

Peer Review File

Article Information: <http://dx.doi.org/10.21037/cdt-20-560>

Review Comments:

Reviewer A:

Comment #1: please explain the long time interval between data acquisition and article submission

Reply #1: *I apologize lack of explanation about the long time interval between data acquisition and manuscript submission. Actually this work was first started in 2016-2017 during my fellowship at Ajou university hospital. The earlier version of this abstract was presented at Korean Society of Cardiology (KSC) 2017 and European Society of Cardiology (ESC) 2018 in the format of poster. I started my new carrier at Seoul Medical Center since 2018 and developed this manuscript. We applied 3D-reconstruction software to the plain angiography image in 2017 although other data were collected between 2011 and 2014.*

Reviewer B:

This is an interesting study that compares the value of 3D QCA vs IVUS as a non-invasive tool to predict whether a stenosis needs to be revascularized with the FFR as the standard. The results of this study indicate that the 3D QCA is not inferior to IVUS to predict the functional significance of a coronary narrowing, although the relationships could be further improved by setting the next step towards angio-based FFR. The AuC for 3D QCA was 0.77, and that of IVUS 0.73. There were no significant differences between for 3D MLA and IVUS-MLA.

Reply : *Thank you for your kind and insightful comment. We absolutely agreed to your comment of setting the next step towards FFR. At borderline 3D QCA cut-off levels, confirming angio-based FFR may still be needed to decide treatment strategy.*

Reviewer C:

Lee et al in the manuscript entitled "comparison of three-dimensional quantitative coronary angiography and intravascular ultrasound for detecting functionally significant coronary lesions" assessed 175 lesions from 175 patients by FFR, IVUS and 3D-QCA. They showed that there were no significant difference between the diagnostic performance of 3D-QCA-derived MLA and IVUS-derived MLA for detecting the functionally significant lesions (AUC=0.77 versus 0.73, p=0.27). The correlation between 3D-QCA-derived MLA with FFR and IVUS-derived MLA with FFR was 0.48 and 0.43, respectively.

Intracoronary images allow detailed assessment of coronary lumen, plaque morphology and stent expansion and apposition. Nonetheless, the performance in

assessing the physiologic significance of coronary stenosis is limited. The topic is clinically relevant since 3D-QCA offers a cheaper modality to assess lesion severity compared with IVUS. I have the following comments.

1. Please specify the inclusion criteria.

Reply #1: *Thank you for your insightful comment. We included 175 patients with stable ischemic heart disease who underwent coronary angiography in Ajou university hospital. We added more detailed inclusion criteria in the Study population section. (see Page 3, line 66-70)*

2. It would be more relevant to report the diagnostic performance of DS% by 3D QCA compared with IVUS-based MLA.

Reply #2: *We absolutely agree with your comment. It would be more relevant to report not only 3D-QCA MLA but also 3D-QCA DS% compared with IVUS-MLA. In our data, diagnostic accuracy of 3D-QCA DS% is slightly lower than that of 3D-QCA MLA and IVUS MLA. The area parameter may reflect much truer vessel geometry than diameter parameter. So we select 3D-QCA MLA for the main comparison target. We added the data of 3D-QCA DS% in the Table 2 and Table 3. We also modified Figure 6. (see Page 6, line 124-130) (see Page 8, line 169-172)*

3. Please report the overall diagnostic accuracy, i.e., diagnostic concordance with FFR, for both 3D-QCA and IVUS. .

Reply #3: *We deeply appreciate your valuable comment. Diagnostic concordance(Accuracy) with FFR for 3D-QCA was 73% and for IVUS was 68%. Location of lesion, burden of myocardial mass, microvascular resistance and clinical situation may affect these discrepancies between anatomical and functional severities. We mentioned this points at Limitations, third. We added diagnostic accuracy for both 3D-QCA and IVUS in the Results and Table 3. (see Page 6, line 126-128)*

4. Please improve the layout of Table 2. Currently it is a little confusing.

Reply #4: *We apologize any lack of clarity. We modified the layout of Table 2. by reducing font size.*

5. The r values in Figure 4 and Figure 5 do not match the values reported in the manuscript.

Reply #5: *We deeply apologize these critical errors. We hope that these errors do not compromise reliability of our manuscript. We modified r and p-values of Figure 3, Figure 4 and Figure 5.*

6. In the Abstract, it is concluded that "3D-QCA is not inferior to IVUS for functional assessment of intermediate coronary lesion". Similar finding has recently been reported by comparing 3D-QCA and OCT by Huang et al (10.4244/EIJ-D-19-01034). The authors should discuss the finding in the context of the finding by Huang et al.

Reply #6: *We sincerely appreciate your introducing novel reference article. OFR is very excellent method in the assessment of both anatomical and functional severity which is superior to 3D-QCA derived DS% and QFR. Our data derived from 3D-QCA are compatible with J. Huang's. We think that the strength of our work is validation of advanced anatomical parameter with physiologic parameter. We modified discussion section in the context of the finding by J. Huang et al. (see Page 8, line 167-182)*

7. Was there any interrogated vessel with myocardial bridge or previously implanted stent. The presence of myocardial bridge or stent might influence MLA result and its diagnostic performance.

Reply #7: *Thank for your pointed comment. We excluded significant myocardial bridge and previous stenting in the target vessel due to possibility of overestimated FFR. We added this content in the exclusion criteria. (see Page 4, line 72-74)*

8. Additional details of the blinding of the measurement of 3D-QCA and IVUS would be helpful.

Reply #8: *Thank you for your brilliant comment. To exclude bias, 3D-QCA analysis was performed blinded to the FFR and IVUS data. We added the comments regarding the blinding of the measurement. (see Page 5, line 88-89, 98-99)*

9. From the example figures it seems that 3D-QCA was performed in very short segment. Is this the standard approach to analyze 3D QCA in your center?

Reply #9: *Thank you for your comment. We usually selected proximal and distal reference about 5mm apart from the lesion when analyzing 3D-QCA. But relatively short segment was analyzed in the example figures to emphasize the three dimensional eccentric structure of the lesion.*