Response to Reviewers

Reviewer 1

topic is of interest. study is well designed and of great important to clarify dose reduction techniques. the authors give general idea about the dose reduction, but evaluation of the factors of the dose reduction and significance of each factor well added much.

Reviewer 2

The manuscript describes the protocol which is performed in the specific institution. Main limitations of this study are the following:

1. There is no correlation in the Discussion paragraph with the protocols which are adopted in other hospitals.

We have now added this to the discussion (page 11) outlining other protocols in use with references:

"The prospective ECG-gated single volume acquisition with AIDR-3D protocol we use at our institution is not the only potential strategy for very low dose CCTA. Another contemporary strategy is Prospective ECG-triggered high-pitch spiral acquisition which also allows the entire heart to be scanned within one single cardiac cycle thus significantly lowering the radiation dose[24-26]. This coupled with IR techniques have shown ultra-low mean effective radiation doses ranging from 0.06 mSv to 0.3 mSv with clinically acceptable diagnostic images[7, 27]. While demonstrating the feasibility of ultra-low dose CCTA, these studies were limited to carefully selected patents with a low and regular heart rate (< 60 bpm) and a body weight of less than 100 kg. Other IR algorithms are also in use including Model-based iterative reconstruction (MBIR, GE Healthcare, Waukesha, Wisconsin) which has also shown promising results for noise reduction in very-low-dose CCTA.[22] iDose4 and Iterative Model Reconstruction (IMR) are alternative IR algorithms released by Philips Healthcare (Philips Healthcare, Best, the Netherlands) that have also maintained image quality at 80% lower radiation exposure.[13] "

Also, it would be useful to have some data from the patients who underwent interventional coronary angiograms in order to compare the findings.

This analysis has now been included. The following has been added to the methods (page 7):

"If any patients went on to undergo invasive coronary angiography then the accuracy of CCTA in determining the presence of significant coronary disease (stenosis >50%) compared with the gold standard of invasive angiography was recorded."

And this has been added to the results (page 8):

"Twenty-one of the patients underwent invasive coronary angiography in addition to CCTA yielding 84 coronary arteries for comparison (21 left main stem, 21 left anterior descending, 21 left circumflex and 21 right coronary artery). CCTA correctly identified a significant (>50%) stenosis in 16 / 17 coronary arteries and correctly excluded significant stenosis in 62/67 coronary arteries. This

gave CCTA a sensitivity of 94%, specificity 93%, negative predictive value 98% and positive predictive value 76% to identify a significantly (>50%) stenosed coronary artery in comparison with the gold standard of invasive angiography. Examples of correct and incorrect CCTA classifications are provided in Figure 3."

In addition, a new figure, Figure 3 has been added showing examples of correlation between invasive angio and CCTA

2. Data such as BMI are lacking. The results of the study concern selected patient population without AF who are not overweight.

This has now been added as a limitation of the study (page 12):

"In addition, patients in atrial fibrillation were not included and whilst the patients were not selected on the basis of body weight, body mass index was not recorded and actual weight measurements were only available for 32% of the patients meaning the effect of patient weight on dose could not be investigated in this study. In view of this, the results may not be generalizable to patients who are overweight or in atrial fibrillation."

Moreover, authors should define clearly the specific characteristics of the patients with poor quality images.

This analysis has been done and added to the results (page 8) with an additional table (Table 2):

"We compared the patient characteristics of the excellent and good scans (Image Quality Score 3 + 4) with those that were poor and unusable (Image Quality Score 1 + 2). There was no difference in mean age or sex between the groups. However, compared with excellent and good scans, poor and unusable scans were more likely to occur in patients with heart rates >65 bpm (31% vs. 9%, p <0.0001) and require a higher effective dose (1.98 ± 1.69 vs. 1.24 ± 1.41, p =0.0041) (Table 2)."

Reviewer 3

Major comments

1. Main limitation of this study is that the definition of the quality of the images was subjective and performed by the authors. In addition no correlation is reported with the gold standard coronary angiography to see if this protocol-technique is clinically adequate. You should mention these limitations in the discussion

This has been added to the limitations as requested on page 12:

"The Image Quality Score used is a subjective assessment and was performed by the authors. Whilst the results of patients who underwent invasive coronary angiography is included, the proportion is relatively small and a more robust assessment of image adequacy would have been obtained if all patients had undergone the gold standard of invasive angiography."

2. Which are the characteristics of the patients with poor quality images? It is important to identify them, in order to establish indications for the use of this low radiation protocol-technique only in those that we will have at least good quality images

This analysis has been done and added to the results (page 8) and additional table added (Table 2):

"We compared the patient characteristics of the excellent and good scans (Image Quality Score 3 + 4) with those that were poor and unusable (Image Quality Score 1 + 2). There was no difference in mean age or sex between the groups. However, compared with excellent and good scans, poor and unusable scans were more likely to occur in patients with heart rates >65 bpm (31% vs. 9%, p <0.0001) and require a higher effective dose (1.98 ± 1.69 vs. 1.24 ± 1.41, p =0.0041) (Table 2)."

3. In a paragraph provide the clinical implications of this study (in view of the limitations)

As requested this paragraph has been added to the Conclusion (page 13):

"We have demonstrated that provided patients are in sinus rhythm and with the judicious use of beta blockers to achieve heart rates <65 bpm a combination of low-dose CCTA scan protocol and AIDR3D with a 320-detector row CT scanner can provide high quality images at exceptionally low radiation dose in patients being investigated for CAD."

Minor comments Abstract: DLP: explain

This abbreviation (Dose Length Product) has been written in full in the abstract.