Estimated Risks of Radiation-Induced Fatal Cancer from Pediatric CT

David J. Brenner[1]
Carl D. Elliston[1]
Eric J. Hall[1]
Walter E. Berdon[2]

OBJECTIVE. In light of the rapidly increasing frequency of pediatric CT examinations, the purpose of our study was to assess the lifetime cancer mortality risks attributable to radiation from pediatric CT.

MATERIALS AND METHODS. Organ doses as a function of age-at-diagnosis were estimated for common CT examinations, and estimated attributable lifetime cancer mortality risks (per unit dose) for different organ sites were applied. Standard models that assume a linear extrapolation of risks from intermediate to low doses were applied. On the basis of current standard practice, the same exposures (milliampere-seconds) were assumed, independent of age.

RESULTS. The larger doses and increased lifetime radiation risks in children produce a sharp increase, relative to adults, in estimated risk from CT. Estimated lifetime cancer mortality risks attributable to the radiation exposure from a CT in a 1-year-old are 0.18% (abdominal) and 0.07% (head)—an order of magnitude higher than for adults—although those figures still represent a small increase in cancer mortality over the natrual background rate. In the United States, of approximately 600,000 abdominal and head CT examinations annually performed in children under the age of 15 years, a rough estimate is that 500 of these individuals might ultimately die from cancer attributable to the CT radiation.

CONCLUSION. The best available risk estimates suggest that pediatric CT will result in significantly increased lifetime radiation risk over adult CT, both because of the increased dose per milliampere-second, and the increased lifetime risk per unit dose. Lower milliampere-second settings can be used for children without significant loss of information. Although the risk–benefit balance is still strongly tilted toward benefit, because the frequency of pediatric CT examinations is rapidly increasing, estimates that quantitative lifetime radiation risks for children undergoing CT are not negligible may stimulate more active reduction of CT exposure settings in pediatric patients.

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[1]Center for Radiological Research, Columbia University, 630 W. 168th St., New York, NY 10032. Address correspondence to D. J. Brenner.

[2]Department of Radiology, Division of Pediatric Radiology, Columbia-Presbyterian Medical Center, 630 W. 168th St., New York, NY 10032.

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The use of CT has increased rapidly in the past two decades, fueled in part by the development of helical CT [1]. For example, the estimated annual number of CT examinations in the United States rose approximately sevenfold from 2.8 million in 1981 [2] to 20 million in 1995 [3]. By their nature, CT examinations contribute disproportionately to the collective diagnostic radiation dose to the population; for example, in Britain it has been estimated that approximately 4% of diagnostic radiology procedures are CT examinations, but their contribution to the collective dose is approximately 40% [4].

Figure 1 shows a breakdown of the number of CT examinations by age at examination, based on the results of a 1989 British survey [5]; in this survey, approximately 4% of CT examinations (which corresponds to about 10^6/year in the United States) were performed on children under the age of 15 years. The proportion of childhood CT examinations is rapidly increasing (indeed, an average value of 6% was estimated in 1993 [6]); for example, Coren et al. [7] reported a 63% increase in requests for pediatric CT between 1991 and 1994.

The recent increase in pediatric CT examinations is particularly marked in the United States. Figure 2 shows the number of abdominal and pelvic CT examinations of children under a given age at a major American children's hospital for 1996 through 1999. This figure shows, for example, a 92% increase between 1996 and 1999 in abdominal and pelvic CT examinations on children less

than 15 years old. The increased frequency of pediatric CT, particularly in the United States, is largely caused by the advent of fast helical CT [1], which reduces the need for sedation [8]. Helical CT makes more types of CT examinations, particularly evaluation of the acute pediatric abdomen [9, 10], more practical in younger, sicker, or less cooperative children [1]; it also allows newer pediatric CT applications such as dynamic studies of pulmonary physiology and three-dimensional airway imaging.

Pediatrics represents a comparatively small, though increasing, fraction of the overall number of CT examinations. However, we show here that the combination of higher radiation doses to children for a given CT examination and, more importantly, the much larger lifetime risks per unit dose of radiation that apply to children, result in lifetime cancer mortality attributable to the radiation exposure from CT that is significantly higher in children than in adults.

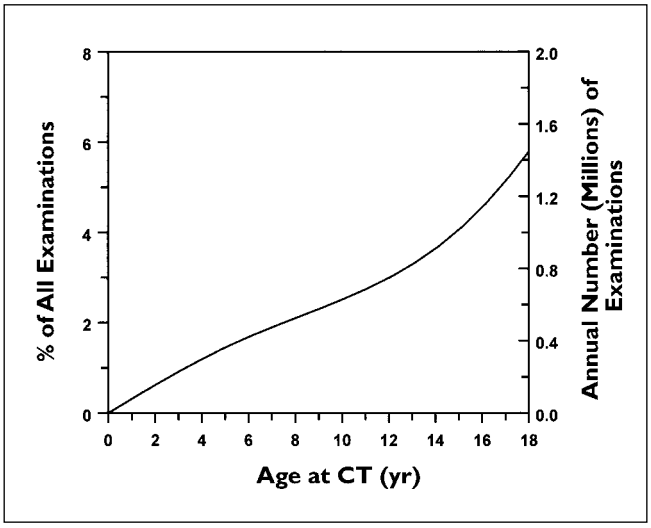

Fig. 1.—Graph shows proportion of total number of CT examinations performed on individuals younger than a given age. Data are from 1989 British study by Shrimpton et al. [5]. Ordinate on right shows estimated absolute numbers of CT examinations now performed annually in United States on patients younger than a given age (based on proportions from Shrimpton et al. [5], an overall annual frequency of CT examinations in the United States of 91/1000 [3], and current United States population of 274,000,000).

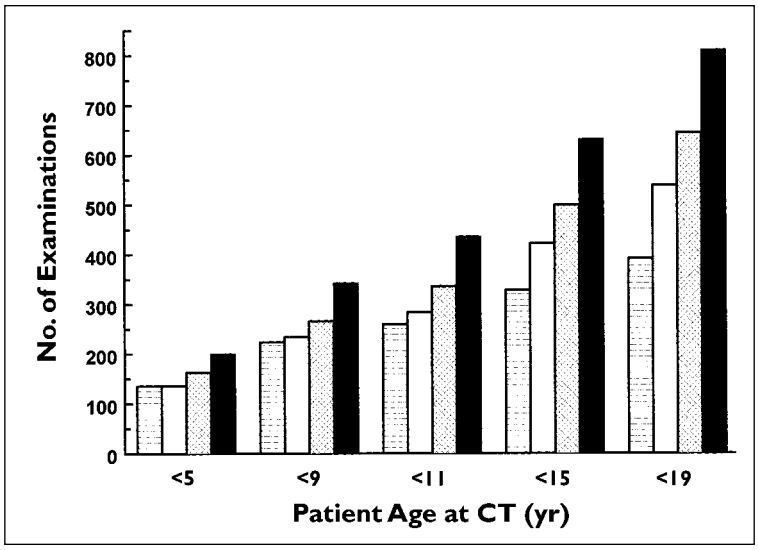

Fig. 2.—Bar graph shows annual number of abdominal and pelvic CT examinations performed at St. Louis Children's Hospital (Mallinckrodt Institute of Radiology, St. Louis, MO) on patients younger than a given age, for years 1996–1999 (*bars* left to right in each group) (McAlister WH, personal communication). Number of pediatric CT examinations almost doubled between 1996 and 1999.

A central issue is that epidemiologic evidence [11] points strongly to a "relative" risk mechanism for radiation-induced cancer; essentially, that the excess probability of cancer mortality after radiation exposure is proportional to the natural background rate of cancer death. In other words, the pattern of excess risk is that of a lifelong elevation (though not necessarily a fixed elevation) of the "natural" age-specific risk. Lifetime radiation risk estimation, both for the analysis of atomic bomb survivor data [11] and for generating resultant risk estimates for Western populations [12, 13], has used relative risk models. The implication of a relative risk mechanism is that the lifetime risk attributable to a single small dose of radiation at a given age is larger for children (who face a large lifetime background risk of cancer mortality) but decreases with age (Fig. 3). This larger attributable lifetime risk after childhood exposure implies that a given radiation dose to a child is of greater public health significance than the same dose in an adult.

Although some estimates have been made of cancer risks to adults attributable to the radiation from CT examinations [14, 15], no such estimates have been made for children. We use here calculated organ doses from CT examinations in combination with age-at-exposure–dependent estimates of attributable lifetime risks per unit dose to provide estimates of the lifetime age-dependent cancer mortality risks associated with common CT examinations.

As we discuss, various uncertainties are associated with these risk estimates, both in terms of the dose for a given CT examination and in terms of the cancer risk per unit dose. However, neither the uncertainties in the doses nor the uncertainties in the risks per unit dose are such that the overall pattern of risks for children relative to adults—a significantly larger lifetime cancer mortality risk associated with pediatric CT—is likely to change.

Materials and Methods

Lifetime Mortality Risks per Unit Dose

Evaluated lifetime cancer mortality risks per unit dose as a function of age at exposure are given both by the National Academy of Sciences Biological Effects of Ionizing Radiations committee [12] and by the International Commission on Radiological Protection [13], as shown in Figure 3. Both are based on relative risk models that depend on sex, age at exposure, and time since exposure, and inherently assume a linear extrapolation of risks from intermediate to low doses.

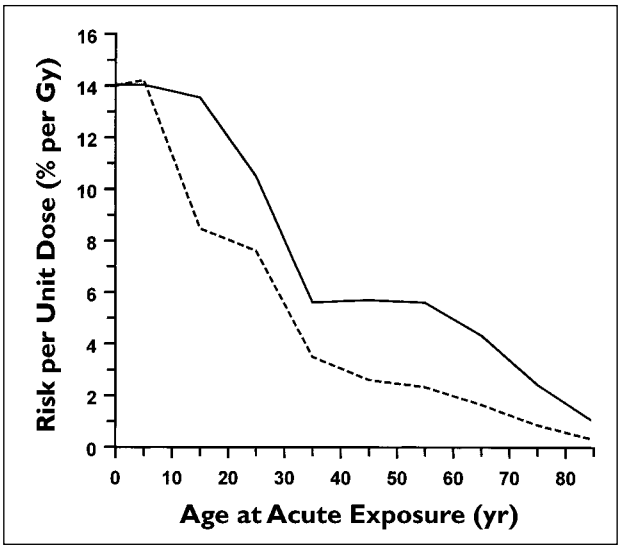

Fig. 3.—Graph shows lifetime attributable cancer mortality risks per unit dose as a function of age at a single acute exposure as estimated by National Academy of Sciences BEIR V (Biological Effects of Ionizing Radiations) committee (*solid line*) [12] and in ICRP (International Commission on Radiological Protection) report 60 (*dotted line*) [13]. Note rapid increase in lifetime risk with decreasing age at exposure.

As discussed in the following text, because of the inhomogeneous nature of the dose distribution produced by CT, we need to evaluate the age-dependent risks separately for each group of potential cancer sites. Figure 4 shows these age-dependent lifetime cancer mortality risks derived from the Biological Effects of Ionizing Radiations committee evaluation.

Overall Methodology

Our basic technique is to multiply age-dependent lifetime cancer mortality risks (per unit dose) by estimated age-dependent doses produced by various CT examinations. In fact, the age dependence of the cancer mortality risk varies considerably from site to site (Fig. 4). Thus, for a highly inhomogeneous dose distribution, as produced by a CT examination, the age dependence of the overall cancer risk cannot be directly inferred from estimates of the total cancer mortality (for all sites combined) per unit effective dose. Rather, the age dependence of the risks for the various groups of sites shown in Figure 4 are each separately calculated by applying appropriate site-specific doses to the age- and site-dependent risks in Figure 4, and these site-specific risks are then summed to yield the overall age-dependent lifetime cancer mortality risk.

Age-Dependent Doses from CT Examinations

For adults, various calculations and measurements are available of the doses produced by a variety of CT examinations under different conditions [16, 17], the most comprehensive being the results of a 1989 survey of CT practice in Britain, in which organ doses were estimated for 17 CT examinations from more than 100 CT scanners [16]. For children, however, less information is available. Doses to specific organs at some ages have been reported [18–20], and systematic effective dose (i.e., organ-weighted average body dose) calculations as a function of age at examination have recently been reported [21]. Therefore, we chose to use estimated organ doses for adult CT examinations, and scale them for children using relative effective doses.

Because of the comprehensive nature of the British survey, we chose to scale adult organ doses as reported in this 1989 survey [16] of CT practice in Britain. These results were averaged over 121 different machines (108 for routine abdominal scans) surveyed at the time. The mean scan parameters, averaged over all the machines surveyed, are 404 mAs, 15.5 slices, and 9.3-mm slice width for routine abdominal CT; and 462 mAs, 12.5 slices, and 9.1-mm slice width for routine head CT. These surveyed exposure settings, reflecting day-to-day practice, are similar to more recent survey results of adult CT in the United States [22] and Norway [23], although probably considerably higher than optimal [24]. As discussed here, all the doses and risks presented vary approximately linearly with exposure (milliampere-seconds), so the results obtained here can easily be scaled to other milliampere-second settings.

To obtain organ doses from pediatric CT examinations, relative changes in effective dose as a function of age, estimated by Huda et al. [21] for head and for abdominal CT examinations, were applied to

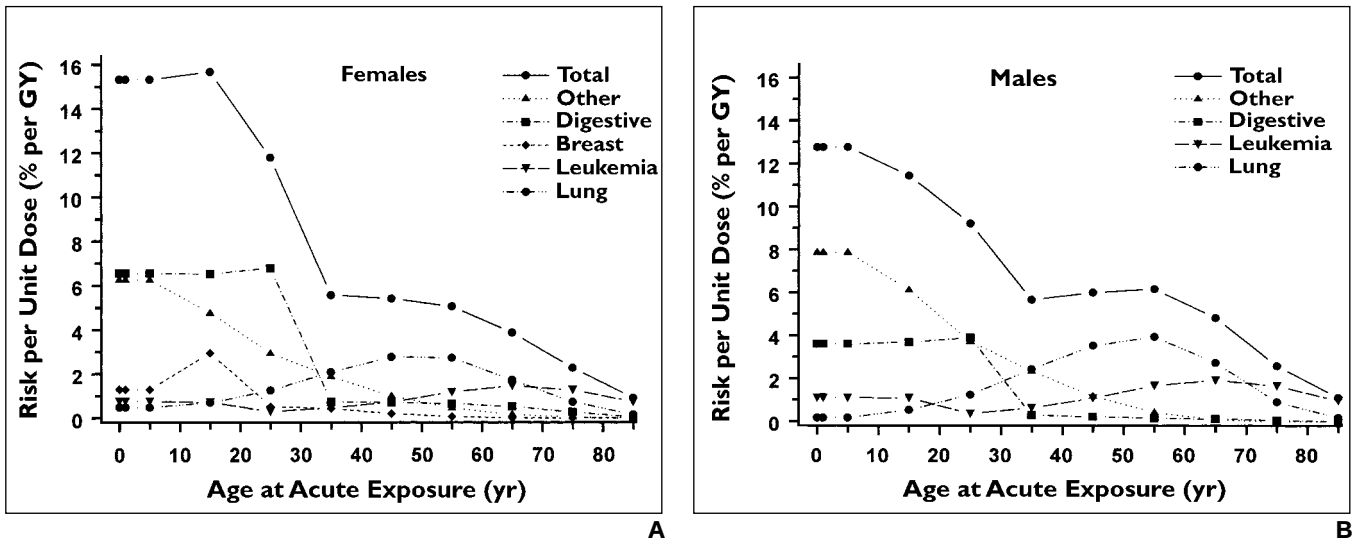

Fig. 4.—Breakdown by cancer type.
A and **B,** Graphs show breakdown by cancer type of risk per unit dose for females (**A**) and males (**B**) of lifetime attributable cancer mortality risks as a function of age at a single acute exposure as estimated by the National Academy of Sciences BEIR V (Biological Effects of Ionizing Radiations) committee [12].

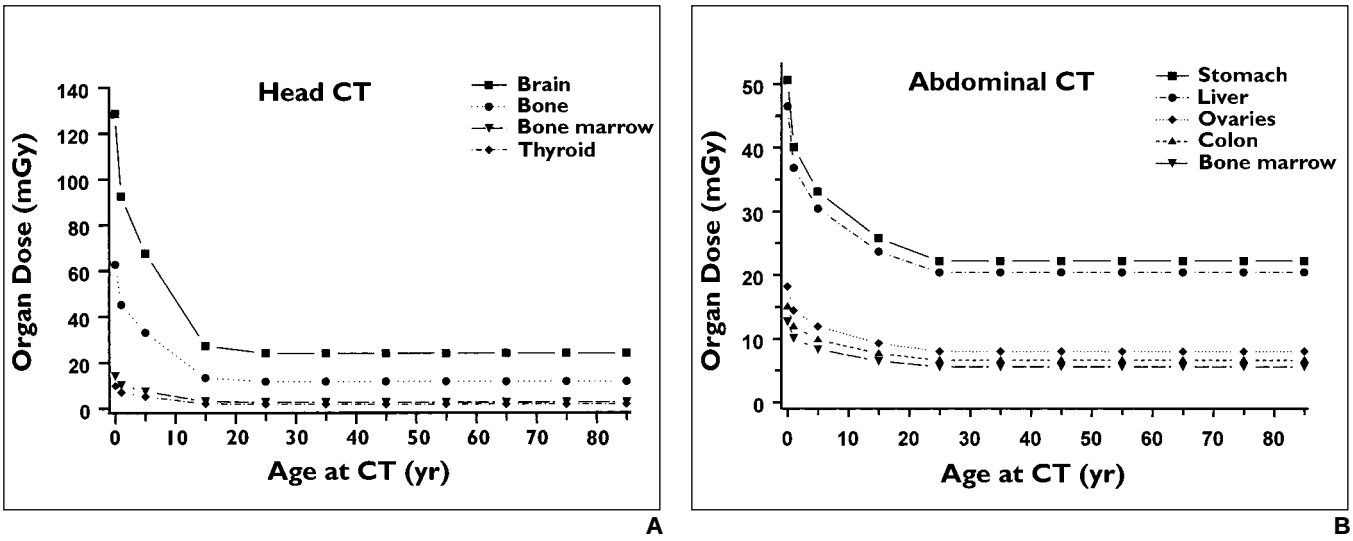

Fig. 5.—Estimated age-dependent CT doses to various organs.
A and **B,** Graphs show estimated age-dependent doses to various organs that contribute significantly to overall estimated risk for typical single CT examination of head (**A**) and of abdomen (**B**). Note different scales for the two graphs. As discussed in text, the same exposure techniques (milliampere-seconds) for all ages are assumed here. For both types of examinations, doses increase markedly with decreasing age.

all these adult organ doses. We assumed that the relative doses to any organ relative to any other organ remain unchanged with age. Typical results are shown in Figure 5.

The relative doses as a function of age obtained with this method are in reasonable agreement with the Monte Carlo calculations by Zankl et al. [17, 19], who used computer-simulated anthropomorphic phantoms of a neonate, a 7-year-old, and an adult. For example, the stomach dose from an abdominal CT examination in a 7-year-old relative to that in an adult, as calculated by Zankl et al. [17, 19] was 1.35; using the current methodology, the same relative dose was 1.39.

The specific groupings of potential types of cancer for which evaluated radiation-induced risks are available are leukemia, digestive organ cancer, lung cancer, breast cancer (for women), and other cancer [12]. Digestive organ cancer includes cancer of the colon, stomach, liver, pancreas, esophagus, and small intestine; "other" cancer includes brain, thyroid, bladder, kidney, adrenal gland, spleen, thymus, skin, bone, testes (for men), and uterus and ovaries (for women). To use the risk data shown in Figure 4, doses appropriate to these sites or groups of sites need to be assigned. For leukemia, lung, and breast cancer in women, doses to the bone marrow, lung, and female breast were respectively used. For digestive cancer, a weighted average of the doses to the relevant organs was used, the weighting consisting of the relative radiation–carcinogenic sensitivities of these organs. Thus, the dose to the digestive organs was computed as

$$D_{digestive} = \sum_T w_T D_T \Big/ \sum_T w_T, \qquad (1)$$

where the summation is over the tissues (T) of the colon, stomach, liver, pancreas, esophagus, and small intestine. Here w_T are weighting factors representing the evaluated relative radiation–carcinogenic sensitivities of the different tissues and were taken from the 1990 International Commission on Radiological Protection recommendations [13]. Similarly,

$$D_{other} = \sum_T w_T D_T \Big/ \sum_T w_T, \qquad (2)$$

where the summation is over the tissues (T) of the brain, thyroid, bladder, kidney, adrenal gland, spleen, thymus, skin, bone, testes (for men), and uterus and ovaries (for women).

Various authors have suggested that pediatric CT exposures (i.e., milliampere-seconds) could be reduced by 30–50% or more relative to adult exposures to obtain essentially the same information [24–28]. However, most institutions do not reduce the exposure for children or other patients with reduced body weight. For example, Huda et al. [29] measured the correlation between patient weight and applied tube current in patients undergoing thoracic CT examinations and found essentially no correlation ($r = 0.06$), indicating that those CT examination protocols did not take into account the size of the patient. Similar results have been shown for other CT examinations and at other institutions [30, 31]. Thus, in accordance with current standard practice, we have assumed that the exposure technique (milliampere-seconds) is not reduced for a pediatric relative to an adult CT examination. Of course, a given reduction in exposure for a pediatric CT examination would result in a corresponding reduction in dose and thus in risk.

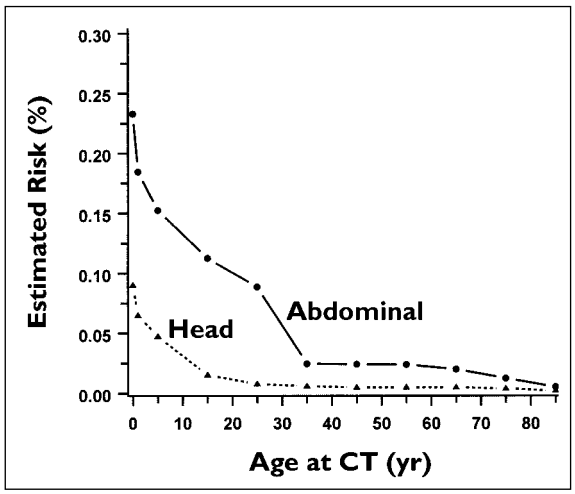

Fig. 6.—Graph shows estimated lifetime attributable cancer mortality risk as a function of age at examination for a single typical CT examination of head (*broken dotted line*) and of abdomen (*broken solid line*). Note rapid increase in risk with decreasing age.

Results

Figure 6 shows the estimated lifetime cancer mortality risk attributable to a single CT

examination performed at different ages. The combination of larger doses and increased lifetime risks in pediatric CT result in a sharp increase in estimated risk relative to adult CT. Results are shown for two of the most common routine CT examinations, CT of the head and CT of the abdomen.

Breakdowns of the estimated lifetime cancer mortality by sex and by site are shown in Figure 7. For head CT examinations, the estimated "other cancer" mortality category is dominated by brain cancer, with a small contribution (≈10%) from thyroid cancer. For abdominal CT examinations, the risks are dominated by digestive organ cancer, primarily stomach, liver, and colon cancer. Overall, the estimated risks for abdominal CT examinations are significantly greater than those for head examinations, primarily because of the larger combined lifetime mortality risks (per unit dose) for exposure of the digestive organs relative to exposure of the brain and thyroid.

Estimated lifetime cancer mortality risks from abdominal CT examinations are somewhat greater for women than for men, an effect that is caused by the significantly greater estimated risks per unit dose for digestive organ cancer in women (Fig. 4). The sex effect for head examinations is smaller because estimated brain tumor risks do not vary greatly with sex. The estimated risk for abdominal CT examinations decreases much more slowly with increasing age at examination than does the risk from head examinations, an effect caused by the near constancy of the estimated lifetime risk (per unit dose) for digestive organ cancer from birth to approximately 25 years old.

To generate an estimate of the absolute numbers of cancer deaths attributable to CT examinations, we first applied the 1995 United States rate of CT examinations (91/1000 population per year) to the current United States population; second, we subdivided this rate, assuming that 40% of CT examinations are of the head and 20% are abdominal [32]; third, we further subdivided this rate into 5-year age-

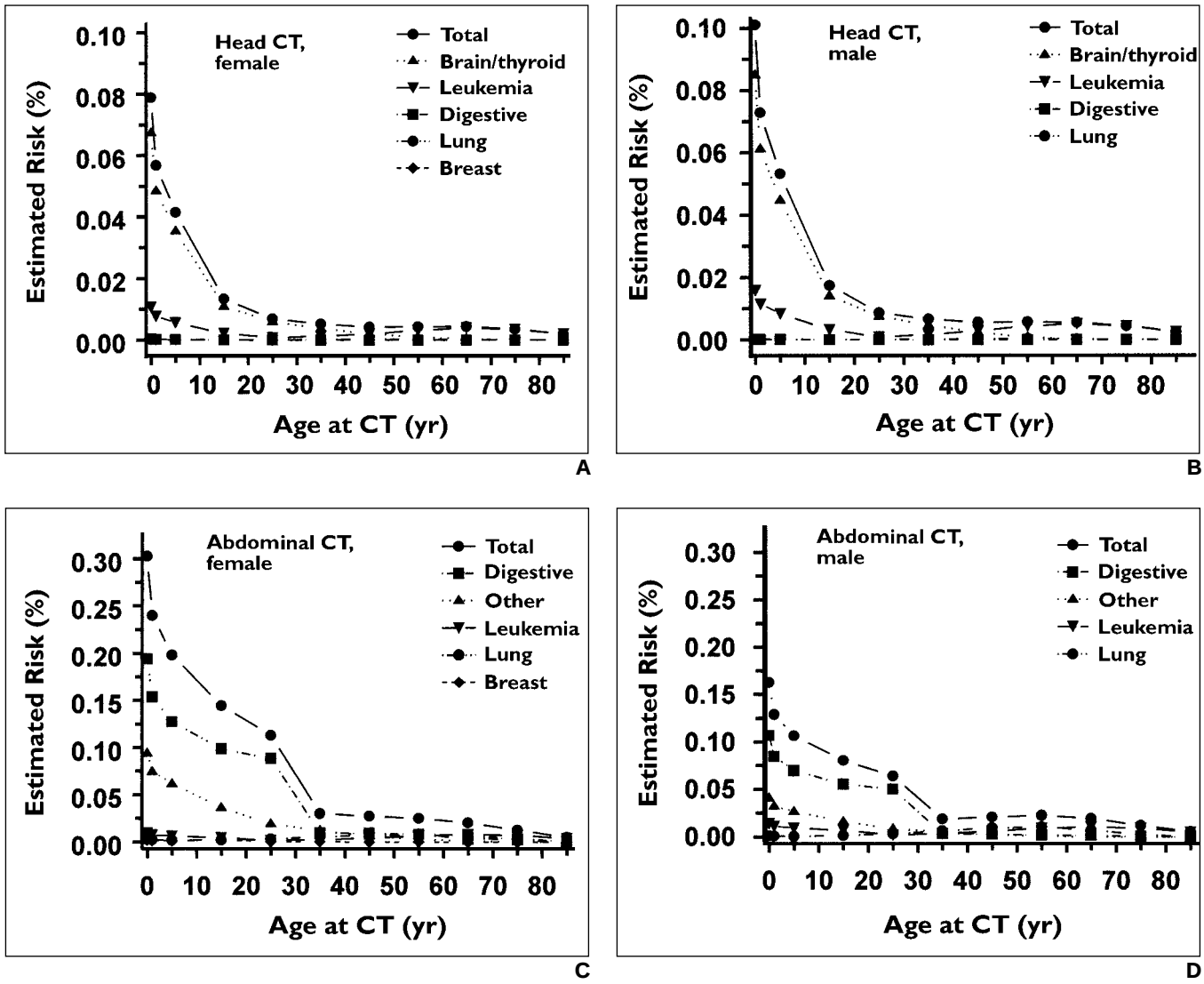

Fig. 7.—Breakdown by cancer type of estimated lifetime CT-attributable cancer mortality risks as a function of age.
A–D, Graphs show breakdown by cancer type of estimated lifetime attributable cancer mortality risks in females and males as a function of age at CT examination for a typical single CT examination of head (**A**, **B**) and of abdomen (**C**, **D**). Note different scales for head and for abdominal data. For all sites, risk rapidly increases with decreasing age.

at-examination intervals, assuming the age distribution for CT examinations from the 1989 British survey [5]; and finally, we applied lifetime mortality risks as a function of age at CT, as calculated here.

On the basis of these assumptions, the predicted total number of deaths attributable to 1 (current) year of CT examinations in the United States is approximately 700 from head examinations and approximately 1800 from abdominal examinations, of which approximately 170 and 310, respectively, would be attributable to head and abdominal CT examinations in individuals who were less than 15 years at the time of examination. In both cases, childhood CT examinations contribute significantly to the overall estimated CT-related potential cancer mortality. For example, although CT examinations of patients less than 15 years old contribute only approximately 4% by number, based on our calculations they are estimated to contribute approximately 20% of the total potential cancer mortality from CT examinations.

Again, the doses and risks estimated here depend roughly linearly on the exposure settings assumed. The survey data [16] from which the doses were estimated yielded average exposure settings of 462 mAs for routine head and 404 mAs for routine abdominal CT and, as discussed previously, these values have been used both for adults and for children. Results for any other exposure settings can be simply scaled from these numbers, so that, for example, if the milliampere-second settings were reduced by 40% for pediatric examinations, all the corresponding pediatric risk estimates would also be reduced by 40%.

Discussion

On the basis of the standard models applied here, the lifetime cancer mortality risks attributable to radiation from a pediatric CT examination are estimated to be considerably higher than for adults. For example, a best estimate of the lifetime cancer mortality risk attributable to the radiation exposure from a single abdominal CT examination in a 1-year-old child is approximately one in 550, and approximately one in 1500 for a head CT examination. These estimated risks are an order of magnitude higher than risks for adults. In the United States, at least 600,000 abdominal and head CT examinations per year are currently performed on children less than 15 years old and, of these individuals, a rough estimate is that approximately 500 will ultimately die from a cancer attributable to the radiation from the CT.

For the two routine CT examinations considered here—abdominal and head—the dominant predicted induced malignancies are, respectively, of the digestive organs and of the brain. Although the brain was once considered a comparatively radioresistant organ, more recent data suggest that it is significantly radiosensitive, particularly at very low doses, with the risk increasing with decreasing age [33]. The risk estimates given here are for lifetime cancer mortality; estimated cancer risks from pediatric CT examinations would, by definition, be larger, particularly for CT examinations of the head, because of the larger contribution of radiation-induced thyroid cancer [34].

Although the absolute estimated risks that we have projected are quite high, the percentage increase in the cancer mortality rate over the natural background rate is very low. For example, of the approximately 600,000 children less than 15 years old who are estimated to undergo CT each year in the United States, approximately 140,000 will ultimately die of cancer. Thus, the estimated projected 500 CT-related deaths represents a small (≈0.35%) percentage increase over this background. This small estimated relative risk suggests that detection of an increased risk in an epidemiologic study would not be easy, although a recent case-control study [35] on the association between pediatric radiologic examination and childhood leukemia did show a significant elevated risk (linearly related to the number of examinations) compared with controls in children who received two or more diagnostic examinations (odds ratio, 1.6; confidence interval, 1.1–2.3).

The CT-related cancer risk estimates provided here are probably the most credible available, but they must be considered with a number of caveats. The most significant caveats relate to the risks per unit dose assumed here (Figs. 3 and 4) for the comparatively low doses (Fig. 5) of relevance to a single CT examination. The assumed risk estimates are ultimately derived from analyses of mortality data based on Japanese atomic bomb survivors [11] exposed to intermediate radiation doses. As illustrated in Figure 8, the atomic bomb data provide strong evidence of an increased cancer mortality risk at equivalent doses greater than 100 mSv, good evidence of an increased risk for doses between 50 and 100 mSv, and reasonable evidence for an increased risk for doses between 10 and 50 mSv [11].

Some supporting evidence for the risk estimates adopted here at doses of relevance to pediatric CT examinations (Fig. 5) comes from studies of childhood cancer risks after fetal exposure from diagnostic radiography. In a 1997 review of the data, Doll and Wakeford [36] concluded that doses to the fetus on the order of 10 mSv produce an excess risk of cancer during childhood of roughly 6% per sievert, which would be consistent with the lifetime cancer mortality risks of 14% per sievert used here for an exposed neonate (Fig. 3).

The linear extrapolation without a dose threshold that is used to extrapolate cancer risks to very low doses has been the subject of much debate [37–40]; however, the main regulatory and advisory groups that have reported on this issue [12, 13, 41, 42] have all concluded that the most scientifically credible approach to risk extrapolation to this dose range is a linear extrapolation from greater doses, which is the assumption implicitly adopted here.

Aside from the correct shape of the dose–risk relationship at low doses, there are further uncertainties in the absolute magnitude of the risks per unit dose shown in Figures 3 and 4, originating in such issues as dosimet-

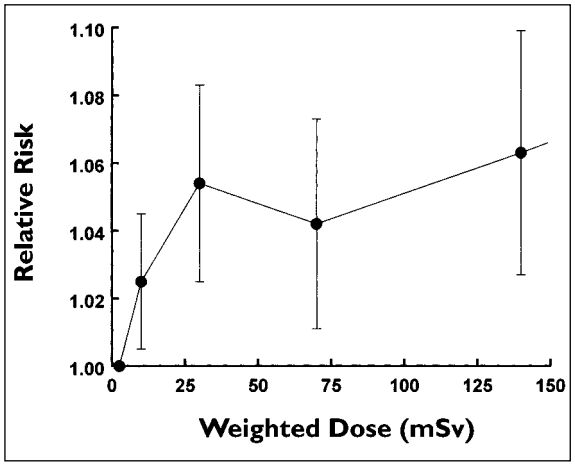

Fig. 8.—Graph shows estimated relative risk and standard errors for solid cancer mortality among Japanese atomic bomb survivors of all ages [11]. Only very low-dose data points are shown. At doses of relevance to CT examinations, these data do not suggest any threshold in dose below which no excess risk exists.

ric uncertainties and risk transfer from Japanese to Western populations. An analysis by Sinclair [43] suggested an overall uncertainty in the low–dose total cancer mortality risk estimates (per unit dose) of approximately a factor of 2 (although the uncertainties in cancer risks for individual organs or groups of organs may be larger than this).

The organ dose estimates used in our work also have significant uncertainties attached to them, although these would be expected to be smaller than the uncertainties in the risks per unit dose. Of more importance here are systematic changes in clinical practice, particularly the potential for dose reduction in pediatric CT examinations. Specifically, in line with the standard clinical practice [29–31], we have assumed that the same milliampere-second techniques are used for pediatric examinations as for the corresponding adult CT examinations. Several studies have suggested that a technique with significant reduction in exposure (milliampere-seconds) could be adopted for pediatric CT examinations without significant loss of information [25–28], and any such reduction would yield a corresponding reduction in dose and in risk.

In summary, the following argument suggests that CT exposure settings should be actively reduced when used in a pediatric setting: First, the frequency of pediatric CT examinations is rapidly increasing, largely because of the improved logistics of helical CT. Second, the best available risk estimates suggest that pediatric CT will likely result in significantly increased lifetime risk over adult CT, both because of the increased dose per milliampere-second and because of the increased lifetime risk per unit dose. Third, lower milliampere-second settings can be used for CT examinations of children without significant loss of information.

Specifically, the dose delivered in most pediatric CT examinations could potentially be reduced by reducing the milliampere-seconds either manually [25–28] or automatically [44] and by increasing the pitch [45]. Various authors [24–28] have suggested that pediatric CT exposures (i.e., milliampere-seconds) could be reduced by at least 30–50% relative to adult exposures to obtain essentially the same information; such reductions would result in a corresponding decrease in radiation risks (whatever they might be) by the same factors.

Of course, in most situations in which pediatric CT is used, the risk–benefit balance is strongly tilted toward benefit [7], which may explain why reduced exposure settings are not routinely used for pediatric CT [29–31]. We hope that pointing out that lifetime radiation risks for children undergoing CT are quantitatively not negligible will encourage more active reduction of CT exposure settings in the pediatric context. Both CT equipment manufacturers and pediatric radiologists could contribute to this end.

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