Committee on Medical Aspects of Radiation in the Environment (COMARE)

TWELFTH REPORT

The impact of personally initiated X-ray computed tomography scanning for the health assessment of asymptomatic individuals.

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Produced by the Health Protection Agency for the
Committee on Medical Aspects of Radiation in the Environment

ISBN 978-0-85951-611-2

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FOREWORD

i The Committee on Medical Aspects of Radiation in the Environment (COMARE) was established in November 1985 in response to the final recommendation of the report of the Independent Advisory Group chaired by Sir Douglas Black (Black, 1984). The terms of reference for COMARE are:

> "to assess and advise Government and the Devolved Authorities on the health effects of natural and man-made radiation and to assess the adequacy of the available data and the need for further research"

In over 20 years of providing advice to Government and the Devolved Authorities, COMARE has produced 11 major reports and many other statements and documents related mainly to exposure to naturally occurring radionuclides such as radon and its progeny or to man-made radiation, usually that emitted by major nuclear installations.

ii Medical exposures account for over 97% of the annual dose to the UK population from artificial sources of radiation, and constitute approximately 15% of the average annual dose to the UK population, although obviously there will be marked variations in the doses received by individuals in the UK depending on their unique exposure characteristics. While technical innovations promise greater diagnostic accuracy and an increased range of clinical applications, there is also the potential for greater radiation doses to individuals, from interventional techniques and from changes of practice within X-ray computed tomography (CT). This potential increase is a marked difference to the trends in radiation dose to patients observed during the 1990s, where doses to patients were seen to be falling consistently.

iii The Department of Health's radiation protection concerns increasingly centre on medical exposures. As a consequence of this concern, the Department of Health in 2005 instructed COMARE to include within its sphere of interest, radiation protection from medical practices. It was decided that the use of CT scanning of the asymptomatic individual was to be addressed as a first priority. To achieve an appropriate review of this topic, COMARE established its Medical Practices Subcommittee. The subcommittee incorporates members from COMARE, the Royal College of Radiologists, the Royal College of Physicians, the independent sector and also a patient representative.

iv The subcommittee's terms of reference are:

> "to advise COMARE on the health effects arising from medical and similar practices involving the use of ionising and non-ionising radiation through assessment of the available data and to inform COMARE of further research priorities"

When the subcommittee had finished its deliberations they were passed to COMARE for consideration by the full committee with the aim that in due

course COMARE would present its advice to the Department of Health. That advice is contained in this, our Twelfth Report.

v The aim of this report has been to provide advice for the Department of Health on the practice of personally initiated CT scanning of asymptomatic individuals. Consequently, this report does not consider the relevance of such scanning techniques to a population screening programme. It focuses solely on the context of scanning the individual.

CHAPTER 1

INTRODUCTION

1.1 X-ray computed tomography (CT), originally known as computed axial tomography (CAT), uses specialised X-ray equipment to obtain image data from different angles around the body. Digital processing of the information results in detailed cross-sectional images of body tissues and organs in either a two- or three-dimensional format.

1.2 The idea of CT was conceived in 1967 in England by Godfrey Newbold Hounsfield at the THORN EMI Central Research Laboratories, being publicly announced in 1972. The system was independently developed by Allan McLeod Cormack at Tufts University and they shared a Nobel Prize in medicine in 1979. The original prototype, developed in 1971, used americium as the gamma source, and took 160 parallel readings over 180 angles, each 1° apart. It took 9 days to collect sufficient information about the object being scanned and a further 2.5 hours to reconstruct the data into an image. Later the gamma source was replaced by a more powerful X-ray source, which reduced the scanning time (Hounsfield, 1973).

1.3 The first commercial CT system (the EMI scanner) was installed in Atkinson Morley's Hospital in Wimbledon. It was limited to making tomographic sections of the brain and the first patient brainscan using the machine was obtained in 1972. To reduce the dynamic range of the radiation reaching the detectors, the machine required the use of a water-filled Perspex tank, with a pre-shaped rubber head cap enclosing the patient's head. However, the machine did acquire the image data, taking between 4.5 and 20 minutes per 180° scan, with 7 minutes required to process each image (Beckmann, 2006).

1.4 CT scanners have gone through multiple phases of technological developments from single slice static machines to single slice spiral/helical machines. In the last six years, there have been further significant advances in CT technology. In particular, the recent development of multidetector or multislice CT has increased the speed of scanning and enabled high resolution reconstruction of images in all planes. Other recent developments allow consideration of volume CT acquisition. A chest examination that previously required 10 separate breath-holds of 10 seconds each can now be performed with a single 10-second breath-hold. Software packages have been developed to utilise these benefits, with modern scanners being able to reconstruct a study of 1000 images in less than 30 seconds. In addition, as with most digital technologies, these developments have been achieved with a decrease in the real costs of equipment. The result has been increased patient throughput at lower costs per capita, which has consolidated CT as a major first-line diagnostic modality and established its potential as an imaging modality for screening.

1.5 Radiation exposure from medical practices accounts for the largest UK population dose from artificial sources of radiation and, within the UK, the use of CT has doubled in the last 10 years. Of the dose received from medical X-rays, more than 47% is contributed by CT scans (Hart and Wall, 2004). The average annual dose from both natural and artificial radiation is 2.7 mSv, of which medical radiation exposure accounts for around 15% (Hughes et al, 2005). Currently in the UK, over 90% of CT scans are undertaken on NHS patients. However, there appears to be an increasing trend for commercial CT scans to be offered to the general population. CT scanning now has the potential to contribute to preventative healthcare through its use in the scanning of asymptomatic individuals, either with whole body scanning or through imaging of specific anatomical regions.

1.6 CT scanning of the asymptomatic individual is marketed directly to the public as a form of preventative medicine to give individuals peace of mind. Under this premise, scanning is currently offered for several anatomical regions:

(i) whole body (from the neck to the pubic symphysis bone),

(ii) cardiac,

(iii) lung,

(iv) colon.

CT scans can reveal the early stages of deformity, deterioration and disease. While there may be benefits from this approach, there are also detriments to be considered, such as those from the radiation dose involved and the psychological impact on the individual. It is important to balance the medical science, patient care, ethics and economics of such tests (Council on Scientific Affairs, 2003).

1.7 Clinically, CT screening is currently performed for people thought to be at risk for specific diseases. Lung cancer is the primary cause of cancer-related deaths worldwide, due to the difficulty of early detection at a surgically curable stage. Indeed CT has been used to screen for lung cancer in Japan since 1993 (Kaneko et al, 2000). There is, however, dispute over the efficacy of using CT screening for lung cancer identification and whether mortality rates are reduced. Atherosclerotic disease is one of the leading causes of death in the western world, and coronary calcification measured by CT is considered to be an early indicator in asymptomatic patients believed to be at risk. Virtual CT colonography has been used to examine the colon and rectum to detect polyps and cancers in asymptomatic individuals who are considered to be at risk of developing a colorectal cancer.

1.8 Dependent on research findings and technological advancements, some pathologies could, ultimately, be considered for the introduction of a screening programme for the general population. However, a screening programme should be developed as part of an integrated system that incorporates the provision of adequate information for the individual being tested as well as the facility for further investigations and treatments (BMA, 2005). In this report, only the scanning of asymptomatic individuals is considered and not the use of these techniques for a population screening programme.

1.9 While CT scanning has advanced the accuracy of diagnostic radiology and its benefits are clear, there are potential detriments also. The level of radiation dose received by the individual may be significant. CT scanning of asymptomatic individuals can result in detection of a range of pathologies

including conditions of no clinical significance and conditions that will not influence an individual's outcome, both situations that can be considered as examples of pseudodisease. Such findings could potentially result in needless further investigations, which themselves carry additional risks and cost implications, increase the individual's anxiety levels and affect their quality of life. These adverse features are discussed further in Chapter 2. There are also important issues concerning sensitivity and specificity. Scans of specific anatomical regions should be optimised for this purpose and may not be able to detect conditions other than those targeted. It may not be possible to give an asymptomatic individual a complete 'all clear' after a scan, even though such reassurance is the expectation of the scanned individual. It is also not clear whether CT imaging detects some cancers (eg lung) that are not as clinically aggressive as those identified following presentation with symptoms. It is possible that some tumours detected are ones that might be present at the individual's death and would not have been life threatening, skewing the apparent benefit of detection by scanning. In this report, the term 'overdiagnosis' refers to the detection of malignant disease that would never present clinically during the lifetime of the individual.

1.10 The level of radiation received by the individual is an additional concern, particularly with whole body CT scanning. For an asymptomatic individual the potential risk may outweigh the benefits. The dose received by an individual can vary substantially depending on the type of scan employed and the machine and protocol used.

1.11 This report looks at the justification of these scanning procedures, including CT scans of the whole body and of key anatomical areas, the latter being designed to allay the concerns of asymptomatic individuals with regard to defined diseases.

1.12 It has taken into consideration published peer-reviewed data and evidence regarding CT scanning of asymptomatic individuals and information provided by a number of independent sector organisations offering such services. The latter included commercially sensitive information which has not been reproduced within the report.

1.13 The report consists of nine chapters, which include this introduction, a chapter on the rationale behind CT scanning of the asymptomatic individual, five chapters on scanning anatomical regions – whole body, lung, heart and colon and more general scanning. The final two chapters provide conclusions and recommendations. A glossary and references are provided.

CHAPTER 2

RATIONALE

Background – radiation protection principles and regulatory factors

2.1 In 1990 the International Commission on Radiological Protection reaffirmed three key principles of radiation protection (ICRP, 1991):

(i) justification – exposure to radiation must produce sufficient benefit to the exposed individuals, or to society, to offset the potential radiation detriment,

(ii) optimisation – implementing procedures and techniques to keep exposures as low as reasonably practicable, economic and social factors being taken into account,

(iii) dose limitation – keeping radiation doses received within specified limits.

2.2 In the context of medical exposures, justification and optimisation apply. Dose limitation is not used for medical exposures but the concept of diagnostic reference levels has been introduced to support the control and periodic reduction of radiation doses from diagnostic procedures.

2.3 The hazards associated with ionising radiation are addressed in a number of European Council Directives and subsequently in legislation in Great Britain and Northern Ireland. For CT scanning, and the protection of the asymptomatic individual, two sets of regulations are of particular importance:

(i) The Justification of Practices Involving Ionising Radiation Regulations (2004),

(ii) The Ionising Radiation (Medical Exposure) Regulations (2000).

2.4 The guidance on the application and administration of The Justification of Practices Involving Ionising Radiation Regulations (2004) indicates a range of types of practice that existed prior to 13 May 2000, the implementation date for the EC Basic Safety Standards Directive 96/29/Euratom. This Directive establishes the need for the justification of new classes or types of practice involving ionising radiation. Medical exposures using CT for diagnosis are included as an existing type of practice within this guidance. CT scanning of the asymptomatic individual is considered to be early diagnosis and is therefore incorporated as an existing practice.

2.5 The Ionising Radiation (Medical Exposure) Regulations 2000 require that all individual medical exposures are referred, justified and optimised. The Regulations require an identified person to take legal responsibility for deciding whether an individual medical exposure is justified. In the UK, this person is known as the ‘practitioner’. Such persons must be adequately trained to carry out the task of justification and be entitled to do so by their employer. Justification of exposures must take into account medical information about the individual provided by a referrer (also a duty holder under the Regulations) and should be based on the available scientific evidence. Both the referrer and the practitioner must be registered healthcare professionals.

2.6 Justification cannot be retrospective. Since all persons exposed suffer radiation detriment, the practitioner's decision as to whether an individual medical exposure is justified must be made prior to the exposure, and must be valid whether the test result is subsequently positive or negative. Procedures can only be justified if the individual for whom the exposure is proposed will receive a predictable benefit that outweighs the detriment, or if there is an overall net benefit to society.

2.7 Optimisation of every medical exposure is the responsibility of the practitioner and of the operator who undertakes the practical aspects of a medical exposure, to the extent of their respective involvement. To assist in optimisation, the employer must ensure that written protocols are in place for all standard procedures which must be specific to each piece of equipment. Such protocols should include exposure factors for each routine examination.

Potential benefits and detriments

2.8 Depending on the initial clinical suspicion as to the presence of disease, the potential benefits from a diagnostic medical exposure are:

(i) evidence in favour of, or against, a suspected diagnosis,

(ii) monitoring the progress of known disease,

(iii) identification of an unsuspected pathology.

2.9 In all cases these benefits must be balanced against the risks, not only from the radiation detriment but also from potentially misleading or inaccurate results. The magnitude of the latter risks depends strongly on the disease prevalence, and the most appropriate diagnostic investigations are likely to be different in groups with suspected, as opposed to unsuspected, disease. A test which is considered justifiable for patients presenting with certain symptoms may not necessarily be justifiable or clinically valuable when applied to an asymptomatic individual.

Testing a potential diagnosis

2.10 Guidance on the balance of risks and benefits for medical exposures has been produced by international bodies (EC, 2001) and UK professional bodies (RCR, 2003). These guidelines are intended primarily to assist the person referring a patient for a medical exposure, and provide clear recommendations stating which procedures are likely to be useful, and which are not, for a wide range of clinical conditions and suspected diagnoses. The guidelines also state the relative radiation detriment for each procedure, assisting the practitioner and others to assess whether the likely benefit justifies the risk.

Monitoring known disease

2.11 In these cases the individual disease status and clinical condition of the patient will primarily determine the justifiable level of risk. Nevertheless, practitioners still have a duty to ensure that the benefit to be gained in terms of improved or altered treatment is sufficient to outweigh the risk, especially in the case of chronic minor disease.

Discovering unsuspected pathology

2.12 There may be benefits from detecting wholly unexpected findings, and there are numerous reported cases where serious pathology has been revealed during an examination undertaken for another purpose. However, the overall likelihood of discovering wholly unsuspected significant disease is low, and the justification for the examination cannot have been based on the benefits that may have been conferred by the unsuspected finding, since by definition the practitioner was not aware of this potential outcome when the procedure was justified. It follows that justification for scanning asymptomatic individuals can be based only on the first potential benefit listed above, which in turn requires a suspected diagnosis.

Risk factors and suspected diagnoses

2.13 The likelihood that an asymptomatic individual has a suspected diagnosis will vary according to the presence or absence of associated risk factors. In some cases, these factors will be sufficiently well correlated with the disease in question as to raise the likelihood to a level at which a higher risk investigation may be justifiable. A practitioner using such factors to justify a medical exposure would require an evidence base indicating probability of disease in relevant populations.

2.14 Earlier diagnosis does not always improve prognosis, and there may be no benefit from diagnosing some indolent pathologies which would have remained asymptomatic. The term pseudodisease is used to describe disease that does not affect the length or quality of a patient's life. A large amount of pseudodisease within a population may render a screening programme ineffective and, for an individual, may result in additional testing with potential morbidity and mortality. Two types of pseudodisease occur. Type I is disease detected on screening that does not necessarily progress to symptomatic disease. Type II is indolent disease that occurs in patients dying from other causes. An example might be prostatic carcinoma, with the vast majority of men diagnosed with clinically localised prostatic carcinoma dying with rather than of their disease (Albertsen et al, 2005; Potosky et al, 2000).

Radiation detriment

2.15 Excess cancer risk has not been demonstrated by epidemiological studies at doses below 100 mSv. The estimated risks from diagnostic medical exposures are based primarily on extrapolation from the observed increased incidence of cancer in exposed populations, generally at higher doses. These groups include the Japanese atomic-bomb survivors (Preston et al, 2004), patients treated with radiotherapy for benign conditions (Weiss et al, 1994), children irradiated *in utero* (Doll and Wakeford, 1997), and workers occupationally exposed (Cardis et al, 1995). The internationally recommended risk factor for fatal cancer induction is 5% per Sv for an adult population or 0.005% per mSv using the linear non-threshold hypothesis (ICRP, 1991). Risks are generally higher in younger patients and are slightly higher in females than in males, as demonstrated in recently published estimates of age-specific death rates (BEIR Committee, 2006 – see Table 12 D-1, D-2 for all cancers).

Figure 2.1 Deaths per 100,000 persons exposed to a single whole body dose of 10 mSv

2.16 A typical CT scan with an effective dose of 10 mSv is associated with a predicted average risk of fatal cancer induction of 1 in 2000 over a lifetime (Figure 2.1). Although this is low compared to the spontaneous fatal cancer risk of approximately 1 in 4 (Quinn et al, 2000), the public health impact in terms of numbers of excess cancer cases is not negligible. If 100,000 people undergo a CT scan every 5 years from age 40 to 70 years, receiving an effective dose of 10 mSv from each scan, then the estimated impact is approximately 240 excess fatalities using the age-specific death rates shown above. For scanning at higher frequencies (every two years or annually) this increases to 600 and 1200 fatalities, respectively. These estimated risks are proportional to dose.

Clinical benefits, detriments and test outcomes

2.17 No diagnostic test is correct in every case. Imaging procedures often have a high sensitivity (eg 95%), but that still means that 1 in every 20 abnormal cases would be missed (false negatives). If a procedure is being used and optimised at an early stage in the diagnostic process then it is likely that the specificity will be slightly lower (eg 85%), meaning that 3 in every 20 normal cases would be wrongly diagnosed (false positives). Sensitivity and specificity values for CT scanning will vary according to the condition being investigated, but these values are representative of published data for major pathologies (Beinfeld et al, 2005). When making judgements about the overall benefits to be gained from a medical exposure, the practitioner must keep in mind all potential outcomes. The principles can be illustrated using the simplest model of this process, in which a diagnostic test is used to detect the presence or absence of a single disease condition. The four possible outcomes are shown in Table 2.1.

Table 2.1 Benefit and detriment from positive and negative scan results in people that have disease or are free from disease

	Test positive	**Test negative**
Person has disease	**'True positive'** Benefit, if the condition is treatable, and early diagnosis improves the outcome	**'False negative'** Detriment, if the condition is progressive and diagnosis is not made by another means
Person free from disease	**'False positive'** Detriment, from additional tests and/or unnecessary treatment, as well as being unnecessarily alarming	**'True negative'** Benefit, in terms of reassurance and also eliminating an incorrect diagnosis

2.18 In the case of medical exposures the exposed person will always suffer a radiation detriment in the form of a predicted increased cancer risk. It is therefore essential that the clinical benefits from true positive and true negative results outweigh the detriments from false positive and false negative results.

Effect of sensitivity, specificity and disease prevalence

2.19 The diagnostic value of a test depends on the disease prevalence as well as on the inherent ability of the test to identify or exclude disease. Patients who report symptoms, and who are referred to secondary care and undergo investigation for a specific suspected condition, will have a high disease prevalence. For a disease prevalence of 30%, and assuming a test with 95% sensitivity and 85% specificity, the distribution of test outcomes is shown in Table 2.2.

2.20 Even in this group, the benefits gained by the 28.5% of patients with true positive results may be significantly offset by the 12% of patients with false positive or false negative results.

Table 2.2 Distribution of test outcomes in people who have disease or are free from disease where the disease prevalence is 30%

	Test positive (%)	Test negative (%)
Patient has disease	28.5	1.5
Patient free from disease	10.5	59.5

Table 2.3 Distribution of test outcomes in people who have disease or are free from disease where the disease prevalence is 3%

	Test positive (%)	Test negative (%)
Person has disease	2.8	0.2
Person free from disease	14.6	82.4

2.21 Individuals who are asymptomatic, in whom the index of suspicion is low and who have not undergone any primary or secondary care assessment, will have a much lower disease prevalence. The corresponding distribution of outcomes for the same test when the disease prevalence falls to 3% is shown in Table 2.3.

2.22 In this group of individuals, those with the greatest benefit (2.8% true positives) are considerably outnumbered by those for whom the test itself has produced detriment (14.8% false positive or false negative). Moreover, the benefits gained by the 82.4% of individuals with true negative results are significantly less in this case. It is true that they do not have the disease in question, but this was true for 97% of these individuals before the test was performed.

2.23 For low disease prevalence (2% or less), there are at least twice as many individuals suffering some detriment as those gaining clear benefit, even for high quality tests combining 95% sensitivity and specificity (Figure 2.2). For lower levels of specificity, which are more likely in clinical practice, there are between five and ten times as many individuals suffering detriment when the disease prevalence is less than 2%.

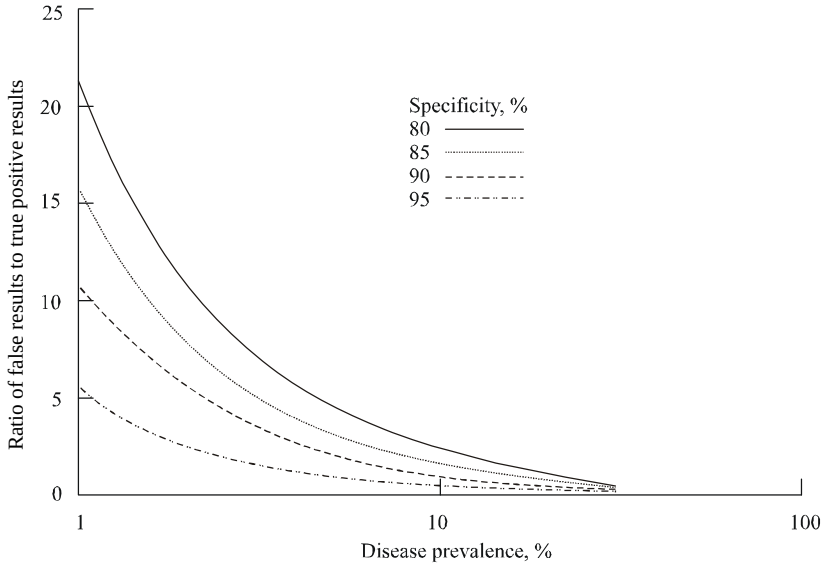


Figure 2.2 Ratio of individuals with detriment (all false test results) to the individuals with the greatest benefit (true positives only) as the disease prevalence alters for specificities in the range 80% to 95%

Imaging for multiple pathologies

2.24 The simple model above is based on a single test applied to a single potential diagnosis. CT imaging is capable of diagnosing a wide range of pathologies, and it may be possible to design imaging protocols which are capable of, if not optimal for, detecting any of several possible conditions. If a true positive result is defined as a positive (correct) test result for any of these, then the fraction of persons benefiting from the examination increases. Unfortunately false positive results increase in a similar manner, so that the ratio of those receiving benefit to those experiencing detriment remains similar. If the test has an independent 85% specificity for each of four potential diagnoses, then the probability that a normal individual will receive at least one false positive result is almost 0.5 (ie almost 50% of normal individuals will receive a false positive result).

Psychological impact – benefit and detriment

2.25 The potential psychological impact of receiving test results from examinations of asymptomatic individuals can be considered on two levels: firstly, how the individual decision-making process might be altered by the receipt of test results, particularly where error exists in the test result, and secondly, the wider social impact of test results. There is little direct research on the potential psychological responses to CT scan results, hence the following information has been generalised from studies in other medical contexts, including other uses of medical radiation.

2.26 Psychological outcomes at an individual level will depend on the motivations of the subjects undergoing investigation. The psychological outcome will be influenced by the positioning put forward by those promoting the procedures. A desire for a healthier lifestyle, as well as increased anxiety about personal health, have been found to be factors that increase demand for personal health screening (Michie et al, 1995).

2.27 Public health campaigns are often based on a fear–reassurance model, creating fear through identifying the negative health consequences of certain behaviours, such as smoking, and reassurance by providing a route for further action to be taken. Research has shown that messages that inspire fear or guilt can be persuasive in making individuals take positive action on their health, provided there is clear information given to act on the fear (Robberson and Rogers, 1988).

2.28 In order to generate demand for personal health screening, the communications models adopted by private firms might employ a similar approach. It is essential therefore that in the case of an adverse test result from an investigation, very clear processes should be in place through which the individual can receive further confirmation and treatment as appropriate. This planning is important because, when the stakes become higher, psychological factors take a more important role in decision making. For example, when given medical results on relatively minor illnesses, patients are able to take in many of the details and evaluate treatment options. However, when given a diagnosis of cancer, patients may respond by remembering only the bad news, and forgetting treatment details. Thus, the problem becomes not the investigation, but the inability of the individuals to deal with the information they receive (Press and Browner, 1994). Additionally, recent studies have found that people are more likely to seek treatment for a disease they see as severe and treatable, than for one that is severe and untreatable (Dawson et al, 2006), which suggests that understanding treatment options can affect the decision to have an investigation in the first place.

2.29 For an individual living in fear of a particular disease, a normal result from an examination can reduce stress and leave a more positive feeling than

before the examination took place. Similarly, and perhaps counter intuitively, an adverse result can reduce uncertainty which may result in greater peace of mind for the individual and an increased likelihood of taking appropriate action to deal with any condition. Research into ovarian cancer screening programmes found that false negative results caused distress (Andrykowski et al, 2004). However, this distress was short term and typically localised around the condition; levels of distress were found to return to baseline levels within four months. These findings suggest that where an individual carries a belief that they are at risk, then personal health screening can provide some positive psychological benefits.

2.30 In the case of somatoform disorders, such as hypochondria, similar benefits of personal health screening may exist, by providing relief from anxiety over health. Yet, if a side effect of the promotion of personal health screening is to increase the general level of health anxiety in the population, then there are some serious potential consequences as a result of the relatively higher false positive and false negative rates that occur when scanning asymptomatic individuals.

2.31 The lower incidence of the illness for which the subject is being investigated means there is an alteration of the 'benefit–detriment' outcome away from benefit and towards detriment. Research has demonstrated that public responses to radiation risks are not uniform. Individual perceptions are highly dependent on both the source of radiation, and the individual context in which the radiation exposure has been received (Slovic, 1996). Although there are few studies to date on risk perception relating to CT scans, a number of more general studies have found that individuals perceive exposure to medical radiation as being very low risk, compared to other sources of radiation such as nuclear power. Studies on radiation risk have shown that public acceptance of radiation in a medical context is a function of the high levels of trust in which medical professionals are held (Slovic, 1996). Trust is based on the capability of the medical professional to remove uncertainty, and the information provided can thus move this uncertainty in a particular direction – for example, by providing greater certainty through a correct diagnosis. This level of trust has translated into an expectation that the results of medical tests will be largely accurate, and conclusive. Even if, by personally initiating CT scans, individuals are contributing to the increase in incorrect results, the responsibility or perception of blame for any incorrect results is likely to lie with the medical professional. At an individual level, receipt of an incorrect result may result in a reduced trust towards the medical professional, and a greater likelihood of requesting many tests in order to achieve certainty in diagnosis.

2.32 Such individual-level impacts can also create group-level effects. Public perception of risks is likely to be amplified or attenuated by a range of social factors. The impacts of incorrect diagnoses, either adverse or reassuring, are not restricted to the individual. The social amplification of risk is a well-documented phenomenon in psychology (Kasperson et al, 1988), with the King's Cross station fire in 1987 and the Three Mile Island radiation incident in 1979, and the future of genetically modified food, being examples where the interpretation of the danger from the risk has been substantially greater than the physical harm. On the other hand, the risks of, for example, naturally occurring radon gas and smoking are socially attenuated, and interpreted as being of lower risk than is actually the case.

2.33 Where there is a large difference between the perceived public benefits of investigation of asymptomatic individuals, as created by promotional activities or the media, and the actual efficacy of the tests then there might be

a reduction in the trust held in medical radiation as a whole. If the trust in the technology, or the way it is applied, fails then the perception of the risk of having a test may be amplified and the public could question the value of medical radiation as a whole, and avoid treatment. This phenomenon is comparable to that seen in the case of the measles, mumps and rubella (MMR) immunisation. Given the current public acceptance of risks associated with medical radiation technology, the psychological impact of unregulated health screening is potentially much wider than that of the individuals receiving their test results. An example of this is a woman who underwent genetic testing, which indicated a likelihood of breast and ovarian cancers. After an operation to remove the ovaries, it was found that the test results were incorrect – having been mistaken for another woman's (Peres, 1999). Although this could be dismissed as an isolated case, it raises questions over how the high level of media coverage may have led to public uncertainty about the accuracy and reliability of the testing procedures (Brashers, 2001).

Specific issues in CT scanning of asymptomatic individuals

2.34 In CT scanning of the asymptomatic individual, as discussed above, a clinical benefit may be the discovery of an unknown or unsuspected pathology, possibly enabling quicker treatment where appropriate, with the potential for an improved outcome for the individual. Where the CT scan demonstrates that there is no untoward pathology present, there may be a psychological benefit to the individual from the reassurance that 'one is well' (Hillman, 2003).

2.35 The most obvious detriment associated with CT scanning is the radiation dose itself, which will be significant, especially if the test is repeated at regular intervals. The dose received by an individual can vary substantially depending on the type of scan and protocol used as well as on the machine itself. The potential risk associated with the radiation dose may outweigh the benefits for an asymptomatic individual.

2.36 CT scans are usually optimised for a specific purpose and therefore may not be able to detect other conditions. Consequently the reassurance provided by a negative or 'all clear' report following a CT scan might be misleading.

2.37 As discussed, a number of CT examinations will result in the detection of lesions that may be clinically unimportant or non-life-threatening. These findings may result in further investigations, which may themselves carry additional risks to the individual (Furtado et al, 2005).

2.38 Further investigations may involve ionising radiation and thus carry an additional associated detriment. They may involve more invasive procedures with associated morbidity and in extreme cases mortality. The risks associated with these investigations may be difficult to quantify, particularly before the CT scan takes place, as their magnitude will depend heavily on initial findings. Nevertheless the individual should be made aware of the potential maximum detriments. Review of commercial websites and client information literature indicates that this is not currently provided. Without comprehensive information, individuals cannot make an informed choice regarding the procedures offered. It is essential that asymptomatic individuals, although starting from a different position, should have similar opportunities for discussion on the benefits and detriments as relevant to their situation.

2.39 Moreover there may be resource and financial implications from the additional investigations (Beinfeld et al, 2005). It may not be possible for these to be carried out at the unit that performed the CT scan, resulting in the individual having to be referred elsewhere. The decision to carry out further, possibly needless, investigations may place additional financial or psychological

burdens on the individual (Hillman, 2003). Furthermore, if the individual is referred to the NHS for the investigations, there may be resource implications for the service.

2.40 This situation contrasts starkly with a national screening programme, which is a whole system, not just a single test. Screening programmes take into account the need to provide the patient with adequate information about the initial and possible subsequent investigations, as well as building in the provision for further investigation and treatment (National Screening Committee, 2003). Such programmes are properly managed and monitored, with effective quality assurance in place to ensure that more good than harm results (BMA, 2005).

2.41 Electing to have a CT scan, even in the absence of symptoms, may have implications for life assurance applications or premiums. When applying for an insurance policy, customers must answer insurance questions accurately and to the best of their knowledge and belief. The results of personally initiated and asymptomatic CT scans must be disclosed when answering the insurer's questions. Customers must inform life assurance companies if they have had CT scans for screening purposes in the absence of symptoms just as they must for any other elective investigations or medical consultations (Personal communication, Association of British Insurers, 2007).

Medical responsibility

2.42 For symptomatic patients who require CT scanning, the established approach within healthcare services in the UK would be a referral after seeing their general practitioner (GP) or hospital specialist. This means that they will be progressing along a care pathway and should receive considerable information and have occasion for discussion. The discussions should include information about risks and potential errors as well as potential benefits. Sufficient information must be provided to enable individuals to make informed decisions about consent to medical exposures.

2.43 For asymptomatic patients, whether or not the CT scan demonstrates any pathology, responsibility for the medical management of the individuals still needs to be considered. This responsibility would normally fall to the individual's GP. However, when an asymptomatic individual has a CT scan performed at an independent centre, that person may elect for the results of the CT scan not to be passed on to their GP. This failure to share information may have implications for the future care of the individual. Coordination of scan results may also be complicated by the increasing use of multiple providers for the diagnosis and treatment of disease.

Summary

2.44 All medical exposures, including CT scans on asymptomatic individuals, are subject to legislative control to ensure that risks and benefits are properly considered. Duty holders have specific and personal responsibilities to ensure that adequate medical information about the individual is provided as part of the referral, that this information is sufficient to justify the proposed procedure in an individual showing no symptoms of disease, and that CT scan parameters are optimised for that specific procedure.

2.45 The radiation dose from a CT scan is significant, with a consequent predicted increase in cancer risk. Current estimates of age-related radiation risks indicate approximately 240 radiation-induced fatalities in a population of 100,000 individuals undergoing CT scans every 5 years from age 40 to 70 years. The personal risk is small compared to the natural incidence of cancer, but the population health impact of frequent scanning would be measurable.

2.46 CT scans, as all diagnostic tests, are not perfect. A population of asymptomatic individuals will have a relatively low prevalence of serious disease, and hence will yield a large fraction of false positive results. Even for excellent quality tests (95% sensitivity and specificity) the number of false positive results will exceed the number of true positive results whenever the prevalence of disease is less than 5%. In addition to diagnostic errors, scanning a low prevalence population will also produce pseudodisease, either by detecting precursor conditions of unknown clinical significance (Type 1) or by correctly diagnosing indolent disease which would not have progressed (Type 2).

2.47 At an individual level there can be a number of benefits of investigation, such as a reduction in anxiety provided through reassurance. Such benefits are likely to be greatest where the individual has a close emotional connection to a disease, such as through a family history. However, at a broader level, the number of false positives and false negatives present with investigation of asymptomatic individuals could result in an overall reduction in the trust held in medical professionals and uncertainty over the efficacy of medical radiation technology, an impact that could be amplified to a wider mistrust in the general use of radiation for medical purposes.

2.48 Asymptomatic individuals undergoing CT scanning will require information on radiation risks, the potential for diagnostic error, the likelihood of further investigations being required, and any risks associated with subsequent scans. They will also require advice on how any follow-up should be undertaken, and how to integrate any findings from the examination with existing care pathways. If follow-up procedures are undertaken in NHS facilities, then a considerable additional burden can be anticipated in order to resolve uncertainties arising from the original investigation.

CHAPTER 3

CT SCANNING OF THE WHOLE BODY

Introduction

3.1 At present, full or whole body CT scanning is only performed in the USA, where a whole body scan refers to a scan of the entire body. In the UK, whole body CT scanning is the term generally used to refer to scanning of the torso – ie chest, abdomen and pelvis – and may include multiple scans of different anatomical regions to investigate the 'whole body'. It usually does not include the head, neck or limbs. This chapter presents the evidence for potential benefit and detriment from the use of such scans in asymptomatic adults, who may be encouraged to seek them without medical indication in response to their recent availability in the commercial sector in the UK, where they are marketed as having the potential to confer significant health benefit.

Whole body CT scanning: rationale and scope

3.2 The torso includes major vital organs such as heart, lungs, kidney, liver, pancreas, spleen and ovaries, also the breasts, digestive tract and major blood vessels (in particular, the aorta and coronary arteries). The potential health benefit of CT scans targeted at these organs would include the detection of early or pre-cancerous lesions, aneurysms and atheroma. Such scans would have no role to play in the detection of other common illnesses for which screening for early detection, using other specific methodologies, has been demonstrated to have clear health benefit – for example, in breast cancer (mammography), cervical cancer (Pap screening), diabetes, hypertension, obesity and osteoporosis.

Health benefits of whole body CT scanning

3.3 There are two mechanisms by which whole body CT scanning could conceivably lead to health benefits to the individual:

(i) early detection of disease leading to earlier and more effective intervention with concomitant increase in survival and decrease in morbidity,

(ii) enhanced peace-of-mind and hence well-being due to the positive psychological benefits of a normal CT scan demonstrating absence of disease.

3.4 The evidence for each of these potential benefits is discussed below.

Early detection of disease and reduced mortality (true positives)

3.5 To contribute to the avoidance of future ill-health in otherwise asymptomatic individuals any screening programme must fulfil the following criteria.

(i) It must lead to the earlier diagnosis of disease for which there is effective treatment.

(ii) This treatment is more effective in the earlier rather than later stages of the disease.

(iii) The disease progresses at a rate sufficiently slow for there to be a suitable interval in which to implement effective treatment.

(iv) The disease so identified must also be one which would progress during the lifetime of the individual.

(v) The disease must contribute to severe ill-health or the death of the individual, ie a condition that the individual would be likely to die from rather than die with.

3.6 Examples around this last issue abound. For example, in the current controversy over screening for prostate cancer by measuring the blood-borne prostate specific antigen (PSA), the use of this test may lead to the detection of slowly developing prostate cancer at very early stages in men in whom there might not be symptomatic disease in their lifetime.

3.7 Generic to all cancer screening programmes are the issues of lead and length time bias, of which the prostate cancer controversy is a good example.

3.8 Whilst there are one or two anecdotal reports of early detection of malignant tumours (Henschke et al, 2006), there are no population based data reporting the efficacy of whole body CT scanning as a screening tool for detecting early disease in asymptomatic adults.

3.9 The radiation dose from any medical exposure should be optimised. The 'low dose' whole body settings fail to optimise the images of a specific organ, reducing the sensitivity for potential early detection of any specific condition or anomaly within a specific organ. For example, protocols for settings of the scanner, dosage of contrast agent, sequence and timing of images would all be specific to individual organs. Those for lung masses would be very different from those for liver tumours and different again for colonic masses.

Positive health benefits from a negative scan (true and false negatives)

3.10 There have been no studies reported in the literature in which the perceived benefit to individuals of a negative whole body CT scan has been evaluated. There are a number of high-profile celebrity reports of such benefit (including Oprah Winfrey in the USA and Richard Madeley and Judy Finnegan in the UK) and these individuals support these procedures. Such support is likely to be highly influential on public opinion. However, there are three important issues to be considered in this respect.

(i) There is the potential for those with negative scans (true negatives) to interpret this as a 'clean bill of health' thus reinforcing reluctance to change an 'unhealthy' lifestyle.

(ii) It may lead to a failure to seek appropriate medical advice with regard to symptoms of conditions which would be outside the scope of the whole body CT scan in the mistaken belief that no abnormality was present.

(iii) It may deter individuals from engaging in other screening programmes of demonstrated effectiveness – for example, for hypertension or diabetes.

3.11 Inevitably, false negatives may be reported in individuals who have malignant disease (for which they believe they have been scanned) but the malignancy has not been detected due to the suboptimal quality and lack of specific targeting as above. This lack of detection may lead to delayed diagnosis and treatment with potentially dire consequences. It may, however, result in inappropriate psychological reassurance.

3.12 Because of the high rate of false positive findings with this technology, a substantial proportion of individuals who undergo a whole body CT will require further investigation to evaluate suspected pathology which has a high likelihood of being insignificant in terms of morbidity and mortality. The frequency of findings increases dramatically with age and is not related to the detection of early disease and, where applicable, earlier treatment and longer survival.

3.13 Thus many of those undergoing whole body CT scanning will not receive the comfort of an 'all clear' result, which is one of the main planks of the commercial marketing of this procedure.

Potential harm

3.14 There are a number of serious potential risks associated with whole body CT scanning and these are currently unavoidable.

Radiation exposure

3.15 The radiation exposure from a whole body CT scan is between 4 and 24 mSv (biologically effective dose). An effective dose of 10 mSv (equivalent to 500 chest radiographs – Hart and Wall, 2004) results in a risk of cancer death of 1 in 2000.

3.16 Of particular concern with regard to radiation exposure from whole body CT scans are the following issues.

(i) The dose varies substantially between scans depending on technical and anatomical characteristics. The dose to individuals for similar scans may vary by a factor of ten. This variation may be due to differing size of the individual being scanned, and the type of CT procedure, system and operating technique. Thus, in extreme cases, an individual may be exposed to up to 100 mSv during a whole body CT scan, conferring a substantially higher risk of malignant disease to some (Anderiesz et al, 2004). Further, newer and increasingly sophisticated CT scanners tend to lead to higher rather than lower exposures (Allan and Williams, 2003) unless every effort is made to optimise the protocol.

(ii) The high rate of anomalies detected leads to a high rate of investigations for what are identified eventually as benign conditions of no clinical significance. Many of these further investigations will involve further CT scans with intravenous contrast with further radiation exposure of the individual. As discussed later in this section, it is likely that these further investigations will be performed within the NHS rather than in the private sector and the potential cost and resource implications of this are profound.

(iii) Some commercial sector marketing of whole body CT scans recommends repeating the procedure either annually or every five years from the age of 40 years onwards. This practice would imply a very high cumulative radiation exposure for any individual complying with these recommendations, which could lead to 1 in 50 of those individuals so exposed dying from a malignancy induced by the CT scanning (Brenner and Elliston, 2004).

(iv) It is estimated that over a recent three year period 15,000,000 men and women elected for whole body CT scanning in the USA (Margo, 2003), which would represent a cumulative exposure to ionising radiation of around 200,000,000 mSv. This level of cumulative population dosage is comparable to that seen in the Japanese survivors of the atomic bombings at Hiroshima and Nagasaki, who are known to have significant excess mortality from cancer (BEIR Committee, 2006).

3.17 In conclusion, the radiation exposure to an individual from one whole body CT scan is high. Together with the high rate of false positive findings leading to further investigation and the implication that whole body CT scans should be repeated at frequent intervals, there is a very high potential for cumulative radiation exposure at individual and population level. This exposure does not at the present time appear to be balanced by tangible benefit to the individual.

Overdiagnosis and findings of unknown clinical significance (false positives)

3.18 *Overdiagnosis* is used here to denote the identification of a lesion – lump, bump or irregularity – which appears on scan and on pathological invasive biopsy to be a malignant tumour. However, these tumours would never have presented as clinical disease during the lifetime of the individual. Failure to present as symptomatic disease could be because the tumour would have undergone spontaneous regression – as is the case with many screening-detected neuroblastoma tumours in infants (Katzenstein et al, 1998; Nickerson et al, 2000) – or would grow so slowly that the individual would die from other causes before they had overt disease from that tumour. Such overdiagnosis is a manifestation of all cancer screening programmes, but it has not been quantified in the context of whole body CT scanning. In all programmes, however, overdiagnosis leads to unnecessary investigations and invasive and potentially hazardous interventions which may include surgery and drug therapy, exposing the individual to significant health risk.

3.19 The major challenge in whole body CT scanning is *findings of unknown clinical significance*. They refer to the identification, from a whole body CT scan, of an anatomical anomaly the clinical significance of which is unknown. The vast majority of such anomalies are of no importance to the individual but they will lead to uncertainty on behalf of both the health professionals and the individual. Unnecessary investigations will result, which may themselves be hazardous and may cause distress and anxiety in the individual.

3.20 One of the few studies reporting follow-up of a large number of individuals undergoing whole body CT scanning encompassed 1192 patients who received whole body CT scans at an outpatient imaging centre in Southern California during January–June 2000 (Furtado et al, 2005). The majority (76%) of patients had personally initiated the procedure and only 4% of patients had significant medical history. Only 14% of patients had no findings, while 11% had six or more findings (see Table 3.1).

3.21 The probability of a finding increased with age: in those under 40 years, 43% had at least one finding but for those over 70 this rose to 99%. A variable number of these findings were followed by recommendations for referral (see Table 3.2). Overall, 37% of individuals screened were recommended for follow-up investigations. This was age dependent, 11% of those referred for follow-up investigations were aged under 40 years old and 56% were over 70 years old. Of the total recommendations, 69% of findings required further imaging investigation, the majority of which involved a further CT scan with additional radiation exposure (see Table 3.3). The authors of this paper expressed additional concern over the general inconsistency in referral patterns. There was little difference in the findings and referral patterns for either men or women.

3.22 The vast majority of these findings were harmless and it is estimated that less than 20% of abnormalities detected by whole body CT scanning are of clinical importance (Johns Hopkins Medicine, 2002). The ‘hit rate’ for successive scans would be lower as they would be predominantly of conditions arising rapidly in the time interval since the previous scan.

Table 3.1 Number of findings per scan (Furtado et al, 2005)

Number of findings per scan	Percentage of patients scanned (%)
0	14
1	19
2	18
3	15
4	14
5	9
6+	11

Table 3.2 Number of recommendations for investigation (Furtado et al, 2005)

Number of recommendations for investigation	Percentage of patients scanned (%)
0	63
1	28
2	7.2
3	1.3
4	0.42
5	0.08

Table 3.3 Type of imaging employed in further investigations (Furtado et al, 2005)

Type of follow-up imaging	Percentage of patients (%)
CT	67
Ultrasound	14
MRI	10
Non-specific	6
Mammogram	2
Upper GI tract	1

Inappropriate reassurance

3.23 A negative scan – even a true negative scan – may lead to a belief by the individual that they are 'healthy'; this idea is certainly implied by the advertising of many private companies operating in this area. There is a wide range of life-limiting conditions, however, which are not addressed by asymptomatic whole body CT scanning, eg obesity, hypertension, hyperlipidemia, diabetes and some forms of cancer. A misconception of 'normality' in this respect could lead to the perpetuation or adoption of an unhealthy lifestyle and delayed referral in the face of symptoms, if the individual believed that no disease was present.

Economic costs

3.24 The findings of economic modelling of the cost-effectiveness of whole body CT scanning have been investigated (Beinfeld et al, 2005). In particular, comparisons of cost estimates for scanning, follow-up investigations and treatment of disease have been made in hypothetical screened and unscreened populations. Beinfeld et al estimated that whole body CT scanning provided a gain in life expectancy of around six days at an average cost of $2513 per patient or $151,000 per life-year gained (equivalent to £1250 and £75,000, respectively). They concluded that this expenditure was not cost effective and would add a substantial burden to the healthcare system. However, the

findings of this study are likely to overestimate the benefit in life-years gained and underestimate the costs as the authors used sensitivity and specificity estimates from organ-specific imaging which are likely to be superior to those of whole body CT scanning for the reasons discussed elsewhere in this report. Furthermore, the cost of whole body CT scanning is higher in the UK than in the USA and is nearer to $1500 than $1000 per scan.

International opinion

3.25 There is a general consensus from the international radiology community that whole body CT scanning is not to be recommended. In particular, the following organisations have issued statements advising against the use of whole body CT scanning:

American Medical Association (2005)

American College of Radiology (2002)

American College of Cardiology/American Heart Association (2000)

American Association of Physicists in Medicine (AAPM) (2002)

US Agency for Healthcare Research (2005)

US Health Physics Society (2003)

US Food and Drug Administration (2002)

NSW Environment Protection Authority (2003)

Australia and New Zealand Health and Safety Advisory Council (2002)

Radiation Advisory Council of Australia (2003)

Royal Australian and New Zealand College of Radiologists (2002)

College of Radiology, Academy of Medicine of Malaysia (2005)

3.26 In New South Wales it is illegal to perform whole body CT scans without a written request from an independent medical practitioner.

Summary

3.27 There is little evidence of benefit from whole body CT scanning either in its ability to identify disease at a more treatable stage or in its ability to reassure.

3.28 Conversely there is substantial evidence of significant health cost to individuals undergoing this procedure such that in excess of a third will undergo investigations for findings which will turn out to be of no health consequence but which themselves carry risk. There is a risk of induced malignancy from the associated exposure to ionising radiation – while for an individual undergoing a single scan the risk may be small, the risk increases substantially with repeated scans and collectively the population burden could be substantial. Additionally, during referral and subsequent further investigations, there is increased anxiety for the individual, which may be entirely unwarranted.

3.29 Follow-up investigations and repeated imaging will put a substantial burden on the NHS without any evidence of benefit.

3.30 In the absence of tangible benefit from whole body CT scanning, the potential for a substantial risk of malignancy at the population level, which would follow wide-scale adoption of this procedure, results in an unavoidable, substantive drain on NHS resources.

3.31 The apparent lack of regulation of the procedure and the ability of asymptomatic individuals to personally initiate is inappropriate and both should be addressed urgently.

CHAPTER 4

CT SCANNING OF THE LUNG

Introduction

4.1 Lung cancer is responsible for approximately 1,300,000 deaths per year worldwide, with smokers making up to 80% of these (IARC, 2005). There are a number of predisposing factors other than smoking that substantially increase the risk of developing lung cancer, such as the presence of underlying pulmonary fibrosis, or prior exposure to asbestos (Alberg and Samet, 2003). Surgical resection is currently the only hope of cure, but is of benefit only to patients with early stage disease, and in patients with adequate lung function to withstand pulmonary resection. Unfortunately, even in Stage I disease, the five-year survival after surgery is 70% (Coleman et al, 2004) and more disappointingly only 20% of lung cancers are currently diagnosed at Stage I. The advanced stage of disease at presentation for the majority of patients results in an overall survival of 10% at five years (Coleman et al, 2004).

4.2 Given the poor outlook for the majority of patients presenting with lung cancer, a number of investigators have focused on the use of imaging as a method of detecting disease prior to clinical presentation, and in this way detect earlier resectable disease.

4.3 Initial attempts at lung cancer screening with imaging began shortly after its association with smoking became known, and led to at least ten screening trials using the chest X-ray (CXR), of which four were prospective and randomised. The most analysed study, the Mayo Lung Project, at both initial analysis and 20 year follow-up, not only failed to show a benefit from screening, but showed an increase in mortality in the screened patients (Fontana et al, 1984, 1986; Marcus et al, 2000).

4.4 More recently published work in lung cancer screening reported on the use of single slice spiral CT (Gray, 1997) and multidetector CT (MDCT) to detect earlier stage, smaller lung cancers that, if screening is effective, should result in patient benefit from resection (Lee and Sutedja, 2007).

Basic principles of screening including its application to individuals

Prevalence of disease

4.5 The prevalence of lung cancer is sufficiently high, and can be increased by selection of a high risk population (for instance, smokers over the age of 60 years) that it is possible to fulfil Wilson and Jeung's criteria of high disease prevalence for a screening test (Gray, 1997). In the context of a non-selected population, these criteria are unlikely to be met, such that screening is not of value. It has been suggested that those most suitable for lung cancer screening are unlikely to volunteer on an individual basis, and that the 'worried well', for whom there is no proven benefit and who have a low prevalence of disease, are likely to personally initiate screening (Silvestri et al, 2007).

Low incidence of pseudodisease

4.6 Pseudodisease has been described in Chapter 2. This is disease that does not affect the length or quality of a patient's life. A large amount of pseudodisease within a population may render the screening programme ineffective and, for the individual, may result in additional testing with potential morbidity and mortality.

4.7 In lung cancer CT scanning, Type I disease is seen as atypical adenomatous hyperplasia (AAH) in patients screened for lung cancer. For individuals undergoing lung cancer screening, the prevalence of Type I pseudodisease is dependent on age and smoking history, with an increase occurring from both. Most radiologists were unaware of the existence of AAH prior to the advent of CT screening for lung cancer, let alone that it is found in 2–3% of patients at autopsy and in 8–10% of patients undergoing resection for lung cancer (Kayser et al, 2003). It is typically a focal lesion often 5 mm or less in diameter and may be reported variably by pathologists. There is, as yet, not enough information available to be confident on the incidence of AAH detected in lung cancer screening programmes.

4.8 The concept of Type II pseudodisease is controversial in lung cancer, but by definition exists. Screening for lung cancer in any individual with reduced life expectancy from other causes will result, in some, in the detection of disease that will not affect their life expectancy. An example might be screening in a patient with markedly reduced lung function from pulmonary fibrosis. The reduced life expectancy in a patient with severe pulmonary fibrosis (Gribbin et al, 2006) is such that detection of an early malignancy would not result in an improvement in their survival.

4.9 The report analysing data from a 20 year follow-up of patients from the original Mayo Lung Project (Marcus et al, 2000) raises concerns voiced almost 20 years ago; namely that screening may detect lung cancers that are not of importance. The screened group, even after a 20 year follow-up, had a higher incidence of lung cancer but unchanged mortality compared with the control group. This would suggest that some cancers detected at screening behave differently from cancers presenting symptomatically. It is known that adenocarcinomas make up a larger proportion of cancers detected at screening than that in clinically presenting lung cancers, suggesting that some screen-detected adenocarcinomas may be a different biological entity. At one extreme, in a series of screen-detected lung cancers, 31% of the tumours were well-differentiated adenocarcinomas: all were Stage I and their mean volume doubling time was 831 days (Hasegawa et al, 2000). Screening may detect biologically benign lung cancers leading to unnecessary biopsy, thoracotomy and resection in some patients.

4.10 Will the problem of identifying cancers of little importance be made more complex by utilising even more sensitive MDCT technology? T1 adenocarcinomas in the lung of less than 2 cm in size can been subdivided into six histological subgroups (A–F, where F is the most advanced), which are associated with different prognoses (Aoki et al, 2001). In one series the five-year survival of types A and B was 100%. Modern high resolution CT of adenocarcinomas can help to differentiate between histological subtypes, particularly with reference to the amount of ‘ground glass’ opacification present. In one study, 94% of small peripheral lung adenocarcinomas detected by screening were type A, ie pure ‘ground glass’ opacities. In another study, the presence of a higher percentage of ‘ground glass’ appearance was confirmed as a useful prognostic marker, with these lesions having a significantly improved survival. This is further evidence of the variable biological nature of lung cancers, fuelling the argument for the presence of significant pseudodisease.

Detection in the pre-clinical phase of disease

4.11 For lung cancer screening to be successful, the disease has to be detectable pre-clinically. MDCT has the ability to detect disease prior to symptom development in some patients and incidental detection of early stage disease can result in improved survival. For an individual, this incidental

disease detection – for instance, on a pre-operative CXR or on a CT pulmonary angiogram (CTPA) – may result in an increase in life expectancy, but this fortuitous disease detection has as yet not been shown to be transferable to screening programmes, nor to personally initiated screening by individuals.

4.12 Unfortunately there is no correlation between tumour size and the presence of metastatic disease that would make early detection of small tumours definitely beneficial. There is a wide variation in biological behaviour in lung cancers and one reported study has shown no correlation in T1 Stage 1A carcinoma size and survival (Patz et al, 2000), while another study reported on the presence of tumour cells in the bone marrow of 55% of T1 and T2 tumours undergoing resection (Cote et al, 1995). These studies suggest that simply detecting smaller cancers may not result in improved survival for a screened population and therefore that detecting smaller cancers may not be of benefit for an individual patient.

Effective treatment

4.13 Surgical resection remains an effective treatment for early stage disease but, if screening is to be effective in a personally initiated non-screening programme population, these individuals must be both suitable for and willing to undergo resection. They must, as in a screening programme, be made aware of the risks of thoracotomy and lobectomy.

Lung cancer screening trials

4.14 There is at present no UK lung cancer screening trial from which to draw information. There are a number of trials in progress around the world. These trials are predominantly prospective, single arm and non-randomised outcome studies, although there is a single, very large, prospective randomised trial running at present in the USA, the NLST trial (NCI, 2002). This trial has recruited 50,000 participants, is powered to detect a 20% reduction in mortality and has randomised patients to either low dose spiral CT or a CXR. The non-randomised trials that have reported so far include: the Mayo Lung Cancer Screening Trial (Swensen et al, 2002), a German Lung Cancer Screening Trial (Diederich et al, 2002), a Canadian Lung Cancer Screening Trial (McWilliams et al, 2003), the Early Lung Cancer Action Project (ELCAP) (Henschke et al, 1999), the Japanese Anti-Lung Cancer Association (ALCA) (Sobue et al, 2002), the Irish Lung Cancer Screening Trial (PALCAD) (MacRedmond et al, 2004) and the Italian Lung Cancer Screening Trial (Pastorino et al, 2003). The last of these included the use of PET scanning as part of the trial. A trial in smokers in the USA suggests that screening for lung cancer with low dose CT may increase the rate of lung cancer diagnosis and treatment, but may not meaningfully reduce the risk of advanced lung cancer or death from lung cancer (Bach et al, 2007a). In addition, the American College of Chest Physicians (ACCP) has recommended against the use of low dose CT in screening for lung cancer in the general population, including smokers and others at high risk, except in the context of a well-designed clinical trial (Bach et al, 2007b).

4.15 Clinical trials have shown that spiral CT has the ability to detect non-calcified pulmonary nodules, some of which are malignant, and that it is superior to CXR in detection of both non-calcified nodules and lung cancer. None of the trials has shown benefit in regard to improved survival, although a non-randomised trial design makes this a difficult, if not impossible, trial objective. The five-year report from the Mayo Clinic trial has compared survival and mortality data to historical data, and has suggested that there is no benefit (Swensen et al, 2005). The PALCAD trial suggests that in the Republic of Ireland the identification rate of incidence cancers is lower than that reported in other trials, and that there may be significant morbidity associated with investigation following on from screening (MacRedmond et al, 2004, 2006). Indeed, the Mayo Clinic trial resulted in a number of unnecessary pulmonary

resections for benign disease and has also suggested that screening will result in a large number of investigations for incidentally detected and clinically irrelevant disease (Swensen et al, 2003).

Detection of unimportant incidental disease

4.16 In the context of lung cancer screening unimportant incidental disease predominantly relates to the detection of small benign pulmonary nodules, usually granulomas. The detection of clinically irrelevant pulmonary nodules has been reported by most of the screening trials, and these nodules have required further investigations to confirm that they do not represent malignant disease.

4.17 The prevalence of non-calcified pulmonary nodules in smokers is high and there are no data on non-smokers. In ELCAP, 23% of the screened population had non-calcified nodules (Henschke et al, 1999) and this figure was even higher in the Mayo Clinic study (Swensen et al, 2002), with 69% of the screened patients having at least one non-calcified nodule at three years of screening. The prevalence of non-calcified malignant nodules is much lower, being less than 3% in most of the screening studies. Unfortunately, further investigations are required to investigate the detected non-calcified nodules to determine whether they are benign or malignant. For the majority of patients, this is a repeat CT scan at specified intervals, dependent on the trial protocol. Some nodules will be of sufficient size that other investigations may be performed, again according to trial protocol. These investigations may be a dynamic contrast enhanced CT, a PET scan, biopsy or resection. If a follow-up scan is performed, this is usually used to detect growth, a surrogate marker for possible malignancy and, if demonstrated, the patient may then be referred for further investigation or resection.

4.18 Clearly the detection of a non-calcified nodule results in a significant workload and may result in further radiation exposure for the patient together with possible interventional procedures such as image guided biopsy or even thoracotomy.

4.19 Although the initial report from ELCAP (Henschke et al, 1999) raised the possibility of being able to exclude all patients with benign disease from undergoing unnecessary biopsy or thoracotomy, other groups have not been so successful. The Mayo Clinic group had five patients who underwent thoracotomy (21% of surgical procedures resulting from lung cancer screening) for benign disease (Swensen et al, 2002). In a study from Vancouver three patients – 20% of those undergoing lung resections – had thoracic surgery for benign disease (McWilliams et al, 2003).

4.20 The use of contrast enhancement as part of a protocol for lung nodule assessment, as performed by Pastorino et al (2003)**,** may reduce the incidence for unnecessary surgery, but is in itself not a perfect test. The large multicentre study assessing nodule enhancement reported by Swensen et al also included false positive results, with a sensitivity of 98% and specificity of 58% (using a threshold of 15 Hounsfield Units, HU, as significant enhancement) (Swensen et al, 2000). To try to exclude these false positives, Pastorino et al (2003) raised the threshold for calling a test positive. PET scanning as reported in the same cancer screening trial may also be of value but is yet another test with reporting failings, particularly in the assessment of small nodules and indolent disease.

4.21 Assuming that a particular nodule has been labelled as suspicious as a result of the above investigations, percutaneous biopsy is usually the next step in order to obtain a histological diagnosis. Unfortunately, the majority of nodules that require biopsy will be 1 cm or less in size. To biopsy these lesions will be more technically difficult than other biopsies in most radiologists'

current practice and the expected consequence of this will be a lower sensitivity, despite the outstanding results reported from ELCAP (Henschke et al, 1999).

4.22 Even if the detected nodule is malignant there will be a morbidity and mortality risk from thoracotomy. A recent review reported the average operative mortality for patients undergoing all forms of pulmonary resection was 3.5%, with a mortality of 3% for lobectomy (Smythe, 2003). One critique of lung cancer screening suggests that the consequent slow but accelerated decline in lung function secondary to pulmonary resection in the screened patients may be a further cause of death (Reich, 2002).

Detection of non-pulmonary incidental disease

4.23 Screening with MDCT results in the detection of incidental disease both within and outwith the chest. The Mayo Clinic study resulted in almost 700 additional abnormalities detected in 1500 patients. These included 114 abdominal aortic aneurysms, 4 renal cell carcinomas, 63 indeterminate renal masses, 56 adrenal masses, 21 hepatic masses and 28 breast nodules (Swensen et al, 2002). All of these required further investigation. The frequent finding of incidental disease is further confirmed by the recent report of the NELSON study group, the lung cancer screening trial in the Netherlands. The group reported that of 1929 participants in the study, 1410 had incidental findings, of which only one was malignant, and this was incurable and so without benefit to the patient (van de Wiel et al, 2007).

Failure to detect important screened disease

4.24 The initial trials in lung cancer screening make sobering reading for radiologists. In the original Mayo Lung Project, even with triple reading of CXRs (with the sole purpose of detecting malignancy), up to 75% of peripheral and 90% of central lung cancers were visible in retrospect on review of previous films, ie ‘missed’ (Fontana et al, 1986). Recent reports suggest that a lesser number of lung cancers are ‘missed’ using CT. Nevertheless up to a third of CT screen-detected cancers are visible in retrospect: in the Mayo Clinic study, four out of eleven cancers detected on repeat screening had been present in retrospect on the previous scan, including one Stage IIIA tumour (Swensen et al, 2002). Characteristic misses include cancers that are predominantly ‘ground glass’ in appearance or associated with scars. Help may be at hand via computer aided detection (CAD) software programmes, although these will have their own disadvantages, such as cost, reliability and increased time requirements.

Interval cancers

4.25 Even in an intensive screening programme such as ELCAP, some lung cancer patients present symptomatically between the screening rounds (so-called interval cancers) (Henschke et al, 2001). Prior to the first interval scan following initial screening, two patients presented symptomatically, both with endobronchial abnormalities on CT: one of these patients had a limited small cell carcinoma, and the other had Stage IIB non-small cell lung cancer (NSCLC) resected successfully. These were two of nine carcinomas diagnosed by the end of the first interval screening round.

4.26 The Mayo Clinic study also documented interval cancers (Swensen et al, 2002). Within the screening period there were ten NSCLCs and one small cell cancer detected by CT, but there were two interval cancers in the same period: one of these was Stage IV NSCLC and the other was a small cell cancer.

4.27 These data raise concerns as the proportion of interval cancers is high compared to the screen-detected cancers, and although expected for a lung cancer presenting symptomatically, they are at a comparatively more advanced stage. This appears to be further evidence of the biological variability in

disease and it would seem unlikely that the outcome of such highly aggressive cancers will be altered, even by an intensive screening programme.

Opportunity costs

4.28 Most actions in medicine have a consequence and this is obviously the case in lung cancer screening. The limited resources available for healthcare suggest that, until a lung cancer screening programme is proved to be successful in reducing disease-specific mortality, any such strategy might be a net user of resources. Indeed it is possible that even if it successfully reduced lung cancer mortality it would continue to consume resources. After all, most symptomatic patients with lung cancer only survive for a limited period, whereas the screened population are likely to require screening for life, along with the other identified additional costs such as PET scans, biopsies, and the investigation of incidental disease. Probably, at least in the UK, the screening programme would consume resources by taking them from elsewhere within the healthcare environment. It may be that a greater patient benefit would occur if the funding of a screening programme were to be utilised in an alternative manner.

Summary

4.29 The pitfalls in CT scanning of the lung are comparable to those in screening programmes already in place in medicine. These include the identification of unimportant disease, the failure to identify important disease successfully, the consequence of investigating and treating disease identified, and the expenditure of money that may be better utilised elsewhere. All of these issues would be best assessed following a prospective randomised trial of MDCT, when true efficacy and cost benefit could be assessed.

4.30 For a personally initiated, self-funded asymptomatic 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.

CHAPTER 5

CARDIAC CT SCANNING

Background

5.1 Coronary heart disease is the commonest cause of death in industrialised countries including the UK. In 2004, it was estimated over 230,000 people had a heart attack and more than 105,000 were known to have died from coronary heart disease in the UK (Allender et al, 2006). There are many recognised risk factors for coronary heart disease which include increasing age, smoking, hypertension, diabetes, hyperlipidaemia (increased low density lipid protein cholesterol and decreased high density lipid protein cholesterol), obesity, physical inactivity and family history of premature coronary artery disease.

5.2 These risk factors only explain about 60% of the variability seen in the prevalence of coronary heart disease. More importantly approximately 50% of incident presentations are with sudden cardiac death or myocardial infarction (Tunstall-Pedoe et al, 1996) which results in irreversible heart muscle damage and leads to heart failure in later life. The total cost of heart failure care accounts for 2% of all health care costs (Department of Health, 2000).

5.3 The UK government has set targets to reduce mortality from coronary heart disease by 40% by 2010. To improve the outcome from coronary heart disease significantly, two strategies have been highlighted: lifestyle changes to improve primary prevention and the identification of high risk asymptomatic individuals who will benefit from proven therapies that reduce mortality (Department of Health, 2000).

CT scanning to detect coronary artery calcification

5.4 CT scanning of the heart can be performed to assess coronary artery calcification or arterial patency (coronary angiography). Coronary artery calcification occurs as part of the atherosclerotic process which leads to coronary heart disease. It can be detected easily by either ultrafast electron beam CT (EBCT) or multidetector CT (MDCT), see Figure 5.1. Calcification is defined as attenuation greater than 130 HU in three or more consecutive pixels.

5.5 The coronary artery calcium score can be calculated by adding all areas of calcification from the base of the heart down to the apex (Agatston et al, 1990). Protocols for EBCT have been standardised usually using 40 slices that are 3 mm thick from the base to the apex and are acquired in one-two breath-holds. Prospective electrocardiogram (ECG) gating is always used with data acquisition limited to less than 100 ms in diastole, at 60–80% of the RR (time between successive heartbeats) interval to limit cardiac motion (Schoepf et al, 2004).

5.6 Effective doses using EBCT and specific protocols for coronary artery calcification using EBCT are usually less than 1.5 mSv. In MDCT, ECG gating can be performed either retrospectively when scanning is carried out throughout the cardiac cycle or prospectively where data acquisition is limited to short periods in diastole. The latter approach significantly reduces radiation exposure, usually to less than 2 mSv. The extent of coronary artery calcification is related to the number of cardiovascular risk factors, age and sex (Figure 5.2);

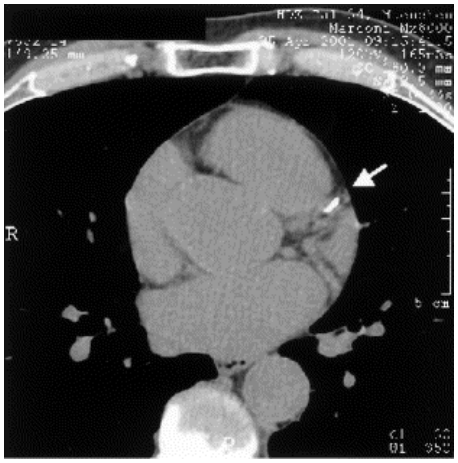


Figure 5.1 Coronary artery calcification detected by four-slice MDCT. The arrow indicates a calcified plaque in the left anterior descending artery (Schmermund et al, 2002)

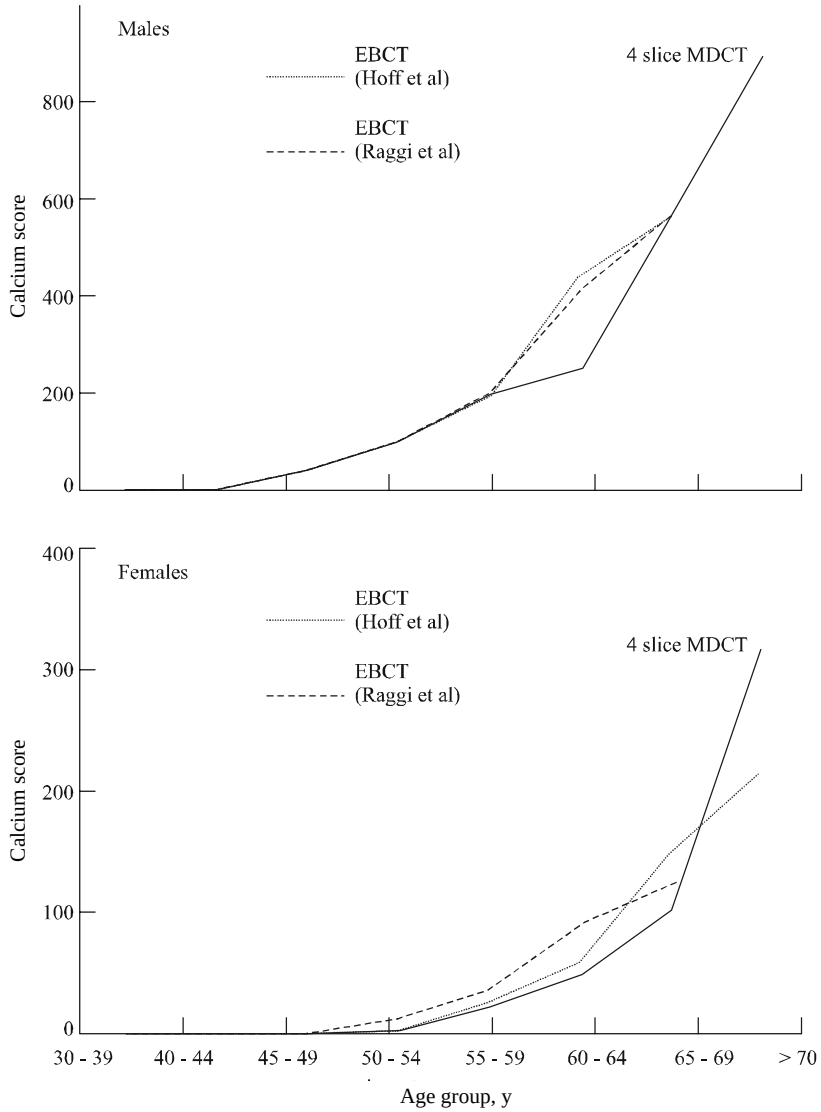


Figure 5.2 Age-related calcium score normal ranges for EBCT and four-slice MDCT (Schmermund et al, 2002) in men and women. Comparison of the 75th percentile value for EBCT taken from two independent studies (Raggi et al, 2000, and Hoff et al, 2001)

the calcium scores calculated by EBCT and MDCT are closely correlated but not identical, at least with four-slice MDCT (Schmermund et al, 2002; Stanford et al, 2004).

5.7 The extent of inter-study and inter-observer variability is around 10% and may be improved by calculating total calcium volume or mass compared to the traditional Agatston method (Schoepf et al, 2004). All the major CT manufacturers have automatic calcium scoring software which generates scores, but trained operators should confirm that the area of calcification lies directly over a coronary artery. Inter-study variation is greater at lower calcium scores. The calcium score is correlated to the total atherosclerotic burden but underestimates this by approximately 80% and is not related to stenosis severity (Rumberger et al, 1995; Sangiorgi et al, 1998). Significant plaques may be present which do not contain calcium. Myocardial perfusion defects are rarely seen with calcium scores less than 100, but are frequently seen when the score is greater than 400 (Berman et al, 2004; He et al, 2000).

Calcium score in asymptomatic patients

5.8 Several early studies using EBCT have shown that higher calcium scores were associated with adverse cardiovascular events. However, it was unclear from these early studies whether the calcium score gave additional information to that of traditional risk factors (O'Rourke et al, 2000) and indeed one study in high risk subjects showed that the calcium score did not predict short-term outcome (Detrano et al, 1999). More recently, however, multiple well-controlled studies involving tens of thousands of asymptomatic subjects have demonstrated that EBCT calcium scoring is an independent predictor of outcome even when considered in a multivariant model with other risk factors (Arad et al, 2000, 2005a; Greenland et al, 2004; Kondos et al, 2003; Raggi et al, 2000, 2001; Shaw et al, 2003; Taylor et al, 2005; Wayhs et al, 2002; Wong et al, 2000).

5.9 The calcium score confers modest additional information to that of conventional risk estimates using Framingham calculations, but in those deemed to have a low ten-year risk (less than 10%) after initial assessment there have been contradictory results reported (Greenland et al, 2004). The Framingham risk score gives estimates for 'hard coronary heart disease' which includes myocardial infarction and coronary death. The risk factors included in the Framingham calculation are age, total cholesterol, HDL cholesterol, systolic blood pressure, treatment for hypertension, and cigarette smoking. The absolute and relative risks are incrementally related to age- and sex-standardised calcium scores (Raggi et al, 2001; Shaw et al, 2003; Taylor et al, 2005) – see Table 5.1. Concern about the prediction of soft endpoints such as revascularisation, which

Table 5.1 Absolute and relative risk for fatal or non-fatal myocardial infarction by age- and sex-specific calcium scores in centiles. (Adapted from Raggi et al, 2001)

Calcium score (%)	Annual absolute risk (%)	Odds ratio (95% CI)
0	0.4	1.0 (1.0–1.0)
10	0.5	1.4 (1.2–1.6)
20	0.7	2.0 (1.6–2.5)
30	1.0	2.8 (1.9–4.0)
40	1.4	3.9 (2.4–6.4)
50	1.9	5.5 (3.0–10.1)
60	2.6	7.8 (3.8–1.60)
70	3.6	10.9 (4.7–25.4)
80	4.9	15.4 (5.8–40.4)
90	6.5	21.6 (7.3–64.1)

may be driven by the result of calcium scoring (O'Rourke et al, 2000), has been unequivocally laid to rest.

5.10 Several authors have suggested that cardiovascular risk can be best predicted using conventional Framingham risk factors and adjusting biological age according to the calcium score (Nasir et al, 2006; Shaw et al, 2006). Recently an influential group in the USA has gone one step further and recommended complete population screening of intermediate risk groups with calcium scoring or carotid ultrasound to more accurately quantify risk and tailor preventative therapies accordingly (Naghavi et al, 2006).

Randomised trial of treatment by calcium scoring

5.11 There have been no large-scale population studies which have randomised patients to receive therapy on the basis of the calcium score and shown significant improvement in medium-term outcome. One report randomised 1005 asymptomatic patients to a combination of atorvastatin 20 mg, vitamin C and E or matching placebos and demonstrated a trend for reduced cardiovascular events (p=0.08) at four years of follow-up (Arad et al, 2005b). The low overall event rate in this study may be partly explained by the fact that patients in the active and placebo arms were prescribed aspirin. The trial was therefore underpowered to detect a treatment effect, although there was a statistically significant reduction in those with the highest calcium scores (over 400) who had the highest event rates.

CT coronary angiography

5.12 MDCT coronary angiography is a technique which should be regarded separately from calcium scoring. For coronary angiography, an ECG-gated MDCT is performed with the addition of contrast. The radiation exposure is at least equal to, and often double (5–10 mSv), that of conventional invasive coronary angiography and also carries inherent risks of contrast administration.

5.13 It is a rapidly emerging clinical tool in assessment of patients with coronary artery bypass grafts, or anomalous coronary arteries and may be useful in the assessment of patients presenting with chest pain (Schoenhagen et al, 2004). Satisfactory results are generally only obtained with heart rates less than 60 beats per minute and intravenous beta-blockers may have to be administered. MDCT coronary angiography has excellent negative predictive value in the detection of obstructive coronary heart disease but is still limited by un-interpretable segments and low specificity due to heavy calcification or motion artefacts (Ropers et al, 2006).

5.14 There are no outcome studies on the use of MDCT coronary angiography in asymptomatic subjects and this technique will not discussed further, although clinical applications will continue to develop with technological advances (Schoenhagen et al, 2004).

Coronary artery calcification versus other predictors of cardiovascular risk

5.15 There is a lack of long-term comparative data on calcium scoring versus tests of reversible ischaemia such as exercise ECG, myocardial perfusion scanning and stress echocardiography which also confer prognostic information (O'Rourke et al, 2000). Other tests which look at subclinical atherosclerosis such as carotid intima-media wall thickness, left ventricular hypertrophy, ECG abnormalities, and traditional risk factors will be compared in the Multi-Ethnic Study of Atherosclerosis (MESA) in different ethnic populations in the USA (Bild et al, 2002).

5.16 Cardiac MRI, which does not involve ionising radiation, is very useful in the assessment of patients with ischaemic heart disease but there is general agreement that the technology will not advance rapidly enough to allow accurate assessment of coronary artery plaque burden or coronary angiography in the short to medium term (Pennell et al, 2004).

Safety

5.17 CT coronary artery calcification scoring is a completely non-invasive test when performed without the use of intravenous beta-blockers. There is no injection of contrast and there are no short-term adverse effects. The major consideration is radiation protection of the patient and the long-term risk of radiation-induced cancer.

5.18 There is general agreement that cardiac CT scanning is not justified in subjects with low risk cardiovascular disease, such as young adults (under 30 years) and in very high risk patients (age over 75 years) or in those with established coronary heart disease (Naghavi et al, 2006; O'Rourke et al, 2000). Optimisation of the examination for the individual should include a weight-adjusted protocol with prospective gating and complete coverage of the heart but not the whole chest or torso.

5.19 The radiation dose (1–2 mSv) is approximately 50 to 100 times that of a standard chest radiograph but just less than annual background radiation. The lifetime risk of a radiation-induced cancer depends on the age at screening and in a 45 year old male undergoing calcium scoring every five years to the age of 75 years gives a total risk of radiation-induced cancer of less than 0.1%. This radiation risk may be justified in individuals deemed to be at intermediate risk of cardiovascular events after careful assessment by a cardiac specialist to allow appropriately tailored medical therapy (Naghavi et al, 2006; O'Rourke et al, 2000). The risks from further investigation of individuals with high calcium scores, using myocardial perfusion scanning or invasive coronary angiography, are difficult to determine at this time due to the lack of randomised controlled trials.

Training issues

5.20 EBCT is scarcely available in the UK, although MDCT scanners are in most large hospitals. There are no outcome data for coronary artery calcification by MDCT and agreed standardised protocols and normal ranges for different MDCT scanners have yet to be established, particularly scanners with 16, 64 and potentially 128 row MDCT on which calcium scoring in this country is likely to be performed. Although calcium scores are calculated automatically by computer software programmes, manual checking of calcific lesions should be performed by a specialist familiar with the coronary anatomy but there is a shortage of trained cardiac radiologists in the UK.

Detection of incidental findings

5.21 Although the field of view is limited in calcium scoring, large areas of the lungs, mediastinum, liver, vertebrae and ribs are visualised. Incidental findings are detected in 8% of patients undergoing calcium scoring with EBCT, the majority of which are pulmonary nodules (Elgin et al, 2002; Horton et al, 2002). Many of these findings will require clinical follow-up which, as discussed in Chapter 4, may entail yet further CT scanning.

Impact on NHS resources

5.22 Asymptomatic individuals who require further cardiac investigation are likely to be referred to the NHS, probably to a cardiologist in the outpatient clinic to determine which test(s) is(are) most appropriate. A greater number of individuals may make appointments to discuss their results with their GP who is extremely unlikely to be familiar with calcium scoring and will probably refer on to secondary care even though the individual may not need any further investigation or treatment. Incidental findings are also likely to be investigated in the NHS.

Patient information

5.23 Individuals should be informed that, although the test is non-invasive, there is a small long-term increase in the risk of fatal cancer developing. This risk is less than 0.01% for adults in the potential screening age with a single examination. The risk will rise correspondingly with repeated scans. The results of calcium scoring are most useful when combined with a

comprehensive cardiovascular risk assessment; the test should not be routinely performed in asymptomatic individuals unless requested by the patient's own GP or cardiac specialist.

5.24 The finding of coronary artery calcification on cardiac CT is common and increases with age. The test does not accurately reflect the presence of narrowed arteries and further testing may be recommended by the patient's GP or cardiac specialist, particularly for high age-adjusted scores which may involve further radiation exposure. A completely normal scan does not mean that there is no risk of suffering from a heart attack in the next few (three to five) years, although the risk is very low. On the basis of test results, a GP or cardiac specialist may recommend lifestyle changes or medication for conditions such as high blood pressure or high cholesterol.

Summary

5.25 Coronary artery calcium scoring by EBCT is a well-validated technique for predicting cardiovascular risk in asymptomatic populations. However, there are only a few EBCT scanners in the UK and so calcium scoring is most likely to be performed by MDCT. Normal age- and sex-specific calcium scores for 16 and 64 row MDCT are likely to be similar to those of EBCT but they have not been validated for predicting cardiovascular outcome. Calcium scoring provides moderate improvement over conventional risk factors in the prediction of cardiovascular adverse events, particularly in patients with intermediate ten-year risk. No large-scale screening trials have shown improvement in cardiovascular outcome in patients undergoing therapy following calcium scoring. It should not be performed in subjects deemed to be at high or low risk of cardiovascular disease since it is extremely unlikely to alter treatment and calcium scoring is of no proven benefit in patients with established coronary heart disease (Greenland et al, 2007).

5.26 Individuals considering calcium scoring should be informed of the radiation exposure and the possibility of requiring further investigation, which may involve more radiation exposure, as a result of the test. A significant proportion of people undergoing calcium scoring are likely to be referred to the NHS for discussion of results and/or further investigation.

CHAPTER 6

CT SCANNING OF THE COLON

Diagnostic pathway for colorectal cancer

6.1 *Symptomatic patients* would include individuals over the age of 50 years with a history of rectal bleeding or mucous, or a sustained change in bowel habit. The criteria for access to the diagnostic team, and the pathway of investigations undertaken, are defined by the agreed cancer standards for the relevant area of the UK. The first investigation may be by flexible sigmoidoscopy, or by colonoscopy, depending on symptoms (for example, whether they suggest a lesion in the distal colorectum or the ascending/transverse colon). These procedures allow for biopsy of any abnormal lesion found, and subsequent management can be determined in the light of a firm diagnosis. Barium enema may be used in the assessment of a colorectal lesion, but is less often performed than previously, and is unlikely to be the sole investigation in the diagnostic workup. Virtual colonoscopy is not yet routinely performed in the UK, and is only likely to be part of the diagnostic workup in centres with a particular interest in it.

6.2 *Asymptomatic patients* are usually individuals with colorectal cancer, diagnosed via one of the NHS screening programmes. In general terms, the first investigation will be with faecal occult blood testing, those individuals who test positively being further investigated, with flexible sigmoidoscopy and/or colonoscopy as appropriate. Individuals who are found to have an adenomatous polyp will generally undergo subsequent screening by colonoscopy at two- or three-year intervals. In England, the pilot bowel cancer screening programme, based on faecal occult blood testing at two-year intervals in individuals between 60 and 69 years, finished in March 2007 (NHS Cancer Screening Programmes, 2007). The programme is currently being rolled out across England and Scotland, although the age range in Scotland is between 50 and 74 years. In Wales, the programme is being planned to roll out from 2008/09, screening individuals, also between the ages of 50 and 74 years, every two years. Planning is also underway in Northern Ireland, with a view to beginning bowel cancer screening in 2009, although the age range is still under discussion.

Colorectal cancer screening

6.3 There are a number of investigations which are options for population based screening for colorectal cancer.

Tests available

(i) *Faecal occult blood* testing has been available for many years. Despite its reputation for high false positive rates, recent trials have suggested that it can perform well enough to be used in a screening setting, with or without enhancements such as immunohistochemistry to improve detection rates. More recently, studies have addressed whether faecal DNA analysis (Wu et al, 2006), focusing on the molecular abnormalities associated with colorectal cancer, or on the detection of epithelial cells, might further refine faecal screening and this may become more widely available in the future.

(ii) *Flexible sigmoidoscopy* enables visualisation of the rectum, sigmoid colon, and descending colon, as far as the splenic flexure, and is clearly superior to rigid sigmoidoscopy. It can be performed on an out-patient basis without sedation.

(iii) *Colonoscopy* enables visualisation of the entire colon, as far as the caecum. It can be performed also as a day-case procedure, but is generally done under sedation, making it somewhat more cumbersome than flexible sigmoidoscopy in the general population (Lieberman et al, 2000).

(iv) *CT colonography* is the topic of this chapter. It is possible that it will find a role in population screening, but large-scale population based studies have not yet been performed in this context.

(v) *Barium enema*, once the standard investigation for large bowel pathology, is not as popular as an option in a population screening context, although some studies using it are underway (Kung et al, 2006).

Effects on mortality

6.4 There are now a number of published studies providing evidence that mortality can be reduced by screening for colorectal cancer (Cotterchio et al, 2005). Studies have generally focused on faecal occult blood testing, flexible sigmoidoscopy and colonoscopy. Results from randomised trials and large-scale studies suggest, in addition to the effects on mortality:

(i) that there is generally a high enough take-up of tests to justify population screening (Segnan et al, 2005),

(ii) that any of the three methods of screening above have acceptable sensitivity and specificity (Cotterchio et al, 2005; Lieberman et al, 2000; Weissfeld et al, 2005).

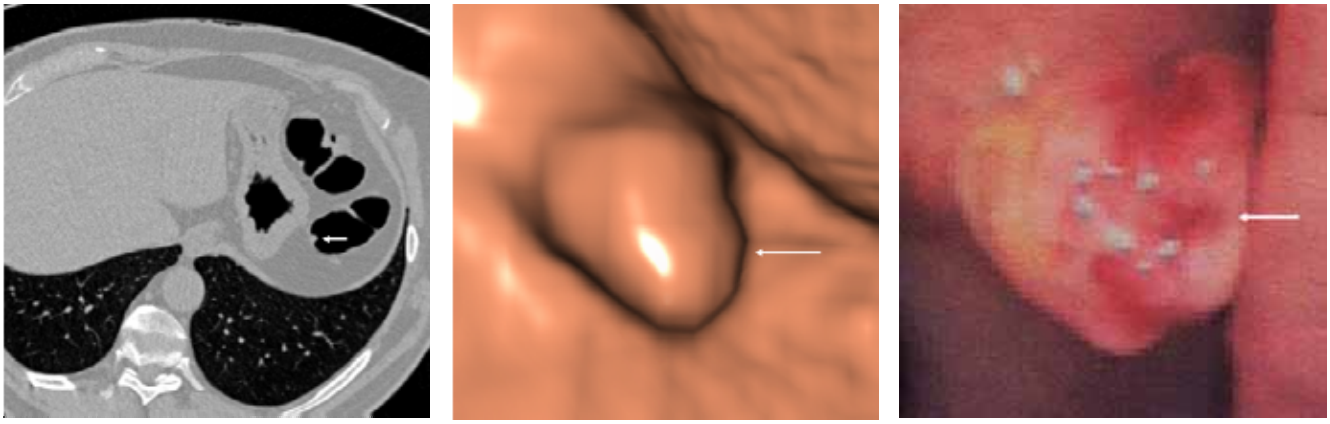
There have been few direct comparisons between tests, although there have been, for example, comparisons of biennial faecal occult blood testing and one-off flexible sigmoidoscopies. As yet, no trials have demonstrated a reduction in mortality as a consequence of population screening using CT colonography. However, given the performance of CT colonography, which is now becoming very close to colonoscopy (see below), in the setting of the investigation of symptomatic patients, it seems reasonable to expect that it, too, would reduce mortality from colorectal cancer in a population screening setting.

What is CT colonography?

6.5 CT colonography (also known as ‘virtual colonoscopy’ or ‘CT colonoscopy’) is a technique whereby three-dimensional reconstruction of the large intestine from conventional CT images (acquired using a thin-section helical technique) can be used to generate high resolution images of diagnostic quality. The images obtained show strikingly similar morphology to the appearances of conventional colonoscopy, as seen in Figure 6.1 (Macari and Bini, 2005).

6.6 The quality and elegance of the images obtained has led to a huge upsurge of interest in the technique, mainly from research institutions. However, before this procedure can be recommended for more widespread use, data on its sensitivity/specificity profile, safety, reproducibility and cost-effectiveness will need to be evaluated. The emphasis of this technique would be on the detection of colonic polyps (which in some cases are pre-cancerous lesions, whose removal would prevent their development into overt cancer) and of occult cancers of the colon and rectum.

6.7 The natural history of colorectal cancer is relatively well understood. It is accepted that all such cancers are potentially life threatening (in contrast to, say, prostate cancer), and that the removal of an early cancer or pre-cancerous lesion is curative. Such treatment does not, however, prevent the development of further, separate cancers elsewhere in the colon or rectum.



(a) **(b)** **(c)**

Figure 6.1 A 4.5 mm splenic flexure polyp in a 53 year old man. (a) Transverse CT image shows small polypoid lesion (arrow) in the splenic flexure. (b) Endoluminal CT colonographic image shows polypoid morphology (arrow) of the lesion. (c) Image from conventional colonoscopy performed one week later shows identical morphology (arrow). Histological evaluation indicated an inflammatory polyp

Sensitivity and specificity analyses

6.8 Two systematic reviews have been performed, which have included evaluation of sensitivity and specificity. In the first analysis (Halligan et al, 2005) on 24 studies and 4181 patients, selected for key methodological criteria including a verification colonoscopy, sensitivity for the detection of colonic polyps was reported to be high (93%), and specificity was also high for large polyps (97%). However, both sensitivity and specificity fell when the analysis was broadened to include medium-sized polyps (86% and 86%, respectively), and a very wide range was noted when polyps of any size were included (45–97% for sensitivity and 26–97% for specificity). It was noted that studies were often poorly reported. The second study (Mulhall et al, 2005) reviewed data on 33 studies and 6393 patients. The review was restricted to those studies comparing CT colonography to standard colonoscopy for verification, employing state-of-the-art (according to the authors' definition) technology, but there was still substantial heterogeneity between studies. Once again, polyp size emerged as a significant determinant, with sensitivity falling from 85% to 70% to 48% for the detection of polyps of size >9, 6–9 and <6 mm, respectively. In this study, the specificity was more homogeneous, ranging from 97% to 93% to 92% for the detection of polyps of size >9, 6–9 and <6 mm, respectively. The authors also commented that CT colonography was particularly sensitive for detecting cancer in symptomatic patients – a different population from those 'well' individuals who might take part in a screening exercise. It should also be noted that some clinicians regard polyps less than 4 mm in size as being 'clinically unimportant', although the evidence for this assertion needs to be critically evaluated (Barish et al, 2005). The low and often variable specificity seems to be a major limitation of this technique. It could be related to a number of issues – equipment, technique, training, and so on, but it remains a significant variable and a barrier to the widespread introduction of CT colonography for population based screening.

6.9 A wider question arises as to the effects of combined screening methods (eg CT colonography, plus colonoscopy, plus faecal occult blood detection), but there do not appear to be any studies addressing this. There would, inevitably, be questions about the acceptability to patients of these combined methods, in addition to health economic evaluation.

Technique and patient information

6.10 Conventionally, CT colonography requires full bowel preparation in the same way as is required for colonoscopy or for barium enema. Full bowel preparation is the practice by over 90% of specialists in the UK (Burling et al, 2004), although there are several different protocols by which it may be performed.

6.11 Some investigators, as well as using different purgatives (Forbes et al, 2005; Ginnerup et al, 2002; Macari et al, 2001; Taylor et al, 2003a), the use of bowel contrast (Ginnerup et al, 2002; Nagata et al, 2007), intravenous contrast (Morrin et al, 2000), or intravenous hyoscine (to achieve bowel distension) (Taylor et al, 2003b), have advocated the use of minimal bowel preparation prior to CT colonography (Bielen et al, 2003). Minimal bowel preparation has been used in frail patients (Kealey et al, 2004; Robinson et al, 2002). Of some concern, however, is the possibility that residual stool is responsible for the misinterpretation of abnormalities on CT colonography (Arnesen et al, 2005).

6.12 The need for colonic distension has already been referred to, and is achieved either manually or by automated insufflation, which may be superior (Burling et al, 2006b). Also already described, detection rates may be higher when the examination is performed in both supine and prone positions (Barish et al, 2005; Chen et al, 1999), and occasionally others (Gryspeerdt et al, 2004).

6.13 There are, thus, a number of points purely related to technique, about which patients need to be informed prior to CT colonography, namely:

(i) possible need for bowel preparation (which itself carries some morbidity),

(ii) possible need for intravenous contrast and/or intravenous hyoscine,

(iii) need for bowel insufflation,

(iv) need for the examination to be repeated in (usually) two positions.

6.14 In addition, current practice would indicate that the finding of a suspicious lesion on CT colonography would require a conventional colonoscopy, both for verification and also to obtain a histological diagnosis.

Complications and safety – perforation

6.15 In general, the technique of CT colonography is regarded as being safe, with few complications reported in large groups of patients. The most common complication appears to be bowel perforation, related to the need to insufflate the colo-rectum with CO_2 in order to distend it.

6.16 In a UK review of 17,067 examinations from 50 centres, a total of 13 patients suffered a potentially serious adverse event (0.08%), nine of which were perforations (Burling et al, 2006a). In a second study of 11,870 examinations from 11 Israeli centres, the risk of perforation was 0.06% (Sosna et al, 2006). Six of the seven cases of perforation occurred in symptomatic patients in the latter study, and in five out of the nine cases in the UK study. In the US Virtual Colonoscopy Working Group review of 21,923 studies there were no perforations in 11,707 screening examinations, and two cases in 10,216 diagnostic examinations in symptomatic patients, yielding an overall complication rate of 0.02%, which included two cases of renal failure secondary to bowel preparation and one patient with chest pain (Pickhardt, 2006). In this study the overall perforation rate in asymptomatic cases was 0.009%, substantially lower than in the other studies. It would appear that complication rates might be minimised if CT colonography were restricted to asymptomatic patients without known bowel pathology. In addition, at least

some perforations appear to be associated with manual insufflation of the colon, as opposed to using automated CO_2 delivery (Pickhardt, 2006).

Safety – radiation doses

6.17 One major difference between CT colonography and standard colonoscopy is that the former involves a dose of radiation in a healthy person, who would not otherwise receive that dose. A systematic review of practice in 36 institutions indicated that in 2004, the median effective radiation dose for CT colonography was 5.1 mSv per scan, and 10.2 mSv per complete examination, with a range of 1.2–11.7 mSv per examination position (prone and supine) (Jensch et al, 2006). The median effective dose appeared to be relatively constant between 1996 and 2004. The lifetime risks of exposure-related death (principally from a radiation-induced cancer), associated with CT colonography with a dose of 10 mSv per examination, have been estimated as 0.4% for males and 0.6% for females who begin screening at the age of 40 years with a three-year screening interval (Wise, 2003). This would obviously fall in subjects beginning screening at an older age, or with a longer screening interval. A second estimate gives a lifetime risk of 0.14% in subjects beginning screening at the age of 50 years (Brenner and Georgsson, 2005). Research is underway to reduce further the dose of radiation associated with this technique.

6.18 Image quality deteriorates as the dose is lowered; the deterioration becomes more noticeable below an effective dose of 3.6 mSv per position with standard techniques (van Gelder et al, 2002). However, preliminary data suggest that, using noise reduction techniques, it might be possible to perform CT colonography with doses as low as 1 mSv per examination (Cohnen et al, 2004); this goal appears achievable when using modern equipment (Iannaccone et al, 2003).

Training issues

6.19 The competence and experience of the radiologist are important determinants of the sensitivity and specificity of any procedure, and CT colonography will be no exception. Nonetheless, there are no specific professional guidelines in the UK, and there is no regulatory mechanism to ensure that supervising radiologists have a minimum level of competence.

6.20 The need to optimise training has been cited in several studies as a factor where CT colonography performed less well than colonoscopy (Cotton et al, 2004), and considerable variation in investigators' abilities has been seen in a prospective study (Taylor et al, 2004). Furthermore, this study also indicated that prior expertise in gastrointestinal radiology was an advantage and, importantly, that competence could not be assumed, even after the completion of a formal training process (Taylor et al, 2004).

6.21 Studies that yield good results tend to come from single-centre institutions, involving a small number of highly dedicated investigators. Results appear to be less good when the technique is taken into the general medical community (Soto et al, 2005). Indeed, some recent prospective studies have mandated a specific course of training prior to investigators being allowed to participate, and for the US ACRIN II trial this has been made compulsory for any radiologist who has reported fewer than 500 colonographies with endoscopic correlation (Soto et al, 2005).

Detection of extra-colonic lesions

6.22 There is no doubt that the use of CT colonography will result in the detection of extra-colonic lesions in a significant proportion of cases. Indeed, a proposed system to code and track such lesions has been published (Zalis et al, 2005).

6.23 In a small study of 75 patients under surveillance for previous cancer or polyps, 68 instances of extra-colonic findings were reported in 49 patients (65%), requiring additional investigations in eight patients, including surgery in two (Ginnerup et al, 2003). The prevalence of extra-colonic findings is variable, but ranges from modest rates of 24% (Ng et al, 2004) to very high rates of 85% (Gluecker et al, 2003) or 89% (Spreng et al, 2005), which have also been reported. It seems reasonable to conclude that additional findings will be detected in the majority or a substantial proportion of patients undergoing CT colonography, especially if this is being done as part of a whole body CT examination.

6.24 Extra-colonic findings are often classified as being of 'little' and 'variable' significance (Pickhardt and Taylor, 2006), or as clinically 'relevant' or 'irrelevant' (Chin et al, 2005). In the latter study from Australia, the cost of following up relevant extra-colonic findings was estimated as $24.37AUD per case (around £10), which is modest (Chin et al, 2005). However, there are no studies that demonstrate a reduction in mortality arising from this practice and in some instances – for example, in very small renal carcinomas – the natural history of even 'relevant' lesions is unclear. Furthermore, no studies have quantified the additional psychological morbidity, or effects on quality of life of the detection, further investigation, and interventional procedures for incidentally-found extra-colonic lesions as a result of CT colonography.

CT colonography in context

6.25 Even as CT colonography continues to evolve, other techniques are becoming available, most notably magnetic resonance colonography (Hart and Wall, 2004; Hartmann et al, 2006; Lauenstein, 2006; Purkayastha et al, 2005), which may supersede CT within or shortly after the timescale that would be envisaged to collect and evaluate enough mature data to indicate the potential routine use of the latter. Although consideration of magnetic resonance colonography is beyond the scope of this report, its development is of relevance to the future of CT colonography.

6.26 The risk of developing colorectal cancer in adults increases by around 20 per 100,000 per year with every five-year increase in age range from 40–44 years. Thus, in 40–44 year olds, the annual risk of developing colorectal cancer is around 1 in 10,000, increasing to 1 in 4,000 for ages 45–49, 1 in 2,000 for ages 50–54, 1 in 1,250 for ages 54–59 and 1 in 800 for those aged 60–64 years.

6.27 There would appear to be little justification in screening those under the age of 50 years since such a small proportion of cases will occur in this age group, and even for the 50–54 year olds, the likely rate of diagnosis is very low. The colorectal cancer screening programme in England will be based around faecal occult blood testing, and will be restricted to the 60–69 year olds (NHS Cancer Screening Programmes, 2007). In Scotland, the screening age range is 55–69 years. In Wales, screening may be extended to a younger age group, but there are no plans in the UK to screen patients below the age of 50 years. Screening patients younger than this using CT colonography is not, therefore, in line with the UK screening programme. In its 2005 guidance, the National Institute for Health and Clinical Excellence (NICE) recognised that CT colonography may be used in asymptomatic patients with a high risk of developing colorectal cancer (NICE, 2005).

Summary

6.28 CT colonography has variable sensitivity and (especially) variable specificity in the screen detection of colonic polyps, with better results in large, specialist centres. It is best for detecting lesions over 6 mm in diameter. The technique requires an experienced, specialised, and highly trained radiologist

for the accurate interpretation of images. CT colonography has a high likelihood of generating further investigations and/or interventions for extra-colonic findings, an outcome that is especially likely in the context of whole body CT scanning.

6.29 The procedures involved with CT colonography are generally safe, with very low rates of complications, the principal one being bowel perforation. There is an associated estimated lifetime risk of causing cancer of between 0.1% and 0.4%, depending on the age of onset of screening and screening interval.

6.30 CT colonography may be associated with the need for bowel preparation, intravenous agents and bowel insufflation, with their attendant discomfort. If a lesion is found, an additional colonoscopy would be required.

6.31 There may be a place for CT colonography as an investigation for colorectal cancer. However, the risk–benefit ratio depends on the age at which it is done, with relatively less benefit and more risk in patients under the age of 50 years compared with patients aged over 60 years.

6.32 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 comprehensive programme. This should be undertaken in conjunction with specialist units, where there is full access to expertise in medical genetics, a colorectal cancer multidisciplinary team, and a dedicated screening programme targeted to such high risk groups. It is inappropriate for such patients to be investigated in commercial scanning centres.

6.33 Radiologists interpreting CT colonography images should be trained appropriately and should have had adequate experience in doing so.

CHAPTER 7

CT SCANNING FOR OTHER CONDITIONS

7.1 As indicated in Chapter 3, whole body CT scanning is the term generally used in the UK to refer to scanning of the torso – ie chest, abdomen and pelvis. The torso includes major vital organs such as heart, lungs, kidney, liver, pancreas, spleen and ovaries. Other areas of the torso including the digestive tract and major blood vessels (in particular, the aorta) may be scanned as part of a whole body CT scan or independently (eg coronary arteries). It should be noted that imaging to detect some abnormalities may require special preparation and it is unlikely that a general whole body CT scan could detect a range of possible conditions (eg scanning of the gallbladder to detect gall stones).

7.2 This chapter considers the evidence for potential benefit and detriment from scanning other parts of the body or types of tissue in asymptomatic individuals.

7.3 The basis of any scanning of asymptomatic individuals should be proven value of the modality from its diagnostic use. CT has established diagnostic applications throughout the body, and this chapter considers a number of these that have been or might be offered as part of commercial services addressed towards the asymptomatic individual, but that are not specifically identified in Chapter 3.

7.4 Three specific areas have been identified:

(i) spinal problems,

(ii) osteoporosis,

(iii) body fat assessment.

Spinal problems

7.5 Spinal problems affect a large proportion of the population but usually have associated symptoms such as aches and acute pain. Nevertheless, CT scanning services have indicated that such conditions may be detected with CT.

7.6 Degenerative changes are present in most people from middle age onwards. The value of any imaging investigation for asymptomatic spinal conditions is questionable but MRI or radiography, in specific circumstances, would be the modalities of choice.

7.7 CT in particular is considered to be the diagnostic investigation of choice only when a high degree of bony detail is required, or as a specialised investigation to demonstrate sequestra, for diagnosis of some tumours and as part of biopsy techniques. Patients with the former conditions would be expected to present with symptoms.

Osteoporosis

7.8 Osteoporosis is a common condition in the elderly that has been linked to poor diet and hormonal changes in women. Approximately 29% of women

and 18% of men aged over 45 years exhibit some degree of osteoporosis, the differential widening markedly as women reach the menopause. Treatments using hormone replacements can be offered which may influence the onset and development of osteoporosis. CT scanning is offered commercially for this purpose.

7.9 Quantitative CT can provide objective measurement of bone mineral content when considering metabolic bone disease and specific software packages have been available for many years from CT equipment manufacturers. CT is the only modality which can produce three-dimensional volumetric bone density assessment.

7.10 The most commonly used modality for assessment of osteoporosis is purpose-designed Dual Energy X-ray Absorptiometry (DEXA). These systems provide an areal projection of the three-dimensional structure. DEXA has a large body of calibration data and is widely regarded as the method of choice for serial measurement of bone density. A typical effective dose for a DEXA study can be 2.5 μSv compared to 300 μSv – 1 mSv for single and dual energy CT techniques, respectively (Huda and Morin, 1996).

7.11 Ultrasound methods, particularly calcaneal (heel bone) measurement, have been used to obtain bone mineral density information without any radiation dose, which could be regarded as a significant advantage when used with asymptomatic individuals, although it should be noted that the radiation dose associated with DEXA is low. Calcaneal ultrasound measurements have been regarded as too inaccurate for screening in low risk populations (Fenton and Deyo, 2003). Sim et al (2005) studied the possibility of using ultrasonic measurement as a pre-screen for DEXA but found it not to be cost-effective.

7.12 There are no randomised clinical trials relating CT to selection of patients for drug therapy or to reducing the risk of fracture, although a 36% difference in fracture rate between (non-randomised) groups which did and did not undergo bone mineral density testing has been reported (Kern et al, 2005). This surprisingly large difference is thought to be due largely to confounding factors between the groups. Because of its sensitivity, CT appears to over-report and mis-categorise osteoporosis (Damilakis et al, 2007). It is unlikely that clinical trials with fracture outcomes would be carried out on the basis of CT inclusion criteria.

7.13 International opinion on the utility of bone mineral measurement varies. The US Preventive Services Task Force (Nelson et al, 2002) and other organisations have recommended that measurement of bone mineral density is cost-effective in women over 65 years of age. Guidelines also recommend measurement in younger, post-menopausal women who have at least one strong risk factor for fracture. The Swedish Council on Technology Assessment in Health Care reviewed the literature and reached the conclusion that there is no scientific evidence to support the use of bone density measurement as a screening method in healthy, middle-aged individuals (Swedish Council on Technology Assessment in Health Care, 2003).

7.14 Comparison of DEXA and CT for measurement of bone mineral density of the lumbar spine of thalassaemia patients has shown that these methods cannot be used interchangeably; it was not possible to determine which technique measured the overall vertebral strength more exactly (Angelopoulos et al, 2006).

7.15 DEXA and calcaneal ultrasound are considered to be the best methods for predicting fracture risk (Placide and Martens, 2003). For the longer-term study of patients undergoing therapy, these authors considered that DEXA was the optimal technique.

Body fat assessment

7.16 Body fat is a major factor in a range of clinical conditions, although the conditions themselves (eg diabetes) are not generally assessed through imaging.

7.17 Body fat is also the subject of a multi-million pound industry that encourages weight loss and body change in the interests of fashion. Liposuction is becoming one of the more common cosmetic surgery procedures.

7.18 CT demonstrates body fat well, in terms of position and amount and indeed the imaging of some organs is greatly enhanced through structural delineation by fat. CT has been used to demonstrate fat deposition in a number of research studies. Although not currently offered commercially, it might be possible to use CT to identify fat deposits prior to cosmetic procedures, or following such procedures to demonstrate removal or redistribution of body fat as required.

7.19 Accurate determination of body fat can be achieved through the use of other modalities. Recently, software modifications have been introduced which permit the use of DEXA. There is a long history of fat measurement by anthropometric (skinfold) techniques also, and, within the last 20 years, bioelectrical impedance analysis techniques have been developed.

7.20 Measurements of percentage body fat using DEXA and abdominal CT showed that the former gave consistently lower values (34% versus 54%), although the coefficient of variation was around 2% (Lane et al, 2005). Similarly, DEXA measurements of leg fat were significantly lower than multislice CT values for leg adipose tissue volume, although they were highly correlated; the differences were consistent with the 10–15% non-fat components of adipose tissue (Levine et al, 2000). This study found poor correlations for DEXA with single slice CT.

7.21 In contrast, the differences in fat mass estimated by DEXA and CT were small, although significantly different; DEXA was felt to be sufficiently accurate (Salamone et al, 2000). The same group had previously compared body fat-free mass estimation by DEXA and a four-compartment body composition model, and found a high correlation (Visser et al, 1999).

7.22 Bioelectrical impedance analysis measures the resistance of the body to a small alternating electric current, typically at several frequencies. All such techniques employ some form of predictive modelling (Chumlea, 2004). Although widely used, bioelectrical impedance analysis appears to underestimate fat-free mass when compared to DEXA (Lerario et al, 2006). Chumlea (2004) recommended that, while useful for group measurements, it should not be used for individual measurements due to the large predictive error. However, skinfold measurements have greater precision than bioelectrical impedance analysis and should be used instead of bioelectrical impedance analysis wherever possible, in the presence of trained staff (Utter et al, 2005).

7.23 In HIV/AIDS patients, skinfold measurements of central subcutaneous fat correlated with both DEXA and abdominal CT, suggesting that the simpler, non-radiation methodology is adequate for both research and healthcare purposes (Florindo et al, 2004).

7.24 The cost of the CT study is higher than the alternative assessment techniques, eg the cost of CT for the determination of osteoporosis is some five times that for DEXA.

Summary

7.25 There is a range of established approaches for assessing spinal problems, osteoporosis and body fat. These approaches involve very small doses of ionising radiation or use non-ionising radiation, and consequently have lower or no radiological risk consequences. CT is the diagnostic investigation of choice in only a very few circumstances and should be considered a specialised investigation, none of which is applicable to the investigation of the asymptomatic individual.

CHAPTER 8

CONCLUSIONS

8.1 This, our Twelfth Report, follows the Department of Health's request that radiation protection aspects of medical practices should be included within our sphere of interest. This is a significant development in the work programme of COMARE.

8.2 CT scanning of the asymptomatic individual may provide benefits to that person. However, these benefits will not be the same as those in the use of diagnostic CT where the patient presents with symptoms. Therefore the justification of CT scanning of the asymptomatic individual cannot be considered in the same way as justification for patients.

8.3 Scanning of the asymptomatic individual by using CT is a practice that has implications for public health. There are limited resources available for state provided healthcare. Where CT scanning of the asymptomatic individual is proved to result in reducing disease-specific mortality, there is a basis for consideration of increasing or diverting resources into investigations and treatment following this CT scanning. If, however, CT scanning of the individual results in additional procedures without high expectation of benefits, then the likely impact on NHS resources provides a basis for controlling such practice.

8.4 Care needs to be taken when comparing the benefits of CT for diagnosis of patients with symptoms, national CT screening programmes (of which there is none at present in the UK) and the use of CT in the assessment of asymptomatic individuals. While this report addresses only the last of these, it must in part draw on the experience of the other two scenarios.

8.5 It is recognised that CT is a fast evolving modality. The capability of CT in terms of its spatial and contrast resolution and the time in which scans are performed will continue to evolve. This may improve sensitivity and specificity (ie reduce false positive and false negative rates).

8.6 Within the context of this report, other factors must be taken into account such as the time taken for a scan, the relative costs of scanners and the subsequent cost per scan. These will all influence the availability of CT services offered for asymptomatic individuals.

8.7 The expected increased use of dose reduction technology within CT over the next few years will significantly influence its use in asymptomatic individuals. This might be provided by hardware changes or software control but both can affect the benefit to detriment ratio.

8.8 Improvements in some or all of these factors may influence advice on the appropriateness of CT scanning for asymptomatic individuals. These factors will need to result in new research evidence demonstrating improved benefit, such as impact on outcome, before the recommendations within this report are reviewed. The adoption of CT scanning in national screening

programmes will also depend on these factors and will require a different evaluation, but the mechanisms to do so are already in place within the NHS.

8.9 In considering this topic, we have reviewed the evidence available from a wide range of sources. In contrast to the data on specificity and sensitivity of CT in the diagnostic symptomatic arena, reliable data are not abundant on its use for assessment of asymptomatic individuals outside, or even within, a screening programme.

8.10 We have also considered, in producing this report, the amount and type of information that is made available to individuals who take advantage of commercially available services.

8.11 We have noted that the available data, such as they exist, are not generally made available to individuals. The amount of information given regarding radiation dose and risk of the procedure itself is not always consistent or well presented. Information relating to follow-on procedures that will be necessary to confirm initial findings and how these are provided is not clear. Commercial companies do not tend to explain that a percentage of results will be false positives and that these may have physical and psychological implications.

8.12 The ownership and availability of results to inform subsequent care of the individual need to be made clearer and in many cases more care needs to be given to the integration of such services into a clinical care pathway, if such services are to have real benefit.

8.13 Finally, we have considered the regulation of these services themselves rather than the regulatory framework that addresses medical exposures in all circumstances. These and the points highlighted above are addressed in the recommendations of this report.

CHAPTER 9

RECOMMENDATIONS

In this report we have reviewed the literature regarding the benefit and detriment associated with X-ray computed tomography (CT) scanning in the health assessment of asymptomatic individuals. We have not restricted our evaluation to the detriment caused by radiation alone. Indeed, the detriment associated with a single targeted CT scan, when expressed in terms of the risk of cancer induction alone, is usually below that considered to be unacceptable. Instead we have considered the total potential detriment from the first and subsequent scans, that from other investigations which might be necessary to confirm a diagnosis, and balanced this against the benefit to the individual of the first CT scan. While reviewing this type of practice, we have also considered alternative techniques using lower doses of ionising radiation or non-ionising radiation.

Recommendation 1

Medical exposures using ionising radiation and the equipment used to undertake these exposures are controlled by a number of regulations, including the Ionising Radiation (Medical Exposure) Regulations 2000 and Ionising Radiations Regulations 1999. These regulations apply to exposures undertaken both in the NHS and in the commercial sector. Commercial CT services themselves, however, are not subject to additional regulation as they do not involve interventions or treatment. We recommend that the Department of Health should review this situation and consider regulating these services against agreed standards. Any regulation should address and provide guidelines on appropriate referral processes, justification and optimisation of CT scans. It should also require that providers of CT services should submit agreed datasets to the regulator regarding the rate of reported findings.

Recommendation 2

The information supplied to asymptomatic clients attending commercial CT services is inconsistent and incomplete. We recommend that all such services should provide comprehensive information regarding eligibility criteria and the dose and risk of the initial CT scan. The rates of false negative and false positive findings associated with CT scanning of asymptomatic individuals should be independently audited and explained. In particular, the range of further investigations that may be required to confirm initial findings and the risks associated with subsequent scans if recommended, should be discussed. The provision of these investigations will need to be clarified. An outline of this information should be made available to individuals before they present for scanning, as part of websites, advertising literature, etc.

Recommendation 3

Any medical intervention will be most effective when part of a locally agreed and coordinated clinical care pathway that is under the supervision of a multidisciplinary team. We recommend that commercial CT services should have well-developed, robust and confidential mechanisms for integrating the results of their examinations into an established care pathway, including the availability of scans and data relating to any individual scanned in formats consistent with NHS information technology programmes. This intended transfer of medical data must be discussed with and agreed by patients prior to medical exposures taking place.

Recommendation 4 Any individual with symptoms relevant to conditions likely to be identifiable by CT scanning, should be entered into an appropriate care pathway as soon as possible. The customary process is for this to be initiated by a referral from a general practitioner (GP). Therefore commercial CT services, which may not be able to provide a full range of diagnostic capabilities, should in most circumstances refer personally initiating symptomatic individuals back to their GP without delay. This will, of course, not apply where a patient has been referred for a CT scan by their GP or a relevant NHS hospital-based medical specialist who is responsible for the individual's care.

Recommendation 5 There is a regulatory requirement that all medical exposures using ionising radiation should be referred, justified and optimised. Referral and justification must be carried out by registered healthcare professionals. Justification of any medical exposure should be based on the scientific evidence available. There is little evidence that demonstrates, for whole body CT scanning, the benefit outweighs the detriment. We recommend therefore that services offering whole body CT scanning of asymptomatic individuals should stop doing so immediately. Where scans are offered for a number of discrete anatomical regions within a single scanning procedure, the advertising should clearly state which regions are examined and for which conditions the scan is optimised. In CT scanning it is not possible to optimise exposure parameters for scans of the whole of the body.

Recommendation 6 Investigation of a number of clinical conditions can be better undertaken using modalities other than CT. We recommend that where there is evidence that CT is not the modality of choice for diagnostic purposes, then it should not be made available for the assessment of asymptomatic individuals. In particular, CT scanning primarily for spinal conditions, osteoporosis and body fat assessment should cease, since there are more appropriate methods available and which have lower radiological risk consequences. If analysis of data available from a scan intended for other purposes provides clinically useful and reliable information on, for example, osteoporosis, it would be permissible to include these data in the results.

Recommendation 7 Current evidence suggests that there is no benefit to be derived from CT scanning of the lung in asymptomatic individuals. Further research is required in this area but, until this is available, CT scanning of the asymptomatic individual cannot be justified for the lung and should not be made available.

Recommendation 8 Electron beam CT scanning to determine coronary artery calcification is valuable for predicting cardiovascular risk in asymptomatic individuals. Further studies with multidetector CT are expected to have similar results. We recommend that CT scanning should only be undertaken on individuals with intermediate risk identified by a comprehensive cardiovascular Framingham risk score assessment, unless the referral is by a cardiac specialist. Research will be required to determine the feasibility and efficacy of a combined coronary artery calcification score/conventional risk score approach in reducing coronary heart disease events in this population. It is recommended that scans should not be performed routinely more frequently than once every three years.

Recommendation 9 CT colonography has the potential to detect small lesions in asymptomatic individuals, although the finding of a suspicious lesion on CT colonography would require a conventional colonoscopy for histological diagnosis or treatment. Despite this, CT colonography may find a place in routine diagnostic and screening practice. We recommend that screening for colorectal cancer outside of the NHS screening programmes should only be undertaken in individuals in the appropriate age group, and not, therefore, under the age of

50 years, unless they have been referred by an appropriate medical specialist. In keeping with the NHS screening programmes, scans should not be performed routinely more frequently than once every two or three years. Individuals at high risk of developing colorectal cancer (eg with familial adenomatous polyposis, or those with a family history of colorectal cancer) should be assessed in a specialist unit that includes access to medical genetics, and specialist services in surgery, histopathology and oncology. Screening of high risk individuals by CT colonography should only be performed as part of a multidisciplinary care package with input from an appropriate specialist unit.

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ACKNOWLEDGEMENTS

Michael Macari MD for supplying composites for Figure 6.1 (Department of Radiology, Division of Abdominal Imaging, NYU Medical Center, NYU School of Medicine, 560 First Avenue, Suite HW 207, New York, NY 10016).

Elsevier Publishing and the Radiological Society of North America for permission to use figures.

THE APPENDICES

APPENDIX A

GLOSSARY

ABSORBED DOSE	The quantity of energy imparted by ionising radiation to a unit mass of matter such as tissue. Absorbed dose has the units J kg^{-1} and the specific name gray (Gy), where 1 Gy = 1 joule per kg.
ADENOCARCINOMA	A carcinoma formed from glandular tissue.
ADIPOSE TISSUE	Body tissue that provides insulation and serves as an energy reserve, consisting of large spherical cells specialised for the storage of fat and oil.
AGATSTON SCORING	Agatston scoring, introduced in 1990, is the traditional method for quantifying coronary calcium with EBCT. The method is based on the maximum X-ray attenuation coefficient, or CT number (measured in Hounsfield Units), and the area of calcium deposits.
ANEURYSM	A localised widening (dilatation) of an artery, vein or the heart. At the area of an aneurysm, there is typically a bulge and the wall is weakened and may rupture.
ANGIOGRAM	An X-ray image of the blood vessels, with a radiocontrast agent added to the blood via a catheter to make visualisation possible.
ANOMALY	A marked deviation from the usual; something different, peculiar or abnormal.
ASYMPTOMATIC	Without obvious symptoms of disease.
ATHEROMA	A fatty deposit in the intima (inner lining) of an artery, resulting from atherosclerosis. Also called an atherosclerotic plaque.
ATHEROSCLEROSIS	A process of progressive thickening and hardening of the walls of medium-sized and large arteries as a result of fat deposits on their inner lining. This build-up of fat may slow down or stop blood flow. This is known to occur to some degree with ageing, but other risk factors that accelerate this process have been identified. These factors include high cholesterol, high blood pressure, smoking, diabetes and family history for atherosclerotic disease. Atherosclerosis is responsible for much coronary artery disease (angina and heart attacks) and many strokes.
ATORVASTATIN	Atorvastatin is a drug used to lower levels of cholesterol and fats in the blood.
ATYPICAL ADENOMATOUS HYPERPLASIA (AAH)	A putative precursor lesion of pulmonary adenocarcinoma, according to many immunohistochemical and genetical studies.
BENIGN	Non-cancerous or non-malignant. A benign tumour may grow but it does not invade surrounding tissue or spread to other parts of the body.
BETA-BLOCKERS	A large group of medications that act to block specific receptors in the nervous system. The effect of beta-blockade results in slowing of the heart rate, and reduction in blood pressure. Beta-blockers are used in the treatment of high blood pressure and other heart conditions.
BIOPSY	A medical test involving the removal of cells or tissues for examination.

BODY FAT ASSESSMENT *See obesity.*

CARCINOMA A malignant growth. Carcinomas invade surrounding tissues and organs, and may spread to lymph nodes and distal sites (metastasis).

CARDIAC GATING Using an electrical signal from the contraction of the heart to trigger the imaging of separate phases of the cardiac cycle. The ECG comprises various waves, of which the R wave is the most prominent. The RR interval is the time between successive heart contractions.

COLONOSCOPY A procedure in which a long flexible viewing tube (a colonoscope) is threaded up through the rectum for the purpose of inspecting the entire colon and rectum and, if there is an abnormality, taking a biopsy of it or removing it. The colonoscopy procedure requires a thorough bowel cleansing to assure a clear view of the lining.

COLORECTAL Pertaining to the colon and the rectum, or the entire large bowel.

COMPUTED TOMOGRAPHY (CT) A special radiographical technique that uses a computer to assimilate multiple X-ray images into a two-dimensional cross-sectional image.

CONTRAST AGENT A substance that is introduced into or around a structure and, because of the difference in absorption of X-rays by the contrast medium and the surrounding tissues, allows radiographical visualisation of the structure.

CORONARY CALCIFICATION Coronary calcification is an organised, regulated process similar to bone formation that occurs only when other aspects of atherosclerosis are also present. Calcification is found more frequently in advanced lesions, but it may also occur in small amounts in earlier lesions that appear earlier in life. Plaques with microscopic evidence of calcification are larger and associated with larger coronary arteries than are plaques or arteries without calcification. The relation of arterial calcification to the probability of plaque rupture is unknown, and further research is needed to better elucidate the relation of calcification to the pathogenesis of both atherosclerosis and plaque rupture.

DIABETES Refers to diabetes mellitus or, less often, to diabetes insipidus. Diabetes mellitus and diabetes insipidus share the name ‘diabetes’ because they are both conditions characterised by excessive urination (polyuria).

When ‘diabetes’ is used alone, it generally refers to diabetes mellitus. The two main types of diabetes mellitus – insulin-requiring type 1 diabetes and adult-onset type 2 diabetes – are distinct and different diseases in themselves.

DIASTOLE The time, in between ventricular contractions of the heart, at which ventricular filling occurs.

DISTAL In anatomy, the farthest from the point of attachment.

DISTENSION Stretched or enlarged, as in distended bowel.

DOSE A measure of the amount of radiation received. More strictly it is related to the energy absorbed per unit mass of tissue *(see absorbed dose)*. Doses can be estimated for individual organs or for the body as a whole.

EFFECTIVE DOSE Effective dose is the sum of the weighted equivalent doses in all the tissues and organs of the body. It takes into account the biological effectiveness of different types of radiation and variation in the susceptibility of different organs and tissues to radiation damage. Thus it provides a common basis for comparing exposures from different sources. It has the unit of sievert (Sv).

EQUIVALENT DOSE The quantity obtained by multiplying the absorbed dose by a factor to allow for the different effectiveness of the various ionising radiations in causing harm to tissue. It has the unit of sievert (Sv).

ELECTROCARDIOGRAM A recording of the electrical activity of the heart.

ELECTRON BEAM COMPUTED TOMOGRAPHY (EBCT)

A high resolution volume X-ray scanning method used to identify calcification in and around the coronary arteries.

FALSE NEGATIVE

This is an erroneous test result which occurs when the test result is *negative* but the individual *does have* the condition under test.

FALSE POSITIVE

This is an erroneous test result which occurs when the test result is *positive* but the individual *does not have* the condition under test.

FRAMINGHAM CORONARY RISK CALCUATION

The Framingham risk score gives estimates for 'hard coronary heart disease' which includes myocardial infarction and coronary death. The risk factors included in the Framingham calculation are age, total cholesterol, HDL cholesterol, systolic blood pressure, treatment for hypertension and cigarette smoking.

GRANULOMA

Granulomas are small nodules that are seen in a variety of diseases such as Crohn's disease, tuberculosis, sarcoidosis, berylliosis and syphilis, or as a reaction to a foreign body in the tissues. They are often seen in the lungs and typically cause no signs or symptoms. Although they are benign, they may resemble cancer on an X-ray.

GRAY (Gy)

The international (SI) unit of absorbed dose. 1 gray is equivalent to 1 joule of energy absorbed per kilogram of matter such as body tissue.

HETEROGENEITY

The quality of being made of many different elements, forms, kinds or individuals, each distinct from each other.

HISTOLOGY

The microscopic study of tissue sectioned as a thin slice. It can also be described as microscopic anatomy and is an important tool of anatomical pathology, eg in the accurate diagnosis of cancer.

HOMOGENEITY

The opposite of heterogeneity.

HOUNSFIELD UNIT

A normalised index of X-ray attenuation based on a scale of –1000 (air) to +1000 (bone), with water being 0.

HYOSCINE

An alkaloid drug that acts on the autonomic nervous system to prevent muscle spasm and nausea.

HYPERLIPIDAEMIA

A disorder of lipoprotein metabolism, including lipoprotein overproduction or deficiency. Hyperlipidaemias may be manifested by elevation of the total cholesterol, the 'bad' low density lipoprotein (LDL) cholesterol and the triglyceride concentrations, and a decrease in the 'good' high density lipoprotein (HDL) cholesterol concentration in the blood.

Hyperlipidaemia comes under consideration in many situations including diabetes, a common cause of lipidemia. For adults with diabetes, it has been recommended that the levels of LDL, HDL, and total cholesterol, and triglyceride be measured every year. Optimal LDL cholesterol levels for adults with diabetes are less than 100 mg dL^{-1} (2.60 mmol L^{-1}), optimal HDL cholesterol levels are equal to or greater than 40 mg dL^{-1} (1.02 mmol L^{-1}), and desirable triglyceride levels are less than 150 mg dL^{-1} (1.7 mmol L^{-1}).

HYPERTENSION

This is a condition of a consistently high arterial blood pressure. Hypertension can cause blood vessel changes in the back of the eye (retina), abnormal thickening of the heart muscle, kidney failure and brain damage. There may be no known cause or it may be associated with other primary diseases (secondary hypertension). The condition may be treated with regular aerobic exercise, weight loss, salt restriction, and medications. Hypertension is considered a risk factor for the development of heart disease, peripheral vascular disease, stroke and kidney disease.

IMMUNO-HISTOCHEMISTRY

Immunohistochemistry is a method of analysing and identifying cell types based on the binding of antibodies to specific components of the cell.

INCIDENCE	This is the number of new cases of a disease arising in a population over a specific period of time, usually one year.
INDOLENT	An indolent condition is such that it is recognised as not rapidly spreading, in contrast to an 'aggressive' condition.
INSUFFLATE	Injection of a gas (such as carbon dioxide) or powder into the body cavity.
INTRAVENOUS CONTRAST	A dye injected into the vein used to provide contrast between blood vessels and other tissues, or to enhance the visibility of tumours on an image.
IONISING RADIATION	Radiation that is sufficiently energetic to remove electrons from atoms in its path. In human or animal exposures ionising radiation can result in the formation of highly reactive particles in the body which can cause damage to individual components of living cells and tissues.
ISCHAEMIA	A low oxygen state usually due to obstruction of the arterial blood supply or inadequate blood flow leading to hypoxia in the tissue.
LEAD TIME	Lead time is the interval by which the time of diagnosis is brought forward by screening.
LEAD TIME BIAS	This is the apparent prolongation in survival for screened individuals following early diagnosis by screening due to lead time.
LENGTH TIME	This is the interval during which a tumour may be detected by screening before it is of sufficient size to be detected clinically or cause symptoms.
LENGTH TIME BIAS	Tumours which are slow growing are generally associated with more favourable outcome. These tumours have a longer period during which they may be detected pre-clinically by screening and so are more likely to be detected by pre-clinical screening. Hence, length time bias is the apparent improved outcome in screen-detected patients due to the fact that slow growing tumours are more likely to be detected.
LIPOSUCTION	A type of cosmetic surgery in which localised areas of fat are removed from beneath the skin using a suction-pump device inserted through a small incision.
LOBECTOMY	Surgical removal of one lobe of the lung.
MALIGNANT	Cancerous growth, a mass of cells showing uncontrolled growth, a tendency to invade and damage surrounding tissues and an ability to seed daughter growths to sites remote from the primary growth.
MAMMOGRAPHY	Mammography is a specific type of imaging that uses an X-ray system for the examination of breasts. The technique is used as a screening tool to detect early breast cancer in asymptomatic women. A mammogram is able to detect early breast cancer when a lump is less than 2 cm in size. Currently, it is believed that routine mammography is life saving in women over the age of 50 years, useful between 40 and 50 years and not normally recommended as a routine test for women under 40 years, and useful to detect and diagnose breast disease in women with symptoms.
METASTATIC DISEASE	A disease which is able to spread from the organ or tissue of origin to another part of the body.
MORBIDITY	Morbidity is the presence of symptomatic disease or illness in a population.
MORTALITY	This is the rate of death in a population.
MYOCARDIAL PERFUSION	Blood flow through the heart.
MULTIDETECTOR CT (MDCT)	A form of CT technology used in diagnostic imaging, where a two-dimensional array of detector elements replaces the linear array typically used in conventional and helical CT scanners. This arrangement allows the acquisition of multiple slices or sections simultaneously and therefore greatly increases the speed of image acquisition.

NEUROBLASTOMA	A leading childhood form of cancer that arises in the adrenal gland or in tissue of the nervous system relating to the adrenal gland. It is often present at birth but usually is not detected until later in infancy or childhood.
NODULES	A small aggregation of cells, which are usually benign and often painless. They may, however, affect the function of the organ.
OBESITY	An increase in body weight beyond the limitation of skeletal and physical requirement, as the result of an excessive accumulation of fat in the body. A person is considered obese if he or she has 20 per cent (or more) extra body fat for his/her age, height, sex and bone structure. Extra body fat is thought to be a risk factor for many conditions, including diabetes, stroke and coronary artery disease.
OPACIFICATION	The process of becoming cloudy or opaque.
OSTEOPOROSIS	This is a condition where thinning of the bones occurs with a reduction in bone mass brought about by a depletion of calcium and bone protein. Osteoporosis predisposes a person to fractures, which are often slow to heal and fail to heal properly. It is more common in older adults, particularly post-menopausal women, in patients on steroids, and in those who take steroidal drugs. Unchecked osteoporosis can lead to changes in posture, physical abnormality, and decreased mobility. Osteoporosis can be detected by using tests that measure bone density. Treatment of osteoporosis includes ensuring that the diet contains adequate calcium and other minerals needed to promote new bone growth, and for post-menopausal women, oestrogen or combination hormone supplements.
OVERDIAGNOSIS	The identification during a screening examination of a lesion, which appears both on a scan and on biopsy to be a malignant tumour, but would not have presented as clinical disease during the lifetime of the individual.
PATENCY	The state of being freely open or expanded or unblocked.
PERCUTANEOUS	A surgical procedure where access to inner organs or other tissue is gained via needle-puncture of the skin, instead of using an ‘open’ approach where inner organs or tissues are exposed.
PIXEL	Picture element (pix for picture, el for element). A single, finite-sized element of a digitised video picture. A pixel is defined by its *X* and *Y* coordinates and its grey level or colour, commonly expressed by binary numbers.
PLACEBO	A substance that is administered as a drug but has no medicinal content, either given to a patient for its reassuring and therefore beneficial effect, or used in a clinical trial of a real drug, in which participants who have been given a placebo (though believing that it is the real drug) serve as untreated control subjects for comparison with those actually given the drug.
PNEUMONECTOMY	Surgical removal of a whole lung.
POLYPS	A mass of tissue that develops on the mucosal wall of a hollow organ, such as in the colon or rectum. Polyps are usually benign, but some have the potential to become cancerous.
POSITRON EMISSION TOMOGRAPHY (PET) SCAN	A diagnostic examination involving the acquisition of physiological images based on the detection of radiation through the emission of positrons. The positrons are emitted from a short-lived radioactive isotope incorporated into a metabolically active substance administered to the patient prior to the examination.
PREVALENCE	This is the number of cases of disease present in a population at any one time.
PRONE	With the front surface downwards; an individual lying prone has their face downwards.
PROGNOSTIC	A sign or symptom indicating the course and termination of a disease.

PROSTATE CANCER (PROSTATIC CARCINOMA)	Cancer that begins in the prostate. Cells in the prostate start to divide and grow out of their normal pattern, and grow into lumpy bundles of cells called tumours. Tumours disrupt the normal function of the prostate, and cells that come free from the tumour can travel elsewhere in the body, and begin to grow tumours there.
PSEUDODISEASE	A disease that does not affect the quality or the length of a patient's life.
PUBIC SYMPHYSIS	The join between the pubic bones at the front of the pelvis.
PULMONARY FIBROSIS	The formation or development of excess fibrous connective tissue in the lung as a reparative or reactive process.
PURGATIVE	An agent that stimulates evacuation of the bowel.
RADIOLOGIST	A medically qualified doctor who specialises in the use of imaging techniques (X-rays, ultrasound, CT, MR, fine needle biopsy, etc) for diagnosis (diagnostic radiologist) or one who specialises in the use of imaging techniques in assisting treatment (in inserting catheters into blood vessels, in choking the blood supply of a tumour by injection of a type of glue, etc) (interventional radiologist).
RECONSTRUCTION	The computerised creation of images from a series of X-ray projections in computed tomography.
REGRESSION	A subsidence of symptoms or of a disease process to an earlier state, particularly that of a tumour.
RESECTION	A surgical procedure to remove part of an organ or structure.
REVASCULARISATION	The regrowth of blood vessels.
RISK	The probability that an event will occur, eg that an individual will become ill or die before a stated period of time or age. This is also a non-technical term encompassing a variety of measures of the probability of a (generally) unfavourable outcome.
SCREENING PROGRAMME	This is the performance of a test or examination in a population aimed at early detection of disease. Screening may be targeted at a high risk group, or be population based and therefore include symptomatic and asymptomatic individuals, or include asymptomatic individuals only.
SENSITIVITY	A measure for assessing the results of diagnostic and screening tests. Sensitivity is the proportion of diseased persons who are identified as being diseased by the test. It is the probability of correctly diagnosing a condition in a person who has that disease.
SEQUESTRUM	A fragment of dead tissue, usually bone, that separates from surrounding living tissue.
SIEVERT (Sv)	The international (SI) unit of effective dose obtained by weighting the equivalent dose in each tissue in the body with the ICRP recommended tissue weighting factors and summing over all tissues. Because the sievert is a large unit, effective dose is commonly expressed in millisieverts (mSv) – ie one-thousandth of one sievert. The average annual radiation dose received by members of the public in the UK is 2.7 mSv.
SIGMOIDOSCOPY	A procedure in which an endoscope is used to inspect the sigmoid section of the colon.
SOMATOFORM	A group of disorders in which there are physical symptoms suggesting physical disorders for which there are no demonstrable organic findings or known physiological mechanisms, and for which there is positive evidence, or a strong presumption, that the symptoms are linked to psychological factors (eg hysteria, conversion disorder, hypochondriasis and pain disorder).
SPECIFICITY	A measure for assessing the results of diagnostic and screening tests. Specificity is the proportion of normal individuals who are so identified by the screening test. It is the probability of correctly excluding a disease in a normal individual.
STENOSIS	The narrowing of an artery or vessel.

SUPINE	With the back surface downwards; an individual lying supine has their face upwards.
SYMPTOMATIC	A person with symptoms of disease.
T1 AND T2 TUMOURS	Tumours can be classified using the TNM (Tumour Node Metastases) system. The T classifies the extent of the primary tumour, and is normally given as T0 through T4. T0 represents a tumour that has not even started to invade the local tissues. T4, however, represents a large primary tumour that has probably invaded other organs by direct extension, and which is usually inoperable.
THORACOTOMY	A surgical incision to the chest to allow a surgeon access to the thoracic organs, eg the heart or the lungs.
TORSO	The main part of the human body, without the limbs and head; the trunk.
TRANSVERSE	In anatomy, lying in a crosswise direction.
TRUE NEGATIVE	This is a correct test result which occurs when the test result is *negative* and the individual *does not have* the condition under test.
TRUE POSITIVE	This is a correct test result which occurs when the test result is *positive* and the individual *does have* the condition under test.
TUMOUR	Mass of tissue formed by unregulated growth of cells; can be benign or malignant.
X-RAY	An image obtained using high energy radiation with waves shorter than those of visible light. X-rays possess the properties of penetrating most substances (to varying extents), of acting on a photographic film or plate (permitting radiography), and of causing a fluorescent screen to give off light (permitting fluoroscopy). In low doses X-rays are used for making images that help to diagnose disease, and in high doses to treat cancer.

APPENDIX B

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Department of Trade and Industry

Environment Agency

Food Standards Agency

Health Protection Agency – Radiation Protection Division (formerly NRPB)

Health and Safety Executive

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APPENDIX C

DECLARATION OF MEMBERS' INTERESTS CODE OF PRACTICE

Introduction

1 This code of practice guides members of COMARE as to the circumstances in which they should declare an interest in the course of the Committee's work.

2 To avoid any public concern that commercial interests of members might affect their advice to Government, Ministers have decided that information on significant and relevant interests of members of its advisory committees should be on the public record. The advice of the Committee frequently relates to matters which are connected with the nuclear industry generally and, less frequently, to commercial interests involving radioactivity and it is therefore desirable that members should comply with the Code of Practice which is set out below.

Scope and definitions

3 This code applies to members of COMARE and sub-groups or working groups of COMARE which may be formed.

4 For the purposes of this code of practice, the 'radiation industry' means:

(a) companies, partnerships or individuals who are involved with the manufacture, sale or supply of products processes or services which are the subject of the Committee's business. This will include nuclear power generation, the nuclear fuel reprocessing industry and associated isotope producing industries, both military and civil;

(b) trade associations representing companies involved with such products;

(c) companies, partnerships or individuals who are directly concerned with research or development in related areas;

(d) interest groups or environmental organisations with a known interest in radiation matters.

It is recognised that an interest in a particular company or group may, because of the course of the Committee's work, become relevant when the member had no prior expectation this would be the case. In such cases, the member should declare that interest to the Chairman of the meeting and thereafter to the Secretariat.

5 In this code, 'the Department' means the Department of Health, and 'the Secretariat' means the secretariat of COMARE.

Different types of interest – definitions

6 The following is intended as a guide to the kinds of interests which should be declared. Where a member is uncertain as to whether an interest should be declared he or she should seek guidance from the Secretariat or, where it may concern a particular subject which is to be considered at a meeting, from the Chairman at that meeting. Neither members nor the

Department are under an obligation to search out links between one company and another, for example where a company with which a member is connected has a relevant interest of which the member is not aware and could not reasonably be expected to be aware.

If members have interests not specified in these notes but which they believe could be regarded as influencing their advice they should declare them to the Secretariat in writing and to the Chairman at the time the issue arises at a meeting.

Personal interests

6.1 A personal interest involves payment to the member personally. The main examples are:

(a) *Consultancies or employment:* any consultancy, directorship, position in or work for the radiation industries which attracts regular or occasional payments in cash or kind.

(b) *Fee-paid work:* any work commissioned by those industries for which the member is paid in cash or kind.

(c) *Shareholdings:* any shareholding in or other beneficial interest in shares of those industries. This does not include shareholdings through unit trusts or similar arrangements where the member has no influence on financial management.

Non-personal interests

6.2 A non-personal interest involves payment which benefits a department for which a member is responsible, but is not received by the member personally. The main examples are:

(a) *Fellowships:* the holding of a fellowship endowed by the radiation industry.

(b) *Support by industry:* any payment, other support or sponsorship by the radiation industry which does not convey any pecuniary or material benefit to a member personally but which does benefit their position or department, eg:

(i) a grant from a company for the running of a unit or department for which a member is responsible;

(ii) a grant or fellowship or other payment to sponsor a post or a member of staff in the unit for which a member is responsible. This does not include financial assistance for students, but does include work carried out by postgraduate students and non-scientific staff, including administrative and general support staff;

(iii) the commissioning of research or work by, or advice from, staff who work in a unit for which the member is responsible.

(c) *Support by charities and charitable consortia:* any payment, other support or sponsorship from these sources towards which the radiation industry has made a specific and readily identifiable contribution. This does not include unqualified support from the radiation industry towards the generality of the charitable resource.

Trusteeships: where a member is trustee of a fund with investments in the radiation industry, the member may wish to consult the Secretariat about the form of declaration which would be appropriate.

Members are under no obligation to seek out knowledge of work done for or on behalf of the radiation industry within departments for which they are responsible if they would not reasonably expect to be informed.

Declaration of interests

7 Members should inform the Department in writing when they are appointed of their current personal and non-personal interests and annually in response to a Secretariat request. Only the name of the company (or other body) and the nature of the interest is required; the amount of any salary, fees, share-holding, grant, etc, need not be disclosed to the Department. An interest is current if the member has a continuing financial involvement with the industry, eg if he or she holds shares in a radiation company, has a consultancy contract, or if the member or the department for which he or she is responsible is in the process of carrying out work for the radiation industry. Members are asked to inform the Department at the time of any change in their personal interests, and will be invited to complete a form of declaration once a year. It would be sufficient if changes in non-personal interests are reported at the next annual declaration following the change. (Non-personal interests involving less than £1000 from a particular company in the previous year need not be declared to the Department.)

Declaration of interests to the department

Declaration of interests at meetings and participation by members

8 Members are required to declare relevant interests at Committee meetings and to state whether they are personal or non personal interests. The declaration should include an indication of the nature of the interest.

(a) If a member has a current (personal or non-personal) interest in the business under discussion, he or she will not automatically be debarred from contributing to the discussion subject to the Chairman's discretion. The Chairman will consider the nature of the business under discussion and of the interest declared (including whether it is personal or non-personal) in deciding whether it would be appropriate for the relevant member to participate in the item.

(b) If a member has an interest which is not current in the business under discussion, this need not be declared unless not to do so might be seen as concealing a relevant interest. The intention should always be that the Chairman and other members of the Committee are fully aware of relevant circumstances.

9 A member who is in any doubt as to whether he or she has an interest which should be declared, or whether to take part in the proceedings, should ask the Chairman for guidance. The Chairman has the power to determine whether or not a member with an interest shall take part in the proceedings.

10 If a member is aware that a matter under consideration is or may become a competitor of a product process or service in which the member has a current personal interest, he or she should declare the interest in the company marketing the rival product. The member should seek the Chairman's guidance on whether to take part in the proceedings.

11 If the Chairman should declare a current interest of any kind, he or she should stand down from the chair for that item and the meeting should be conducted by the Deputy Chairman or other nominee if he or she is not there.

12 Some members of the Committee may, at the time of adoption of this note, or (in the case of new members) of their joining the Committee, be bound by the terms of a contract which requires them to keep the fact of the contractual arrangement confidential. As a transitional measure, any member so affected should seek to agree an entry for the public record (see paragraph 14) with the

other party. If such agreement does not prove possible, the members shall seek a waiver permitting them to disclose their interest, in confidence, to the Chairman and the Secretariat. The Secretariat will maintain a confidential register of such disclosures which will not form part of the public record.

13 On adoption of this note members shall not enter into new contractual obligations which would inhibit their ability to declare a relevant interest.

Record of interests

14 A record will be kept in the Department of the names of members who have declared interests to the Department on appointment, as the interest first arises or through an annual declaration, and the nature of the interest.

15 Information from the record will be made available by the Secretariat to bona-fide enquirers and published by any other means as and where the Department deems appropriate.

Members' declarations of interests – 2006

Member	Company	Personal interest	Company	Non-personal interest
Prof T C Atkinson		None	UKAEA	Consultancy
Dr H R Baillie-Johnson		None		None
Prof R Dale		None		None
Prof A Elliott		None		None
Dr C J Gibson		None		None
Prof S V Hodgson		None	CR-UK	Support for research
Prof P A Jeggo		None		None
Prof G McKenna		None		None
Prof P McKinney		None		None
Dr G Maskell		None		None
Prof M D Mason		None		None
Dr C D Mitchell		None		None
Dr M Murphy		None		None
Dr R A Shields		None		None
Prof I Stratford	Oxford Biomedica AstraZeneca UCB/Celltech	Shares Grants and consultancy Grants		None
Dr J Verne		None		None
Prof R Waters		None		None