SPECIAL REPORTS AND REVIEWS

Mass Screening With CT Colonography: Should the Radiation Exposure Be of Concern?

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Background & Aims: **Computed tomography colonography (CTC), particularly using noncathartic techniques, has the clear potential to increase compliance for colorectal cancer screening. Because the geometry for CTC is highly advantageous, it can be performed with lower radiation doses than almost any other CT examination. If CTC were to become a standard screening tool for the population age 50 years and older, the potential market in the United States would soon be over 100 million people. Therefore, it is pertinent to consider the radiation exposure and any potential radiation risk to the population from such a mass CTC screening program.** ***Methods:*** **Organ doses from CTC examinations can be estimated with standard techniques. These doses can be applied to organ- and dose-specific radiation cancer risk estimates to estimate the excess cancer risk resulting from the radiation from a paired (supine and prone) CTC examination.** ***Results:*** **The cancer risks associated with the radiation exposure from CTC are unlikely to be zero, but they are small. A best estimate for the absolute lifetime cancer risk associated with the radiation exposure using typical current scanner techniques is about 0.14% for paired CTC scans for a 50-year-old, and about half that for a 70-year-old. These values probably could be reduced by factors of 5 or 10 with optimized CTC protocols.** ***Conclusions:*** **In terms of the radiation exposure, the benefit-risk ratio potentially is large for CTC.**

There is no doubt that colonoscopy-driven polypectomy can result in a significantly decreased incidence of colorectal cancer,[1,2] and that there is suboptimal compliance with current guidelines for colorectal cancer screening.[3,4] Screening using computed tomography colonography (CTC), sometimes referred to as *virtual colonoscopy*, first was suggested in 1983,[5] but only recently has become a potential option for mass screening.[6–8] Figure 1 shows that CTC is of increasing interest to the clinical community.

In the most common current usage of CTC, after bowel preparation, the colon is inflated and the colon is scanned by CT. The resulting data then can be analyzed for polyps based on 2-dimensional images, or by using a 3-dimensional endoluminal view. In general, CTC is an excellent application of CT because of the radiologic contrast exhibited by colonic polyps projecting into an air- or CO_2-filled lumen (Figure 2).[5,6,9]

CTC may well have the potential to increase colorectal cancer screening compliance, largely because of the possibility that it can be performed with noncathartic preexamination bowel preparation. Current compliance with screening guidelines clearly is poor—at most, about one third of adults over age 50 in the United States have had an endoscopic examination within the past 10 years.[3,4]

From a technologic perspective, CTC is not quite ready for use in mass-screening programs. The 3 main outstanding issues, all of which seem relatively close to solution, are as follows.

1. Sensitivity and Specificity of CTC for Detecting Lesions From 5 to 10 mm. CTC sensitivity and specificity for lesions greater than 10 mm in diameter generally are well over 90%—about as good as those for optical colonoscopy.[10] There is evidence that a well-designed CTC screening program can achieve at least 90% sensitivity and specificity in the size category from 7 and 10 mm,[7,11] but not all studies have achieved this.[12]

2. Use of Noncathartic Pre-Examination Bowel Preparation Regimens. In general, it may be less the invasive nature of conventional colonoscopy that results in poor compliance, but more the necessity for cathartic bowel preparation.[13–17] CTC offers the potential for noncathartic bowel preparation through the use of barium or iodinated tagging agents that impart a high density to both stool and residual fluid, allowing increased contrast

Abbreviations used in this paper: CTC, computed tomography colonography.

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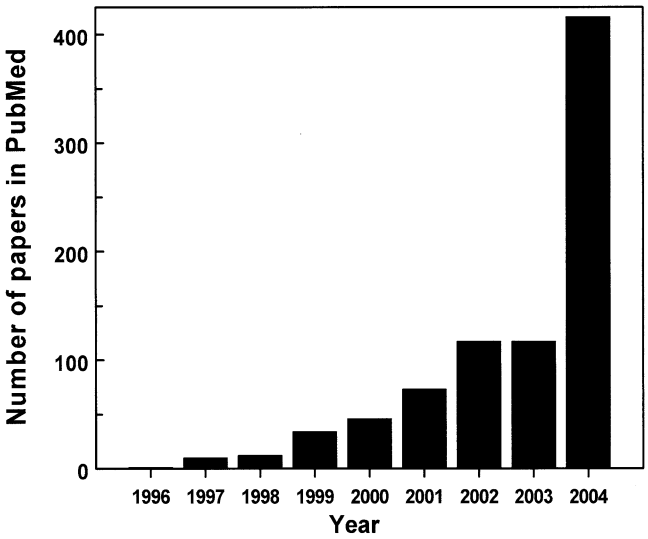

Figure 1. Number of articles listed in PubMed (Medline) on CTC or virtual colonoscopy.

with soft-tissue polyps. Recent results with noncathartic CTC (Figure 2*B*) have been very encouraging.[8,18–20]

3. Optimization and Standardization of CT Parameters. Just as mammographic examinations are now well standardized[21] and regulated,[22] so CTC should be optimized and standardized if it is to be used for mass screening. Particularly until the previous 2 points are settled, it probably is premature to consider standardizing CTC scanner parameters.

If CTC were to become a standard screening tool for patients over age 50 years, the potential market in the United States soon would be greater than 100 million people. Even if the recommended CTC frequency were to be that currently recommended for optical colonoscopy (every decade), this would imply that several million CTC scans might be performed each year. Should the relative simplicity of the CTC tests result in the recommended examination frequency being increased, then several tens of millions of these CTC scans might be expected to be performed in the United States each year. Therefore, it is pertinent to consider the radiation exposure and any potential radiation risk to the population from such a mass screening program.

Cancer Risks Associated With Exposure to Low Doses of X-Rays

Some typical low doses of societal relevance are shown in Table 1. Radiation dose is a measure of ionizing energy absorbed per unit mass and has units of Gy (Gray) or mGy; it often is quoted as an equivalent dose, in units of Sv (Sievert) or mSv. For x-rays, which is the radiation produced in CT scanners, 1 mSv = 1 mGy.

The biological effects of low-dose x-ray exposure have been investigated and debated for more than a century.[23] There is little question that intermediate and high doses of ionizing radiation, for example, greater than 100 mSv, given acutely or over a prolonged period, produce deleterious effects in humans, the most significant being cancer induction.[24] At lower doses, however, the situation is less clear. Compared with higher doses, the risks for low doses of radiation are lower, and progressively larger epidemiologic studies are required to quantify the cancer risk to a useful level of precision. This is because

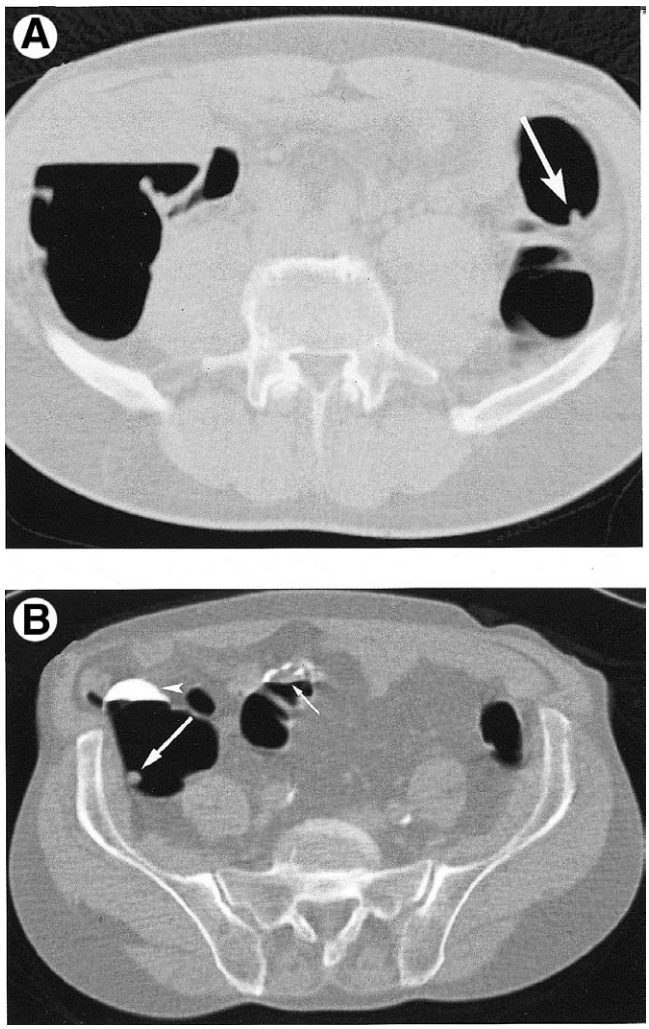

Figure 2. Excellent radiologic contrast between a soft-tissue polyp and the air-filled lumen, with or without cathartic preparation. Two-dimensional transverse images are shown here from extremely low-dose CTC examinations.[8,36] The scanner settings used here (Siemens Plus 4 Volume Zoom, Erlangen, Germany; 9 mAs; pitch, .9; collimation, 4 × 2.5 mm; 140 kV) result in doses less than one fourth of the currently typical values tabulated in Table 2. (*A*) A 9-mm sessile polyp imaged in a cathartically prepared colon (*arrow*).[36] (*B*) CTC without cathartic preparation.[8] Liquid fecal material is tagged homogeneously (*arrowhead*); 8-mm polyp (*long arrow*); 20-mm polyp identified while completely submerged in liquid fecal material (*short arrow*). Reproduced courtesy of Dr. Riccardo Iannaccone, University of Rome.

Table 1. Typical Mean Doses Relevant to Some Low-Dose Radiation Exposures to Different Populations

Radiation exposure scenario	Approximate mean individual dose (mSv)[a]
Round-trip flight, New York–Seattle[57]	0.06
Single-screening mammogram (breast dose)[21]	3
Background dose caused by natural radiation exposure[58]	3/y
Adult CT scan (stomach dose from abdominal scan)[59]	10
Excess dose (>15 y) to 4 million individuals in Ukraine in the vicinity of the Chernobyl accident[60,61]	13
Typical dose to an A-bomb survivor at a distance of 2.3 km from the explosion hypocenter at Hiroshima[25]	13
Dose range over 20-block radius from hypothetical nuclear terrorism incident[62]	3–30
Radiation worker annual exposure limit[43]	20/y
Exposure on international space station[63]	170/y

[a]All doses are effective whole-body doses with the exception of the medical exposures (mammography, CT scan), which are to specific organs.

as the dose decreases, the signal-to-noise ratio (radiation risk to natural background risk) decreases.

Most of the quantitative information that we have regarding radiation-induced cancer risks comes from studies of A-bomb survivors. A-bomb survivor cohorts generally are used as the basis for predicting radiation-related risks for a general population because (1) they are the most thoroughly studied (over many decades) large exposed population, (2) the cohorts are not selected for disease, (3) all age groups are covered, and (4) a substantial subcohort of about 25,000 survivors, typically those who were approximately 2–2.7 km from the explosion hypocenters,[25] received radiation doses comparable with those of concern here.

The key questions here are: (1) What is the lowest dose of x-rays for which there is convincing evidence of significantly increased cancer risks in humans? (2) What is the most appropriate way to extrapolate these risks to even lower doses? (3) What is the dependence of cancer risks on age at exposure? These issues recently have been reviewed extensively.[23]

Effects of Radiation Dose on Cancer Risk

In summary, there is good epidemiologic evidence of increased cancer risk for children exposed to acute doses of 10 mSv (or greater), and for adults exposed to acute doses of 50 mSv (or greater).[23] As we discuss later, relevant organ doses for a paired (supine and prone) CTC examination are of the order of 15 mSv or less.

Extrapolation of Risks for Lower Radiation Doses

The issue here is how to estimate risks at doses somewhat (although not a great deal) lower than those for which there is statistically significant evidence of increased cancer risks. The current consensus[26] is that the measured risks reasonably can be extrapolated linearly to somewhat lower doses, although as the dose of interest becomes progressively lower, the uncertainties inherent in this extrapolation become progressively greater. Relatively small extrapolations from epidemiologic data are required (eg, from 50 to 15 mSv), however, to estimate cancer risks at the doses relevant to CTC examinations.

Effect of Age at Exposure

Regarding age at exposure, as can be seen in Figure 3, radiation risks generally decrease markedly with age. This is because sensitivity is related to the proportion of dividing cells in an organ, which decreases with increasing age, and other competing risks play an increasing role with increasing age.

CT

At present, medical X-rays are responsible for about 17% of all the ionizing radiation exposure to which an average US resident is exposed (Figure 4). Within this fraction of the total radiation pie, about two-thirds is from CT examinations.[27] This large proportion is despite the fact that only about 1 in 10 of all radiologic examinations are CT scans, and reflects the fact (Table 2) that CT scans produce a much larger radiation dose than conventional radiographs such as dental radiographs, chest radiographs,

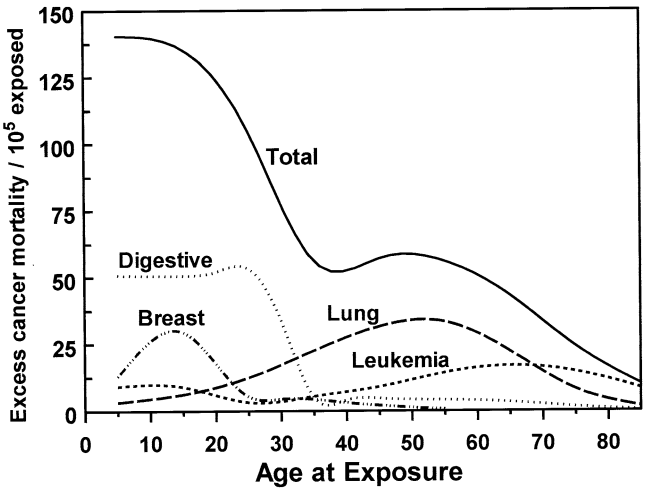

Figure 3. Estimated radiation-related absolute cancer mortality risk/10^5 individuals in the United States exposed at different ages to a whole-body dose of 10 mSv. Estimates from the 1990 NAS BEIR-V report.[46]

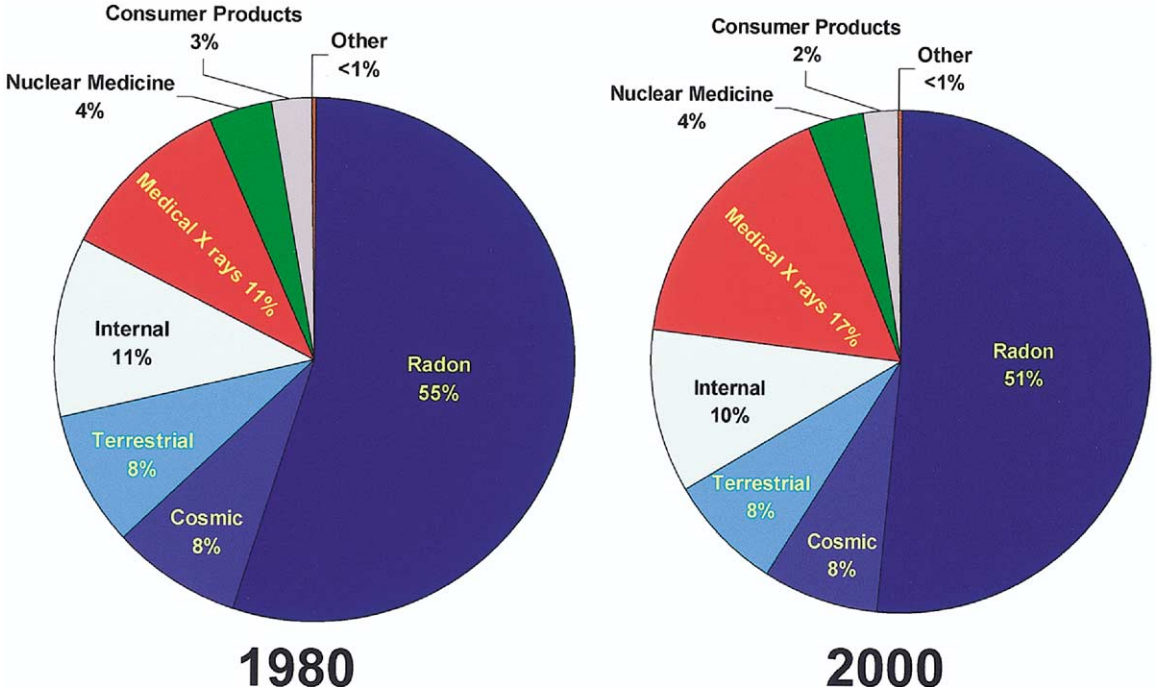

Figure 4. Sources of ionizing radiation exposure (technically the collective effective dose) to an average individual in the United States. The difference in the contribution of medical x-rays between 1980[64] and 2000 is caused primarily by the increase in CT scans—from about 2 million per year in 1980 to about 58 million in 2000.[65]

or mammograms. This is inherent in the nature of a CT scan, which essentially involves the generation of multiple X-ray images.

The basic principle of helical, or spiral, CT scanning is shown in Figure 5. Essentially, the patient is moved through a continuously rotating x-ray source/detector combination. A more modern version is the multidetector CT, which gives the advantage of short scan times, coupled with potentially very thin slice widths.

A relatively new CT dose-reduction technique is automatic tube current modulation (Figure 6),[28–31] now available from all the major scanner manufacturers. These systems continuously lower or raise the x-ray tube current to compensate for different instantaneous levels of attenuation of the x-ray beam by the patient. For example, when the beam is aimed in the posteroanterior direction, fewer x-rays are needed (for the same image quality) compared with the lateral-medial direction; or when the beam is passing through the region of the transverse colon, fewer x-rays are needed compared with the pelvic bone region.

For helical CT scans, the speed that the patient table moves relative to the rotation speed of the x-ray tubes/detectors is an important determinant of the radiation dose; it is defined through the pitch, which is the linear table motion feed per 360° rotation, divided by the total beam width (the slice width × the number of detectors).

The radiation dose from CT depends on a number of factors. The most important are the tube current, the scan time, the pitch, the tube voltage, the number of detectors, the slice thickness, and the particular scanner design.[32] For a given CT scanner operating at a given voltage, the organ dose is proportional to the mAs (current [mA] × rotation time) and is inversely proportional to the pitch. It is always the case, however, that the relative noise in CT images will increase as the radiation dose decreases; thus, there always will be a trade-off between the need for low-noise images and the desirability of using low radiation doses.[33]

Table 2. Typical Organ Doses From Various Radiologic Examinations

Examination	Relevant organ	Relevant organ dose (mSv)
Dental radiograph	Brain	0.005
Posteroanterior chest radiograph	Lung	0.01
Lateral chest radiograph	Lung	0.15
Screening mammogram	Breast	3
Adult abdominal CT	Stomach	10
Neonate abdominal CT	Stomach	25

CTC

Radiation Doses From CTC Examinations

Because of the advantageous geometry of a CTC scan, the dose/noise trade-off can be very much weighted toward low-dose, higher-noise images.[9,10,34–36] Several studies have examined systematically the various scanner

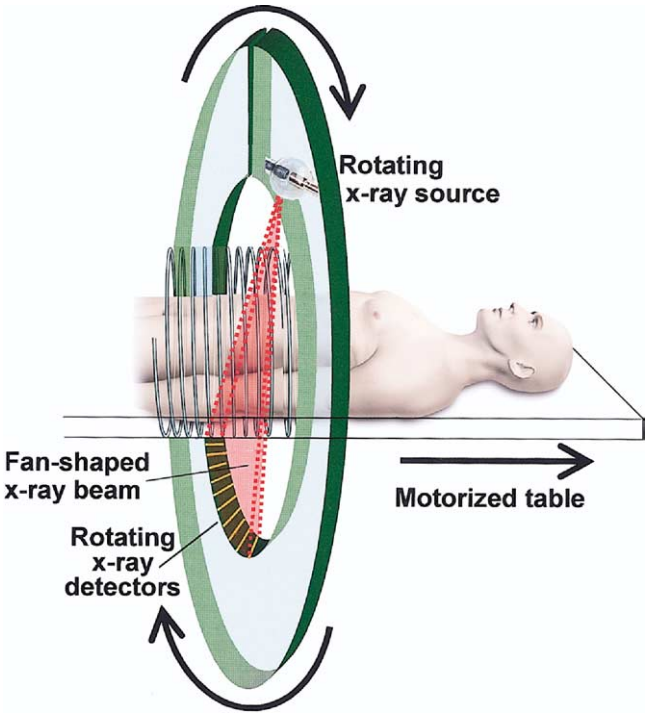

Figure 5. Helical (spiral) CT scanning. Both the x-ray source and, on the other side of the patient, the x-ray detectors, rotate around the patient. If the table were not moving, a single slice of the patient would be imaged (axial CT). Because the table is moving at the same speed as the source-detector combination is rotating, the result is a helical or spiral CT scan of the patient, as depicted here. A single row of detectors is shown; modern multidetector scanners have several rows of detectors alongside each other, which allow both for thinner slice widths and shorter scan times.

parameters discussed earlier, and generally have come to the conclusion that more noise can be accepted in a CTC scan compared with other CT scans, while still maintaining sensitivity and specificity, at least for polyps greater than approximately 7 mm in diameter.[10,11,34,37,38]

To estimate the radiation dose to different organs from adult CTC scans, we used the ImPACT CT Dosimetry Calculator[39] (London, England), for a given CT scanner with given scanner settings, this tool, which is available online, uses standard calculational techniques[39] to estimate generic doses to the organs of a simplified anthropomorphic phantom (Figure 7). Our own work, using direct measurements in a realistic anthropomorphic phantom, suggests that the estimated doses from ImPACT calculations generally are within 30% of measured values.

It is important to note that, in general, paired CTC examinations are given, 1 in the supine and 1 in the prone position. Several studies have suggested that this technique improves colonic distention,[40–42] decreasing the number of collapsed colonic segments.

Table 3 shows estimated organ doses using the ImPACT calculator for one of the more common CT scanners (LightSpeed Ultra; GE, Waukesha, WI). The scanner parameters were taken from a recent Mayo Clinic study by Johnson et al,[11] and are toward the low-dose end of published CTC protocols.[34] To provide an estimate of scanner-to-scanner dose variations, Table 4 shows the radiation dose to the colon estimated for 5 of the more common CT scanners in use today, using identical scanner parameters in each case; the coefficient of variation of the dose to the colon is about 20%.

Table 3 shows that typical organ doses are less than 20 mSv, even for organs directly in the x-ray beam such as the colon, stomach, bladder, and kidneys. The subcohort of approximately 25,000 A-bomb survivors[25] who received comparable radiation doses (A-bomb dose range

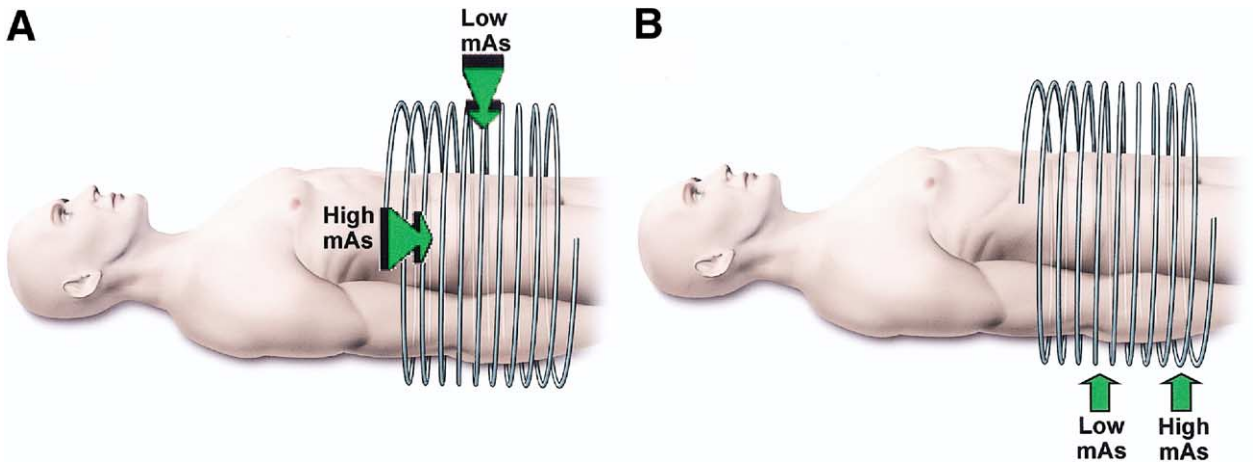

Figure 6. Principles of automatic tube current modulation. (*A*) Angular modulation in which the x-ray tube current is lowered as the x-rays are aimed in the anteroposterior directions, and increased when the x-rays are aimed in the lateral-medial directions, when there will be more x-ray attenuation. (*B*) Z-axis modulation in which, for example, fewer x-rays are required in the abdominal region superior to the pelvic bones compared with the pelvic region.

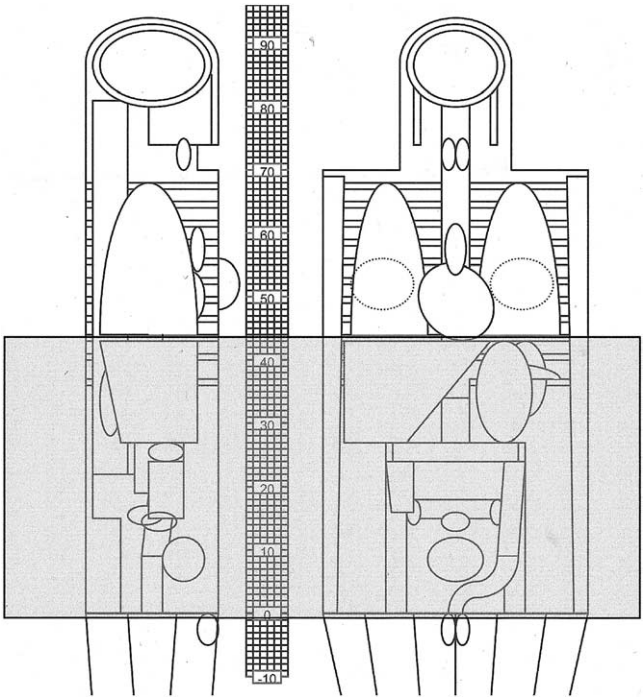

Figure 7. Idealized computer representation of internal organs used in ImPACT calculations[39] of organ doses from CTC examinations. *Shaded area* indicates scanning region for CTC assumed in this study.

5–50 mSv; mean, 20 mSv) does show a slight increase in cancer mortality compared with the control population,[24] but this increase is of marginal statistical significance ($P = 0.15$). It also is pertinent to point out that this A-bomb subcohort consists of individuals covering all age groups, and thus it is reasonable to assert that there is no direct statistically significant evidence from A-bomb survivor data that a pair of CTC scans increases cancer risks in adults. It does not follow, of course, that the radiation risk is zero; rather that it is likely to be small.

It also is pertinent to note (Figure 3) that the largest radiation risks for individuals over age 50 years are for lung cancer and leukemia. Table 3 shows that neither the lung nor bone marrow are among the organs most exposed during a CTC scan.

Table 4. Estimated Colon Doses From Paired CTC Scans Using the Same Machine Settings With Different CT Scanners

Scanner	Colon dose from paired CTC scans[a] (mSv)
GE LightSpeed Ultra	13.2
GE QX/I, LightSpeed, LightSpeed Plus	11.6
Philips Mx8000 (Andover, MA)	9.0
Siemens Volume Zoom, Access	8.6
Siemens Sensation 16	7.6

[a]Paired CTC examinations at 65 mAs, 120 kVp, 10-mm collimation, pitch 1.35.

Estimation of Radiation Risks Associated With CTC Examinations

In this section we provide estimates of the cancer risks associated with the organ doses that are shown in

Table 3. Typical Organ Doses, Background Lifetime Cancer Risks, and Additional Absolute Lifetime Cancer Risks, From a Paired CTC Examination of a Healthy 50-Year-Old

	Organ dose from paired CTC scans[a] (mSv)	Background organ-specific remaining lifetime cancer risk[b] (%)	Additional absolute lifetime cancer risk[c] from paired CTC scans at age 50 (%)
Colon (man)	13.2	5.9	0.044
Colon (woman)	13.2	4.8	0.038
Bladder (man)	16	3.7	0.025
Bladder (woman)	16	1.1	0.016
Stomach (man)	14.8	1.2	0.013
Stomach (woman)	14.8	0.7	0.031
Kidney (man)	16.1	1.3	0.012
Kidney (woman)	16.1	0.8	0.017
Liver (man)	13.8	0.8	0.016
Liver (woman)	13.8	0.4	0.005
Leukemia (man)	6.6	1.3	0.032
Leukemia (woman)	6.6	0.8	0.018
Lung (man)	2.2	7.7	0.006
Lung (woman)	2.2	5.4	0.008
Total (man)		45.7	0.15
Total (woman)		32.9	0.13

[a]D_o (see text for equation) for paired (supine and prone) CTC examinations with GE LightSpeed Ultra CT scanner: 130 mA, 120 kVp, .5-s rotation time, collimation 8 × 1.25 mm, pitch 1.35.[11] As discussed in the text, dose reductions by factors of 5 or even 10 beyond the standard parameters used here potentially are practical.
[b]B_o: background organ-specific cancer risks for healthy individual aged 60 (50 + 10 y).
[c]R_o.

Table 3, from CTC scans. (Note that the commonly quoted "effective dose," which is an age-independent weighted average of organ doses,[43] is useful as a relative measure of the total radiation detriment from different scanners or scanner settings, but gives no better than order-of-magnitude estimates of absolute cancer risks. The organ-weighting factors used in the effective dose calculation are expected to be changed significantly in the near future.[44])

To generate risk estimates that are applicable to US populations, we have used as a basis the dose-, organ-, and sex-specific excess relative risks for cancer incidence in Japanese A-bomb survivors.[45] Standard risk-transfer methodologies[46,47] then are applied to these A-bomb data to generate estimates of organ-specific lifetime excess relative risk for cancer induction that are applicable to low-dose radiation exposures in US populations.

Thus, we can estimate dose-, organ-, and sex-specific excess relative risks for cancer induction caused by low-dose radiation exposure in US populations, and the radiation doses to the various organs (Table 3) from a CTC examination. Based on these, we can estimate the excess relative cancer risk caused by radiation exposure from CTC scans at a given age, and thus the absolute cancer risks caused by the radiation exposure. The basis of this approach is that the radiation-associated organ-dependent cancer risks can be scaled from the natural cancer background risk, by using the estimated radiation-related excess relative risks, and that a latency period of 10 years is assumed after radiation exposure before any cancer risk is manifest.[46] Thus, the absolute excess organ-specific lifetime cancer risk, R_o, associated with the radiation from a paired CTC scan at a given age (A) in an individual of gender G, can be estimated as

$$R_o(A, G) = ERR_o(D_o, G) \times B_o(A + 10, G) \times P_{10}(A, G)$$

where D_o is the organ-dose from a paired CTC scan (Table 3), ERR_o is the estimated organ-specific excess relative risk at organ dose D_o in an individual of gender G, and $B_o(A,G)$ is the lifetime organ-specific cancer risk for an individual alive at age A (from US tumor registries data[48]). $P_{10}(A, G)$ are the probabilities of living at least 10 years from age A, from US life tables.[49] This equation, or similar variants, has been used in most recent national and international radiation risk estimation studies for solid cancers.[43,46,47,50,51]

Table 3 shows the estimated absolute lifetime cancer risks, R_o, associated with the radiation exposure from paired CTC scans in a 50-year-old. For comparison, the lifetime background cancer risks, B_o (see equation), also are shown. As expected, the main organs at risk are the colon, stomach, and bladder, as well as the leukemic cancers. All the estimated absolute radiation risks are relatively small, the largest being less than 0.05% (1 in 2000). Summed over all the organs at risk, the estimated absolute lifetime risk for cancer induction from a pair of CTC scans (with the scanner parameters from Table 3) in a 50-year-old is about 0.14% ($\simeq$1 in 700). Estimated risks for cancer mortality would, of course, be considerably less.

Several points need to be considered regarding the estimated risks in Table 3.

First, the risks are highly dependent on the scanner settings used, particularly the mAs and the pitch. The settings used in Table 3 are on the low-dose side of those used in current reported studies,[34] but there is good evidence[8,11,36] suggesting that the mAs and thus the dose could be decreased further, by at least a factor of 5 (and perhaps as much as a factor of 10) from these settings, while still maintaining sensitivity and specificity for polyps larger than approximately 5 mm. As an example, the low-dose settings used for the CTC scans shown in Figure 2[8,36] result in estimated digestive-organ doses that are only 22% of those listed in Table 3. Still further reductions of up to 50% in CTC doses may be possible (A. Graser, University of Munich, personal communication, March 2005) through the use of automatic tube current modulation (Figure 6),[30,31] now available from all the major CT scanner manufacturers.[30]

Second, the estimated absolute cancer risks are highly age dependent. Although the radiation-related excess relative risk will not change greatly over the age range of interest, both the background cancer risk and the probability of surviving 10 years (B_o and P_{10}) will decrease with increasing age. Thus, for example, the estimated radiation-associated absolute lifetime risk for colon cancer induction decreases from 0.044% for a CTC scan at age 50 (Table 3), to 0.022% for a scan at age 70. If individuals receive multiple CTC screenings over a period of years, the radiation dose will, of course, increase proportionately. The most likely case is that any radiation risks also will increase proportionately. Specifically, at high doses, theory,[52] animal data,[53] and epidemiologic data[54] suggest that fractionating a radiation exposure decreases the overall risk at a given dose, but at the low doses of relevance here, both theory[52] and animal data[53] suggest that the risks are roughly independent of fractionation.

Third, there are quantifiable uncertainties involved in these radiation risk estimates. The largest is the uncertainties in transferring risk estimates from a Japanese population to a US population, but there also are uncertainties associated with the extrapolation of risks from

somewhat higher doses, for which the risks statistically are significant, and uncertainties associated with the reconstructed dosimetry estimates at Hiroshima and Nagasaki.[55] Based on Monte-Carlo simulations of the various uncertainties,[47] the upper and lower 90% confidence limits of the radiation risk estimates are approximately a factor of 3 higher and lower, respectively, than the point estimates.

Conclusions

There is persuasive evidence that colonoscopy-driven polypectomy can result in a significantly decreased incidence of colorectal cancer,[1,2] and there is poor compliance with current guidelines for colorectal cancer screening.[3,4] CTC, particularly using noncathartic or minimally cathartic techniques, has the clear potential to increase compliance.[13,14] It is pertinent to note that should noncathartic CTC result in a significant increase in colorectal screening compliance, the overall colonoscopy demand probably would not change greatly, the decrease in the number of screening colonoscopies being compensated for by the increased demand for polypectomies of CTC-discovered lesions.[56]

Because the geometry for CTC is highly advantageous (soft-tissue polyps projecting into an air- or CO_2-filled lumen), it can be performed using lower radiation doses than almost any other CT examination.

The cancer risks associated with the radiation exposure from CTC are unlikely to be zero, but they are small. A best estimate for the absolute lifetime cancer risk associated with the radiation exposure using typical current scanner techniques is approximately 0.14% for paired CTC scans for a 50-year-old, and about half that for a 70-year-old. These values probably could be reduced by factors of 5 or 10, with optimized protocols.

Thus, it seems clear that in terms of the radiation exposure the benefit-risk ratio potentially is large for CTC.

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