Radiation exposure in adult and pediatric patients with osteogenesis imperfecta[☆]

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ABSTRACT

Diagnostic radiographs, computed tomography (CT), nuclear medicine studies, and intraoperative fluoroscopy durations were analyzed for radiation exposure. Cumulative and yearly effective ionizing radiation doses, cumulative background radiation, and total radiograph studies were compared between pediatric and adult populations. In 24 patients with 1,246 imaging studies (average 5.5 years longitudinal treatment duration), the mean estimated cumulative effective radiation dose per patient was 30.0 mSv (range 2.3–115.0), with an average yearly dose of 4.9 mSv (range 0.4–24.8). Pediatric patients had significantly more radiograph studies per year than adults and greater average yearly effective radiation doses.

1. Introduction

Osteogenesis imperfecta is the most common inheritable disease that leads to bone fragility. Occurring in 1 in 5,000 to 1 in 10,000 births, OI can lead to errors in collagen folding, processing, stability, and production.^{1,2} Patients with OI are at increased risk of fracture as well as growth retardation, hearing loss, communicating hydrocephalus, and seizures.^{3,4} Effective management of OI requires frequent imaging studies, including CT scans, diagnostic radiographs, intraoperative fluoroscopic radiographs, and nuclear medicine studies. Because of frequent fractures and the need for skeletal surveillance, patients with OI are subjected to high levels of ionizing radiation.^{5–7}

Radiation exposure is associated with the development of thyroid cancer, breast cancer, brain cancer, and leukemia. The radiation dosage of any one study is unlikely to increase the risk of cancer development; the radiation of the imaging studies has an additive effect.^{8–10} Although the radiation of any single imaging examination may be low, the radiation has a cumulative effect over years of skeletal surveillance.¹¹ Additionally, younger children are at a higher risk of developing complications due to ionizing radiation because they still have active growth centers and they have a longer life expectancy, meaning they have a longer time to accumulate radiation exposure.^{11,12}

As awareness of the effects of pediatric radiation exposure has

increased, attempts have been made to minimize pediatric exposure to ionizing radiation by avoiding unnecessary imaging.^{13,14} The purpose of this study was to quantify and evaluate the longitudinal cumulative and yearly effective ionizing radiation exposure, frequency of radiograph procedures, and cumulative background radiation in adults and pediatric populations undergoing treatment for OI. Information from this study could be helpful in reducing the dosage and frequency of radiographic studies and decreasing ionizing radiation exposure.

2. Materials and methods

After Institutional Review Board approval, data were collected from medical records at an urban pediatric Level-1 trauma center and four surrounding outpatient clinics. Patients with OI were identified using ICD-9 codes (756.51). Patients with a confirmed diagnosis of OI were included if they had radiograph studies performed and a minimum longitudinal treatment duration of 2 months. All radiographic imaging studies of patients who were treated for OI between September, 2002, and December, 2014, were reviewed. Longitudinal treatment duration for each patient was defined individually from the date of the first medical imaging study to the last recorded imaging study date. Medical imaging studies, including CT scans, diagnostic radiographs, intraoperative fluoroscopic radiographs, and nuclear medicine studies

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related to the treatment of OI, were collected for each patient. Imaging studies for evaluation and treatment of conditions other than OI were excluded.

Effective ionizing radiation dose estimates were measured in millisieverts (mSv) and calculated based on reference values for each radiograph and CT scan specific to each patient's age group. Because there are no established reference values for pediatric patients, the Sievert (Sv) scale was used. This is the International System of Units (SI) unit of dose equivalent radiation which attempts to quantitatively evaluate the biological effects of ionizing radiation as opposed to simply indicating the absorbed dose of radiation energy, which is measured in gray (Gy) ($1 \text{ Gy} = 1 \text{ Sv} = 1 \text{ J/kg}$). For the fluoroscopic radiographs obtained during surgery, information about the amount of radiation designated to a specific surgical procedure was recorded by the radiology technician, because at the end of each procedure the fluoroscopy machine provides the cumulative dose of ionizing radiation in mSv based on a ratio of time and technique (kilovolt [kV] and milliampere [mA]). In regards to intraoperative fluoroscopic radiation, radiation doses were recorded for each procedure by a radiology technician after the procedure once the fluoroscopy machine provided the cumulative dose of ionizing radiation in mSv based on a ratio of time and technique (kV and mA).

Patients were divided based on age during treatment duration. The pediatric population included all patients who were younger than 18 years for their entire treatment duration, and the adult population included all patients who were 18 years old or older for the entirety of their treatment. For patients who spanned pediatric and adult age groups at any point during treatment duration, that individual's specific data as a pediatric patient and an adult patient were analyzed separately.

Results were calculated as total effective radiation dose during treatment, total number of imaging studies, background radiation, and effective ionizing radiation dose per year for pediatric and adult groups. All groups were analyzed using D'Agostino and Pearson omnibus tests for normality, F-tests to compare variances, and subsequent unpaired t-tests or linear regression analyses.

3. Results

Twenty-four patients met study inclusion criteria and had complete records for review. The average age of subjects in the study was 10 years (range, birth to 56 years), with an average follow-up of 5.5 years (range, 4 months to 12 years) and average study endpoint age of 16 years (range, 6 months to 58 years). Of the 24 patients, 15 were male and 9 were female; 15 were exclusively pediatric patients, 5 were exclusively adult patients, and 4 contributed both pediatric and adult data. The total number of radiographic studies performed on the 24 patients was 1,246 with a mean of 8.8 radiographs per year and 44.5 cumulatively. The average cumulative radiation dose per patient was 30.0 mSv (range 2.3–115.0).

Pediatric OI patients had significantly more radiograph procedures overall and per year (Fig. 1 and Fig. 2), but this difference did not translate to a significantly greater cumulative radiation exposure. Pediatric OI patients had a total of 1098 radiographic studies and adult patients had a total of 148. The pediatric patients received an average of 57.8 radiographs per patient, which was significantly more than the adult patients, who received an average of 16.4 radiographs per patient ($p = 0.0055$). Pediatric and adult OI patients received an average of 11.4 and 3.4 radiographs per year, respectively ($p = 0.011$).

While pediatric patients with OI did have greater radiation doses cumulatively and per year, these differences were not significant (Fig. 3 and Fig. 4). The total cumulative effective dose of radiation accrued by the pediatric OI patients was 630.6 mSv, and the adult cumulative effective radiation dose was 208.7 mSv. Pediatric patients had an average cumulative radiation exposure of 40.5 mSv, and adult patients averaged 28.3 mSv ($p = 0.42$); average radiation doses per year were 5.5 mSv

and 3.7 mSv for pediatric and adult patients, respectively ($p = 0.22$).

Effective radiation dose per year was variable for pediatric patients, ranging from 13.69 mSv to 0.38 mSv, without a significant correlation between age and yearly effective radiation dose. Linear regression of effective radiation dose per year by patient age yielded an R^2 value of 0.00015 and did not demonstrate a significant deviation from zero (Fig. 5). Conversely, for patients above the age of 18 years, there was a significant correlation between age and effective radiation dose. The yearly radiation dose in adult OI patients ranged from 0.59 mSv to 8.90 mSv per year, with older patients receiving less radiation than younger patients. In adult OI patients, there was a negative correlation between age and yearly radiation dose (R^2 value = 0.43; $p = 0.028$).

4. Discussion

Ionizing radiation is a well-known carcinogen, and among the most vulnerable to the effects of ionizing radiation are children.^{12–15} The particular sensitivity of children to ionizing radiation exposure is multifocal. A longer life expectancy with a resultant increased likelihood of repeated and compounding radiation damage and a relatively longer time frame in which to develop complications contribute to the vulnerability of younger patients exposed to ionizing radiation.¹⁶ Damage to the DNA molecule is the primary cause of the biological effects of ionizing radiation, and, because the rate of cell division and tissue growth is greater in children than in adults, children are at higher risk of developing complications of radiation exposure.^{17,18} While pediatric patients received a significantly higher number of radiographic studies per year and cumulatively, this difference did not translate to a significantly higher cumulative radiation dose. This result was possibly due to protocols used by many pediatric practitioners and children's hospitals that preferably use lower radiation studies for pediatric patients.¹⁹ Pediatric patients did not show a consistent relationship between age and number of radiographic procedures and cumulative radiation dose. It is possible that several factors contribute to the decrease in number of radiograph studies with age in adult OI patients. OI patients surviving into adulthood are more likely to have milder variations of the disease, making them less susceptible to minor trauma and fracture.^{1–3,20} Additionally, adult patients with OI often learn to live with their disease by participating in fewer activities that have an associated fracture risk, leading to a lower fracture rate and a lower rate of radiation exposure.^{1,20} They also may learn how to manage simple fractures without seeking healthcare for each minor injury.

In a retrospective cohort study, Pearce et al.²¹ followed patients under the age of 22 years without previous cancer diagnoses who had received radiation exposure from CT scans for the development of leukemia and brain cancer. Compared with patients who received a dose of less than 5 mGy, the relative risk of leukemia for patients who received a cumulative dose of at least 30 mGy was 3.18 and the relative risk for brain cancer for patients who received a cumulative dose greater than 50 mGy was 2.82. The levels of low-dose radiation from medical imaging procedures are defined as low-moderate (3–5 mGy), moderate (3–20 mGy), high (20–50 mGy), or very high (more than 50 mGy), with low-moderate being the radiation exposure of an average person.²² The threshold exposures identified for development of leukemia and brain cancer by Pearce et al. qualify as high and very high. Our patients received an average of 33.7 mGy per year, which qualifies as high level exposure and in the range of increased risk for the development of leukemia.^{21,22}

Limitations of this study include the calculations used for determining radiation exposure using established values for plain radiographs, computed tomography, ventilation-perfusion studies, and swallowing studies for an adult population since values for children have not yet been defined. Using adult values may have resulted in an overestimation of the amount of ionizing radiation for our pediatric population; however, using the standard values allow comparisons among studies that use the same radiation exposure scales. These values

Osteogenesis Imperfecta Adult vs Pediatric Cumulative Radiograph Procedures

Table Analyzed	Total xrays
Column A	Adult
vs	vs
Column B	Pediatric
Unpaired t test	
P value	0.0111
P value summary	*
Are means signif. different? (P < 0.05)	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=2.736 df=26

Fig. 1. Comparison of total numbers of radiographic procedures in pediatric and adult populations with osteogenesis imperfecta.

OI Adult vs Pediatric Radiograph Studies per year

Table Analyzed	xrays per yr
Column A	adult
vs	vs
Column B	pediatric
Unpaired t test	
P value	0.0025
P value summary	**
Are means signif. different? (P < 0.05)	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=3.348 df=26

Fig. 2. Comparison of total numbers of radiograph procedures each year in pediatric and adult populations with osteogenesis imperfect.

Osteogenesis Imperfecta Adult vs Pediatric Cumulative Radiation Exposure

Table Analyzed	Cumulative Radiation
Column A	Adults
vs	vs
Column B	Pediatric
Unpaired t test	
P value	0.4179
P value summary	ns
Are means signif. different? (P < 0.05)	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.8231 df=26

Fig. 3. Comparison of cumulative ionizing radiation in pediatric and adult populations with osteogenesis imperfect.

are widely used because of the differences in regional tissue exposure, differences between beam source, and general difficulty in measuring the exact amount of radiation exposure for each study. Further limitations include a small sample size. Because OI is a rare condition, it would likely be necessary to expand the project to other centers to increase sample size. Our project focused on two distinct patient groups, pediatric and adult patients with OI. It may be of value in future projects to examine ionizing radiation exposure and number of radiograph studies by age as a continuous variable. Additionally, as awareness increases regarding the risks of repeated imaging procedures in the pediatric population, many institutions have adopted measures to reduce radiation exposure and optimize imaging for pediatric

patients.^{19,23}

5. Conclusions

Awareness of radiation exposure from imaging techniques and effects of ionizing radiation exposure in the pediatric population is imperative to the reduction of radiation exposure. Several techniques aid in reducing radiation exposure when imaging is indicated. Taking care to image only involved areas, using lower radiation studies, such as plain radiographs instead of computed tomography, and using low-dose radiation devices and non-radiation based techniques, such as MRI and ultrasound, all aid in reducing cumulative radiation dose.^{19,23} The

Table Analyzed	mSv per yr
Column A	adult
vs	vs
Column B	pediatric
Unpaired t test	
P value	0.2209
P value summary	ns
Are means signif. different? (P < 0.05)	No
One- or two-tailed P value?	Two-tailed
t, df	t=1.254 df=26

Fig. 4. Comparison of average effective ionizing radiation received each year in pediatric and adult populations with osteogenesis imperfecta.

Goodness of Fit	
R square	0.0001525
Sy.x	3.768
Is slope significantly non-zero?	
F	0.001677
DFn, DFd	1.000, 11.00
P value	0.9681
Deviation from zero?	Not Significant

Fig. 5. Linear regression of average effective ionizing radiation doses received each year according to age of subject.

number of radiographic studies per year was significantly higher in the pediatric population, so care must be taken to image only when appropriate. Although necessary imaging studies should not be delayed when strongly indicated, imaging should be reserved for situation I in which the results of imaging will affect the course of management.^{7,22} The risk and benefit of imaging studies must be considered, with the intention of minimizing radiation exposure in patients with OI.

Declarations of interestd

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jor.2019.03.008>.

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