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Revised Cover Letter

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To the Editor:

Dear Dr Nightingale,

Please find attached the author's manuscript for a revised submission to the journal Radiography, with our responses to the reviewers comments attached also.

The manuscript is still not under consideration for any other journals nor has it been submitted for publication previously.

Full details of the authors and identification of the first author and corresponding author is given below. All authors have agreed to the submission of the manuscript and have participated in the work. Publication is approved by all authors and by Professor Paul Keane, the Dean of School of Health and Social Care, Teesside University, where the work was carried out.

The authors (or their relations) have no conflict of interest to declare.

Best wishes

Mark Widdowfield

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***Response to Reviewers**

Reviewer #1	
This is a very important topic and I am happy to see an article on this.	Thank you.
The n of the articles leaves me unconvinced that your finding are valid. I suspect they are but I believe you do not have adequate data to draw a solid conclusion.	Our conclusion has been revised to reflect this.
It is not clear to me why you excluded retrospective studies unless you were hoping to do a meta-analysis. That was not explained. Even though the n of CCTA studies was reasonable, Perhaps re-analysing the data to include the retrospective that meet the other appropriateness criteria might lead to a stronger study.	We were uncertain as to the meaning of 'retrospective'. We have therefore attempted to answer this two fold and this has been added to the script: 'As retrospective ECG gating has been identified as a variable responsible for the increased dose in CCTA[23] it was felt that this could add to the heterogeneity of the studies, and for that reason only prospectively triggered ECG CCTAs were included. Prospective studies were included due to the opportunity for bias in data collection and data analysis that exists within retrospective studies[24].'
Review #2	
This was an interesting review that may be of interest to those working within this area. The introduction sets the scene well and justifies the systematic review.	Thank you.
The methodology is clear but it may help if justification for some of the exclusion and exclusion criteria was explained more fully	This has been performed within the text with particular emphasis around the exclusion of retrospective studies and retrospective gating.
I appreciate that "a priori" is a commonly used term but some of the readership may not be aware of this term so may benefit from an explanation.	This has been added into the 'search strategy and article selection' section.
The results are reasonably clear but on line 45 you mention 4 studies then go down to 3 without a clear link so this may just need some explanation	Apologies. This was a typographical error and has been corrected.
In the conclusion you do concede that this review is based on limited evidence but could I suggest that you would recommend more empirical studies rather than more systematic review as your concluding statement suggests.	We agree and the conclusion has been changed to reflect this.

The author may wish to include a table with the full references and highlights of the review as this may make the discussion easier to understand.	We have included a table with the study characteristics of the papers found and a comparison of the studies findings. We have also re-worked the review highlights.

***Title Page (with author details)**

Title Page

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Publication is approved by all authors and by Professor Paul Keane, the Dean of School of Health and Social Care, Teesside University, where the work was carried out. All authors confirm that this is their own work and they agree to the submission.

Conflict of interest statement: The authors (or their relations) have no conflict of interest to declare

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***Abstract**

Abstract

Introduction: Coronary computed tomography angiography (CCTA) is a reliable, minimally invasive technique used in the diagnosis and characterisation of coronary artery disease. Within this modality iterative reconstruction has the potential to maintain image quality whilst reducing radiation dose.

Methods: A priori search terms and inclusion/exclusion criteria were developed.

Results: Three studies were included in the review which analysed a total of 227 participants. As $CTDI_{vol}$ decreased there was no significant change in objective image quality, although some subjective image quality scores decreased.

Discussion: The decrease of subjective image quality scores may be explained as a reaction to the difference in image appearance of the iterative reconstruction images, a potential reduction in dynamic range and the number of scorers used.

Conclusion: Iterative reconstruction can be utilized as a tool to significantly reduce patients' exposure to ionising radiation; however there may be implications for radiologists/cardiologist in the interpretation of these images.

*Highlights (for review)

- Explores the use of iterative reconstruction in reducing radiation exposure.
- Objective image quality can be maintained with reduced tube current output..
- Subjective image quality scores decreases with reduced tube current output.
- The appearance of IR images may explain the decrease in subjective image quality.
- High quality studies are needed with the addition of the clinical utility.

Introduction

The control of coronary artery disease (CAD) requires reliable diagnosis, intervention, and regular follow-up. Each of these may involve some form of radiological investigation[1]. One such investigation is coronary computed tomography angiography (CCTA) as this has the potential to produce high quality diagnostic images of the entire coronary anatomy[2] without the invasiveness and arterial contrast administration of an interventional diagnostic procedure. CCTA is capable of evaluating lesion morphology and disease severity which is important for informing invasive interventions such as percutaneous coronary intervention (PCI)[3]. In addition, CCTA may also be used for follow-up investigations such as the evaluation of in-stent stenosis[4]. CCTA is advantageous because it is minimally-invasive, fast, and has few complications[5]. Furthermore, CCTA is accurate in the detection of CAD with a sensitivity of 88-100% and a specificity of 64-92% which is comparable with invasive coronary catheter angiography[6].

CCTA has an effective dose ranging between 4-19mSv per investigation; this does vary and is dependent upon the patient, the protocol used and manufacturer of the computed tomography (CT) scanner[7]. In patients who are scanned repeatedly throughout the course of their disease, this may increase the risk of developing a potential malignancy, especially when considered against the potential effective dose received from PCI (potentially >50mSv)[8]. Concerns regarding these risks have been raised by the International Commission on Radiation Protection (ICRP) [7], and the International Atomic Energy Agency (IAEA)[9]. These concerns are justified due to the radiosensitive tissues, such as the lungs and female breasts, which are included within the CCTA scan field[10]. Understandably, the ICRP are prioritising the development and validation of methods that keep the ionising radiation dose in cardiac CT as low as reasonably achievable (ALARA)[7]. Examples of dose-reduction techniques include prospective ECG-triggering[11]; automated exposure control[12]; and a reduction of the Z-axis length[13].

The efficiency of these dose reduction techniques can be restricted by filtered back projection (FBP). In FBP the image reconstructions are based upon ideal assumptions and approximations which can leave the acquired data inaccurate and under-sampled, particularly when radiation dose is not sufficient. In turn this produces images which are susceptible to noise and streak artefact. Ultimately, when using FBP in clinical practice, radiation dose reduction can only be achieved at the expense of image quality[14]. Iterative reconstruction (IR) differs as it interrogates the acquired CT data iteratively and converges upon the solution which is closest to the real object[15]. Despite being slower and more computationally demanding, IR is suggested to reduce radiation dose without compromising image quality[16]. Research to date has explored the application of IR in chest CT[17] and coronary stent analyses[18]. Both of these studies suggest that IR is able to reduce radiation dose while maintaining diagnostic image quality.

A recent systematic review explored the application of IR across a range of clinical examinations, including CCTA[19]. This review provides a valuable overview of the available research relevant to the application of IR in CCTA. There has been a focus on the ability of IR to improve image quality rather than reduce dose[20, 21]; however there have been studies which have shown that CCTA with FBP is already sufficient to diagnose coronary artery stenosis[2, 22]. What is now required are focussed systematic reviews which isolate the effect of IR on reducing patient dose in CCTA examinations to achieve the ALARA principle. Therefore the aim of this systematic review is to assess whether IR techniques are able to reduce radiation dose whilst maintaining image quality.

Method

Inclusion and Exclusion Criteria

Studies meeting the following criteria were included:

- Symptomatic patients (>18 years) with known or suspected coronary artery disease (CAD) undergoing routine CCTA.
- Only those studies which use prospective ECG triggering were included.
- Studies must have used ≥ 64 slice CT. Those studies which used dual-source CT were also included.
- Assessed outcomes in terms of objective measures of image noise, subjective image quality and $CTDI_{vol.}$
- Studies included were prospective experimental studies which compare CCTA using IR and FBP.
- Peer reviewed publications.

As retrospective ECG gating has been identified as a variable responsible for the increased dose in CCTA[23] it was felt that this could add to the heterogeneity of the studies, and for that reason only prospectively triggered ECG CCTAs were included. Prospective studies were included due to the opportunity for bias in data collection and data analysis that exists within retrospective studies[24].

Studies that were excluded included those studies that included patient cohorts recruited specifically with BMI's outside of the normal range. Also excluded were studies that focussed solely on reducing the ionising radiation dose on phantoms, as these were not felt to adequately reflect the clinical environment. Studies that included phantoms and human participants were included, although only the data from human participants were extracted from the papers and included in the review.

Search strategy and article selection

A comprehensive literature search was undertaken using the keywords detailed in table 1 using a PICO methodology[25]. The search terms were developed prior to the searching the databases (*a priori*). MEDLINE, EMBASE, CINAHL, Science-Direct, and Scopus were electronically searched between January 2009 (when the first iterative reconstruction technique was approved by the FDA) and October 2013. Searches were restricted to English language and human participants only.

A hand search was undertaken of the following journals between August and October 2013: Clinical Radiology; Radiology; European Journal of Radiology; European Radiology; International Journal of Cardiovascular Computed Tomography; and JACC: Cardiovascular Imaging. These were searched as they regularly publish studies pertinent to the topic area. The reference lists of all the studies identified were also reviewed for extant literature.

Steps taken to reduce bias
Two independent reviewers were used to ensure that the included studies met the inclusion criteria. Any disagreements resolved by discussion or arbitration by a third reviewer. Conference proceedings, theses, and other forms of grey literature were not searched, leading to the possibility of publication bias within the review.

Methodology Quality Assessment
Quality assessment was undertaken using a modified McMaster's tool[24], using two reviewers. The tool was adapted to: challenge the reproducibility of the scanning and reconstruction protocols; identify any affiliation or funding biases; and assess the ethical implications of the study design.

Data Extraction
Only studies that were deemed of good quality were included within the review and had data extracted. This was performed by the primary reviewer using a previously developed extraction pro-forma to extract relevant data. The primary outcomes were the objective measure of image noise; the subjective measure of image quality; and the $CTDI_{vol}$. Other data collected was limited to the variables that could affect these measures. This included study design; participant data; heart rate and medication used; scan protocols; scanner type; and IR technique.

Data Analysis
Due to the heterogeneity of the studies a meta-analysis was not possible. Bar charts and tables were produced to show the different outcome measures (i.e. objective image noise, subjective image quality, $CTDI_{vol}$) for the different studies. Inferential statistical data was also extracted from the individual reviews.

Results

Results of the Search
A total of 216 papers were identified by the initial search of electronic databases (see fig. 1). Following the removal of duplicates a total of 164 titles and abstracts were assessed using the *a priori* inclusion/exclusion criteria. Following this process a total of 33 studies were included for full text analysis. Hand searches were performed of relevant journals, which returned no results. Of these 33 studies only 4 met the inclusion criteria; of the 29 studies that were reject via full-text review 11 were excluded as these were retrospective rather than prospective studies, 7 studies were rejected as they either did not report the $CTDI_{vol}$ or they did not control for image quality. The QUORM chart (fig 1) shows the other 4 reasons for study rejection.

Characteristics of Included Studies
Table 2 provides a characteristics summary for the three studies included in the assessment of image quality and dose. The three studies recruited a total population of 227 participants with only two of the studies providing details of the excluded participants. The range of mean ages reported in the three studies was 52-59.6 years old (ranging across all studies from 28-87 years old).

The study designs varied between all studies (e.g. number of participant groups, contrast protocols etc.), although there were similarities, particularly with the reporting of the image quality. All studies gave both objective and subjective measures of image quality. Objective measures were measurements of image noise (standard deviation of Hounsfield Units at the aortic root) signal-noise and contrast-noise ratios. Subjective image quality was defined on a 4-point Likert scale following assessment by two experienced practitioners (the professional title of those performing this function was not always given). The variation in the studies came from the amount of tube current reduction and application of IR (see table 2).

Differences are also appreciable in the technology used and contrast injection protocols. Two studies used a 256-slice single-source CT machine[25,26] and one used a 2nd generation 64-slice dual-source CT machine[27]. Two studies used iDose[25,26] and one used SAFFIRE[27] as their iterative reconstruction software. The amount of contrast injected also varied although all studies utilized a contrast injection of between 50-80mL of contrast media (350/370 mgI/mL) with a saline bolus chaser. Yin et al[27] also added a 30:70 saline/contrast mixture (see table 2) to their injection protocol.

Subjective Image Quality
Subjective image quality (SIQ) was scored via a 4 point Likert scale (1 = unacceptable/poor SIQ; 2=fair/acceptable SIQ; 3=good SIQ; 4 = Excellent SIQ), based on the observers interpretation of contrast, sharpness, subjective image noise and overall acceptability. (Yin et al[27] reversed the scoring system with 4 = unacceptable/poor SIQ through to 1=Excellent SIQ). Papers varied in the reporting of whether these judgments were based on the entire series (i.e. per patient)[25, 26] or an individual artery (i.e. per segment)[27].

All studies reported a decline in overall acceptability of the IQ with decreasing tube current and application of IR (see fig. 2). In some cases this decline in SIQ was statistically significant. Hou et al[25] reported a statistically significant between the FBP series and the 65mAs tube output groups (i.e. between the control and most extreme tube current reduction).

Objective Image Quality
Objective image quality was measured with minor differences between the three papers. The three papers provided the same measurements for image noise, contrast-noise ratio (CNR) and signal-noise ratio (SNR) (equations for CNR and SNR measurements were consistent across all papers). All papers reported noise as the standard deviation of Hounsfield Units within the aortic root[25, 26, 27] (at either the left or right coronary artery level); however Yin et al[27] also described measurements been taken within the individual coronary arteries, although the results of these measurements are not specified by artery, they are only reported by series. Collations of results across all studies are given in figs. 3-5.

No papers reported statistically significant differences between the modified tube current/IR groups and the FBP groups for any of the objective image quality measures provided (i.e. image noise, SNR and CNR).

$CTDI_{vol}$

$CTDI_{vol}$ was extracted from the studies as this is the most widely applicable comparison variable (rather than another measure such as dose length product). $CTDI_{vol}$ for FBP only protocols ranged from 6.12 – 19.56mGy. For the IR protocols it is difficult to directly compare these due to the varying nature of the dose-reduction protocols employed in each of the studies; however the lowest value reported in all studies was 2.93mGy[27] and the largest intra-study reduction was from an FBP only of 19.56mGy to 5mGy[25]. All studies showed a reduction in $CTDI_{vol}$ (see fig 6) and all studies described these reductions as statistically significant.

Discussion

To our knowledge this is the first systematic review to interrogate prospectively-triggered CT cardiac angiography specifically, to evaluate the dose reduction potential of IR. Other previous systematic reviews have shown that IR has the potential to improve image quality and reduce dose[19] (Willemink *et al.,* 2013b); however the review in question was wide ranging in its consideration of clinical applicability and therefore it was considered that a more focused question was needed to evaluate the potential of IR in CCTA clinical practice.

As with individual CT machines, each IR technique differs in its method and is proprietary. Techniques such as IRIS (Siemens Healthcare; Munich; Germany) interrogate only the reconstructed image[28]. IRIS is able to distinguish fine-grained noise from true anatomical structures; however is unable to significantly counteract streak-artefacts[29]. This is because streak-artefacts originate within the acquired-data and are amplified during the reconstruction process. ASIR (GE Healthcare; Little Chalfont; UK), SAFIRE (Siemens Healthcare; Munich; Germany), iDose (Phillips; Eidhoeven; Netherlands), AIDR (Toshiba Medical Systems Corporation; Tochigi-ken; Japan) and Intelli-P (Hitachi Medical Corporation; Tokyo; Japan) on the other hand, interrogate both the raw projection-data and the reconstructed image[30] (Willemink *et al.,* 2013a). These techniques can correct the inaccuracies which propagate streak-artefact formation prior to the reconstruction of the images[31]. All of these techniques, however, continue to assume an ideal system and are therefore limited in accuracy[32]. Model Based Iterative Reconstruction (MBIR) in comparison, attempts to model the entire x-ray beam as it travels between the cathode and the detector. MBIR captures the volumetric nature of the focal spot; the divergence of the X-ray beam; the 3-dimensional nature of the voxel; and the volumetric interaction between the X-ray beam and the detector[30]. Preliminary evidence suggests that MBIR produces superior image quality when compared with iDose and ASIR[20, 33]. Unfortunately, IRIS, Intelli-P and MBIR were not represented in this review. Therefore, these results may not be applicable to these techniques. Of the techniques which were represented, similarity was observed in that they all interrogate both the projection-data and the reconstructed image. This suggests inter-study comparability. At present, there is minimal research which directly compares the efficacy of different manufacturers IR techniques. Research of this nature is impractical because IR techniques are only compatible with their respective manufacturer's scanners[34].

Radiation exposure (to patients and staff) within cardiac catheter angiography is a significant concern of cardiology intervention and therefore the utilisation of CCTA could be beneficial. However, radiation dose in this area has been higher than for other CT angiographic examinations, with CCTA effective doses of up to 30 mSv[35] especially when using retrospective gating. Comparing this to the dose received to the patient in cardiac catheter angiography of between 3.1 – 22.7mSv[36], further dose reduction is required. Also with further generations of CT scanners able to scan the heart in one heartbeat, then the need for retrospective ECG-gating may be removed[6], further reducing the ionising radiation exposure to the patient when combined with iterative reconstruction. This is of particular importance when one considers that prospectively triggered-ECG CCTA, despite the evidence suggesting lower ionising radiation dose than retrospective-gating, can be susceptible to heart rate fluctuation and therefore requires low and consistent heart rates[37]. Although CCTA reduces the risk of interventional complications associated with cardiac catheterisation, the risk of artificially reducing a patient's heart rate must be taken into consideration in these examinations. For example, apart from some of the common side effects of beta-blockers (e.g. dizziness, headaches) care should be taken in those patients with bronchospastic diseases, due to the drugs pharmacology[38]. Although no studies discussed individual images, variability of heart rate can be more of an issue than rate, with respect to image quality[39].

A finding of this review is that the use of iterative reconstruction within CCTA could significantly reduce patients' exposure to ionising radiation whist maintaining diagnostic image quality. $CTDI_{vol}$ was used in all three studies to estimate exposure to ionising radiation. Both Hou et al[25,26] studies included dose length product (DLP) and effective dose and Yin et al[27] included DLP also, $CTDI_{vol}$ was chosen for data extraction as this was constantly reported throughout the papers. $CTDI_{vol}$ is also preferable as this indicates the exposure per rotation and is therefore independent of patient length[40]. Given the high tissue weighting given to breast tissue in the latest update of the tissue weighting factors[41] this reduction in $CTDI_{vol}$ can be seen as a positive step forward.

The ALARA principle would not be achieved if the resultant decrease in ionising radiation exposure leads to the production of poor quality, un-diagnostic images. The studies reviewed here used both objective and subjective measures of image quality. Subjective image quality is routinely measured using a multiple-point Likert-type scale. The results showed that as the tube current was decreased, so the number of scores within the lower sections of the Likert scale increased. It should however be noted that the image quality never dropped below the acceptable range (i.e. all scores were >1). A possible reason for this gradual decrease is that it is very difficult to blind participants to whether or not the images are produced from FBP or IR due to the so-called 'plastic' appearance of the IR images[4] and perhaps this indicates that whilst the images were acceptable, the observers were not accustomed to viewing these types of image. The difference seen between the extremities of the Hou et al[25] study (i.e. FBP and the and the 70% tube current reduction images) may be due a number of factors; namely: the decreased dynamic range caused through the use of IR; the decrease in the raw data signal through the decrease in tube current; or a combination of the two. The use of only 2 observers in each of the studies may also have affected the subjective image quality scores. As diagnosis was only taken into account in one of the studies, it is difficult to state what effect this phenomena may have on the clinical utility of IR.

Objective image quality was ascertained though image noise, SNR and CNR measurements within all of the studies. These do not give a true reflection of the diagnostic acceptability of the images, merely a ratio of signal to noise or contrast to noise within a specific area. It is also a task dependent analysis, as some tasks may be able to cope with more noise than others[42]. The results reported here appeared to show that although signal to noise ratio fluctuated marginally, the observers opinions of the quality of the film appeared to decrease, however as stated above the subjective measures of the image quality never moved into unacceptable limits. None of the studies measured signal to noise ratios at specific areas of diagnosis (rather areas of potential diagnosis); therefore a task dependent threshold level for signal to noise and contrast to noise ratio for CCTA may be useful to provide a more useful, clinically relevant objective image quality threshold.

Conclusion

Iterative reconstruction can be used to maintain objective image quality whilst reducing tube current output and subsequent ionising radiation dose to the patient. It may be useful to use a task dependent objective measure of image quality, as the amount of noise acceptable may fluctuate with the task being performed. It is noted that as tube current is reduced and IR applied the subjective measures of image quality scores show a decrease, this may be due more to the appearance of the images than their diagnostic acceptability. The amount of papers found reflects the paucity of research in this area and it may be that further prospective experimental trials into the application of IR and the resultant diagnostic measures in this area are needed.

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Figure(s)

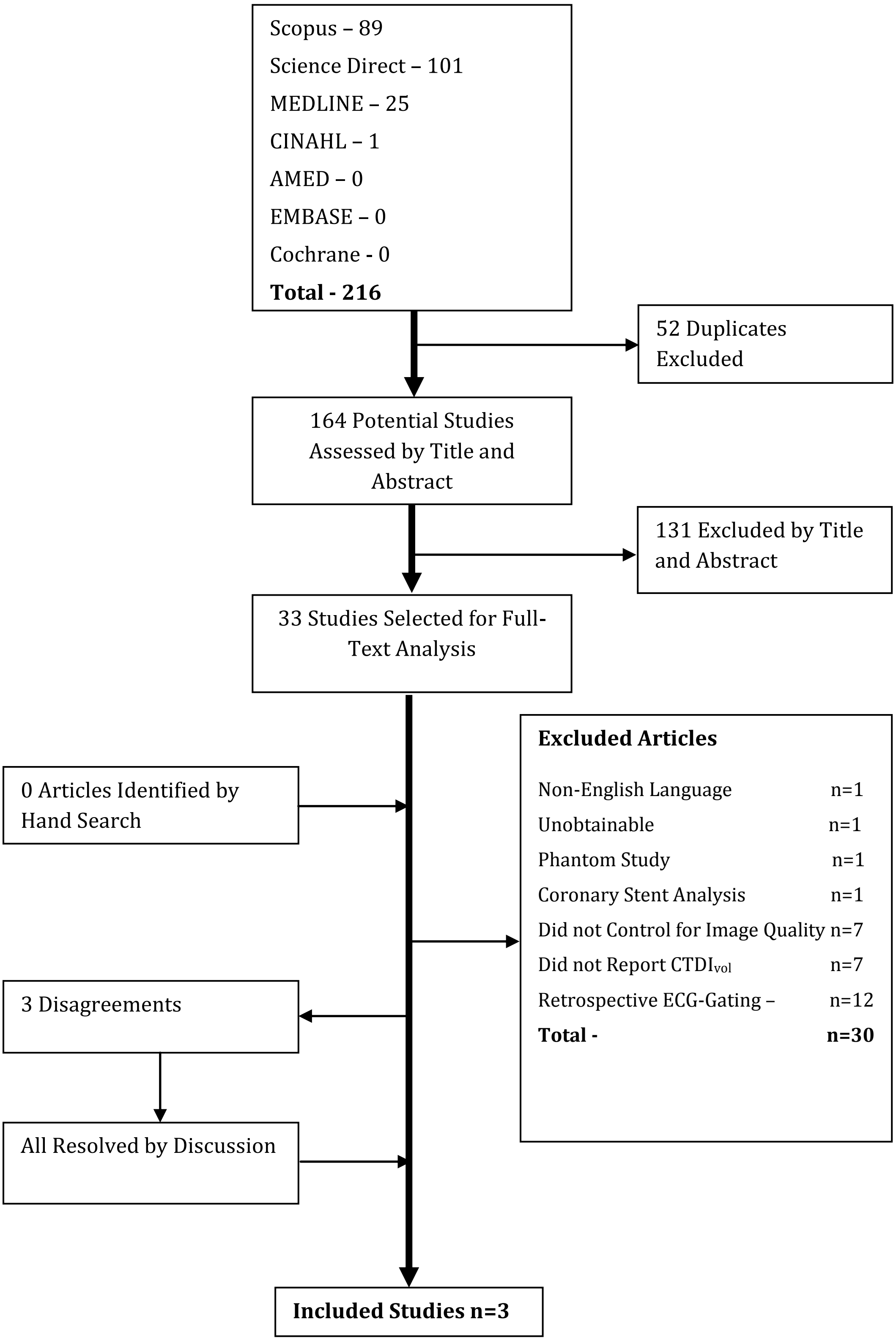

Figure 1
Results of the Systematic Search. Adapted from Qurom Statement (Moher et al., 1999)

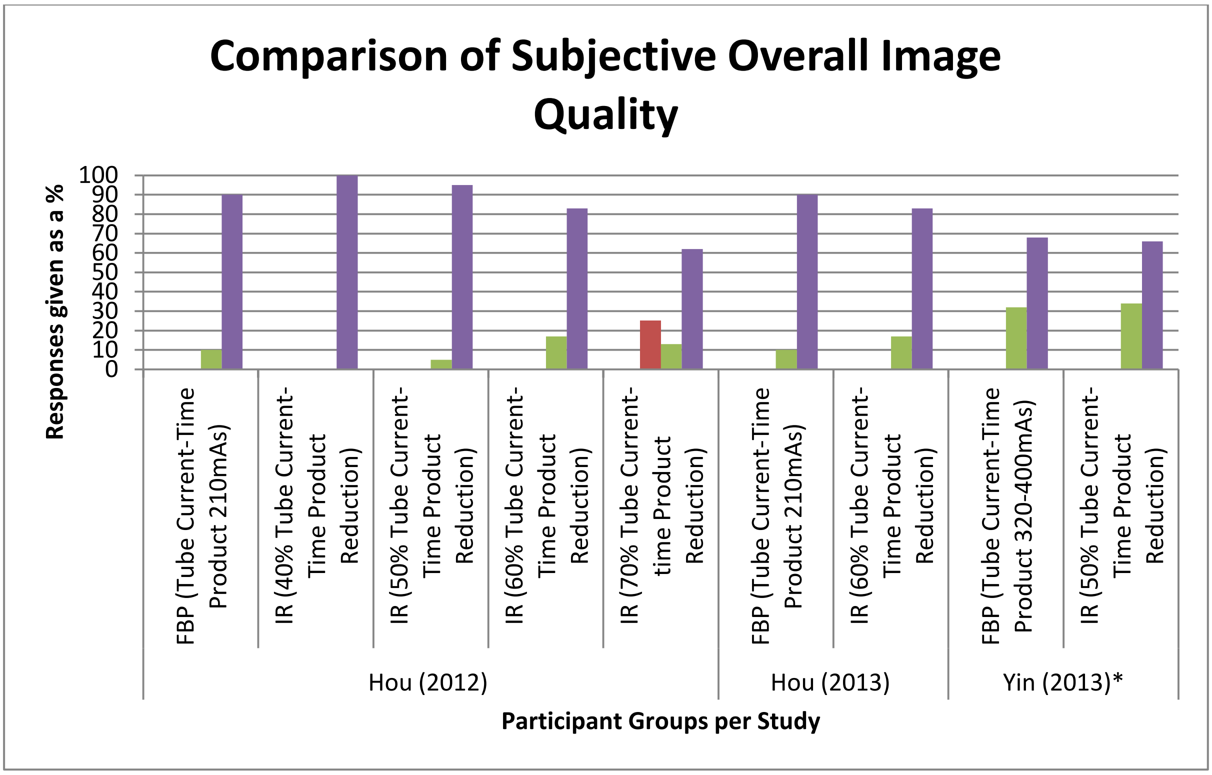

Fig. 2: Graph showing changes in perceived acceptability of the within the three papers identified. (* in the interests of comparability values for Yin et al were reversed as the same scale was used but the direction was altered)

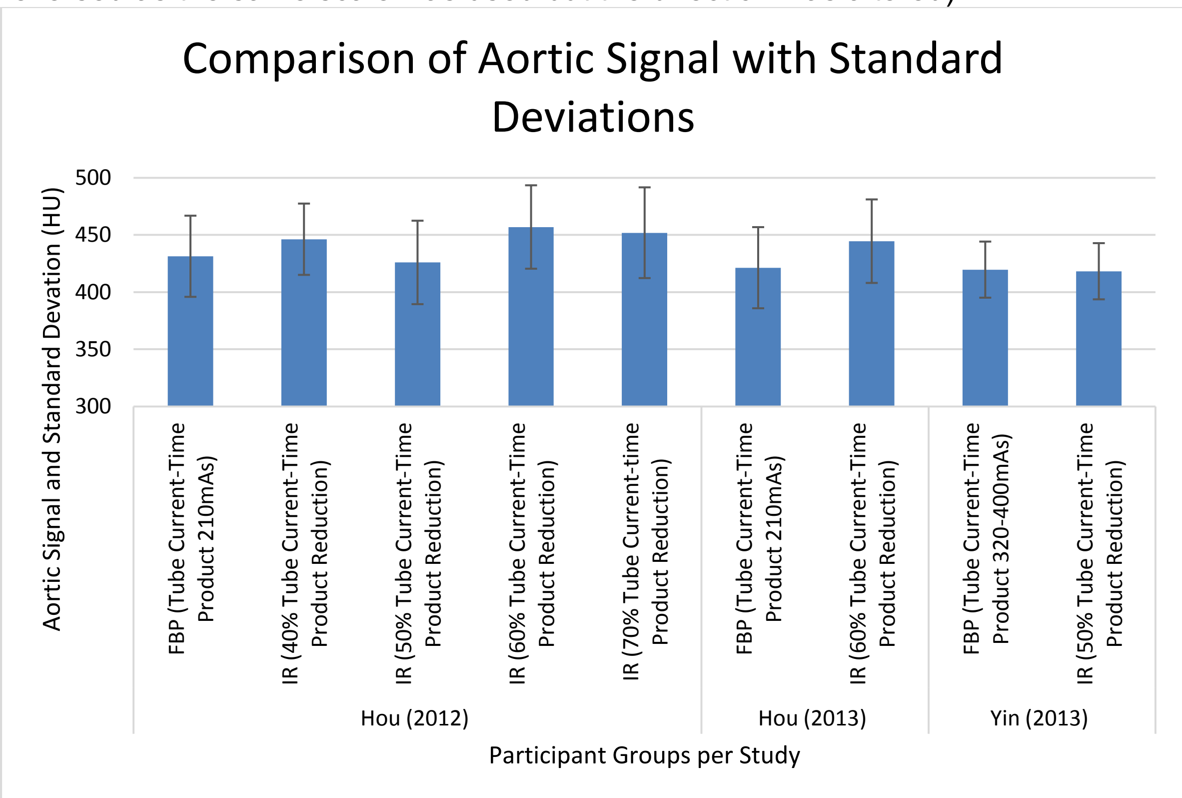

Fig. 3: Graph showing aortic signal and standard deviation (i.e. noise metric) at the level of the aortic root, used as an objective measure of signal and image noise for each experimental group within the papers found.

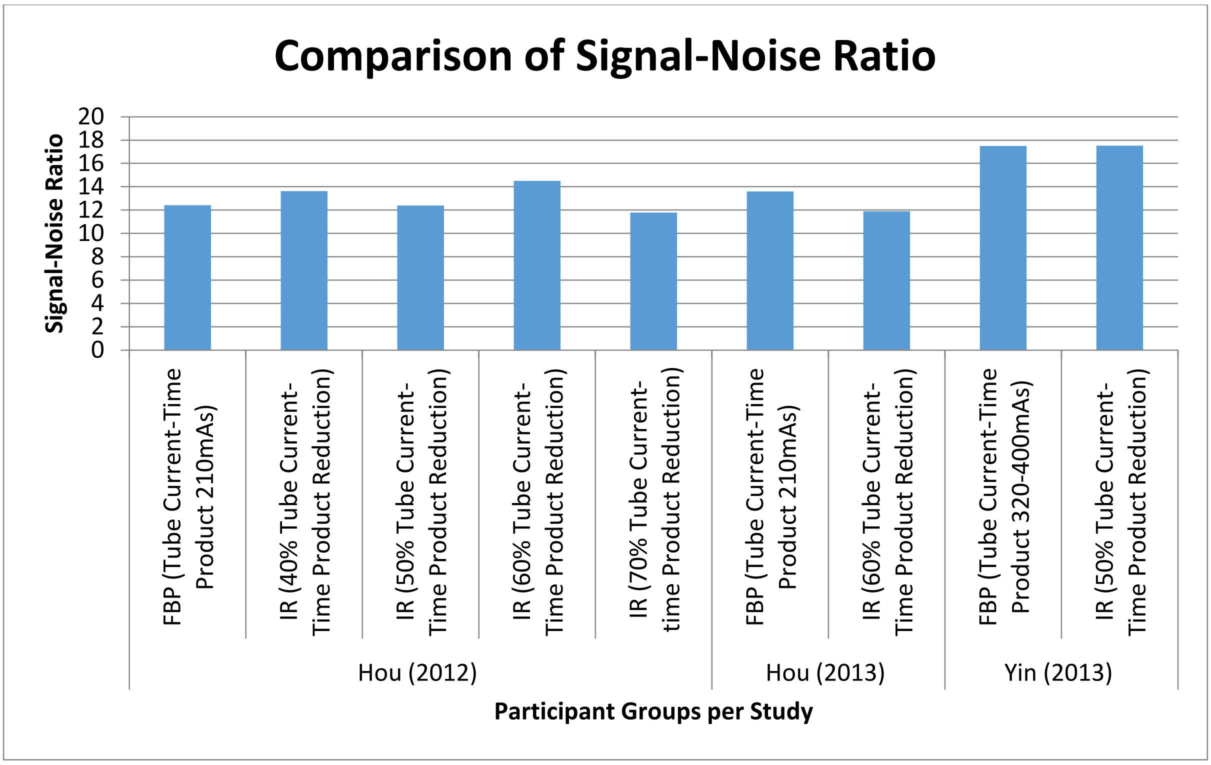

Fig. 4: Graph showing comparison of signal to noise ratios provided by each study.

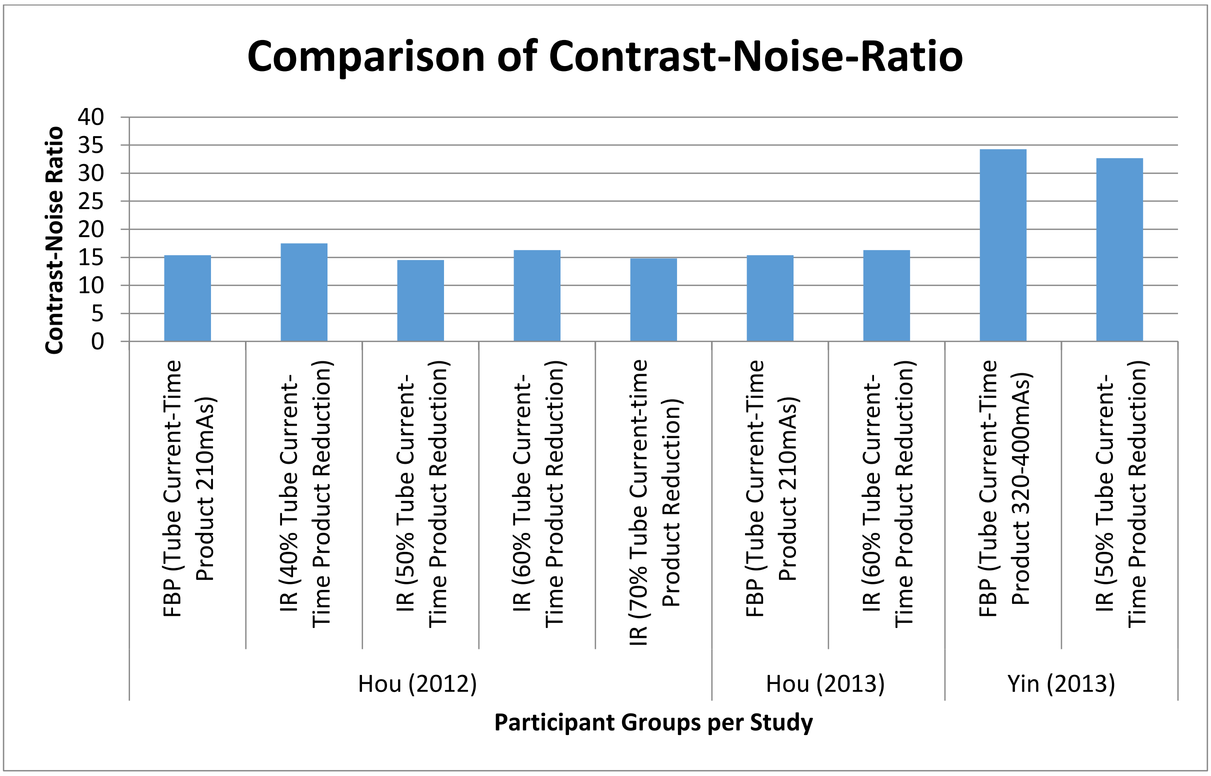

Fig. 5: Graph showing a comparison of contrast-noise ratios in each study.

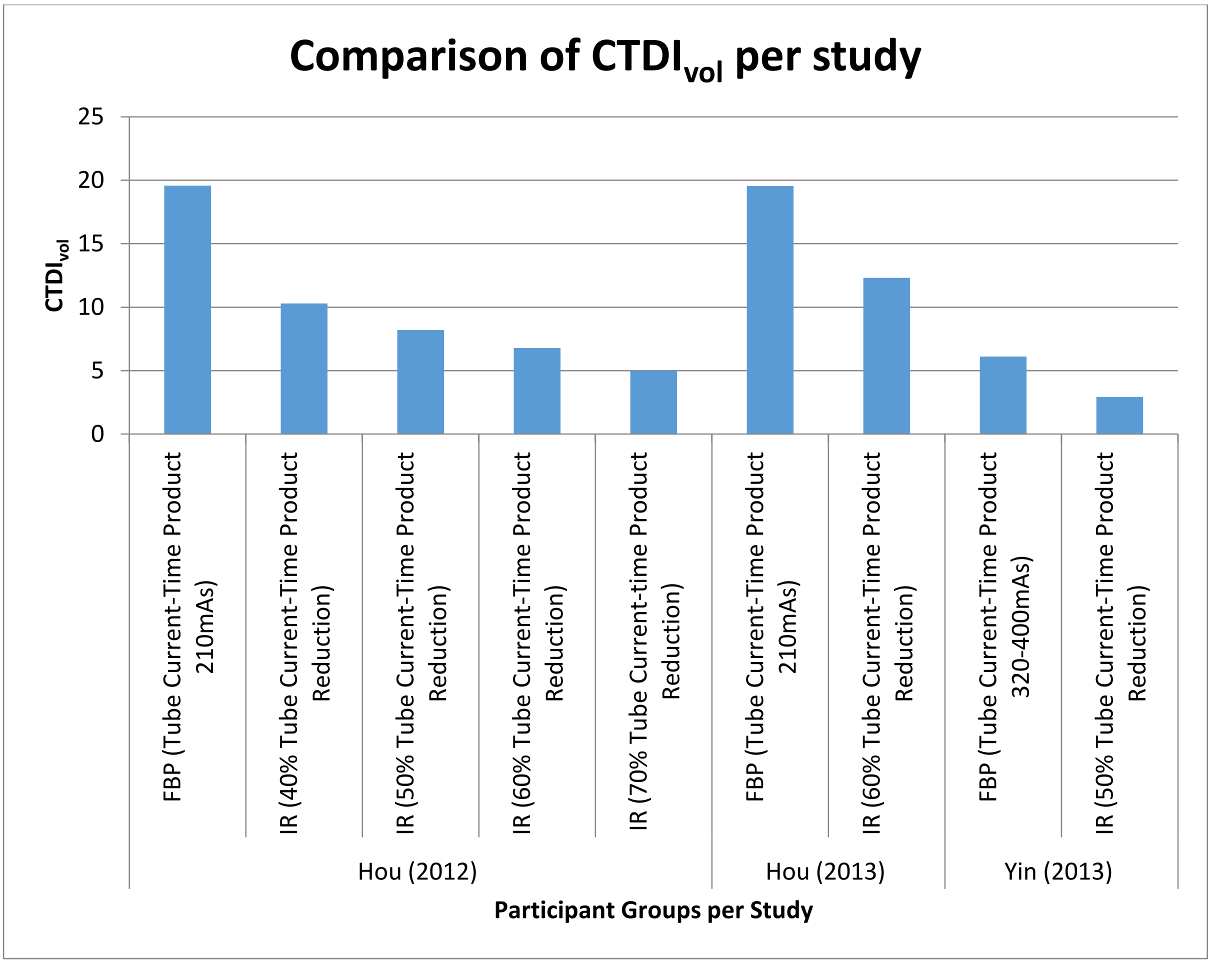

Fig. 6: $CTDI_{vol}$ values for each participant group per study.

Table 1- Boolean operators and keywords used for the systematic search.

((CAD OR "Coronary Artery Disease" OR CHD OR "Coronary Heart Disease" OR "Coronary Disease" OR Stenosis OR Atherosclerosis OR Arteriosclerosis OR Plaque*))
AND
(("Iterative Reconstruction" OR "Adaptive Statistical Iterative Reconstruction" OR ASIR OR "Model Based Iterative Reconstruction" OR MBIR OR VEO OR "Iterative Reconstruction in Image Space" OR IRIS OR "Sinogram Affirmed Iterative Reconstruction" OR SAFIRE OR IDose OR IDose4 OR "Adaptive Iterative Dose Reduction" OR AIDR OR AIDR3D OR I26f OR I46f OR "Intelli IP"))
AND
(("Filtered Back Projection" OR "FBP" OR "Convoluted Back Projection" OR "Back Projection with a Convoluted Filter" OR B26f OR B46f OR QDS+))
AND
(("Objective Image Quality" OR "Image Noise" OR "Contrast-Noise-Ratio" OR "CNR" OR "Signal-Noise-Ratio" OR "SNR" OR "Subjective Image Quality"))

Table 2 - Summary of study characteristics.

Study	Study Design	Sample Characteristics	CT Scanner	Contrast Media Protocol	Iterative Reconstruction
Hou et al[25] (2012)	Prospective Experimental Group 1 – FBP (210mAs) Group 2 – IR 60% Tube Current-Time Product Reduction Group 3 – IR (50% Tube Current-Time Product Reduction) Group 4 – IR (40% Tube Current-Time Product Reduction) Group 5 - IR (30% Tube Current-Time Product Reduction)	110 Adult Patients. 63% Males. Age Range 28-87 Years. Mean BMI 24.7.	Philips Brilliance iCT 256-slice Rotation Time 270ms Detector-Configuration 128x0.625mm	Automatic bolus tracking ROI – ascending aorta at level of pulmonary artery 180 HU threshold 70-80mL Iohexol 350mgI/mL 30mL saline bolus chaser 5-6mL/sec	iDose Slice Thickness 0.9mm Increment 0.45mm
Hou et al[26] (2013)	Prospective Experimental Phantom Study to Optimise Tube-Current Reduction Group 1 – FBP (210mAs) Group 2 – IR 60% Tube Current-Time Product Reduction	57 Adult Patients. 61% Male. Age Range 28-77 Years. Mean BMI 25.4.	Philips Brilliance iCT 256-slice Rotation Time 270ms Detector-Configuration 128x0.625mm	Automatic bolus tracking ROI – ascending aorta at level of pulmonary artery 180 HU threshold 60-70mL Iohexol 350mgI/mL 20mL saline bolus chaser 5 mL/sec	iDose Slice Thickness 0.9mm Increment 0.45mm
Yin et al[27] (2013)	Prospective Experimental All Patients Subjected to Both Full-Dose Scans (320-400mAs) With FBP and 50% Tube Current-Time Product Reduction with IR.	60 Adult Patients. 75% Males. Age Range 36-69 Years. Mean Bodyweight 72kg	SOMATOM Definition Flash, Siemens Healthcare 64-slice Dual-Source Rotation Time 280ms Detector-Configuration 2x64x0.6mm	Automatic bolus tracking ROI – ascending aorta at level of pulmonary artery 100 HU threshold 50-60mL iopromide 370mgI/mL then 30mL of contrast/saline mixture (30:70) 40 mL saline bolus chaser 4-5mL/sec	SAFIRE Slice Thickness 0.75mm Increment 0.5mm