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Original article

Long term radiological features of radiation-induced lung damage

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A B S T R A C T

Purpose: To describe the radiological findings of radiation-induced lung damage (RILD) present on CT imaging of lung cancer patients 12 months after radical chemoradiation.
Material and methods: Baseline and 12-month CT scans of 33 patients were reviewed from a phase I/II clinical trial of isotoxic chemoradiation (IDEAL CRT). CT findings were scored in three categories derived from eleven sub-categories: (1) parenchymal change, defined as the presence of consolidation, ground-glass opacities (GGOs), traction bronchiectasis and/or reticulation; (2) lung volume reduction, identified through reduction in lung height and/or distortions in fissures, diaphragm, anterior junction line and major airways anatomy, and (3) pleural changes, either thickening and/or effusion.
Results: Six patients were excluded from the analysis due to anatomical changes caused by partial lung collapse and abscess. All remaining 27 patients had radiological evidence of lung damage. The three categories, parenchymal change, shrinkage and pleural change were present in 100%, 96% and 82% respectively. All patients had at least two categories of change present and 72% all three. GGOs, reticulation and traction bronchiectasis were present in 44%, 52% and 37% of patients.
Conclusions: Parenchymal change, lung shrinkage and pleural change are present in a high proportion of patients and are frequently identified in RILD. GGOs, reticulation and traction bronchiectasis are common at 12 months but not diagnostic.

Radiation-induced lung damage (RILD) is a side effect of radical radiotherapy (RT) and a significant cause of reduced quality of life in cancer survivors [1]. While the early, acute phase has been extensively investigated, the late, chronic phase of RILD is less well studied and described [2–6]. The historically poor prognosis of lung cancer patients has led to a lack of objective and standardised criteria to describe and quantify the process [4,7,8], leading to variable reporting across centres and trials. As lung cancer survivorship improves, the importance of long term treatment side effects grows [9–14].

Repetitive or severe lung injuries result in permanent radiological scarring, often referred to as fibrosis, that impairs lung function [15]. CT imaging is a sensitive indicator of RILD [16–22]. In addition to parenchymal density changes many other related abnormalities exist that are under-reported in the literature and poorly understood [5,17,20,21,23–29]. These include more obvious changes such as segmental collapse and pleural effusions, and more subtle changes such as traction bronchiectasis, elevation or tenting of the hemidiaphragm, mediastinal shift and rotation, distortion of major airways and pleural thickening.

Using patient data from the completed IDEAL CRT trial we studied the incidence of anatomical abnormalities found on CT imaging of lung cancer patients 12 months after RT, compared to their pre-treatment CT. This study is the first step towards developing a CT-based scoring system for RILD. The aim was to describe key radiological findings to inform the diagnosis of RILD.

Methods and materials

Study design

Patient data were derived from the IDEAL CRT trial cohort [11]. This was a stage I/II clinical trial of isotoxic chemoradiation for patients with stage II–III non-small cell lung cancer (NSCLC). Patients received 63–73 Gy RT in 30 fractions over 6 weeks or 63–71 Gy in 30 fractions over 5 weeks (with one day of twice daily RT weekly) with two concurrent cycles of cisplatin and vinorelbine. The lung EQD2 mean dose was planned to be 18.2 Gy in all

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Table 1
Demographics and baseline characteristics of all patients.

	No. patients ($N = 27$)
Age (y)	
≥70	5
<70	22
Mean (±SD)	66 (±7)
Median (range)	65 (53–83)
Sex	
Male	20
Female	7
Stage[+]	
IIA	0
IIB	1
IIIA	16
IIIB	10
Fractionation scheme	
6-Weeks protocol	17
5-Weeks protocol	10
Radiotherapy technique	
Conformal	24
IMRT/VMAT	3
GTV size[*] (cm^3)	
Mean (±SD)	104 (±57)
Median (range)	101 (14–211)
PTV size[*] (cm^3)	
Mean (±SD)	400 (±149)
Median (range)	358 (203–832)
Prescription dose (Gy)	
Mean (±SD)	67.9 (±3.8)
Median (range)	69.1 (63.0–73.0)

[*] Calculated on 3D or 4D-CT used for planning. On 4D-CT a composite volume was formed by merging the GTV outlined on different phases.
[+] IASLC 7th edition staging.

patients, so that although the tumour dose varied between patients, the lung dose was homogeneous across the entire cohort. The protocol called for CT scans to be performed at 12 months post-RT in all patients. Median overall survival (OS) for the 6-week protocol was 36.9 months. The 5-week outcomes are pending full follow-up. Baseline and 12 month CT scans were collected centrally. Information on tumour stage and patient characteristics are presented in Table 1.

CT scans

Each patient underwent a baseline PET/CT or diagnostic CT before treatment and a diagnostic CT 12 months after treatment. Pairs of baseline and follow-up CT images were rigidly co-registered using the open-source NiftyReg software [30]. The transformation was optimised to match the anatomy of the thoracic vertebrae.

Scoring of radiological findings of RILD

Analysis of CT abnormalities was achieved by consensus in a multidisciplinary team: AD, thoracic radiologist, DL, clinical oncologist and CV, medical physicist. Scans were inspected in pairs (baseline vs follow-up) to assess new findings indicative of lung damage. There was no knowledge of the patient's identity or RT treatment details. Window and level settings were the same for all images ($W = 1300$, $L = -350$). The abnormalities identified were categorised as follows: (1) parenchymal, (2) lung volume reduction, and (3) pleural.

Classification of radiological changes

Parenchymal findings of four types were noted as defined in Gotway et al. (2005) (Fig. 1): ground-glass opacities (GGOs), consolidation, reticulation and traction bronchiectasis [31]. Since rounded consolidation and residual masses may have a similar radiological appearance [32,33], residual masses were defined as opacities with rounded shape in the same anatomical location of the initial tumour. Follow-up clinical and imaging data from the trial were used to identify residual masses with local recurrence.

Lung volume reduction measurement was recorded in five ways (Fig. 2): reduction in lung height, distortion of ipsilateral pleural fissure anatomy, changes in the position and shape of the ipsilateral hemidiaphragm [23], displacement and/or thickening of the anterior pleural junction line [34], and gross distortions of the anatomy of the main bronchi. Reduction in lung height was assessed on coronal reconstructed images. Fissure distortion was identified through changes in the relationship between the oblique fissure and diaphragm on axial images. Distortions of the bronchial tree were identified on coronal views.

Pleural changes included thickening and effusion (Fig. 3). Effusion is a region of homogeneous liquid at the boundary between the lung and thoracic cage. Thickening is an increase in the size of the pleural reflection, with the intensity of soft tissue and occurring at any interface between lung and thoracic cage.

In total three categories and eleven sub-categories of lung damage were analysed. For each patient, the presence or absence of each category and sub-category was annotated. Qualitative details on sub-types of patterns of damage were also recorded for future analysis. For the purposes of this analysis changes were not empirically measured but were recorded as present or absent based on routine inspection.

Results

Out of 120 patients in IDEAL CRT, baseline and 12-month scans were available for central review in 33 patients at the time of this analysis. All available pairs of baseline and 12-month scans were reviewed by the multidisciplinary team. For a total of six patients there was radiological evidence of major radiation damage that did not correspond to typical RILD. In five patients there was partial lung collapse due to airways damage. One patient had a lung abscess with extensive inflammatory change. These anatomical changes obscure the described findings of RILD. 27 patients are included in this analysis. The median time from end of treatment to time of second scan was 353 days, range: 265–364 days.

The number of patients with each category and sub-category of change is shown in Fig. 4. Parenchymal changes were detected in all patients and volume reduction in all patients but one. Pleural changes were found in 82% of patients. All patients had at least two categories of lung damage and all three categories were present in 78% of patients.

Within the parenchymal category, the sub-category of consolidation was most commonly present, affecting 93% of patients. GGOs, reticulation and traction bronchiectasis were present in 44%, 52% and 37% of patients respectively.

In the volume reduction category, fissure and diaphragm distortion were present in 78% and 67% of patients respectively. Lung height was reduced in 59%. Major airways distortion and anterior junctional change were present in 63% and 78% respectively, representing mediastinal change.

Pleural thickening was present in 70% and pleural effusion in 19%.

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