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Pilot Feasibility Study of Comprehensive Pulmonary Evaluation Following Lung Radiation Therapy

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Abstract

Background—Symptoms of pulmonary injury following lung irradiation may not manifest clinically in childhood. We performed comprehensive pulmonary evaluation of patients who had received lung irradiation for treatment of cancer.

Methods—Patients underwent a focused history and physical examination, computed tomography (CT) of the chest, pulmonary function test (PFT) and cardio-pulmonary exercise stress test (CPET). Health related quality of life (HRQOL) was also measured.

Results—Fourteen patients were recruited with median age of 16 years (range 6-21 years). Median time from pulmonary radiation to testing was 5 years (range 2-11 years). Five patients reported pulmonary symptoms. Twelve patients (85.7%) had at least one PFT abnormality. Nine patients demonstrated CPET abnormalities; seven patients had abnormal pulmonary limitation to exercise, and five patients had exercise-induced bronchospasm. The pulmonary limitations included abnormal ventilatory response to exercise in five patients, and gas exchange abnormalities in four patients. Chest CT demonstrated grade 1-2 radiation induced lung changes in four patients, and grade 3 abnormalities in one patient.

Conclusion—Significant pulmonary dysfunction was observed in childhood cancer survivors who had received lung irradiation. CPET is feasible in childhood cancer survivors and can be valuable for assessment of pulmonary function and exercise capacity.

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Keywords

Exercise testing; lung irradiation; radiation therapy; pulmonary toxicity; childhood cancer

INTRODUCTION

With current advances in therapy, the 5-year survival rates for childhood cancer are approaching 80%.¹ However, increased survival can be associated with comorbidities and treatment related complications.²⁻⁴ Chemotherapy and radiation therapy can both result in pulmonary injury.⁵ Pulmonary complications in childhood cancer survivors have been associated with increased mortality risk with a standard mortality ratio of 8.8.^{2,3} In children, pulmonary effects of cancer therapy may be more pronounced due to skeletal immaturity and impaired lung growth.

Radiation therapy is an important adjunct treatment for many childhood malignancies including Hodgkin lymphoma, Wilms tumor, neuroblastoma, and bone and soft tissue tumors. Pulmonary injury due to irradiation may result in pneumonitis within 1-3 months of therapy, and can progress to irreversible damage and fibrosis over 1-2 years.^{6,7} In addition, children may develop chest wall deformity as a result of impaired skeletal growth.^{8,9} Pulmonary function test (PFT) abnormalities following radiation therapy can range from an obstructive defect to a restrictive pattern of reduced lung volumes with or without gas exchange and diffusion abnormalities.^{10,11} Symptoms of pulmonary injury may not manifest in childhood, but as pulmonary reserves decrease with age, clinical symptoms may develop. Routine PFTs can measure lung function but not the aerobic or functional capacity of a patient.

Aerobic fitness has been found to be lower in children with cancer even in the absence of cardiac and pulmonary dysfunction.¹²⁻¹⁴ There are only a few pediatric studies on cardiopulmonary exercise stress testing (CPET) in childhood cancer survivors and these were performed in leukemia and brain tumor survivors.¹⁵⁻¹⁷ Furthermore, very few studies have addressed cardiopulmonary limitations of exercise test in patients following chest radiation therapy.¹³ Previous studies have evaluated cardiac limitations and fitness in response to exercise stress testing, but, did not focus on the pulmonary limitations. CPET can measure the body's physiological responses to the stress and increased metabolic demand of exercise and serve as an objective measure of the functional status of the cardiovascular and ventilatory systems. CPET may also uncover subtle ventilatory abnormalities and gas exchange defects, and can help in the diagnosis of exercise induced bronchospasm.

Our objective was to perform a comprehensive evaluation of pulmonary function including assessment of pulmonary fitness by exercise stress testing in pediatric cancer survivors who had received radiation therapy to the chest. We performed a cross-sectional pilot study that included history and directed clinical examination for pulmonary signs and symptoms, arterial blood gas (ABG) analysis, PFT, CPET, high resolution computed tomography (CT) of the lungs, and measurement of Health Related Quality of Life (HRQOL).

MATERIALS AND METHODS

Study Population

Patients who had received whole lung or partial lung irradiation were identified from the radiation oncology treatment database at Children's Hospital Los Angeles (CHLA). The institutional review board approved the conduct of the study. Patients between 0-21 years of age at the time of lung irradiation, and currently not receiving anticancer therapy were eligible. Patients had to be at least six years of age at the time of study entry. Patients with history of myocardial infarction, cardiac arrhythmias, congestive heart failure, uncontrolled hypertension, or ventricular outflow tract obstruction were excluded because of safety concerns related to CPET. Participants were recruited during routine follow up visits or contacted by telephone and invited to participate in the study. Written informed consent/ assent was obtained from all subjects.

Study Procedures

On the day of the study, a focused history and physical examination was performed followed by a blood draw for ABG analysis. A single, non-contrast, high resolution CT scan of the chest was obtained (if one had not been done in the previous 6 months). Pulmonary function tests were performed prior to exercise. All PFTs were performed in the PFT laboratory at CHLA in accordance with the American Thoracic Society (ATS) guidelines.¹⁸⁻²⁰ Testing was performed using CareFusion Vmax Encore 22 spirometer, CareFusion Vmax Autobox V62J, and V62W body plethysmograph (San Diego, California). PFT data collected included spirometry, lung volumes, slope of phase III of single breath N₂ washout curve (Phase III N₂), and diffusing capacity of the lung for carbon monoxide (DLCO). A pneumotach was used to obtain flow values, and lung volumes were determined by body plethysmography. Flows [forced expiratory volume in 1 second (FEV₁) and forced expiratory flow between 25-75% of forced vital capacity (FEF_{25-75%})] and lung volumes [forced vital capacity (FVC), residual volume (RV), and total lung capacity (TLC)] were reported as raw values and as a percent of predicted based on standard reference values.²¹⁻²³ DLCO was measured using the single-breath technique. Lung disease was defined based on percent predicted (%pred) of normal lung volumes for age. Restrictive lung disease was defined as a TLC < 80% pred. Obstructive lung disease was defined as an abnormal FEV₁/FVC < 80% with or without an abnormal FEV₁ < 80%, or an abnormal FEF_{25-75%} < 68%. Hyperinflation was defined as a RV > 120% pred or a RV/TLC ratio > 28%. DLCO adj < 80% or DLCO adj/V_A < 4 ml/mmHg/min/L was considered abnormal and indicative of diffusion defect.

Exercise testing was also performed in the PFT laboratory in accordance with the ATS guidelines.²⁴ At the beginning of the test, subjects were asked to walk or run on a treadmill at an initial speed of 1.9 km per hr. The treadmill speed was then increased gradually over the first 7 minutes to a maximum of 7 km per hr followed by an increase in the grade on the treadmill by 2.5% each minute to a maximum of 20% or until the subject was exhausted. Subjects were encouraged to exercise until they were exhausted. Subjects breathed through a mouthpiece, and inspired and expired gas concentrations were continuously analyzed with tidal volumes measured using a computerized breath-by-breath exercise system

(Medgraphics, CardioO2, St. Paul, MN). Minute ventilation ($\dot{V}_E$), volume of oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), respiratory exchange ratio ($RER = \dot{V}CO_2 / \dot{V}O_2$), and ventilatory equivalents for oxygen ($\dot{V}_E / \dot{V}O_2$), and carbon dioxide ($\dot{V}_E / \dot{V}CO_2$) were calculated on a breath-by-breath basis. Heart rate (HR) and oxygen saturation were continuously monitored by electrocardiogram and pulse oximetry (Capnograph plus with oximetry, BCI international, Smiths Medical, Kent, UK) respectively. Effort was considered to be maximal if the highest observed heart rate was >170 bpm and the peak RER was >1.0 . The $\dot{V}O_2$ max was recorded as the highest $\dot{V}O_2$ achieved during exercise. HR at $\dot{V}O_2$ max and O2 pulse ($\dot{V}O_2$ max/HR at $\dot{V}O_2$ max) were also recorded. Anaerobic threshold (AT) was determined at the point at which $\dot{V}CO_2$ increased non-linearly compared to $\dot{V}O_2$. This was calculated by the exercise system (Medgraphics, CardioO2) and checked manually. $\dot{V}_E / \dot{V}CO_2$ at AT and $\dot{V}_E / \dot{V}O_2$ at maximum exercise ($\dot{V}_E / \dot{V}O_2$ max) were used for interpretation. The highest minute ventilation ($\dot{V}_E$) during exercise was recorded as the $\dot{V}_E$ max. The maximum voluntary ventilation (MVV) was calculated using the formula $40 \times FEV1$.²⁵ Breathing reserve was calculated using the formula $(MVV - \dot{V}_E \text{ max}) / MVV \times 100$. Pulmonary limitation to exercise was defined as an abnormal ventilatory response or an abnormal gas exchange. At the end of exercise stress testing PFTs were performed at 5, 10 and 15 minutes. If there was evidence of bronchospasm on PFT (defined by a decrease in FEV1 by greater than 10% or FEF25-75% by greater than 25%) or if subjects had evidence of shortness of breath and wheezing clinically, they were thought to have exercise-induced bronchospasm, and were given a nebulized treatment with a bronchodilator following which PFTs were repeated.

The Pediatric Quality of Life Inventory (PedsQL) Version 4 Generic Core Scales, which have established validity and reliability as a health outcome measure in pediatrics,^{26,27} were used to measure Health Related Quality of Life (HRQOL). The PedsQL includes subject self-report for ages 5 to 25 and parent proxy-report for ages 2 to 18. Items were scored on a scale of 0 to 100. The scale consists of 4 sub-categories: physical functioning (8 items), emotional functioning (5 items), social functioning (5 items), and school functioning (5 items). Social, emotional, and school scores were combined to generate a psychosocial score. The average HRQOL scores for all domains for patient self-report and parent proxy reports were obtained. The scores were compared with reference population scores in healthy children obtained as part of reliability and validity study of the PedsQL 4.0 Generic Core Scales.²⁷ A score of less than 1 SD from the mean score of healthy children in this study was considered abnormal.

RESULTS

Fourteen subjects were enrolled between July 2011 and March 2013. Median age of the 14 patients (Table 1) was 16 years (range 6-21 years). The median time from radiation therapy was 5 years (range 2-11 years). The majority of patients were male, and most patients were of Hispanic ethnicity. The median Body Mass Index (BMI) was 20.71; two patients were obese, three were overweight and one was underweight. The tumor and treatment characteristics are described in Table 1. All patients had received chemotherapy, and one patient with metastatic Wilms tumor had pulmonary wedge resections for right lower lobe and left upper lobe metastases.

Initially ABG testing was attempted in 11 patients; three patients declined the test. Of the remaining eight patients, arterial sample could not be obtained in two. Only one patient had an abnormal ABG, while in two other patients the results were suggestive of hyperventilation. Three patients had normal values. We concluded that ABG testing was not a reliable way of testing lung function abnormalities in our cohort given the high amount of variability of the results and the difficulty of obtaining good samples, and the test was removed from the study protocol.

Clinical symptoms of respiratory disease were present in five patients. Three patients reported having asthma. Three patients reported experiencing shortness of breath with mild to moderate activity. All patients were able to perform PFT. Twelve of the 14 patients (85.7%) had a PFT abnormality in the form of obstructive defect, restrictive defect, hyperinflation or diffusion defect (Table 2). The individual results of PFT testing for all patients are presented in Supplementary Table 1. One patient was excluded from performing exercise testing due to high blood pressure. Two patients did not exercise to their maximum capacity due to poor effort. Of the 11 patients who completed exercise testing, only two patients had a normal exercise study (Table 3). Four patients had abnormal pulmonary limitation to exercise, two patients had exercise induced bronchospasm, and three patients had both. The pulmonary abnormalities noted were abnormal ventilatory response in five patients (insufficient increase in tidal volume in three patients, increased $\dot{V}_E/\dot{V}CO_2$ ratio at AT in five patients, elevated $\dot{V}_E/\dot{V}O_2$ max in two patients), and gas exchange abnormalities in four patients leading to hypoxemia and/ or hypercarbia.

CT scan findings demonstrated radiation induced lung changes in 5 of 14 patients. The Common Terminology Criteria for Adverse Events (CTCAE) version 4 grading system was used to assess severity of interstitial disease. Four patients had grade 1-2 abnormalities and only 1 patient had >50% lung involvement with scarring (grade 3). The patient with grade 3 abnormalities had received hemithorax radiation with 5580 cGy.

The average HRQOL scores for all domains for patient self-report and parent proxy reports were obtained. Thirteen of 14 subjects had available data for child reports and 8 of 9 subjects less than 18 years had data available for parent-proxy report. Four subjects had a low PedsQL global score, while two had low parent proxy scores. However, the mean scores for child report (75.86) and parent-proxy report (86.09) were within 1 SD of the means (83 ± 14.79 for child report and 87.6 ± 12.33 for parent proxy report) for healthy normal population (Table 4).²⁷ A summary of the comprehensive evaluation for each of the study patients is given in Table 5.

DISCUSSION

Our pilot study was designed for comprehensive evaluation of pulmonary function in survivors of childhood cancer who received radiation therapy to the chest. At a median of 5 years from radiation therapy, one third of the patients had signs or symptoms of respiratory disease. All patients were able to perform pulmonary function testing. Cardio-respiratory exercise stress testing was a feasible test to perform in this population but two young patients (age 6 and 7 years) were unable to yield an adequate test result due to poor effort.

The majority of patients tested had either a pulmonary limitation to exercise or exercise-induced bronchospasm. ABG analysis was deemed to be not feasible in our study as a quarter of the patients declined having the test performed and the results were not a reliable measure of pulmonary function or gas exchange. CT scan testing was performed in all patients but very few patients had significant radiological abnormalities. The mean HRQOL scores for patient and parent proxy scores were within the normal range of healthy pediatric populations.

There are few studies that have evaluated exercise stress testing following cancer therapy in children.^{13,15–17} In previous studies, the cardiopulmonary exercise response was evaluated from the perspective of physical fitness or cardiovascular responses to exercise. Peak $\dot{V}O_2$ or $\dot{V}O_2$ max is the best indicator of functional exercise capacity or aerobic fitness. During cardiopulmonary exercise stress testing, the increased oxygen consumption is a reflection of increased cardiac function, peripheral circulation, oxygen carrying capacity of blood, oxygen extraction by the muscles, and increased ventilation. In normal subjects, maximal exercise and oxygen consumption is limited by a maximized cardiac response. However, exercise can also be limited by poor effort, abnormal cardiac conditions, or abnormal ventilatory and gas exchange mechanisms. In normal cardio-respiratory response to exercise, there is a large breathing reserve or potential capacity of the pulmonary system that prevails even when maximum heart rate and cardiac output are reached. In patients with lung parenchymal, interstitial or obstructive airway disease, the pulmonary system is challenged and is less efficient. This can be evaluated during exercise stress testing as an abnormal ventilatory response to exercise. In our study, an abnormal ventilatory response was seen in five patients, and four patients had gas exchange abnormalities with hypoxemia and/or hypercarbia. An increased $\dot{V}_E/\dot{V}CO_2$ ratio at AT was seen in all 5 patients with ventilatory defects. An abnormally low $\dot{V}_E/\dot{V}CO_2$ at AT can be a reflection of ventilation perfusion mismatch, pulmonary vascular disease or increased dead space ventilation in subjects.²⁵

In the study by Järvelä et al,¹⁵ the average peak $\dot{V}O_2$ in 21 adolescent and young adult survivors of acute lymphoblastic leukemia (ALL) was significantly lower than the control population. Even though only two of our patients had decreased aerobic capacity and fitness, nine (81%) patients had a pulmonary limitation to exercise or exercise induced bronchospasm. The pulmonary factors that limited exercise included abnormal gas exchange (hypoxemia and hypercarbia) and abnormal ventilatory response to increasing work load. De Caro et al²⁸ evaluated cardiac function and response to cardiopulmonary exercise stress testing in childhood cancer survivors, most of whom had received anthracyclines, and did not find a significant difference in exercise responses between subjects and controls. In the study by Elbl,²⁹ 27% of adult patients had a decreased peak $\dot{V}O_2$ that was significantly correlated with left ventricular dysfunction, cumulative dose of doxorubicin (median 240 mg/m²), female gender and age. On multivariate analysis diastolic dysfunction was correlated with dose of doxorubicin and radiation therapy among other factors. Eleven of our patients had received doxorubicin therapy with a median cumulative anthracycline dose of 150 mg/m² but none of our patients had an abnormal cardiac limitation to exercise. The younger age of our population could have accounted for the absence of this problem.

In our study, all nine patients who had pulmonary abnormalities on exercise testing also had abnormal findings on PFT testing. In addition, two of the three patients who did not have exercise data available had abnormal PFT parameters. The two patients with normal exercise stress tests had normal PFTs. Several studies have previously evaluated PFT abnormalities in patients with radiation therapy.¹¹ In our study population, a significant number of patients (36%) had airways obstruction on PFTs even in the absence of a history of asthma. In another study by our group,¹⁰ a similar prevalence of obstructive airway disease was noted on long-term follow up of patients with chest radiation. About 50% of our patients had exercise-induced bronchospasm. Exercise-induced bronchospasm can be seen in 80% patients with asthma or airway reactivity but may also present in patients without an underlying diagnosis of asthma. Preclinical evidence suggests that radiation induced cytokine changes can trigger asthma-like inflammatory pathways in the lungs and may be responsible for these findings.³⁰ The higher frequency of exercise-induced bronchospasm is a crucial finding and warrants further studies to establish guidelines for routine evaluation of this condition in childhood cancer survivors following radiation therapy. In this pilot study, the anatomical findings on CT scan did not provide additional information on the functional pulmonary status.

There can be several potential reasons for decreased exercise capacity in cancer patients including generalized weakness, fatigue, peripheral neuropathy, obesity following cancer therapy, sedentary lifestyle, as well as psychosocial factors. Participation in physical activity can enhance physical and emotional well-being as well as quality of life in cancer survivors. However, assessment of baseline pulmonary function and physical fitness may be essential before making appropriate physical activity recommendations for patients. Assessing pulmonary function by PFTs alone does not provide a holistic assessment of physical fitness in these patients, and thus additional methods of testing and strategies for screening and monitoring these patients need to be explored. In adult patients with chronic obstructive pulmonary disease (COPD), peak $\dot{V}O_2$ has been found to be a better predictor of outcomes than FEV1 alone.³¹ CPET has also been found to be useful for pre-operative risk assessment for major surgery^{32,33} as well as for predicting survival time in patients with heart failure.^{34–36} Thus performance of CPET in a young cancer survivor population has several potential future implications and needs to be investigated further.

Extensive testing was performed in our patients as part of a pilot feasibility study and may seem to be an expensive proposition. However, these tests performed at a single point in time can provide valuable information on the pulmonary function status of cancer survivors. Exercise studies and PFTs were valuable in providing this information prior to onset of clinical symptoms, more so than chest CT scan. This evaluation can be used to tailor fitness prescriptions to patients as well as allow early interventions to limit further damage. Effective treatment strategies for exercise induced bronchospasm and airway reactivity can be instituted in patients with subclinical dysfunction. Clinical benefits from such interventions may make the comprehensive pulmonary evaluation cost effective. Moreover, these patients may be eligible for therapeutic strategies currently under investigation, to limit progression of radiation induced lung damage, such as, pentoxifylline, enalapril, and statins^{37–40}.

There are several limitations to our study. In addition to irradiation, several other treatment and patient related factors could have influenced pulmonary outcomes. Due to limited patient numbers, we cannot determine causality in this study. There was no control group of comparable subjects. Young age was a barrier to exercise testing. However based on this study, we can establish that comprehensive assessment of pulmonary function employing PFT, exercise stress testing and HRQOL is feasible in a young cancer survivor population and can serve as a useful and important tool for pulmonary assessment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1**Patient and Treatment Demographics**

Characteristic	N=14
Age, years; Median (range)	16 (6-21)
Age at diagnosis, years; Median (range)	7.8 (2 -16)
Age at radiation, years; Median (range)	8.9 (2.1-18.2)
Years since radiation; Median (range)	4.8 (2.1 -10.8)
Male /female, n	10/ 4
Ethnicity, n	
Hispanic	8
Non-Hispanic White	2
Asian	1
African- American	2
Other	1
BMI (kg/m ²); Mean $\pm$ SD (range)	21.1 $\pm$ 4.7 (14.5-30.8)
Cancer Type, n	
Hodgkin lymphoma	6
Rhabdomyosarcoma	3
Neuroblastoma	2
Wilms tumor	2
Ewing sarcoma	1
Received adjuvant chemotherapy, n	14
Cyclophosphamide	12
Doxorubicin	11
Bleomycin	5
Received surgery, n	1
Type of radiation, n	
Chest	7
Whole lung radiation	4
Mantle radiation	2
Total lymphoid irradiation	1
Dosimetric characteristics	
Prescribed dose, cGy; Median (range)	2100 (1440- 5580)
Mean lung dose, cGy; Median (range)	1187 (109- 3106)
Maximum lung dose, cGy; Median (range)	2262 (1200-6526)

SD, Standard deviation; BMI, Body mass index

Table 2**PFT Abnormalities**

PFT parameter	Number of Abnormal (%) N=14
FVC	4 (29)
FEV ₁	4 (29)
FEV ₁ /FVC	4 (29)
FEF _{25-75%}	4 (29)
TLC	3 (21)
RV	5 (36)
RV/TLC	5 (36)
Phase III N ₂	3 (23)
DLCO corr %pred	6 (50)
DLCO corr/V _A	0
Airways Obstruction	5 (36)
Restrictive	3 (21)
Hyperinflation	7 (50)
Any PFT abnormality	12 (86)

PFT, Pulmonary function test; FVC, Forced vital capacity; FEV₁, Forced expiratory volume in 1 second; FEF_{25-75%}, Forced expiratory flow rate between 25-75% of forced vital capacity; RV, Residual volume; TLC, Total lung capacity ; Phase III N₂, Slope of phase III of the single breath N₂ washout curve; DLCO corr %pred, Diffusing capacity of the lung for carbon monoxide adjusted for hemoglobin; DLCO corr/V_A, Diffusing capacity of the lung for carbon monoxide adjusted for hemoglobin and corrected for alveolar volume; SD, standard deviation

Table 3**Exercise Test Abnormalities**

Variables	Number of Abnormal N=11 (%)
VO ₂ /kg max	2 (18)
VO ₂ /kg AT	2 (18)
RER max	7 (64)
HR max	3 (27)
V _E /V _{CO2} at AT	5 (45)
V _E /V _{O2} max	2 (18)
Vt max did not double baseline	3 (27)
Hypercarbia during CPET	1 (9)
Hypoxemia during CPET	3 (27)
Pulmonary Limitation	7 (64)
Exercised induced bronchospasm	5 (45)
No Exercise Abnormality	2 (18)

VO₂/kg max, Volume of oxygen consumption at maximum exercise per kilogram body weight; VO₂/kg AT, Volume of oxygen consumption at maximum exercise per kilogram body weight at anaerobic threshold; RER max, Respiratory exchange ratio at maximum exercise; HR max, Heart rate at maximum exercise; V_E/V_{CO2} at AT, Ventilatory equivalent for carbon dioxide production at anaerobic threshold; V_E/V_{O2} max, Ventilatory equivalent for oxygen consumption at maximum exercise; CPET, Cardio-pulmonary exercise test; SD, Standard deviation

Table 4

Pediatric Quality of Life Inventory Version 4.0 Generic Core Scales for Subjects Compared with Healthy Patient Populations

	Study Population			Overall Healthy Children Population Score [¶]			
	n	Mean	SD	n	Mean	SD	>1SD score
Child report	13	75.86	14.28	401	83	14.79	68.2
Parent-proxy report	8	86.09	11.69	717	87.6	12.33	75.3

SD, standard deviation

[¶]Reference for healthy population- Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care*, 2001 39: 800–812

Table 5

Comprehensive Assessment of Patients

Patient No.	Radiation Field	Dose of Radiation (cGy)	Clinical Symptoms and Signs	PFT Abnormality	Exercise Testing	Interstitial changes on CT scan (grade)	PedsQL Score
1	Mantle radiation	2100	None	Obstructive, Hyperinflation, Diffusion defect	Exercise induced bronchospasm	1	84.7
2	Hemithorax	5580	SOB with mild activity; scoliosis	Restrictive, Hyperinflation, Diffusion defect	Pulmonary limitation; Exercise induced bronchospasm	3	71.7
3	Neck and supraclavicular - Bilateral	2100	None	Obstructive	Pulmonary limitation	0	92.3
4	Neck and Supraclavicular - Bilateral	5040	None	Hyperinflation, Non-uniform distribution of ventilation	Poor effort	0	63
5	Neck and supraclavicular - Bilateral	2100	None	No abnormality	No abnormality	1	86.9
6	Whole lung radiation	2100	None	Restrictive; Non-uniform distribution of ventilation, Diffusion defect	Pulmonary limitation; Exercise induced bronchospasm	0	78.2
7	Mediastinal	2160	None	No abnormality;	Poor effort	0	Not available
8	Mediastinal	2160	Asthma, cough	No abnormality;	No abnormality	0	69.5
9	Neck and supraclavicular -Unilateral	2100	None	Obstructive, Non-uniform distribution of ventilation	Pulmonary limitation	0	86.9
10	Total lung irradiation	2100	Asthma, SOB with moderate activity	Obstructive, Hyperinflation	Exercise induced bronchospasm	2	92.3
11	Whole lung radiation	1440	SOB with moderate activity	Restrictive, Diffusion defect	Pulmonary limitation	2	60.8
12	Whole lung radiation	1500	None	Hyperinflation	Pulmonary limitation	0	47.8
13	Mantle radiation	2100	Asthma	Obstructive, Diffusion defect	Did not exercise	0	63
14	Whole lung radiation	1500	None	Hyperinflation	Pulmonary limitation	0	89.1

cGy, Centigray; SOB, Shortness of breath; LPM, Liter per minute; FEV1, Forced expiratory volume in 1 second; CT, Computed tomography