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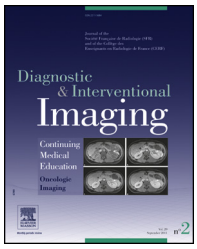

CONTINUING EDUCATION PROGRAM: FOCUS. . .

Imaging after radiation therapy of thoracic tumors

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Abstract Radiation-induced lung disease (RILD) is frequent after therapeutic irradiation of thoracic malignancies. Many technique-, treatment-, tumor- and patient-related factors influence the degree of injury sustained by the lung after irradiation. Based on the time interval after the completion of the treatment RILD presents as early and late features characterized by inflammatory and fibrotic changes, respectively. They are usually confined to the radiation port. Though the typical pattern of RILD is easily recognized after conventional two-dimensional radiation therapy (RT), RILD may present with atypical patterns after more recent types of three- or four-dimensional RT treatment. Three atypical patterns are reported: the modified conventional, the mass-like and the scar-like patterns. Knowledge of the various features and patterns of RILD is important for correct diagnosis and appropriate treatment. RILD should be differentiated from recurrent tumoral disease, infection and radiation-induced tumors. Due to RILD, the follow-up after RT may be difficult as response evaluation criteria in solid tumours (RECIST) criteria may be unreliable to assess tumor control particularly after stereotactic ablation RT (SABR). Long-term follow-up should be based on clinical examination and morphological and/or functional investigations including CT, PET-CT, pulmonary functional tests, MRI and PET-MRI.

Surgical resection remains the mainstay of therapy for early non-small cell lung cancer (NSCLC) but only 20% of those patients are eligible for surgery. Sixty percent of patients with lung cancer will benefit from radiation therapy (RT) at one time during their treatment. Complete response has been reported in 33—61% after conventional RT but the rate

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of success has more recently improved due to refinements in RT techniques [1—3]. The indications of RT in lung cancer are four types:

- *curative* in patients with medically non operable stage I or II NSCLC;
- *adjuvant* in patients with resected or resectable stage IIIa N2 single-station NSCLC;
- *combined* with chemotherapy in patients with unresectable stage IIIa N2 NSCLC, stage IIIb NSCLC or with limited-stage SCLC;
- *palliative* in order to decrease some intractable symptoms in locally advanced or metastatic lung cancer [4].

Lung injury is frequent after thoracic RT and features of radiation-induced lung disease (RILD) are important to know for correct diagnosis and appropriate management [5]. CT is more sensitive than chest X-ray for diagnosing RILD and demonstrates the related features earlier. However, interpretation of imaging examinations after RT may be difficult, as the treatment planning, including the beams arrangement and the dose distribution, is individualized for each patient. The aim of the paper is therefore to review the general principles of RT techniques that will aid in the interpretation of images obtained after treatment and to describe the typical and atypical patterns of RILD.

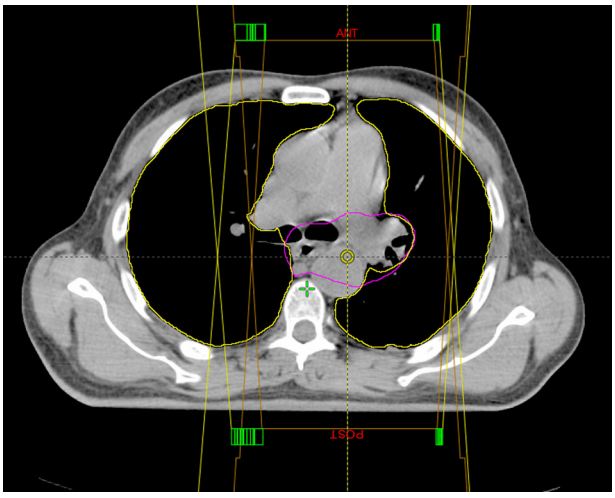

Figure 1. Basic principles of conventional 2D-RT. Example of a patient with left hilar NSCLC treated by 2D-RT. 2D-RT treatment is delivered by two opposed anterior and posterior beams generating a rectangular-shaped radiation field. Classical treatment delivers 60 Gy to the target volume in 2 Gy per fraction. Due to the limited beam orientation, the volume of normal tissue that is irradiated adjacent to the treatment field is relatively large. This technique is no longer in use nowadays.

Basic principles of two-dimensional (2D)-conventional RT

Although conventional 2D-RT is no longer in use nowadays, the principles of RT treatment and their side effects, including RILD, may be easier to understand when considering this basic technique. 2D-RT uses a single or few beams, usually 2 parallel and opposed beams generating a rectangular-shaped radiation field. The classical treatment delivers 60 Gy to the target volume in 2 Gy per fraction (Fig. 1) [6]. Typically, treatment portals for NSCLC are designed with a 2 cm margin around the tumor and a 1 cm margin around lymph node areas. For extensive mediastinal involvement, the homolateral supraclavicular area is generally included in the irradiated volume [7]. Due to the rough beam orientation, the volume of normal tissue that is irradiated adjacent to the treatment field is relatively large [5].

Radiation-induced lung disease

The pattern of RILD evolves depending of the occurrence of events from the day of completion of the RT treatment, which is also termed as the *reference point*. Clinically, pathologically and radiologically, RILD is separated in two successive phases, namely the early or acute phase and the late or chronic fibrosis phase [5,8].

Pathology and clinical manifestations

Early phase

The early or acute phase is also named as the transient radiation pneumonitis. It appears between 1 and 3 months after the end of the treatment and lasts up to 6 months. The early phase is pathologically characterized by an acute exsudative phase with injury to small vessels and capillaries resulting in vascular congestion and increased capillary permeability. Afterwards, interstitial infiltration by mononuclear and other inflammatory cells, and early deposition of collagen fibrils define the organising phase [8,9]. Lesions will gradually resolve without leaving any sequelae when injury to the lung is limited. During this phase, most patients do not present with symptoms although dyspnea, cough, low-grade fever and chest discomfort may be reported in some patients [4]. Noteworthy, symptoms may develop before any radiological change [9]. Symptomatic patients will be treated by steroids in order both to decrease their symptoms and, most of all, to prevent the development of the late phase [5,8].

Late phase

The late phase is also named as the chronic radiation fibrosis. It results from an unresolved acute radiation pneumonitis and may last from the 6th to the 12th month after RT or even the 24th month in some conditions. Lesions are usually considered as stable and definite after 2 years [5]. The late phase is pathologically characterized by a marked increase in the deposition of fibrous tissue, fibroblasts proliferation, progressive vascular sclerosis, collapse and obliteration of alveolar air spaces [8,9]. Patients are mostly non symptomatic but depending on the extent of the lesions may present with progressive dyspnea, dry cough or even *cor pulmonale* due to pulmonary hypertension [4].

Imaging of typical pattern or RILD

The imaging findings of RILD will also change according to the pathological alterations. The typical findings will be

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