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Cancer risks from diagnostic radiology

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ABSTRACT. In recent years, there has been a rapid increase in the number of CT scans performed, both in the US and the UK, which has fuelled concern about the long-term consequences of these exposures, particularly in terms of cancer induction. Statistics from the US and the UK indicate a 20-fold and 12-fold increase, respectively, in CT usage over the past two decades, with *per caput* CT usage in the US being about five times that in the UK. In both countries, most of the collective dose from diagnostic radiology comes from high-dose (in the radiological context) procedures such as CT, interventional radiology and barium enemas; for these procedures, the relevant organ doses are in the range for which there is now direct credible epidemiological evidence of an excess risk of cancer, without the need to extrapolate risks from higher doses. Even for high-dose radiological procedures, the risk to the individual patient is small, so that the benefit/risk balance is generally in the patients' favour. Concerns arise when CT examinations are used without a proven clinical rationale, when alternative modalities could be used with equal efficacy, or when CT scans are repeated unnecessarily. It has been estimated, at least in the US, that these scenarios account for up to one-third of all CT scans. A further issue is the increasing use of CT scans as a screening procedure in asymptomatic patients; at this time, the benefit/risk balance for any of the commonly suggested CT screening techniques has yet to be established.

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The use of X-rays as a diagnostic tool is so well established that it is hard to imagine contemporary medicine without them. At the same time, X-rays are a known and proven human carcinogen. It is the purpose of this review to address the benefit/risk balance associated with these two observations.

Two findings have recently combined to spark concern over the long-term effects of diagnostic X-rays, particularly the induction of cancer. Firstly, as illustrated in Figure 1, CT usage over the past quarter of a century has risen ~12-fold in the UK and >20-fold in the US [1–3]. Current annual usage is estimated to be more than 3 million scans per year in the UK and more than 60 million per year in the US. Overall, the mean effective dose in the US from all medical X-rays has increased ~seven-fold over this period [4], with the result that medical exposures now represent, for the first time, the majority of the effective dose to which individuals in the US are exposed.

These increases, driven in large part by the increases in CT usage, are a reflection of the fact that CT is such a rapid, simple and accurate diagnostic tool. Concerns arise because a CT scan results in organ radiation doses that are, typically, 100 times larger than those from conventional radiological procedures such as chest X-rays.

The second recent development, as we shall discuss, is that there is now direct credible epidemiological evidence for a small risk of radiation-associated cancer at doses comparable to a few CT scans, or from other high-dose radiological procedures [5–8]. Indeed, as early as 2002, the International Commission on Radiological Protection (ICRP) commented that: ''*The absorbed dose to tissue from CT can often approach or exceed the levels known to increase the probability of cancer*'' [9].

Radiation exposure should always operate under the ''As Low As Reasonably Achievable'' (ALARA) principle and, as we discuss, opportunities do exist in the CT field for collective dose reduction, both by reducing the numbers of CT scans and by reducing the doses per scan. It is hoped that this review will promote ongoing dialogue [10] among radiologists, emergency room (ER) staff and other physicians, and indeed the public, as to practical ways to slow the increase in CT usage and CT doses, without compromising patient care.

CT and its usage

From its inception in the 1970s, the use of CT has increased rapidly in all developed countries, although usage rates vary greatly from country to country. In a survey from the mid-1990s, illustrated in Figure 2 [11], the number of CT scanners per million population was 64 in Japan, 26 in the US and 6 in the UK, the country where CT was invented.

Figure 1 quantifies the increase in CT usage in the UK and the US over the past quarter of a century [3]. It is estimated that close to 3 million CT scans per year were

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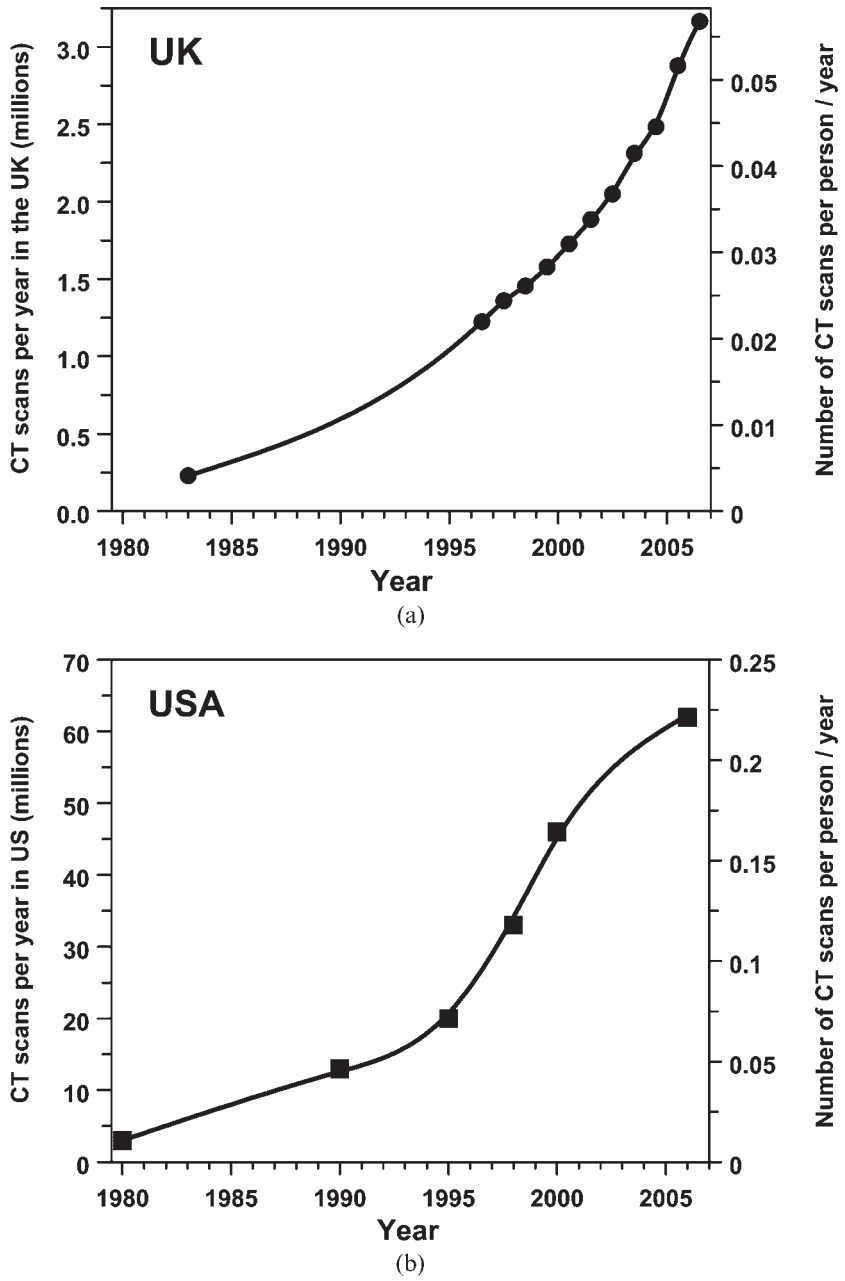

Figure 1. Graphs illustrating the rapid increase in the number of CT scans per year in (a) the UK and in (b) the US, as well as the number of CT scans per person per year [1–3]. Note that the number of scans per person per year is about five times lower in the UK than in the US.

performed in the UK in 2005–2006, compared with 0.25 million in 1980 [2, 7]. The corresponding figures for the US are 69 million scans in 2007, compared with ~2 million in 1980 [1, 7]. Taking into account the relative populations, the data indicate that the number of CT scans per person is five times greater in the US than in the UK. There is perhaps a suggestion from the data in Figure 1 that the rate of increase in scans is slowing in the US, but continuing to rise sharply in the UK.

A significant part of the UK increase is probably for pre-surgical diagnosis of acute appendicitis. For example, Dixon and Goldstone [12] report that UK radiology departments are currently experiencing a massive increase in requests for CT of the acute abdomen. A particular concern here, as discussed below, is that appendicitis is largely a disease of young people [13], for whom the radiation risks are correspondingly higher.

In 1997, the European Union issued a Directive on ''Health protection of individuals against the dangers of ionizing radiation in relation to medical exposure'' [14], from which followed corresponding UK regulations [15] and a detailed set of referral criteria guidelines [16]. No corresponding regulatory framework exists in the US, although the American College of Radiology has recently published a valuable white paper on radiation dose in medicine [17], which contains a series of recommendations designed to slow the increase in US population exposure from diagnostic radiology.

Organ doses produced by CT scans

Organ doses from CT examinations are considerably larger than those from the corresponding conventional radiograph (Table 1). For example, typical doses to the lung from a conventional chest X-ray range from about 0.01 mGy to 0.15 mGy, whereas a typical dose to an organ examined with CT, as discussed below, is around

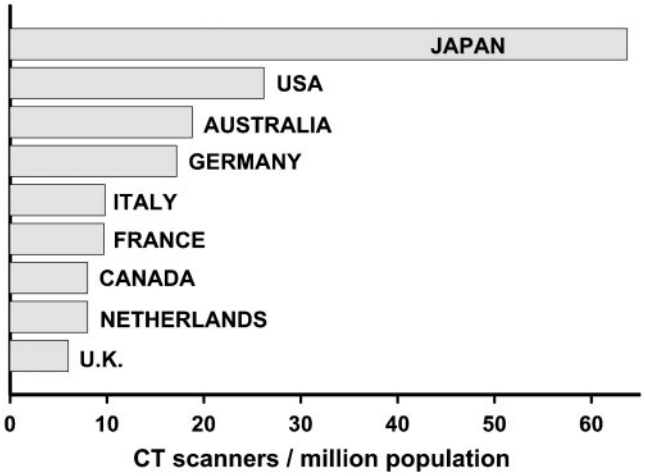

Figure 2. Number of CT scanners per million population in selected countries in the 1990s. Data from a 1991–1996 survey reported by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) [11].

10 mGy to 20 mGy, and can be as high as 80 mGy for 64-slice CT coronary angiography.

The radiation doses to particular organs from any given CT scan depend upon a number of factors: the most important are the number of scans, the product of tube current and scan time (the ''mAs''), the patient size, the axial scan range, the scan pitch (the degree of overlap between adjacent CT ''slices''), the maximum tube voltage (the kV_p) and the particular scanner design [18]. Many of these parameters are under the control of the radiologist or radiographer, and ideally should be tailored to the individual examination type and the individual patient size, a practice that is increasing but is by no means universal [19]. It is always the case that the relative noise in CT images will increase as the radiation dose decreases, and so there will always be a trade-off between the need for low-noise images and the desirability to use low radiation doses [20].

Representative calculated organ doses from single CT scans are shown in Figure 3 for commonly used machine settings [22] for either a single head scan or a single abdominal scan, the two most common CT scans. The number of CT scans in a given study is, of course, an important factor in determining the dose. For example, Mettler et al [23] reported that almost all patients having CT scans of the abdomen or pelvis had more than one CT scan on the same day; for all patients having CT scans, they reported that 30% had at least three scans, 7% had more than five scans, and 4% had nine or more CT scans.

It should also be borne in mind that doses associated with a given CT scan may vary considerably between different machines and institutions. For example, the US Food and Drug Administration conducted a survey of CT head scans in 203 facilities and found, as illustrated in Figure 4, that the institution-to-institution multiple-scan average dose varied by as much as a factor of 10 [24].

Radiation carcinogenesis at low doses

Data from atomic bomb survivors represent the ''gold standard'' in the quantitative assessment of radiation carcinogenesis risks at low doses. There are several reasons for this:

1. The study involves a large non-selected population (~100 000), including all ages and both genders.
2. Approximately 30 000 of the survivors were exposed to low doses — specifically in the range of 5–100 mSv — which is roughly the relevant dose range for single and multiple CT examinations.
3. Both cancer incidence and mortality data are available.
4. Mortality follow-up is close to complete among individuals exposed as adults, and is more than 50% complete for exposed children.
5. The study has continued for 60 years (and is ongoing), and has cost over 0.5 billion dollars. It is (hopefully) highly unlikely that any comparable study will ever be performed.

Two major conclusions from the A-bomb studies are, firstly, that the risk of all solid cancers is consistent with a linear increase in radiation dose, from low doses up to ~2.5 Sv (Figure 5). The second major conclusion is that children are much more radiosensitive than adults; indeed, there is a continuous decline in radiosensitivity with age for most cancers (Figure 6). Lung cancer is a notable exception, with the radiation-associated relative risk for lung cancer apparently increasing with age, up to middle age [6], implying that the absolute radiation-associated risk of lung cancer may not decrease significantly with age. The significance of this observation for a variety of adult CT scans will be discussed below.

Radiation risks are reviewed at regular intervals by a variety of national and international organizations. At the international level, there are the ICRP and the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). At national levels, there are the

Table 1. Typical organ doses from various radiological examinations

Examination	Relevant organ	Relevant organ dose (mGy)
Dental X-ray	Brain	0.005
PA chest X-ray	Lung	0.01
Lateral chest X-ray	Lung	0.15
Screening mammogram	Breast	3
Adult abdominal CT	Stomach	10
Barium enema	Colon	15
Neonate abdominal CT	Stomach	20
CT coronary angiography	Lung	40–100

PA, posteroanterior.

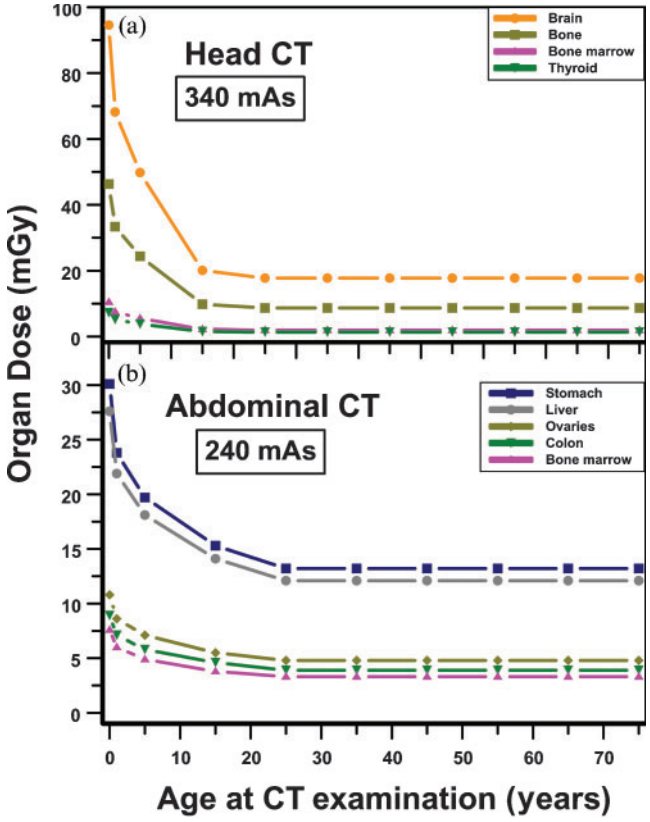

Figure 3. Estimated organ doses in mGy from typical single CT scans of the (a) head and the (b) abdomen [3]. As expected, the main exposed organs are the brain for head CT, and the digestive organs for abdominal CT. As described in the text, these doses depend on a variety of factors, including the number of scans (data here are for a single scan) and the mAs setting. The data here refer to the median mAs settings reported in the 2000 NEXT survey of CT usage [22, 24]. Note that, for a given mAs setting, paediatric doses are much larger than adult doses, as there is less self-shielding, but mAs settings can be (but only sometimes are [19]) reduced for children, which proportionately reduces the paediatric dose and the risk. The dose estimation methodology used for these calculations has been described elsewhere [38], but software to estimate organ doses for specific ages and CT settings is now generally available [21].

UK Radiation Protection Division of the Health Protection Agency and the US National Council on Radiological Protection and Measurements (NCRP), as well as the US National Academy of Sciences Biological Effects of Ionizing Radiation (BEIR) committees. The current unanimous consensus of all of these bodies is that, for doses <100 mSv, the most appropriate risk model for radiation protection purposes is one in which the risk of radiation-induced stochastic effects, is particular cancer induction, is assumed to decrease linearly with decreasing dose with no threshold (the so-called ''linear no-threshold'' (LNT) model) [11, 25, 26].

This LNT hypothesis is often described as prudent and possibly conservative, but it is certainly not proven. What can be said is that the measured cancer risks are consistent with linearity. Not surprisingly, this hypothesis has been assailed on both sides — by those who believe that low radiation doses are more damaging than linearity (specifically, a linear extrapolation of risks from higher doses) predicts [27, 28], as well as by those who

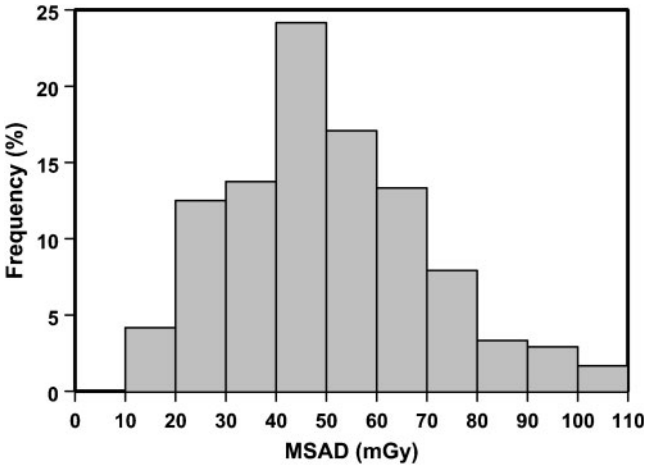

Figure 4. During 2000–2001, the US Food and Drug Administration conducted measurements in 203 institutions [24] to estimate the institution-to-institution variation in multiple scan average doses (MSADs) involved in a no-contrast axial CT head scan. The frequency distribution of results, shown here, exhibits a 10-fold variation in the MSAD.

believe that low radiation doses are less damaging than linearity would predict [29], or even that they are beneficial [30].

In the present context, it is not necessary to take a position on this LNT controversy. This is because the doses involved in CT scans, interventional radiology and barium enemas, which account for the majority of the collective

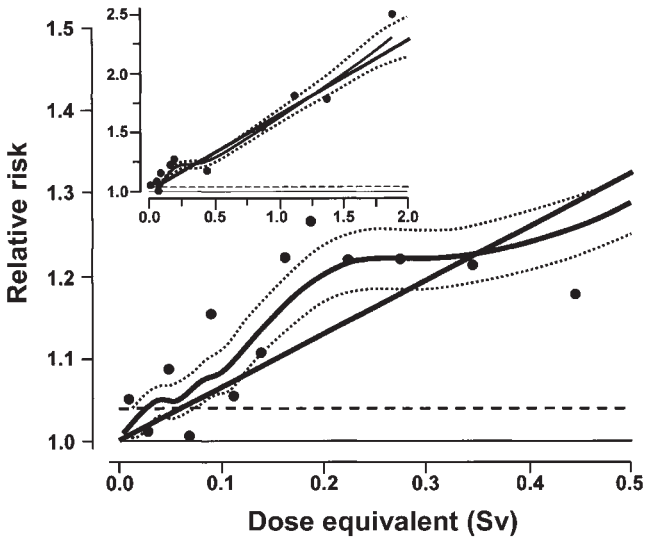

Figure 5. Estimated relative risks for cancer incidence in A-bomb survivors during the 1958−1994 follow-up period relative to controls [5]. The dotted curves represent ±1 standard error for the smoothed curve. The inset shows data over the whole dose range of 0–2 Sv, to which a straight line is fitted, *i.e.* the relative risk is proportional to the dose, with no threshold. The main figure is an expanded version of the low-dose region up to 0.5 Sv. The straight line is taken from the inset data for the whole dose range. Because of an apparent distinction between distal and proximal zero-dose cancer rates, the unity baseline corresponds to zero-dose survivors within 3 km of the bombs. The dashed line represents the alternative baseline if the distal survivors were not omitted.

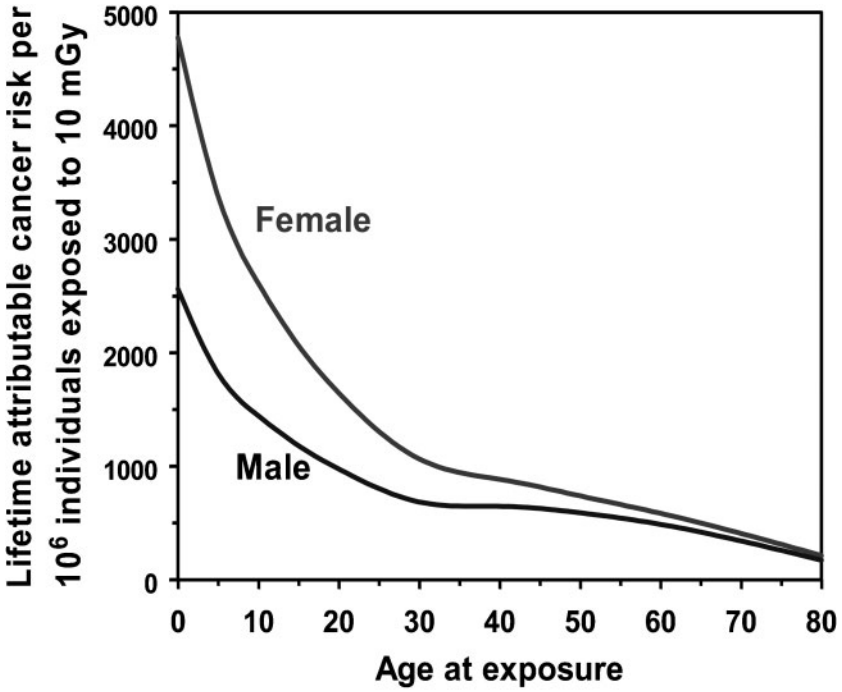

Figure 6. Estimated attributable lifetime risk from a single small dose of radiation as a function of age at exposure [74]. Note the dramatic decrease in radiosensitivity with age. The higher risk for the younger age groups is not expressed until late in life.

dose from diagnostic radiology, are just within the range where we have credible and direct epidemiological evidence for an increased cancer risk in human populations [5–8]. By contrast, for example, a single-plane chest X-ray results in a maximum organ dose of less than 0.2 mGy (see Table 1), which is much lower than the smallest dose for which significant epidemiological data are available. Estimating the risk for very low dose procedures does indeed involve a significant extrapolation, over as much as two orders of magnitude of dose, and is the subject of much controversy; however, it is not directly relevant to the higher radiological doses of interest in this review.

Limitations of epidemiological radiation-attributable cancer risk data

Report 126 from the NCRP [8] addressed the question of uncertainties in the total fatal cancer risk estimates used in radiation protection. The report considered epidemiological uncertainties, dosimetric uncertainties, transfer of risk between populations, projections to a lifetime risk, and extrapolation to low dose and/or low dose-rate. The results suggest an overall uncertainty of approximately a factor of 3 below and above the estimated value. By far the biggest source of uncertainty involves the extrapolation to low doses and the application of a dose-rate effectiveness factor. This uncertainty was estimated to be a factor of 2–2.5, but much of this component of the uncertainty may not apply to the doses involved in CT, in that we do not need to significantly extrapolate risks to lower doses or dose rates. Epidemiology-based uncertainties were estimated at $\pm$25%, dosimetric uncertainties at 0−30%, transfer between populations at −30% to +65%, and projections to a lifetime risk at −50% to +10%.

A limitation of the Japanese A-bomb data that must always be kept in mind is that the cohort size is large (~100 000 individuals), but not infinitely large. Thus, stratification of the results, *e.g.* by age, results in a marked decrease in statistical power. As such, when investigating the variation of radiosensitivity with age, all doses must be used, and when investigating the lowest dose for which a significant excess cancer risk is evident, all ages must be used. Thus, it is probably not possible to answer some detailed questions, such as ''what is the lowest dose at which an excess cancer incidence is evident in children less than 10 years of age?''.

What is the lowest dose for which cancer excess has been demonstrated?

A-bomb survivors

Several analyses have addressed the question of the lowest dose for which a statistically significant increase in cancer risk is apparent [6, 7], with the caveat, as discussed above, that age-averaged data must be used for the analysis. A summary of the conclusions [7] is shown in Figure 7. The survivors are stratified into progressively larger dose bins, with the lowest being 5–50 mSv; the excess relative risk (ERR) is then plotted as a function of the mean dose. The mean dose in the lowest dose bin at which the ERR is statistically significant is ~35 mSv, which corresponds to the typical maximum organ dose from two or three CT scans.

Nuclear workers

In 1995, the International Agency for Research on Cancer (IARC) published the results of a large study involving over 95 000 nuclear industry workers in the US, UK and Canada, who received an average occupational dose of ~40 mSv [31]. Because the confidence intervals were wide, the results were consistent both with zero risk and with the risk based on analysis of the

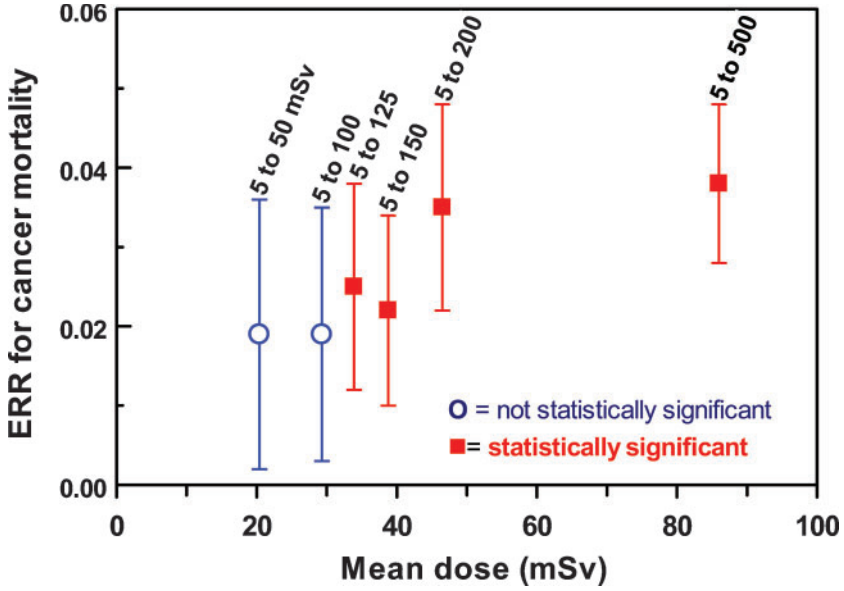

Figure 7. Estimated excess relative risk (ERR ± 1 standard error (SE)) for solid cancer mortality among groups of survivors in the lifespan cohort of atomic bomb survivors, who were exposed to low doses of radiation [7]. The dose groups correspond to progressively larger maximum doses, with the ERR plotted against the mean dose in each group. The first two data points are not statistically significant compared with the comparison population who were exposed to <5 mSv, whereas the remaining four higher dose points are statistically significant ($p<0.05$).

A-bomb survivors. In particular, for all solid cancers combined, there was no evidence for an increased cancer mortality risk associated with occupational radiation, whereas a statistically significant increased risk was observed for leukaemia [31].

Thus, even a population as large as 95 000 was not sufficient to assess radiation-associated cancer risks at the low doses received occupationally. Consequently, IARC embarked on a still larger 15-nation study involving over 400 000 nuclear workers and a lower mean dose of 20 mSv [32, 33]. The results, illustrated in Figure 8, indicate a statistically significant ERR estimate of 0.97 per Sv, consistent with that derived from the A-bomb survivors (illustrated in Figure 9). It should be noted that there is considerable variation between the results from the various countries, with one data set showing a negative risk and one showing a noticeably larger risk than the others, although detailed analysis did not reveal any of the data sets to be statistical outliers [32, 33].

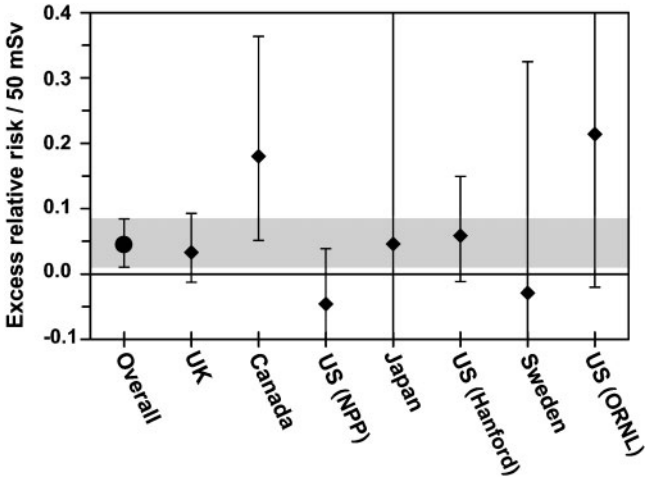

Figure 8. Estimated radiation-associated excess relative risks (with 90% confidence limits) for solid-cancer mortality, from the IARC 15 country study of radiation workers in the nuclear industry [32 33]. Overall, there is a small but statistically significant increase in the cancer mortality risk, as indicated by the "overall" data point for all of the cohorts combined, and the corresponding shaded region. Cohort-specific risk estimates are also shown for the cohorts with the largest numbers of cancers for which risks could be estimated, indicating the variability associated with low-dose radiation risk estimation. Note that the Canadian result, and the corresponding overall risk estimate, include data from the Ontario Hydro plant for which socio-economic data are not available, although this does not significantly affect the overall risk estimate [33].

The results of both the earlier and the newer IARC studies emphasise the point that exceedingly large and careful studies are needed to assess the risks associated with low radiation doses, such as those of relevance to CT.

It might finally be noted here that other large-scale, low-dose cohort studies are in progress, such as at the Techa River in Russia [34], where the mean dose was 40 mGy. Results to date suggest overall cancer risks per unit dose that are consistent with those from the A-bomb survivors [35].

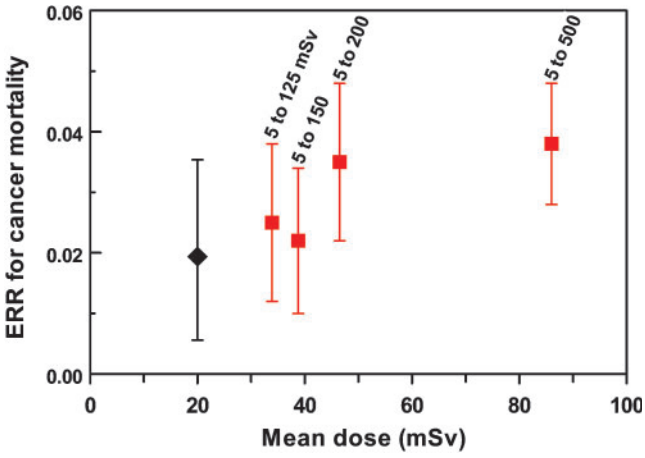

Figure 9. Estimated excess relative risk (ERR) for cancer mortality: The results from the 15-country study [32, 33] of nuclear workers (diamond, see Figure 8) is superimposed onto the statistically significant low-dose data [7] derived from A-bomb survivors (squares, see Figure 7).

Methodologies for assessing the potential risks associated with high-dose radiological examinations

The potential health risk associated with a high dose (in a radiological context) examination can be quantitatively assessed in several different ways. One simple approach uses the effective dose concept [36], which represents an attempt to provide a single number that is proportional to the radiobiological ''detriment'' from a particular radiation exposure — with detriment representing a balance between carcinogenesis, life shortening and hereditary effects. Specifically, it is the sum of the equivalent doses to a number of radiosensitive organ/tissues, with each organ being weighted by a tissue-specific committee-determined weighting factor. The effective dose is commonly used in radiology to allow comparisons of the risks associated with different spatial dose distributions produced by different imaging techniques. If the effective doses to all of the involved individuals are summed, the result is the collective dose [37]. If the collective dose is then multiplied by a generic fatal cancer risk estimate for whole-body exposure (*e.g.* 5% Sv^{-1} from ICRP Publication 60 [25]), the result is a very crude estimate of the number of fatal cancers resulting from the procedure.

Such risk estimates based on effective dose and collective dose are crude for two reasons:

1. Collective dose from radiological procedures includes contributions from the many low-dose procedures, such as routine chest X-rays and mammograms, which involve doses far below those for which we have direct evidence of cancer induction, *i.e.* it assumes validity of the LNT hypothesis down to the lowest doses. However, as we discuss below, most of the collective dose is actually from high-dose procedures (*e.g.* CT, interventional radiology and barium enema).
2. Risk estimates based on effective dose are highly generic and include, for example, hereditary effects that are unlikely to be significant at doses relevant to diagnostic radiology. In addition, the weighting factors used in the calculation of effective dose do not take into account the strong variations of radiosensitivity with age and gender.

In the next section, we use the collective dose concept to make some generic estimates of cancer risks from diagnostic radiology in the UK. Although we make a rough correction by excluding low-dose procedures, the risk estimates for which would be highly speculative, the results are still highly generic and, in the following sections, more reliable risk estimates are described. In particular, rather than using effective dose and collective dose, with all their inherent assumptions, a potentially more satisfactory method to assess the risk associated with a high-dose (in the radiological context) examination is first to measure (in an anthropomorphic phantom) or calculate (using Monte Carlo techniques) individual organ doses. Given these organ doses, risks can be applied (ultimately derived from A-bomb survivors) that are dose specific, organ specific, age specific, gender specific and country specific; finally, the resulting organ-specific risks can be summed. Such an approach to CT risk estimation has been used by several groups [3, 38–40].

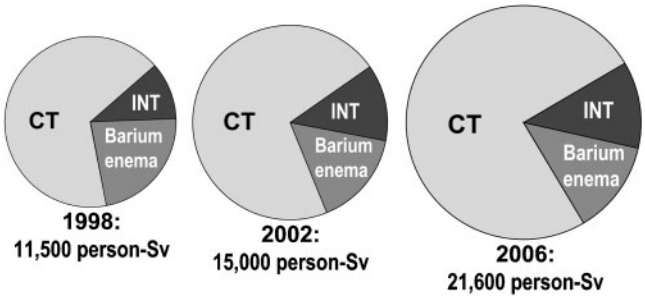

Figure 10. Diagram illustrating the recent increase in the UK collective dose from high-dose radiological procedures. Only the main high-dose diagnostic procedures are included, *i.e.* CT, interventional radiology (INT) and barium enemas. The number of procedures in each category was obtained from the UK Department of Health KH12 returns [2], and the average effective doses per procedure from Hart and Wall [41].

Radiology in the UK, 2005–2006: generic risk estimates

Figure 10 shows the increase with time of the UK collective dose from radiology, restricted to the three major radiological procedures (CT, interventional radiology and barium enema) where organ doses are sufficiently high that there is plausible direct evidence from epidemiological studies (see above) of an increased cancer risk. For the time period 2005–2006, this restricted collective dose is ~21 600 man Sv per year, based on the number of procedures [1] and the average effective dose per procedure [41]. If all radiological procedures were included, the corresponding collective dose would be ~28 000 man Sv per year (thus, approximately three-quarters of the total radiology collective dose is from high-dose procedures).

CT contributes the bulk of the collective dose, but interventional radiology is also very much a growth area, both in the US and the UK. In 2006, as illustrated in Figure 10, interventional radiology in the UK accounted for ~11% of the high-dose collective dose from radiology procedures [1, 41]. Although it represents a much smaller contribution to the collective dose than CT, it is growing just as rapidly. In fact, some patients undergoing interventional radiology receive doses sufficiently high as to cause deterministic effects in the skin, from erythema to desquamation and, very occasionally, even necrosis [42–45]. A mitigating factor is that most patients receiving interventional radiology are older and suffering from life-threatening illnesses, so that the radiation risks must be viewed in a broader context.

Barium enemas involve doses, and therefore risks, that are comparable to CT. The number of barium enemas performed is not increasing as rapidly as CT and interventional radiology, so that it represents a declining proportion of the collective dose.

With all the caveats discussed above, by applying the risk factor for fatal cancer suggested by the ICRP of 5% Sv^{-1} [37], a collective dose of 28 000 man Sv implies that the practice of diagnostic radiology in the UK would be predicted to result in $5/100 \times 28\,000$ or 1400 fatal cancers per year. If only high-dose (in the radiological context) procedures are included, the rationale for which is described above, the corresponding predicted number

of fatal cancers would be just over 1000 per year in the UK, of which about 750 would be from CT examinations. As discussed above, this is a highly generic risk estimate with, for example, no allowance for variations in age or gender, but it does give an order of magnitude estimate of the public health problem that is accumulating by the burgeoning use of diagnostic radiology.

Radiation risks associated with CT scans

As yet, no large-scale epidemiological studies of the cancer risks associated with CT scans have been reported, although one is just beginning [46]. While the results of such studies will not be available for some years, it is possible [38] to estimate the cancer risks associated with the radiation exposure from any given CT scan by measuring or calculating the organ doses involved, and applying organ-specific cancer incidence/mortality data that were ultimately derived from A-bomb survivors. As we have discussed, the organ doses for a typical CT study involving two or three scans are in the range where there is direct statistically significant evidence of increased cancer risk, and thus the corresponding CT-related risks can be directly assessed from epidemiological data, without the need to extrapolate measured risks to lower doses.

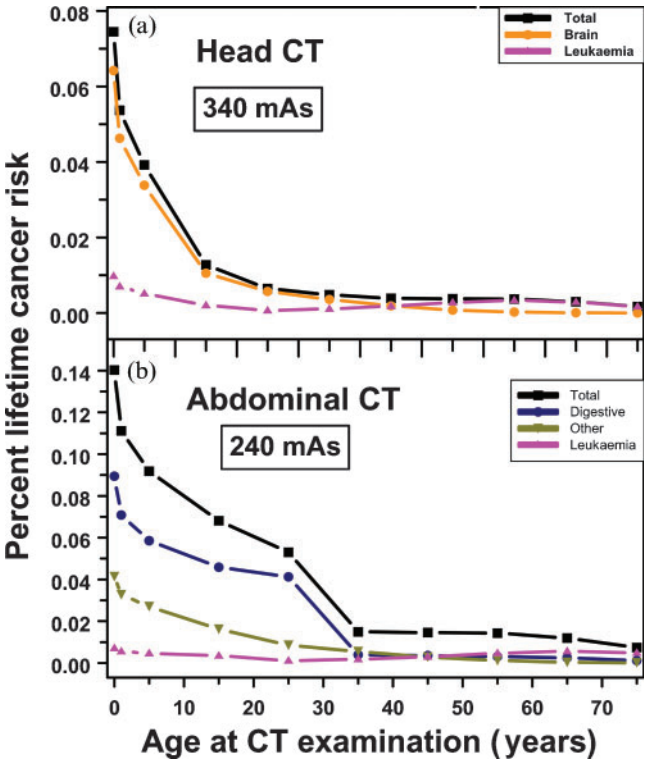

Figure 11. Estimated age-dependent, gender-averaged percentage lifetime radiation-attributable cancer risks from typical single CT scans of (a) the head and (b) the abdomen [3], based on estimated organ doses shown in Figure 3. The methodology used is summarized in the text. The risks are highly age dependent, both because the doses are age dependent (Figure 3) and because the risks per unit dose are age dependent (Figure 6). Despite the fact that doses are higher for head scans, the risks are higher for abdominal scans, because the digestive organs are more sensitive to radiation-induced cancer than is the brain.

Figure 11 shows estimated lifetime cancer mortality risks from a single ''generic'' CT scan of the head or the abdomen, estimated by summing the estimated organ-specific cancer risks. These risk estimates were estimated using the organ doses shown in Figure 3, derived for average [22] CT machine settings.

There are quantifiable uncertainties involved in the radiation risk estimates discussed here. Based on Monte-Carlo simulations of the various uncertainties [8, 47], the upper and lower 90% confidence limits of the radiation risk estimates are about a factor of 3 higher and lower, respectively, than the point estimates.

Although the individual risk estimates shown in Figure 11 are small, the concern over CT risks is related to the current rapid increase in CT usage — small individual risks applied to an increasingly large population may result in a potential public health issue some years in the future. For example, based on methodologies similar to those described here and radiology usage data for the years 1991–1996, Berrington de González and Darby [40] estimated that 0.6% of the cumulative risk of cancer in the UK population up to 75 years of age could ultimately be attributable to diagnostic X-rays, with the corresponding estimates in the US and Japan being 0.9% and 3%, respectively. Allowing for the rapid growth of CT scan usage in the UK and the US since 1991–1996 (see Figure 1), these estimated proportions would now be correspondingly larger.

Screening with CT

Although CT has been in use for over 20 years, its use for mass screening of asymptomatic patients is a recent innovation, driven in part by the increased availability and convenience of CT machines. Four primary applications, each of which will be briefly discussed, have been suggested for CT-based screening:

1. Screening for colon polyps (virtual colonoscopy);
2. Screening for early-stage lung cancer in smokers and ex-smokers;
3. Screening for cardiac disease;
4. Screening the whole body (full-body screening).

All four of these applications are quite new, and a consensus has not yet been reached about the efficacy of any of them. General issues regarding the efficacy of these new modalities are, in essence, the same as for other mass screening modalities such as mammography, pap smear screening and colonoscopy. However, as we will discuss, there is an added issue for CT-based screening, namely the significant X-ray radiation exposures involved. Thus, the potential benefits of any CT-based screening procedure should, in addition to the more general efficacy issues, significantly outweigh any potential cancer risks associated with repeated CT exposures.

CT colonography (CTC or virtual colonoscopy)

There is no doubt that colonoscopy-driven polypectomy can result in a significantly decreased incidence of

Table 2. Typical organ doses and estimated additional absolute gender-averaged lifetime cancer risks associated with a paired CTC screening examination of a healthy 50 year old [65].

	Organ dose from paired CTC scans[a] (mGy)	Additional absolute lifetime cancer risk from paired CTC scans at age 50 years (%)
Colon	13.2	0.042
Bladder	16	0.020
Stomach	14.8	0.022
Kidney	16.1	0.014
Liver	13.8	0.010
Leukaemia	6.6	0.025
Lung	2.2	0.007
Total		0.14

[a]Paired CT colonography (CTC) examinations at 65 mAs, 120 kVp, 10 mm collimation and pitch 1.35

Table 3. Estimated colon doses from paired CTC scans using the same machine settings with different CT scanners [65]

Scanner	Colon dose from paired CTC scans[a] (mGy)
GE LightSpeed Ultra[b]	13.2
GE QX/I, LightSpeed, LightSpeed Plus[b]	11.6
Phillips Mx8000[c]	9.0
Siemens Volume Zoom, Access[d]	8.6
Siemens Sensation 16[d]	7.6

[a]The doses were estimated for paired CT colonography (CTC) examinations at 65 mAs, 120 kVp, 10 mm collimation, and pitch 1.35.
[b]GE Healthcare, Waukesham, USA.
[c]Phillips Healthcare, Eindhoven, the Netherlands.
[d]Siemens Healthcare, Erlangen, Germany.

colorectal cancer [48], and that there is suboptimal compliance with current guidelines for colorectal cancer screening [49]. Screening using CT colonography, often referred to as CTC or ''virtual colonoscopy'', was suggested as early as 1983 [50], but has only recently become a potential option for mass screening [51, 52].

Several recent large-scale studies have shown that CTC is at least as sensitive and specific as conventional optical colonoscopy in detecting adenomas of diameter $\geqslant$10 mm [53, 54] — a result confirmed by preliminary results of the National US CT Colonography Trial [55]. CTC may well have the potential to increase colorectal cancer screening compliance, in part because of the possibility that it can be performed with reduced laxative [56, 57] or non-cathartic [58, 59] pre-examination bowel preparation.

It is clear that CTC, at least in the US, is reasonably close to being used for mass screening, although it is not yet approved for most US third-party reimbursements. An issue that confronts CTC is its reduced sensitivity and specificity for detecting lesions $<$10 mm, although lesions smaller than this typically have no more than a 1% chance of containing a frank malignancy. Another issue is the relatively early developmental stage of non-cathartic or minimally cathartic protocols, with standardized approaches still to be established.

If CTC were to become a standard screening tool for the over-50s, the potential ''market'' would be ~100 million people in the US and 20 million in the UK. Even if the recommended CTC frequency were to be that currently recommended for optical colonoscopy (every decade), this would imply that millions of CTC scans might be performed each year. It is pertinent, therefore, to consider the radiation exposure and any potential radiation risk to the population from such a mass screening programme. Because of the advantageous geometry of a CTC scan, the dose/noise trade-off can be very much weighted towards low-dose higher-noise images, while still maintaining sensitivity and specificity, at least for polyps $>$10 mm in diameter [60–64].

Table 2 [65] shows estimated CTC organ doses for one of the more common CT scanners, with typical scanner parameters. To provide an estimate of scanner-to-scanner dose variations, Table 3 [65] shows the radiation dose to the colon estimated for five of the more common CT scanners in current use, using identical scanner parameters in each case; the coefficient of variation of the dose to the colon is ~20%.

Table 2 also shows the estimated absolute lifetime cancers risks associated with the radiation exposure from paired CTC scans in a 50-year-old individual [65]. As expected, the main organs at risk are the colon, stomach and bladder, as well as the leukaemic cancers. All of the estimated absolute radiation risks are relatively small, with the largest being $<$0.05% (1 in 2000). Summed over all of the organs at risk, the estimated absolute lifetime risk of cancer induction from a pair of CTC scans (with the scanner parameters from Table 2) in a 50-year old is ~0.14%, approximately 1 in 700. Estimated risks for cancer mortality would, of course, be less.

The estimated risks are, of course, dependent upon the scanner settings used, particularly the mAs and the pitch. There is good evidence [62, 66] to suggest that the mAs and thus the dose for CTC could be decreased considerably further. In addition, automatic tube current modulation, discussed elsewhere in this review, has been shown to reduce CTC doses by a further 35% [67]. Thus, it seems clear that, in terms of the radiation exposure, the benefit/risk ratio is potentially large for virtual colonoscopy.

Low-dose CT screening for early-stage lung cancer in smokers and ex-smokers

Lung cancer is the leading cause of cancer-related mortality and is, of course, strongly associated with past smoking history. Thus, there is much interest in using low-dose CT scans for the regular screening of smokers and former smokers for early-stage lung cancer. This is a logical next step after the failure of earlier attempts to screen this population with conventional chest X-rays [68]; low-dose lung CT clearly has a much greater sensitivity for detecting small pulmonary lesions than does conventional radiography [69]. A National Lung Cancer Screening Trial is currently underway in the US [70].

As with virtual colonoscopy, the geometry for lung CT is quite advantageous, and this allows the use of relatively low-dose (*i.e.* noisier) images, while still maintaining good sensitivity for detecting small lesions [71].

The potential mortality benefits of lung cancer screening have been much debated [72, 73], and it is fair to say that, at the very earliest, the issue will not be resolved until the completion of the National Lung Cancer

Screening Trial in 2009. Less attention has been paid to the potential radiation risks, specifically radiation-induced lung cancer, associated with the radiation from these CT scans. In part, this is because the screening technique involves ''low dose'', rather than standard, CT lung scans, and partly because ERRs of radiation-induced cancer generally decrease markedly with increasing age [74].

There are, however, indications that the radiation risk to the lung associated with this screening technique may be significant. Firstly, cancer risks from radiation are generally multiplicative of the background cancer risk [75], which is of course high for lung cancer in smokers; this general observation has been borne out in terms of the interaction between radiation and smoking, which most authors have suggested is near-multiplicative [76–79], although an intermediate interaction between additive and multiplicative has also been suggested for radon exposure [80], and there is one suggestion of an additive interaction [81] in A-bomb survivors. Secondly, although ERRs for cancer generally decrease markedly with increasing age at exposure, radiation-induced lung cancer does not show this decrease in ERR with increasing age [6].

These considerations suggest that the risk of radiation-induced lung cancer associated with the radiation from repeated low-dose CT scans of the lung in smokers may not be negligible. A recent estimate [82], based on the organ-specific risk estimation techniques described above, suggests that a 50-year-old smoker planning an annual lung screening CT would incur an estimated radiation-related lifetime lung cancer risk of 0.5%, in addition to his/her otherwise expected lung cancer risk of ~14% (the radiation-associated cancer risk to any other organ is far lower). The estimated radiation risk set a baseline of benefit that annual CT screening must substantially exceed. This risk/benefit analysis suggests that a reduction in mortality from annual CT screening of more than 3% would be necessary to outweigh the potential radiation risks [82].

CT-based cardiac screening for heart disease

Since the introduction of Agatston's scoring system [83] for quantifying artery calcium levels, there has been increasing interest in using CT as a screening test for cardiovascular risk [84–86]. A variety of studies has suggested that coronary artery calcium might indeed be a good predictor of cardiovascular events such as acute myocardial infarction, coronary revascularization and sudden death [87–90]. These results have contributed to the SHAPE (Screening for Heart Attack Prevention and Education) task force call for non-invasive screening, either with CT or ultrasound, of all asymptomatic men 45–75 years of age and asymptomatic women 55–75 years of age (except those defined as very low risk) to detect individuals with sub-clinical atherosclerosis [91]. In the US, this amounts to 61 million people, and in the UK to approximately 12 million people.

Neither the sensitivity nor the specificity of CT-based calcium screening has yet been well established [92, 93]. In particular, many dangerous patches of arterial disease are not yet calcified, and so would be missed, leading to decreased sensitivity; furthermore, many calcified arteries will have normal blood flow, leading to decreased specificity.

Because of its rapid motion, CT screening of the heart presents special problems. In particular, information can only be obtained when the heart is relatively still, *i.e.* in diastole. Typically, this is done using retrospective gated techniques, so that the dose delivered in other parts of the heart's cycle is effectively wasted, leading to high organ doses, particularly to the lung and breast [39, 94]. For adults aged over 45 years, it would be expected that the lung risks would considerably outweigh any risks to the breast [74]. Assuming the SHAPE recommendations for screening all asymptomatic men and women aged 45–75 years and 55–75 years, respectively, Table 4 shows estimates of the predicted radiation-associated lung cancer mortality if all of these 61 million people in the US were screened with multi-detector row CT once, involving a lung dose of 10 mGy [94]. The total predicted mortality is ~7000, or about 1 in 8000.

As discussed elsewhere in this review, the use of prospective electrocardiogram-triggered coronary CT, where the machine is off during other parts of the cardiac cycle, has the potential to reduce the dose and therefore the risk significantly, perhaps by a factor of 4 [95]. Thus, the radiation concerns will be significantly reduced if CT were to become a realistic option.

Full-body CT screening

There has been a recent wave of interest in the use of full-body CT screening of non-symptomatic adults [96–99]. The technique is intended to be an early detection device for a variety of diseases including lung cancer, coronary artery disease and colon cancer. At present, the evidence for the utility of this technique is anecdotal, and there is considerable controversy [100] regarding its efficacy; to date, no studies have reported a life-prolonging benefit. Because of the nature of the scan, the false-positive rate is expected to be high, and a study on full-body CT screening [101] found that 37% of those screened were recommended for further evaluation, whereas the overall evaluable disease prevalence is probably ~2% [102].

Another aspect that is important in assessing full-body screening is the potential risk from the radiation exposure associated with full-body CT scans. Typical organ doses from a single full body scan are ~9 mGy to the lung, 8 mGy to the digestive organs and 6 mGy to the bone marrow [103]. The effective dose is ~7 mSv, and therefore if, for example, five such scans were undertaken in a lifetime, the effective dose would be ~35 mSv. To put these doses into perspective, a typical screening mammogram produces a dose of ~2.6 mGy to the breast [104], with a corresponding effective dose of ~0.13 mSv. Based on the risk estimation methodologies described above, the estimated lifetime cancer mortality risks from a single full-body scan are $\sim 4.5 \times 10^{-4}$ (about 1 in 2200) for a 45 year old and $\sim 3.3 \times 10^{-4}$ (about 1 in 3000) for a 65 year old [103]. The risk estimates for multiple scans, which would be necessary if full-body CT screening was to become a useful screening tool, are correspondingly larger. For example, a 45 year

Table 4. Estimated radiation-associated mortality risks for CT cardiac screening

Female age group (years)	Population (10^6)	Mortality risk/ 10^6/10 mSv	Predicted lung cancer deaths	Male age group (years)	Population (10^6)	Mortality risk/10^6/ 10 mSv	Predicted lung cancer deaths
				45–49	9.9	105	1040
				50–54	8.6	100	860
55–59	7.0	190	1330	55–59	6.5	95	620
60–64	5.7	170	970	60–64	5.1	90	460
65–69	5.1	150	765	65–69	4.4	75	330
70–74	5.0	130	650	70–74	3.9	65	235
All (55–74)	22.8		3715	All (45–74)	38.4		3545

Estimates are for lung cancer mortality, which is expected to dominate the risk. The risk estimates assume the Screening for Heart Attack Prevention and Education (SHAPE) [91] guidelines, calling for screening of all asymptomatic women 55–75 years of age (left four columns) and asymptomatic men 45–75 years of age (right four columns). It was assumed that each of the 61 million individuals in this age group in the US receives one multidetector row CT for calcium scoring, with a typical lung dose of 10 mGy [94]. The total predicted lung cancer deaths is ~7000 out of the 61 million population.

old who plans on undergoing 10 three-yearly full-body scans would potentially accrue an estimated lifetime cancer mortality risk of 0.33% (about 1 in 300) [103].

The issue of whole-body screening has recently been addressed by the UK Committee on Medical Aspects of Radiation in the Environment (COMARE) [105]. They concluded that ''*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*''.

Can CT doses be reduced?

The short answer is yes. There are a variety of CT parameters that can be optimized in order to deliver a minimum dose while obtaining the desired information, and there is much published research in this area [106, 107]. In particular, mAS, filtration, collimation and peak tube voltage can all be optimized.

Much interest has focused on automated exposure control. In general, exposure control is based on the notion that lower CT image noise will typically be achieved at the cost of higher doses, so the image noise level should be no better than sufficient for the diagnostic task at hand. Given a desired noise level and the geometry of the patient, either manual [108] or automated [106, 107, 109, 110] exposure control techniques can be used to generate a CT setting that will minimize the patient dose.

All of the major CT scanner manufacturers now offer some type of automated exposure control, in which the user defines the desired image quality, resulting in machine-recommended settings [106]. The CT control system can then adjust the tube current according to the patient's size, and can also optionally adjust the tube current continuously during a given rotation and/or during movement along the *z*-axis, according to the patient's size and body habitus, to produce an image consistent with the image quality requirements.

Patient size is a particularly important issue. It has been known for many years that, for the same image quality requirement, smaller (*e.g.* paediatric) patients require lower mAs settings [111]; however, for many years, paediatric CT was often performed with the same settings as adult CT [19]. Automated and semi-automated exposure-control systems, as well as increased physician awareness, have resulted in significant improvements in this regard.

Finally, one area in which much technological improvement has recently occurred is CT coronary angiography. Because of cardiac motion, cardiac CT has generally been retrospectively gated, obtaining useful information only during diastole and resulting in unnecessary exposure throughout the rest of the heart cycle [39]. Prospective electrocardiogram-triggered 64-slice helical CT, in which CT is only ''on'' during diastole, can result in a sharp decrease in radiation dose [95].

Can CT usage be reduced?

Irrespective of the absolute levels of CT-associated risk, it is clearly desirable to reduce CT usage, as long as patient care is not compromised. However, this will not be an easy task. Physicians are often subject to significant pressures (some country specific) from the medical system, the medico-legal system and from the public to prescribe CT. As we have discussed, in most (non-screening) scenarios, CT is the appropriate choice, but there is undoubtedly a significant proportion of potential situations where CT is not medically justifiable or where equally effective alternatives exist.

Tellingly, a straw poll [112] of paediatric radiologists suggested that perhaps one-third of CT exams could be replaced by alternative approaches, or not performed at all [113]. Examples include the use of CT, or the use of multiple CT scans, for the management of blunt trauma [114–118], seizures [119, 120] and chronic headaches [121].

There is also a variety of scenarios in which CT usage could be replaced by other imaging modalities, without significant loss of efficacy. For example, patients with a history of nephrolithiasis and flank pain, or with known chronic kidney stones, are at increased risk for multiple CT exams, resulting in potentially high cumulative doses. In such cases, combinations of sonography and unenhanced abdominal radiography (kidneys, ureters and bladder) would be an appropriate alternative to

multiple CT scans [122–124]. Another example is the use of CT in screening for abdominal aortic aneurysm in patients at risk; although CT is an excellent solution, several ultrasound-based devices have been shown to be equally effective and practical to use in an ER situation [125, 126].

A third area is the use of CT as a primary tool for pre-surgical diagnosis of acute appendicitis [127]. CT is largely replacing ultrasound for this purpose [128], and has a very high sensitivity and specificity for diagnosing appendicitis. A particular issue here is that appendicitis is predominantly a young person's disease [13], and so the radiation risks per unit dose are higher than for adults. Several recent reports [129, 130] have highlighted the utility and practicality of clinical practice guidelines for diagnosing paediatric appendicitis, using selective CT and ultrasound scans. Specifically, the guidelines recommend immediate surgery or further evaluation with either CT or ultrasound depending on the patient's specific clinical presentation. Selective imaging guidelines for paediatric appendicitis have been shown to decrease markedly the number of CT scans performed (by a reported 40% [129]) with minimal diminution in diagnostic accuracy.

Beyond these clinical issues, however, a problem arises when CT scans are requested in the practice of defensive medicine, or when a CT scan, justified in itself, is repeated as the patient passes through the medical system, often simply because of a lack of communication. It is possible that the wider use of electronic radiology information systems and patient records will reduce this problem in the future.

Part of the issue is that physicians often view CT exams in the same light as other radiological procedures, despite the fact that CT-related doses are typically much higher. In a recent survey of radiologists and ER physicians [131], about three-quarters of physicians significantly underestimated the radiation dose from a CT scan, whereas 53% of radiologists and 91% of ER physicians did not believe that CT scans increased cancer risks.

This concern is encapsulated by an Editorial comment regarding CT angiography [132], but which applies equally well to many CT applications: ''*due to its easier availability, CT of the pulmonary arteries may, however, be used more liberally in patients with low clinical suspicion*''. This trend towards a somewhat less selective use of diagnostic CT, for better or worse, has occurred in many different applications of CT, and is in considerable part responsible for the rapid increases in CT use.

Understanding, using and communicating CT risk estimates

In 1983, the Royal Society introduced a useful stratification of risks [133]. They proposed that a risk of one in a million is acceptable as part of everyday life activities such as commercial air travel. Conversely, an annual risk of 1 in 100, *e.g.* that associated with coal mining in the 19th century, was considered unacceptable. Between these extremes, a risk of 1 in 1000 (which corresponds approximately to an abdominal CT in a child) was considered acceptable, provided:

1. the individual receives a potential benefit that outweighs the potential risk;
2. everything possible has been done to reduce or minimize the risk;
3. the individual or parent is aware of the risk.

We discuss the first two points elsewhere in this review. The risk/benefit balance, which is well established as being highly favourable in the majority, although not all, of diagnostic CT examinations, is currently far less well established for CT-based screening exams. With regard to the second point, we discuss elsewhere the new technologies being introduced to lower CT doses and the issue of paediatric CT dose reduction.

Regarding the third point — risk communication — a recent US survey concluded that, although most academic medical centres currently have guidelines for informed consent regarding CT, only a minority of institutions inform patients about the possible radiation risks and alternatives to CT [134]. There may well be some concern here that a patient who needs a CT scan might refuse it because of anxiety over received cancer risk information, but the evidence does not support this concern; for example, in a recently published US study [135], when parents were informed about CT risks, their willingness to have their child undergo a CT did not significantly change, although they became more willing to consider other imaging options if equally effective. No CTs were cancelled or deferred after receiving risk information. It appears that, given the appropriate information, patients can make a balanced judgment as to the risk/benefit balance for CT [135–138].

In the UK, the Royal College of Radiologists (RCR) has recommended [139], with regard to high-dose procedures such as CT, that ''*all examinations having a known potential risk of complications of the order of ⩾1:2000 should be brought to the attention of the patient when seeking consent*''. The RCR suggests that ''*the clinical radiologist will already have reviewed the clinical indication for the examination in order to ensure that risk/benefit has been properly evaluated. However, the patient may wish to discuss further the necessity for or the desirability of the radiation exposure involved. Additional information may be needed. The time and effort of the radiological team in discussing these aspects of radiological care require special workload and timetabling arrangements within the imaging department*''. This is a highly desirable, although possibly somewhat idealized, scenario. For example, in a recent UK survey [140] of 500 outpatient non-emergency first-time attendees for ultrasound (300 patients), CT (150 patients) or MRI (50 patients), less than half of the patients indicated they even knew the type of investigation for which they had been referred.

Finally, when assessing risk, it is important to distinguish between individual risk and collective public health risk. Although the risk to the individual is small and acceptable for the symptomatic patient, the exposed population is large and increasing. Even a small individual radiation risk, when multiplied by such a huge number, adds up to a significant long-term public health problem that will not become evident for many years. One is reminded of examples from the past, such as the use of multiple fluoroscopies in the management

of artificial pneumothorax in TB patients. This was considered an acceptable use of radiation from about 1930 to 1950, and only in the mid 1960s was there a suggestion of an increased breast cancer risk [141], which has since been well established and quantified in subsequent decades [142, 143]. The fluoroscopic doses were an order of magnitude larger than the doses of relevance to CT, but the number of individuals exposed to CT in the modern era is undoubtedly several orders of magnitude larger than the number of TB patients who received multiple fluoroscopies.

Conclusions

- There has been a major increase in the collective dose from medical radiation within the past two decades, fuelled mostly by the rapid increase in the use of CT scans.
- About three-quarters of the collective dose from radiology is the result of high-dose procedures, in particular CT, interventional radiology and barium enemas. For these procedures, the organ doses involved are sufficiently large that there is direct statistically significant evidence of small increased cancer risks, based on epidemiological data.
- Lower-dose procedures, such as mammography or conventional radiography, require models to estimate any associated cancer risk.
- The ''gold standard'' for risk estimates of radiation-induced cancer at doses relevant to CT is the study of the A-bomb survivors: ~30 000 survivors were exposed to doses corresponding to one or a few CT scans. The low-dose A-bomb cancer risk data are consistent with the results from large-scale epidemiological studies in nuclear workers.
- Risk to an individual from a high-dose radiological procedure, such as a specific CT scan, is optimally estimated by measuring or calculating organ doses, and then applying organ-specific, age-specific, gender-specific and country-specific cancer risk estimates. For CT doses, such risk estimates are probably good to within a factor of approximately 3 in either direction.
- The majority of diagnostic radiological procedures, including CT, in symptomatic patients involve an extremely small individual risk, which is justified by the medical need.
- In contrast, the various proposed applications of CT-based health screening of asymptomatic populations are not yet in a position where the potential benefits can be quantitatively balanced against the potential radiation risks.
- There is considerable potential, using ongoing technological developments, to reduce CT doses, and therefore the associated risks.
- Even in symptomatic patients, there is a significant number of situations where a CT scan either need not be done or could be reasonably replaced with another imaging modality — perhaps one-third of all diagnostic CT scans fall into this category. Common examples include (i) pre-operative diagnosis for appendicitis, particularly in children, where selective guidelines could reduce CT usage considerably, and (ii) patients with a history of flank pain or kidney stones, where sonography plus radiography is an alternative to multiple CT scans.
- Regardless of individual risk, the burgeoning collective dose from CT must signal the possibility that we are creating a future public health problem. Ongoing dialogue is important among radiologists, ER physicians and other physicians, and indeed the public, to establish practical ways to slow the increase in CT usage and CT doses, without compromising patient care.

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