

National Institute for Health and Clinical Excellence
Computed tomography (CT) scanners for cardiac imaging –
Somatom Definition Flash, Aquilion One, Brilliance iCT and Discovery CT750 H
Diagnostics Assessment Report (DAR) – comments

Responder reference no.	Comment no.	Page no.	Section no.	Comment	
1	1	16	2.2	One scanner being evaluated is a 64 slice machine.	
1	2	16	2.3	Flash can scan high and unstable heart rates and patients intolerant to Beta blockers	
1	3	20	2.5	Flash can scan obese patients, having a power reserve of 2 x 100KW generators.	
1	4	25	3.2.1	This is not a '2 x 64 dual source scanner'. See your own definition of Dual Source scanner on page 11, Glossary, Multi Slice CT coronary angiography: A dual source scanner has two pairs of X-ray sources and multi-slice detectors mounted at 90 degrees to each other	
1	5	25	3.2.1	Misleading temporal resolution stated here of 0.44ms. This is using multi segment reconstruction. Either this should be used for all statements of temporal resolution in later sections (see pg 26, 3.2.3 where the true temporal resolution is stated), or better still adjust this section to state the true temporal resolution.	

1	6	26	3.2.3	To be consistent with the method of stating temporal resolution used in 3.2.1, this should read 'temporal resolution of 36ms'.	
1	7	26	3.2.3	Should read '2 x 64 x 0.6. Coverage stated is misleading and takes no account of Flash spiral mode which has a much greater coverage per rotation. Flash spiral allows acquisition speeds of up to 43cm/sec by interleaving the spiral data acquired at high pitch from each source detector.	
1	8	27	3.2.4	This machine ACQUIRES 320 slices per rotation. Why is it stated as a 640 slice CT scanner? The 640 slices refers to a reconstruction mode. All the other scanners could cite much higher slices if this philosophy was universally adopted. We would argue that common terminology should be adopted across all vendors.	
1	9			Throughout the report, many references are made about intolerance of beta blockers. Is this project going to assess the financial savings to be obtained through avoiding use of beta blockers, (in patients who could nevertheless tolerate them)? Isn't this also an area of potential benefit?	
2	1	25	3.2.1	The GE 750HD is not a dual source scanner as it only has one x-ray tube and one detector array. It is capable of dual energy scanning but so are all the other CT scanners in the study	
2	2			In general the amount of published literature on all but the Siemens system is limited so can this be considered an accurate evaluation.	
3		16	2.1	Line 10: in the sentence discussing the possible advantages over CT scanners e.g. Shorter imaging times, reduced radiation dose, more accurate diagnosis in specific patient groups. Might we suggest that the latter of	

				these advantages is further clarified to put it into context perhaps; 'improved image quality allowing more accurate diagnosis in specific patient groups'	
3	2	16	2.2	We would be grateful if all references to CT750 HD could be rephrased to Discovery CT750 HD.	
3	3	17	2.3	Line 2 – can the dates of the systematic literature review please be corrected.	
3	4	18	2.3	Line 7 – this sentence was somewhat confusing on a first read. The assessment group might like to consider rephrasing the sentence, perhaps 'While there were differences in sensitivity and specificity between the patient groups, it was assumed that these were the same for the different populations, suspected and known CAD.'	
3	5	20	2.4	It would be good to have a consistent terminology e.g. NGCCT with ICA or NGCCT-ICA to help clarity	
3	6	20	2.5	It is noted within the conclusion that data were sparse, particularly for obese patients, etc. Given a review of the included studies we feel that there are more studies that could be included to enhance the data set considered. The majority of the studies included in the analysis are actually based on a prior generation CT scanner (Somatom Definition Dual Source rather than on Somatom Definition Flash). Given this, we believe there are studies on the prior generation of GE CT (Lightspeed VCT) that could also be considered as relevant. For example, Herzog 2008 (see Appendix 2 of the additional data submitted 4 th April 2011) considers cardiac CT to ICA over a range of BMI's including BMI>30. We would ask the assessment group to reconsider the evidence submitted from GE Healthcare with this in mind as we believe additional data could be included to strengthen the	

				evidence base.	
3	7	21	2.6	There is mention of the NICE Clinical Guidelines on chest pain. We feel it is worth noting at this point that there may be a need to update these guidelines to not just consider NGCCT for low risk patients but also for moderate risk patients who currently are sent for functional imaging such as SPECT. While not within the scope of this evaluation it should be noted for future reference.	
3	8	25	3.2.1	<p>We would be grateful if the description of Discovery CT750 HD could be refined to fully reflect its capabilities. The below amended text provides a more accurate description of the technology:</p> <p>Discovery CT750 HD, GE Healthcare</p> <p>The Discovery CT750 HD is a 128-slice CT scanner. It has a 40 mm wide detector array with 64 rows of 0.625 mm elements. The detector also doubles samples in the x-direction to achieve a higher resolution cardiac scanning. In the z-direction the measured cardiac spatial resolution is 18lp/cm; which translates to visualisation of objects as small as 0.23 mm across.</p> <p>The Discovery CT750 HD has a gantry aperture of 70 cm, a gantry tilt of $\pm 30^\circ$ and a gantry rotation speed of 0.35 seconds. The table has a maximum load of 227 kg and a horizontal speed of 137.5 mm/s. The Discovery CT750 HD has a cardiac temporal resolution of 0.44 ms. The maximum scan field is 50 cm.</p> <p>The GemstoneTM detector uses a fast scintillator made of a complex rare earth based oxide with a chemical structure of garnet crystal. This contributes to high image quality and a low amount of afterglow. It has a single X-ray source which switches between two energy levels, allowing two data sets – high energy and low energy – to be acquired simultaneously. This imaging technique has</p>	

				<p>the ability to detect very small concentrations of contrast agent and can deliver non-contrast-like images by subtracting the detected agent from the images.</p> <p>The SnapShot Pulse™, a prospectively gated axial scanning technique allows a complete picture of the heart to be captured in three or four “snapshots” taken at precise patient table positions and timed to correspond to a specific phase of the cardiac cycle.</p> <p>An Adaptive Statistical Iterative Reconstruction (ASiR) algorithm is used to enhance low contrast detection at a reduced level of radiation and reduced image noise. In clinical use, the Discovery CT750 HD has been shown to perform adult CCTA exams at or below a 1mSv dose.</p> <p>Other features to reduce radiation dose are:</p> <ul style="list-style-type: none"> • Dynamic z-axis tracking provides automatic and continuous correction of the X-ray beam position to block unused radiation at the beginning and end of a helical scan. • Filters reduce noise providing dose reduction while maintaining image quality and spatial resolution. • 3D Dose Modulation allows dose protocols to be easily personalised to each patient. 	
3	9	35	5.1	<p>We suggest the assessment group make a distinction between the evidence that is specifically NGCCT and that which is based on the precursor products within the defined patient populations of this evaluation. We are concerned that the reader will be left with the inaccurate perception that only Siemens have conducted ICA comparator studies in the patient population of concern.</p> <p>Within the assessment report there are actually only 2 studies which compare NGCCT to ICA (LaBounty 2010; Pflederer 2010). Another reference that should be considered (Mihara ACC 2010 ACC abstract, Noninvasive</p>	

				<p>Assessment of In-Stent Restenosis).</p> <p>We find the majority of the evidence for the accuracy of NGCCT is demonstrated in multi-reader, observational studies. The baseline accuracy of 64-slice CT vs coronary angiography is well-established (Min et al, JACC Vol 52:21; 2008; Herzog et al, Eur Heart J 29: 24, 2008 and LaBounty et al, AJR 194; 2010).</p> <p>Studies with an ICA comparison were less frequent by the time of the arrival of the in-scope NGCCT, and so there are relatively few examples of the NGCCT compared to ICA.</p> <p>The ICA comparator studies included in this assessment still provide value allowing a valid assessment of the clinical and economic evidence, but it should be made clear to the reader when such studies are not specifically NGCCT.</p>	
3	10	36	5.1	<p>It is noted that phantom studies were excluded however we would question if this is appropriate for two reasons.</p> <p>Firstly, ethical practice dictates using histological and phantom models in place of humans whenever possible. This is especially true in pediatric imaging where randomisation and informed consent are not feasible. The following is an example of a relevant abstract that has been automatically excluded as it is a phantom model.</p> <p>Wallner – paediatric protocol evaluation in phantom models</p> <p>Secondly, there are studies such as Min 2009 and Siu 2009 (see Appendix 2, additional data submitted by GE Healthcare, 4th April 2011) which while being phantom studies are specifically designed to look at coronary artery stents therefore providing potentially valuable evidence in one of the noted patient populations for this evaluation. Another abstract that could add value is:</p>	

				Moravitch-Horvath. – ex vivo human heart stenosis	
3	11	40	5.6	<p>20 of the 21 Siemens papers cited were not performed on Somatom Definition Flash, but on the prior generation Somatom Definition Dual Source CT Scanner. We therefore request that the assessment group also consider relevant publications comparing Lightspeed VCT to ICA within the relevant patient populations:</p> <p>Results From the Prospective Multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) Trial</p> <p>Core 64, Min</p> <p>Comparison of radiation dose between CT and Catheterization – 42 patients; Herzog</p> <p>http://heart.bmj.com/content/95/20/1656.full.pdf</p> <p>Diagnostic Accuracy of Coronary Computed Tomography Angiography; Pontone – 180 patients</p> <p>http://www.sciencedirect.com/science?_ob=MIimg&_imagekey=B6T18-4WS7955-B-5&_cdi=4884&_user=9156398&_pii=S0735109709014351&_origin=&_coverDate=07%2F21%2F2009&_sk=999459995&view=c&wchp=dGLzVlz-SkWz&md5=163f9b4d819bfa0e6181cd2d6e310670&ie=/sarticle.pdf</p> <p>Determinants of vessel contrast in BMI-adapted low dose CT; Kaufman – 70 patients</p>	

				http://www.springerlink.com/content/v6872882l472l986/fulltext.html A comparison of radiation doses between state-of-the-art multislice CT coronary angiography with iterative reconstruction; Gosling – 84 Patients http://heart.bmj.com/content/96/12/922.abstract In vivo reduction of radiation exposure with a single-source coronary CT angiography, Tavildari – 135 Patients http://www.sciencedirect.com/science/article/pii/S1878648010701373	
3	12	46	5.6	Please note that LaBounty 2010 uses Discovery CT750 HD. References to HD-CT are generally always referring to Discovery CT750 HD. In addition to support this statement it should be noted that HD-CCTA using ASIR (as per the abstract) – ASIR is a GE trademark and is used on the Discovery CT750 HD. Other references to the LaBounty paper can be found on pages 84 and 295.	
3	13	109	6.2.1.4	There is no table 20 for review	
3	14	213	Appendix 1	Additional Search Criteria The search strategies may be using overly restrictive search criteria. The terms Dual Source, Dual Energy and DSCT are synonymous with Siemens Definition Flash and, the now obsolete Definition Dual Source scanners. No publications on Discovery CT750 HD were located using the more restrictive CT750 and CT-750. Common alternative names for the GE CT customers are HDCT and HD 750. In addition, some studies list only the GE CT low dose SnapShot Pulse	

			<p>trademarked feature.</p> <p>The query of HDCT NOT chemotherapy reveals another ACC paper on CT750 vs. ICA on 40 stent patients</p> <p>http://circ.ahajournals.org/cgi/content/meeting_abstract/122/21_MeetingAbstracts/A13277</p> <p>Along with additional phantom/histological studies, one from Min and one from Moravitch-Horvath.</p> <p>http://linkinghub.elsevier.com/retrieve/pii/S1934592509002597</p> <p>http://circ.ahajournals.org/cgi/content/meeting_abstract/120/18_MeetingAbstracts/S303-a</p> <p>HD 750 CT reveals the following</p> <p>Blinded read studies with expert observers</p> <p>Leipsic et al – 292 patients</p> <p>http://www.ajronline.org/cgi/reprint/195/5/1095</p> <p>Earls et al – 202 patients</p> <p>http://www.sciencedirect.com/science/article/pii/S0002914910014931</p> <p>Earls et al – 886 patients</p> <p>http://www.ajronline.org/cgi/content/abstract/194/4/933</p> <p>Accuracy established against prior versions</p> <p>Leipsic – 50 patients</p> <p>http://www.ajronline.org/cgi/content/abstract/196/4/801</p> <p><u>SnapShot Pulse</u> (a GE trademarked product feature), reveals the following:</p> <p>Comparison of radiation dose between CT and Catheterization – 42 patients; Herzog</p>	
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				<p>http://heart.bmj.com/content/95/20/1656.full.pdf</p> <p>Diagnostic Accuracy of Coronary Computed Tomography Angiography; Pontone – 180 patients</p> <p>http://www.sciencedirect.com/science?_ob=MIimg&_imagekey=B6T18-4WS7955-B-5&_cdi=4884&_user=9156398&_pii=S0735109709014351&_origin=&_coverDate=07%2F21%2F2009&_sk=999459995&_view=c&_wchp=dGLzVlz-zSkWz&md5=163f9b4d819bfa0e6181cd2d6e310670&ie=/s/article.pdf</p> <p>Determinants of vessel contrast in BMI-adapted low dose CT; Kaufman – 70 patients</p> <p>http://www.springerlink.com/content/v6872882l472l986/fulltext.html</p> <p>A comparison of radiation doses between state-of-the-art multislice CT coronary angiography with iterative reconstruction; Gosling – 84 Patients</p> <p>http://heart.bmj.com/content/96/12/922.abstract</p> <p>In vivo reduction of radiation exposure with a single-source coronary CT angiography, Tavildari – 135 Patients</p> <p>http://www.sciencedirect.com/science/article/pii/S1878648010701373</p> <p>We believe inclusion of these publications would expand the evidence base for NGCCT and strengthen the evaluation.</p>	
3	15	295	Appendix 4	<p>Index Test column should read CT scanner – Discovery CT750 HD, GE Healthcare, Waukesha, WI.</p>	

3	16	331-2	Appendix 5	<p>We would request that the external assessment group reconsider the following publications that were initially excluded from their assessment:</p> <ul style="list-style-type: none"> • [20] LaBounty TM, Earls JP, Leipsic J, Heilbron B, Mancini GBJ, Lin FY, et al. Excluded because did not meet criteria in section 5.1. Paper specifically states that it included patient with BMI as high as 33kg/m³ while demonstrating reduced dose. Demonstrates the Discovery CT750 HD can be used on this patient category with low dose and high accuracy. • [21] LaBounty TM, Leipsic J, Min JK, Heilbron B, Mancini GBJ, Lin FY, et al. Excluded because the outcomes were not included. The paper specifically states that <u>equal</u> outcomes were attained at very low dose in patients with BMI up to 33kg/m³. Demonstrates the Discovery CT750 HD can be used routinely on this patient category with low dose and high accuracy. • [14] Heilbron BG, Leipsic J. Submillisievert coronary computed tomography angiography using adaptive statistical iterative reconstruction: a new reality. Can J Cardiol 2010;26(1):35-6 <p>We believe that the evidence of GE Healthcare NGCCT performance is clearly demonstrated in these multi-reader, observational studies for the patient population considered within the scope of this evaluation.</p>	
3	17	333	Appendix 5	<p>We would request that the external assessment group reconsider reference [24] Leipsic et al. Estimated radiation dose reduction using adaptive statistical</p>	

				iterative reconstruction in coronary CT angiography: the ERASIR study. AJR 2010; 195 (3):655 – 60. We believe the evidence provided here will add to the evidence base for this evaluation demonstrating the benefits of NGCCT.	
4	1	General		This report suffers from an inadequate understanding of the complexities of CT scanner technology, particularly as applied to cardiac scanning. This undermines the basis of the modelling.	
4	2	General		<p>A number of assumptions have been made in this report which are incorrect and so may prejudice the conclusions of the review:</p> <p>'NGCCT' assumes a generic scanner type, with the same dose and imaging performance, for all the 4 systems. However all four systems are very different, and have distinct advantages and disadvantages in imaging different patient groups. The results obtained for one of the systems cannot be extrapolated to the others. Some specific examples are given:</p> <p>The Siemens Definition Flash (as well as the original Siemens Definition Dual source) can achieve approximately double the temporal resolution of the other systems when using 'single sector reconstruction' mode, therefore should show advantages in imaging patients with high heart rates. Improved temporal resolution will result in improved effective spatial resolution, therefore benefits should be seen in patients with a high calcium score, as well as those with stents,</p> <p>The Toshiba Aquilion ONE is the only scanner with a detector whose coverage extends over the whole cardiac volume. It can therefore image the whole</p>	

				<p>heart in a single heartbeat which is advantageous for patients with arrhythmia. Although the Definition Flash also has the capability of 'single beat coverage' when used in Flash mode, there are other disadvantages to this mode.</p> <p>The GE Discovery CT750 HD has an increased spatial resolution in the x-y plain compared to other GE scanner models. This could have advantages in scanning patients with stents or a high calcium level. However, its spatial resolution in the z-axis, and its temporal resolution, is the same as on previous GE models.</p> <p>The Philips Brilliance iCT has an increased z-axis coverage compared to other Philips scanners, so can cover the cardiac volume in fewer rotations.</p> <p>There is little technical reason to suppose that there will be advantages on e.g. obese patients on any of the 'NGCCT' scanners.</p>	
4	3	General		<p>Assumption 2:</p> <p>Most of the studies identified in the literature search were performed on Siemens scanners and the results have been extrapolated to the other three models.</p> <p>Furthermore, many of the studies were not on the Definition Flash, the Siemens model identified as NGCCT. They were on the Definition Dual source, the precursor of the Flash, and it has been assumed that the results apply to the Flash.</p>	
4	4	General		<p>Assumption 3:</p> <p>It has been assumed that the systems included in the review will have improved sensitivity and</p>	

				specificity over non- NGCCT scanners in the patient groups defined as 'difficult to image'. However, as stated above, some of these systems may only have advantages in scanning particular patient groups, but not in all of the 'difficult' patient groups mentioned.	
4	5	General		<p>Assumption 3:</p> <p>It cannot be assumed that the systems defined as 'NGCCT' will perform cardiac studies at lower dose. Most approaches used for dose reduction in cardiac CT are now available on a wide range of scanner models. For example, the dose from a cardiac CT scan is largely dependant on scan mode (prospective triggering versus retrospective gating) and both these modes are available on a wide range of scanners. It is also dependent on kV, and use of low kV is not restricted to these scanner models. Iterative reconstruction methods, which are being used to reduce dose, are also now available on a wide range of scanner models.</p> <p>In fact, the dose used on a patient is very dependent on patient characteristics, and the 'difficult to image patients' usually require a higher dose.</p>	
4	6	General		<p>Assumption 4:</p> <p>It has been assumed that the patients in the included studies could not have been imaged on non NGCCT scanners.</p>	
4	7	General		It was felt unnecessary to examine the tables in detail due to the more pressing fundamental flaws in the methodology and analysis.	

4	8	16	2.2	<p>It is not clear how NGCCT were defined. Why were these particular scanners selected – explanation and justification is required.</p> <p>The inference is that NGCCT scanners are scanners with '>64 slices' but two of the scanners identified as 'NGCCT' are 64 detector row scanners.</p>	
4	9	16	2.3, para 1	<i>'Search strategies were be based on...'</i> Delete 'be' from sentence.	
4	10	17	2.3, para 1	<i>'The following databases were searched from 2000 to 2000 to February/March 2011...'</i> Delete 'to 2000'.	
4	11	17, para 3	2.3	<i>'The latter of these five models...'</i> Replace with 'The last of these five models...'	
4	12	18, para 1	2.3	Is it valid to assume that sensitivity and specificity for patients with known CAD and suspected CAD are equal?	
4	13	18, para 2	2.3	<p><i>'The impacts of radiation reduction on life-time risk of cancer incidence and subsequently related life expectancy, health related quality of life and costs were assessed based using the YRM model.'</i></p> <p>It has been assumed above that 'NGCCT' models covered in this report result in dose reduction as compared to other CT scanners. This assumption has not been justified. Manufacturers often incorporate new dose reduction features on their latest top-of-the-range models, but these features are subsequently available on other scanners in their range. For example, iterative reconstruction techniques were first introduced on the Discovery HD750 CT, but now are available on most of GE's</p>	

				<p>scanner range.</p> <p>Also, the word 'based' in the quoted sentence is superfluous.</p>	
4	14	18	2.4, para 1	<p>It is not clear that patients included in these studies could not be imaged on non-NGCCT scanners? The criteria for defining a 'difficult to image patient' are fairly arbitrary. For example:</p> <p>the criteria for 'high heart rate' patients were changed from 70 bpm to 65 bpm</p> <p>obese patients will be imaged more successfully on scanners with iterative reconstruction which is available on systems other than just those defined as 'NGCCT'</p>	
4	15	18 para 3	2.3	How was the reduced radiation dose associated with NGCCT measured or otherwise deduced?	
4	16	19 para 1	2.4	<p>"Further, though there were no data specifically for β-blocker intolerant patients, it should be noted that no study reporting per patient data for patients with high heart rates used additional β-blockers before scanning. It may therefore be inferred that new generation cardiac CT could reasonably be used to image patients who are intolerant to β-blockers who could not otherwise be reliably imaged by 64-slice CT."</p>	
4	17	19	2.4, para 2	<p><i>'It may therefore be inferred that new generation cardiac CT could reasonably be used to image patients who are intolerant to β-blockers who could not otherwise be reliably imaged by 64-slice CT.'</i></p>	

				<p>Is this a reasonable inference?</p> <p>The majority of studies included are from scanner models of a single CT manufacturer which have a definite advantage in terms of temporal resolution. It cannot be assumed that all the other 'NGCCT' scanner models will be able to scan without beta blockers.</p>	
4	18	19	2.4, para 2	<p><i>'The high per patient estimates of sensitivity (>95%) indicate that new generation cardiac CT could be used to reliably rule out significant stenosis and thus potentially avoid invasive investigations such as ICA in these patient groups.'</i></p> <p>The specificity of these systems has been ignored. The specificity of these systems was ~80%, meaning that 2 out of 10 patients without significant stenosis would receive unnecessary intervention.</p>	
4	19	20, para 3	2.4	Replace 'mSV' with 'mSv'.	
4	20	20	2.5	The conclusions reached in this review have been applied to all NGCCT scanners, whereas the majority of papers are from one manufacturer's scanners. As all the scanner models considered have very different specifications, the conclusions reached on one model cannot be applied to another.	
4	21	24 - 27	3.2.1, 3.2.2, 3.3.3,	This section generally reads as though the scanner descriptions have been taken from manufacturer's literature, with neither independent verification of the claims, nor caveat that the claims have not been	

			3.2.4	<p>verified.</p> <p>The summaries of the equipment contain different types of information and lack consistency of approach, therefore are difficult to compare. E.g. section 3.2.4 does not give the rotation time, whereas all the others do.</p> <p>For this reason it is not obvious that the four systems have very different levels of performance and so cannot be treated as a generic 'NGCCT' scanner.</p> <p>Furthermore the descriptions are not always accurate. E.g. to describe the Discovery CT750 HD as a dual source scanner is misleading. It is not true dual source scanner in the same way as a Siemens Definition Flash, which has two x-ray tubes resulting in a number of advantages.</p> <p>Although the authors refer to the CEP report on advanced CT scanners for coronary angiography, the fact that these scanners were shown to be very different has not been considered in this review.</p>	
4	22	25	3.2.1	<p><i>"The Discovery CT750 HD is a 2 x 64-slice dual source CT scanner"</i></p> <p>It is not a dual source scanner</p>	
4	23	25	3.2.1 Para 1	<p>Replace 'gantry rotation speed' with 'gantry rotation time'.</p> <p>This section generally reads as though it has been taken from manufacturer's literature with neither independent verification of the claims nor caveat that</p>	

				the claims have not been verified.	
4	24	28	3.3.1	<p><i>“the total risk, for all major complications from ICA (mortality, MI, cerebrovascular accident, arrhythmia, vascular complications, allergic reaction to contrast media, hemodynamic complications, perforation of heart chamber), is <2%.^{22, 23}”</i></p> <p>Risk from MSCT needs to include allergic reaction to contrast media</p>	
4	25	31	3.4.2	<p><i>“We are not aware of any nationally accepted guidelines on the diagnosis and management of newborns, infants and children with congenital heart disease have been identified.”</i></p> <p>Sentence construction needs to be addressed. (Delete ‘<i>have been identified</i>’, or replace ‘<i>We are not aware of any</i>’ with ‘<i>No</i>’</p>	
4	26	31	3.4.2	<p><i>“The main disadvantage of using MRI in this population is the procedure length, which requires babies and young children to be under general anaesthetic, however, there is no associated radiation exposure”.</i></p> <p>Have noise levels in MRI been considered? http://www.mhra.gov.uk/home/groups/dts-iac/documents/publication/con2033065.pdf cf page 18</p>	
4	27	31	3.4.2	<p><i>CT imaging has the advantage of rapid acquisition time, removing the need for general anaesthetic.</i></p> <p>Not all (NG) CT scanners remove the need for general anaesthetic.</p>	

4	28	31	3.4.2	<p><i>“that are too high to benefit from the low radiation modes of scanning in NGCCT.”..</i></p> <p>This is an incorrect assumption about NGCCT. Not all the scan modes give lower radiation dose, indeed some of these scanners may give higher radiation dose. It all depends on what mode they are used in, scan parameters used, and patient characteristics e.g. BMI, heart rate.....</p> <p>Dose reduction also depends on whether or not iterative reconstruction techniques are implemented on the scanner. It is a development that offers high dose reduction, but that can also be implemented on some of the standard 64 slice models.</p>	
4	29	33	4.1	<p>Report appears to be making the assumption that the 4 scanners selected for inclusion in this report have identical performance and that studies performed using one scanner have results that are directly applicable to each of the other scanners.</p>	
4	30	34	5.1	<p><i>“Difficult or impossible to image patient groups defined a priori were:</i></p> <p>...</p> <p><i>High heart rate (HHR) (>65 bpm) ...”</i></p> <p>65 bpm is not that high. Current 64 slice scanners are used for these patients.</p> <p>The ‘new generation ‘ collection do not necessarily have any benefits for high HRs as they do not all have an improved temporal resolution. One particular model, in one particular mode, is the opposite – it requires a low HR of < 65 bpm.</p>	
4	31	35	5.1	<p><i>“The only relevant comparator for the assessment of difficult to image CAD patients was ICA.”</i></p>	

				This assumes that difficult to image patients are automatically excluded from normal 64 slice scanning. Not sure that is entirely true. Sometimes a poorer image is still deemed to have diagnostic value.	
4	32	34	5.1, <i>Participants</i>	High heart rate has been defined as >65 bpm. Have the authors considered the Sensitivity and Specificity of 'non-NGCCT' scanners at heart rates in this region e.g. 65 – 70 bpm? What is the maximum heart rate considered in the included studies?	
4	33	35	5.1, <i>Interventions</i>	<p><i>'No additional equivalent technologies were identified during the review process.'</i></p> <p>The authors have not defined what is meant by a 'NGCCT scanner'. It is assumed that they consider them to be scanners with 'more than 64 slices'. However, at least one of the scanners included is a 64-slice system. One other is sometimes described as such.</p> <p>Furthermore, the Toshiba Aquilion Premium is a scanner with more than 64 detector banks, but has not been included in the list of 'NGCCT' scanners. There are also a number of other scanners, which are referred to as > 64 slices. There is an important technical distinction between '>64-slice scanners' and '>64-detector bank scanners'.</p> <p>The authors do not distinguish between the original Siemens dual source scanner, the Somatom Definition, and the new generation Siemens dual</p>	

				source scanner (the Somatom Definition Flash). These two scanners have different dose and imaging specifications, but papers on both systems have been included in the review, even though the original dual source scanner has not been identified as a 'NGCCT' system. It is possible that some papers on the single source Definitions have also been included in the review.	
4	34	35	5.1	<p><i>"Studies reporting the diagnostic accuracy of NGCCT for the detection of significant CAD were required to use ICA as the reference standard."</i></p> <p>What was the comparison with standard 64 slice scanners?</p>	
4	35	40	5.6	<p><i>"Twenty of the 24 included studies reported using Somatom Definition; three studies did not specify the instrument used,39-41"</i></p> <p>Does this not invalidate the whole exercise ? Since the scanners have not been proved to give similar results. (They are very different technologies, so they would need to have a sufficient representation).</p>	
4	36	40	5.6, para 4	<p>The authors refer to the Somatom Definition. This is not specific enough. There are a number of 'Somatom Definition' scanners:</p> <p>'Definition': The Mark 1 Siemens dual source scanner, a 40 detector bank scanner</p> <p>'Definition Flash': The Mark 2 dual source, 64 detector bank scanner described in this report, and included in the 'NGCCT' scanner list</p>	

				<p>'Definition AS': a single source, 32 detector bank scanner</p> <p>'Definition AS+': a single source, 64 detector bank scanner</p>	
4	37	70	5.6.3 Table 7	<p>Have the authors considered that the dose in mSv may have resulted from differing conversion factors from the DLP. (there are at least two different factors in use in the literature).</p> <p>Also applies to tables 5, 9,11,13</p>	
4	38	87	5.6.7 Table 13	<p><i>"DLP (mGy*cm) 1.726±596"</i></p> <p>This can't be correct. Is it meant to be 1726 ?</p>	
4	39	89	5.6.8 Table 15	<i>Ditto</i>	
4	40	90	5.7	<p><i>"It may therefore be inferred that NGCCT could reasonably be used to image patients who are intolerant to β-blockers who could not otherwise be reliably imaged by 64-slice CT. "</i></p> <p>Incorrect inference</p>	
4	41	90	5.7	This analysis does not make sense unless research is also carried out on scanners excluded from this study. (This should be considered also as a general comment).	
4	42	90	5.7, para 2	See comment 0 (page 19, section 2.4, para. 2) and comment 0 (page 19, section 2.4, para. 2).	

4	43	90	5.7, para 3	<p><i>"Data on the numbers of difficult to image patients in whom NGCCT was non-diagnostic were sparse;"</i></p> <p>Therefore extreme caution is needed in making any conclusions.</p>	
4	44	95, 99, 101		Text blacked out. Assume deliberate ?	
4	45	107 (last line)	6.2.1.4	Should be 'chance' not 'change'	
4	46	109		Table 20 missing	
4	47	120	6.2.1.5 (cf YRM Models)	This comment refers to the related YRM models (spreadsheets): Why is adult scoliosis as a heading in tab 'Adjusted YRM' on all YRM models ?	
4	48	122	6.2.1.5	<p><i>"we conducted expert surveys to obtain the relevant dosages by scanning strategy. The results are shown in Table 52 (for coronary artery disease patients) and Table 66(for congenital heart disease patients)."</i></p> <p>Table 52 is based on two experts. This is not very robust. There needs to be evidence for these views. For example the source of the knowledge of the experts could be based on one scanner or type of scan only.</p>	
4	49	122	6.2.1.5	'Table 66' incorrect. It should read table 69. (Occurs twice on this page)	

4	50	122	6.2.1.5	<p><i>“The results of our expert surveys are in line with the literature that focuses on general chest CTs (see Table 27)”.</i></p> <p>Chest CT’s are a very different scanning mode from cardiac CT. Therefore this statement loses weight without clarification.</p>	
4	51	122 para 2	6.2.1.5	Should read ‘CT is’ not ‘CTs are’; should be ‘multi-slice CT allows’ not ‘multi-slice CTs allow’.	
4	52	123	6.2.1.6, last line	Seems an odd way to end a sentence – perhaps it should be ‘mean’ not ‘men’?	
4	53	127	6.2.2.1	Lots of blank text. Intended ?	
4	54	142 and 145	6.2.2.5 Para 2, and table 52.	<p>The dose value for NGGCT is based on the expert view of only 2 people. This is not adequate.</p> <p>The dose is very dependent on the type of scanner, the scan mode and options available on the scanner, as well as patient characteristics (eg BMI, heart rate, arrhythmia).</p>	
4	55	175	6.3.2.1, para 3	<p><i>“No clear evidence exists on to what extent NGCCT reduces the radiation dose at each scan. The general, NGCCT favourable assumption, supported by expert opinion, was to assume a reduction of 50% as compared to the standard 64-slice CT.”</i></p> <p>This is an incorrect statement, and should not be included or used in this report. The level of 50 % reduction in dose, which can be achieved on some scanners can be due to iterative reconstruction</p>	

				techniques. These iterative techniques, whilst maybe initially offered on top range systems, are available on scanners other than the NGCCT scanners given in this report.	
4	56	176	6.3.2.1, Table 69	As above.	
4	57	175, 176, 142, 145	6.2.2.5 and 6.3.2.1,	(See above comments on pages 175, 176 , 142, and 145). In addition, any dose data should be referenced. There is a wide body of literature on doses from cardiac CT and this has not been utilised.	
4	58	187	6.4, para 3	See comment 0 (page 17, para 3, section 2.3).	
4	59	190	7.1.1, para 2	See comment 0 (page 19, section 2.4, para 2).	
4	60	211	Searches	Some searches include 'Somatom' and 'DSCT' as well as 'Definition' and 'Flash', whereas others only include the first two terms. The term '64-row', '64-detect\$' etc., has not been included in the searches, although some of the scanners defined as 'NGCCT' are '64-row' scanners.	
4	61	292	App. 4	"Somatom Definition " Which Siemens Definition scanner does this refer to ? This could be the single tube system, or the original two tube system which is not the Definition Flash)	

4	62	321	App. 5	<p>“outcomes – The study did not report any of the outcomes specified in section 5.1, OR, for diagnostic test accuracy studies, insufficient data were reported to allow the construction of 2 x2 contingency tables (numbers of TP, FN, FP, and TN test results).</p> <p>study design – The study design was not one of those specified in section 5.1, OR the study included <10 participants in the relevant patient groups.”</p> <p>‘Bold’ text IS the wrong way round. ‘outcomes’ and ‘study design’ need to be bold Other text should not be in bold.</p>	
5	1			<p>For challenging patients with suspected and known coronary artery disease: NGCCT (Next-Gen Cardiac Computed Tomography) is both cost- and clinically-effective. For patients with suspected CAD, the NGCCT-only strategy could be cost-effective; for patients with known CAD, the NGCCT + ICA (invasive cath) strategy is cost-effective.</p>	
	2			<p>For people with congenital heart disease (CHD), the finding is that the use of NGCCT instead of 64-slice is not cost effective when only considering radiation exposure.</p> <p>It is stated that “The reduction in radiation by replacing a single 64-slice CT scan by a NGCCT scan is small and leads to only a minor decrease in radiation related cancer incidence, therefore it cannot justify the additional costs of the NGCCT scan.”</p> <p>We propose two amendments with regards to this statement.</p> <p>a) While the above comment may be OK for</p>	

				<p>adults, NGCCT could be useful in challenging sub-groups with this disease, for example infant and pediatric population where it is extremely helpful to have speed and coverage (to deal with high cardiac motion) *and* new and available iterative reconstruction techniques to reduce radiation dose since the imaging clinician may want to verify the origin of the coronary arteries.</p> <p>OR</p> <p>b) It could be considered unnecessary since only 9 in 1000 people (0.9%) are born with a congenital heart defect (reference [1] listed below) – this may form a small portion of the patients who go in for CCTA scans.</p> <p>[1] "<i>Congenital Heart Defects in Children Fact Sheet</i>". American Heart. http://www.americanheart.org.</p>	
6	1			<p>Clinical evidence / cost effectiveness</p> <p>My interpretation of the evidence presented – and other evidence on new generation cardiac imaging technologies that I have independently sourced – is that whilst there does seem to be reasonable evidence of the improved incremental performance of the new generation cardiac CT technologies (over imaging and other diagnostic technologies that are currently in use) the evidence that this changes management decisions and improves outcomes is far sparser. Evidence on technical performance might well be good in theory; evidence of real world performance is also required. For existing technologies evidence of real world performance seems to be drawn from largely level III studies, often with poor recording of data on outcomes and short follow up. Good evidence of improved</p>	

			<p>incremental sensitivity and specificity is not in itself a compelling reason to introduce a new technology – there also needs to be persuasive evidence that such improvements are borne out in real world clinical settings, they lead to improved outcomes, are worth it (cost effective) within acceptable thresholds and are affordable. My read of the NIHR report leads me to conclude that new generation cardiac CT would fail these latter tests.</p> <p>Other evidence leads in the same direction. The 2009 HTA from the Institute of Clinical and Economic Review at the Massachusetts General Hospital suggests that there is no robust evidence to suggest that dual source 128-slice/256-slice CT scanners offer any advantage over dual source 64-slice CT scanners in cardiac imaging.</p> <p>More importantly the evidence that investment in such technologies, considering the likely significant capital investment, would be a cost effective use of scarce NHS resources (at a time when services are under extreme financial pressure) is sparse in the extreme. The evidence presented in the HTA review was a far from compelling clinical or economic case (Health Technol Assess 2008;12(17):1–164). Use of 64 slice cardiac CT was recommended in NICE CG 95 (2010). This CG highlights problems with the technique, notably the ‘poor correlation with coronary angiography in calcified vessels, the poor correlation for quantifying stenosis severity when > 50% and in vessels <2mm, no functional assessment of myocardial ischaemia’. NICE also highlights to possibility of publication bias so that using CTA in low to</p>	
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			<p>intermediate risk patients may affect the test performance ‘the diagnostic performance of the test requires evaluation in unselected populations’. It should be noted that NICE guidance on the management of stable angina is due in July 2011. NICE CG 95 also recommends that work comparing the cost effectiveness of CT angiography versus stress testing is still required. For these reasons, many NHS commissioners are of the view that NICE need to look far more critically at the dual source 64-slice CT scanner before considering newer technologies.</p> <p>More specifically on the Somatom Definition Flash, Aquilion One, Brilliance iCT and Discovery CT750 HD report that was circulated, we consider that a great deal of faith is being placed in the evidence of clinical and cost effectiveness with respect to the “difficult to image” groups. The economic evidence presented, and the point estimates of ICERS do not appear to support the conclusions that the NIHR report comes to, we find this odd and would wish to study this in great detail.</p> <p>There might well be sub groups in which new imaging techniques have a place, NHS commissioners would wish these to be exceptionally tightly defined – and closely monitored through an agreed contract. Such a contract would need to very carefully estimate the likely numbers of patients in whom new imaging techniques should be used.</p>	
6	2		<p>Economics and affordability</p> <p>It is of note that there is relatively little (if any) mention of affordability of introduction of new technologies to commissioners, we feel this should be</p>	

			<p>considered very prominently in the deliberations of NICE. The NHS budget is fixed, and introduction of new technologies will necessitate consideration of whether they will be inflationary – using a commissioner perspective. Belgian data cited by CADTH note significant costs of installing CT angiography capability in a hospital (ranging from initial investment of €850k-2million, and additional software costs). American estimates are of \$700-1000 per angiogram. Caveats remain that positive CT angiograms will then require invasive angiography (references can be supplied if needed).</p> <p>Consideration of the different perspectives on affordability and economics between providers and commissioners is warranted. Given the likely capital costs of investment in new generation scanners, it seems likely there will be an inbuilt pressure and economic incentive on providers to scan as many as possible, thereby recouping the cost of capital investment. NHS commissioners will not accept that strategy.</p> <p>NHS Bradford and Airedale would wish to make exceptionally clear, on behalf of all NHS Commissioners that were NICE to make a positive recommendation for new generation cardiac imaging this should not be seen as representing a commissioning intention to fund such technologies.</p> <p>We would strongly urge providers who might be wishing to introduce such technologies following any NICE recommendation to hold discussions with their commissioners at the earliest opportunity. The pot of</p>	
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				<p>funding available to commissioners is fixed, in 2009 10 the NHS in England spent £2.11bn on CHD (Programme Budget data), £22m in Bradford and Airedale. Prior to any push to introduce new generation cardiac CT, NHS Commissioners would certainly require a detailed analysis of the estimated costs of introduction within the context of existing pathways of care, including recommended reductions in services elsewhere in the same pathway. It seems inevitable that were providers seeking to introduce such technologies they would seek assurances that other services will be stopped to ensure the CHD budget remain neutral overall.</p>	
6	3			<p>Summary In summary, NHS Commissioners do not see a compelling case to appraise new generation cardiac CT. Moreover were NICE to make a positive recommendation for the introduction of such technologies, unless the evidence was exceptionally compelling they would not be seen as a high priority investment for the NHS. There seems reasonable evidence of improved technical performance of new generation cardiac CT. There seems, on the face of it, far less evidence that this improved technical performance translates to real world improved outcomes, nor is it a cost effective or affordable development.</p>	

Ends.