Chest CT Scan at Radiation Dose of a Posteroanterior and Lateral Chest Radiograph Series

A Proof of Principle in Lymphangioleiomyomatosis

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BACKGROUND: Given the rising utilization of medical imaging and the risks of radiation, there is increased interest in reducing radiation exposure. The objective of this study was to evaluate, as a proof of principle, CT scans performed at radiation doses equivalent to that of a posteroanterior and lateral chest radiograph series in the cystic lung disease lymphangioleiomyomatosis (LAM).

METHODS: From November 2016 to May 2018, 105 consecutive subjects with LAM received chest CT scans at standard and ultra-low radiation doses. Standard and ultra-low-dose images, respectively, were reconstructed with routine iterative and newer model-based iterative reconstruction. LAM severity can be quantified as cyst score (percentage of lung occupied by cysts), an ideal benchmark for validating CT scans performed at a reduced dose compared with a standard dose. Cyst scores were quantified using semi-automated software and evaluated by linear correlation and Bland-Altman analysis.

RESULTS: Overall, ultra-low-dose CT scans represented a 96% dose reduction, with a median dose equivalent to 1 vs 22 posteroanterior and lateral chest radiograph series (0.14 mSv; 5th-95th percentile, 0.10-0.20 vs standard dose 3.4 mSv; 5th-95th percentile, 1.5-7.4; $P < .0001$). The mean difference in cyst scores between ultra-low- and standard-dose CT scans was $1.1\% \pm 2.0\%$, with a relative difference in cyst score of 11%. Linear correlation coefficient was excellent at 0.97 ($P < .0001$).

CONCLUSIONS: In LAM chest CT scan at substantial radiation reduction to doses equivalent to that of a posteroanterior and lateral chest radiograph series provides cyst score quantification similar to that of standard-dose CT scan.

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ABBREVIATIONS: IR = iterative reconstruction; LAM = lymphangioleiomyomatosis; MBIR = model-based iterative reconstruction

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Because of rising use of medical imaging, radiation exposure is an increasing concern. Ionizing radiation damages tissues and alters DNA structure, which has been shown to increase long-term cancer risk on the basis of radiation dose and repeated exposure.¹⁻⁴ In fact, since the 1980s, the number of CT scans performed increased 20-fold in the United States, and CT scans now account for about one-half of the total radiation exposure in imaging.⁴⁻⁸ An approach to reducing radiation risks is to lower the radiation doses used in CT imaging.

Lymphangioleiomyomatosis (LAM), a cystic lung disease, is an ideal model in which to evaluate CT scans at chest radiography doses.⁹ The potential harms of cumulative radiation exposure with repeated imaging over a lifetime are of particular concern in patients with LAM, a rare multisystem disease diagnosed primarily in young women.⁹⁻¹¹ LAM also occurs sporadically in the presence of tuberous sclerosis complex, an autosomal dominant disorder. Pulmonary LAM is characterized by cystic lung destruction secondary to proliferation of smooth muscle- and cancer-like LAM cells.^{9,12} CT scan demonstrates thin-walled cysts that range from 2 to

40 mm in diameter and are distributed diffusely throughout the lungs.¹³ These characteristic cysts can be quantified in terms of a cyst score, which correlates with LAM disease severity and is defined as the percentage of lung occupied by cysts.¹⁴ The cyst score in LAM is therefore an ideal benchmark for validating CT scans performed at radiation doses equivalent to that of a posteroanterior and lateral chest radiograph series compared with standard doses.

Ultra-low-dose CT scan in combination with model-based iterative reconstruction (MBIR) has been shown to enable reductions in radiation required for diagnostic imaging, including lung cancer screening,¹⁵ identification of emphysema in patients screened for lung cancer,¹⁶ emphysema quantification,¹⁷ and ventricular systolic function in adult congenital heart disease.¹⁸ The purpose of this study is to investigate as proof of principle whether chest CT scan with MBIR at radiation doses equivalent to that of a posteroanterior and lateral chest radiograph series retains the ability to accurately quantify the extent of LAM pulmonary cysts (cyst score) compared with standard dose chest CT scan.

Methods

This study was performed in patients enrolled in two ongoing National Heart, Lung, and Blood Institute institutional review board- and radiation safety-approved, prospective single-center protocols (National Institutes of Health National Heart, Lung, and Blood Institute No. IRB000000004, project approval Nos. 95-H-0186 and 96-H-0100) at the National Institutes of Health in Bethesda, Maryland. Patients in the study provided written informed consent. A total of 105 consecutive subjects with LAM underwent radiologic evaluation from November 2, 2016, to May 31, 2018. To monitor disease or complications, subjects received a clinically indicated chest CT scan at standard radiation dose and an additional chest CT scan at ultra-

low dose (goal of dose equivalent to a posteroanterior and lateral chest radiograph series).

Imaging was performed on a multidetector CT system (Aquilion Genesis; Canon Medical Systems) using 80 × 0.5 mm helical acquisition mode with 275 milliseconds gantry rotation time. Radiograph tube potential and current for standard dose scans were determined by automatic exposure control (^{SURE}Exposure 3D) based on scout image attenuation and used an image quality factor of SD10. Ultra-low-dose scans used a fixed tube current of 10 mA and tube potential of 135 kV if BMI was ≥ 30 kg/m² or 120 kV if BMI was < 30 kg/m². Scanner-reported radiation dose parameters were documented. The effective radiation dose in millisieverts was calculated by multiplying dose-length-product by a conversion coefficient of 0.014 (mSv·mGy⁻¹·cm⁻¹).¹⁹

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Images were reconstructed with a 512 × 512 matrix, 1.0-mm slice thickness, and 1.0-mm slice interval. Standard and ultra-low dose CT images, respectively, used routine clinical iterative reconstruction (IR) and MBIR techniques. Sample images are shown in [Figure 1](#). The routine clinical IR (Adaptive Iterative Dose Reduction in 3 Dimensions, AIDR3D enhanced FC51; Canon Medical Systems) is a hybrid blend between filtered back projection and IR. It is approved by the US Food and Drug Administration and is used routinely for clinical CT image reconstruction. Therefore, IR was used to reconstruct our standard dose images because it is the current clinical practice. For ultra-low-dose CT images, we used MBIR (FIRST Lung Standard; Canon Medical Systems), a fully model-based IR algorithm that uses a forward projection at each iteration and compares the forward projection with the original projection data. This MBIR algorithm takes into account statistical noise (photon, anatomic, and electronic noise), scanner characteristics (detector geometry, collimation, source, and detector distances), optics

Figure 1 – Standard- and ultra-low-radiation-dose chest CT images in a 46-y-old woman with lymphangioleiomyomatosis. Lungs are shown in axial view. Cystic lesions are shown in yellow. The upper panel shows the standard dose iterative reconstruction images, whereas the lower panel shows the ultra-low dose model-based iterative reconstruction images (93% radiation reduction).

(variations or scatter in photon path), and cone beam geometry to yield improved image quality.

Volumetric cyst score quantification was performed using semi-automated image processing software, Lung Volume Analysis (Canon Medical Systems). Trachea, bronchi, and lungs were automatically segmented based on anatomic atlas modeling. Cystic regions were identified by low areas of attenuation based on Hounsfield values and systemically applied to the entire lung field. Cyst scores were calculated as the percentage of cyst volume within total lung volume. In general, the cyst threshold was -940 Hounsfield units but was manually edited in 17 subjects for the

ultra-low-dose images and one subject for the standard-dose images because of initial inclusion of noncystic lung parenchyma. Each cyst score measurement was performed blinded to other results. None of the subjects required manual editing of the lung, trachea, or bronchi segmentation from other organs or the chest wall.

Cyst scores were compared between the ultra-low MBIR and standard IR chest CT images. The isolated effect of MBIR on cyst score was also investigated by comparing standard radiation dose CT images reconstructed with MBIR and IR methods. Statistical analysis was performed using MedCalc (MedCalc Software), paired t tests, linear regression, and Bland-Altman techniques.²⁰

Results

Demographics are detailed in Table 1. Nearly all subjects were women (98.1%). Mean age was 47.8 ± 12.1 years, and mean BMI was 27.0 ± 9.0 kg/m².

TABLE 1] Demographics of 105 Subjects With Lymphangioleiomyomatosis

Demographic	Value
Sex, female/male	103 (98.1)/2 (1.9)
Age, y	47.8 ± 12.1
Height, cm ^a	163.6 ± 10.1
Weight, kg	71.7 ± 20.3
BMI, kg/m ^{2,a}	27.0 ± 9.0
Race, white/Asian/white Hispanic/black/multirace/unknown	80 (76.2)/6 (5.7)/4 (3.8)/3 (2.9)/3 (2.9)/2 (1.9)/7 (6.7)

Data are presented as No. (%) or mean $\pm$ SD.

^an = 104 because one patient did not have height data available.

Overall, standard dose IR scans represented a median radiation dose equivalent to 22 posteroanterior and lateral chest radiograph series (3.4 mSv; 5th-95th percentile, 1.5-7.4). Ultra-low-dose MBIR scans represented a 96% dose reduction, resulting in a median dose equivalent to one posteroanterior and lateral chest radiograph series (0.14 mSv; 5th-95th percentile, 0.10-0.20; $P < .0001$) (Fig 2, Table 2).

The mean cyst score measured by standard-dose IR images was $9.9\% \pm 10.5\%$, whereas that measured by ultra-low-dose MBIR images was $11.1\% \pm 10.2\%$. Bland-Altman analysis comparing ultra-low-dose MBIR with standard-dose IR images demonstrated a mean difference in cyst score quantification of $1.1\% \pm 2.0\%$ ($P < .0001$), with a relative difference in cyst score of 11%. The linear correlation coefficient between ultra-low- and standard-dose CT scans was excellent at 0.97 ($P < .0001$) (Fig 3).

Analyzing the isolated effect of MBIR compared with routine IR at standard radiation dose, we found that

Figure 2 – Radiation level of ultra-low-dose chest CT scan over time. Median radiation dose was 0.14 mSv (5th-95th percentile, 0.10-0.20). One subject required a larger radiation dose because of morbid obesity (BMI, 48 kg/m²).

MBIR slightly overestimated cyst scores. The linear correlation coefficient between MBIR and routine clinical IR cyst scores was excellent at 0.99 ($P < .0001$). Bland-Altman analysis demonstrated a mean difference in cyst score of $2.1\% \pm 1.4\%$ ($P < .0001$) (Fig 4).

Discussion

With increased concern regarding radiation exposure and rising utilization of medical imaging, it is necessary to find new techniques of lowering radiation doses. CT scans account for a large portion of ionizing radiation exposure in imaging and is a prime target for radiation dose reductions.^{4,7} In this study, we start with LAM as a

proof of principle for validating the utility of CT scans performed at radiation doses equivalent to that of a posteroanterior and lateral chest radiograph series. LAM is an ideal model because the cysts are well defined and can be quantified to facilitate comparison between ultra-low and standard dose CT scans.¹⁴

The average dose of a posteroanterior and lateral chest radiograph is 0.1 to 0.15 mSv, with a range of 0.05 to 0.24 mSv reported in the literature, and further dose reductions with advances in imaging technology.^{10,16,21,22} The average dose of a standard chest CT scan in the literature is 4.9 mSv^{23,24}; however, standard-dose CT scans at our institution are currently lower at 3.4 mSv. This study demonstrates that ultra-low-radiation-dose chest CT scans at doses equivalent to a posteroanterior and lateral chest radiograph series are achievable for clinical assessment of LAM disease extent and severity. Overall, ultra-low-dose CT scans represented a 96% dose reduction, with a median dose equivalent to 1 vs 22 posteroanterior and lateral chest radiograph series (0.14 mSv; 5th-95th percentile, 0.10-0.20 vs standard dose 3.4 mSv; 5th-95th percentile, 1.5-7.4; $P < .0001$).

We demonstrate that in LAM, ultra-low-dose chest CT scan at a radiation dose of a posteroanterior and lateral chest radiograph series provides similar cyst score quantification as a standard-dose chest CT scan. The linear correlation coefficient between ultra-low- and standard-dose CT scans was excellent at 0.97. The mean difference in cyst score measured by ultra-low MBIR

TABLE 2] Radiation Dose Parameters (N = 105)

Parameter	Standard-Dose CT Scan	Ultra-Low-Dose CT Scan	P Value
kVp	100: 48 (45.7) 120: 57 (54.3)	100: 3 (2.9) 120: 50 (47.6) 135: 52 (49.5)	< .0001
CT dose index, mGy	6.0 (2.7-12.5)	0.3 (0.2-0.5)	< .0001
Dose-length-product, mGy·cm	232.6 (100.7-508.0)	10.2 (7.2-14.1)	< .0001
Exposure time, s	3.5 (3.0-3.8)	3.9 (3.3-4.1)	< .0001
Range, mm	360 (300-390)	360 (300-390)	...
Body size anterior-posterior, cm	21.6 (18.5-28.6)	21.6 (18.5-28.6)	...
Body size lateral, cm	28.5 (23.3-35.8)	28.5 (23.3-35.8)	...
Effective dose, mSv	3.4 (1.5-7.4)	0.14 (0.10-0.20)	< .0001
Cyst score (%)	9.9 ± 10.5 (with IR) 12.0 ± 11.2 (with MBIR)	11.1 ± 10.2 (with MBIR)	...

Data are presented as No. (%), median (5th-95th percentile), mean ± SD, or as otherwise indicated. P values comparing ultra-low- with standard-dose chest CT scans used Wilcoxon rank-sum tests, with the exception of kVp, which used the χ^2 test. Range and body size parameters were not compared because they have the exact same values in ultra-low- and standard-dose scans. IR = routine clinical iterative reconstruction; MBIR = model-based iterative reconstruction.

Figure 3 – Linear regression and Bland-Altman plots of ultra-low-dose compared with standard-dose chest CT images. Ultra-low dose images used MBIR, whereas standard-dose images used routine IR. IR = iterative reconstruction; MBIR = model-based iterative reconstruction.

and standard IR images was clinically insignificant at $1.1\% \pm 2.0\%$, with a relative difference in cyst score of 11%.

This study also elucidates that, at a standard radiation dose, the isolated effect of MBIR yields a small 2.1% overestimation of cyst scores when compared with routine clinical IR, which is a minimal and clinically insignificant difference. The observed effect of MBIR is similar to that shown in a prior study in which MBIR methods were found to overestimate emphysema area by 2%.¹⁶

In summary, ultra-low-dose chest CT scans using MBIR may be performed at radiation doses equivalent to that of a posteroanterior and lateral chest radiograph series in patients with LAM. The substantial radiation reduction promises to minimize cumulative radiation exposure in patients with LAM while retaining the ability to monitor disease. A limitation of the study was

Figure 4 – Linear regression and Bland-Altman plots of MBIR compared with routine IR in standard dose chest CT images. See Figure 3 legend for expansion of abbreviations.

that the cyst threshold was changed in a minority of subjects because of initial inclusion of noncystic lung parenchyma in cyst volume; however, this would be easily identifiable in routine clinical workflow. Although LAM manifests as pulmonary cysts, nodular opacities such as multifocal micronodular pneumocyte hyperplasia can be present especially in the presence of tuberous sclerosis complex, and would need to be considered for a more comprehensive assessment of disease extent and severity. Nevertheless, chest CT scans at a radiation dose equivalent to that used in a posteroanterior and lateral chest radiograph series are the future for imaging in these patients. Further research is ongoing to evaluate the use of ultra-low-dose CT scan in other more common pulmonary diseases, such as COPD, cystic fibrosis, pulmonary nodules, and ground glass opacities. Application of chest CT scans at a radiation dose equivalent to that of a posteroanterior and lateral chest radiograph series will considerably lower radiation exposure during medical imaging.

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