National Institute for Health and Clinical Excellence

NATIONAL INSTITUTE FOR HEALTH AND CLINCIAL EXCELLENCE

Diagnostics Assessment Programme

Computed tomography (CT) scanners for cardiac imaging – Somatom Definition Flash, Aquilion One, Brilliance iCT and Discovery CT750 HD

Final scope

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1 Introduction

The Medical Technologies Advisory Committee identified the Somatom Definition Flash computed tomography (CT) scanner as potentially suitable for evaluation by the Diagnostics Assessment Programme (DAP) on the basis of a briefing note. The Somatom Definition Flash CT scanner is manufactured by Siemens AG, Healthcare. Scoping research carried out by the DAP team identified three other CT scanners for potential inclusion in the evaluation: Aquilion One (Toshiba Medical Systems), Brilliance iCT (Philips Healthcare) and Discovery CT750 HD (GE Healthcare). Attendees at the scoping workshop held on the 13th December 2010 supported the inclusion of these technologies in the evaluation. The scope outlines the approach for assessing the clinical and cost effectiveness of these four CT scanners for use in cardiac imaging. For the purpose of this document the four CT scanners are described as high definition CT scanners.

2 Description of the technologies

Although the high definition CT scanners identified can be used for all routine diagnostic imaging procedures (for example, orthopaedic, oncology, neurology, gastrointestinal, vascular and interventional), they have specialised functionality for cardiac patients, severely traumatised or unconscious patients, paediatric patients and patients for whom a breath hold is difficult.

The high definition CT scanners described below have advanced technical features which address the drawbacks, including spatial resolution, low contrast detection, noise and artefacts, plus high levels of radiation, that are associated with conventional 64-slice CT scanners.

The sections below describe the properties of the high definition CT scanners based on information provided to NICE from the manufacturers and on information available in the public domain. NICE has not carried out an independent evaluation of these descriptions.

2.1 Somatom Definition Flash

The Somatom Definition Flash is a second generation dual source 128-slice CT scanner designed to provide high resolution images at a fast scanning speed with low dose radiation. The scanner has two X-ray tubes and two detector arrays mounted at 95° to each other. There are 64 x 0.6 mm detector rows giving a total z-axis coverage of 38.4 mm per rotation. Each detector row is double sampled to give 128 data channels.

The gantry opening measures 78 cm and the table has a maximum load of 220 kg as standard, with an option to increase maximum load to 300 kg. The maximum scan field is 50 cm, with an option to increase the scan field to 78 cm. The gantry has a rotation time of 0.28 seconds which, combined with the fast table feed, results in a maximum scan speed of 458 mm/s.

The use of two source-detector assemblies facilitates dual energy scanning by operating the two tubes at different peak kilovoltages. The dual energy data are acquired at the same time which enables a temporal resolution of 75 ms and allows scanning in a high pitch helical ‘Flash’ mode.

The Somatom Definition Flash employs a selective photon shield which filters the high kilovoltage X-rays to improve material separation and substantially reduce radiation dose. In addition, Iterative Reconstruction in Image Space (IRIS) is used to reconstruct an image from raw data, which allows a further reduction in radiation dose to the patient while maintaining image quality, or improved image quality from full dose imaging.

Using the Flash mode, which is recommended for heart rates up to 65 beats per minute (bpm), data projections of the entire heart can be captured in approximately 250 ms with a radiation dose of less than 1 mSv. For heart rates above 65 bpm, different scan modes are recommended which result in slightly higher acquisition times and radiation doses. These scan modes provide the option of scanning patients with high heart rates without the need to use beta blockers to regulate the heart rate.

2.2 Aquilion One

The Toshiba Aquilion One is a 640-slice CT scanner with 320 x 0.5 mm detector rows giving z-axis coverage of 160 mm. This specification allows the imaging of whole organs in a single non-helical rotation, for example an image of the heart can be captured within a single heart beat. In addition to reducing the exam time, the radiation and the contrast dose are also reduced. In helical scanning mode the z-axis coverage is 80 mm from 160 x 0.5 mm detector rows.

Advanced features include:

- Adaptive Iterative Dose Reduction: rapidly produces diagnostic images with low noise levels and minimal operator input.
- Automated parameter selection to ensure consistent image quality for all patients, regardless of size.
- PhaseXact: automatically selects the cardiac phase that displays the least amount of motion to improve temporal accuracy and reduce review time.
- ConeXact volume reconstruction: removes artefacts related to the wide cone angle to produce high quality images.
- Automatic arrhythmia rejection software: terminates radiation exposure if abnormal heart beat is detected and acquires the next normal beat for image reconstruction.
- Adaptive multisegment reconstruction: improves temporal resolution in patients with high or variable heart rates.

It is also claimed that the Aquilion One can perform cardiac functional analysis and anatomical analysis in one scan, reducing the need to perform multiple examinations using different modalities.

2.3 Brilliance iCT

The Philips Brilliance iCT is a new generation 256-slice multi detector CT scanner. It has 128 x 0.625 mm detector rows providing a total z-axis coverage of 80 mm per rotation. Each detector row is double sampled which increases spatial resolution. In cardiac step and shoot mode the Brilliance iCT can capture an image of the heart in two heart beats. It has a gantry rotation time of 0.27 seconds, a gantry aperture of 70 cm, a maximum table load of 204 kg (with an option to increase to maximum load to 295 kg) and a 50 cm scan field.

The Brilliance iCT has several features to manage radiation dose. It uses filters to reduce dose through absorption of unwanted X-rays and to provide a uniform dose delivery across the scan field. It uses automatic current selection to optimise the dose for each patient based on the planned scan and also to increase or decrease the signal over different areas of the scan. It has a collimator that lowers patient exposure during helical scanning by removing radiation at the beginning and end which would not contribute to image formation.

Additional benefits of the Brilliance iCT scanner are:

- A powerful X-ray tube: for improved durability, image quality and spatial resolution, particularly in patients with high BMIs.
- 120 kW generator: provides instantaneous power to maximise the image quality of short scans.
- Innovative NanoPanel detectors: reduce electronic noise, enabling fast, low-dose scans with high spatial resolution (up to 24 lp/cm) which gives better definition of small structures.
- iDose iterative reconstruction technique: uses advanced reconstruction algorithms to enable diagnostic images at low dose without the problems noise and image artefacts. The faster reconstruction of data means higher throughput and less waiting for large volume datasets.

It is claimed that when using low dose Step and Shoot imaging, patients with heart rates of up to 75 bpm can be imaged successfully.

2.4 Discovery CT750 HD

The Discovery CT750 HD from GE Healthcare is a 2 x 64-slice dual energy CT scanner. There is a 40 mm wide detector array with 64 rows of 0.625 mm elements. The Discovery CT750 HD has a gantry aperture of 70 cm, a gantry tilt of ±30° 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 maximum scan field is 50 cm.

The Discovery CT750 HD has advanced features which give a spatial resolution of 0.23 mm. It has a Gemstone™ detector which 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 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. It also gives a cardiac temporal resolution of 0.44 ms.

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.

An Adaptive Statistical Iterative Reconstruction algorithm is used to enhance low contrast detection at a reduced level of radiation and to give a reduction in image noise. Other features to reduce radiation dose are:

- 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 Description of the comparators

3.1 Invasive coronary angiography

Coronary angiography (CA), or cardiac catheterisation, is an invasive anatomical imaging technique which uses a contrast dye and X-rays to provide anatomical information about the degree of stenosis in the coronary arteries. A catheter is generally inserted into an artery in the groin and is moved up the aorta and into the coronary arteries. Once in place, the dye is injected through the catheter, and a rapid series of X-ray images are taken to show how the dye moves through the branches of the coronary arteries. Any narrowing of the arteries will show up on the X-ray images. In babies and children a general anaesthetic would be required to perform the procedure.

Invasive CA is considered the 'gold standard' for providing anatomical information and defining the site and severity of coronary artery lesions despite the significant inter and intra reader variation in interpretation. However, there are serious complications associated with the technique, including death, non fatal myocardial infarction and stroke. In addition, it only provides a 2D image as oppose to the 3D image produced by other imaging techniques.

3.2 Conventional 64-slice CT scanners

Multi-slice CT scanners combine the use of X-rays with computerised analysis of series of 2D X-ray images to create 3D images. The technology has been rapidly advancing, with 4-slice CT scanners first appearing in 1998, 16-slice scanners in 2001 and 64-slice scanners at the end of 2004. Multi-slice CTCA is a minimally-invasive investigation which uses a contrast dye injected through a cannula in the forearm and provides anatomical information about the degree of stenosis in the coronary arteries. Cardiac CT has particular challenges due to the continuous motion of the heart.

4 Target indications

This topic was selected by the NICE Medical Technologies Advisory Committee and routed to the Diagnostics Assessment Programme for evaluation for use in cardiac imaging. Within the field of cardiac imaging however, there are several potential indications which may benefit from the use of high definition CT scanners.

Discussions at the scoping workshop resulted in the focusing of the evaluation on people with suspected or known coronary artery disease (CAD) who are difficult to image and on children and adults with congenital heart disease.

In addition to these target indications, there is a potential benefit for anyone undergoing a CT scan in that high definition CT scanners are associated with reduced levels of radiation exposure compared to conventional 64-slice CT scanners. As radiation exposure is linked to an increase risk of cancer in later life, the benefit of lower radiation exposure in the general population is fewer cases of cancer in the future.

4.1 Detection of coronary artery stenosis in people with suspected or known CAD

CAD is a major cause of cardiovascular disability and death in the UK. It is caused by narrowing of the coronary arteries, most commonly by atherosclerotic deposits of fibrous and fatty tissue, leading to a reduction in the flow of blood to the heart. The primary symptom is angina, but CAD may also cause myocardial infarction. For the purpose of this document, patients with suspected CAD will be defined as those who have chest pain or have other symptoms suggestive of CAD.

The NICE clinical guideline CG95 (Chest pain of recent onset) defines significant CAD as ≥ 70% diameter stenosis of at least one major epicardial artery segment or ≥ 50% diameter stenosis in the left main coronary artery.

Some factors intensify ischaemia and allow less severe lesions (for example ≥ 50% diameter stenosis of one major epicardial artery segment) to produce angina, for example, reduced oxygen delivery, increased oxygen demand, large mass of ischaemic myocardium, or longer lesion length. Similarly, some factors reduce ischaemia and may render lesions (≥ 70% diameter stenosis of one major epicardial artery segment) asymptomatic, for example a well developed collateral supply or small mass of ischaemic myocardium.

CA or CT coronary angiography (CTCA) is used to assess the state of the arteries and to identify significant narrowing (stenosis) as recommended by NICE clinical guideline CG95. The guideline recommends use of a 64-slice (or above) CT scanner. For most patients there will be little benefit associated with the use of a high definition CT scanner over the use of a conventional 64-slice CT scanner. However CTCA using high definition CT scanners may be particularly beneficial in difficult to image patients, for example, those who cannot hold their breath, have an irregular or fast heartbeat, are obese, have high levels of coronary calcium or have a stent. In these patients image quality using a conventional 64-slice CT scanner is often decreased or is imaging using a conventional 64-slice CT scanner not recommended.

4.2 Detection of congenital heart disease and coronary artery anomalies

High definition CT scanners may also be used in children and adults with complex congenital heart disease for refining a diagnosis and for deciding upon the best operational approach. Congenital heart disease is a general term which describes birth defects that affect the heart. There are over 30 different types of heart defect, the most common being ventricular or atrial septal defects, pulmonary or aortic stenosis, patent ductus ateriosus, tetralogy of Fallot, and transposition of the great arteries. More complex conditions include vascular ring and vascular issues peripheral to the heart. The incidence rate for congenital heart disease in the UK is estimated to be one in every 145 babies born and approximately 85% of children born with congenital heart disease respond well to treatment and will survive into adulthood.

Congenital coronary artery abnormalities are rare conditions occurring in less than 1% of the UK population and are often found in association with other congenital heart defects. These complications may also occur as a consequence of Kawasaki disease. Coronary artery anomalies in the absence of additional heart defects are often the cause of sudden death in young adults, particularly in athletes.

For patients with uncomplicated congenital heart diseases, CT imaging is not required as enough information can be collected from echocardiography. For patients with complex congenital heart disease and/or coronary artery abnormalities CT imaging may be beneficial.

4.3 Care pathways

4.3.1 Coronary artery disease

Diagnosis

NICE clinical guideline CG95 (Chest pain of recent onset) details the care pathway recommended to make a diagnosis of stable angina in people with chest pain. The guideline describes that a diagnosis of significant CAD can be made using anatomical imaging and a diagnosis of reversible myocardial ischaemia can be made using functional imaging. Both significant CAD and reversible myocardial ischaemia are treated as a diagnosis of stable angina.

People with chest pain who have an estimated likelihood of CAD of 10-29% should be offered calcium scoring followed by CTCA if the calcium score is 1-400, and invasive CA if the calcium score is greater than 400 (if clinically appropriate). People with chest pain who have an estimated likelihood of CAD of 30-60% should be offered non-invasive functional imaging for myocardial ischaemia. People with chest pain who have an estimated likelihood of CAD of 61-90% should be offered invasive CA if clinically appropriate and coronary revascularisation is being considered.

If non-invasive functional imaging is offered the following should be used:

- myocardial perfusion scintigraphy with single photon emission computed tomography **or**
- stress echocardiography **or**
- first-pass contrast-enhanced magnetic resonance perfusion **or**
- magnetic resonance imaging for stress-induced wall motion abnormalities.

As the guideline on chest pain of recent onset is relatively new and technology advances have been occurring rapidly, it has been noted that the guideline on chest pain of recent onset has not been implemented in all cardiac centres across the UK.

Management with drugs

Patients diagnosed as having significant CAD should be managed as having stable angina. The management of stable angina is currently being evaluated by NICE and the draft clinical guideline has been released for stakeholder consultation (15 December 2010 to 9 February 2011). It should be noted that the provisional recommendations presented do not constitute the NICE's formal guidance on this topic. The recommendations are provisional and may change after consultation. The final clinical guideline is due for publication in July 2011.

Key provisional recommendations from the draft guideline state:

- Functional tests for myocardial ischaemia or anatomical tests for obstructive CAD to stratify risk are not routinely recommended.
- A short-acting nitrate should be offered for preventing and treating episodes of angina.
- Aspirin 75 mg daily should be considered for the secondary prevention of cardiovascular disease.
- Treatment with one or two anti-anginal drugs should be offered for the initial management of stable angina.
- First-line treatment options for stable angina are beta blockers and/or calcium channel blockers.
- For people who cannot tolerate beta-blockers or calcium channel blockers, or these drugs are contraindicated, monotherapy with a long-acting nitrate, ivabradine, nicorandil[1] or ranolazine can be considered.
- For people on beta blocker or calcium channel blocker monotherapy whose symptoms are not controlled and the other option is contraindicated or not tolerated, one of the following can be considered as an additional drug: a long-acting nitrate, ivabradine[2], nicorandil[1] or ranolazine.
- A third drug can be considered when symptoms are not controlled with two anti-anginal drugs and the person is waiting for revascularisation or it is not considered appropriate or acceptable.

The NHS Clinical Knowledge Summaries publication on the management of stable angina provides similar information. Primarily, it states that patients with a newly confirmed diagnosis of angina should be treated for symptom relief and to improve their prognosis.

For symptom relief:

- Sublingual glyceryl trinitrate should be used for the rapid relief of the symptoms of angina and before performing activities known to cause symptoms of angina.
- Beta-blockers should be prescribed as a first-line regular treatment to reduce the symptoms of stable angina.

[1] At the time of consultation (December 2010), nicorandil did not have UK marketing authorisation for use in this indication.
[2] Ivabradine should only be combined with a dihydropyridine calcium channel blocker.

- If a beta-blocker is not tolerated or is contraindicated, a calcium-channel blocker, a nitrate or nicorandil should be prescribed.

To improve prognosis:

- Low dose aspirin and a statin unless they are contraindicated or not tolerated.
- Consider for treatment with an angiotensin-converting enzyme inhibitor.

Management by revascularisation

The NICE draft clinical guideline on stable angina provisionally recommends considering revascularisation for people whose symptoms are not controlled by drug treatment. Results of any functional and/or anatomical tests performed at diagnosis should be reviewed when revascularisation is being considered. Invasive CA to guide the revascularisation strategy should be offered if not recently completed during diagnosis. Additional non-invasive or invasive functional testing may be required.

Two revascularisation strategies are available. The first strategy, coronary artery bypass grafting (CABG), involves major cardiac surgery. The second strategy, balloon angioplasty, involves non-surgical widening from within the artery using a balloon catheter. This may be performed with or without stenting and is covered by the general term percutaneous coronary intervention (PCI). NICE technology appraisal 71 (Guidance on the use of coronary artery stents) and NICE technology appraisal 152 (Drug-eluting stents for the treatment of coronary artery disease) provide recommendations on the use of stents for revascularisation in CAD.

The NICE draft clinical guideline on stable angina provisionally recommends that PCI should be considered in preference to CABG for people with single-vessel disease or multi-vessel disease, including left main stem disease, and continuing symptoms despite optimal medical treatment if the anatomy is suitable for PCI. The draft guideline also provisionally recommends that CABG should be considered for people with single-vessel disease or multi-vessel disease, including left main stem disease, and continuing symptoms despite optimal medical treatment if the anatomy is unsuitable for PCI, if the person is over 65 years and/or if they have diabetes.

NICE technology appraisal 71 recommends that for patients who are indicated for PCI, stents should be routinely used. Further, NICE technology appraisal 152 states that drug-eluting stents are only recommended for use in PCI for the treatment of CAD if:

- the target artery to be treated has less than a 3 mm calibre or the lesion is longer than 15 mm, and
- the price difference between drug-eluting stents and bare-metal stents is no more than £300.

4.3.2 Congenital heart disease and coronary artery anomalies

Diagnosis of children with congenital heart disease

No nationally accepted guidelines on the diagnosis and management of newborns, infants and children with congenital heart disease have been identified. Other sources of information such as NHS Choices and Patient UK provide limited information. They suggest that if congenital heart disease is suspected a full clinical history of the pregnancy and the mother's health should be taken prior to investigations. This should be followed by echocardiography, which is a non-invasive procedure without ionizing radiation that can provide information on the anatomy and function of the heart. Other tests such as an electrocardiogram, chest X-rays and pulse oximetry may also be used. CT imaging or magnetic resonance imaging (MRI) may be used to provide further anatomical information and to prepare for correction of the defect.

The disadvantage of using MRI is the length of time the procedure takes which requires babies and children to be under general anaesthetic, however, there is no radiation exposure which is a benefit when imaging these patients. The advantage of CT imaging is that the rapid acquisition time removes the need for general anaesthetic and the images allow the clinician to examine the lungs and airways, which is harder to do with MRI. The disadvantage of CT imaging is that it is associated with radiation exposure. Further, small children may have heart rates that are too high to benefit from the low radiation modes of scanning, for example the Flash mode on Somatom Definition.

Coronary imaging is not necessary for most types of congenital heart disease. As such, the use of invasive coronary angiography, which would require a general anaesthetic, is avoided whenever possible. It may be used in children who have tetralogy of Fallot, in which coronary anomalies also occur, and for those with inflammatory problems. Coronary imaging may also be required in children following a heart transplant.

Treatment and monitoring in children with congenital heart disease

Once congenital heart disease is diagnosed, watchful waiting, medical management, non-invasive surgery, invasive surgery or heart transplantation may be used to treat the condition depending on the type of heart anomaly identified. There are several NICE Interventional Procedure Guidelines relating to the treatment of various heart defects (see appendix C).

Diagnosis of adults with congenital heart disease

As many babies born with congenital heart disease survive into adulthood, consideration of the monitoring and care these people receive also needs to be taken into account. In addition, some defects may be diagnosed for the first time in adult life. The European Society of Cardiology (ESC) has recently updated its Guidelines on the Management of Grown-Up Congenital Heart Disease (GUCH).

For the diagnosis of suspected congenital heart disease in adults, the recommended diagnostic work-up in the ESC 2010 guideline is similar to that recommended in paediatric patients. That is, a clinical examination followed by an echocardiogram and pulse oximetry. Chest X-rays may be performed when indicated, but are not routinely recommended. Further investigation of anatomy and physiology has shifted away from invasive studies to non-invasive protocols involving cardiovascular magnetic resonance (CMR) and CT. Invasive coronary angiography is reserved for the resolution of specific anatomical and physiological questions, or for intervention.

Treatment and monitoring in adults with congenital heart disease

For adults with congenital heart disease, medical management generally focuses on prevention or control of cardiac problems, for example, heart failure, arrhythmias, hypertension, thrombo-embolic events and endocarditis. Sudden cardiac death is a particular concern. Interventional treatment may be required in people who have undergone intervention in childhood but have residual or new complications or in people with conditions not diagnosed or not considered severe enough to require surgery in childhood. Care of adults with congenital heart disease also needs to take into account several non-cardiac issues, including recommendations for exercise and sports, and issues around pregnancy, contraception and genetic counselling (ESC 2010 guideline).

Due to the range of different congenital heart defects, specific conditions require specific treatments and follow-up strategies. For example, people with an atrial septal defect successfully treated with surgery under the age of 25 years do not require regular follow-up. Patients with more complicated defects or sequelae following interventional treatment may require regular follow-up, with frequencies ranging from yearly to once every five years (ESC 2010 guideline).

5 Scope of the evaluation

5.1 Populations

Two populations have been identified in which high definition CT scanners are likely to have additional clinical benefits over conventional 64-slice CT scanners.

1. People with suspected CAD (defined as those who have chest pain or other symptoms suggestive of CAD) or known CAD (defined as those who have previously been diagnosed with CAD and whose symptoms are no longer controlled by drug treatment and/or are being considered for revascularisation) who are difficult to image. In these people a diagnosis of significant CAD is difficult or impossible to make using a conventional 64-slice scanner. These patients include, but are not limited to:

   - Obese patients
   - Patients with high levels of coronary calcium
   - Patients with arrhythmias
   - Patients with high heart rates (>70 bpm)
   - Patients intolerant of beta-blockers
   - Patients with stents
   - Patients with bypass grafts

2. Babies, children and adults with complex congenital heart defects, or babies, children and adults with congenital heart defects who are not suitable for MRI scanning or general anaesthetic, where CT imaging is used for refining a diagnosis to help decide upon the best treatment approach.

Populations that will not be considered in the assessment, but for which NICE acknowledges there may be a benefit from the use of high definition CT scanners are: patients presenting with acute chest pain to the emergency department; patients with suspected CAD who do not have features making them difficult to image; non-cardiac patients.

5.2 Interventions

The interventions for this evaluation are the Somatom Definition Flash, the Aquilion One, the Brilliance iCT and the Discovery CT750 HD, as described in sections 2.1, 2.2, 2.3 and 2.4.

5.3 Comparators

For the evaluation of suspected or known CAD in difficult or impossible to image patients the relevant comparator is invasive CA. This is also the reference standard against which the diagnostic accuracy of high definition CTCA would ideally be measured. Conventional 64-slice CT scanners will not be considered a comparator for this group of patients as they are assumed to have already had a non-diagnostic image on a conventional 64-slice CT scanner or to have been identified as impossible to image with a conventional 64-slice CT scanner.

For the evaluation of complex congenital heart disease, CT scanning is likely to be used as an add-on test following initial imaging with echocardiography and as a complementary technique to MRI. Depending on the technologies available to the consultant, CT imaging with a high definition scanner may be an add-on test to echocardiography, or may be a replacement test for CT scanning with a 64-slice CT scanner. Invasive CA would be used extremely rarely in this population. As such, the comparators for high definition CT scanners are conventional 64-slice CT scanners and no CT imaging.

5.4 Healthcare setting

Secondary and tertiary care setting.

5.5 Outcomes

5.5.1 Clinical considerations

For the evaluation of suspected or known CAD in difficult or impossible to image patients, intermediate measures from the diagnostic procedures include:

- diagnostic test accuracy (sensitivity and specificity)
- indeterminacy (test failure rate)
- radiation exposure.

Direct outcomes from the test include side effects associated with the use of contrast agents, and the risk of death, myocardial infarction and stroke related to the invasive CA procedure. Side effects from beta-blockers in patients with a high heart rate may be a relevant direct outcome as their use is not always necessary when imaging using a high definition CT scanner.

The indirect clinical outcomes as a result of being classified as true negative, true positive, false negative or false positive, may include:

- impact on medical management, for example: treatment with preventative drugs and interventions such as PCI and CABG
- long term rate of coronary heart disease events such as angina, myocardial infarction and stroke
- overall mortality
- rate of cancer due to radiation exposure.

The impact of radiation exposure may be reduced in this population as patients with known or suspected CAD tend to be older adults, however, the outcome should still be examined in order to more fully understand the benefits of the high definition CT scanners.

For the evaluation of complex congenital heart disease diagnostic test accuracy is not considered to be an outcome of interest for the assessment as initial diagnoses are made using alternative techniques. The level of radiation exposure is an important intermediate measure in this population as babies, children and young adults are more susceptible to the risks associated with radiation exposure compared to older adults. Direct outcomes may include side effects from the use of general anaesthetic in children and infants as its use is not always necessary when imaging using a high definition CT scanner, but may be necessary if using a conventional 64-slice CT scanner.

The primary indirect clinical outcome associated with CT imaging in babies, children and adults with congenital heart disease is the impact on medical management, for example, surgical planning including the length of time spent in surgery. The rate of cancer and infertility in later life due to radiation exposure is a secondary outcome to be considered, however, this patient group would likely be receiving only one CT scan rather than repeated scans for monitoring, so the impact may be reduced.

Data on these indirect outcomes should be used along with clinical utility scores to estimate QALYs as final health outcomes.

Patient relevant non-health outcomes could also be considered. These may include improved patient experience due to the faster scan. For example, breath hold is not required, claustrophobia is reduced, and there is no inconvenience resulting from the need to follow dietary rules prior to a scan. For children there would be a benefit associated with not having to hold still for an extended period of time.

5.5.2 Cost considerations

High definition CT scanners will have large non-recurrent set-up costs including purchase of equipment and room setup. Modifications to existing CT rooms may be required, for example some high definition CT scanners require additional energy sources. Further costs to be considered include:

- Maintenance of equipment
- Staff and training of staff
- Examination time
- Consumables (e.g. contrast dye, beta-blockers)
- Hospital costs associated with invasive CA
- Medical costs arising from ongoing care following test results.

6 Modelling approach

In the modelling, the included high definition scanners listed in section 2 should be analysed as a group rather than as individual technologies due to the limited data available on each.

6.1 Extant models

6.1.1 Coronary artery disease

As CAD has been studied extensively, there are several related clinical guidelines and many economic models looking at the diagnosis and treatment of the disease. In addition, there are systematic reviews available on the different diagnostic techniques and management strategies and there are studies reporting costs and clinical utility data in patients with CAD (Melsop 2003, Longworth 2005, Arnold 2010).

Diagnostic models

The guideline development group for NICE clinical guideline 95 considered a short-term model for the diagnosis of stable angina, looking at the cost per correct diagnosis for a variety of diagnostic strategies. The diagnostic accuracy and the costs for the comparators (conventional 64-slice CTCA and invasive CA) used in this model should be considered for use in the model built for this assessment.

Other published models have performed full cost-utility analyses which may be useful in designing the model for this assessment. Mowatt et al (2004) evaluated myocardial perfusion scintigraphy with single photon emission computed tomography relative to stress echocardiography and CA for the diagnosis and management of CAD. The model consisted of a decision tree model for the diagnosis decision and a Markov model for the management of patients with suspected CAD. Amemiya and Takao (2009) used a decision model to compare four strategies: (1) no examination, (2) routine coronary angiography (CAG), (3) CTCA, or (4) medication without CAG or CTCA in persons at risk for stable CAD from a US perspective.

Treatment models

The NICE technology appraisal guidance 152 (Drug-eluting stents for the treatment of coronary artery disease) included an economic evaluation of drug-eluting stents versus bare-metal stents in patients currently revasularised for angina in NHS hospitals. Data from this model could be considered for use in the model built for this assessment.

Other studies have looked more generally at treatment. Fidan et al (2007) examined the cost-effectiveness of coronary heart disease treatments in England and Wales, including aspirin, beta-blockers, cardiac rehabilitation, ACE inhibitors, statins, CABG surgery and angioplasty. Some studies have compared the different revascularisation procedures. Wang et al (2008) compared on-pump CABG, off-pump CABG, PCI with bare metal stents and PCI with drug eluting stents for the treatment of CAD in patients with stable angina form the prospective of the Canadian health care system. Further studies have limited analyses to medical treatments, for example statins (Mark et al, 2008 and Wagner et al, 2009).

6.1.2 Congenital heart disease

Several cost studies were identified which examine the costs and benefits associated with monitoring and treatment of children and adults with congenital heart disease (Price 2007, Garson 1994, Danford 1995). No useful economic evaluations on the diagnosis congenital heart disease in children or adults were identified.

6.2 Care pathway structures

For the patient population with suspected or known CAD the diagnostic pathway in the model should be based around that presented in CG95. Variations to this pathway which could potentially be investigated are that patients do not receive coronary calcium scoring prior to anatomical testing, and that the availability of a high definition CT scanner may lead to more people having CTCA rather than undergoing an invasive CA. The care pathway for patient management following diagnosis will need to be pulled from several sources, including NICE guidelines and expert clinical opinion.

For the patient population with congenital heart disease it is suggested the care pathway could be based around the information discussed in section 4.3.2, supported by expert opinion.

6.3 Model structure

As no end-to-end studies have been identified during the scoping phase, it is likely that a linked evidence approach will need to be used in the modelling. That is, intermediate measures and direct outcomes of the diagnostic strategies to be assessed will need to be related to changes in final heath outcomes.

6.4 Time horizon

CAD is a condition which once diagnosed needs to continue to be managed over a patient's lifetime. Patients tend to be diagnosed with CAD in their early 60s or later, but patients with a family history may develop the disease earlier. As such, a lifetime time horizon is appropriate.

Congenital heart disease tends to be diagnosed early in childhood, but some people may be diagnosed in early adulthood. The management of congenital heart disease varies depending on the severity of the defect, but monitoring of the condition may continue over a lifetime.

7 Equality issues

It has been noted that the data used to validate the coronary calcium scoring method was collected from a Caucasian population. Caution should be taken when making treatment decisions based on calcium scoring in a non-Caucasian patient. No other evidence has been found to indicate variation in effectiveness according to age, gender, class or ethnicity.

8 Implementation issues

There are non-recurrent set-up costs associated with high definition CT scanners, including the acquisition cost of the equipment plus any modification to existing CT rooms. In addition, hospitals need to be sure that IT systems can handle the increased amount of data generated from high definition CT scanners as compared to lower slice CT scanners. These issues will need to be fully understood in relation to an optimised implementation strategy.

Appendix A Glossary of terms

Acute chest pain	Chest pain / discomfort which has occurred recently and may still be present, is of suspected cardiac origin and which may be due to acute myocardial infarction or unstable angina.
Coronary angiography	An invasive diagnostic test which provides anatomical information about the degree of stenosis (narrowing) in a coronary artery. It involves manipulation of cardiac catheters from an artery in the arm or top of the leg. A contrast medium is injected into the coronary arteries, and the flow of contrast in the artery is monitored by taking a rapid series of X-rays. It is considered the 'gold standard' for providing anatomical information and defining the site and severity of coronary artery lesions.
Coronary artery	An artery which supplies the myocardium.
Coronary artery disease	A condition in which atheromatous plaque builds up inside the coronary artery leading to narrowing of the arteries which may be sufficient to restrict blood flow and cause myocardial ischaemia.
Calcium scoring	A technique by which the extent of calcification in the coronary arteries is measured and scored.
Gantry	Found in CT machines, a gantry rotates around a patient for cross-sectional views.
Material separation	The contrast resolution of the image between the iodine agent and the soft tissues. Improved material separation enables a lower dose of contrast agent to be used.
Multi-slice CT coronary angiography	A non-invasive investigation which provides coronary calcium scoring and anatomical information about the degree of stenosis (narrowing) in the coronary arteries. The scanner has a special X-ray tube and rotation speed and as the technology has advanced the number of slices in each rotation has increased. A dual source scanner has two pairs of X-ray sources and multi-slice detectors mounted at 90 degrees to each other.
Myocardial perfusion scintigraphy with SPECT	Myocardial perfusion scintigraphy involves injecting small amounts of radioactive tracer to evaluate perfusion of the myocardium via the coronary arteries at stress and at rest. The distribution of the radioactive tracer is imaged using a gamma camera. In SPECT the camera rotates round the patient and the raw data processed to obtain tomographic images of the myocardium. Cardiovascular stress may be induced by either pharmacological agents or exercise.
Patent ductus ateriosus	A duct or passage in the heart that is meant to close shortly after birth. In cases of PDA, the duct fails to completely close, which means that some oxygen-rich blood leaks through the duct, into the pulmonary valve and into the lungs.
Septal defects (atrial or	A group of common congenital anomalies consisting of a hole in the septum (the wall) between the chambers of the heart. The hole may

ventricular)	be between the left and right atria or the left and right ventricles. The result is that the blood can't circulate as it should and the heart has to compensate by working harder.
Stenosis	A narrowing of the arteries leading to a reduction in blood flow. May be due to the build up of atherosclerotic deposits of fibrous and fatty tissue or may be a congenital defect.
Stable angina	There are no case definitions of stable angina that have been agreed internationally. Working definition angina is a symptom of myocardial ischaemia that is recognised clinically by its character, its location and its relation to provocative stimuli. Angina is usually caused by obstructive coronary artery disease that is sufficiently severe to restrict oxygen delivery to the cardiac myocytes. Generally speaking angiographic luminal obstruction estimated at ≥70% is regarded as 'severe' and likely to be a cause of angina, but this will depend on other factors
Stress echocardiograph	An ultrasound examination of the heart. Exercise or pharmacological stress may be used to look for reversible systolic regional wall motion abnormalities consistent with the development of myocardial ischaemia.
Stress magnetic resonance imaging (stress MRI)	MRI is a diagnostic procedure that uses radio waves in a strong magnetic field. The pattern of electromagnetic energy released is detected and analysed by a computer to generate detailed images of the heart. Stress MRI is a specific application in which a contrast agent is used to detect myocardial blood flow at stress and at rest. Pharmacological stress is used to induce cardiovascular stress.
Tetralogy of Fallot	A complex congenital heart defect condition comprising of: a ventricular septal defect; pulmonary obstruction; a displaced aorta; an enlarged right ventricle.
Transposition of great arteries	A congenital heart defect in which the aorta and pulmonary artery are transposed so that the aorta arises from the right ventricle and the pulmonary artery arises from the left ventricle. This leads to oxygen-low blood being pumped around the body.
Unstable angina	New onset chest pain / discomfort, or abrupt deterioration in previously stable angina, with chest pain / discomfort occurring frequently and with little or no exertion, and often with prolonged episodes. This often presents in the same way as myocardial infarction but without biomarker evidence of myocardial necrosis.
z-axis	The direction that the scanning table travels in (i.e. head to toe).

Appendix B Abbreviations

BMI	Body mass index
bpm	Beats per minute
CMR	Cardiovascular magnetic resonance
CA	Coronary angiography
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CG	Clinical guideline
CT	Computed tomography
CTCA	Computed tomography coronary angiography
DAP	Diagnostics Assessment Programme
ECG	Electrocardiogram
kW	Kilowatts
MR	Magnetic resonance
ms	Milliseconds
mSv	Millisieverts
NICE	National Institute of Health and Clinical Excellence
PCI	Percutaneous coronary intervention
SPECT	Single photon emission computed tomography
TA	Technology appraisal

Appendix C Related NICE guidance

Chest pain of recent onset. NICE clinical guideline 95 (2010). Available from www.guidance.nice.org.uk/CG95

Unstable angina and NSTEMI. NICE clinical guideline 94 (2010). Available from www.guidance.nice.org.uk/CG94

Stable angina: NICE draft clinical guideline for consulatation.

Guidance on the use of coronary artery stents. NICE technology appraisal guidance 71 (2003). Available from www.guidance.nice.org.uk/TA71

Drug eluting stents for the treatment of coronary artery disease. NICE technology appraisal guidance 152 (2008). Available from www.guidance.nice.org.uk/TA152

SeQuent Please balloon catheter for in-stent coronary restenosis. NICE medical technologies guidance 1 (2010). Available from www.guidance.nice.org.uk/MTG1

Off-pump coronary artery bypass grafting. NICE interventional procedure guidance 35 (2004). Available from www.nice.org.uk/guidance/IPG35 (currently being updated with an expected publication in January 2011)

Balloon dilatation of pulmonary valve stenosis. NICE interventional procedures guidance 67 (2004). Available from www.guidance.nice.org.uk/IPG67

Balloon angioplasty with or without stenting for coarctation or recoarctation of aorta in adults and children. NICE interventional procedures guidance 74 (2004). Available from www.guidance.nice.org.uk/IPG74

Balloon dilatation with or without stenting for pulmonary artery or non-valvar right ventricular outflow tract obstruction in children. NICE interventional procedures guidance 76 (2004). Available from www.guidance.nice.org.uk/IPG76

Balloon dilatation of systemic to pulmonary arterial shunts in children. NICE interventional procedures guidance 77 (2004). Available from www.guidance.nice.org.uk/IPG77

Balloon valvuloplasty for aortic valve stenosis in adults and children. NICE interventional procedures guidance 78 (2004). Available from www.guidance.nice.org.uk/IPG78

Endovascular atrial septostomy. NICE interventional procedure guidance 86 (2004). Available from www.guidance.nice.org.uk/IPG86

Radiofrequency valvotomy for pulmonary atresia. NICE interventional procedure guidance 95 (2004). Available from www.guidance.nice.org.uk/IPG95

Endovascular closure of atril septal defect. NICE interventional procedure guidance 96 (2004). Available from www.guidance.nice.org.uk/IPG96

Endovascular closure of patent ductus arteriosus. NICE interventional procedure guidance 97. Available from www.guidance.nice.org.uk/IPG97

Intraoperative fluorescence angiography in coronary artery bypass grafting. NICE interventional procedure guidance 98 (2004). Available from www.nice.org.uk/guidance/IPG98

Percutaneous pulmonary valve implantation for right ventricular outflow tract dysfunction. NICE interventional procedure guidance 237 (2007). Available from www.guidance.nice.org.uk/IPG237

Hybrid procedure for interim management of hypoplastic left heart syndrome in neonates. NICE interventional procedures guidance 246 (2007). Available from www.guidance.nice.org.uk/IPG246

Percutaneous laser revascularisation for refractory angina pectoris. NICE interventional procedures guidance 302 (2009). Available from www.nice.org.uk/guidance/IPG302

Transmyocardial laser revascularisation for refractory angina pectoris. NICE interventional procedures guidance 301 (2009). Available from www.nice.org.uk/guidance/IPG301

Transcatheter endovascular closure of perimembranous ventricular septal defect. NICE interventional procedure guidance 336 (2010). Available from www.guidance.nice.org.uk/IPG336

Endoscopic saphenous vein harvest for coronary artery bypass grafting. NICE interventional procedures guidance 343 (2010). Available from www.guidance.nice.org.uk/IPG343

Appendix D References

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