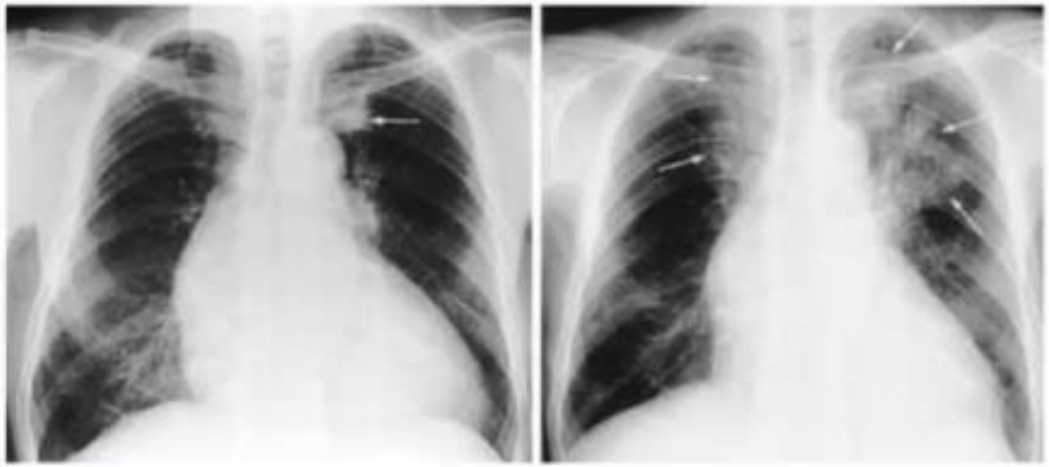
Management of Radiation Toxicity: Lung

Dr. Manish Gupta
Professor & Head
Department of Radiation Oncology
AIIMS Bhopal

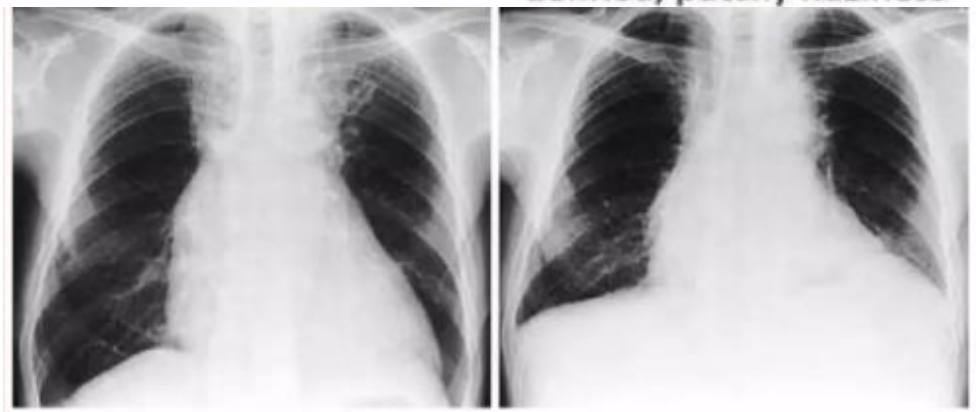
ICRO 20/04/2024

Introduction



Pre-treatment: nodule

3 month after RT: ill-defined, patchy haziness

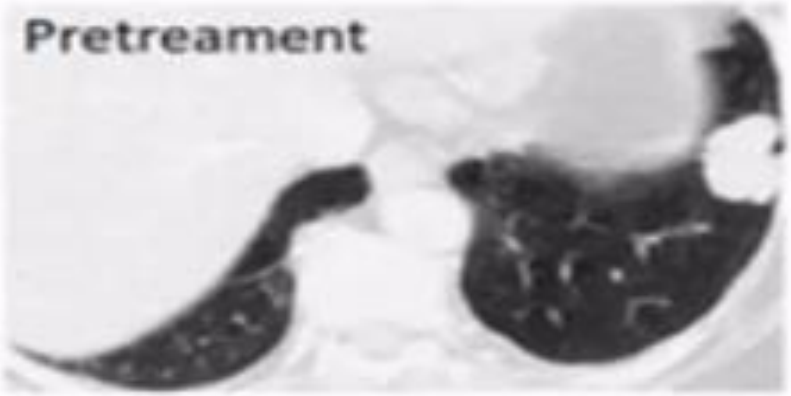


6 mo and 1 yr after RT: increasing volume loss, homogeneity of opacity, sharpness of lateral margins

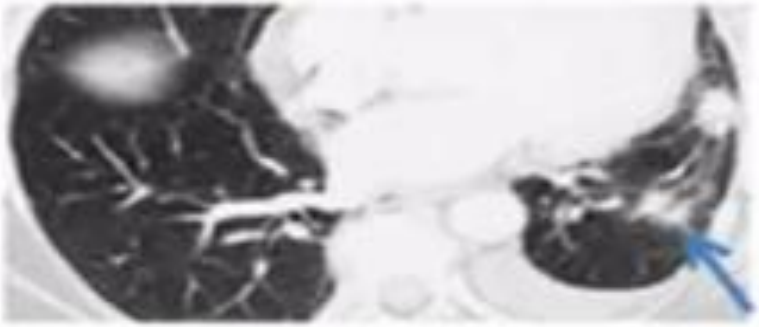
Tumor →Radiotherapy→Pneumonitis→Fibrosis

65 yo, female
adenoCA LLL

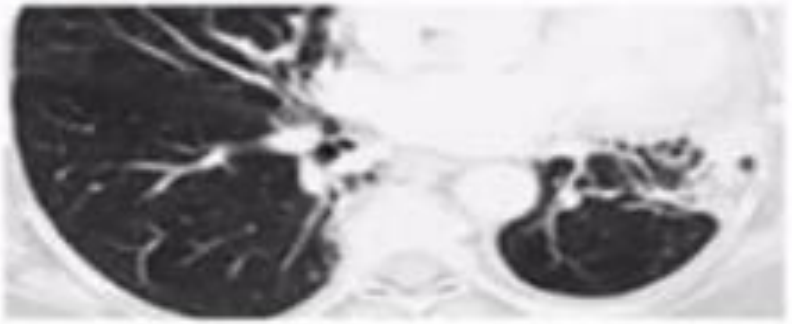
Pretreament



5 mo: nodular
radiation pneumonitis



9 mo: fibrosis



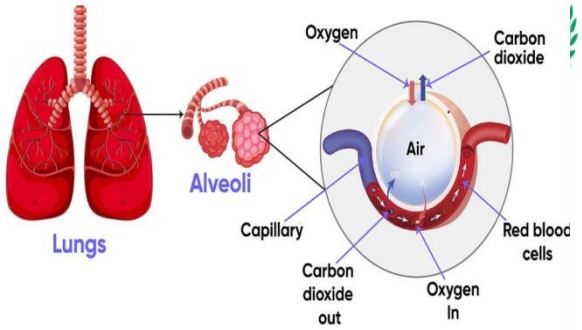
Introduction

- Radiation therapy: Role in the management of various thoracic tumors
  - Lung cancer
  - Breast Cancer
  - Esophageal cancer
  - Mesothelioma
- Radiation Induced Lung Injury (RILI): First described in 1898
- 1925: two types of RILI
  - Radiation Pneumonitis
  - Radiation Fibrosis
- RILI:
  - a dose-limiting factor is chest radiotherapy
  - most common side effects during the treatment of thoracic tumours resulting in limitation of dose of radiation.

contd..

Radiation damage to the lung:

- **Stages**
  - Asymptomatic / Silent
  - Symptomatic pneumonitis
  - Lung Fibrosis
  - Symptomatic bronchial stenosis



Exchange of oxygen for CO2

- Challenging to distinguish radiation-related pulmonary symptoms from comorbid illnesses (e.g., exacerbation of chronic obstructive pulmonary disease , infection, cardiac events)
- Objective reductions in the lungs ability to move and exchange gas can be measured by formal pulmonary function tests (PFTs)
- RILI: pathogenesis
  - Indirect effect through free radicals
  - Direct effect

Histopathological Stages

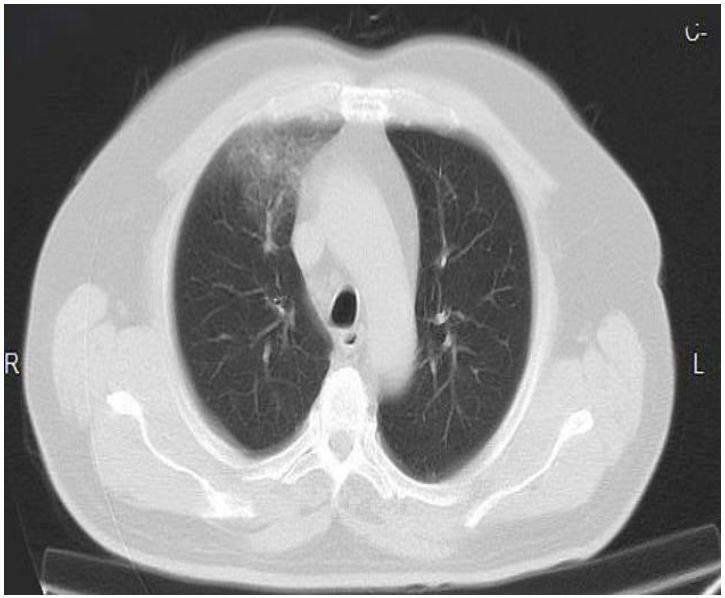
- **Acute Phase**: 1-2 months post RT
  - Early/Exudative : vascular congestion, edema, inflammatory response
  - diffuse alveolar damage
  - Clinically silent
- **Intermediate phase** / Proliferative Phase : 2-9months
  - Hyaline membrane formation
  - Type II pneumocyte proliferation
  - Continued edema
- **Reparative Phase**: 6-9 months
  - Thickened basement membrane
  - Capillary regeneration
- **Late**/Chronic Phase/ Fibrotic Phase : >9months
  - Pulmonary fibrosis
  - Type I pneumocyte (non-dividing) replaced with scar tissue

Symptomatic Radiation Pneumonitis –

- 4 - 12 weeks post radiotherapy, (may be seen as early as one week, especially in a high total dose.)
- Symptoms include

  Non-specific

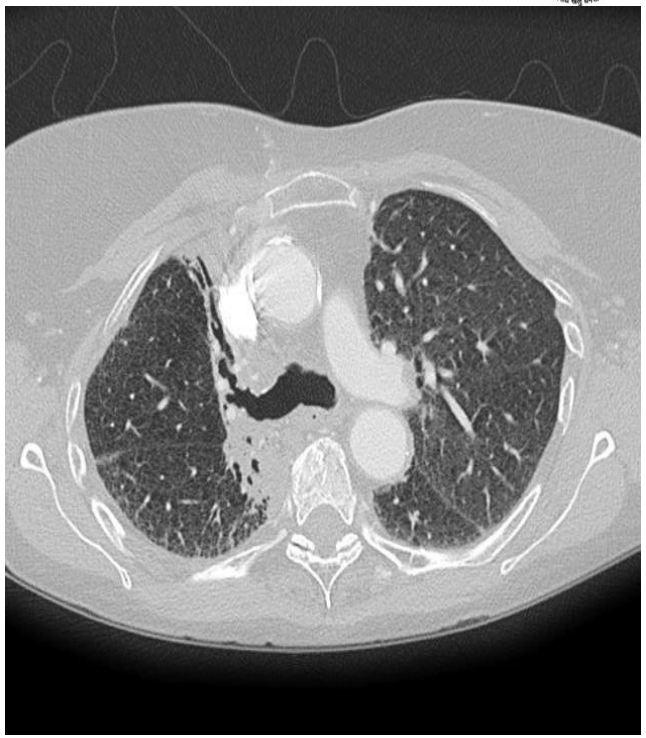
  - Dyspnoea
  - non-productive Cough
  - Low-grade transient fever (Occasionally)
  - Chest discomfort
  - small pleural effusion Hemoptysis
  - Crackles on auscaltation
  - Increased WBC, ESR



CT : Radiation Pneumonitis – Ground glass Opacities

Radiation-induced pulmonary fibrosis –

- 6 and 12 months post radiotherapy (continue to progress for up to 2 years)
- Symptoms :
  - Persistent dry cough
  - Shortness of breath
- Extent and severity of fibrosis remains stable after 2 years RT
- Radiation-induced chronic lung injury can progress to
  - Chronic respiratory failure
  - Pulmonary hypertension
  - Chronic cor-pulmonale



CT changes with Radiation induced pulmonary fibrosis (Thyroid Ca)-

- volume loss
- linear scarring
- chronic consolidation
- hilar vascular displacement
- mediastinal shift
- pleural thickening

Radiation-induced Bronchial Stenosis- >12 Months

- Symptoms
  - Cough
  - Shortness of breath

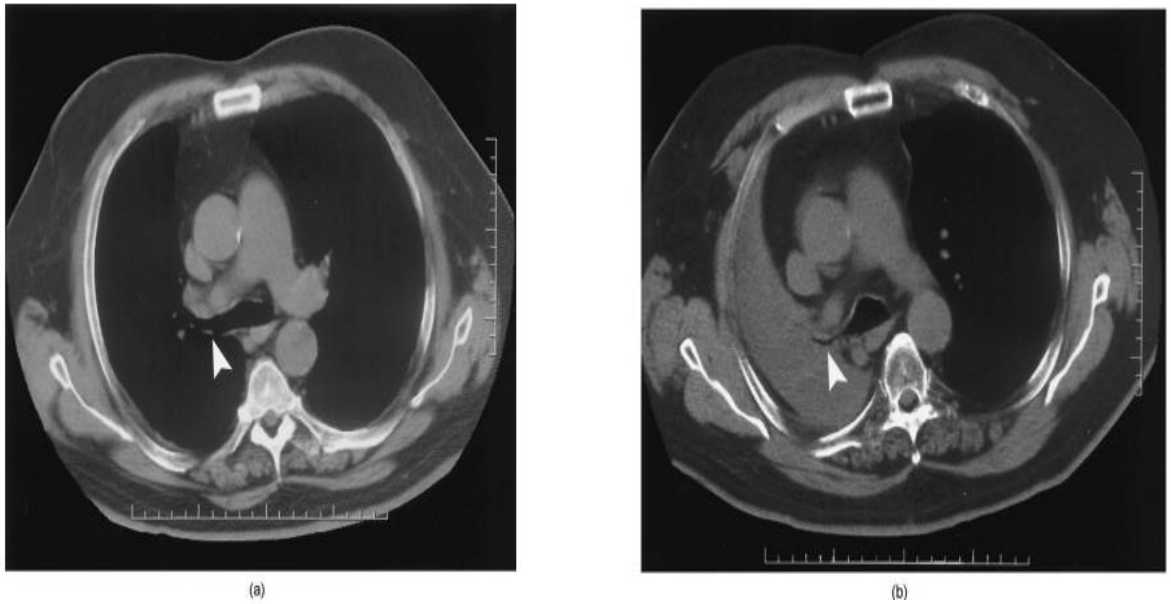


Fig.(a) Pretreatment and (b) posttreatment thoracic computed tomographic scans of showing development of marked bronchial stenosis of right mainstem bronchus (arrow)

Radiographic Changes

- X-ray:
  - ill defined patchy haziness
- CT :
  - more sensitive
  - Evaluate precise distribution and pattern of RILI
  - CTPA to exclude pulmonary thromboembolism
  - Findings:
    - Patchy or dense consolidation
    - Ground glass opacity
    - Limited to radiation port
    - May gradually disappear but may lead to fibrotic changes

Treatment related risk factors

- Risk of lung toxicities can vary based on Treatment Approaches-
  - Conventional radiation therapy
  - Conformal Radiotherapy (IMRT/VMAT)
  - Stereotactic body radiation therapy (SBRT)

- This difference is due to differences in treatment delivery and dose distribution

Patient related risk factors

- Meta-analyses (DA palma 2013) findings on patient-related adverse risk factors for Radiation Pneumonitis:

- Identified risk factors: in NSCLC and breast cancer patients
  - Older age
  - History of chronic lung disease
  - Diabetes
  - Smoking:

Defining volumes and challenges

- Inaccuracies in defining lung volume due to movement and volume changes during respiration
- Lung mass remains relatively constant, but density declines with increased volumes
- Proposal to use dose-mass histograms instead of DVHs, though not widely applied
- Likelihood of dose/volume/outcome data dependency on respiratory control type
- Majority of data derived from free breathing scans/treatment, may not apply to techniques like breath hold
- Uncertainties in defining lung borders near central airways

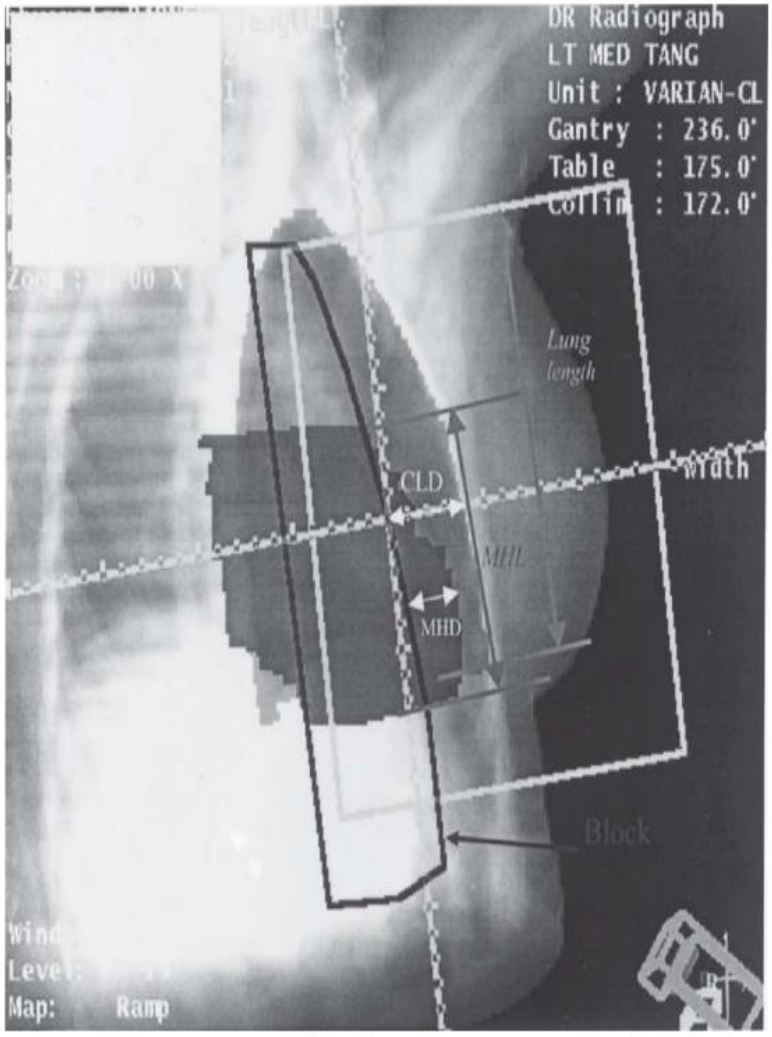


FIG. Measurement of the radiographic parameters using virtual simulator.
The contoured heart is shown in black, the lung in gray.
The central lung distance (CLD) is the lung distance in the projection of the tangential fields at the level of the central axis.
Lung length is the vertical lung distance included in the radiation port.
The maximal heart distance (MHD) is the width of heart in the tangent fields at its maximal level, whereas the maximal heart length (MHL) is the maximal length in tangential fields referring to the heart contour in a digitally reconstructed radiograph (DRR).

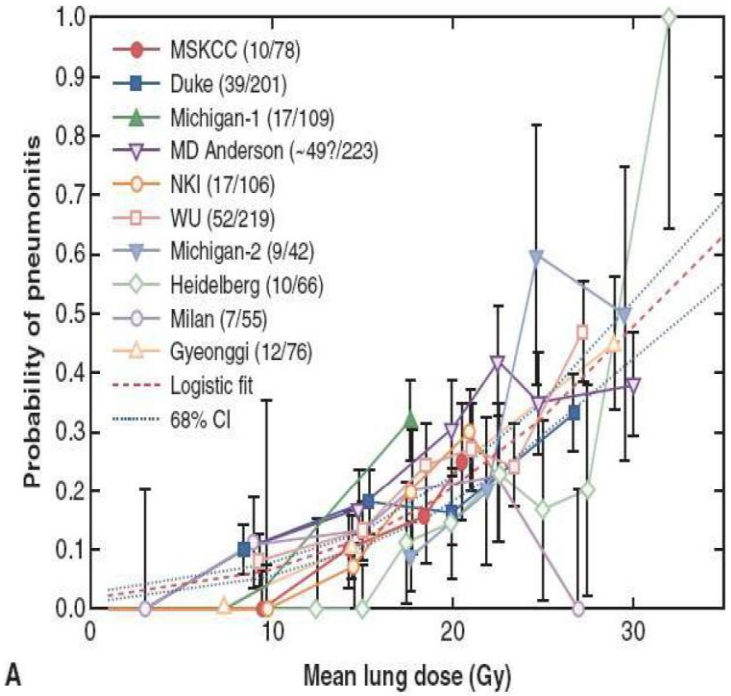
(Reprinted from Kong F-M, Klein EE, Bradley JD, et al.. Int J Radiat Oncol Biol Phys 2002;54[3])

- The anterior chest wall slopes downward from the mid chest to the neck.
- Techniques to ensure the posterior edge of the tangential beam follows this contour:
  - Rotate the collimator of the tangential beam or position the patient on a slant.
  - Use a rotating beam splitter mounted on a tray without collimator rotation.
  - Utilize multi-leaf collimation for precise beam shaping.
- The superior edge of the tangential beam remains vertically aligned.
- Typically, up to 2 to 3 cm of underlying lung may be included in the tangential portals.

- Parameters measured from simulator films for treatment planning:
  - Central lung distance (CLD): Perpendicular distance from posterior tangential field edge to posterior part of anterior chest wall at center of the field.
  - Maximum lung distance (MLD): Maximum perpendicular distance from posterior tangential field edge to posterior part of anterior chest wall.
- Length of lung at posterior tangential field edge on simulator film.
- CLD is the best predictor of percentage of ipsilateral lung volume treated by tangential fields:
  - CLD of 1.5 cm predicts approximately 6% of ipsilateral lung inclusion.
  - CLD of 2.5 cm predicts approximately 16% of ipsilateral lung inclusion.
  - CLD of 3.5 cm predicts approximately 26% of ipsilateral lung inclusion.

Studies Assessing dose volume parameters

- Several parameters have been shown to be associated with the risk of radiation pneumonitis, including V5 to V70, mean lung dose (MLD), and model-based parameters.
- These dosimetric parameters are mutually correlated, accounting for the fact that in most studies examining a range of *Vx*'s, many appear statistically significant.



Recommended dose

Multiple studies have investigated the dose and volume parameters associated with lung toxicity. Consequently, recommendations are:

1. **Emami trial**
    - Suggested keeping the Mean Lung Dose (MLD) below 20 Gy would result in a low risk (<5%) of symptomatic radiation pneumonitis
    - while MLD values exceeding 30 Gy were associated with a high risk (>20%) of complications.
2. **QUANTEC (**Quantitative Analyses of Normal Tissue Effects in the Clinic)

    (recommended several dose-volume parameters to minimize the risk of radiation pneumonitis, including:

    - Limiting the MLD to ≤20 Gy whenever feasible.
    - Keeping the volume of lung receiving ≥20 Gy (V20) as low as possible, ideally below 30%.
    - Avoiding or minimizing the volume of lung receiving high doses (>40 Gy) to reduce the risk of severe toxicity.

SBRT

- Typically involves a few large fractions (e.g., three 18-Gy or five 10-Gy fractions) over 5 to 20 days.
- High-dose volumes are small, and dose gradients are steep, minimizing dose to surrounding critical structures.
- However, multiple beams used may result in large volumes of lung receiving low to medium doses.
- Dose-volume characteristics of lung SBRT differ significantly from conventional RT and warrant special consideration.

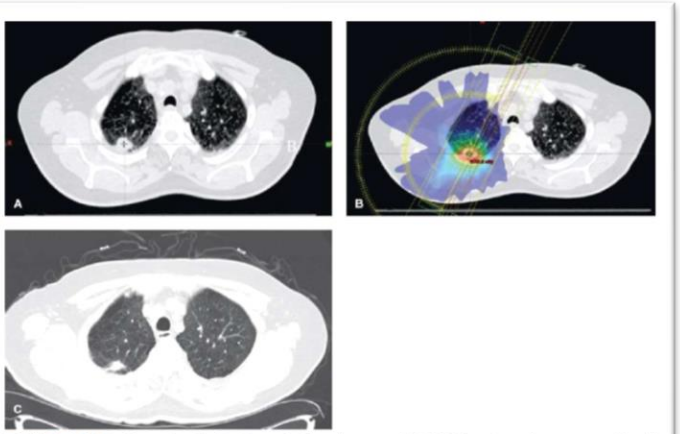


FIGURE 54.2. Stereotactic body radiation therapy (SBRT) in stage I non–small cell lung carcinoma (NSCLC). The patient was diagnosed as having T1N0M0 right upper lobe NSCLC and was treated with SBRT. **A:** Pretreatment tumor volume. **B:** Treatment plan with dose color wash. **C:** CT showing response 6 weeks after

Radiation Pneumonitis after SBRT

- Incidence:
  - Radiation-associated lung injury is relatively uncommon, typically occurring in less than 10% of cases, although one study reported rates as high as 25%.
  - Bronchial Injury: Conventional fractionation rarely leads to bronchial injury or stenosis, but SBRT targeting perihilar or central tumors may increase the risk.
- Factors from Zhao et al. Review (2021)
  - Risk of lung injury after lung SBRT is 10-15%.
  - MLD of combined lungs should be <8 Gy.
  - V20 (percent of total lung volume receiving more than 20 Gy) should be <10-15%.
  - Patients with interstitial lung disease are particularly susceptible to severe radiation-associated lung toxicity.

Dose constrains in SBRT

- Dose-response relationship for radiation pneumonitis noted in individual studies based on various metrics.
- **QUANTEC analysis of pooled data**: (Known as **HyTEC**)

  - No specific threshold identified for pneumonitis.

  - Risks increase gradually as dose increases.

- Correlation among dose-volume parameters of the lung:

  - Many parameters (V5 through V30, MLD) are correlated.

  - No "optimal" parameter identified.

- Recommendations for patients with non-small cell lung cancer:
  - Limit V20 to <30% to 35%.
  - Limit MLD to <20 to 23 Gy.
  - Aim to reduce risk of pneumonitis to <20%.
- Recommendations for patients irradiated after pneumonectomy for mesothelioma:
  - Limit V5 to below 60%.
  - Limit V20 to <4% to 10%.
  - Limit MLD to <8 Gy.

Diagnosis

Imaging Studies:

- Chest X-rays
- CT scans
- PET scans

-used to assess changes in lung parenchyma, including inflammation, fibrosis, or pneumonitis.

Pulmonary Function Tests (PFTs):

PFTs can help evaluate lung function by measuring parameters such as

- Forced vital capacity (FVC),
- Forced expiratory volume in one second (FEV1), and
- Diffusion capacity of the lung for carbon monoxide (DLCO)

Pulmonary Function Tests (PFTs):

- **Spirometry**: Spirometry measures lung volumes and airflow
- **Lung Volume Measurements**: Lung volumes, such as forced vital capacity (FVC) and total lung capacity (TLC), can be measured using spirometry or body plethysmography.
- **Diffusion Capacity**: Diffusion capacity of the lung for carbon monoxide (DLCO) measures the ability of the lungs to transfer gases from the air into the bloodstream. This test involves inhaling a small amount of carbon monoxide and measuring its uptake in the lungs.
- **Arterial Blood Gas (ABG) Analysis**: ABG analysis assesses oxygen and carbon dioxide levels in the blood, providing information about gas exchange in the lungs

Treatment

Radiation Pneumonitis

- **Corticosteroids**:

➢ Systemic corticosteroids such as prednisone or methylprednisolone (1-2 mg/kg loading dose followed by 0.5 mg/kg X 15 days as maintenance) may be used to reduce inflammation and alleviate acute symptoms of radiation pneumonitis.

- **Symptomatic Relief**:

➢ Medications such as bronchodilators or oxygen therapy may help alleviate symptoms such as cough or dyspnoea.

- **Radiation-induced pulmonary fibrosis :**
  - **Pulmonary Rehabilitation**: Structured pulmonary rehabilitation programs may help improve exercise tolerance, lung function, and quality of life in patients with chronic lung toxicities.
  - **Medication**: In cases of chronic fibrosis or pulmonary dysfunction, medications such as
    - Bronchodilators
    - Inhaled corticosteroids
    - Antifibrotic agents may be considered to manage symptoms and slow disease progression.
  - **Oxygen Therapy**: Long-term oxygen therapy may be necessary for patients with severe chronic lung disease to improve oxygenation and relieve dyspnea.

Follow-Up and Monitoring

- Imaging studies
- Pulmonary function tests

repeated periodically to evaluate treatment efficacy and disease progression.

- Thank you

- Acknowledgment:
  - Dr Arvind Padmanabhan