Implications of Ionizing Radiation in the Pediatric Urology Patient

Kelly L. Stratton, John C. Pope, IV, Mark C. Adams, John W. Brock, III and John C. Thomas*

From the Division of Pediatric Urology, Department of Urologic Surgery, Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, Tennessee

Purpose: We reviewed the literature on the effects of ionizing radiation in pediatric patients, and discuss current recommendations and challenges facing radiologists and pediatric urologists.
Materials and Methods: We performed a MEDLINE® search to identify articles evaluating the risk of ionizing radiation in pediatric patients. Particular attention was focused on computerized tomography. Standard radiography, fluoroscopy and nuclear imaging were also evaluated.
Results: To date the literature relating radiation exposure to imaging has primarily focused on the role of the pediatrician and radiologist as decision makers. However, these imaging modalities are important to treat and monitor many conditions treated by the pediatric urologist. Conflicting reports have made clinical decision making and patient education challenging.
Conclusions: A lack of consensus on the risk of radiation exposure in pediatric patients increases the need for heightened awareness by the urologist requesting radiographic evaluation. Monitoring future studies is required to better understand the impact of radiation on children and ensure prompt implementation of appropriate guidelines for patient care.

Key Words: diagnostic imaging, urology, radiation dosage, risk, child

Abbreviations and Acronyms

ALARA = as low as reasonably achievable

CT = computerized tomography

MRI = magnetic resonance imaging

MRU = magnetic resonance urogram

VCUG = voiding cystourethrogram

VRPFL = variable rate pulsed fluoroscopy

Submitted for publication June 21, 2009.

* Correspondence: Division of Pediatric Urology, Department of Urologic Surgery, Monroe Carell Jr. Children's Hospital at Vanderbilt, 2200 Children's Way, 4102 DOT, Nashville, Tennessee 37232-9820 (telephone: 615-343-8195; FAX: 615-936-1061; e-mail: john.thomas@vanderbilt.edu).

Recently attention has been drawn to the risk of ionizing radiation exposure from diagnostic radiographic studies, primarily CT. Several new studies have attempted to evaluate the risk and effect of ionizing radiation in pediatric patients. Although controversy regarding radiation safety has been ongoing since the first days of radiography, recognizing the potential risks of inducing cancer in children is of utmost importance to parents, radiologists and clinicians.[1] As a pediatric urologist, imaging studies are integral for evaluating and treating several common disease processes. Counseling parents on the need for examinations is already important but with increased scrutiny placed on medical necessity pediatric urologists will be faced with an increasing burden of responsibility when ordering these studies. We reviewed current understanding of the risk associated with different imaging modalities in children.

COMPUTERIZED TOMOGRAPHY

As access to quality CT has increased, the number of CTs done nationally has rapidly increased.[2,3] Thus, the number of CTs done to evaluate the pediatric patient has increased dramatically, reportedly up 800% since the 1980s.[4] Brenner et al reported that the number of abdominal and pelvic CTs in children younger than 15 years increased 92% between 1996

0022-5347/10/1836-2137/0
THE JOURNAL OF UROLOGY®

Vol. 183, 2137-2142, June 2010
Printed in U.S.A.
DOI:10.1016/j.juro.2010.02.2384

and 1999 alone.[5] Although CT represents only 5% of imaging studies in the pediatric population, it provides more than 40% of the radiation exposure.[6] A factor explaining the increased use of CT in pediatric patients is the advent of helical CT, which obtains accurate imaging so rapidly that sedation is not routinely required.[1,5,7] In conventional radiography an increased radiation dose leads to radiograph overexposure and is readily identifiable. Conversely CT has a wide range of technical variables that can change the radiation dose in the patient but may not affect image quality.[8] The table lists estimated radiation doses of various imaging modalities.[9–11]

The principal concern about ionizing radiation delivered during CT is potential carcinogenesis from direct damage to DNA strands.[12] In children the effects are more concerning due to relatively higher organ doses of radiation at each examination and longer life expectancy during which malignancy can arise.[5] Since more cells are actively dividing in children, they are more sensitive to radiation effects.[2] Based on these factors Brenner et al determined the risk of fatal malignancy caused by exposure to ionizing radiation in pediatric patients.[5] They obtained estimates of the risks of radiation induced lifetime cancer mortality from the National Academy of Sciences Biological Effect of Ionizing Radiation committee and the International Commission on Radiological Protection, and multiplied the age based risk of cancer mortality per radiation dose to each organ by group estimates of the age specific dose to the same organ. This produced organ specific estimates of cancer mortality risk based on age and examination. They concluded that a single abdominal CT in a 1-year-old child would result in 1 CT related death per 550 scans. Also, in the United States the combined annual head and abdominal CTs in patients younger than 15 years would result in approximately 480 cancer related deaths with a total number of deaths at all ages estimated at 2,500. Of all CT related potential deaths this accounted for approximately 20% of the total mortality (480 of 2,500) while accounting for only 4% of the total CTs done. For study purposes Brenner et al used adult CT settings, which can provide up to 50% more exposure than suggested pediatric settings. The basis of their choice related to the lack of implementation of pediatric settings at most hospitals at the time of study publication.

Estimated radiation doses[9–11]

Body Area Imaged	Effective Dose (mSv)	Equivalent Chest X-Ray (mSv)
5-Yr-old child:		
Annual Denver, CO natural background	3.5	175
2-View chest	0.02	1
Anteroposterior + lat abdomen	0.05	2.5
^{99m}Tc radionuclide cystogram	0.18	9
Fluoroscopic cystogram	0.33	16
Chest CT	3	150
Head CT	4	200
Abdomen CT	5	250
Adult:		
Renogram	1.8–3.3	90–165
Excretory urography	3	150

In 2007 Brenner and Hall provided additional theoretical insight into the consequences of ionizing radiation from CT in patients in regard to cancer risk.[13] They extrapolated data gathered from prospective studies in survivors of the atomic bombs dropped on Japan in 1945, and compared their exposure and cancer rates to those of CT exposure. For instance, they estimated that a 5-year-old child who underwent CT of the abdomen would be at about 1% lifetime risk of death from cancer. They also estimated that at the current rate of CT 1.5% to 2% of all cancers in the United States would be attributable to CT. However, in response to this article some members of the radiological community thought that the assumptions made when comparing bomb survivors to patients, namely the linear no threshold extrapolation model, exaggerated the CT risk.[14] This model, which is based on well-founded studies of the effects of high radiation doses and cancer risk, claims that the effects are linearly proportional even at small doses and even the smallest radiation dose has a small potential to increase cancer risk.[8]

Other than comparative studies, there is a lack of data on experimental laboratory animals or humans showing a direct connection between the low dose exposure of CT and cancer.[14] A 15-country study of more than 400,000 radiation workers who received low levels of radiation exposure during long periods showed a statistically significant association between radiation dose and cancer mortality.[15] However, analysis of 31 specific cancer types revealed that only lung cancer was statistically increased with radiation exposure. Potential confounding by smoking or exposure to other carcinogens was not addressed since the data were not available.

Sound epidemiological data would be widely accepted as a measure of cancer risk but this is not possible. For instance, the general population is at 1/5 lifetime risk of cancer. The potential risk of cancer due to exposure to ionizing radiation during CT in an adult is thought to be around 1/5,000. A study proving an increased risk of cancer above what is already a significant baseline risk would require thousands if not millions of patients to be definitive.[8]

Regardless of the studies, it is known that children who undergo radiographic examination are potentially at higher risk for consequences due to radiation exposure than adults. To prevent unnecessary overexposure to patients the ALARA concept[16] has been widely adopted. As a radiation safety philosophy, ALARA is applicable to all forms of ionizing radiation and attempts to limit radiation exposure as much as can be accomplished while still obtaining the images required for diagnosis and treatment. Obtaining the required information without ionizing radiation would be the ultimate success of the ALARA concept. ALARA has been helpful in motivating discussions on decreasing radiation exposure and advocating new technology.

To increase awareness the multidisciplinary Alliance for Radiation Safety in Pediatric Imaging group was formed. Focusing mainly on educating radiologists and radiation technologists, the group launched the Image Gently campaign (http://www.imagegently.org).[4,17] They developed 4 messages to convey to their audience. 1) They advocate decreasing the amount of radiation used during imaging to a more appropriate quantity. 2) They recommend imaging only when necessary. 3) They advocate limiting the scan to only the area under investigation. 4) They encourage limits to multiphase imaging, which results in repeat scans for 1 study that may not add additional significant information. Regardless of the suspected risk it is evident that CT in the pediatric population has become more common. This has resulted in more rapid, more accurate imaging, which hopefully leads to better outcomes in these children.

VOIDING CYSTOURETHROGRAM

Radiographic and fluoroscopic imaging, such as plain x-ray of the kidneys, ureters and bladder or VCUG, is not exempt from scrutiny since it comprises almost 90% of the pediatric imaging burden.[18,19] Studies to determine the effects of radiation exposure in pediatric patients during VCUG have been done for almost 30 years. As early as 1979, groups of researchers showed concern for the exposure level during these examinations. Seppänen et al estimated that almost 25% of genetically significant radiation to children was provided during urological evaluation.[20] They went on to estimate the dose of gonadal radiation received during excretory urography and micturition cystourethrography. Using ionization chamber dosimeters they found that the total genetic risk would be 9 to 60 genetic deaths per 10 million children examined. They also determined that 7 to 9 cases of leukemia would occur in each 10 million children examined. Since the time of that study, the advent of digital fluoroscopy has decreased the radiation exposure delivered during VCUG. Digital fluoroscopes have greater sensitivity in the imaging system as well as special factors that decrease mA seconds during the examination.[21] Cleveland et al evaluated decreased exposure using digital fluoroscopy for VCUG.[21] Using child-sized phantoms they estimated that digital fluoroscopy decreased the radiation dose by almost 50% compared to 105 mm films.

Advances in fluoroscopic technology have not stopped with image digitalization. Pulsed fluoroscopy offers a new method of dose reduction by limiting exposure duration in each patient.[19] Earlier fluoroscopes used continuous fluoroscopy producing 30 image frames per second.[22] The advent of VRPFL allowed the radiologist to alter the pulse of the x-ray beam, increasing image sharpness and potentially decreasing radiation exposure.[22] Ward et al quantified the decrease in radiation exposure using VRPFL.[22] In a porcine model of pediatric vesicoureteral reflux they compared exposures at varying cross-sectional widths and found that pulsed fluoroscopy resulted in 4.6 to 7.5 times decreased radiation exposure depending on animal girth. They also retrospectively compared radiation exposure in pediatric patients who underwent VCUG with continuous fluoroscopy or grid controlled VRPFL and noted 8 to 10-fold decreased radiation exposure in those imaged by VRPFL.[23] As technology continues to advance, achieving ALARA will hopefully become easier. In the future it may become feasible to study children without exposure to ionizing radiation. Some studies comparing Doppler ultrasound to VCUG have provided comparable results, as described.[24,25]

NUCLEAR MEDICINE APPLICATIONS

Currently there is limited information on radiation exposure during nuclear medicine studies, particularly nuclear cystography. Nuclear renography is the current standard imaging modality to estimate renal function, diagnose urinary obstruction and evaluate renal scaring due to pyelonephritis. Nuclear cystography serves as an alternative to VCUG in children with vesicoureteral reflux. Understanding the potential effects of radiation exposure from these tests would help clinicians make better clinical decisions and assist with patient and parent counseling. Studies in adults showed that renography provides an effective dose of between 1.8 and 3.3 mSv.[11] In comparison the average yearly background radiation exposure in an adult is about 3 mSv. While the studies show administered doses of 370 MBq in adults, recommended administered doses in children begin at 37 MBq and increase based on weight.[26,27] Further complicating comparisons are reports that at institutions doses are decreased to as low as 5 MBq (effective dose 0.04 mSv) to decrease radiation exposure.[28] Exposure levels during nuclear renography are low but concern arises due to adult models of well functioning kidneys with hydronephrosis or obstruction that result in increased absorbed doses 5 to 40 times greater than normal.[29]

ALTERNATIVE STUDIES

Ultrasound

Monitoring vesicoureteral reflux requires VCUG or radionuclide cystography, which results in radiation exposure. An alternative has been contrast enhanced voiding urosonography. In 1 series echo enhancement by the microbubble compound SH U 508 A was used to evaluate 188 patents.[24] Patients with microbubbles located in the upper tracts were considered to have reflux. Patients were catheterized, the bladder was filled with saline to determine bladder capacity and saline was replaced with microbubble solution. When comparing echo enhanced ultrasound to VCUG, there was 92% concordance in results. The group concluded that SH U 508 A enhanced voiding ultrasound would be an acceptable alternative to VCUG. Since then, Darge reviewed the urosonography literature and found that almost each study yielded greater than 90% diagnostic accuracy when comparing contrast enhanced ultrasound to VCUG.[30] While contrast enhanced voiding urosonography appears to be a promising technique to assess reflux without radiation, the contrast agents have yet to be approved by the Food and Drug Administration, preventing any widespread implementation. Also, this modality does not image the urethra and, thus, it would be most appropriate for followup studies or a first examination in girls.

Avoiding patient catheterization helps decrease patient discomfort during reflux evaluation. Color flow Doppler ultrasound has been evaluated to identify reflux and it does not require catheterization or instillation of enhancement material. Oak et al compared color flow Doppler to VCUG in 36 patients, in whom result concordance was found in 86%.[25] Oak et al thought that ultrasound was a reliable, less invasive alternative than VCUG to monitor reflux. In a subsequent study in 35 patients with a mean age of 7.1 years Koşar et al found 90% sensitivity and 93% specificity for color flow Doppler compared to VCUG.[31] However, a lack of large, confirmatory prospective studies along with nonstandardized technique, operator dependence and suboptimal anatomical resolution has limited the widespread use of color flow Doppler ultrasound to detect or manage reflux.

Magnetic Resonance Imaging

MRI, developed more than 30 years ago as a powerful body imaging modality, has become an alternative to CT. Since its inception several advances in technique have been made, including the development of contrast materials that are excreted into the urinary system. Using gadolinium excretory MRI or MRU can be done. MRU can provide structural and functional information. Three-dimensional reconstruction with evaluation of split renal function and drainage is available.[32] Most importantly imaging is done without exposure to ionizing radiation. There is an association between gadolinium exposure in patients with renal failure and nephrogenic systemic fibrosis but contrast material can be administered in patients allergic to iodinated contrast medium.[32]

A comparative study of ultrasound, nuclear imaging and MRI in patients with hydronephrosis by Perez-Brayfield et al showed that MRI provides superior anatomical detail and comparable functional information.[33] The anatomical detail provided by MRU can be beneficial to evaluate hydronephrosis and renal scarring but it is not yet appropriate in patients with vesicoureteral reflux or nephrolithiasis.[32] Other drawbacks to MRU are its high cost and the requirement of sedation to ensure good image quality and decrease motion artifact. Ultimately MRU will be another valuable tool to evaluate pediatric urology patients but it still requires further advancement before widespread implementation.

Renal Trauma Special Situation

Improvements in imaging, particularly CT, have allowed a change in management plans for various conditions. This certainly pertains to renal trauma, for which imaging has advanced diagnosis and enabled more conservative management for renal injury. However, a balance between limiting radiation exposure and obtaining high quality imaging must be achieved. This balance makes the ALARA concept challenging to investigate or bring into practice. Recently Eeg et al evaluated the efficacy of serial imaging for stable renal trauma by ultrasound rather than CT.[34] They retrospectively reviewed their trauma database and identified 71 children treated for blunt renal trauma with a mean injury grade of 2.4. Of these children only 11 required repeat CT, of whom only 2 underwent repeat CT for urological evaluation. The remaining patients were followed by ultrasound. No complications or delayed diagnoses were identified in this cohort. Eeg et al concluded that ultrasound was an appropriate followup study in stable patients with renal trauma that would potentially result in decreased unnecessary radiation exposure.

CONCLUSIONS

Concern for ionizing radiation exposure in pediatric patients continues to increase. As a group of specialists who rely heavily on imaging for common ailments, pediatric urologists face the responsibility of understanding the risks associated with imaging and the appropriate justification for studies. As a liaison between radiologist and parents, the urologist should also be able to explain the possible risks and alternatives to the patient family. The Image Gently website can serve as a starting point for any urologist who may want additional information on pediatric imaging safety. It also provides publications outlining methods to discuss the risks and benefits of imaging with parents along with free informational handouts.[35,36]

Additional concern from the pediatric urologist should come from knowing that many conditions that lead to early studies with ionizing radiation are chronic and require repeat imaging throughout the patient life. Particularly children who are chronic stone formers can expect to have several more episodes of stone disease throughout life. Although preventing stone episodes is ideal, many patients ultimately go on to repeat surgical intervention. In a British study in adults followed primarily without CT John et al noted that an average stone episode resulted in 5.3 mSv of radiation exposure.[37] They also observed that patients requiring CT had even higher average exposure. Following patients with ultrasound or conventional radiography when appropriate would help decrease unnecessary radiation exposure.

Collaboration with radiologists would ensure that imaging requests are appropriately obtained and alternative studies are not available. Also, practitioners with office based imaging should be fully aware of the mechanics of the machines used and any possible available dose reducing measures. Discussing technical parameters with product experts can greatly increase the urologist understanding of equipment use before studies are performed.

Imaging resulting in radiation exposure will continue to be an invaluable tool for diagnosing and treating pediatric urology conditions. Avoiding a study that is clearly indicated is not justified by concerns of radiation exposure and does not follow recommendations from the Image Gently campaign. In the end it is our responsibility as clinicians to ensure that the health and safety of each patient remain the focus of our efforts as we continually learn more about the implications of ionizing radiation.

REFERENCES

1. Donnelly LF: Lessons from history. Pediatr Radiol 2002; **32:** 287.
2. Brenner DJ: Estimating cancer risks from pediatric CT: going from the qualitative to the quantitative. Pediatr Radiol 2002; **32:** 228.
3. Mettler FA Jr, Wiest PW, Locken JA et al: CT scanning: patterns of use and dose. J Radiol Prot 2000; **20:** 353.
4. Goske MJ, Applegate KE, Boylan J et al: The 'Image Gently' campaign: increasing CT radiation dose awareness through a national education and awareness program. Pediatr Radiol 2008; **38:** 265.
5. Brenner D, Elliston C, Hall E et al: Estimated risks of radiation-induced fatal cancer from pediatric CT. AJR Am J Roentgenol 2001; **176:** 289.
6. Frush DP, Donnelly LF and Rosen NS: Computed tomography and radiation risks: what pediatric health care providers should know. Pediatrics 2003; **112:** 951.
7. White KS: Invited article: helical/spiral CT scanning: a pediatric radiology perspective. Pediatr Radiol 1996; **26:** 5.
8. Brody AS, Frush DP, Huda W et al: Radiation risk to children from computed tomography. Pediatrics 2007; **120:** 677.
9. Rice HE, Frush DP, Farmer D et al: Review of radiation risks from computed tomography: essentials for the pediatric surgeon. J Pediatr Surg 2007; **42:** 603.
10. Brody AS, Frush DP, Huda W et al: Radiation risk to children from computed tomography. Pediatrics 2007; **120:** 677.
11. Mettler FA Jr, Huda W, Yoshizumi TT et al: Effective doses in radiology and diagnostic nuclear medicine: a catalog. Radiology 2008; **248:** 254.
12. Hall EJ: Radiation biology for pediatric radiologists. Pediatr Radiol, suppl., 2009; **39:** S57.
13. Brenner DJ and Hall EJ: Computed tomography—an increasing source of radiation exposure. N Engl J Med 2007; **357:** 2277.
14. Tubiana M: Computed tomography and radiation exposure. N Engl J Med 2008; **358:** 850.
15. Cardis E, Vrijheid M, Blettner M et al: The 15-Country Collaborative Study of Cancer Risk among Radiation Workers in the Nuclear Industry: estimates of radiation-related cancer risks. Radiat Res 2007; **167:** 396.
16. Strauss KJ and Kaste SC: The ALARA (as low as reasonably achievable) concept in pediatric interventional and fluoroscopic imaging: striving to keep radiation doses as low as possible during fluoroscopy of pediatric patients—a white paper executive summary. Pediatr Radiol 2006; **36:** 110.
17. Goske MJ, Applegate KE, Boylan J et al: The Image Gently campaign: working together to change practice. AJR Am J Roentgenol 2008; **190:** 273.
18. Frush DP: Introduction: the role of the pediatric radiologist in dose reduction. Pediatr Radiol 2002; **32:** 285.
19. Hernanz-Schulman M: Science to practice: can fluoroscopic radiation dose be substantially reduced? Radiology 2006; **238:** 1.
20. Seppänen U, Torniainen P and Kiviniitty K: Radiation gonad doses received by children in intravenous urography and micturition cysto-urethrography. Pediatr Radiol 1979; **8:** 169.
21. Cleveland RH, Constantinou C, Blickman JG et al: Voiding cystourethrography in children: value of digital fluoroscopy in reducing radiation dose. AJR Am J Roentgenol 1992; **158:** 137.
22. Ward VL, Barnewolt CE, Strauss KJ et al: Radiation exposure reduction during voiding cystourethrography in a pediatric porcine model of vesicoureteral reflux. Radiology 2006; **238:** 96.
23. Ward VL, Strauss KJ, Barnewolt CE et al: Pediatric radiation exposure and effective dose reduction during voiding cystourethrography. Radiology 2008; **249:** 1002.
24. Darge K, Troeger J, Duetting T et al: Reflux in young patients: comparison of voiding US of the bladder and retrovesical space with echo enhancement versus voiding cystourethrography for diagnosis. Radiology 1999; **210:** 201.

25. Oak SN, Kulkarni B and Chaubal N: Color flow Doppler sonography: a reliable alternative to voiding cystourethrogram in the diagnosis of vesicoureteral reflux in children. Urology 1999; **53:** 1211.

26. Conway JJ and Maizels M: The "well tempered" diuretic renogram: a standard method to examine the asymptomatic neonate with hydronephrosis or hydroureteronephrosis. A report from combined meetings of The Society for Fetal Urology and members of The Pediatric Nuclear Medicine Council—The Society of Nuclear Medicine. J Nucl Med 1992; **33:** 2047.

27. Sfakianakis GN, Sfakianaki E, Georgiou M et al: A renal protocol for all ages and all indications: mercapto-acetyl-triglycine (MAG3) with simultaneous injection of furosemide (MAG3-F0): a 17-year experience. Semin Nucl Med 2009; **39:** 156.

28. Ritchie G, Wilkinson AG and Prescott RJ: Comparison of differential renal function using technetium-99m mercaptoacetyltriglycine (MAG3) and technetium-99m dimercaptosuccinic acid (DMSA) renography in a paediatric population. Pediatr Radiol 2008; **38:** 857.

29. Nikiforidis G, Karatrandou A and Vassilakos P: In vivo determination of radiation dose in kidneys and bladder during renogram: a new approach. Nucl Med Commun 1993; **14:** 611.

30. Darge K: Voiding urosonography with US contrast agents for the diagnosis of vesicoureteric reflux in children. II. Comparison with radiological examinations. Pediatr Radiol 2008; **38:** 54.

31. Koşar A, Yeşildağ A, Oyar O et al: Detection of vesico-ureteric reflux in children by colour-flow Doppler ultrasonography. BJU Int 2003; **91:** 856.

32. Cerwinka WH, Damien Grattan-Smith J and Kirsch AJ: Magnetic resonance urography in pediatric urology. J Pediatr Urol 2008; **4:** 74.

33. Perez-Brayfield MR, Kirsch AJ, Jones RA et al: A prospective study comparing ultrasound, nuclear scintigraphy and dynamic contrast enhanced magnetic resonance imaging in the evaluation of hydronephrosis. J Urol 2003; **170:** 1330.

34. Eeg KR, Khoury AE, Halachmi S et al: Single center experience with application of the ALARA concept to serial imaging studies after blunt renal trauma in children—is ultrasound enough? J Urol 2009; **181:** 1834.

35. Bulas D, Goske M, Applegate K et al: Image Gently: improving health literacy for parents about CT scans for children. Pediatr Radiol 2009; **39:** 112.

36. Bulas DI, Goske MJ, Applegate KE et al: Image Gently: why we should talk to parents about CT in children. AJR Am J Roentgenol 2009; **192:** 1176.

37. John BS, Patel U and Anson K: What radiation exposure can a patient expect during a single stone episode? J Endourol 2008; **22:** 419.