Comparison of 0.3-mSv CT to Standard-Dose CT for Detection of Lung Nodules in Children and Young Adults With Cancer

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BACKGROUND. CT is the imaging modality of choice to identify lung metastasis.

OBJECTIVE. The purpose of this study was to evaluate the performance of reduced-dose CT for the detection of lung nodules in children and young adults with cancer.

METHODS. This prospective study enrolled patients 4–21 years old with known or suspected malignancy who were undergoing clinically indicated chest CT. Study participants underwent an additional investigational reduced-dose chest CT examination in the same imaging encounter. Separated deidentified CT examinations were reviewed in blinded fashion by three independent radiologists. One reviewer performed a subsequent secondary review to match nodules between the standard- and reduced-dose examinations. Diagnostic performance was computed for the reduced-dose examinations using the clinical examinations as the reference standard. Intraobserver agreement and interobserver agreement were calculated using Cohen kappa.

RESULTS. A total of 78 patients (44 male patients and 34 female patients; mean age, 15.2 ± 3.8 [SD] years) were enrolled. The mean estimated effective dose was 1.8 ± 1.1 mSv for clinical CT and 0.3 ± 0.1 mSv for reduced-dose CT, which is an 83% dose reduction. Forty-five of the 78 (58%) patients had 162 total lung nodules (mean size, 3.4 ± 3.3 mm) detected on the clinical CT examinations. A total of 92% of nodules were visible on reduced-dose CT. The sensitivity and specificity of reduced-dose CT for nodules ranged from 63% to 77% and from 80% to 90%, respectively, across the three reviewers. Intraobserver agreement between clinical CT and reduced-dose CT was moderate to substantial for the presence of nodules (κ = 0.45–0.67) and was good to excellent for the number of nodules (κ = 0.68–0.84) and nodule size (κ = 0.69–0.86). Interobserver agreement for the presence of nodules was moderate for both reduced-dose (κ = 0.53) and clinical (κ = 0.54) CT. A median of one nodule was present on clinical CT in patients with a falsely negative reduced-dose CT examination.

CONCLUSION. Reduced-dose CT depicts more than 90% of lung nodules in children and young adults with cancer. Reviewers identified the presence of nodules with moderate sensitivity and high specificity.

CLINICAL IMPACT. CT performed at a 0.3-mSv mean effective dose has acceptable diagnostic performance for lung nodule detection in children and young adults and has the potential to reduce patient dose or expand CT utilization (e.g., to replace radiography in screening or monitoring protocols).

TRIAL REGISTRATION. ClinicalTrials.gov NCT03681873

CT is the imaging modality of choice to diagnose and monitor lung metastasis in patients with cancer [1, 2]. Despite dramatic improvements in CT technology (e.g., automated tube current modulation, iterative and deep learning–based image reconstruction) and the success of campaigns such as Image Gently, CT is still considered to be a "high radiation dose" examination by referring clinicians, patients, and families [3]. This perception has the potential to drive avoidance or decreased utilization of CT.

Data are emerging that CT can be performed at doses approaching that of chest radiography with excellent diagnostic performance. However, most of the available stud-

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ies have been performed in adult populations or in phantoms or performed using simulated images [4–7]. In two simulation studies based on clinically acquired pediatric chest CT examinations, Li et al. [8, 9] both simulated a lower-dose technique by introduction of noise and simulated the presence of 3- to 5-mm nodules. By doing so, they showed that although nodule conspicuity was dependent on image noise, detection accuracy was only weakly related to simulated dose [8, 9].

To our knowledge, no direct comparative study of reduced-versus standard-dose chest CT has been performed in children, particularly related to the task of lung nodule detection. If shown to have satisfactory diagnostic performance, then reduced-dose CT could not only reduce patient radiation exposure, but also potentially replace or augment radiography in diagnostic paradigms.

The purpose of this study was to evaluate the diagnostic performance of reduced-dose chest CT for the detection of lung nodules in children and young adults with cancer.

HIGHLIGHTS

Key Finding

- *Among 78 children and young adults with cancer who underwent standard-dose chest CT and reduced-dose chest CT (mean effective dose, 0.3 ± 0.1 [SD] mSv [representing an 83% dose reduction]) in the same imaging encounter, the reduced-dose protocol detected more than 90% of lung nodules identified on the standard-dose examination.*

Importance

- *Reduced-dose CT has acceptable diagnostic performance for nodule detection in children and young adults with cancer and may facilitate expanded CT utilization in clinical protocols.*

Methods

This was an institutional review board–approved prospective HIPAA-compliant study designed to test the diagnostic performance of a reduced-dose CT technique for the detection of lung nodules in children and young adults with known or suspected malignancy. This study was registered on ClinicalTrials.gov (NCT03681873). Written informed consent was obtained from all study participants 18 years old or older or from a parent or guardian for participants younger than 18 years old. In addition, children 11–17 years old provided written assent to participate.

Between November 30, 2018, and August 31, 2020, patients 4–21 years old undergoing chest CT for a history of known or suspected malignancy at Cincinnati Children's Hospital Medical Center were recruited to undergo an additional investigational reduced-dose chest CT examination immediately after the clinically indicated CT examination. All enrolled patients underwent both the clinically indicated CT examination and the investigational reduced-dose CT examination. Patients were recruited until reaching a target sample size based on an a priori power calculation. Patients were invited to participate in the study only a single time over the study period.

CT examinations were performed on one of two CT scanners: an Aquilion One or Aquilion One Genesis, both manufactured by Toshiba Medical Systems (now, Canon Medical Systems). According to routine clinical practice, clinical CT protocols were acquired using the helical mode (pitch, 0.813) and optimized by weight. Patients weighing 15–70 kg were imaged at 100 kV, and patients weighing more than 70 kg were imaged at 120 kV. Images were initially acquired at 0.5-mm axial thickness. Tube current modulation was used for all examinations, and IV contrast material was used when clinically indicated. All clinical CT images were reconstructed using iterative reconstruction (Adaptive Iterative Dose Reconstruction [AIDR3D], Canon Medical Systems).

A reduced-dose CT technique was developed by imaging three adult cadavers (22.4-, 26.0-, and 27.2-cm effective diameters of the chest). Diagnostic confidence for visualization of lung detail and of vasculature (as a surrogate for lung nodules) on images from these cadavers was subjectively characterized by a single board-certified pediatric radiologist (A.T.T. with 8 years of experience) at different levels of dose reduction. Acquisition settings for the reduced-dose CT were developed for each CT scanner independently. For the Aquilion One Genesis, helical mode, pitch of 0.813, 100 kV, 40 mA, and 0.275-second rotation time were used. For the Aquilion One, helical mode, pitch of 0.813, 100 kV, 25 mA, and 0.35-second rotation time were used. The final reduced-dose protocols were built on the CT scanners, and the investigational reduced-dose CT examinations were performed by the clinical technologist performing the clinically indicated CT examination. No additional IV contrast material was administered for the reduced-dose CT examinations. All reduced-dose CT images were reconstructed using AIDR3D.

Patient Radiation Dose Estimates

Postacquisition patient dose estimations were performed using commercial dose-reporting software (Radimetrics v2.9b, Bayer). Radimetrics software uses a Cristy phantom library to estimate patient organ doses [10]. Each patient's CT examination was matched to a size-based phantom on the basis of a midvolume scan diameter. To calculate phantom organ doses, Radimetrics used previously calculated Monte Carlo simulations of various scanning protocols and of different CT scanners with different examination parameters. The volume CT dose index ($CTDI_{vol}$) values for each examination were used to scale the Monte Carlo phantom organ doses. Phantom organ doses were used to calculate population-based representative effective dose using tissue weighting factors published in Report 103 of the International Commission on Radiological Protection [11].

Image Review

The clinical and reduced-dose CT examinations were reformatted in the axial, coronal, and sagittal planes at 2-mm axial and 3-mm coronal and sagittal intervals (standard thicknesses for our clinical practice). The examinations were then separated, deidentified, and loaded in random order to a research version of our clinical PACS (Merge PACS, Merge Healthcare). Default PACS settings were established to display all images in lung windows to reduce unblinding related to the presence of IV contrast material. Deidentified examinations, including images in all three planes were reviewed by three board-certified pediatric

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radiologists (M.P.N., E.J.C., C.G.A., with 15, 20, and 22 years of experience, respectively), blinded to acquisition technique and to overall study purpose.

Reviewers were asked to review images only in lung windows and to report only lung nodules (i.e., not to report infection or masses [defined as lesions > 3 cm]). Reviewers reported the presence or absence of nodules, the number of nodules, and the size and location of each individual nodule. Reviewers also categorized nodules as definite nodules (possible metastasis), definite atelectasis (unlikely to reflect metastasis), or perifissural nodules (possible intrapulmonary lymph nodes). Reviewers were instructed to perform this categorization as they would in clinical practice, without further explicit criteria provided. For patients with more than 20 nodules, reviewers simply indicated the presence of more than 20 nodules without measuring or describing individual nodules in detail.

Reviewers recorded the image number for identified nodules. Annotations of the nodules were not stored on the images to avoid unblinding. Image numbers and nodule size were used to match nodules between observers and between examinations. Nodule matching between observers for the same examination required lobar concordance and an image number discrepancy of no more than two images in either direction. Nodule matching between examinations required lobar concordance and an image number discrepancy of no more than five images in either direction, allowing differences in breath-holding. For global assessment of the visibility of lung nodules on the reduced-dose CT examination, nodules detected on reduced-dose CT by any observer that met between-examination matching criteria were considered visible. Nodules identified on the clinical CT examination that could not be definitively matched to nodules reported by reviewers on the reduced-dose CT were secondarily reviewed on a nodule-by-nodule basis by a single observer (C.G.A.). This secondary review occurred after completion of the primary review and consisted of a side-by-side review of the clinical CT and reduced-dose CT to define the visibility of nodules on the reduced-dose CT. For this secondary review, nodules were classified as visible, poorly visible, or not visible on the reduced-dose CT.

Power Calculation

An a priori power analysis showed that a total of 78 enrolled patients would be required to detect a change in sensitivity and specificity from 0.7 to 0.9 with a power of 80% and a significance level of .05, assuming a 40% disease prevalence for pulmonary nodules in patients with cancer.

Statistical Analysis

Data were summarized using counts, percentages, medians, interquartile ranges, means, and SDs. For assessment of diagnostic performance, including sensitivity and specificity, the clinical CT examination, as interpreted by each individual reviewer, was considered the reference standard for nodule presence, size, and number. Nodules considered to reflect atelectasis by all reviewers who reported that nodule were not included in performance analyses because the focus of the study was metastatic disease. Analyses were performed twice: once inclusive of only nodules classified as definite by one or more reviewers and once inclusive of nodules classified as definite or as perifissural by all reviewers. Analyses of intraobserver agreement between clinical CT and reduced-dose CT examinations and of interobserver agreement for the same examination type (clinical CT or reduced-dose CT) were performed using the Cohen kappa statistic for the binary determination of nodules present or absent and the intraclass correlation coefficient (ICC) for the number of nodules and largest nodule per patient. To assess the effect of dose reduction on lung nodule detection, the difference in mean effective dose between the clinical CT and reduced-dose CT examinations was compared between examinations for which readers did and did not achieve intraobserver agreement.

Statistical analyses were performed using statistics software (MedCalc v20.009, MedCalc Software). Means were compared using *t* tests. Kappa coefficients were interpreted as follows: less than 0 to 0, poor agreement; 0.01–0.20, slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial; and 0.81–1, almost perfect [12]. ICCs were interpreted as follows: 0–0.39, poor; 0.40–0.59, fair; 0.60–0.74, good; and 0.75–1.0, excellent [13].

Results

A total of 81 patients were recruited. Of these patients, parental consent was not obtained for one patient, and two patients declined to participate due to the additional radiation exposure. Thus, the final study sample included 78 enrolled patients (44 male patients, 34 female patients; mean age, 15.2 ± 3.8 [SD] years; age range, 4.9–20.9 years) (Fig. 1). No enrolled patients were subsequently excluded. Demographic characteristics and clinical indications are detailed in Table 1. The most common known tumor types were Ewing sarcoma (*n* = 16) and osteosarcoma (*n* = 15). A total of 37 (47%) of the clinical CT examinations were performed using IV contrast material. An example of paired images in each of the three reconstruction planes is provided in Figure 2. Considering clinical CT as the reference standard, 45 (58%) patients had nonatelectatic lung nodules present, four of whom had more than 20 nodules. Mean nodule size on clinical CT was 3.4 ± 3.3 mm.

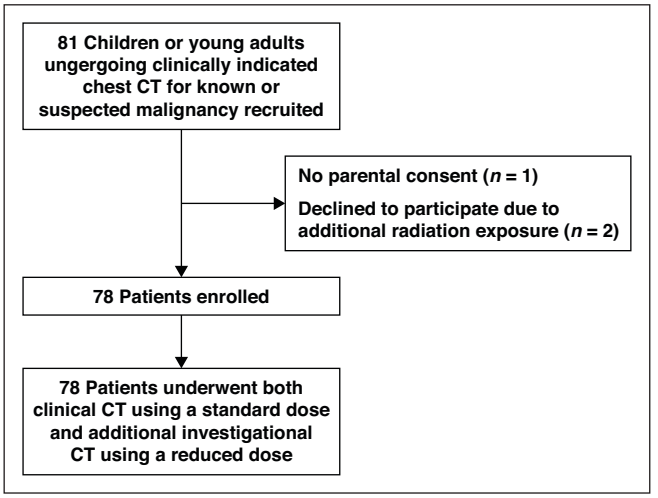


Fig. 1—Flow diagram shows process for selection of study cohort.

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TABLE 1: Study Cohort Characteristics

Characteristic	Value
Total no. of participants	78
Age (y), mean ± SD	15.2 ± 3.8
Age group	
4–5.99 y	2 (3)
6–7.99 y	2 (3)
8–9.99 y	4 (5)
10–11.99 y	11 (14)
12–13.99 y	9 (12)
14–15.99 y	11 (14)
16–17.99 y	19 (24)
18–19.99 y	13 (17)
20–20.99 y	7 (9)
Weight (kg), mean ± SD	60.2 ± 25.4
Sex	
Male	44 (56)
Female	34 (44)
Tumor type, no. of patients	
Ewing sarcoma	16
Osteosarcoma	15
Rhabdomyosarcoma	5
Papillary thyroid carcinoma	5
Germ cell tumor	5
Synovial cell sarcoma	4
Nasopharyngeal carcinoma	3
Wilms tumor	2
Neuroblastoma	2
Hepatocellular carcinoma	2
Squamous cell carcinoma	2
Carcinoma NOS	2
Other[a]	15
Clinical CT	
With IV contrast material	37 (47)
Without IV contrast material	41 (53)
Estimated effective dose (mSv), mean ± SD	
Clinical CT	1.8 ± 1.1
Reduced-dose CT	0.3 ± 0.1
Nonatelectatic lung nodules	
Present	45 (58)
Absent	33 (42)

Note—Unless indicated otherwise, values are reported as number of patients with percentages in parentheses. NOS = not otherwise specified.

[a]Multiple types of tumors, one patient for each of the following types: desmoid tumor, adamantinoma, chondroblastoma, chondrosarcoma, clear cell sarcoma, epithelioid hemangioendothelioma, fibrosarcoma, follicular thyroid carcinoma, pancreatic acinar cell carcinoma, pancreatic neuroendocrine tumor, pancreatoblastoma, renal cell carcinoma, round cell sarcoma, malignant melanoma, and sarcoma not otherwise specified.

CT Dose

The $CTDI_{vol}$ value for the reduced-dose CT examinations performed on the Aquilion One Genesis was 0.4 mGy and on the Aquilion One was 0.6 mGy. The mean estimated effective dose was 1.8 ± 1.1 mSv for the clinical CT examinations and 0.3 ± 0.1 mSv for the reduced-dose CT examinations, yielding an 83% reduction in mean dose (Fig. 3). Calculated organ doses are detailed in Supplemental Table 1, which can be viewed in the *AJR* electronic supplement to this article at www.ajronline.org.

Comparison of Reduced-Dose CT and Clinical CT for Intraobserver Agreement, Sensitivity, and Specificity

Intraobserver agreement for the presence of nodules was moderate (κ = 0.48–0.57) for all three reviewers when perifissural nodules were included (Table 2) and was moderate to substantial (κ = 0.45–0.67) when perifissural nodules were excluded (Table 2). Sensitivity and specificity relative to the reference standard clinical CT images are detailed in Table 2 and were similar for each reviewer whether perifissural nodules were included or excluded. Across reviewers, sensitivity ranged from 63% to 77%, and specificity ranged from 80% to 90%. Across reviewers, between 10 and 13 reduced-dose CT examinations were falsely negative for the presence of nodules when perifissural nodules were included, and between 9 and 12 reduced-dose CT examinations were falsely negative when perifissural nodules were excluded. A median of one nodule (range, one to five nodules) was present on clinical CT in patients with a falsely negative reduced-dose CT examination. Reduced-dose CT was falsely negative for all three reviewers in two patients when perifissural nodules were included and in one patient when perifissural nodules were excluded.

For each reviewer, the mean effective dose difference (clinical CT – reduced-dose CT) was not significantly different between pairs of examinations in which the reviewer agreed on the presence of any lung nodule versus pairs of examinations in which the reviewer did not agree ($p = .36$, $p = .93$, $p = .52$ for the three reviewers).

Intraobserver agreement for the number of nodules and nodule size was good to excellent for all three reviewers (Table 3). Specifically, when perifissural nodules were included, ICC was 0.68–0.84 for the number of nodules and 0.69–0.86 for the maximum diameter of the largest nodule. When perifissural nodules were excluded, ICC was 0.59–0.84 for the number of nodules and 0.69–0.88 for the maximum diameter of the largest nodule.

Interobserver Agreement

The interobserver agreement analysis is summarized in Table 4. For clinical CT, agreement between observers for the presence of any nodule was moderate (κ = 0.54) and for the number and size of nodules (among all nodules) was good (ICC = 0.66–0.72). For reduced-dose CT, agreement for the presence of any nodule was moderate (κ = 0.53) and for the number and size of nodules (among all nodules) was good (κ = 0.72–0.74).

Secondary Review of Nodules

A total of 162 individual nodules were identified across the clinical CT examinations. Four patients had more than 20 nodules, with those nodules not included in the count of 162 nodules. A total of 79 of 162 (49%) nodules were readily matched to nodules reported on the reduced-dose CT based on image number and nodule location reported by reviewers. The remaining 83 nodules underwent secondary review. On secondary review, 52

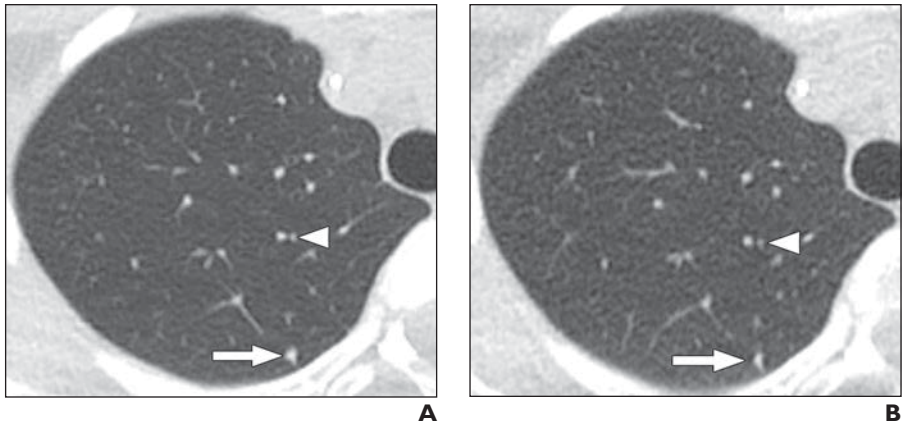


Fig. 2—Representative clinical (1.45 mSv) and reduced-dose (0.45 mSv) CT images of 13-year-old girl with osteosarcoma.
A and **B,** Both clinical (**A**) and reduced-dose (**B**) CT images depict two right upper lobe nodules (*arrow* and *arrowhead*).

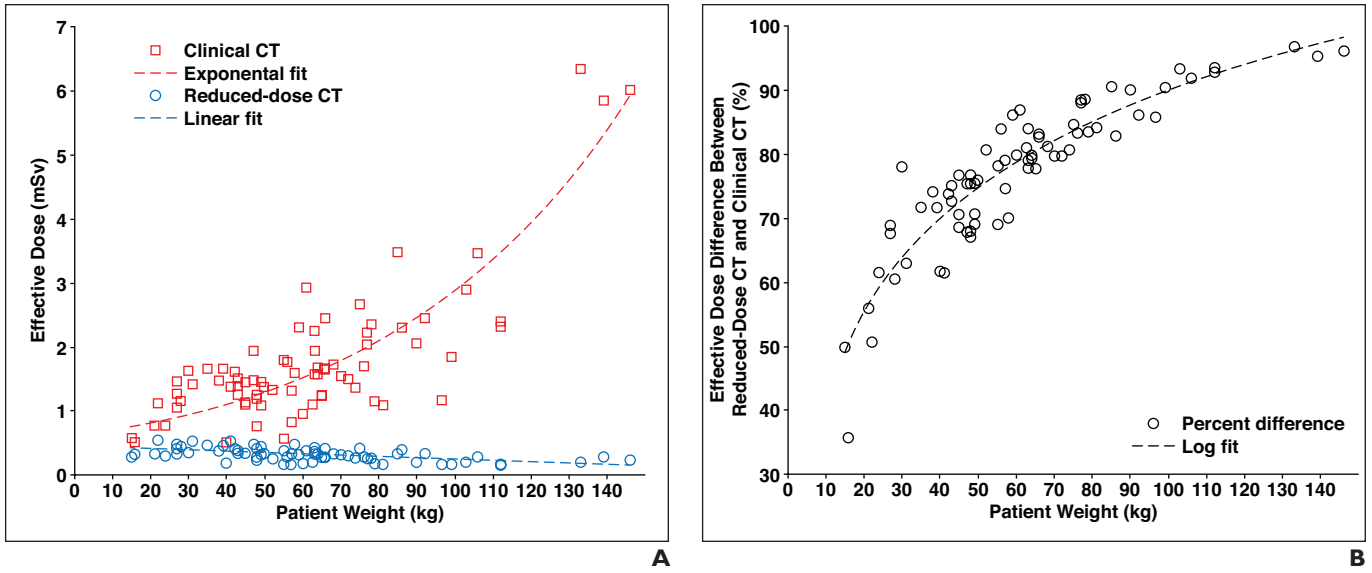


Fig. 3—Dose estimates.
A, Scatterplot of effective dose calculations for clinical CT examinations (*red squares*) show typical exponential increase in dose with patient weight when CT scanner uses tube current modulation to balance image noise and patient dose. Effective dose for reduced-dose CT (*blue circles*) shows linear dose across all patient weights since CT output was held constant. Distance between red and blue lines reflects dose reduction using reduced-dose CT protocol.
B, Scatterplot shows percent difference in estimated effective dose between reduced-dose and clinical CT examinations.

TABLE 2: Intraobserver Agreement for Presence of Lung Nodules Between Clinical and Reduced-Dose CT and Sensitivity and Specificity of Reduced-Dose CT for Presence of Lung Nodules[a]

Outcome	Reviewer 1	Reviewer 2	Reviewer 3
All nodules			
Agreement (Cohen κ) for presence of nodules	0.56 (0.38–0.75)	0.48 (0.29–0.68)	0.57 (0.40–0.75)
Sensitivity (%)	77 (61.4–88.2)	63 (43.7–78.9)	70 (53.9–82.8)
Specificity (%)	80 (63.1–91.6)	85 (71.1–93.7)	89 (73.3–96.8)
Definite nodules only			
Agreement (Cohen κ) for presence of nodules	0.67 (0.50–0.83)	0.45 (0.25–0.66)	0.61 (0.43–0.80)
Sensitivity (%)	76 (59.8–88.6)	63 (43.7–78.9)	70 (50.6–85.3)
Specificity (%)	90 (76.3–97.2)	85 (71.1–93.7)	90 (77.3–96.5)

Note—Values in parentheses are 95% CIs.
[a]Clinical CT was used as the reference standard.

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TABLE 3: Intraobserver Agreement (ICC) for Number of Nodules and Largest Nodule Size Between Clinical CT and Reduced-Dose CT

Outcome	ICC		
	Reviewer 1	Reviewer 2	Reviewer 3
No. of nodules			
All nodules	0.74 (0.61–0.83)	0.84 (0.75–0.89)	0.68 (0.54–0.79)
Definite nodules only	0.80 (0.69–0.87)	0.84 (0.76–0.90)	0.59 (0.43–0.72)
Largest nodule size			
All nodules	0.86 (0.79–0.91)	0.69 (0.55–0.80)	0.85 (0.77–0.90)
Definite nodules only	0.88 (0.82–0.92)	0.69 (0.55–0.79)	0.88 (0.81–0.92)

Note—Values in parentheses are 95% CIs. ICC = intraclass correlation coefficient.

TABLE 4: Interobserver Agreement for Presence of Any Nodule (Cohen κ) and Number and Size of Nodules (ICC)

Outcome	Presence of Any Nodule		No. of Nodules		Largest Nodule Size	
	Clinical CT	Reduced-Dose CT	Clinical CT	Reduced-Dose CT	Clinical CT	Reduced-Dose CT
All nodules	0.54 (0.39–0.68)	0.53 (0.39–0.68)	0.66 (0.54–0.76)	0.74 (0.64–0.82)	0.72 (0.63–0.80)	0.72 (0.62–0.80)
Definite nodules only	0.56 (0.42–0.71)	0.58 (0.43–0.72)	0.65 (0.53–0.75)	0.72 (0.62–0.81)	0.75 (0.65–0.82)	0.72 (0.63–0.80)

Note—Values in parentheses are 95% CIs. ICC = intraclass correlation coefficient.

were classified as visible on the reduced-dose CT examination, 18 were classified as poorly visible (Fig. 4), and 13 (8% of total 162 nodules) were classified as not visible (Fig. 5). The mean size of the nodules that were visible, poorly visible, and not visible was 3.0 ± 2.4 mm (range, 1–7 mm), 1.8 ± 0.8 mm (range, 1–3 mm), and 1.7 ± 0.5 mm (range, 1–2 mm), respectively. Nodules that were poorly visible were significantly smaller (p = .04) than those that were visible. Nodules that were visible and those that were not visible were not significantly different in terms of size (p = .06).

Discussion

In this study, we investigated the performance of a reduced-dose CT protocol for the detection of lung nodules in pediatric and young adult patients with cancer. Reduced-dose CT images were obtained with a mean estimated effective dose of 0.3 ± 0.1 mSv, representing an 83% reduction from clinical doses at our institution. Based on independent review by three pediatric radiologists, reduced-dose CT exhibited a sensitivity of 63–77% for any lung nodule with a specificity of 80–90%. Agreement between reduced-dose CT and clinical CT in terms of the number and size of nodules was good to excellent.

The level of sensitivity achieved in our study may not seem adequate to consider implementing reduced-dose CT. However, the intra- and interradiologist variability in detecting pulmonary nodules is large regardless of CT technique. In a study comparing combinations of standard-dose CT reconstructions to identify lung nodules, Verhagen et al. [14] showed suboptimal interobserver agreement with a maximal kappa of 0.3 as well as a sensitivity of 71%. Similarly, in a study comparing standard-dose maximum-intensity-projection images to axial images, Kilburn-Toppin et al. [15] achieved a maximal sensitivity of 78% for nodules. Further, results from our own study show that interobserver agreement on the presence, size, and number of nodules is similar for the reduced-dose CT and clinical CT examinations, suggesting that observer performance, not CT technique, drives diagnostic performance. Thus, the observed diagnostic performance of reduced-dose CT in our study is within the expected range for CT for lung nodules in general.

The moderate observed intra- and interobserver agreement for lung nodule detection and characterization do not fully reflect the ability of reduced-dose CT to depict lung nodules. To more completely define the ability of reduced-dose CT to depict lung nodules on a nodule-by-nodule basis, we matched each individual nodule between the clinical CT and reduced-dose CT examinations. Based on nodule-by-nodule matching, 92% of nodules identified on clinical CT were identifiable on reduced-dose CT. Although nodules not visible on reduced-dose CT were smaller than visible nodules, this difference was not statistically significant, and multiple 1- to 2-mm nodules were detected by reviewers on the reduced-dose CT, suggesting nodules size is not the only relevant factor. Overall, these findings suggest good technical performance of reduced-dose CT and are similar to the performance of reduced-dose CT in a recent study in adults, which showed 91% detection of nodules on the reduced-dose examinations [4].

To our knowledge, no prior study has directly compared clinical CT to reduced-dose CT for the detection of lung nodules in children. However, our results compare favorably to a prior study in children by Villanueva-Meyer et al. [16] in which readers estimated their diagnostic confidence for various diagnoses, including identification of metastatic disease, based on review of standard-dose CT images and reduced-dose CT images that had been obtained in different children for other clinical indications. In this hypothetical environment, the authors suggested that confidence for diagnosis of lung metastases was significantly reduced, from 98% to 75–78%, on the reduced-dose CT images.

The reduced-dose CT technique used in this study used a fixed technique regardless of patient weight. This translates to less dose reduction for smaller children and greater dose reduction

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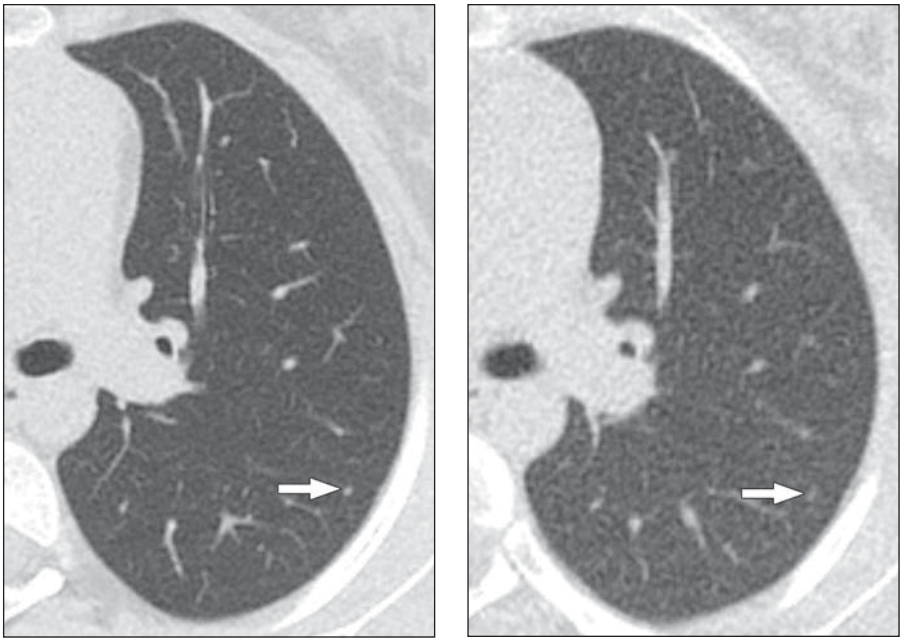


Fig. 4—CT images of 17-year-old girl with osteosarcoma.
A, On axial reformatted clinical (1.083 mSv) CT image, 2-mm left lower lobe nodule (*arrow*) is clearly visible in left lower lobe.
B, Same nodule (*arrow*) shown in **A** is vaguely apparent on reduced-dose CT image (0.318 mSv) and was classified as present but poorly visible.

for larger children and young adults. The use of dose modulation to achieve uniform image noise and/or dose reduction would be an alternative approach that might allow greater dose reduction in smaller children and greater image quality, albeit at a higher dose, in larger children. Despite the use of a fixed technique, effective dose reduction and agreement on the presence of any lung nodule were not significantly related.

At a minimum, our demonstration of adequate diagnostic performance of reduced-dose CT allows this technique to be used for patients with increased radiation sensitivity (e.g., ataxia telangiectasia) without significantly compromising clinical care. In broader application, reduced-dose CT has the potential to further decrease patient radiation dose in clinical practice. Further, lowering dose may reduce the perception that CT is a high-dose examination, increasing patient and provider acceptance. Finally, reduced-dose CT could expand the use of CT in clinical care [17]. For example, reduced-dose CT might replace chest radiography in screening or monitoring protocols [18].

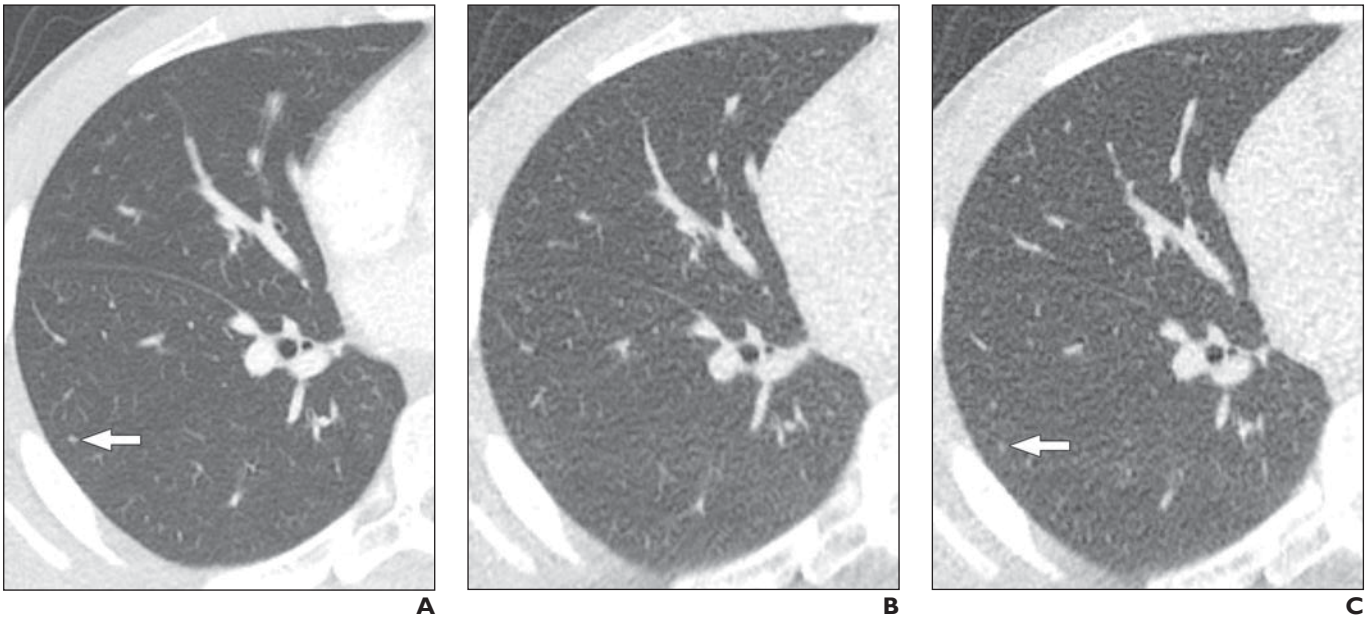


Fig. 5—CT images of 18-year-old man with rhabdomyosarcoma.
A, On axial reformatted clinical (2.457 mSv) CT image, 2-mm right lower lobe nodule (*arrow*) is visible.
B, Same nodule shown in **A** is not apparent on 2-mm reconstructed reduced-dose (0.344 mSv) CT image and was classified as not visible on reduced-dose CT.
C, Same nodule (*arrow*) shown in **A** is visible on source reduced-dose (0.5 mm) CT image.

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Our study has important limitations, the first of which is that only iterative image reconstruction was used. Deep learning reconstruction, which can achieve greater image noise reduction, might further improve the quality of reduced-dose CT images, possibly allowing improved nodule detection or characterization [19]. Second, in the context of this study, observers were presented with a large number of examinations (n = 156) to review in a short period of time without any clinical history to support their reviews. The impact of this artificial design on diagnosis and nodule identification is uncertain, although readers' attention to nodule identification might have been less due to reader fatigue. Third, although observers were blinded to technique and to study purpose, the reduced-dose CT images have a distinct appearance that might have been recognizable, thereby resulting in unavoidable unblinding. Performance of 47% of the clinical examinations with IV contrast material might also have resulted in unblinding. It is also possible that the presence of contrast material may have affected lung nodule conspicuity. Fourth, reviewers only reviewed 2-mm axial reconstructed images. Nodule identification may have been affected by differences in slice positioning between the clinical CT and reduced-dose CT examinations, and discrepancies may have been resolved with review of 0.5-mm images or maximum-intensity-projection images, which have been shown to increase sensitivity [15]. Fifth, children younger than 4 years old were not included, which limits generalizability to these children and possibly to cancers more common at that age. Sixth, this study focused entirely on the detection of lung nodules, which is a high-contrast-resolution detection task. We have not studied the efficacy of this technique for the assessment of soft tissues. Further, the clinical impact of detecting (or missing) lung nodules has not been studied, and the clinical significance of detecting nodules smaller than 3–5 mm is uncertain [18, 20, 21].

We have shown that reduced-dose CT with a fixed technique can depict most (> 90%) lung nodules in a cohort of children and young adults with cancer. Further, multiple reviewers were able to identify the presence of nodules with moderate sensitivity and high specificity. Given the acceptable performance, reduced-dose CT may be a feasible option for the detection of pulmonary metastatic disease in situations in which radiation dose is a primary consideration or as an option to reduce dose in patients undergoing serial chest CT examinations to monitor known disease.

References

1. Ajani JA, D'Amico TA, Almhanna K, et al. Gastric cancer, version 3.2016, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2016; 14:1286–1312
2. Kemppainen J, Hynninen J, Virtanen J, Seppänen M. PET/CT for evaluation of ovarian cancer. *Semin Nucl Med* 2019; 49:484–492
3. Greenwood TJ, Lopez-Costa RI, Rhoades PD, et al. CT dose optimization in pediatric radiology: a multiyear effort to preserve the benefits of imaging while reducing the risks. *RadioGraphics* 2015; 35:1539–1554
4. Messerli M, Kluckert T, Knitel M, et al. Ultralow dose CT for pulmonary nodule detection with chest x-ray equivalent dose: a prospective intra-individual comparative study. *Eur Radiol* 2017; 27:3290–3299
5. Fletcher JG, Levin DL, Sykes AG, et al. Observer performance for detection of pulmonary nodules at chest CT over a large range of radiation dose levels. *Radiology* 2020; 297:699–707
6. Ebner L, Bütikofer Y, Ott D, et al. Lung nodule detection by microdose CT versus chest radiography (standard and dual-energy subtracted). *AJR* 2015; 204:727–735
7. Punwani S, Zhang J, Davies W, Greenhalgh R, Humphries P. Paediatric CT: the effects of increasing image noise on pulmonary nodule detection. *Pediatr Radiol* 2008; 38:192–201
8. Li X, Samei E, Barnhart HX, et al. Lung nodule detection in pediatric chest CT: quantitative relationship between image quality and radiologist performance. *Med Phys* 2011; 38:2609–2618
9. Li X, Samei E, DeLong DM, et al. Pediatric MDCT: towards assessing the diagnostic influence of dose reduction on the detection of small lung nodules. *Acad Radiol* 2009; 16:872–880
10. Cristy M. Mathematical phantoms representing children of various ages for use in estimates of internal dose. Oak Ridge National Laboratory, June 1, 1980: Report NUREG/CR-1159
11. [No authors listed]. The 2007 recommendations of the International Commission on Radiological Protection: ICRP publication 103. *Ann ICRP* 2007; 37:1–332
12. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; 33:159–174
13. Hallgren KA. Computing inter-rater reliability for observational data: an overview and tutorial. *Tutor Quant Methods Psychol* 2012; 8:23–34
14. Verhagen MV, Smets AMJB, van Schuppen J, Deurloo EE, Schaefer-Prokop C. The impact of reconstruction techniques on observer performance for the detection and characterization of small pulmonary nodules in chest CT of children under 13 years. *Eur J Radiol* 2018; 100:142–146
15. Kilburn-Toppin F, Arthurs OJ, Tasker AD, Set PA. Detection of pulmonary nodules at paediatric CT: maximum intensity projections and axial source images are complementary. *Pediatr Radiol* 2013; 43:820–826
16. Villanueva-Meyer JE, Naeger DM, Courtier JL, et al. Pediatric chest CT at chest radiograph doses: when is the ultralow-dose chest CT clinically appropriate? *Emerg Radiol* 2017; 24:369–376
17. Zaleska-Dorobisz U, Olchowy C, Łasecki M, et al. Low-dose computed tomography in assessment of pulmonary abnormalities in children with febrile neutropenia suffering from malignant diseases. *Adv Clin Exp Med* 2017; 26:695–701
18. Grundy PE, Green DM, Dirks AC, et al. Clinical significance of pulmonary nodules detected by CT and not CXR in patients treated for favorable histology Wilms tumor on national Wilms tumor studies-4 and -5: a report from the Children's Oncology Group. *Pediatr Blood Cancer* 2012; 59:631–635
19. Brady SL, Trout AT, Somasundaram E, Anton CG, Li Y, Dillman JR. Improving image quality and reducing radiation dose for pediatric CT by using deep learning reconstruction. *Radiology* 2021; 298:180–188
20. Davison R, Hamati F, Kent P. What effect do pulmonary micronodules detected at presentation in patients with osteosarcoma have on 5-year overall survival? *J Clin Med* 2021; 10:1213
21. Raciborska A, Bilska K, Rychłowska-Pruszyńska M, et al. Management and follow-up of Ewing sarcoma patients with isolated lung metastases. *J Pediatr Surg* 2016; 51:1067–1071

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