Department of Health

Justification of Computed Tomography (CT) for Individual Health Assessment

Expert Working Party Report

July 2014

Title: Justification of Computed Tomography (CT) for Individual Health Assessment
Author: Directorate/ Division/ Branch acronym / cost centre Public health/Health Protection/Environmental Hazards
Document Purpose: Independent Report
Publication date: June 2014
Target audience: Members of the public CT scanning providers Health Enforcement Authorities
Contact details: Ian Chell, Policy Manager, Health Protection, Department of Health, 79 Whitehall, London SW1A 2NS Ian.chell@dh.gsi.gov.uk

Published to gov.uk, in PDF format only.

www.gov.uk/dh

Justification of Computed Tomography (CT) for Individual Health Assessment

Expert Working Party Report

Prepared by
Dr Giles Maskell, Royal College of Radiologists (Chair)
Dr David Baldwin, Royal College of Physicians
Mr Steve Ebdon-Jackson, Public Health England
Dr Chris Gibson, Medical Physicist
Prof Fergus Gleeson, Royal College of Radiologists
Dr Steve Hughes, Royal College of Physicians
Dr John Reid, Royal College of Radiologists
Dr Nick Summerton, Royal College of General Practitioners
Prof Stuart Taylor, Royal College of Radiologists
Mrs Helen Warner, lay member
Dr Mark Westwood, Royal College of Physicians

Contents

Contents 4
Executive summary 5
Chapter 1 - Justification of Individual Health Assessment using Computed Tomography 6
Chapter 2 - CT Scanning For Lung Cancer Detection 10
Chapter 3 - CT Scanning For Colorectal Cancer & Polyp Detection 20
Chapter 4 - CT in Coronary Heart Disease 31
Summary of Recommendations 39
Membership 41

Executive summary

Purpose

The working party was commissioned by the Department of Health (DH) to assess the latest available body of scientific evidence on certain indications for CT scanning.

Working Party constitution

The expert working party members who drafted this report were recruited by the Royal College of Radiologists and the Royal College of Physicians.

Terms of Reference

The Group will produce a report:-

Which considers the recommendations contained in the COMARE 12th report and the evidence on which they were based.

Which considers any new evidence which has arisen since publication of the COMARE report, specifically in the use of CT scanning for lung disease, colonic disease and coronary heart disease in asymptomatic individuals.

Which advises on those circumstances in which CT scanning for Individual Health Assessment (IHA) may be justified on currently available evidence

Which will alert DH to areas in which the evidence base is uncertain or incomplete and in which any recommendations are likely to require early review.

Chapter 1 - Justification of Individual Health Assessment using Computed Tomography

1.1 Background

The traditional model for healthcare of individuals focuses on patients who present to a medical practitioner with recognised symptoms. This may prompt a range of diagnostic investigations to confirm the existence or the extent of a condition and these will help to determine a treatment pathway for the individual. This model can be extended to include asymptomatic individuals in certain populations, where apparently healthy people may be investigated, on the basis of a high likelihood of disease. In such cases, diagnostic investigations may also be appropriate. Such approaches are particularly helpful when early detection of disease can result in more successful treatment and improved outcomes. In both cases, radiological procedures using ionising radiation may be performed.

For asymptomatic individuals, the diagnostic test may demonstrate findings associated with the development of a disease, or the disease itself. Investigation of such individuals falls into two categories:

1. Screening as part of a programme
2. Individual health assessment

1.1.1 Screening as part of a programme

Where screening is performed as part of a programme, a national or regional body will have assessed the potential benefits of the programme for the population as a whole and compared these with any detriments and costs. Detriments associated with diagnostic interventions may include stress, morbidity and mortality, whether in the short or long term. For diagnostic investigations using imaging with ionising radiation, the main detriments will be an increased probability of cancer associated with exposure to ionising radiation and any morbidity or mortality associated with follow-up procedures, whether or not the presence of an abnormality is confirmed and whether or not this relates to the condition for which the test was primarily performed.

Before any screening programme is approved, there needs to be a strong evidence base for the net positive effect of the programme and processes put in place to ensure that sufficient quality is assured and maintained and that

information from the programme is included in any subsequent care pathway for the detected disease, for the population and for the individual.

The first established screening programme using ionising radiation was developed for the early detection of tuberculosis. Currently, the most widely used screening programmes involving the use of ionising radiation are those established for breast cancer.

1.1.2 Individual Health Assessment

In recent years, investigations for asymptomatic individuals have been made available to those who may consider they are at risk of a disease. To differentiate these from screening programmes, this practice has been termed ***individual health assessment (IHA)***. Although the principles of early detection and more successful outcome remain the driver behind such investigations, the fact that they are targeted at individuals rather than populations, and performed in independent institutions, has meant that the evidence base, quality assurance, arrangements for information transfer into established care pathways and assessment regarding the net benefit have not been conducted to the same standard as is applied to screening programmes.

As a consequence, in 2007, the Committee on Medical Aspects of Radiation in the Environment (COMARE) published its 12th report and made a number of recommendations regarding the justification of Computed Tomography (CT) procedures undertaken as part of individual health assessment. In addition, the Department of Health has reviewed the legal basis for such practices and asked the Royal College of Radiologists and the Royal College of Physicians to review the current evidence for individual health assessment. Abroad, the recently introduced International Basic Safety Standard Directive and the Euratom Basic Safety Standard Directive to addresses individual health assessment, with almost identical requirements and in 2012, the Heads of the European Radiological protection Competent Authorities (HERCA) Medical Applications Working Group on Medical Applications published a position paper on screening and individual health assessment.

1.2 Legislative Background

Published in 1997, Council Directive 97/43/Euratom provides the basic framework for the protection of individuals against the dangers of ionising radiation in relation to medical exposures. In Great Britain this was implemented largely by the Ionising Radiation (Medical Exposure) Regulations 2000 (IR(ME)R 2000) which includes within its scope the exposure of patients as part of their own medical diagnosis or treatment AND the exposure of individuals as part of health screening programmes.

1.2.1 Because individual health assessment using ionising radiation, and in particular CT, was not undertaken in 2000, the Regulations did not specifically address this practice, but in subsequent years, officials at the Department of Health were of the view that individual health assessment constituted a form of "early diagnosis" and that IR(ME)R 2000 applied. In its 12th Report, COMARE shared this view, but in 2011, the Department of Health removed any doubt by amending IR(ME)R 2000 and explicitly included individual health assessment within the scope of the Regulations.

1.2.2 IR(ME)R 2000 includes a number of requirements but prominent are the key radiation protection principles of justification and optimisation. For individual health assessment, optimisation of imaging should be no more complex than it is for procedures undertaken for diagnostic purposes, as long as the procedure is limited to specific suspected pathology in a restricted area of the body. Where the procedure is less closely defined, and is being used as a trawl for a range of possible diagnoses, optimisation will be more difficult. The Ionising Radiations Regulations 1999 address quality assurance and control of equipment.

Justification is also more difficult because the benefit for asymptomatic individuals may be significantly less than for patients, due to the limited evidence base to support the investigation and the potential increased detriment from false positive results which would require further investigation. The benefit v detriment balance is different for a patient with symptoms compared to an asymptomatic individual.

1.2.3 The importance of the transfer of data from individual health assessments into the healthcare record and subsequent influence of the care pathway has already been highlighted, but there may be legal considerations to this as well as ones relating to good medical practice. Under IR(ME)R 2000, a medical exposure can only be carried out if justified, with appropriate weight given to the total potential diagnostic (or therapeutic) benefits to the individual. This may have implications for CT examinations undertaken as part of individual health assessment, where currently there is no identified mechanism to transfer findings into the health record of the patient.

1.3 Further considerations

While legal considerations must underpin the use of CT in individual health assessment, a range of additional factors, which might be considered as ethical, scientific, logistical, psychological and financial, should be taken into account including:

a. The extent of provision of information for potential clients before appointments are made, including the significant likelihood of false positive findings where the probability of disease is low

b. The detail provided on possible findings (whether clinically significant or not), potential risks, possible further investigations and where and how these would be conducted,
c. The support provided to individuals when results of scans are positive or indeterminate,
d. The impact or otherwise of negative findings on those who have unhealthy lifestyles,
e. The logistical arrangements for transfer of data into the individual's healthcare record,
f. The mechanisms in place to develop an evidence base for justification of CT examinations for asymptomatic individuals with varying risk factors,
g. The relationship between the healthcare professional acting as referrer for the procedure and the practitioner justifying that the scan should be undertaken.

Some of these factors will need to be addressed by the organisations providing individual health assessments, others will be for those providing and funding the established healthcare system within the UK. The impact of these services on NHS resources should not be underestimated.

This report confines itself to a review of the current evidence base for imaging with CT of asymptomatic individuals as part of individual health assessment.

Chapter 2 - CT Scanning For Lung Cancer Detection

DR Baldwin & FV Gleeson

2.1 Introduction

2.1.1 Lung cancer is responsible for approximately 1.4 million deaths per year worldwide, with over 80% caused by tobacco smoking[1]. It is estimated that there will be 47,600 new lung cancers annually in the UK by 2020, an increase of almost 20% from 2008, and this increase is predicted to continue until at least 2030[1]. The age adjusted incidence is declining, especially in men due to smoking cessation but because of the ageing population, the overall numbers are increasing.

2.1.2 Although the major determinants of risk of lung cancer are tobacco smoking and age, other associated factors are asbestos exposure, family history of cancer, previous pneumonia and chronic obstructive pulmonary disease (COPD). A number of risk scores have been developed and validated to help predict the risk of malignancy but none of these is currently used in routine clinical practice.

2.1.3 Surgical resection is the current gold standard for treatment with curative intent, although there are alternatives which may be more applicable to those patients with co-morbidity unsuitable for surgical resection or at high risk of surgical complications. These include stereotactic ablative radiotherapy and percutaneous thermal ablation. Treatment with curative intent is only available to those patients with early stage disease and these currently comprise around a quarter of patients who are diagnosed with lung cancer.

Fewer than 15% of lung cancers are currently diagnosed at Stage I[2] and even in this patient group, the 5-year survival after surgery is only 70%. The advanced stage of disease at presentation for the majority of patients results in an overall survival of approximately 8% at 5 years[2].

2.2 Screening for lung cancer

2.2.1 Initial attempts at lung cancer screening with imaging began shortly after its association with smoking became known, and led to at least 10 screening trials using the chest X-Ray (CXR), of which four were prospective and randomised. The most analysed of these, the Mayo Lung Project, failed to show a benefit from screening at initial analysis and at 20 year follow-up, and in fact showed an increase in mortality in the screened individuals[3-5].

More recently published work in lung cancer screening has reported on the use of single and now multi-detector computed tomography (MDCT) to detect earlier stage, smaller lung cancers, and has for the most part suggested that screening may be effective.

2.2.2 There are now at least 13 non-randomised screening trials using MDCT, that have recruited over a hundred thousand patients, and at least 9 randomised screening trials that are currently in progress or have reported early results[6]. These trials have recruited a variety of subjects; smokers and non-smokers, of variable gender ratios and have utilised a variety of screening protocols. In the randomised trials, some have no intervention in the control arm; others use the CXR as the control intervention. There is also no uniform CT screening regime, with some having limited incidence screens and others having annual screens for more than 5 years[6].

2.2.3 The difficulties in applying these varied screening regimes to an individual in the UK are compounded by the different definitions of a positive or indeterminate screen used in the different studies and the variety of methods used for follow up. For instance, some of the screening programmes such as the National Lung Screening Trial (NLST) have no defined protocol for work up, whilst others such as Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON) and Danish Lung Cancer Screening Trial (DLCST) use volumetric nodule analysis at specified intervals and or PET-CT[7-11].

2.2.4 The non-randomised trials have shown that CT has the ability to detect non-calcified pulmonary nodules, some of which are malignant, and that it is superior to the CXR in detection of both non-calcified nodules and lung cancer. The lung cancer detection rates and intervention for both benign and malignant disease in these trials are variable, being dependent upon the screening regime, work up protocols and the underlying ratio of benign to malignant nodules in the screened population[6].

In the non-randomised screening trials the prevalence of cancers detected ranges from 0.5% to 2.7%, with 4% to 33% of those undergoing intervention doing so for benign disease[6].

2.2.5 Whilst it is not possible to determine whether MDCT screening is definitively of value from these trials, the recent report from a multicentre randomised trial from the United States, the National Lung Screening Trial (NLST), raises hope that screening will be of benefit[8]. This very large randomised trial of MDCT compared to CXR in current or former heavy smokers aged 55 to 74 years recruited over 50,000 subjects, and demonstrated a relative reduction in death from lung cancer of 20% with an all-cause mortality reduction of 6.7%.

2.2.6 Some caution is necessary when attempting to translate these results to a UK or European population. The non-randomised ProActive Lung Cancer Detection (PALCAD) trial from Ireland[18] and the randomised DLCST from Denmark[11] suggest that there may be important differences in both the prevalence of lung cancers detectable by screening and the benefit from screening in Europe compared to the USA. The DLCST successfully identified more cancers in the CT screened arm than in the control arm, 69 compared to 24, and these were at an earlier stage; but there were more deaths in the screened versus the control arm, 61 compared to 42, and more deaths due to lung cancer, 15 compared to 11. Two further RCTs have reported mortality, the MILD and DANTE. All are underpowered and have insufficient follow-up periods to comment on mortality. Nevertheless if these results are combined with those of NLST, the mortality benefit remains at 19% [12]. These results indicate the urgent need for a decision on screening policy. The United Kingdom Lung Screen trial (UKLS) employs a single screen design and has completed recruitment of over 4000 subjects in the pilot phase. Currently the full trial (an additional 28000 subjects) has not been funded because of the NLST publication and the financial climate. NELSON will publish results in 2015/16 and if negative will cast doubt on the applicability of the NLST results to other countries. There is also the intention to pool the results from all of the European trials where trial design is sufficiently similar [13].

2.3 Screening a non-selected population or individual

2.3.1 The effectiveness of screening for lung cancer using MDCT can be increased by selection of a high-risk population, preferably by using an individual risk score or by selecting a population at risk, for instance smokers over a certain age with an occupational history of asbestos exposure. The latter method was used in NLST but led to many subjects being screened that were at relatively low risk by virtue of their age: 43% were aged less than 60. Recently it has been established that an individual risk model developed from the PLCO study would have resulted in the selection of 81 additional persons for screening who received a diagnosis of lung cancer in follow-up that would have resulted in 12 fewer deaths [14]. The Liverpool Lung Project criteria[15] are used to select patients with a 5% risk of developing lung cancer over 5 years for randomisation into UKLS[16]. In the context of a non-selected population the benefit of screening will be reduced.

2.3.2 This position is supported by the paper by Silvestri et al[17], which suggests that those most suitable for lung cancer screening are unlikely to volunteer on an

individual basis, and the “worried well” for whom there is no proven benefit and who have a low prevalence of disease are likely to self-select for screening.

2.4 Evidence relating to the frequency of false negatives

2.4.1 Recent reports suggest that very few significant lung cancers are “missed” using MDCT. In NELSON, the chances of finding a lung cancer 1 and 2 years after a negative first-round test were 1 in 1000 and 3 in 1000, respectively[10].

2.5 Radiation dose considerations

2.5.1 If MDCT protocols are optimised for lung cancer detection, the radiation dose involved can be very small – of the order of 0.5 to 1.4 mSv , equivalent to approximately 50 to 140 chest X-Rays or 61 to 170 days of background radiation in the UK. Potential harms from ionising radiation are therefore a relatively minor consideration in this situation compared with other CT applications although the legal requirement to minimise radiation dose remains.

2.6 Over-diagnosis and length-time effect

2.6.1 Over-diagnosis and length time bias are two ways in which screening can apparently result in improvements in survival but do not, in fact, change mortality. Over-diagnosis is common in all screening trials for lung cancer and reflects the ability of the screening test to detect cancers that do not affect life expectancy and that would have never presented during the patient’s life span. However, once detected these need further investigation, treatment and follow-up and all of this results in morbidity and a small but measurable mortality. There is a significant risk that self-selected patients will be subject to over-diagnosis, although even with this effect the evidence so far (from NLST) is for an overall benefit.

2.6.2 Related to over-diagnosis is length time bias. This is the tendency for a screening test to detect more indolent tumours because these have a longer time interval between becoming detectable by CT and causing symptoms sufficient for the person to present. Thus, some of these tumours may not affect life expectancy, especially in the elderly. In lung cancer a further consideration is that some lesions may regress spontaneously. This applies to atypical adenomatous hyperplasia, (AAH) which is found in 2-3% of patients at autopsy, and in 8-10% of patients undergoing resection for lung cancer[19]. It is typically a focal lesion often 5mm or less in diameter and is variably reported by pathologists. There is as yet not enough information available to be confident of the incidence of AAH detected in individuals being screened for lung cancer in the UK.

2.6.3 These biases are particularly important in patients with a poor life expectancy from co-morbidities, but the potential futility (as well as increased complications of investigation and treatment) should be clearly explained to this group of patients if they seek to be screened. This should be done by clinicians fully conversant with the latest diagnostic and therapeutic technology. Individuals with respiratory disease wishing to be screened may not benefit from screening because of their impaired lung or cardiac function and may in any case already have had a prior CT for diagnostic evaluation at presentation[20].

2.7 Evidence relating to the frequency and importance of incidental findings

Incidental pulmonary disease

2.7.1 In the context of lung cancer screening, unimportant incidental pulmonary disease predominantly relates to the detection of small benign pulmonary nodules, usually subpleural lymph nodes or granulomas. The detection of clinically irrelevant pulmonary nodules has been reported by most of the screening trials, and these nodules often result in the need for further investigation[6, 21]. For the majority of patients, this is a repeat CT scan at a specified interval to detect growth, a surrogate marker for possible malignancy[10]. The detection of growth in these small nodules is of itself difficult: some trials have used calliper measurement whilst others have used volumetric software analysis. Some of the nodules detected will be of sufficient size that investigations other than follow up CT scanning may be performed. These investigations may be a dynamic contrast enhanced CT, a PET-CT scan, trans-thoracic biopsy or resection.

2.7.2 The prevalence of non-calcified pulmonary nodules in smokers is high. In the Early Lung Cancer Action Project (ELCAP) 23% of the screened population were found to have non-calcified nodules[22]. This figure was even higher in the Mayo Clinic study, with 69% of the screened patients having at least one non-calcified nodule after 3 years of screening[23]. The prevalence of clinically insignificant pulmonary nodules has been reported in European trials: the NELSON trial reported that 21.8% of patients were investigated or recalled because of nodules detected on the prevalence screen, with only 0.9% of those screened shown to have a lung cancer[10].

2.7.3 Clearly the detection of a non-calcified nodule may result in patient anxiety, further radiation exposure for the patient from follow up or other scans, and possible interventional procedures such as image guided biopsy or even thoracotomy. Although the initial report from ELCAP[22] raised the possibility of being able to exclude all patients with benign disease from undergoing unnecessary biopsy or thoracotomy, other groups also using volumetric scanning techniques and software to detect growth have not confirmed this.

The Mayo Lung Cancer Screening Project reported five patients who underwent thoracotomy (21% of surgical procedures resulting from LCS) for benign disease[24]. In NELSON, 27% of interventions were for benign disease[10].

2.7.4 Specific follow up scanning regimes to help confirm a diagnosis of a benign nodule have been included in most of the lung cancer screening trials in an attempt to avoid unnecessary interventional procedures. The use of contrast enhancement as part of a protocol for lung nodule assessment, as performed by Pastorino *et al*[25], may reduce the incidence of unnecessary intervention, but is in itself not a perfect test. The large multicentre study assessing nodule enhancement reported by Swensen et al. had a sensitivity of 98% and specificity of 58% (using a threshold of 15HU as significant enhancement)[26], but included nodules up to 4 cm in size, far larger than would be included in a screening study. PET-CT scanning, when combined with volume doubling time to assess patients with indeterminate nodules in DLCST, achieved a sensitivity of 90% and a specificity of 82%[9].

Incidental finding of non-pulmonary disease

2.7.5 Screening with MDCT results in the detection of incidental disease both within and outside the chest. The Mayo Clinic study resulted in almost 700 additional abnormalities detected in fifteen hundred patients[23]. These included 114 abdominal aortic aneurysms, 4 renal cell carcinomas, 63 indeterminate renal masses, 56 adrenal masses, 21 hepatic masses and 28 breast nodules. All of these required further investigation.

2.7.6 This high incidence of non-pulmonary incidental disease is also found in other screening studies such as NELSON, which reported that of 1929 participants in the study, 1410 had incidental findings, of which only one was malignant, and this was incurable so that its detection was of no benefit to the patient[27].

2.7.7 The current IELCAP[28] protocol routinely assesses coronary artery calcification score and recommends referral for cardiological assessment for individuals with scores of more than 4 out of 12.

2.8 Risks and consequences of interventions associated with screening

2.8.1 The morbidity and mortality figures from interventional procedures including biopsy, mediastinoscopy, thoracotomy and resection associated with the lung cancer screening programmes worldwide appear excellent, possibly because of the patient criteria required to enter the programmes, and the quality of the centres involved. The results reported are better than those published for the investigation and treatment of symptomatically detected lung cancer.

2.8.2 In the NLST, a total of 0.06% of the positive screening tests in the low-dose CT group that did not result in a diagnosis of lung cancer and 11.2% of those that did, were associated with a major complication after an invasive procedure[8]. A total of 16 participants in the low-dose CT group (10 of whom had lung cancer) died within 60 days after an invasive procedure. Similarly excellent results have been shown in I-ELCAP[28], with a 30-day mortality of 0.5% in patients undergoing resection for their screen detected lung cancer.

2.9. Final Considerations

The pitfalls in lung cancer screening are comparable to those in screening programmes already in place in medicine, so it is important to learn from these. These include the identification of unimportant disease, the failure to identify important disease successfully, the physical and psychological consequences of investigating and treating disease identified, and the expenditure of money that may be better utilised elsewhere. For a self-funded individual, the cost to the taxpayer relates to the consequences of disease detected on the scan, and whether the individual continues to fund the further investigations and possible surgery. The costs differ whether the disease is benign or malignant, but occur in both instances. Furthermore both the individual and taxpayer may be paying for investigations and treatment without proven benefit, and with potential harm. It is essential that any clinician providing this service is fully conversant with the latest research and that the patient has access to all relevant information provided in a form that they can understand.

Summary:

CT has been shown to reduced lung cancer mortality in the US in a specified risk group.

There are a number of uncertainties that make it difficult to recommend screening implementation in the UK. It is important to establish whether mortality can be reduced in a cost effective way taking into account the frequency of screens, population at risk, participation rates, harms associated with screening and other associated cost effective interventions such as smoking cessation.

Recommendations:

1. IHA CT for lung cancer detection should not be offered to people under the age of 55 as they are unlikely to benefit.
2. IHA CT for lung cancer detection should not be offered to people who have never smoked, or those with a pack history of less than 20 years with no other risk factors as they are unlikely to benefit.
3. Individual risk prediction models should be used to select those patients at risk of developing lung cancer. IHA CT may be offered if the risk is equivalent to 5% in 5 years. If the risk is lower IHA CT may still be offered but the balance of risk and benefit is not known. Annual or biennial screening may be offered from age 55 to 74 but few people aged 55 to 60 will be at sufficiently high risk.
4. IHA CT should only be offered by expert clinicians (radiologists and respiratory physicians), able to explain the risks and benefits of CT for IHA.
5. Information packs on the risks and benefits of CT for IHA, detailing in lay persons' language the limitations, and the risks and benefits of IHA should be made available to individuals prior to undergoing CT scanning.

References:

1. GLOBOCAN 2008. Cancer Incidence, Mortality and Prevalence Worldwide in 2008
2. http://info.cancerresearchuk.org/cancerstats/types/lung/survival/lung-cancer-survival-statistics
3. Fontana RS, Sanderson DR, Taylor WF et al. Early Lung Cancer Detection: Results Of The Initial (Prevalence) Radiologic And Cytologic Screening In The Mayo Clinic Study. Am Rev Respir Dis 1984;130:561-5
4. Fontana RS, Sanderson DR, Woolner LB et al. Lung Cancer Screening: The Mayo Program. J Occup Med 1986;28:746-750
5. Marcus PM, Bergstralh EH, Fagerstrom RM et al. Lung Cancer Mortality In The Mayo Lung Project: Impact Of Extended Follow-Up. J Natl Cancer Inst 2000;92:1308-1316
6. Pastorino U. Lung Cancer Screening. Br J Cancer 2010;102:1681-1686
7. National Cancer Institute. National Lung Screening Trial. www.cancer.gov/nlst
8. National Lung Screening Trial Research Team. Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening. N Engl J Med 2011;365:395-409
9. van't Westeinde S, de Koning HJ, Thunnissen FB et al. The Role Of The (18)F-Fluorodeoxyglucose-Positron Emission Tomography Scan In The Nederlands Leuvans Longkanker Screenings Ondrzoek Lung Cancer Screening Trial. J Thorac Oncol 2011;6:1704-1712

10. van Klaveren RJ, Oudkerk M, Prokop M et al. Management of Lung Nodules Detected by Volume CT Scanning. N Engl J Med 2009;361:2221-9
11. Saghir Z, Dirksen A, Ashraf H et al. CT Screening For Lung Cancer Brings Forward Early Disease. The Randomised Danish Lung Cancer Screening Trial: Status After Five Annual Screening Rounds With Low Dose CT. Thorax 2012;67:296-301
12. Field JK, Hansell DM, Duffy SW, Baldwin DR. Computed Tomography Screening for Lung Cancer: Countdown to Implementation? Lancet Oncology 2013 in press
13. Field JK, Smith RA, Duffy SW, et al. The Liverpool Statement 2005: priorities for the European Union/United States spiral computed tomography collaborative group. J Thorac Oncol 2006; 1: 497-8.
14. Tammemagi MC, Katki HA, Hocking WG, et al. Selection criteria for lung-cancer screening. N Engl J Med 2013; 368: 728-36.
15. Cassidy A, Myles JP, van Tongeren M et al. The LLP Risk Model: An Individual Risk Prediction Model For Lung Cancer. Br J Cancer 2008;98:270-6
16. www.ukls.org/index.html
17. Silvestri G, Nietert P, Zoller J, Carter C, Bradford D. Attitudes Towards Screening For Lung Cancer Among Smokers And Their Non-Smoking Counterparts. Thorax. 2006 Nov 13; [Epub ahead of print]
18. MacRedmond R, Logan PM, Lee M et al. Screening For Lung Cancer Using Low Dose CT Scanning: Results Of 2 Year Follow Up. Thorax 2006;61:54-56.
19. Kayser K, Nwoye JO, Kosjerina Z et al. Atypical Adenomatous Hyperplasia Of Lung: Its Incidence And Analysis Of Clinical, Glycohistochemical And Structural Features Including Newly Defined Growth Regulators And Vascularization. Lung Cancer 2003;42:171-182
20. J Gribbin, R B Hubbard, I Le Jeune, C J P Smith, J West, and L J Tata. Incidence And Mortality Of Idiopathic Pulmonary Fibrosis And Sarcoidosis In The UK. Thorax 2006; 61: 980 - 985
21. Spiro S. Screening For Lung Cancer: We Still Need To Know More. Thorax 2012;67: 283-4
22. Henschke CI, McCauley DI, Yankelevitz DF et al. Early Lung Cancer Action Project: Overall Design And Findings From Baseline Screening. Lancet 1999;354:99-105
23. Swensen SJ, Jett JR, Hartmann TE et al. Lung Cancer Screening With CT: Mayo Clinic Experience. Radiology 2003;226:756-761
24. Swensen S, Jett JR, Hartmann TE et al. CT Screening For Lung Cancer: Five-year Prospective Experience. Radiology 2005;235:259-265
25. Pastorino U, Bellomi M, Landoni C et al. Early Lung Cancer Detection With Spiral CT And Positron Emission Tomography In Heavy Smokers: 2 Year Results. Lancet 2003;362:593-7

26. Swensen SJ, Viggiano RW, Midthun DE et al. Lung Nodule Enhancement at CT: Multicenter Study1. Radiology, January 1, 2000; 214(1): 73 - 80
27. van de Weil JC, Wang Y, Xu DM et al. Neglectable Benefit Of Searching For Incidental Findings In The Dutch-Belgian Lung Cancer Screening Trial (NELSON) Using Low-Dose Multidetector CT. Eur Radiol 2007;17:1474-1482
28. www.ielcap.org/professionals/protocols.html

Chapter 3 - CT Scanning For Colorectal Cancer & Polyp Detection

S Hughes & SA Taylor

3.1 Introduction

3.1.1 Colorectal cancer is the third most frequently diagnosed cancer worldwide, accounting for more than 1 million cases and 600,000 deaths every year[1]. In England in 2007, 30,727 people were diagnosed with colorectal cancer and 12,841 people died from it. 5-year survival rates for colorectal cancer are 50.9% in men and 52.6% in women. Survival is strongly related to stage at diagnosis with survival rates of 90% for localised cases[2].

3.1.2 Colorectal cancer can occur at any age but the incidence increases with age with a peak incidence in the 70 to 79 yrs age group in men and over 85 yrs in women. It is well established that most sporadic colorectal cancers develop from malignant transformation of benign adenomatous polyps. Early diagnosis of CRC leads to better survival but the identification and removal of adenomatous polyps will reduce the risk of cancer development and is therefore a more attractive strategy.

3.1.3 The NHS Bowel Cancer Screening Programme (BCSP) offers screening by faecal occult blood testing (FOBt) followed by colonoscopy for those with a positive FOBt. Individuals between the ages of 60 and 69 years are screened at present but this is in the process of being extended to 69 to 75 year olds. By 2016, in addition all 55year olds will be offered screening by a one-off flexible sigmoidoscopy. The British Society of Gastroenterology (BSG) guidelines recommend that individuals with increased risk of CRC due to a positive family history are examined at between 50 and 55 yrs depending on how many family members are affected[3].

3.1.4 Since the 12th COMARE report, there has been rapid dissemination of CT colonography (CTC) as a diagnostic test in patients with symptoms possibly attributable to colorectal cancer. Up to date audit data is lacking, but in 2004 36% of surveyed NHS departments offered a CTC service[4]. A re-audit is currently under way under the auspices of BSGAR (British Society of Gastrointestinal and Abdominal Radiology), and this percentage will undoubtedly be considerably larger. As described below, data from the completed SIGGAR 1 trial provide definitive evidence that CTC is similar to optical colonoscopy and more sensitive than barium enema for detecting colorectal cancer and large (>10mm) polyps.

3.2 Evidence for accuracy of CTC in diagnosing colon polyps and cancers

Symptomatic patients

3.2.1 In 2002, The UK Department of Health via the Health Technology Assessment programme (HTA) commissioned a study to determine the likely future role of CTC within the National Health Service (NHS). The resulting SIGGAR trial[5] was restricted to symptomatic patients and used detection of colorectal cancer or polyps ≥10mm as its primary end point. The trial had two parallel arms-one comparing CTC to barium enema, and the other CTC to colonoscopy. The randomised controlled trial comparing CTC with barium enema recruited 3,838 patients. In an intention-to-treat analysis, colorectal cancer or polyps ≥10mm were diagnosed significantly more frequently in patients assigned CTC than barium enema (7.4% vs. 5.6%, p=0.03). Using national registry data to capture cancer miss rates (diagnosed within 2-years of randomization), barium enema had twice the miss rate of CTC (14% vs 7%). A recent meta- analysis specifically assessed the diagnostic accuracy of CTC for colorectal cancer detection considered 49 studies including 11141 patients. CTC had a sensitivity of 96% for cancer detection, comparable to colonoscopy[6].

Asymptomatic individuals

3.2.2 The NHS Bowel Cancer Screening Programme has been described in outline above. Colonoscopy is the default whole colon examination for those with positive FOBt. However for those in whom colonoscopy is inappropriate (for example due to medical co-morbidity) or incomplete, guidance has been issued indicating that CTC rather than Barium enema is the preferred imaging method (http://www.cancerscreening.nhs.uk/bowel/publications/nhsbcsp05.pdf). This guidance reflects the increasing evidence for diagnostic superiority of CTC over barium enema.

3.2.3 Large trials of primary population screening using CTC are underway in Europe, but have not currently reported. In the USA, Johnson et a[l7] studied 2531 asymptomatic individuals aged 50 or over across 15 centres. The reference standard was optical colonoscopy (OC). For cancer and large polyps (≥10mm), mean per-patient sensitivity, specificity, positive and negative predictive values for CTC were 90%, 86%, 0.23, and 0.99 respectively. The per-patient sensitivity for detecting adenomas that were 6 mm or more in diameter was 78%. The Munich

Colorectal Cancer Prevention Trial8 examined 307 patients undergoing same day CTC and colonoscopy. CTC detected 93.9% of adenomas larger than 10mm. Per-patient specificity for polyps larger than 6 mm was 93.1%. A third large trial (Italian IMPACT study)[9] recruited 1103 patients at increased risk of colonic neoplasia such as those with a personal or family history of adenomatous polyps or positive faecal occult blood test (FOBT). CTC sensitivity for polyps ≥10mm was 90.8% with positive and negative predictive values of 0.62 and 0.96.

A study of 510 asymptomatic patients from Madeira reported a per patient, sensitivity, specificity, PPV and, NPV for adenomas ≥6mm of 98.11% (88.6-99.9% 95% CI), 90.97% (87.8-93.4% 95% CI), 56.52% (45.8-66.7% 95% CI), 99.75% (98.4-99.9% 95% CI, CTC was interpreted by experienced radiologists using tele-radiology [10].

3.2.4 A non-randomised cohort study by Kim et al compared advanced neoplasia detection in 3120 adults screened using CTC with a separate cohort of 3163 screened using optical colonoscopy[11]. Advanced neoplasia was confirmed in 3.2% of the CTC group and 3.4% of the colonoscopy group. However the total numbers of polyps removed in the CTC and colonoscopy group to achieve this yield were 561 and 2434, respectively. There were seven colonic perforations in the colonoscopy group and none in the CTC group.

3.2.5 A meta-analysis by Chaparro et al[12] considered forty-seven studies including 10,546 patients. Overall per-polyp sensitivity of CTC was 59% for polyps 6-9 mm in size and 76% for polyps larger than 9 mm. The meta-analysis however included many studies using outdated CT scanner technology, and confirmed higher sensitivity in studies using state of the art technique. As noted above, further meta-analysis by Pickhardt at al[6] restricted its focus to colon cancer detection alone and included 49 studies. The sensitivity of CTC for cancer detection was 96.1% with no statistical heterogeneity between studies.

3.2.6 Based on the accrued data, in 2008 a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology recommended screening CTC every 5 years in asymptomatic average risk individuals aged 50 years or older[13.]

3.3 CTC technique and patient information

3.3.1 There have been refinements in CTC technique since publication of the 12th COMARE report. Further data on the use of reduced laxative protocols supplemented by oral contrast (faecal tagging) have been published[14, 15]. The data suggest that diagnostic accuracy can be maintained with reduced laxative

protocols[16] but large scale studies are lacking and full bowel purgation remains standard practice, with its associated risks. The use of faecal tagging even with full purgation is however gaining wide acceptance and its use is recommended by expert consensus guidelines[17]. Use of iodinated oral contrast carries a very small risk of allergic reaction, of which the patient should be informed.

3.3.2 Computer aided detection (CAD) algorithms are increasingly robust for detecting colonic neoplasia in CTC datasets. A retrospective study in a cohort of 3042 screened individuals found standalone CAD per-patient sensitivities of 93.8% and 96.5% at 6 and 10-mm thresholds respectively, with a median false-positive rate of 3 per CTC series[18]. The impact of CAD on radiologist performance has been evaluated in two multi-reader, multi-case studies using CAD as a second reader (ie applied only after a first unassisted radiologist read) [19, 20]. Both found that CAD increased reader sensitivity by up to 7%, although at least one[20] also showed a slight reduction in specificity by 0.025 (P = .05). It is anticipated that the use of CAD as part of CTC interpretation will increase.

3.3.3 Patients attending for endoscopic procedures generally receive high quality, patient friendly information covering risks and benefits of the proposed procedure and the incidence of missed pathology. Patients attending for CTC should receive similar information prior to their procedure as outlined in section 6.13 of the COMARE 12th report.

3.4 Complications and safety

3.4.1 There has been no significant updated information on the small but well documented perforation risk of CTC. Combined data suggests the risks of perforation is around 0.035%, and likely lower in asymptomatic patients[21]. Other reported complications include vaso-vagal reactions, cardiovascular effects of spasmolytics (notably tachycardia) and complications related to bowel preparation

3.5 Radiation dose considerations

3.5.1 Low dose protocols are now considered the norm during CTC, especially in asymptomatic individuals in whom intravenous contrast is usually not administered. New techniques such as dose modulation are increasingly employed. In an update to their 2004 survey[22], Stoker and colleagues surveyed 109 institutions of whom 62 replied. Median effective dose for routine protocols was 7.6 mSv (4.3 mSv and 2.0 mSv for supine and prone, respectively) and for screening 4.4 mSv (2.6 mSv and 2.0 mSv, respectively; P = .01). There was a trend of reducing effective dose since 2004, (from 11 mSv in 2004)

3.5.2 On-going developments in CT scanner and detector technology are likely to reduce doses further in the future.

3.6 Training issues, standards and audit

3.6.1 Consensus guidelines concur that training prior to CTC interpretation is mandatory, although the optimum training format is uncertain. Many training workshops are available, many under the auspices of national radiological bodies, and commonly last 2 days. It has however been shown that competence in CTC cannot be guaranteed after a single training workshop[23]. Despite strong recommendations to train prior to interpreting CTC, uptake of specific CTC training amongst radiologists is patchy. A recent survey of European CTC workshop participants[24] showed that 69% of respondents had been interpreting CTC in daily practice despite having no previous hands-on training and limited experience.

3.6.2 Audit of performance metrics including patient safety, technical adequacy, positive predictive values and adenoma detection rate is currently recommended for those performing CTC in the context of the NHS bowel cancer screening program (http://www.cancerscreening.nhs.uk/bowel/publications/nhsbcsp05.pdf).

3.6.3 Preliminary data has been published concerning non radiologist interpretation of CTC. In a small study, Young *et al*[25] reported suitably trained gastroenterologists achieved a mean sensitivity of 83.5% and 87.8% for detecting polyps larger than 6 and 10mm respectively, although specificity was low at 70%. In a study of 303 consecutive symptomatic patients[26] , the performance of radiographic technicians assisted by CAD was compared to that of experienced consultant radiologists. Technicians detected 100% of cancers, 72% of large polyps and 70% of medium (6-9mm) sized polyps, although specificity was low and based only on the technician report, inappropriate management would have occurred in 37% of patients. A recent systematic review of studies investigating primary reporting by radiographers reported per lesion sensitivity 68% (95% CI: 65-71%) and 75% (95% CI: 72-79%) for polyps >5 and >10 mm respectively[27]. Independent reporting of CTC by non-radiologists remains under investigation but is not currently recommended[17].

3.6.4 An international standards document has recently been published detailing minimum standards and best practice in patient information and consent, bowel preparation, acquisition protocols, patient safety, team working, patient management, interpretation and training[17].

3.7 Detection of extra-colonic findings

3.7.1 The impact of extra colonic findings on CTC remains unclear. A retrospective review of 10,286 outpatient adults undergoing screening CTC[28] reported [36] unexpected extra-colonic malignancies (0.35%) including 11 renal cell carcinomas, eight lung cancers and six cases of non-Hodgkin's lymphoma. Another study of 2777 screening patients identified extra colonic findings in 46%, and 'significant' findings in 11%. Further evaluation resulted in 280 radiology procedures and 19 surgical interventions[29]. Pickhardt et al assessed incidental indeterminate adnexal masses in 2869 asymptomatic women undergoing CT colonography screening[30] and found that while ovarian lesions were common (4.1%), subsequent work-up revealed no ovarian cancers. Importantly, a normal CTC did not exclude subsequent development of ovarian cancer. A recent review of 24 studies reported the median positive predictive value of CTC for suspected renal cancers was 20.5%, but much lower for suspected cancers of the lung, liver, ovary and pancreas (range 0 to 2.8%)[31].

3.7.2 Markov modelling has predicted that CTC detection of unsuspected aortic aneurysm in the context of a screening program could significantly increase both lives saved and cost effectiveness[32]. Other reported "benefits" of extra colonic assessment include derivation of bone mineral density and body fat[33], which is considered in chapter 7 of the 12th COMARE report.

3.7.3 There remains no prospective trial data on the impact of extra colonic findings in asymptomatic individuals. Patients considering undergoing CTC should be informed of the negative as well as potential positive outcome of incidental extra colonic findings.

3.8 Alternative techniques

3.8.1 Optical colonoscopy (OC) remains the most accurate test for the identification of colonic polyps, particularly those less than 10mm in size. OC has the potential for endoscopic removal of polyps and biopsy of suspicious lesions. The safety of OC has been underlined by the recent National Colonoscopy Audit in the UK, which revealed only 8 perforations and no deaths in a series of over 20.000 procedures[34]. Despite this, the procedure requires rigorous bowel cleansing and is an invasive test usually performed under sedation. Whilst it remains the procedure of choice for managing known colonic polyps and the surveillance of high risk groups, a non-invasive test which can be performed in an unsedated patient is an attractive alternative as an initial screening test in asymptomatic individuals.

3.8.2 Wireless capsule colonoscopy is an emerging technology which is capable of identifying colonic tumours and polyps[35] but so far data are limited and the procedure is not widely available in the UK.

3.8.3 Development of magnetic resonance colonography continues, although use remains restricted to mainly academic centres with a research interest. A meta-analysis of thirty-seven studies and 1,285 patients by Zijta et al[36] reported significant heterogeneity and estimated sensitivity for polyps less than 9mm was not possible. The pooled sensitivities were 100% for colon cancer, and 88% (95% CI 63-97%) for polyps 10 mm or larger. A recent trial of MRI colonography in 286 asymptomatic individuals undergoing same day colonoscopy reported the sensitivity of MRI for adenomas ≥6mm was 78.4%[37]

3.9 Polyp management, surveillance and follow up

3.9.1 When polyps are identified, usual practice is to perform OC to remove the polyp. If the polyp is proven at histology to be a neoplastic (adenomatous) polyp rather than a hyperplastic polyp, OC is performed at intervals depending on the perceived CRC risk as judged by the number and size of the adenomatous polyps identified. If polyps are identified at CTC it is recommended that the patient is referred to an appropriate specialist for advice regarding removal of the polyp (or polyps) and for consideration of endoscopic surveillance. CTC is advocated for surveillance, although long term outcome data is awaited. Studies are on-going regarding a 'watch and wait' policy for polyps 6-9mm identified at CTC, but the safety of this strategy has not been established

3.9.2 The process of developing polyps is a continuous process and therefore a single negative screening procedure is insufficient and the procedure should be repeated at suitable intervals. If CTC may fail to identify small polyps, the interval between a normal CTC and the next examination should be equivalent to that recommended for patients with small polyps found at OC. BSG recommends that when investigation reveals a single small adenomatous polyp (<10mm) the patient should be re-examined after 5 yrs. This is also the interval recommended by the joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology[13].

3.9.3 While much is known about the natural history of colorectal cancer, it remains unclear whether detection of small adenomas is clinically desirable in the context of screening. For example, a metaanalysis of four studies comprising 20562 screening patients by Hassan et al[38] found advanced adenomas were detected in 1155 (5.6%) subjects, with the overall incidence in diminutive, small and large polyps of 4.6%, 7.9% and 87.5% respectively. They concluded that a 10-mm threshold for colonoscopy referral would identify 88% of advanced neoplasia while a 6-mm polyp size threshold would identify over 95%. However NICE recognises individuals with multiple small polyps (5 or more polyps < 10 mm) which may be missed at CTC as being a high risk group. NICE recommends a 1yr surveillance interval for these patients[39]. If multiple small polyps are confidently identified at CTC these guidelines should be followed if they are confirmed to be adenomata.

Summary

Since the 12th COMARE report, dissemination of CTC into routine radiological practice has increased and randomised trial data has shown its superiority over barium enema for detection of large polyps and cancer.

New trial data in asymptomatic patients together with updated and meta analysis review has confirmed good sensitivity of CTC for polyps ≥6mm, although diagnostic performance remains limited for polyps below 6mm.

The average radiation dose imparted by the procedure continues to decrease with improved CT technology, and new diagnostic aids such as computer aided detection are entering clinical practice. Whilst research into reduced laxative regimens shows considerable promise, bowel preparation remains the norm.

The need for adequate training of reporting radiologists is reaffirmed.

CTC generates additional investigations for detected extracolonic findings. The impact of extra-colonic findings remains uncertain.

Clear patient pathways need to be identified so that when pathology is identified at CTC (eg polyps or cancer) there is a clear management plan for the patient.

CTC is established for the investigation of individuals with suspected colorectal cancer. The literature increasingly supports its role in the investigation of asymptomatic individuals when implemented according to published guidelines pertaining to age, follow up interval and polyp surveillance. As per the recommendations of the 12th COMARE report, individuals identified as having a high risk of developing colorectal cancer (eg those with a family history of colorectal cancer or of polyposis coli) should be managed as part of a multi-disciplinary comprehensive programme.

Recommendations

6. CTC for IHA and outside the NHS bowel cancer screening programme should only be undertaken in individuals in the appropriate age group and not, therefore, under the age of 45 years. Subjects aged under 45 should only be screened if they have an increased risk of colorectal cancer and then in accordance with published guidelines.

7. Individuals with a negative CTC or CTC demonstrating polyps less than 6mm in size and who remain asymptomatic should not undergo further CTC for IHA in an interval less than five years from the initial examination.

References:

1. WHO. Cancer, fact sheet 297. Geneva: World Health Organisation, 2009.

2. Cancer Research UK. Bowel cancer survival statistics by stage at diagnosis. London: Cancer Research UK, 2009
3. Cairns SR, Scholefield JH, Steele RJ, et al. Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). Gut 2010; 59:666-689
4. Burling D, Halligan S, Taylor SA, Usiskin S, Bartram CI. CT colonography practice in the UK: a national survey. Clin Radiol 2004; 59:39-43
5. Halligan S, Wooldrage K, Dadswell E, et al Computed tomographic colonography versus barium enema for diagnosis of colorectal cancer or large polyps in symptomatic patients (SIGGAR): a multicentre randomised trial. Lancet 2013; 381 (9873): 1185-93
6. Pickhardt PJ, Hassan C, Halligan S, Marmo R. Colorectal cancer: CT colonography and colonoscopy for detection--systematic review and meta-analysis. Radiology 2011; 259:393-405
7. Johnson CD, Chen MH, Toledano AY, et al. Accuracy of CT colonography for detection of large adenomas and cancers. N Engl J Med 2008; 359:1207-1217
8. Graser A, Stieber P, Nagel D, et al. Comparison of CT colonography, colonoscopy, sigmoidoscopy and faecal occult blood tests for the detection of advanced adenoma in an average risk population. Gut 2009; 58:241-248
9. Regge D, Laudi C, Galatola G, et al. Diagnostic accuracy of computed tomographic colonography for the detection of advanced neoplasia in individuals at increased risk of colorectal cancer. JAMA 2009; 301:2453-2461
10. Lefere P, Silva C, Gryspeerdt S, et al Teleradiology based CT colonography to screen a population group of a remote island; at average risk for colorectal cancer. Eur J Radiol. 2013; 82:e262-7.:
11. Kim DH, Pickhardt PJ, Taylor AJ, et al. CT colonography versus colonoscopy for the detection of advanced neoplasia. N Engl J Med 2007; 357:1403-1412
12. Chaparro M, Gisbert JP, Del Campo L, Cantero J, Mate J. Accuracy of computed tomographic colonography for the detection of polyps and colorectal tumors: a systematic review and meta-analysis. Digestion 2009; 80:1-17
13. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Gastroenterology 2008; 134:1570-1595
14. Campanella D, Morra L, Delsanto S, et al. Comparison of three different iodine-based bowel regimens for CT colonography. Eur Radiol 2010; 20:348-358

15. Liedenbaum MH, Denters MJ, Zijta FM, et al. Reducing the oral contrast dose in CT colonography: evaluation of faecal tagging quality and patient acceptance. Clin Radiol 2011; 66:30-37
16. Mahgerefteh S, Fraifeld S, Blachar A, Sosna J. CT colonography with decreased purgation: balancing preparation, performance, and patient acceptance. AJR Am J Roentgenol 2009; 193:1531-1539
17. Burling D. CT colonography standards. Clin Radiol 2010; 65:474-480
18. Lawrence EM, Pickhardt PJ, Kim DH, Robbins JB. Colorectal polyps: stand-alone performance of computer-aided detection in a large asymptomatic screening population. Radiology 2010; 256:791-798
19. Halligan S, Mallett S, Altman DG, et al. Incremental benefit of computer-aided detection when used as a second and concurrent reader of CT colonographic data: multiobserver study. Radiology 2011; 258:469-476
20. Dachman AH, Obuchowski NA, Hoffmeister JW, et al. Effect of computer-aided detection for CT colonography in a multireader, multicase trial. Radiology 2010; 256:827-835
21. Pendse DA, Taylor SA. Complications of CT colonography: A Review. Eur J Radiol 2012
22. Boellaard TN, Venema HW, Streekstra GJ, Stoker J. Effective Radiation Dose in CT Colonography: Is There a Downward Trend? Acad Radiol 2012; 19:1127-1133
23. Fletcher JG, Chen MH, Herman BA, et al. Can radiologist training and testing ensure high performance in CT colonography? Lessons From the National CT Colonography Trial. AJR Am J Roentgenol 2010; 195:117-125
24. Boone D, Halligan S, Frost R, et al. CT colonography: who attends training? A survey of participants at educational workshops. Clin Radiol 2011; 66:510-516
25. Young PE, Ray QP, Hwang I, et al. Gastroenterologists' interpretation of CTC: a pilot study demonstrating feasibility and similar accuracy compared with radiologists' interpretation. Am J Gastroenterol 2009; 104:2926-2931
26. Burling D, Wylie P, Gupta A, et al. CT colonography: accuracy of initial interpretation by radiographers in routine clinical practice. Clin Radiol 2010; 65:126-132
27. Meertens R, Brealey S, Nightingale J, et al. Diagnostic accuracy of radiographer reporting of computed tomography colonography examinations: a systematic review. Clin Radiol. 2013; 68:e177-90.
28. Pickhardt PJ, Kim DH, Meiners RJ, et al. Colorectal and extracolonic cancers detected at screening CT colonography in 10,286 asymptomatic adults. Radiology 2010; 255:83-88
29. Veerappan GR, Ally MR, Choi JH, Pak JS, Maydonovitch C, Wong RK. Extracolonic findings on CT colonography increases yield of colorectal cancer screening. AJR Am J Roentgenol 2010; 195:677-686
30. Pickhardt PJ, Hanson ME. Incidental adnexal masses detected at low-dose unenhanced CT in asymptomatic women age 50 and older: implications for

clinical management and ovarian cancer screening. Radiology 2010; 257:144-150
31. Wernli KJ, Rutter CM, Dachman AH, et al. Suspected Extracolonic Neoplasms Detected on CT Colonography: Literature Review and Possible Outcomes. Acad Radiol. 2013; S1076-6332
32. Pickhardt PJ, Hassan C, Laghi A, Kim DH. CT colonography to screen for colorectal cancer and aortic aneurysm in the Medicare population: cost-effectiveness analysis. AJR Am J Roentgenol 2009; 192:1332-1340
33. Pickhardt PJ, Lee LJ, del Rio AM, et al. Simultaneous screening for osteoporosis at CT colonography: bone mineral density assessment using MDCT attenuation techniques compared with the DXA reference standard. J Bone Miner Res 2011; 26:2194-2203
34. Gavin DR, Valori RM, Anderson JT, Donnelly MT, Williams JG, Swarbrick ET. The national colonoscopy audit: a nationwide assessment of the quality and safety of colonoscopy in the UK. Gut 2012
35. Gay G, Delvaux M, Frederic M, Fassler I. Could the colonic capsule PillCam Colon be clinically useful for selecting patients who deserve a complete colonoscopy?: results of clinical comparison with colonoscopy in the perspective of colorectal cancer screening. Am J Gastroenterol 2010; 105:1076-1086.
36. Zijta FM, Bipat S, Stoker J. Magnetic resonance (MR) colonography in the detection of colorectal lesions: a systematic review of prospective studies. Eur Radiol 2010; 20:1031-1046.
37. Graser A, Melzer A, Lindner E, et al. Magnetic resonance colonography for the detection of colorectal neoplasia in asymptomatic adults. Gastroenterology 2013; 144 :743-750.
38. Hassan C, Pickhardt PJ, Kim DH, et al. Systematic review: distribution of advanced neoplasia according to polyp size at screening colonoscopy. Aliment Pharmacol Ther 2010; 31:210-217.
39. NICE guideline. CG118 Colonoscopic surveillance for prevention of colorectal cancer in people with ulcerative colitis, Crohn's disease or adenomas. March 2011.

Chapter 4 - CT in Coronary Heart Disease

MA West wood & JH Reid

4.1 Background

4.1.1 Despite continuing advances in diagnosis, treatment and management, coronary artery disease remains a significant burden. It remains the leading cause of death worldwide and World Health Organisation estimations are that it was responsible for 7.25 million deaths worldwide in 2008[1]. In the UK there were 82,000 deaths from coronary artery disease in 2009[2].

4.1.2 Earlier detection of coronary artery disease coupled with improved treatment options have led to significant reductions in morbidity and mortality. The role of various non-invasive imaging techniques to detect coronary artery disease and its sequelae has increased dramatically with faster and more reliable imaging. One of these techniques is CT coronary angiography. The role of these tests is now recognised in national guidelines for the assessment of patients with chest pain[3].

4.2.The technique of Coronary Assessment by CT

4.2.1 Currently, cardiac CT scanning is mainly used in two distinct ways:

a. quantification of coronary artery calcium and by association the atheromatous plaque burden (coronary calcium scoring, CTCS).
b. direct visualization of the coronary arteries (CT coronary angiography – CTCA), cardiac chambers and mediastinal structures (pericardium and thoracic aorta).

In technical terms, while both types of examination are electrocardiographically (ECG) gated the first technique requires no intravenous contrast and carries a slightly lower radiation dose and the second technique exposes the patient to intravenous iodinated contrast media and a higher radiation dose.

For the purposes of clarity in the sections below CTCS and CTCA will be considered separately.

4.3 CT Coronary Assessment in symptomatic individuals

4.3.1 The role of both CTCS and CTCA in the risk stratification of patients with chest pain and for CTCA the assessment of significant coronary artery disease is well established. The use of CTCS to predict the risk of future events and the coronary artery disease is well described with electron beam CT (EBCT)[4], 4 slice CT[5-7] and 64 slice CT[8]. CTCS is now a routine investigation for this purpose.

4.3.2 Similarly the role of CTCA in the assessment of patients with chest pain to assess for significant coronary artery disease is well established[9-11] . CTCS and CTCA in the UK are indicated as a first line investigation for those patients presenting with new onset chest pain with a pre-test risk of coronary artery disease of 10-29%[3].

4.4 CT Coronary Assessment in asymptomatic self-referred individuals

4.4.1 CTCS and CTCA have not to date been studied as a formal screening test for coronary artery disease and currently there are no plans for formal screening programmes utilizing these techniques. There are also to date no trials to assess this as a potential role for CTCS or CTCA.

4.4.2 The role of cardiac CT has evolved considerably in the last decade[12] and now seems reasonably well established. There is however no evidence to date that patient directed cardiac CT is of benefit either in terms of diagnosis or in terms of prognosis. There are no large randomised studies that have assessed potential benefits for self directed CT coronary angiography and conclusions within this document are extrapolations of existing trials in symptomatic patients.

4.4.3 If CT coronary angiography is to be used in the context of self-referral then the pre-test likelihood of an abnormal result will need to be considered. In many cases this is likely to be low and the potential benefits of a scan are therefore likely to be small. The potential small benefit should be balanced against the known effects of ionising radiation exposure[13] and the potentially deleterious effects of uncovering incidental findings.

4.5 False Negatives

4.5.1 The specificity of CT calcium scoring and CT coronary angiography are extremely high with specificities for CTCS of 95-100%[4,5,8] and for CTCA 97-100%[10,11]. It is therefore likely that the incidence of false negatives even in the context of asymptomatic self-referred individuals will remain low.

4.5.2 It should be borne in mind that in particular for CTCA the study populations were frequently patients awaiting coronary angiography where the incidence of significant coronary artery disease would be high. It is possible that whilst remaining low the occurrence of false negatives will increase in lower risk cohorts (which is likely to be the case for asymptomatic self-referring individuals) as problems with artefacts are likely to be more significant.

4.6 Training and Expertise required for Reporting

4.6.1 There are clear UK, European and international guidelines for training in the reporting of CTCA and CTCS. Any clinician reporting these scans should have level III accreditation. They should also be able to provide evidence of ongoing training and education in CTCA and CTCS as part of their annual appraisal. More specific guidance on this can be found at http://www.scct.org/credentialing/updates.cfm.[14]

4.7 Alternative imaging techniques

4.7.1 Several imaging techniques have been employed to give direct (conventional catheter angiography) or indirect evidence (MRI, cardiac scintigraphy, echocardiography) for the presence of coronary artery disease.

4.7.2 Conventional catheter angiography is the most invasive technique (and is still considered the most accurate) but carries a radiation burden of approximately 2-4mSv and also measurable (~2%) morbidity (stroke and femoral / radial artery false aneurysms) and mortality.

4.7.3 Magnetic resonance imaging (MRI) does not require ionising radiation. It can supply useful information on chamber morphology, regional wall motion abnormality and myocardial perfusion. It is also able to display scar tissue by delayed contrast enhancement. Unfortunately the technique does not have sufficient spatial resolution to demonstrate the coronary vessels themselves.

4.7.4 Cardiac scintigraphy (also known as nuclear cardiology) gives a visual demonstration of wall motion and regional perfusion abnormalities but also carries one of the highest radiation doses of between 10-18mSv depending on which isotope and technique is used.

4.7.5 Echocardiography and especially stress echo which are completely free of radiation have been used as useful adjuncts to or filters for more invasive techniques by delineating wall motion abnormalities. These techniques have moderate sensitivity and specificity but do not allow direct visualisation of the coronary vessels.

4.8 Radiation dose considerations

4.8.1 In the very recent past all the major CT manufacturers have focused on radiation dose reduction to such an extent that cardiac CT has moved from one of the highest dose studies (15 – 20 mSv) to among the lowest (0.8 – 2.0 mSv) on most new machines. Considerable variability remains and close attention is required to dose optimization[15] .

4.9 Incidental findings

4.9.1 Several studies have analysed the frequency and spectrum of incidental findings related to cardiac CT. Additional cardiac and non cardiac findings are frequent but the vast majority of these are of minimal or no clinical significance[16-20]. Onuma et al found that 58% of patients referred for CT coronary angiography for clinical indications had a non cardiac finding[20]. In the only study that included self referring patients Horton et al found additional non cardiac findings in 7.8% of patients [18]. The proportion of self referring patients in this study is not known. The use of EBCT and also the exclusion of patients with previous coronary artery bypass grafting (resulting in a smaller acquired field of view) may partly explain some of this difference.

4.9.2 A more recent study by Machaalany et al with a cohort of 966 patients referred for cardiac CT angiography for clinical indications looked at the implications of these additional findings over 18 months[19]. 42% of patients scanned had incidental findings of which only 1% were significant (ranging from confirmed malignancy to vascular thrombus, aortic dissection and ruptured breast implants). The commonest incidental findings were lung nodules, none of which became significant during the 18 month follow up period. There was a significant cost associated with additional tests (around $1,000 per patient) and one patient suffered a major complication related to the investigation of an incidental finding.

4.9.3 In another study Burt et al analysed a cohort of 459 healthy asymptomatic persons who underwent CT scans to assess coronary artery calcification[16]. 59% were recommended for additional follow up and further CT scans to assess non cardiac findings with an average additional 1.3 CT scans per patient in the 24 month follow up period.

4.9.4 Although evidence has not been sought for this, it is likely that in addition to the financial costs and additional radiation exposure there is a psychological burden for previously well individuals being diagnosed with these non-cardiac findings even if the vast majority are non-significant.

Recommendations:

8. Patients should only undergo investigations using ionising radiation for the diagnosis of CHD if there is a clear care pathway in place to deal with both the consequences of identification of cardiovascular risk and the consequences and implications of incidental findings. Preferably that pathway should be dictated and supervised by a cardiologist.
9. In general, IHA CTCA should **not** be offered to patients without the involvement of a cardiologist.
10. Based on the pre-test probability of coronary artery disease (NICE Guidance CG 95, 2010) it is reasonable to offer CTCS to those with a risk of significant coronary artery disease of greater than 10%. Given that self-referrers are asymptomatic, the nearest group for comparison is low risk patients presenting with no angina chest pain (table 1 NICE Guidance CG95, 2010). Therefore only individuals aged over 45 should be able to self-refer for this test.
11. Given the excellent prognosis of a normal CTCA and CTCS, repeat assessment by either CTCA or CTCS for IHA should only be permitted after 5 years in the context of a previous normal scan.

References:

1. WorldHealthOrganisation. http//www.Who.Int/mediacentre/factsheets/fs310/en/index.html 2008
2. British Heart Foundation: *Keep your heart healthy*. February 2009
3. National Institute for Clinical Excellence. Clinical Guidelines, CG95. Chest Pain Of Recent Onset: Assessment And Diagnosis Of Recent Onset Chest Pain Or Discomfort Of Suspected Cardiac Origin. 2010
4. Budoff MJ, Diamond GA, Raggi P, Arad Y, Guerci AD, Callister TQ, Berman D. Continuous Probabilistic Prediction Of Angiographically Significant Coronary Artery Disease Using Electron Beam Tomography Circulation 2002;105(15):1791-6
5. Herzog C, Britten M, Balzer JO, Mack MG et al. Multidetector-Row Cardiac CT: Diagnostic Value Of Calcium Scoring And CT Coronary Angiography In Patients With Symptomatic, But Atypical, Chest Pain. Eur Radiol. 2004; 14 (2) :169-177
6. Kitamura A, Kobayashi T, Ueda K, Okada T et al. Evaluation Of Coronary Artery Calcification By Multi-Detector Row Computed 388 Of 393 Tomography For The Detection Of Coronary Artery Stenosis In Japanese Patients. J Epidemiol. 2005; 15 (5) :187-193
7. Lau GT, Ridley LJ, Schieb MC, Brieger DB et al. Coronary Artery Stenoses: Detection With Calcium Scoring, CT Angiography, And Both Methods Combined. Radiology. 2005; 235 (2) :415-422
8. Raff GL, Gallagher MJ, O'Neill WW, Goldstein JA. Diagnostic Accuracy Of Noninvasive Coronary Angiography Using 64-Slice Spiral Computed Tomography. J Am Coll Cardiol. 2005; 46 (3) :552-557
9. Abdulla J, Abildstrom SZ, Gotzsche O, Christensen E et al. 64- Multislice Detector Computed Tomography Coronary Angiography As Potential Alternative To Conventional Coronary Angiography: A Systematic Review And Meta-Analysis. Eur Heart J. 2007; 28 (24) :3042-3050
10. Sun Z, Lin C, Davidson R, Dong C et al. Diagnostic Value Of 64-Slice CT Angiography In Coronary Artery Disease: A Systematic Review. Eur J Radiol. 2008; 67 (1) :78-84
11. d'Othee Janne B, Siebert U, Cury R, Jadvar H et al. A Systematic Review On Diagnostic Accuracy Of CT-Based Detection Of Significant Coronary Artery Disease. Eur J Radiol. 2008; 65 (3) :449-461
12. Perrone-Filardi P, Musella F, Savareses G et al. Coronary Computed Tomography: Current Role And Future Perspectives For Cardiovascular Risk Stratification. European Heart Journal Cardiovascular Imaging. 2012;13 453-458
13. Brenner DJ, Hall EJ. Computed Tomography – An Increasing Source Of Radiation Exposure. N Eng J Med 2007;357:2277-84

14. Budoff MJ, Cohen MC, Garcia MJ, et al. ACCF/AHA Clinical Competence Statement On Cardiac Imaging With Computed Tomography And Magnetic Resonance: A Report Of The American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training. J Am Coll Cardiol 2005;46:383–402
15. Hausleiter J, Meyer T, Hermann F et al. Estimated Radiation Dose Associated With Cardiac CT Angiography. JAMA 2009 301:500-507
16. Burt JR, Iribarren C, Fair JM, et al. Incidental Findings On Cardiac Multidetector Row Computed Tomography Among Healthy Older Adults. Prevalence And Clinical Correlates. Arch Intern Med 2008;168:756–61
17. Hlatky MA, Iribarren C. The Dilemma of Incidental Findings on Cardiac Computed Tomography. J. Am Coll Cardiol 2009;54;1542-1543
18. Horton KM, Post WS, Blumenthal RS, Fishman EK. Prevalence Of Significant Noncardiac Findings On Electron-Beam Computed Tomography Coronary Artery Calcium Screening Examinations. Circulation 2002;106:532– 4
19. Machaalany J, Yam Y, Ruddy TD, et al. Potential Clinical And Economic Consequences Of Noncardiac Incidental Findings On Cardiac Computed Tomography. J Am Coll Cardiol 2009;54:1533– 41
20. Onuma Y, Tanabe K, Nakazawa G, et al. Noncardiac Findings In Cardiac Imaging With Multidetector Computed Tomography. J Am Coll Cardiol 2006;48:402– 6

Summary of Recommendations

1. IHA CT for lung cancer detection should not be offered to people under the age of 55 as they are unlikely to benefit.

2. IHA CT for lung cancer detection should not be offered to people who have never smoked, or those with a pack history of less than 20 years with no other risk factors as they are unlikely to benefit.

3. Individual risk prediction models should be used to select those patients at risk of developing lung cancer. IHA CT may be offered if the risk is equivalent to 5% in 5 years. If the risk is lower IHA CT may still be offered but the balance of risk and benefit is not known. Annual or biennial screening may be offered from age 55 to 74 but few people aged 55 to 60 will be at sufficiently high risk.

4. IHA CT should only be offered by expert clinicians (radiologists and respiratory physicians), able to explain the risks and benefits of CT for IHA.

5. Information packs on the risks and benefits of CT for IHA, detailing in lay persons' language the limitations, and the risks and benefits of IHA should be made available to individuals prior to undergoing CT scanning.

6. CTC for IHA and outside the NHS bowel cancer screening programme should only be undertaken in individuals in the appropriate age group and not, therefore, under the age of 45 years. Subjects aged under 45 should only be screened if they have an increased risk of colorectal cancer and then in accordance with published guidelines.

7. Individuals with a negative CTC or CTC demonstrating polyps less than 6mm in size and who remain asymptomatic should not undergo further CTC for IHA in an interval less than five years from the initial examination.

8. Patients should only undergo investigations using ionising radiation for the diagnosis of CHD if there is a clear care pathway in place to deal with both the consequences of identification of cardiovascular risk and the consequences and implications of incidental findings. Preferably that pathway should be dictated and supervised by a cardiologist.

9. In general, IHA CTCA should not be offered to patients without the involvement of a cardiologist.

10. Based on the pre-test probability of coronary artery disease (NICE Guidance CG 95, 2010) it is reasonable to offer CTCS to those with a risk of significant coronary artery disease of greater than 10%. Given that self-referrers are asymptomatic, the nearest group for comparison is low risk patients presenting with no angina chest pain (table 1 NICE Guidance CG95, 2010). Therefore only individuals aged over 45 should be able to self-refer for this test.

11. Given the excellent prognosis of a normal CTCA and CTCS, repeat assessment by either CTCA or CTCS for IHA should only be permitted after 5 years in the context of a previous normal scan.

Membership

Dr Giles Maskell, RCR (Chair)
Dr David Baldwin, RCP
Mr Steve Ebdon-Jackson, PHE
Dr Chris Gibson, Medical Physicist
Prof Fergus Gleeson, RCR
Dr Steve Hughes, RCP
Dr John Reid, RCR
Dr Nick Summerton, RCGP
Prof Stuart Taylor, RCR
Mrs Helen Warner, lay member
Dr Mark Westwood, RCP

Mr Ian Chell DH (observer)

Acknowledgements

Thanks are due to Ms Kim Cyrus (RCR) and to Dr Pat Keep (DH) for administrative support and note taking.