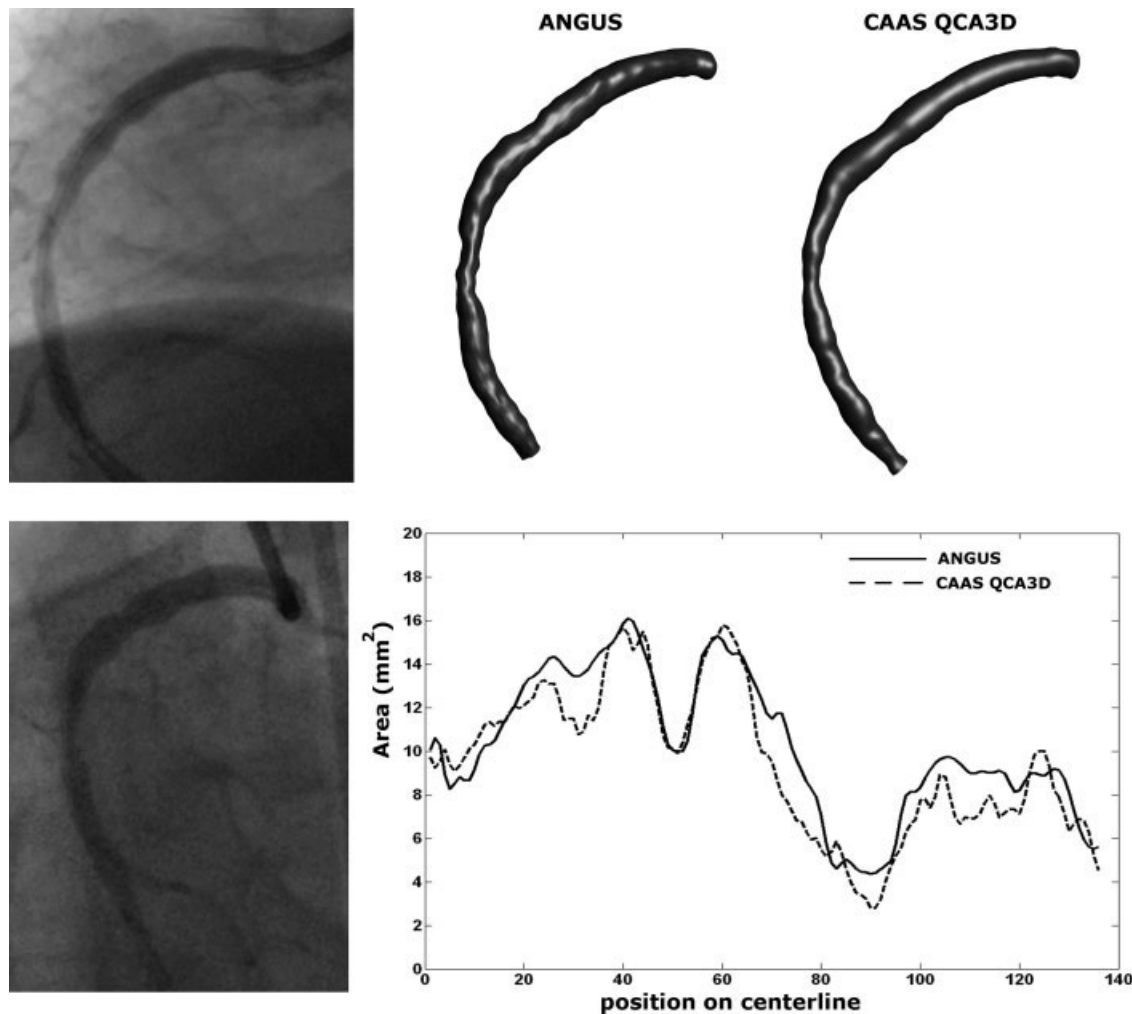


Fig. 1. Three-dimensional reconstruction of a right coronary artery of a patient applying biplane angiography (CAAS QCA-3D) or a combination of biplane angiography and IVUS (ANGUS)—Lower right panel shows the very similar appearance of the area for both systems when relating them to the position on the centerline.

areas systematically by $0.45 \pm 1.49 \text{ mm}^2$, while the proportional error was very small (difference lumen area = $0.013 - 0.058 \times \text{average lumen area}$, $P < 0.05$).

Linear regression analysis of the maximal and minimal diameters of the cross-sections of ANGUS versus CAAS QCA-3D showed a correlation of 0.84 and 0.80, respectively. The maximal diameters were systematically underestimated, while the minimal diameters were overestimated by 0.49 ± 0.35 and $0.37 \pm 0.37 \text{ mm}$, respectively. There was no significant proportional error.

The intra- and inter-observer variability of lumen areas obtained with CAAS QCA-3D were based on biplane angiograms of four patients of which both diluted contrast and full contrast images of the same region of interest with the same x-ray geometry as used in the study were available. The intra-observer variability for area

measurements with CAAS QCA-3D for the diluted contrast images was: $0.18 \pm 0.82 \text{ mm}^2$. The intra- and inter-observer variability for the full contrast images was equal to $-0.09 \pm 0.48 \text{ mm}^2$ and $-0.06 \pm 0.50 \text{ mm}^2$.

DISCUSSION

The present study demonstrates a good correlation between the CAAS QCA-3D system and the validated ANGUS 3D reconstructions [9] for the assessment of 3D vessel geometry in patients. Previous studies on the accuracy of QCA-3D techniques using intravascular phantoms and stents showed a good correspondence as well [3,7,8]. However, these studies were performed for short, circular shaped segments, not taking realistic variations in lumen geometry of human atherosclerotic coronary arteries into account. In this study, we inves-

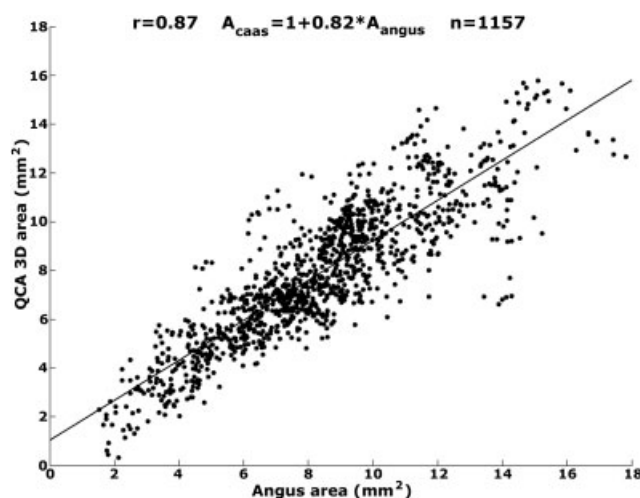


Fig. 2. Regression plot of lumen areas obtained with the CAAS QCA-3D system and the lumen areas obtained with the ANGUS system.

tigated in vivo the accuracy of 3D reconstructions based on CAAS QCA-3D of human coronary arteries with a length up till 78 mm; thus including irregular lumen cross-sections and segments with foreshortening as found in daily clinical practice.

Compared with the ANGUS measurements, the CAAS QCA-3D system showed only a slight underestimation of length in the studied segments. A good estimation of the length is important in clinical practice to guide PCI procedures. For instance, errors in the lesion length assessment because of foreshortening impacts the selection, number, and placement of stents [1,2,11]. In the study of Gollapudi et al. [2] it was shown that in 16% of the cases, experienced operators overestimated the required stent length for a given target lesion with the 2D angiography technique. In those cases, 3D vessel reconstruction would have provided information that could have changed the operator decision. Overestimation of stent length enhances restenosis rates as increasing stent length is associated with a higher risk of restenosis [12]. Stent length mismatch might produce other undesirable results as the covering of a side branch. Moreover, the assessment of the exact location of side branches, even if based on two-directional views, might also result in a wrong estimation of the true 3D location. The use of a 3D reconstruction to select the optimal views to perform a PCI (with minimal foreshortening or overlap) may also reduce the radiation time and the amount of contrast needed [1].

The measured curvature of the vessel with the CAAS QCA-3D system was not statistically different from the one determined with the ANGUS system. Measurement of vessel curvature changes might be useful in predicting angiographic stent restenosis severity [13].

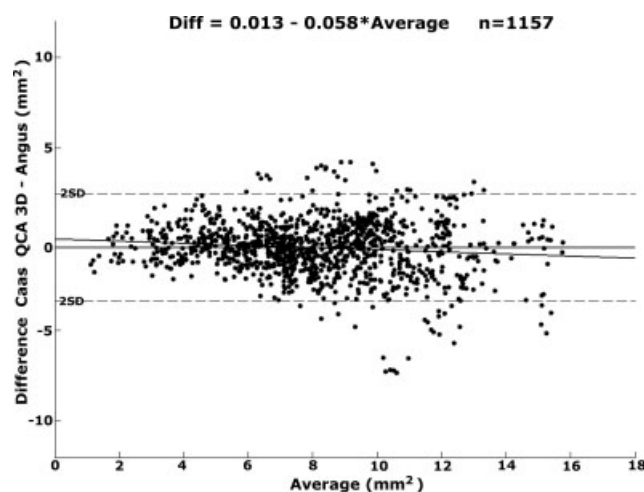


Fig. 3. Bland-Altman plot of the lumen areas obtained with the CAAS QCA-3D system and the ANGUS system.

In the slice by slice comparison, a good correlation between the luminal areas obtained with the ANGUS and CAAS QCA-3D system was found. The CAAS QCA-3D system systematically underestimated the luminal cross-sectional areas by 0.45 mm^2 . This is in concordance with the results of another 3D quantitative coronary angiography system that evaluated stented vessel segments showing slight underestimation of the proximal and distal stent diameters [3,7]. In our study, the use of diluted contrast could have been responsible for this small underestimation. Previous studies comparing 2D angiography measurements of the minimal lumen area to IVUS showed larger absolute differences [7,14], which might be caused by spatial mismatch between the two measurements techniques. Accurate lumen area measurements assists in stent selection and deployment. It has been reported that 2D angiography-guided coronary stent implantation results in suboptimal dilatation and some authors have claimed the need of IVUS to verify an adequate stent expansion [15,16]. However, acquisition and analysis of IVUS data requires the use of additional intracoronary devices and increases the procedural time. In the present study, the CAAS QCA-3D system (that can be performed online during the procedure) has shown a good correlation in the measurement of the lumen area with the ANGUS technique that uses IVUS to create the 3D reconstruction. Therefore CAAS QCA-3D reconstructions could be helpful to assess the result of stent implantation.

The accurate estimation of the vessel geometry might open possibilities for computational fluid dynamics. The wall shear stress patterns have been related with the location and progression of atherosclerotic lesions and in stent restenosis [17,18]. So far, these

patterns have been evaluated using 3D reconstruction systems based on ANGUS like procedures [9,19–21]. These techniques have demonstrated high accuracy in vivo, but require a complex and time consuming off-line analysis. Although attempts are made to automate this 3D reconstruction technique, it still requires at least 10 minutes for rather short segments (25 mm) [22]. The CAAS QCA-3D system provides, regardless the segment length, the 3D information in real-time without the need of additional intracoronary devices and is suitable for routine use in the catheterization laboratory. Nevertheless, it only supplies information about the lumen not allowing the evaluation of the vessel wall.

Limitations

This study was performed in a limited number of patients. Since our methods allowed slice by slice comparisons, the final analysis was performed using 1,157 cross-sections, which we believe is a large enough sample to detect systematic errors and to give a good estimation of the accuracy of the method.

In this study, a slight reduction in image quality of the angiograms was present, because diluted contrast agent was used for the biplane angiograms, which was necessarily for the ANGUS technique. Since the intra- and inter-observer variability of the full contrast images was approximately half of the variability of the angiograms obtained with diluted contrast, it is anticipated that the validation result will improve when full contrast agent is used.

Small errors between the IVUS lumen cross-sectional areas and the CAAS QCA 3D system might have been introduced, because with the IVUS technique cross-sections perpendicular on the IVUS catheter are used to determine the lumen area, while with the CAAS QCA-3D this is perpendicular to the lumen centerline. Research on the angle between the IVUS catheter and the centerline showed that the average angle is 5.0 ± 1.2 . This means that the average error in lumen area because of this reason is smaller than 1%. This is of minor influence on the presented results.

CONCLUSION

The CAAS QCA-3D system allows 3D reconstruction of human coronary arteries based on biplane angiography. Comparison of this system with the ANGUS system showed that both the 3D geometry and lumen areas are highly correlated, which makes the CAAS QCA-3D reconstruction a promising tool for applications in the catheterization laboratory and opens possibilities for computational fluid dynamics.

REFERENCES

1. Green NE, Chen SY, Hansgen AR, Messenger JC, Groves BM, Carroll JD. Angiographic views used for percutaneous coronary interventions: A three-dimensional analysis of physician-determined vs. computer-generated views. *Catheter Cardiovasc Interv* 2005;64:451–459.
2. Gollapudi RR, Valencia R, Lee SS, Wong GB, Teirstein PS, Price MJ. Utility of three-dimensional reconstruction of coronary angiography to guide percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2007;69:479–482.
3. Gradaus R, Mathies K, Breithardt G, Bocker D. Clinical assessment of a new real time 3D quantitative coronary angiography system: Evaluation in stented vessel segments. *Catheter Cardiovasc Interv* 2006;68:44–49.
4. Chen SY, Carroll JD, Messenger JC. Quantitative analysis of reconstructed 3-D coronary arterial tree and intracoronary devices. *IEEE Trans Med Imaging* 2002;21:724–740.
5. Klein JL, Hoff JG, Peifer JW, Folks R, Cooke CD, King SB, 3rd Garcia EV. A quantitative evaluation of the three dimensional reconstruction of patients' coronary arteries. *Int J Card Imaging* 1998;14:75–87.
6. Shechter G, Devernay F, Coste-Maniere E, Quyyumi A, McVeigh ER. Three-dimensional motion tracking of coronary arteries in biplane cineangiograms. *IEEE Trans Med Imaging* 2003;22:493–503.
7. Tsuchida K, van der Giessen WJ, Patterson M, Tanimoto S, García-García HM, Regar E, Ligthart JM, Maugenes A-M, Maatrijk G, Wentzel JJ, et al. In vivo validation of a novel three-dimensional quantitative coronary angiography system (CardiOp-B™): Comparison with a conventional two-dimensional system (CAAS II™) and with special reference to optical coherence tomography. *Eurointervention* 2007;100–108.
8. Ramcharitar S, Daeman J, Patterson M, van Guens RJ, Boersma E, Serruys PW, van der Giessen WJ. First direct in vivo comparison of two commercially available three-dimensional quantitative coronary angiography systems. *Catheter Cardiovasc Interv* 2008;71:44–50.
9. Slager CJ, Wentzel JJ, Schuurbijs JC, Oomen JA, Kloet J, Krams R, von Birgelen C, van der Giessen WJ, Serruys PW, de Feyter PJ. True 3-dimensional reconstruction of coronary arteries in patients by fusion of angiography and IVUS (ANGUS) and its quantitative validation. *Circulation* 2000;102:511–516.
10. Gronenschild E. A second generation system for off-line and on-line quantitative coronary angiography. *Cathet Cardiovasc Diagn* 1994;33:61–75.
11. Thomas AC, Davies MJ, Dilly S, Dilly N, Franc F. Potential errors in the estimation of coronary arterial stenosis from clinical arteriography with reference to the shape of the coronary arterial lumen. *Br Heart J* 1986;55:129–139.
12. Mauri L, O'Malley AJ, Popma JJ, Moses JW, Leon MB, Holmes DR, Jr, Teirstein PS, Cutlip DE, Donahoe D, Kuntz RE. Comparison of thrombosis and restenosis risk from stent length of sirolimus-eluting stents versus bare metal stents. *Am J Cardiol* 2005;95:1140–1145.
13. Gyongyosi M, Yang P, Khorsand A, Glogar D. Longitudinal straightening effect of stents is an additional predictor for major adverse cardiac events. Austrian Wiktor Stent Study Group and European Paragon Stent Investigators. *J Am Coll Cardiol* 2000;35:1580–1589.
14. Haase J, Ozaki Y, Di Mario C, Escaned J, de Feyter PJ, Roelandt JR, Serruys PW. Can intracoronary ultrasound correctly assess the luminal dimensions of coronary artery lesions? A comparison with quantitative angiography. *Eur Heart J* 1995;16:112–119.

15. Johansson B, Olsson H, Wennerblom B. Angiography-guided routine coronary stent implantation results in suboptimal dilatation. *Angiology* 2002;53:69–75.
16. Cheneau E, Leborgne L, Canos D, Pichard AD, Satler LF, Suddath WO, Kent KM, Lindsay J, Weissman N, Waksman R. Impact of intravascular ultrasound-guided direct stenting on clinical outcome of patients treated for native coronary disease. *Cardiovasc Radiat Med* 2004;5:15–19.
17. Gijzen FJ, Oortman RM, Wentzel JJ, Schuurbiers JC, Tanabe K, Degertekin M, Ligthart JM, Thury A, de Feyter PJ, Serruys PW, et al. Usefulness of shear stress pattern in predicting neointima distribution in sirolimus-eluting stents in coronary arteries. *Am J Cardiol* 2003;92:1325–1328.
18. Wentzel JJ, Krams R, Schuurbiers JC, Oomen JA, Kloet J, van Der Giessen WJ, Serruys PW, Slager CJ. Relationship between neointimal thickness and shear stress after Wallstent implantation in human coronary arteries. *Circulation* 2001;103:1740–1745.
19. Wentzel JJ, Janssen E, Vos J, Schuurbiers JC, Krams R, Serruys PW, de Feyter PJ, Slager CJ. Extension of increased atherosclerotic wall thickness into high shear stress regions is associated with loss of compensatory remodeling. *Circulation* 2003;108:17–23.
20. Krams R, Wentzel JJ, Oomen JA, Vinke R, Schuurbiers JC, de Feyter PJ, Serruys PW, Slager CJ. Evaluation of endothelial shear stress and 3D geometry as factors determining the development of atherosclerosis and remodeling in human coronary arteries in vivo. Combining 3D reconstruction from angiography and IVUS (ANGUS) with computational fluid dynamics. *Arterioscler Thromb Vasc Biol* 1997;17:2061–2065.
21. Stone PH, Coskun AU, Yeghiazarians Y, Kinlay S, Popma JJ, Kuntz RE, Feldman CL. Prediction of sites of coronary atherosclerosis progression: In vivo profiling of endothelial shear stress, lumen, and outer vessel wall characteristics to predict vascular behavior. *Curr Opin Cardiol* 2003;18:458–470.
22. Bourantas CV, Kalatzis FG, Papafaklis MI, Fotiadis DI, Tweddel AC, Kourtis IC, Katsouras CS, Michalis LK. Angiocare: An automated system for fast three-dimensional coronary reconstruction by integrating angiographic and intracoronary ultrasound data. *Catheter Cardiovasc Interv* 2008;72:166–175.