RADIATION RISKS TO CHILDREN FROM MEDICAL IMAGING

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INTRODUCCIÓN

Medical imaging is extremely important value and role in the care of the ill or injured child. This includes diagnosis of emergent including life threatening conditions, as well as an aid in management, such as appropriate triage to promote efficient and judicious use of medical resources. For example, CT and MR have been heralded as one of the most significant medical advancements in the past 30 years, based on a survey of medical practitioners (1). While much of the following material will discuss the specific risks of ionizing radiation related to medical imaging, one must not lose sight that when used appropriately, the benefits of medical imaging are far in excess of real and potential risks.

Much of medical imaging depends on the use of x-rays, a type of ionizing radiation, for imaging formation. The general modalities that use x-rays consist of radiography, fluoroscopy (including angiography), computed tomography (CT) and nuclear imaging (also known as nuclear medicine). Other modalities which do not use ionizing radiation which are commonly used for medical imaging consist of sonography, and magnetic resonance imaging. Radiation, in relatively high doses, has known biological effects. These effects include the induction of cancer. Almost without exception, diagnostic medical imaging uses low levels of radiation and the types of biological effects and attendant risks of cancer will be different (as discussed below). The topic of radiation risk in medical imaging is also timely, especially in the United States where there has been increased public attention mostly through media scrutiny reporting radiation doses from medical imaging and biological effects. These reports included hair loss from perfusion imaging (a type of brain CT examination) (2), radiation dermatitis from CT examination in a child (3), relatively high doses from radiography in dental evaluation (4), and excessive radiation doses from improperly performed neonatal radiography (5). Because radiation related effects especially cancer may not be evident for years even decades, concern may be long lasting. I have received communications from parents even several years after imaging evaluation who are concerned about what they have heard about cancer risks and radiology in the media. Recently, the first scientific investigation associating pediatric CT with cancer was published in Lancet (6). Taken together, the importance of medical imaging using ionizing radiation, and continued, and in some circumstances, escalating use of this imaging in both adults and children, and the persistent and often pervasive attention to the long lasting possibility of cancer from ionizing radiation in levels found with diagnostic medical imaging necessitates a reasonable understanding of the risk aspect of the risk benefit ratio for diagnostic medical imaging. This basic understanding applies to all medical practitioners, not just those with imaging expertise (i.e. radiologist). These healthcare providers, such as pediatricians or emergency medicine physicians will be potentially involved in discussions with colleagues about risks and benefits in patient management, as well as conversations with patients about the potential risks and benefits.

This topic of radiation risk and medical imaging applies to all ages. However, it is particularly important in children. Children are relatively

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more vulnerable to radiation than adults. This is in part due to the fact that there is a longer life expectancy in which to manifest potential radiation induced cancers, which can be life-long. In addition, the care of children can be more complicated than adults. For those healthcare providers who are not familiar with the different spectrum of pediatric illness and manifestations of injury, there may be a lower threshold to request imaging evaluation. For imaging experts, lack of familiarity with the often special imaging techniques to maximize quality and minimize radiation may result in studies with excessive radiation doses to children. For all care providers, there is often increased anxiety especially when caring for severely ill or injured children that may also affect the choice (e.g. lower thresholds for requesting) of imaging strategies (7). For these reasons, the following material present a summary information on radiation risks for children from diagnostic medical imaging.

ADDITIONAL RESOURCES IN THE LITERATURE

The following list is provided at this point to let those that are interested know that there are excellent resources for additional information to the ensuing discussion. For the following general sections, the reader is referred to select references (note that there will be some overlap of this material and this division into categories is somewhat arbitrary): radiation biology: Hall and Brenner (8); justification for medical imaging: Hendee, et al (9); general review of CT and radiation: Hricak, et al (10); radiation doses of diagnostic medical imaging examination in adults: Mettler, et al (11); radiation doses of studies in children: Fahey, et al (12); current review of cancer risks from diagnostic imaging procedures in adults, children, and in experimental animal studies: Linet (13); controversies in risk estimations for medical imaging: Hendee, O'Connor (14); strategies on dose reduction for medical imaging using ionizing radiation in children: Frush (15), Nievelstein (16); education material (including material specific for parents and non-imaging healthcare providers): Image Gently website (www.imagegently.org) in children and for adults, Image Wisely (www.imagewisely.org); evidence-based assessment of risk and benefit in medical imaging in children using ionizing radiation: Frush, Applegate (17).

RADIATION BIOLOGY

The biological effects of radiation are derived principally from damage to DNA. The x-ray particle, a photon, releases energy when interacting with an electron. The electron may act either directly on DNA (direct action or affect) but may also interact on a water molecule resulting in a free radical, which in turn can damage DNA (indirect action or affect). The indirect effect is the more dominant effect, consisting of approximately 2/3 of photon interactions. DNA damage results in either single stranded breaks or double stranded breaks. Single stranded breaks are usually well repaired with minimum bioeffects. Breaks in both strands of DNA (which are in close proximity) are more problematic to repair and underlie disruptive function that can result in cell death or in impaired cellular function resulting in the development of cancer. These inappropriate repairs with resultant stable aberrations can initiate one of the multi-step processes in radiation induced carcinogenesis. Of note, there are some chemicals, which serve as radioprotectants, primarily in the setting of radiation oncology that have recently been reviewed (18). While not yet applicable to general diagnostic imaging, these DNA stabilizing agents provide a model for radiation protection at the cellular level.

Radiation results in two biological effects: deterministic and stochastic effects. For virtually all diagnostic imaging (CT, nuclear medicine, and radiography and fluoroscopy) radiation doses are at the levels which are stochastic. Stochastic effects are generally disruptions that result in either cancer or heritable abnormalities. For diagnostic imaging, the discussion is limited almost exclusively to the potential for cancer induction; heritable effects (i.e., on gametes) have not been shown to occur in diagnostic levels of radiation in humans. For a stochastic effect, the risk increases with the dose but the severity of the effect (i.e., the severity of cancer) does not increase. There is also no threshold for this risk (see following discussion on models of radiation risks based on dose). The other biological effect is deterministic. Deterministic effects include cataracts, dermatitis (skin burns), and epilation (hair loss). With the deterministic effect, the amount of radiation determines the severity of effect. For example, the greater amount of radiation, the more extensive the hair loss. With deterministic effects, there is a threshold. Below this threshold the injury does not occur. Deterministic effects can be seen with extensive interventional procedures, and certainly with doses delivered from radiation oncology. Deterministic effects are, except for very unusual circumstances, including imaging errors, not encountered in during diagnostic medical imaging examinations.

RADIATION DOSE

A brief review of radiation units will be helpful for the subsequent material. First, radiation can be measured as exposure; however this is not useful in determining risks since it says nothing about what the organs at risk actually receive. Individual patient risk for organ specific cancer can be determined if the absorption of the radiation, the absorbed dose, measured in Gray (Gy), is known. Obviously, this cannot be determined during routine medical imaging for an individual patient but there are estimations for organ doses. The biological impact on the tissue may vary depending on the type of radiation delivered. For diagnostic imaging, this is the x-ray, and the waiting factor ends up being 1.0 so that the equivalent dose (in Sieverts, Sv) is equal to the absorbed dose in Gy (in medical imaging the measure is milli Gy, or mGy since this is the scale of doses encountered). The final unit of import is the effective dose (in Sv, or mSv in the range of diagnostic imaging) which is commonly used metric in discussions of diagnostic imaging radiation dose. It is formally determined by the sum of the exposed organs and their equivalent doses (in mSv) multiplied by weighting factors which depend on the differing radiosensitive of

those organs that are exposed. The effective dose is a very general dose unit. It could be similar to say an average rainfall for a country per year. This average rainfall takes into account regional and seasonal variations into a single number, but there is no way to extract from the average rainfall the specific data on the coastal rainfall in summer months. Effective dose (derived from experiments and models of organ doses since, again we cannot practically measure internal organ doses during medical imaging) represents an equivalent whole body dose (like the yearly average rainfall) from what may be regional exposures. For example, a brain CT may result in an effective dose of 2.0 mSv. A pelvic CT may result in an effective dose of 4.0 mSv. This means that the pelvic CT equivalent for the whole body exposure is twice that of a brain CT. However, it is easy to see that any potential risks from the brain CT to the lens of the eye for example are going to be greater than the pelvic CT. While the effective dose continues to be the most commonly used metric in discussing ionizing radiation dose from imaging modalities in the clinical realm, it is still problematic and often misunderstood measure (19-21).

The doses for imaging modalities can vary widely, more than a factor of a hundred. In general, radiography of the extremities such as the ankle, wrist, or elbow provide very low doses, and computed tomography and nuclear imaging studies tend to provide relatively higher doses. Again, these are effective doses, or whole body equivalents that, allow the various imaging modalities to be compared with respect to an overall population risk but not an individual patient risk. Doses will depend on the various technical factors used for various imaging studies. In particular, fluoroscopy and angiography doses may vary depending on the indication for the evaluation, or various findings during the procedure. An upper gastrointestinal series with a small bowel follow through will in general have a higher fluoroscopic dose than a simple fluoroscopic cystogram in children. Doses for nuclear medicine studies can be quite low or relatively high (11, 12). Single imaging doses in children from a single CT examination may be as low as less than 1.0 mSv to 10-20 mSv (11, 13, 22).

IMAGING UTILIZATIONS: PATTERNS OF USE

Overall, there are nearly 4 billion diagnostic imaging evaluations that use ionizing radiation performed worldwide (23). Given the current world population, this means more than one examination for every individual in the world is performed every other year. Obviously, not everyone has an examination and various populations of patients will have significant number of examinations per year. If one looks at medical imaging use in the United States, it has substantially increased over the past 30 years (24). Previously, about 3.5 mSv was the annual total radiation per capita dose, 85% coming from background radiation (for example, radon, cosmic radiation, naturally occurring radioisotopes). Before 1980, an effective dose of approximately 0.53 mSv (about 15% of the total) was estimated to result from medical imaging. This is now 3.0 mSv (23), a nearly 600% increase. Currently, in the United States, 48% of all radiation to the population is from medical imaging. Nearly half of this is from CT and the vast majority of medical radiation is due to combination of CT and nuclear imaging. In fact, CT in the United States now accounts for nearly 25% of the per capita radiation exposure per year. This is largely due to increase in medical imaging, rather than higher doses per procedure. The reasons for this increased use are complex but, as noted before, CT has provided an increasingly valuable tool in a number of settings, including evaluation of trauma, especially brain injury, in the setting of cardiovascular disease, including thromboembolism, and other cardiovascular abnormalities (such as acquired and congenital heart disease in children), and in the clinical setting of acute abdominal pain, such as appendicitis.

Currently, in the United States, nearly 80 million CT examinations are performed per year (25) which equates to about one CT evaluation performed per year for every four individuals. In the U.S., the use of medical imaging is also frequent in children. For example, Dorfman et al noted that out that over a three year period in a U.S. population consisting of more than 350,000 children from a group of health care networks, nearly 43% underwent at least one diagnostic imaging procedure using ionizing radiation, and nearly 8% had at least one CT examination (26). Larson noted a five-fold increase in the number of CT examinations from 330,000 to over 1.65 million from 1995 to 2008 (27).

While these data do indicate that the use of medical imaging in children has increased substantially over the past few decades, some other data indicate that at least the use of CT imaging in children has declined over the past few years (28, 29), and further investigations will need to determine if this is a sustained trend.

RISK ESTIMATIONS FOR CANCER FROM IONIZING RADIATION IN MEDICAL IMAGING:

In general, risk estimations for medical imaging in both adults and children come from four sources consisting of studies of populations exposed to atomic bombs (the Radiologic Effects Research Foundation-RERF), occupational exposures, medical exposures, and environmental exposures, such as the Chernobyl accident. An excellent review of the RERF data is found in article by Linet (13). The various reports from these sources have comprised the most cited source for determining risks, the Biological Effects of Ionizing Radiation (BEIR) Committee from the National Academy of Sciences. The most recent report is BEIR VII. While BEIR VII report is the foundation for many risk estimates including medical imaging, there are some problems with the report. As noted by Hendee et al, "... many articles that use the BEIR VII report to forecast cancer incidence and deaths from medical studies fail to acknowledge the limitations of the BEIR VII and accept its risks estimates as scientific fact rather than as a consensus opinion of a committee" (14). Rather than a detail discussion of the limitations of the BEIR VII Report, it is probably more worthwhile to just understand that estimations of cancer risks, such as the levels provided by medical imaging, continue to be speculative. We also estimate the dose

provided by imaging (recall effective dose discussion above), so that there are many estimations involved in determining risks. We do know that at effective doses greater than 100 mSv, there is a significant risk of cancer. Below that, and the range of medical imaging examinations, there is a debate (10, 14, 30).

The model most widely accepted for cancer induction risk related to dose (estimations) is a linear no threshold model (LNT) (31, 32). Basically, we know that at high levels of radiation that there is a significantly risk of cancer (above an effective dose of 100 mSv). This model assumes that the risk is only zero when there is no radiation dose. Beginning at the zero point, a line is drawn through these higher points, generally above 100 mSv. This is not the only model and there has been some support in the literature in the other models such as that based on hormesis, where there is a beneficial (e.g. protective function such as improved DNA repair/stability) at low doses, or levels, with risks seen only at higher doses or levels (33). As a rule, the medical and scientific community accepts the linear no threshold model as a "conservative" model; that is, subscribing to this model is a relatively safe posture as opposed to assuming that lower levels of radiation do not have biologic effects.

There is no difference between radiation induced cancer and the same cancers occurring naturally. In addition, leukemia minimum 2-5 years, up to 20 years after radiation exposure; solid tumors occur a minimum 10 years, and risks remain for and extended time (13).

Radiation risks will depend on age, gender, and other factors, including genetic susceptibility, as well as whether the exposure is protracted or acute. While individuals note that there is a significant risk of developing cancer at doses below a 100 mSv (30), other experts, summarized recently by Hendee et al (14) through statements from two professional medical societies caution against such projections. The American Association of Physicists in Medicine (AAPM) statement relates that "risks of medical imaging and patient doses below 50 mSv for single procedures or 100 mSv for multiple procedures over short time periods are too low to be detectable and may be non-existent". The Health Physic Society issued a physician statement indicating "the Health Physic Society recommends against quantitative estimations of health risks below an individual dose of [50 mSv] in one year or a life time dose of [100 mSv] above that received from natural sources. For doses below [50-100 mSv] risks of health effects are either too small to be observed or are non-existent".

Projected risks from cancer from medical imaging include such statements by Brenner and Hall in New England Journal of Medicine that as many as 1-2 percent of all cancers in the United States could be caused by CT alone (34). In addition, in an investigation published in Archives of Internal Medicine in 2009, Berrington and colleagues noted, with current CT use in the United States that nearly 15,000 fatal cancers could be caused by a single CT examination (35).

In 2009, an excellent review of what is known about medical imaging and cancer risks was published in Cancer, authored by Linet, et al. In this review, authors noted that "…epidemiologic studies have … linked diagnostic x-rays with cancer increases in patients, including modest excesses of pediatric leukemia in the offspring of mothers undergoing diagnostic x-rays during pregnancy, and increased breast cancer risks in women with tuberculosis who were monitored using fluoroscopy and in women with scoliosis who were evaluated with repeat x-rays" (13). A detailed discussion underlying these investigations, which have been widely cited over decades, was provided. In addition, authors reviewed cancer risks associated with external radiation from sources other than diagnostic radiologic procedures (highlighting key epidemiologic studies), and summarized epidemiologic studies of cancer risks associated with diagnostic radiologic procedures including in utero x-rays in pediatric cancer risks, childhood and adolescent x-rays in pediatric and lifetime cancer risks, adult x-rays and cancer risks, and animal studies. For childhood and adolescent x-ray in pediatric lifetime cancer risks, authors summarized that studies have produced "ambivalent results" speculated to be due to methodological limitations, including small sample sizes, as well as short follow-up.

Most recently, a study of children in the United Kingdom undergoing CT examinations published in Lancet by Pearce and colleagues is the first to report an association of CT examinations with cancer. In this investigation, there was a significant association of both some leukemia and brain cancer. For example, one brain CT examination performed in the first decade of life was projected to cause one excess brain cancer per 10,000 scans. While this is the first reported association, accepting that now there is a proven link from a single investigation is imprudent and against scientific tenants. There are ongoing investigations in larger patient populations in several countries (6).

STRATEGIES FOR DOSE REDUCTION

A complete discussion of strategies is outside of the scope of this article but can be found in several recent publications (15,16, 36,37). Strategies are targeted to major aspects of radiation protection: justification and optimization. Justification signifies that the examination is indicated. When an examination is indicated, the examination should be optimized, and various dose conscious techniques and parameters should be utilized. For children, these include age appropriate settings, minimizing the number of projections and fluoroscopic time, appropriate radionuclide doses, and for CT minimizing multiphase examinations. Newer techniques including significant noise reduction strategies will likely provide additional opportunities for significant dose reduction in CT examination.

WHAT IS STILL NEEDED?

All healthcare providers must continue to work together to assure appropriate evidence-based data for image utilization. Educational

materials are extremely valuable and provide information on appropriate use, affording dose reduction opportunities. Further technical advancements in imaging modalities using ionizing radiation will also engender improved radiation protection for patients. Consent for radiation risks from medical has also been an item for discussion (38). Dose archiving, monitoring, and reporting are increasing responsibilities of the imaging community (39) and requires a consensus input from all stakeholders involved in medical imaging.

CONCLUSIONS

Medical imaging is an invaluable tool in the care of children. While there are known biological effects of medical radiation at higher doses, the risks at levels used almost exclusively in diagnostic imaging especially in children are speculative. Healthcare providers with a fundamental and informed understanding of what we know and what we don't know can now have better discussions amongst themselves and with their patients and families to improve patient care.

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