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Lessons we have learned from our children: cancer risks from diagnostic radiology

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Abstract The A-bomb survivors represent the best source of data for risk estimates of radiation-induced cancer. It is clear that children are ten times more sensitive than adults to the induction of cancer. The introduction of helical CT has transformed diagnostic radiology, especially in pediatric patients. The undoubted benefits carry the price tag of much higher doses, and in children, even higher effective doses. The A-bomb data have "matured" and we now have cancer risk estimates for a dose range which coincides with the organ doses from pediatric CT. Individuals exposed 50 years ago to doses comparable to those associated with helical CT today, show a small but statistically significant excess incidence of cancer. There are no assumptions, and no extrapolations involved. An abdominal helical CT scan in a young girl results in a risk of fatal cancer later in life that amounts to about one in a thousand. The risk to the individual is small, and readily balanced by the medical benefits. The public health problem is, however, significant when the small individual risk is multiplied by the 2.7 million of such procedures performed annually. Every effort is needed to minimize doses by an appropriate choice of peak kilovoltage (kVp) and milliampere-seconds (mAs), and at the same time to urge a more selective use of pediatric CT.

Keywords Helical CT · Cancer risks · A-bomb survivors · Risk vs benefit

Edward B.D. Neuhauser, 1908–1987

I am greatly honored to give the Neuhauser lecture, established in the name of Edward Neuhauser, the first president of the Society of Pediatric Radiology (Fig. 1). When Dr. Neuhauser became director of the Department of Radiology at the Children's Hospital in Boston in 1941, there began a period of great excitement; in company with Dr. John Caffey at Babies Hospital in New York, and a growing band of associates in the US and abroad, he established pediatric radiology as a scientific discipline. Figure 2 reproduces a painting in the Children's Hospital in Boston, showing Dr. Neuhauser doing what he enjoyed most, namely, teaching residents. Looking at his impressive bibliography, I see a paper from 1952 in which he described unusual benign and malignant tumors resulting from childhood radiotherapy. I like to imagine that he would have been most interested in the subject of my talk today.

The early days

The development of radiology, from the discovery of x-rays in the laboratory to the implementation of their use for diagnosis in medical practice, is one of the most rapid and remarkable examples of translational research.

Within a few years of their discovery in 1895, the enormous and obvious benefit of x-rays to society had been recognized. However, before long, it was realized that there was a downside to the "new kind of ray."

Fig. 1. Edward B.D. Neuhauser, 1908–1987. First president of the Society of Pediatric Radiology. (Courtesy of Dr. Walter Berdon)

As the nineteenth century turned into the twentieth, it became clear that some of the early radiation workers had suffered skin damage and loss of fingers, and at the same time, the first cases of leukemia were reported [1].

Radiation protection

At the Second International Congress of Radiology in Stockholm in 1928, member countries were invited to send representatives to prepare x-ray protection recommendations. The British recommendations were adopted because they were most complete: guidelines on radiation protection had been set up in that country as early as 1915 [1].

The 1928 congress set up the International Committee on X-ray and Radium Protection, which after World War II was remodeled into two commissions that survive to this day:

- The International Commission on Radiological Protection (ICRP)
- The International Commission on Radiological Units and Measurements (ICRU)

The establishment of these international commissions and the national bodies that were to follow represent a watershed in the development of radiology. From this time on, radiation doses were controlled, so that the deleterious effects of radiation do not stand out as obvious in either patients or in staff occupationally exposed. No longer were deterministic effects, such as

Fig. 2. A painting of Dr. Neuhauser in the Radiology Department of the Children's Hospital in Boston. (Courtesy of Dr. Walter Berdon)

erythema, fibrosis, or necrosis seen in staff or (except in exceptional circumstances involving interventional radiology) in patients. At the same time, any small increment in cancer incidence caused by radiation was not readily apparent against the high spontaneous level. This does not mean that there were no deleterious effects, just that they were not obvious or evident against the high spontaneous level. This brings us to the study of the A-bomb survivors.

The A-bomb survivors

The devastation caused by the heat and blast of the A-bombs dropped on Hiroshima and Nagasaki caused over 100,000 casualties and brought about the surrender of Japan and the end of World War II. It also left a large population of over 100,000 that were exposed to a range of radiation doses, and who lived in a devastated country with a military government that made it possible to organize and set up a careful study of these irradiated survivors. Overseen by the U.S. National Academy of Sciences, this study has continued for over 55 years, at a cost to the taxpayer of hundreds of millions of dollars. No population of individuals medically exposed has ever been subject to such an intense scrutiny, and probably never will. A number of important conclusions can be drawn from this study [2, 3].

Radiation-induced cancers tend to appear at the same age as spontaneous cancers of the same type. For this reason it takes half a century or more to judge the impact of radiation exposure, especially when the exposed individuals include children.

1. Exposure to radiation results in an excess incidence of leukemia and a whole spectrum of solid cancers, such as breast, digestive organs, colon, thyroid, and lung – i.e., all of the "lining" cells of the body.
2. To see an excess incidence of radiation-induced cancers, over and above the high natural incidence, requires that a large population be studied, with an equally large and relevant control population, and that the study be continued for at least 50 years. When this is done, the risk of radiation-induced cancer following an acute dose of 1 Sv (1 Gy of x-rays) to a general population is about 10%; if the dose is spread out over a period of time at low dose-rate, or in a series of fractions, the risk is estimated to be halved, at about 5% [4].
3. The above risk estimate is an average for a population comprised of all ages. Now that the data have matured, and individuals exposed at young ages have reached the cancer-prone years, it is apparent that the risk varies dramatically with age [4]. For individuals in the first decade of life, the risk is closer to 15%/Sv, while for adults in late middle age, the risk drops to 1% or 2%/Sv. There is also a clear gender difference, especially at early ages, with girls more radiosensitive than boys (see Fig. 3).
4. The risk of solid cancers appears to be a linear function of dose. Until a few years ago, the data were good down to a dose of about 20 rad; below this, risks were uncertain. More recently, a careful study has been completed of the 35,000 survivors who were exposed to lower doses, and risk estimates are now good down to about 5 rad [5].

Radiology: the past

Table 1 summarizes the organ doses associated with a variety of radiological procedures [6,7]. For the majority of procedures involving plain films, organ doses are a fraction of 1 rad, although there are a few procedures, such as an upper gastrointestinal series, where some organs receive a higher dose than this. However, this is in contrast to the doses involved in helical CT, that are in general an order of magnitude higher.

During the era before the advent of CT, the lowest dose at which cancer risk estimates were available from the Japanese survivors was about 20 rad; estimates below this required an extrapolation and an assumption of a model of some kind (see Fig. 4). Cancer risks were available at high doses, while radiology (plain film) was associated with low doses. Cancer risk estimates for radiology were therefore "theoretical" inasmuch as an extrapolation was needed from high to low

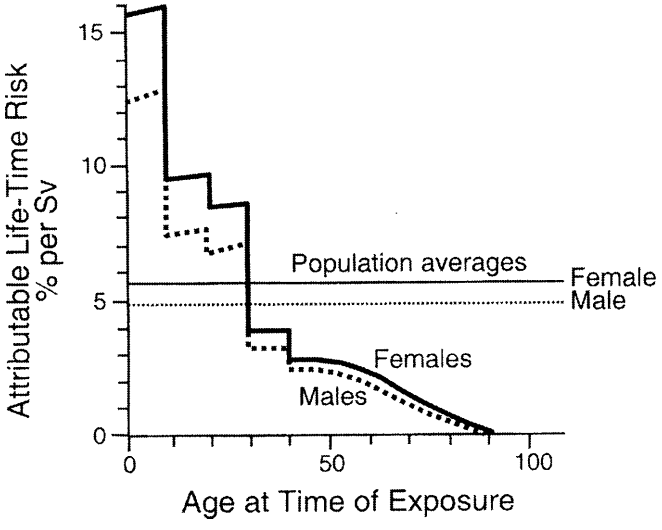

Fig. 3. The attributable lifetime risk from a single small dose of radiation at various ages at the time of exposure. Note the dramatic decrease in radiosensitivity with age. The higher risk for the younger age groups is not expressed until late in life. These estimates are based on a multiplicative model and on a dose and dose-rate effectiveness factor (DDREF) of two. (Adapted from [4])

Table 1. Organ doses from radiographic studies in adults (*N*, no estimate made)

Examination and view	Dose (mrad)					
	Active bone marrow	Thyroid	Breast	Lungs	Ovaries	Testes
Chest						
PA	(2)	(1)	(1)	(7)	N	N
Lateral	(2)	(7)	(15)	(12)	N	N
Skull						
AP	(8)	(6)	–	N	N	N
Lateral	(5)	(21)	–	N	N	N
Cervical spine						
AP	(2)	(100)	–	(2)	N	N
Lateral	(2)	(6)	–	(2)	N	N
Thoracic spine						
AP	(5)	(25)	(95)	(35)	N	N
Lateral	(12)	(5)	(5)	(75)	N	N
Lumbar spine						
AP	(18)	N	–	(40)	(110)	(2)
Lateral	(44)	N	–	(30)	(90)	(2)
Urography						
KUB (AP)	(20)	N	–	(7)	(130)	(10)
Mammography		–	(360)			
Upper gastrointestinal series	(300)	(3)	(50)	(100)	(1,200)	(80)
Barium enema series	(520)	N	–			
Helical CT	Organ doses up to 13,000 mrad					

doses and an assumption was necessary concerning the shape of the dose–response relationship. All this has now changed.

Radiology: the present

Developments in radiological equipment led to the introduction of the helical CT scan. This represents remarkable progress and opens up a new chapter in diagnostic possibilities; however, the benefit comes with the price of much larger radiation doses. CT is a high-dose procedure. Table 2 contrasts effective doses for chest x-rays with an abdominal CT scan, data taken from various publications of The National Radiological Protection Board in the UK [7, 8, 9]. The bottom line is that one abdominal CT scan involves an effective dose equal to 500 chest radiographs and is equivalent to the average national background radiation received over a period of more than 3 years.

The contrast in effective dose between conventional radiology and helical CT is illustrated more graphically in Fig. 5. It should be noted that effective dose is the product of absorbed dose and a tissue weighting factor (W_T) which allows for tissue and organ differences in their susceptibility to cancer (ICRP 60) (see Table 3). At the same time, risk estimates have become available for a lower dose range [5]. The 35,000 A-bomb survivors who received doses lower than 0.25 Sv have been carefully studied. The results are shown in Fig. 6. This is a small but statistically significant excess incidence of cancer at doses down to 50 mSv. This overlaps the organ doses involved in helical CT. In summary, radiation-induced cancer risk estimates are now available from individuals exposed over 50 years ago to doses comparable to those currently involved in

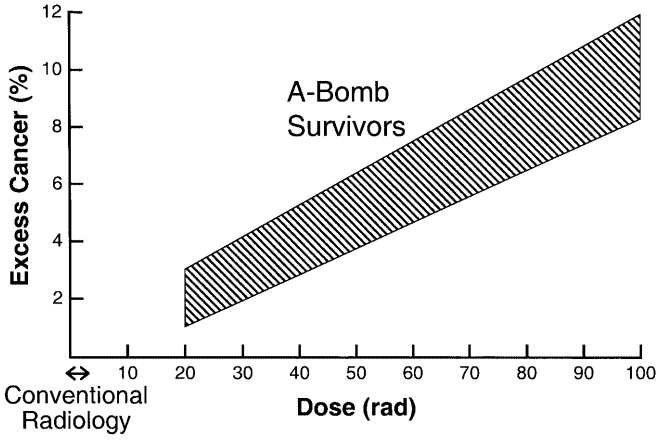

Fig. 4. In the past (the 1980s, for example), radiation-related cancer risks were known from the A-bomb survivors for doses in excess of about 20 rad (0.2 Gy), while organ doses from conventional radiology with plain films were typically of the order of 1 or 2 rad. Consequently, estimating the cancer risks from radiology involved an extrapolation from high to low doses, so that a model or shape of the dose–response relationship had to be assumed

Table 2. CT is a high-dose procedure

Procedure	Effective dose in Sv	Chest surveys equivalent (*n*)	Equivalent background radiation time
Chest PA	0.02	1	2.4 days
Chest CT	8	400	2.7 years
Abdomen CT	10	500	3.3 years

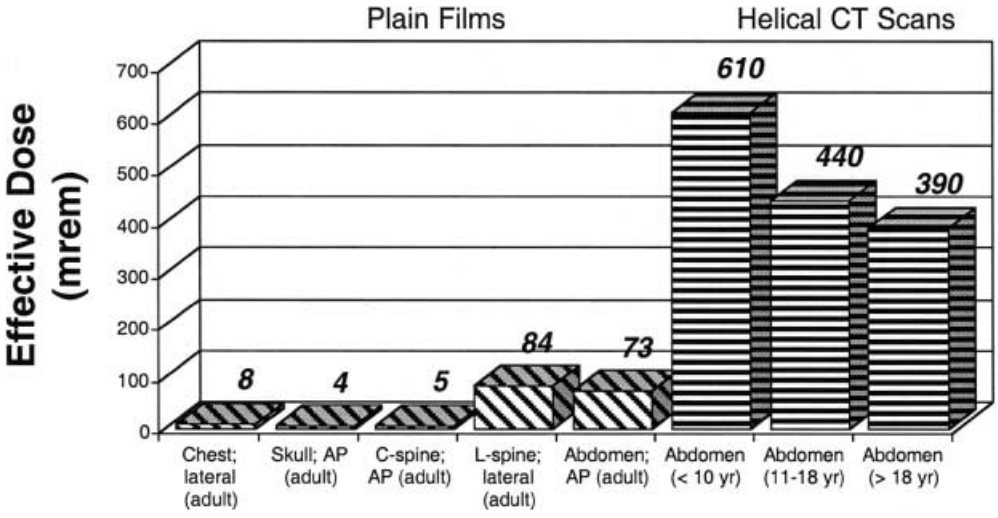

Fig. 5. Effective doses for common diagnostic procedures in radiology involving plain films, compared with the comparable quantity for helical CT scans. Effective dose is the product of absorbed dose and the tissue weighting factor for the tissues exposed. (Data from [18])

helical CT. No theories, no extrapolations, no models are involved.

Pediatric radiology: special considerations

There are three factors of special relevance to the use of helical CT in pediatric radiology.

First, children are much more radiosensitive than adults. A 1-year-old infant is 10–15 times as likely as a 50-year-old adult to develop a malignancy from the same dose of radiation [4].

Second, for a given procedure, the effective dose is larger in a small infant than in an adult. Table 4 illustrates this [10], showing that the effective dose increases as the age decreases. This can be compensated to some extent by reducing the peak kilovoltage (kVp) and milliampere-seconds (mAs) for infants relative to adults (an adjustment not always made in the past); however, organs are closer together in small children, resulting in more radiation dose to nearby organs when the volume of interest is being imaged.

Third, the use of helical CT is increasing even faster in children than in adults, presumably because of the big advantage of a short exposure time that allows for its use without a sedative [11, 12]. This leads to the temptation to use it as a screening procedure. It is estimated that there were 2.7 million CT scans of children under the age of 15 years in the year 2000.

Risk estimates for helical CT

In our paper entitled ''Estimated risks of radiation-induced fatal cancer from Pediatric CT'', we used calculated organ doses from CT examinations, in combination with age-at-exposure-dependent estimates

Table 3. Definitions of dose and effective dose

Dose:	Energy absorbed per unit mass	1 Gray = 100 rad
Effective dose:	Dose×W_T	1 Sv = 100 rem

(i.e., allows for tissue and organ differences in susceptibility to cancer)

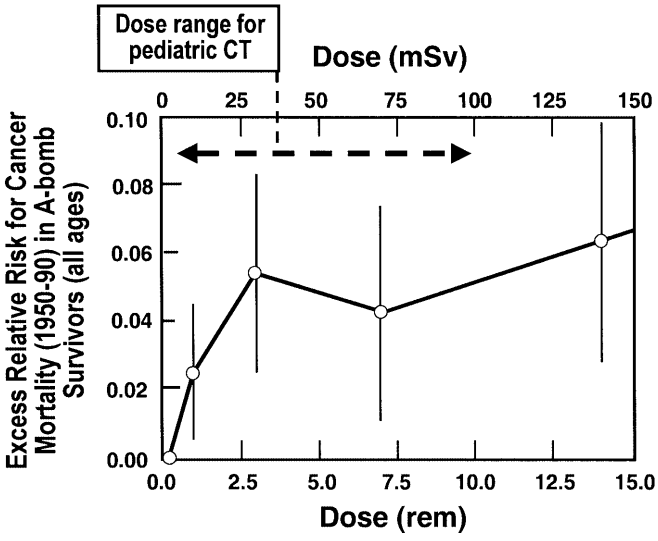

Fig. 6. Estimated radiation-related excess relative risk (and standard error) for solid-cancer mortality among A-bomb survivors. The low-dose data points are shown from Pierce and Preston [5]. Also shown are the range of organ doses characteristic of helical CT. (Adapted from [13])

of attributable lifetime risks per unit dose, obtained from the A-bomb data, to provide estimates of the lifetime age-dependent cancer mortality risks associated with common CT procedures [13]. Figure 7 shows the estimated overall fatal cancer risk, as a function of age at exposure, for typical head and abdominal CT

Table 4. CT dosimetry parameters for three age groups undergoing abdominal examinations

Parameter	≤ 10 years	11–18 years	> 18 years
Section dose, mGy	23.5	18.7	15.7
Energy imparted, mJ	72.1	183.5	234.7
Effective dose, mrem	610	440	390

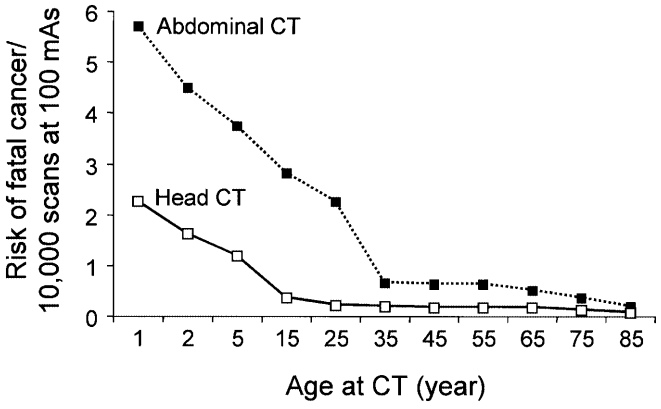

Fig. 7. Graph shows estimated lifetime attributable cancer mortality risk as a function of age at examination for a single typical CT examination of the head or abdomen. Risks are expressed per 10,000 scans for an assumed mAs of 100. Dose, and therefore risk, are proportional to the mAs and can be scaled accordingly. Note rapid increase in risk with decreasing age. (Adapted from [13])

examinations. Much more detail was included in our original paper. Cancer risks are expressed per 10,000 scans, with an assumed mAs of 100. Dose, and therefore risk, are directly proportional to mAs and so risks can be scaled accordingly. For example, risks would be doubled for 200 mAs, and halved for 50 mAs. As a rule of thumb, the lifetime cancer mortality risk attributable to the radiation exposure from a single abdominal CT examination in a 1-year-old child is of the order of one in a thousand, rather less if every effort is made to reduce the mAs and kVp. This risk is an order of magnitude larger than in a similar study in an adult. These estimates are based on cancer *mortality* data from the Japanese survivors. Cancer incidence data are becoming available and of course the risks are about doubled for incidence as opposed to mortality.

It is clear that no evidence of adverse effects is currently being seen, nor is it likely to ever be seen in the present generation of patients undergoing helical CT scans, either as children or as adults. I am unaware of any ongoing studies – which would cost millions of dollars and take 50 years to complete – to see the consequences of radiation over and above the high spontaneous background of cancer. However, applying the available risk estimates from the maturing study of the A-bomb survivors to the doses involved in modern helical CT implies that there will be a consequence. In this context, it is interesting to note that a recent case-control study on an association between pediatric radiologic examinations and childhood leukemia did show a significantly elevated risk in children who received two or more diagnostic examinations compared with controls [14]. In this study, no distinction was made between helical CT and simpler tests involving a plain radiograph.

Perception of risk

Life is a very risky business. Sooner or later we all lose the game of chance. Every day we are confronted by a multitude of risks; some of these are obvious and dramatic, like the risk of an automobile accident or an airplane crash – others are more subtle, remote and not immediate in their effect. Our judgements are often not especially rational. About 50 million Americans continue to smoke, despite the warnings of risk to their health printed on each cigarette pack, and the unequivocal association between smoking and lung cancer. Even more individuals are reluctant to accept the risk of death of one in a million associated with a commercial airline flight, but readily accept a risk of a hundred times greater by driving an automobile every day. The discussion of risk is complicated by the fact that we tend to be willing to accept higher risks in situations where we think (usually wrongly) that we are in control. Driving our own automobile versus being a passenger in an airplane for example. This aside, the general perception of risk can be summarized as follows:

A risk of death of one in a million is generally ignored. We face a multitude of risks of this magnitude every day, from crossing the street, to being killed by lightning or by electrocution in our homes.

A risk of occupational death of one in a hundred per year is totally unacceptable. Coal miners at the turn of the century faced such a risk and this was considered the ultimate "unsafe" industry.

The interesting risk level is intermediate, namely, a risk of death of one in a thousand, which just happens to be the level associated with a helical CT in a child. As long ago as 1983 [15, 16], the Royal Society in the UK made the following statement on risk: "A risk of one in a thousand is not totally unacceptable if:"

a) The individual knew the risk
b) Received some commensurable benefit
c) Understood that everything reasonable had been done to reduce the risk

We need to translate or interpret these general principles to the specific case of helical CT in pediatric radiology.

a) The patient, or the parent in the case of a child, should be told of the small risk involved.
b) The procedure should be restricted to cases where it is specifically indicated, and promises to convey a commensurate benefit in terms of a diagnosis that is difficult to obtain by any other means. It involves too big a dose to be used indiscriminately as a screening procedure.
c) It goes without saying that every effort should be made to decrease the radiation dose by adjusting the kVp and mAs to a suitable level for the size of the child being scanned [17]. One size fits all is no longer appropriate now that the risks have been pointed out.

Conclusion

In pediatric radiology, as in every other aspect of life, there is no free lunch. In general, radiological procedures involve a small risk which must be balanced against the potential for a significant benefit.

Helical CT is a relatively high-dose procedure, and in children involves a risk sufficiently high to merit consideration. These risk estimates are now based on solid data and no longer involve extrapolations and assumptions.

In cases where it is positively indicated, the risk is far outweighed by the potential benefit, and no child should be denied the procedure. It goes without saying that every effort should be made to minimize doses by tailoring the parameters of kVp and mAs to the size of the individual being scanned. However, it is important not to overdo the idea of dose reduction. The ALARA principle mandates that doses should be as low as *reasonably* achievable. Unnecessary dose levels must be eliminated, but it makes no sense to reduce the dose to the point where the diagnostic quality of the scan is compromised, since this defeats the object of the exercise. In the long run, the major concern is the potential public health problem that accumulates when a risk that is acceptable to the individual is multiplied by the 2.7 million procedures performed each year in children.

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