Dear Editor,

Please find enclosed the edited full-text manuscript in Word format (file name ESPC Manuscript No: 5596.doc).

**Title:** Part V: Coronary CT angiography: beyond lumen visualization

**Author:** Zhonghua Sun

**Name of Journal:** World Journal of Cardiology

**ESPS Manuscript NO:** 5596

Reviewer 1:

This is an interesting and well-illustrated paper addressing the capabilities of coronary CT beyond anatomic assessments. Although the authors deal with new developments on computational fluid dynamics (CFD) and fractional flow reserve is mentioned, I miss some information regarding ischemia and viability detection by CT. Minor points; Page 4, 2nd paragraph: Stress echocardiography should be also mentioned here

Response: thank you for your constructive feedback. The manuscript has been revised by taking into account your comments, with inclusion of ischemia and viability detection by dual-energy CT. Echocardiography is also added in the revised manuscript as suggested.

Reviewer 2:

This is an excellent overview about the clinical applications of coronary CT-derived CFD in coronary artery disease. This manuscript is nicely structured and well written. I have no question about this manuscript. I think this manuscript deserves being considered for publication.

Response: thank you very much for your positive feedback.

Reviewer 3:

The authors provide a review about computational fluid dynamics (CFD) with cardiac CT. There are two main issued to be solved. Firstly, the manuscript appears to be more a review of the applications of CFD in coronary atherosclerosis imaging; whereas very few is said or questioned about FFRct. Indeed, FFRct has several limitations and is based on many assumptions. Lastly, I suggest to provide a more comprehensive description of the methods involved in the evaluation of FFRct. I believe the title is not suitable, since "beyond lumen visualization" also implies plaque characterization, trans-stenotic attenuation gradients, stress myocardial perfusion, etc. Figure 6 is unrealistic, since plaque at the ostial LAD typically develops only at the outer vessel wall, opposite to the carina; whereas the inner wall is very rarely diseased as shown in the figure. Minor comments: Do not abbreviate figures (Fig 1). I suggest to include the following reference that was the first in vivo demonstration of the compositional differences in the left main bifurcation according to the shear stress. (Rodriguez-Granillo GA et a. Plaque composition and its relationship with acknowledged shear stress patterns in coronary arteries. J Am Coll Cardiol. 2006 Feb 21;47(4):884-5)

Response: thank you for constructive comments. We agree to the reviewer's comment on the limitation of $FFR_{CT}$ as this is a newly developed technique for identification of flow-limiting lesion. There are some controversial arguments about its clinical value when compared to the gold standard myocardial perfusion SPECT imaging, however, prospective studies confirmed its potential diagnostic value in the diagnosis of coronary artery disease. This has been discussed in the revised manuscript. Figure 7 (I think the reviewer referred to Figure 7 which shows simulation of plaque location in the left coronary artery) is a simulation of different types of plaques in the left coronary artery with more than 50% lumen stenosis, thus the purpose is to analyse hemodynamic changes rather than the exact plaque appearance as observed in realistic situation. As reviewer suggested, we will perform further analysis based on realistic plaque position in the left coronary artery. The title has been revised as suggested. The recommended reference is cited in the section of wall shear stress. A detailed description of $FFR_{CT}$ is provided, and

other relevant changes have been made.

Thank you again for publishing my manuscript in the World Journal of Cardiology.

Sincerely yours,

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