Radiology

ORIGINAL RESEARCH ■ MEDICAL PHYSICS

Impact of Reduced Patient Life Expectancy on Potential Cancer Risks from Radiologic Imaging[1]

David J. Brenner, PhD, DSc
Igor Shuryak, MD, PhD
Andrew J. Einstein, MD, PhD

Purpose: To quantify the effect of reduced life expectancy on cancer risk by comparing estimated lifetime risks of lung cancer attributable to radiation from commonly used computed tomographic (CT) examinations in patients with and those without cancer or cardiac disease.

Materials and Methods: With the use of clinically determined life tables, reductions in radiation-attributable lung cancer risks were estimated for coronary CT angiographic examinations in patients with multivessel coronary artery disease who underwent coronary artery bypass graft (CABG) surgery and for surveillance CT examinations in patients treated for colon cancer. Statistical uncertainties were estimated for the risk ratios in patients who underwent CABG surgery and patients with colon cancer versus the general population.

Results: Patients with decreased life expectancy had decreased radiation-associated cancer risks. For example, for a 70-year-old patient with colon cancer, the estimated reduction in lifetime radiation-associated lung cancer risk was approximately 92% for stage IV disease, versus 8% for stage 0 or I disease. For a patient who had been treated with CABG surgery, the estimated reduction in lifetime radiation-associated lung cancer risk was approximately 57% for a 55-year-old patient, versus 12% for a 75-year-old patient.

Conclusion: The importance of radiation exposure in determining optimal imaging usage is much reduced for patients with markedly reduced life expectancies: Imaging justification and optimization criteria for patients with substantially reduced life expectancies should not necessarily be the same as for those with normal life expectancies.

[1] From the Center for Radiological Research (D.J.B., I.S.) and Departments of Medicine and Radiology (A.J.E.), College of Physicians and Surgeons, Columbia University Medical Center, 630 W 168th St, VC-11-235, New York, NY 10032. Received December 15, 2010; revision requested February 7, 2011; revision received March 16; accepted April 1; final version accepted May 17. **Address correspondence to** D.J.B. (e-mail: *djb3@columbia.edu*).

There has been much concern regarding the potential cancer risks associated with the recent rapid increase in the utilization of radiologic imaging, particularly with regard to higher-dose radiologic protocols such as computed tomography (CT) (1–7). To determine which radiologic imaging procedures are optimal in a given situation, it is useful to have best estimates of the lifetime risks potentially associated with the radiation exposures (8).

The potential public health importance of radiation exposures of the population from CT examinations, which are being performed with increasing frequency, is being recognized, and direct epidemiologic studies of their risks are now beginning (9). Current risk estimates are based largely on data from atomic bomb survivors who were exposed to low radiation doses. There are a number of uncertainties associated with applying these risk estimates to a Western population that have been discussed elsewhere (10). However, one of the largest potential sources of bias for medical imaging risk estimation has been less discussed: That is, that radiation risk estimates are derived almost entirely from studies of general populations exposed to low doses of radiation (ie, individuals with a normal life expectancy). By contrast, given the long latency period (typically 1 or more decades) between radiation exposure and most radiation-associated cancers, if the life expectancy of a patient is lower than average because they have a disease or injury, a lower lifetime radiation-associated risk would be expected because there would be less time available for a radiation-induced cancer to appear (11,12).

Of course, for many scenarios where CT is commonly used, such as mild head trauma (13,14) and the diagnosis of appendicitis (15,16), as well as for CT screening of asymptomatic individuals (17–19), one would not expect the patient to have substantially reduced life expectancy. On the other hand, there are common imaging scenarios, such as those for individuals with cancer (20) or coronary heart disease (21–25), where the life expectancy of the imaged individuals is substantially lower than that of the general population, and so reduced radiation risks would be expected. Thus, the purpose of our study was to quantify the effect of reduced life expectancy on cancer risk by comparing estimated lifetime risks of lung cancer attributable to radiation from commonly used CT examinations in patients with and those without cancer or cardiac disease.

Advances in Knowledge

- Patients with decreased life expectancy have decreased radiation-associated cancer risks (eg, for a 70-year-old patient with colon cancer, the estimated reduction in lifetime radiation-associated lung cancer risk was approximately 92% for stage IV disease, versus 8% for stage 0 or I disease).
- The importance of radiation exposure in determining optimal imaging usage is much reduced in patients with markedly reduced life expectancies.

Materials and Methods

We compared radiation-related lifetime lung cancer risks from commonly used CT examinations in patients with cancer or cardiac disease with estimated radiation risks for the same CT examinations in individuals without such diseases so that we could quantify the effect of reduced life expectancy on these risks. To cover a wide range of reduced life expectancies, we considered patients with different stages of a given cancer type, as well as patients with coronary artery disease at a wide range of ages. In both cases, we chose to make risk estimates of radiation-induced lung cancer, because lung cancer represents the largest radiation-induced cancer risk for the cases studied (26).

Specifically, we estimated radiation-induced lung cancer risks associated with *(a)* follow-up surveillance chest and abdominal CT examinations in patients who were treated for different stages of colon cancer (27,28) and *(b)* coronary CT angiographic examinations in patients of different ages with multivessel coronary artery disease who had undergone coronary artery bypass graft (CABG) surgery (29–31).

For patients undergoing surveillance after treatment for colon cancer, current guidelines recommend annual chest and abdominal CT examinations for 3 years after treatment (28). For patients after CABG surgery, results of several recent studies (29,31) have demonstrated that coronary CT angiography has both high sensitivity and high specificity for the detection of obstructive coronary disease.

Implication for Patient Care

- Imaging justification and optimization criteria for patients with substantially reduced life expectancies should not necessarily be the same as for those with normal life expectancies.

Data Sets Used

The information needed for comparison of the estimated lifetime radiation risks for CT examinations for these patients, relative to the risks for the same CT examinations in individuals with normal life spans, is as follows: *(a)* life tables (age-specific mortality data) for the two scenarios being considered (after treatment for colon cancer or after CABG surgery)

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Abbreviations:
BEIR = Biological Effects of Ionizing Radiation
CABG = coronary artery bypass graft
EAR = excess absolute risk
ERR = excess relative risk
SEER = Surveillance, Epidemiology, and End Results

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See also the editorial by Amis in this issue.

and for the corresponding healthy population, *(b)* the excess relative risk (ERR) per unit dose for radiation-induced lung cancer, and *(c)* the background lung cancer rate for the population.

For patients with colon cancer undergoing surveillance after treatment, we used relative survival data in a population of 129000 patients with colon cancer in the 1998–2001 Surveillance, Epidemiology, and End Results (SEER) database (32), stratified by time since diagnosis, cancer stage, and sex, together with sex-specific U.S. life tables for the year 2000 (33). For patients who had undergone CABG surgery, we used long-term survival data after CABG surgery, stratified by age at surgery and time after surgery, in more than 20000 patients who underwent CABG surgery from 1968 through 2003 in Portland, Oregon (34). Corresponding calendar year–specific life tables for the general population in Oregon were obtained from state-specific U.S. life tables (35).

Method for Estimating Reduction in Lifetime Radiation Risks

Our goal here was to estimate the ratio of lifetime lung cancer risks after radiologic examination in an individual with a normal life expectancy versus the estimated risk in the same individual with a disease-related reduced life expectancy.

The sex-averaged survival probability for a patient with colon cancer (32) or after CABG surgery (34) treated at age X as a function of time after treatment (T) is here denoted as $S_{\text{pat}}(X,T)$ (where "pat" indicates "patient"). The survival probability conditional on surviving to the age of treatment is $S_{\text{con,pat}} = S_{\text{pat}}(X,T)/S_{\text{pat}}(X,0)$, where $S_{pat}(X,0)$ is the patient survival probability immediately after treatment. Likewise, the survival probabilities for male and female individuals in the general population were obtained from U.S. life tables (33,35) and are denoted $S_{\text{norm},g}$, where g denotes sex (g = M and F for male and female individuals, respectively). Conditional survival probabilities of reaching age A having been alive at age X were calculated as $S_{\text{con,norm},g} = S_{\text{norm},g}(A)/S_{\text{norm},g}(X)$. The background lung cancer incidence rates for U.S. male and female individuals since 1973, denoted $I_g(A)$, were obtained from the SEER database (36,37).

To estimate the ratios of radiation risks, we followed the method in the recent Biological Effects of Ionizing Radiation (BEIR) VII National Academies report (38), which provides descriptive equations for the ERRs and excess absolute risks (EARs) at age A for radiation-induced lung cancer in individuals exposed to lung dose D at age X. These risks are denoted by $\text{ERR}_g(X,A,D)$ and $\text{EAR}_g(X,A,D)$.

The radiation risk estimates, as derived in BEIR VII, are based mainly, though not exclusively, on data in Japanese atomic bomb survivors exposed to low radiation doses. Because background incidence rates for some cancers differ substantially between Japan and Western countries, direct application of Japanese ERRs or EARs to Western populations is not considered optimal, and BEIR VII recommends transferring a weighted average of Japanese ERRs (method 1) and EARs (method 2) to a Western population, assigning weighting factors of W_{ERR} and W_{EAR} (ie, = 1 – W_{ERR}), respectively.

The sex-specific radiation-induced EAR for a patient at age A, as estimated by using method 1 (ie, based on ERRs), is the product of three terms: the excess relative risk $\text{ERR}_g(X,A,D)$, the background risk $I_g(A)$, and the survival probability $S_{con,pat}(X,A)$. It is described by Equation (1):

$$\text{EAR}_{\text{pat } g \text{ method1}} = \text{ERR}_g(X,A,D)\, I_g(A)\, S_{\text{con,pat}}(X,A). \quad (1)$$

Thus, the lifetime (up to age 100 years) EAR estimated by using method 1 for the entire patient population, consisting of both sexes, is as follows:

$$\text{EAR}_{\text{lifetime, pat, method1}} = \int_X^{100} [P_{\text{F}}\, EAR_{\text{pat, F, method1}} + P_{\text{M}}\, \text{EAR}_{\text{pat, M, method1}}]\, \text{d}A, \quad (2)$$

where the proportion of female individuals, P_{F} (ie, $1 - P_{\text{M}}$) in the patient populations was 0.24 for the post–CABG surgery population studied by Gao et al (34) and 0.51 in the post–colon cancer SEER cohort (32).

For method 2, where EAR rather than ERR transfer is used, the expression $\text{ERR}_g(X,A,D)\ I_g(A)\ S_{\text{con,pat}}(X,A)$ is replaced by $\text{EAR}_g(X,A,D)\ S_{\text{con,pat}}(X,A)$. The corresponding radiation-induced EAR for a patient at age A, as estimated by using method 2 (ie, based on EARs) is therefore:

$$\text{EAR}_{\text{lifetime, pat, method2}} = \int_X^{100} [P_{\text{F}}\ \text{EAR}_{\text{F}}\ (X,A,D)\, S_{\text{con, pat}}(X,A) + P_{\text{M}}\text{EAR}_{\text{M}}(X,A,D) S_{\text{con, pat}}(X,A)]\ \text{d}A. \quad (3)$$

Combining the ERR and EAR transfer methods (methods 1 and 2), the following equation describes the lifetime radiation-associated EAR for the patient population:

$$\text{EAR}_{\text{life, pat}} = W_{\text{ERR}}\ \text{EAR}_{\text{lifetime, pat, method1}} + W_{\text{EAR}}\ \text{EAR}_{\text{lifetime, pat, method2}}. \quad (4)$$

For radiation-induced lung cancer, W_{ERR} = 0.3. That is, the transfer of the ERR has a weighting of 30%, and the transfer of the EAR likewise has a weighting of 70% (38).

The expected lifetime EAR for an individual with normal life expectancy, $\text{EAR}_{\text{life, norm}}$, is calculated the same way as for the patients, again by using a weighted average of methods 1 and 2 but substituting the appropriate survival function $S_{\text{con, norm, } g}$ in place of $S_{\text{con, pat}}$.

Finally, the required ratio of the lifetime radiation risks in the patient population versus that in the normal-life-span population is simply:

$$R_{\text{risk reduction}} = \text{EAR}_{\text{life, pat}}/\text{EAR}_{\text{life, norm}}. \quad (5)$$

It should be noted that the National Academies' BEIR VII report recommends a dose and/or dose rate effectiveness factor that modifies the estimated low-dose radiation risks, but this factor cancels out of our final risk ratio. It is also the case that the radiation dose D cancels out of this final risk ratio, so we do not need here to estimate lung doses for the CT examinations.

The uncertainties in the estimated risk reduction ratio are mainly due to the relatively small uncertainties in survival functions (life expectancies) of the patient and normal-life-expectancy populations, $S_{con,pat}$ and $S_{con,norm,g}$; the estimated risk reduction ratios are much less sensitive to the larger uncertainties associated with $ERR_g(X,A,D)$ and $EAR_g(X,A,D)$, which essentially cancel out of the ratios, or to variations in smoking patterns. The uncertainties in the risk ratio $R_{risk\ reduction}$ were estimated on the basis of the number of patients in the analyzed data sets and with the assumption that the errors were normally distributed. The 95% confidence intervals for $R_{risk\ reduction}$ were estimated as follows: $R_{risk\ reduction} \pm 1.96\ R_{risk\ reduction}/N^{0.5}$, where N is the number of patients.

Figure 1

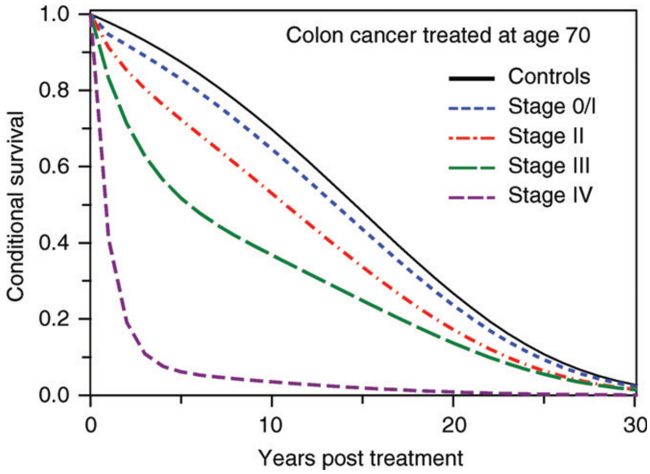

Figure 1: Graph shows comparison of long-term conditional survival functions for patients diagnosed with different stages of colon cancer at age 70 years (the median age for colon cancer diagnosis) and for healthy control subjects. Derived from SEER results reported by Ward et al (32).

Results

Figures 1 and 2 show the conditional survival functions (survival conditional on attaining the starting age) for patients treated for different stages of colon cancer and for patients of different ages after CABG surgery.

Figure 3 shows the ratio of estimated lifetime risks of radiation-induced lung cancer, after surveillance CT examinations, in patients with colon cancer of various stages versus that in individuals with a normal life expectancy (39,40). This ratio is a measure of the decrease in lifetime radiation risk as a result of the reduced life expectancy of the patients with colon cancer. As colon cancer stage increases and life expectancy decreases, the lifetime radiation risk decreases. For example, for a 70-year-old patient with colon cancer, the estimated reduction in lifetime radiation-associated cancer risk was approximately 92% for stage IV disease, versus approximately 8% for stage 0 or I disease.

Correspondingly, Figure 4 shows the ratio of estimated lifetime risks of radiation-induced lung cancer in patients who underwent CABG surgery versus individuals with a normal life expectancy (2). As age at exposure increased, the life expectancy for the two groups converged (Fig 2), and thus the difference in radiation risks decreased. Thus, the estimated reduction in lifetime radiation-associated cancer risk was approximately 57% for a 55-year-old patient, versus only approximately 12% for a 75-year-old patient.

Confidence limits of the ratios shown in Figures 3 and 4 are primarily related to uncertainties in the survival functions for the general population with a normal life span, which are very small, and to uncertainties in the patient survival functions. As an example, the risk ratio at coronary CT angiography for a 65-year-old patient who had undergone CABG surgery is estimated to be 0.58 (Fig 4), with a 95% confidence interval of 0.52, 0.64.

Discussion

Results of numerous previous studies (1,2,5,17–19,23,24,26,41) have demonstrated how lifetime radiation risks from a medical imaging procedure to a typical member of the U.S. population can be estimated by using risk models that incorporate epidemiologic data from atomic bomb survivors and other medically exposed cohorts. Our study expands the applicability of such estimates by providing an approach to quantify the degree to which lifetime radiation risks are likely to be lower in populations with reduced life expectancy. As representative examples, we have considered two radiologic imaging scenarios in patients with a wide range of reduced life expectancies: assessment of graft patency in patients of different ages who have undergone CABG surgery and detection of disease relapse in patients with different stages of colon cancer. In both cases, we compared estimated lifetime lung cancer risks after radiologic examination in an individual with a normal life expectancy versus the estimated risk in the same individual with a disease-related reduced life expectancy. We have chosen here to assess the impact of reduced life expectancy on lung cancer risks because it is the dominant radiation-induced malignancy for the examinations we studied in individuals irradiated in middle age (26), but the general conclusions should be applicable to radiation-induced cancer risks at other sites.

In the examples that we analyzed, for a 70-year-old patient with colon cancer, lifetime lung cancer risks may be drastically reduced by as much as 90% for patients with late stage disease but are comparatively unchanged for patients with early stage disease whose prognosis is good. In the population of patients who had undergone CABG surgery for cardiac disease that we analyzed here, lifetime lung cancer radiation risks may be reduced by a factor of two for younger patients, whose projected life span is much reduced compared with that of a same-age healthy individual. By contrast, older patients who have undergone CABG surgery have essentially the same projected life span as same-age healthy individuals, and thus the estimated lifetime radiation risks are only slightly reduced.

Figure 2

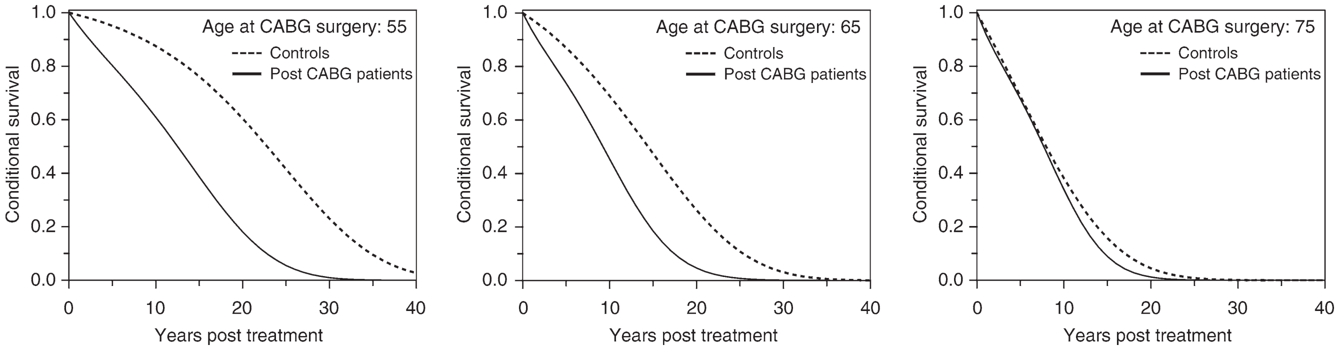

Figure 2: Graphs show comparison of long-term conditional survival functions for patients who had undergone CABG surgery (solid line) and an age-, sex-, and location-matched control population (dashed line). Derived from results reported by Gao et al (34).

Figure 3

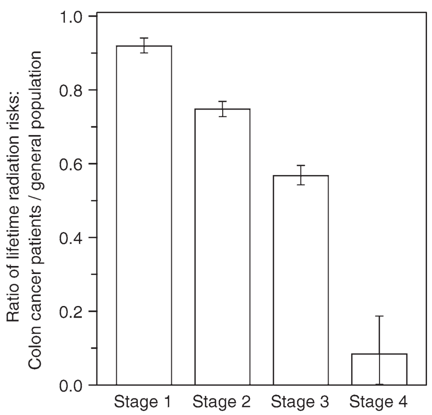

Figure 3: Graph shows ratio, $R_{\text{risk reduction}}$, of predicted lifetime risk for radiation-induced lung cancer due to posttreatment surveillance CT examinations in patients with various stages of colon cancer (mean age at exposure, 70 years) relative to the corresponding lifetime risk of radiation-induced lung cancer in individuals with a normal life span who undergo the same CT examinations. Error bars show 95% confidence intervals for the estimated ratios.

Figure 4

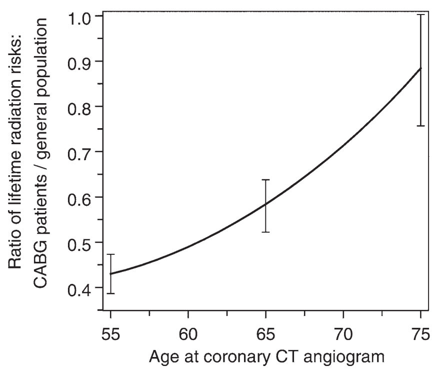

Figure 4: Graph shows ratio, $R_{\text{risk reduction}}$, of predicted lifetime radiation-induced lung cancer risks for a coronary CT angiographic examination in patients who had undergone CABG surgery relative to the lifetime risks for the same CT examination in an age-, sex-, and location-matched normal–life span population. Error bars show 95% confidence intervals for the estimated ratios.

There are clearly other radiologic imaging situations where there will be marked reductions in lifetime radiation risk as a result of decreased life expectancy, such as imaging in patients with congestive heart failure (42) or stroke (43) and in a variety of oncologic scenarios such as cancer of the lung and brain (20). Correspondingly, there are many radiologic imaging scenarios where life expectancy is good, and thus any reduction in lifetime radiation risk will be minimal relative to risk in the general population; examples are early stage breast and prostate cancers and mild head trauma, the diagnosis of appendicitis, and CT screening of asymptomatic individuals.

Limitations of our study included the following: Radiation-induced lung cancer risk per unit dose was quantified by empirical expressions derived from the BEIR VII report, which are driven mainly by analysis of data in Japanese atomic bomb survivors. These risk estimates were then transferred to a Western population, also by using an empirical approach recommended by BEIR VII. This method is the best available to date but should be regarded as only a rough approximation in modeling the processes involved in lung carcinogenesis. In addition, the effects of lifestyle factors such as tobacco smoking, which are known to have a high impact on both background and radiation-induced lung cancer risk, as well as on overall life expectancy, are beyond the scope of this analysis.

We conclude, and have quantified, that reduced life expectancy is an important factor in determining the potential radiation-associated lifetime risk associated with radiologic examinations and thus should play a substantial role in assessing the justification and optimization of these examinations. Estimates of radiation risks in reduced-life-expectancy scenarios that do not take this into account may well result in unrealistically large risk estimates (41). It follows that imaging justification and optimization criteria for patients with substantially reduced life expectancies should not necessarily be the same as for those with normal life expectancies.

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