

Medical Student Module:

Biological Effects of Radiation on Children – You Are Responsible

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A. Background

Diagnostic tests and therapeutic medications are generally safe – the benefits of making the diagnosis and curing the disease outweigh the risks of the procedure or medication. However, each test or medication has risks and with medications, incorrect doses and idiosyncratic reactions can occur.

Imaging tests that use radiation can also be perceived as a medication, with the “correct dose.” Too little radiation may give poor or nondiagnostic images, while too much can cause carcinogenic effects.

Since you, as a future ordering physician, will in part determine which of your patients will receive radiation-producing tests (radiographs, fluoroscopy, CT, nuclear medicine, PET, angiography, etc.), you are responsible for knowing the biological effects of radiation on children and making an informed decision as whether:

1. A test is indicated.
2. This is the correct test vs. a test without ionizing radiation.
3. That the test is administered with minimum dose.

This module is designed to give you information on the biological effects of radiation in children and to learn about those modalities in our diagnostic imaging armamentarium that have radiation and those that do not.

B. Sources of Radiation

Radiation is of two sources – natural and man-made. Natural radiation constitutes 50% of radiation that might effect us. Alpha particles (nuclei of helium atoms and have two protons and two neutrons in close association) are a major source of natural background radiation. They are emitted during the decay of uranium and radium. Radon gas is the largest source of *natural* radiation (Fig. 1).

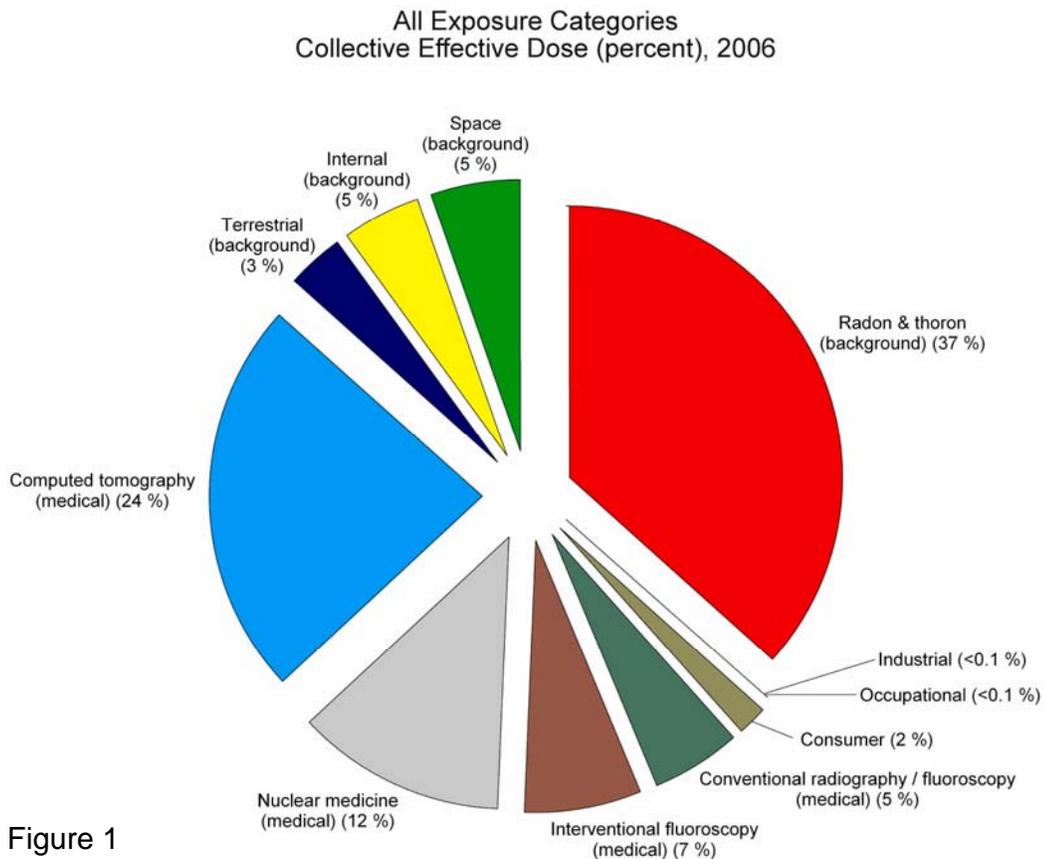


Figure 1
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Man-made sources of radiation have been increasing dramatically in recent years and now account for 50% of our exposure. The largest component of *man-made* radiation is medical procedures. Computed tomography (CT) and nuclear medicine contribute 75% of the medical exposure and 36% of total radiation exposure. Conventional nuclear medicine uses gamma rays and positron emission tomography (PET) uses positron annihilation with short-lived isotopes. X-rays and gamma rays are forms of electromagnetic radiation (Fig. 2).

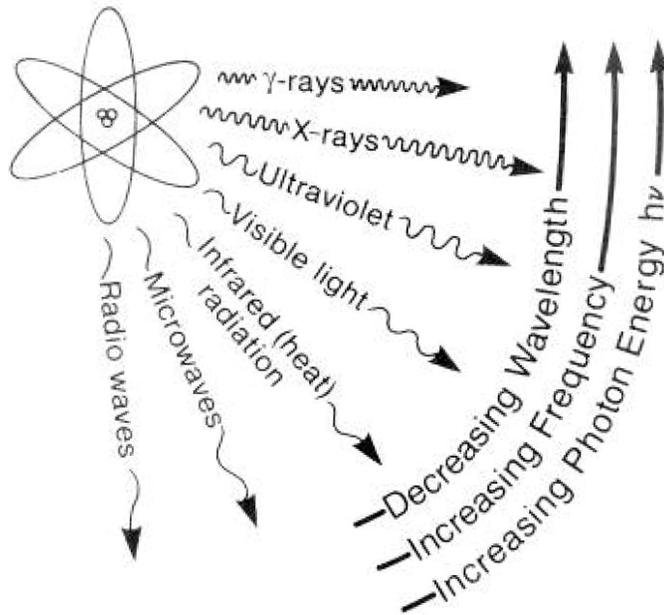


Figure 2 ● Illustration of the electromagnetic spectrum. X-rays and γ -rays have the same nature as visible light, radiant heat, and radio waves; however, they have shorter wavelengths and consequently a larger photon energy. As a result, x- and γ -rays can break chemical bonds and produce biologic effects.

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Other forms of electromagnetic radiation are ultraviolet light, microwaves, and radio-waves. They differ in their wave length and, therefore, their energy. X-rays and gamma rays can be considered packets of energy –photons. It is the deposition (absorption) of these packets of

energy that determine their biological effect. Computed tomography (CT) is the largest source of environmental (man-made) radiation.

C. How Radiation Effects Human Cells

An X-ray can pass through the body or be absorbed. Absorption causes release of the X-rays or photon energy (Fig. 3). The photon energy either indirectly (most often) or directly causes damage of the DNA. The indirect mechanism occurs when the energy of the recoil electron interacts with water (H_2O) to produce an hydroxyl radical ($OH\cdot$), which then damages the DNA. Direct action occurs when the absorbed photons directly damage the DNA.

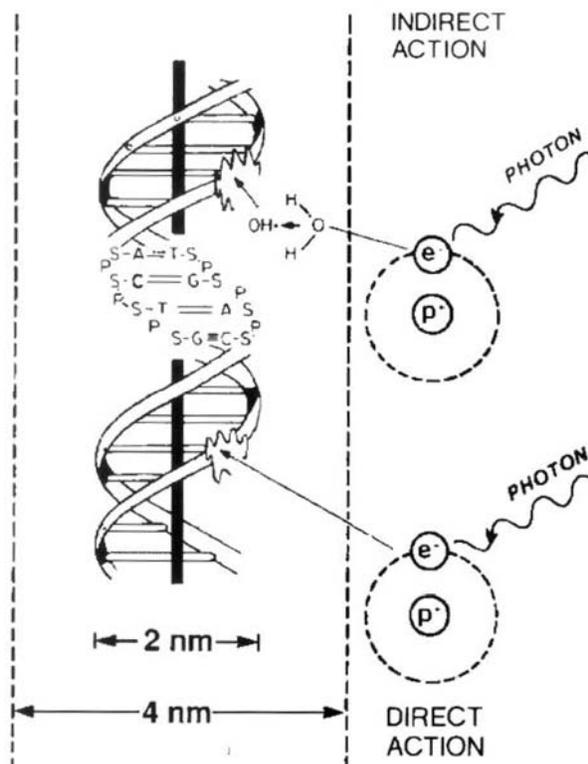


Figure 3 Direct and indirect actions of radiation. The structure of DNA is shown schematically. In direct action, a secondary electron resulting from absorption of an X-ray photon interacts with the DNA to produce an effect. In indirect action, the secondary electron interacts with, for example, a water molecule to produce a hydroxyl radical ($OH\cdot$), which in turn produces the damage to the DNA. The DNA helix has a diameter of about 20 Å (2 nm). It is estimated that free radicals produced in a cylinder with a diameter double that of the DNA helix can affect the DNA. Indirect action is dominant for sparsely ionizing radiation, such as X-rays. *S* sugar, *P* phosphorus, *A* adenine, *T* thymine, *G* guanine, *C* cytosine (Adapted from [1])

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The kind of DNA damage determines the effects of the radiation. The double helix structure of DNA consists of two strands held together by hydrogen bonds. In some instances, there are single-strand breaks, which are usually repairable using the opposite strands as a template (Fig. 4). Therefore, these breaks are of little lasting significance. Double-strand breaks are more of a problem – they can cause chromosomal breakage that can result in cell death or new combinations of chromosomal linkages. This results in various chromosomal sequences that can lead to a translocation or other mal-alignments (Fig. 5). At times, this can cause an oncogene (a gene that contributes to cancer formation when mutated or inappropriately expressed) to be activated.

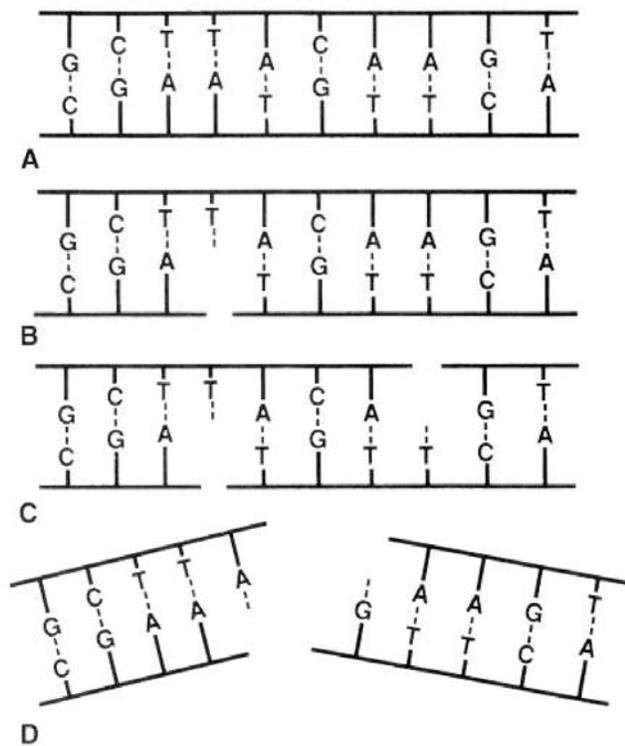


Figure 4 ● Diagrams of single- and double-strand DNA breaks caused by radiation. **A:** Two-dimensional representation of the normal DNA helix. The base pairs carrying the genetic code are complementary (i.e., adenine pairs with thymine, guanine pairs with cytosine). **B:** A break in one strand is of little significance because it is repaired readily, using the opposite strand as a template. **C:** Breaks in both strands, if well separated, are repaired as independent breaks. **D:** If breaks occur in both strands and are directly opposite or separated by only a few base pairs, this may lead to a double-strand break in which the chromatin snaps into two pieces. (Courtesy of Dr. John Ward.)

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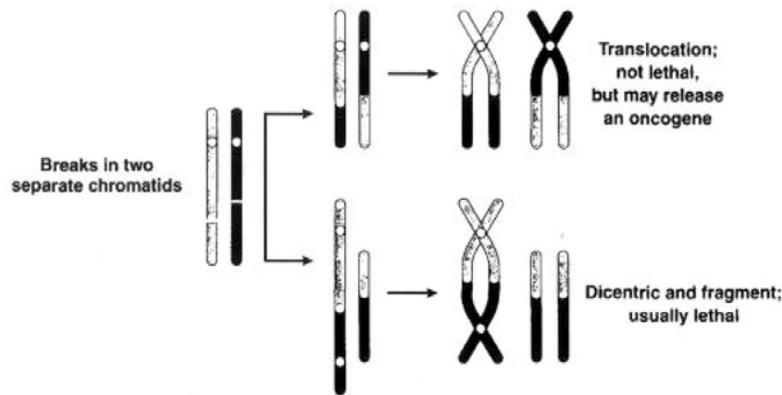


Figure 5 Most biological effects of radiation are caused by the incorrect joining of breaks in two chromosomes. For example, the two broken chromosomes might recombine to form a dicentric (a chromosome with two centromeres) and an acentric fragment (a fragment with no centromere). This is a lethal lesion resulting in cell death. Alternately, the two broken chromosomes might exchange broken ends. This is called a symmetrical translocation. It does not lead to the death of the cell but in a few special cases activates an oncogene by moving it from a quiescent to an active site

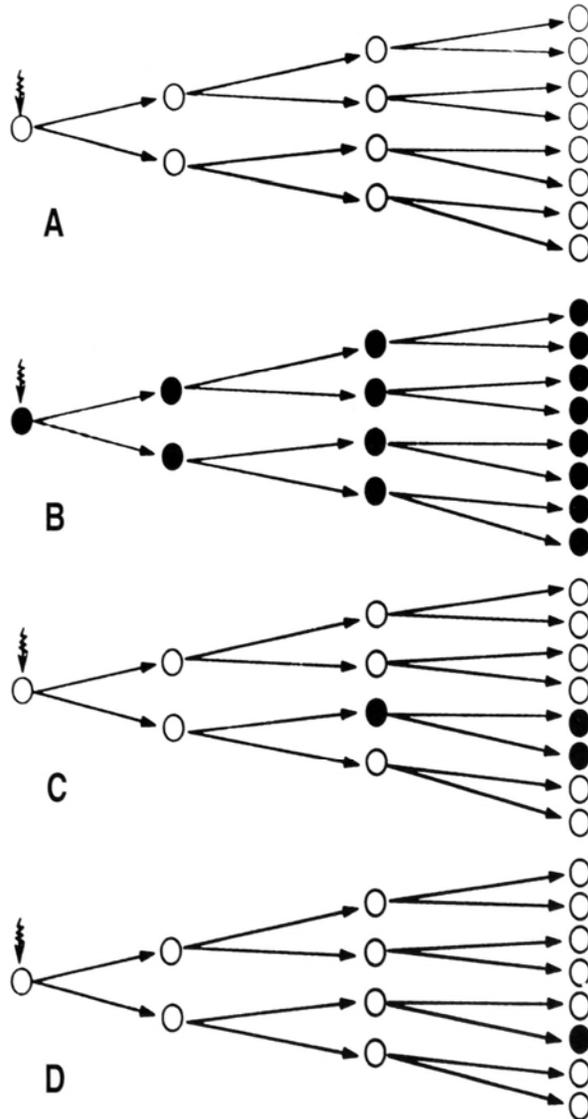
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D. Adverse Effects of Radiation – Carcinogenesis

The most important deleterious effect on the DNA at low doses (5-20 mSv) is carcinogenesis. A stochastic effect is an all-or-nothing effect – the severity of the effect does not depend on the dose, though the probability of it occurring increases with dose. Stochastic means random; i.e. it may or may not cause damage. By contrast, high-doses of radiation (>2,000 mSv) can cause a deterministic effect, such as a cataract, where the severity increases with dose. For example, if a child receives >2,000 mSv acutely to the eye, the child will get cataracts. We are mainly concerned, however, about the stochastic effects.

A good example of a stochastic effect is noted in (Fig. 6) showing us that it is random whether a cell gets hit by radiation and the effects of DNA damage might not be seen for many generations. This explains the 20-40-year lag in expression of radiation-induced cancer.

Figure 6



Little JB: Ionizing Radiation in Cancer in Medicine 2003

E. Evidence of Carcinogenesis Secondary to Irradiation

Steward et al. reported results on the Oxford Survey of Childhood Cancer (OSCC) over 50 years ago. This study linked maternal *in utero* irradiation (for various obstetrical causes) to pediatric cancer mortality in the offspring. This material has been studied with long-term

follow-ups obtained and have now shown that there is increased cancer risk that is approximately >50% greater than baseline.

The best evidence for radiation-induced cancers involves the study of atomic bomb survivors. The study has lasted more than 60 years, involved more than 100,000 people, and has cost the American taxpayers over \$500 million. During the latest part of this study, solid tumors have been appearing at a greater rate than expected. These tumors are the same tumors adults get but appear in a great number and slightly earlier age. The most startling facts arising from this study shows an excess of number of cancers in patients exposed to lower doses of radiation – from 5 mSv to 200 mSv (500 mrad to 20 rads) (Fig. 7). In addition, it became abundantly clear that those who acquired cancer were those exposed at the younger ages (Fig. 8) and that the newborn is 10-15 times more sensitive to radiation than older adults. It also became obvious that females got more cancers than males, principally because of the risk of breast cancer.

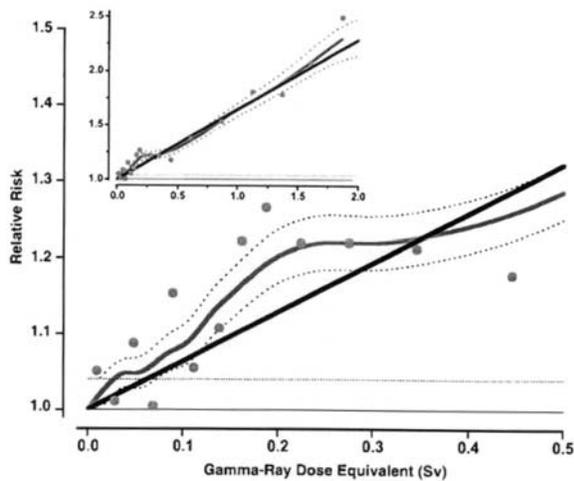
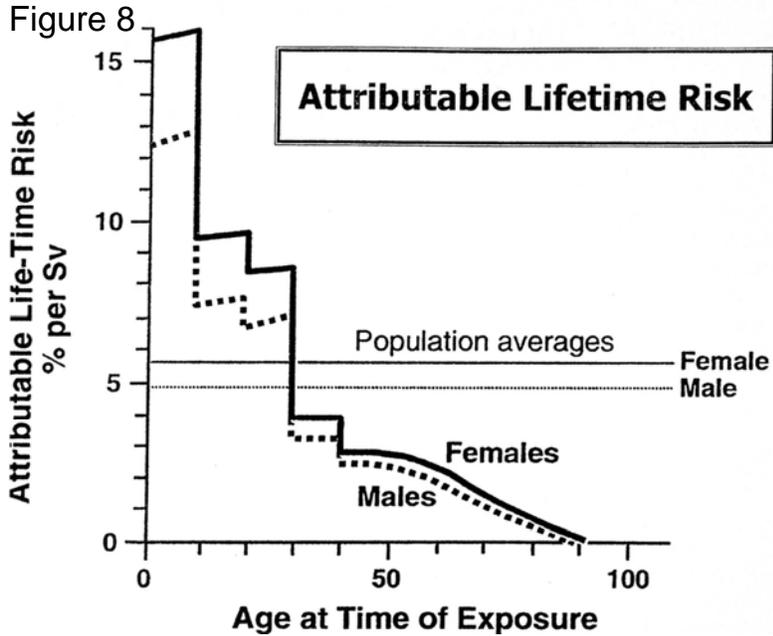


Figure 7 Estimated relative risks for cancer rates in A-bomb survivors during the 1958–1994 follow-up period relative to unexposed individuals. The *dashed curve* represents ± 1 standard error for the *smoothed curve*. The *inset* shows data over the whole dose range 0 to 2 Sv (0–200 rem), to which a straight line is fitted, i.e., relative risk is proportional to dose, with no threshold. The *main figure* is an expanded version of the low-dose region up to 0.5 Sv (500 rem). The *straight line* is taken from the *inset* data for the whole dose range. There is a suggestion that low-dose risks are *above the line*. (Reprinted with permission from [5])

With Permission : Pierce DA, Preston DL, 2000
 Pediatric Research 154: 178-186

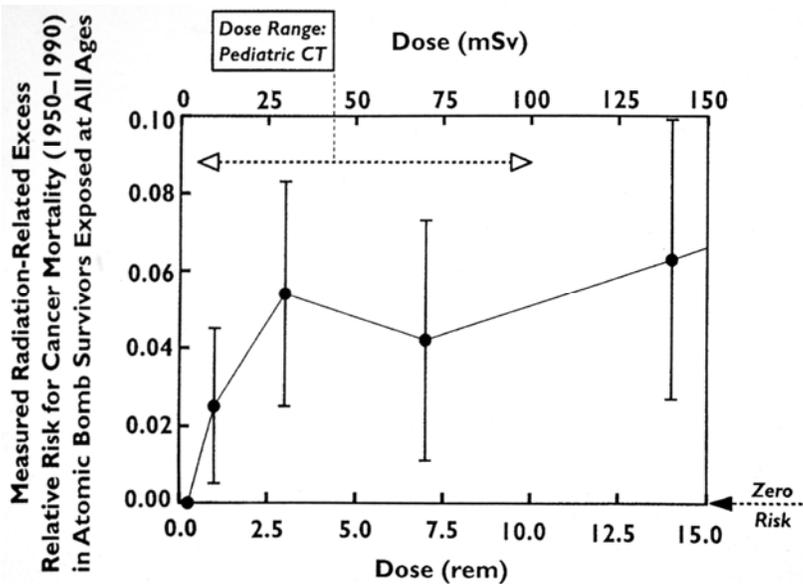


Hall Pediatric Radiology Apr 2002 pg 226

It is clear (Fig. 9) that the doses we are now using in CT overlap these low doses acquired in young individuals at the time of the atomic bomb blast.

All of the data provided are related to *mortality* figures; that is, study of death certificates of individuals exposed to radiation. The *incidence* of cancer is at least double.

Figure 9



Pierce, Preston, Rad Res 151 pg 178-186: 2000

Brenner Pediatric Radiology Apr 2002 pg 230

F. The Metrics of Radiation

Up to this point, we have been talking about various metrics describing radiation dose. (Fig. 10) shows a summary of the doses medical students should know. The unit of *absorbed* dose is the Gray and we usually discuss this in terms of milliGray (mGy). The older unit is rad and most in the U.S. still discuss dosage in terms of rad. The conversion factor from mGy to mrad is simply moving the decimal point two places to the right. The unit describing equivalent effective doses is the Sievert. The effective dose is obtained from a factor to allow for the type of radiation and the part of the body that was exposed. The older term for this estimated dose is the rem.

Figure 10 Dose Chart

- 1 Gy = 100 rads
- 1 cGy = 1 rad
- 1 mGy = 100 mrad
- 1 Sv = 100 rads
- 10 mSv = 1 rad
- (rem = rad)

G. Radiation-producing Tests

Radiation-producing imaging examinations (Fig. 11) are important diagnostic tools and certainly modern medicine would not be possible without them. The properly indicated imaging test has a far greater benefit over risk of any of the complications of radiation. However, it is the frivolous use of radiation-producing tests that provides a greater risk to a child than any benefit.

Figure 11 Table 2. Radiation Dose by Imaging Test*

<u>Exam</u>	<u>mrad or mrem</u>	<u>Site Measured</u>
Chest - 2 views	10-20	entrance (skin)
Abdominal – 2 views	50-100	entrance (skin)
Fluoroscopy nonpulsed	300-500/min	entrance (skin)
pulsed	100-150/min	entrance (skin)
Computed tomography ¹ head	6000 (2000-3000)	middiameter of phantom of 16 cm
abdomen	3000 (1000)	middiameter of phantom of 32 cm
Nuclear medicine ² (^{99m} TcMAG3-renal)	120 mrem	effective dose
Positron emission tomography ² (Brain FDG)	185 mrem	effective dose whole body

*Background radiation is approximately 1 mrad/day (300 mrad/year)

¹Scan explained as CT dose index (CTDI). First dose is with adult factors, second in () are examination adjusted for children.

²This is expressed as effective dose. These are rough guidelines for dose given to a 5-year-old with normal renal function. From ICRP publication 80.

^{99m}TcMAG3 = ^{99m}technetium mercaptoacetyltriglycine
FDG=(F-18) fluoro-2-deoxyglucose

Radiologists have at their disposal through manipulation of the various parameters of all digital radiographic examinations (plain radiograph, CT), the ability to lower the dose of any test and still have diagnostic images. Therefore, it is both the responsibility of the ordering physician (to order appropriately), the technologist and radiologist (performing the test) to use the least radiation resulting in diagnostic pictures (ALARA concept of As Low as Reasonably Achievable dose).

Summary

We are all responsible for the potential biological effects of radiation on children. Children are 10-15 times more sensitive to radiation than older adults. Though the exact excess risk of cancer is not known, it is estimated that a CT abdominal scan results in 1/1,000 to 1/5,000 excess risk of developing cancer at a later date.

We must make sure that it is appropriate to order an imaging test, that we choose the correct test, and that we perform the test consistent with the ALARA principle (As Low As Reasonably Achievable).

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