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

DAVID J. BRENNER* and MARIA A. GEORGSSON†
*Center for Radiological Research, Columbia University Medical Center, New York, New York; and †Hunterdon Healthcare Partners, Flemington, New Jersey

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 exposure 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.

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Abbreviations used in this paper: CTC, computed tomography colonography.
with soft-tissue polyps. Recent results with noncathartic CTC (Figure 2B) have been very encouraging.8,18–20

3. Optimization and Standardization of CT Parameters. Just as mammographic examinations are now well standardized21 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...
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 consensus26 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,
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), 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 thickness × 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. 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.

### Table 2. Typical Organ Doses From Various Radiologic Examinations

<table>
<thead>
<tr>
<th>Examination</th>
<th>Relevant organ</th>
<th>Relevant organ dose (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental radiograph</td>
<td>Brain</td>
<td>0.005</td>
</tr>
<tr>
<td>Posteroanterior chest radiograph</td>
<td>Lung</td>
<td>0.01</td>
</tr>
<tr>
<td>Lateral chest radiograph</td>
<td>Lung</td>
<td>0.15</td>
</tr>
<tr>
<td>Screening mammogram</td>
<td>Breast</td>
<td>3</td>
</tr>
<tr>
<td>Adult abdominal CT</td>
<td>Stomach</td>
<td>10</td>
</tr>
<tr>
<td>Neonate abdominal CT</td>
<td>Stomach</td>
<td>25</td>
</tr>
</tbody>
</table>

### 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. Several studies have examined systematically the various scanner geometries that can significantly reduce the radiation dose.
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.\textsuperscript{10,11,34,37,38}

To estimate the radiation dose to different organs from adult CTC scans, we used the ImPACT CT Dosimetry Calculator\textsuperscript{39} (London, England), for a given CT scanner with given scanner settings, this tool, which is available online, uses standard calculational techniques\textsuperscript{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\textsuperscript{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.,\textsuperscript{11} and are toward the low-dose end of published CTC protocols.\textsuperscript{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\textsuperscript{25} who received comparable radiation doses (A-bomb dose range

![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.](image)

![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.](image)
5–50 mSv; mean, 20 mSv) does show a slight increase in cancer mortality compared with the control population, 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.

### 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

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

\(^a\) \( D_\text{c} \) (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 x 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, 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.

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. Standard risk-transfer methodologies 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. Thus, the absolute excess organ-specific lifetime cancer risk, , associated with the radiation from a paired CTC scan at a given age (A) in an individual of gender , 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 is the organ-dose from a paired CTC scan (Table 3), is the estimated organ-specific excess relative risk at organ dose in an individual of gender , and is the lifetime organ-specific cancer risk for an individual alive at age (from US tumor registries data). are the probabilities of living at least 10 years from age , from US life tables. This equation, or similar variants, has been used in most recent national and international radiation risk estimation studies for solid cancers.

Table 3 shows the estimated absolute lifetime cancer risks, , associated with the radiation exposure from paired CTC scans in a 50-year-old. For comparison, the lifetime background cancer risks, , (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% (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, but there is good evidence 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 28 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) now available from all the major CT scanner manufacturers.

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 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, and animal data, and epidemiologic data suggest that fractionating a radiation exposure decreases the overall risk at a given dose, but at the low doses of relevance here, both theory and animal data 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. Based on Monte-Carlo simulations of the various uncertainties, 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, and there is poor compliance with current guidelines for colorectal cancer screening. CTC, particularly using noncathartic or minimally cathartic techniques, has the clear potential to increase compliance. It is pertinent to note that colonoscopy 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.

Because the geometry for CTC is highly advantageous (soft-tissue polyps projecting into an air- or CO2-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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Address requests for reprints to: David J. Brenner, PhD, Center for Radiological Research, Room VC 11-235, Columbia University Medical Center, 630 West 168th Street, New York, New York 10032. e-mail: dbb3@columbia.edu; fax: (212) 305-3229.
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