Imaging Interpretation of Complications Following Chest Radiation Therapy

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Learning objectives

• Describe some unusual imaging findings and complications following radiation therapy of the chest.
• Discuss the radiologic and clinical features that can help distinguish between radiation therapy-related abnormalities and infection, recurrent disease or new malignancy.
Background

Radiation therapy is widely used to treat or palliate intrathoracic and chest wall malignancies. Several factors are responsible for the severity and extent of damage to the thoracic structures: Total dose, fractionation of the dose, individual susceptibility and previous or concomitant therapy.

In conventional radiation therapy, the dose is delivered to the tumor in two parallel beams that are opposed in orientation. Relatively large volumes of normal tissue are included within the radiation field that may cause unintended damage to the adjacent structures.

Newer radiation delivery techniques: Three-dimensional (3D) conformal therapy and stereotactic body radiation therapy (SBRT), increase the radiation delivered to the tumor while decreasing radiation exposure of normal tissue.

Dramatic changes to normal tissue can be seen following radiation. Some may mimic infection or recurrence of malignancy.

LUNG

Cavitation: Pulmonary necrosis is an uncommon complication, that usually occurs with conventional radiotherapy for lung cancer with dose equal or higher than 50-60Gy. Cavitation due to pulmonary or bronchial necrosis may be seen as early as 6-12 weeks following therapy but has been reported as long as 1-7 years post-radiation.

Cavitation tends to occur within the areas of fibrosis. The possibility of infection should be considered if the cavitory lesion develops before the completion of therapy, is outside of the radiation portal or when the CT findings include centrilobular or branching linear opacities. Fig. 1 on page 8

In patients with a pulmonary solitary lesion treated with stereotactic radiation therapy, cavitation of the tumor has been reported to occur during treatment, presumably secondary to compromise of the tumor vascular supply.

Radiation-Associated Organizing Pneumonia: Organizing pneumonia (OP) is a non-specific pulmonary response to a variety of pulmonary insults including those from infection, drug toxicity, collagen vascular disease, hypersensitivity pneumonitis, chronic eosinophilic pneumonia, or diffuse alveolar damage. It has been described following radiation therapy for the treatment of breast and lung cancer. The classic CT findings of OP include: Peripheral and peribronchovascular consolidation and ground-glass opacities. Atypical imaging features such nodules, crazy paving, bands and the reversed halo sign have also been reported.
The opacities are located within and outside the radiation port and may also involve the contralateral non-irradiated lung. Fig. 2 on page 8 and Fig. 3 on page 9. Infection is the principal differential diagnosis. The diagnosis of radiation-associated OP is made when there has been exclusion of other possible etiologies such as infection, hemorrhage or drug toxicity.

**Infection:** The pulmonary opacities seen with radiation-induced lung disease (RILD) can be confused with infection or tumor recurrence but should be differentiated from them. New opacities occurring prior to completion of radiation therapy or outside of the radiation port may represent infection rather than acute radiation pneumonitis, especially if they evolve rapidly and are associated with abrupt onset and fever. Mycobacterial infection (MAI) may develop in this patient population and should be suspected when bronchiectasis, centrilobular nodules and cavitation are identified. Fig. 4 on page 10. Occasionally the imaging findings of radiation fibrosis may be in a similar distribution to that of MAI infection. The presence of centrilobular nodules, and involvement of non-irradiated lung can be used as a clue to distinguish between infection and RILD.

**Recurrent Disease:** Alteration in the contour of previously stable radiation changes is suspicious for tumor recurrence. Filling in of bronchi within radiation fibrosis is abnormal and usually represents recurrence or superimposed infection. Development of new nodules after completion of radiation, irregularity of the airways, diaphragmatic elevation due to phrenic nerve invasion and bone destruction are signs of recurrence. At times, chest radiograph and CT imaging may not differentiate radiation-induced lung disease from recurrent malignancy. Fluorodeoxiglucose (FDG) positron emission tomography (PET) helps differentiate tumor from fibrosis by demonstrating focal FDG uptake at the recurrence site. Diffuse FDG uptake can be seen with infection and with radiation pneumonitis Fig. 5 on page 10- Fig. 6 on page 11. Because FDG uptake is seen with radiation pneumonitis, FDG PET/CT is recommended later than 3 months following completion of radiation therapy.

**MEDIASTINUM**

**Thymic Cyst:** They may arise in patients irradiated to the thymic bed such as those treated for Hodgkin disease, head and neck or breast cancer. They usually arise years following radiation therapy, are fluid attenuation lesions with thin smooth walls. Fig. 7 on page 12- Fig. 8 on page 13.

**Lymph Nodes:** Calcifications involving lymph nodes after radiation therapy for lymphoma are frequently seen more than one year after treatment. Calcification of a non-enlarging
mass means favorable response to therapy. Keeping this concept in mind avoids confusion with granulomatus disease. Fig. 9 on page 14.

*Heart*: Cardiovascular disease is frequently seen in patients treated with radiotherapy for breast cancer and lymphoma, especially when radiation was delivered in patients younger than 40 years old.

These patients have an increased risk for coronary disease pericardial disease, congestive heart failure and sudden death.

The pericardium is the most frequently affected. Pericardial disease may be seen as pericardial effusion, usually after 12-18 months but has even been reported a few days following initiation of radiation therapy, with or without fever, chest pain and ECG abnormalities. Fig. 10 on page 14. Chronic pericarditis may occur months or several years after radiotherapy. Acute or delayed pericarditis may present with tamponade, enlargement of the cardiomegasternal silhouette, pericardial calcifications, pericardial effusion, and signs of heart failure.

Constrictive physiology is observed in 15-20% of patients with radiation-induced pericarditis. A pericardial thickness of 4 mm with impaired ventricular diastolic filling is consistent with constriction. The aortic and mitral valves are the valves more commonly involved with radiation induced valvular heart disease. The changes can progress from valvular thickening to calcifications. Fig. 11 on page 15.

*Esophagus*: The esophagus is frequently included in the radiation therapy field when patients are treated for mediastinal and lung malignancies. Esophageal dysmotility is the earliest and most common finding. Mucosal changes such as edema, ulceration and fistula formation may occur. These findings can be expected 4-12 weeks after completion of radiation therapy. Esophageal strictures occur 4-8 months after completion of therapy and usually have smooth, tapered margins. On CT esophageal wall thickening and dilation are frequent findings after radiation therapy. Fig. 12 on page 16.

**CHEST WALL**

*Bone*: The spectrum of bone complications includes fractures, osteitis, bone growth alteration (in children) and benign and malignant tumors.

The incidence of rib fractures after radiation therapy is approximately 1.8%. More than one rib is generally involved and non-union of fractures are common. These fractures are linear without expansile changes or cortical destruction. Callus formation may have an atypical appearance that may simulate radiation induced sarcoma. Fig. 13 on page 17.
Osteitis usually develops 2-3 years following radiation therapy. A mottled pattern, with osteopenia, coarse trabeculation and areas of increased density are identified, and may be confused with metastases or new bony malignancy. A previous history of radiation in the area of the bony changes associated to stability at follow-up, favor osteitis. Fig. 14 on page 18. The presence of a mass or new pain is an uncommon finding and is suspicious for malignancy.

**Muscle:** Radiation-induced muscle injury (myositis) is infrequently reported in the literature as a result of radiation therapy. Larger total doses and large doses per fraction appear to be related to development of muscle injury. The onset of symptoms occurs approximately three months following completion of radiation therapy. Thickening or focal collection involving the muscle is identified. The affected regions are often FDG avid on PET/CT Fig. 15 on page 19. Chronic changes typically present as discrete areas of muscle atrophy and fibrosis corresponding to the radiation treatment port. The differential diagnosis include soft-tissue metastasis, focal areas of infection and hematoma. Correlation with previous history of trauma, local signs of infection may help to exclude hematoma or infectious myositis.

Patients previously irradiated for breast cancer and lung cancer are at risk of developing a second breast malignancy such as angiosarcoma, osteosarcoma and spindle cell sarcoma.

In patients with soft tissue sarcoma, such as fibrosarcoma, histiocytoma, spindle cell sarcoma, the presence of mass or new soft tissue in a previously irradiated site raises the possibility of radiation induced malignancy. Fig. 16 on page 20. Infection and metastases are in the differential diagnosis.

Bony changes outside the treatment field are highly suspicious for metastasis. Ultimately confirmation with biopsy is needed. In the case of radiation induced-osteosarcoma, radiation osteitis is the main differential diagnosis. The absence of associated soft tissue mass, favors the diagnosis of osteitis Fig. 17 on page 21

**UPPER ABDOMEN**

Radiation-induced liver disease is associated to radiation therapy for esophageal carcinoma or mesothelioma. The irradiated liver appears hypodense on CT scan with well-defined linear margins that conform to the radiation portals. Fig. 18 on page 22. These patients may be asymptomatic or present with abdominal pain, ascites and hepatomegaly occurring 2 weeks to 4 months after hepatic irradiation. Injury to the spleen and pancreas may occur following radiation for lymphoma, mesothelioma, and esophageal carcinoma. The spleen is a very radiosensitive organ. Splenic fibrosis and atrophy may result, most of the time without clinical significance; rarely pneumococcal
sepsis could be a potential complication. Irradiation to the pancreas causes necrosis and fibrosis similar to chronic pancreatitis, with resultant small size of the pancreas and fatty replacement.
Fig. 1: Cavitation due to radiation therapy in a 58-year-old man after radiation therapy for left upper lobe carcinoma. Contrast enhanced chest CT five months following completion of radiation therapy shows a pulmonary cavity communicating with the bronchial tree (arrow). There are consolidative opacities and volume loss compatible with radiation fibrosis. No additional findings suggestive of infection were seen.

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Fig. 2: Organizing Pneumonia in a 53-year-old woman following radiation therapy for breast cancer. Radiation treatment plan for right breast cancer.

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**Fig. 3:** Organizing Pneumonia in a 53-year-old woman following radiation therapy for breast cancer. CT scan shows scattered areas of consolidation in the right lung inside and outside of the radiation port. Bronchoalveolar lavage and cultures were negative for infection and the opacities resolved after treatment with steroids.

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**Fig. 4:** Pulmonary infection in a 90 year-old woman with left upper lobe malignancy. Contrast enhanced chest CT 2 years following completion of radiation therapy, demonstrates areas of dense consolidation, volume loss and traction bronchiectasis consistent with radiation pneumonitis. There are nodular opacities in a tree-in bud pattern in the right lower lobe (arrows). Bronchoalveolar lavage grew Mycobacterium Kansasii.

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Fig. 5: Radiation fibrosis in a 60-year-old man, with left lung malignancy. Axial unenhanced CT 12 months following radiation therapy shows dense paramediastinal opacities and traction bronquiectasis consistent with radiation pneumonitis.

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Fig. 6: Radiation fibrosis in a 60-year-old man, with left lung malignancy. Fused axial PET/CT shows lower but persistent FDG uptake (arrow), which is consistent with radiation fibrosis and should not be misinterpreted as residual or recurrent tumor.

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Fig. 7: Thymic cyst in a 45-year-old woman 5 years after completion of radiation therapy for papillary thyroid carcinoma. Unenhanced chest CT (lung windows) demonstrates radiation induced fibrotic changes in the lung apices.

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**Fig. 8:** Thymic cyst in a 45-year-old woman 5 years after completion of radiation therapy for papillary thyroid carcinoma. Mediastinal windows, show a hypodense lesion in the thymic bed with imperceptible walls most suggestive of a cyst, confirmed at surgery to represent a thymic cyst.

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**Fig. 9:** Mediastinal calcifications in a 33-year-old woman 4 years following radiation for Hodgkin disease. Contrast enhanced chest CT, mediastinal window, shows residual soft tissue in the anterior mediastinum with coarse calcifications consistent with treated lymphoma.

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Fig. 10: Pericardial effusion in a 45-year-old asymptomatic man, 3 months after completion of radiation therapy for esophageal carcinoma. Contrast enhanced chest CT (mediastinal windows) shows moderate pericardial effusion.

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**Fig. 11:** Pericardial calcifications in a 55-year-old man 5 years following radiation therapy for lymphoma. Unenhanced CT scan axial, shows pericardial calcifications secondary to previous radiation as well as pleural effusions. The patient was asymptomatic.

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Fig. 12: Esophago-pleural fistula in a 58-year-old man after radiation therapy for lung cancer. Contrast enhanced CT scan two years after radiation therapy, demonstrates dilation of the proximal esophagus and esophageal fistula, communicating with the pleural space (arrow).

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Fig. 13: Rib fractures in an 83 year-old woman four years following radiation therapy for a left lower lobe malignancy. CT Scan (bone window). Left rib fractures with exuberant callus formation (arrow) and pleuro- parenchymal opacities due to previous radiation. Stability of the bone changes, which are limited to the radiation ports, ruled-out malignancy.

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Fig. 14: Osteitis in a 63-year-old woman 3 years following radiation therapy for a right upper lobe malignancy. Unenhanced CT scan (bone window), axial shows areas of radiolucency and sclerosis involving the right upper ribs consistent with osteitis, limited to the radiation field. The opacities in the lung are consistent with radiation therapy for lung malignancy.

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Fig. 15: Radiation-induced myositis, two years following radiation therapy for lung cancer. Fused axial PET/CT demonstrates a thickened region in the left pectoralis minor muscle (arrow) with low grade FDG-activity. The fine needle aspiration showed inflammatory material, without malignant cells. Culture was negative. The FDG-uptake in the left upper lobe malignancy is worrisome for recurrent of the disease.

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**Fig. 16:** Radiation-induced fibrosarcoma in a 60-year-old woman following radiation for right upper lobe cancer. Contrast enhanced CT scan at the superior chest wall, demonstrate a large soft tissue mass with enhancement after administration of contrast (arrows). Biopsy of this lesion showed fibrosarcoma.

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**Fig. 17:** Radiation-induced osteosarcoma in a 70-year-old woman following radiation for breast cancer. Axial unenhanced CT demonstrates a partially calcified mass involving the proximal portion of the left clavicle. Biopsy showed osteosarcoma.

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**Fig. 18:** Radiation changes in the liver in a 59-year-old man with right pleural mesothelioma, treated with extrapleural pneumonectomy and adjuvant radiation therapy. Contrast enhanced CT, shows a peripheral hypodense region in the liver (arrows), a region that was included in the radiation portal. Some nodular areas within the irradiated liver correspond to preserved/less injured parenchyma.

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Imaging findings OR Procedure details

Chest CT, axial images with or without contrast. 2.5 mm slice thickness. Fluorodeoxyglucose (FDG) positron emission tomography (PET).
**Conclusion**

Complications from chest irradiation are diverse, and can affect the lungs, pleura, pericardium, thymus, lymph nodes, heart, chest wall and upper abdomen.

Complications from radiation therapy include inflammation, infection and the development of second primary malignancies, and should be differentiated from the expected evolution of radiation changes.

The radiologist should be familiar with the radiological appearance of radiation induced complications in order to positively impact patient management and provide helpful advice on the most useful imaging modalities to be used for investigation and follow up of these patients.
References