Iatrogenic changes in Chest CT after lung and breast cancer treatment - a comprehensive review of imaging features.

Poster No.: C-2222  
Congress: ECR 2015  
Type: Educational Exhibit  
Authors: C. M. Oliveira, R. A. Costa, A. Estevao, F. Caseiro Alves; Coimbra/PT  
Keywords: Lung, Thorax, Breast, CT-High Resolution, CT, Conventional radiography, Treatment effects, Radiation effects, Surgery, Drugs / Reactions, Neoplasia  
DOI: 10.1594/ecr2015/C-2222

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

1- Explain what type of treatments cause iatrogenic changes in the chest CT and in which diseases they are used.

2- Provide the reader with the ability to differentiate those iatrogenic changes from the ones disease-related, providing mainly CT images and radiographs.
Background

In 2012, lung and breast cancers combined accounted for about 25% of all cancers worldwide and were responsible for more than 20% of cancer-related deaths. Nowadays, with the wide variety of treatment options, the radiologist needs to be aware of the changes caused by both the disease and its treatment. Depending on the disease and its stage, different treatments can be used, usually ranging between surgery, radiation and chemotherapy.

This work is divided following these three types of treatment.
Findings and procedure details

Surgery-based treatments

Pulmonary resection techniques include pneumonectomy (intrapleural, extrapleural, intrapericardial, and sleeve pneumonectomy), lobectomy, and limited resection (sleeve lobectomy, segmentectomy, nonanatomic parenchyma-sparing resection). Intrapleural pneumonectomy is the most frequently used procedure and involves resection of the lung and surrounding visceral pleura. (Fig. 1 on page 11 and Fig. 2 on page 11) Extrapleural pneumonectomy involves en bloc resection of the ipsilateral lung, parietal and mediastinal pleura, pericardium, and diaphragm.

Limited resection of the lung and major airways refers to surgical procedures that preserve functioning lung tissues and provide adequate cancer treatment. Sleeve lobectomy, segmentectomy, and wedge resection are examples of these types of surgery.

Sometimes, the only clue guiding the radiologist to the existence of a previous lobectomy is the displacement of a normal fissure in otherwise normal lung parenchyma. (Fig. 3 on page 12)

Complications of Surgery-based treatments

Hemothorax

Inadequate haemostasis of a bronchial artery or systemic vessels in the chest wall usually leads to major haemorrhage following thoracotomy. It infrequently results from the slipping of a ligature from a major pulmonary vessel or an unrecognized injury to a systemic vein. Bleeding related to a coagulation abnormality is rare.

Although hemothoraces are common, the overall mortality rate associated with uncontrolled bleeding is less than 0.1%. Hemothorax often manifests as a rapidly enlarging pleural effusion. (Fig. 4 on page 13) CT can demonstrate hemorrhagic pleural effusions as areas of high attenuation. (Fig. 5 on page 14) CT findings in hemothorax include heterogeneously attenuating pleural fluid with hyperattenuating areas of debris within pleural fluid. Some hyperdense nodular masses within the pleural effusion can be distinguished from pleural-based masses by their high attenuation on unenhanced CT scans. If there is a leak from the pulmonary or systemic vasculature, it is possible to observe contrast product in the pleural space. (Fig. 6 on page 15)
Chylothorax

Chylothorax is defined as an accumulation of chyle in the pleural space caused by disruption of the thoracic duct or one of its major divisions. It is diagnosed by measuring triglyceride levels in the pleural fluid (usually greater than 110 mg/dL). Rapid excessive filling of the postpneumonectomy space with fluid on chest radiographs can be seen as a sign of a developing chylothorax. The attenuation of chylous effusions at CT is variable, going from hipodense (derived from the fat content) to hyperdense because of the high protein content of the fluid (being the latter the commonest appearance).

Persistent Air Leak

If bronchioles or alveolar spaces remain open, bronchioloalveolar leakage develops and an air leak results. Nearly all patients undergoing lobectomy or segmentectomy can be expected to experience some degree of postoperative air leakage. It is also common in pulmonary resection performed in older patients with emphysema. Chest radiography and CT show persistent pneumothorax (Fig. 7 on page 15), pneumomediastinum (Fig. 8 on page 16), or subcutaneous emphysema. Although common, most of the leaks resolve in a day or two without need for re-intervention. Persistent air leak usually leads to prolonged hospitalization and increased costs; however, it does not directly imply a higher morbidity and mortality rate.

Bronchopleural Fistula (BPF)

BPF remains the most dreaded complication following thoracic surgery. Its prevalence is reported to range between 2% and 13% and mortality rates can rise up to 70%. BPF is more common after right pneumonectomy than after left pneumonectomy. This is probably due to anatomic features of the right main bronchus including larger size, greater tendency to spring open, and less mediastinal coverage than the left main bronchus. In the immediate postoperative period, bronchial leaks are rare and are usually due to faulty closure of the bronchus. Delayed BPF is much more common and is usually due to infection or recurrent tumor of the bronchial stump. To avoid avascular necrosis of the stump, the surgeons should aim to preserve the bronchial vascularity. BPF usually develops in the bronchial stump after pneumonectomy or lobectomy and is usually diagnosed with bronchoscopy. Radiologic findings in BPF consist of (a) a continuous increase in the residual intrapleural airspace, (b) the appearance of an air-fluid level, (c) changes in an already present air-fluid level and (d) development of tension pneumothorax. Westcott and Volpe found CT to be useful in the diagnosis and management of peripheral BPF. CT findings in BPF include air and fluid collections in the pleural space and demonstration of a communication or tract from an airway or the lung parenchyma to the pleural space.
Empyema

Empyema is a serious but uncommon complication of pulmonary resection, occurring in 2%-16% of patients. It is also associated with high mortality rates that range from 16% to 71%. Postpneumonectomy empyema occurs more commonly with completion pneumonectomy (ie, pneumonectomy following previous lobectomy), right pneumonectomy or intraoperative contamination of the pleura. (Fig. 9 on page 17) Empyema usually occurs in the early postoperative period but can develop months or even years after surgery. It is usually due to residual infection in the pleural cavity. Empyema may also occur secondary to BPF or esophagopleural fistula.

On CT exams, empyema is characterized for multiple signs:

- Enhancing thickened pleura whereas pleural effusion have thin imperceptable pleural surfaces (Fig. 10 on page 18)
- Absence of gas unless recent thoracocentesis
- Obvious septations
- Associated consolidation (Fig. 11 on page 19)
- Associated adjacent infection (e.g. sub-diaphragmatic abscess)

Atelectasis

Atelectasis resulting from retained secretions and subsequent lack of aeration of various parts of the remaining pulmonary parenchyma is often seen after pulmonary resection. In some patients, infection may be superimposed on unresolved atelectatic areas or may result from unrecognized episodes of aspiration. CT shows ground-glass attenuation and consolidation in the atelectatic lobe, with marked decrease in lobe size.

Pneumonia

The reported prevalence of postthoracotomy pneumonia ranges from 2% to 22%. There can be a time lapse before there is radiographic evidence of pneumonia after clinical presentation. Postoperative pneumonia is most common in patients requiring prolonged ventilatory support or who have ongoing difficulty in clearing tracheobronchial secretions. Postoperative pneumonia is most often caused by aspiration of gastric secretions (Fig. 12 on page 20) and bacterial colonization of the atelectatic lobe. Chest radiographs typically show patchy bronchopneumonic patterns. A prolonged disease course or large aspirations may result in severe necrotizing bronchopneumonia (Fig. 13 on page 21)

Pulmonary Edema
Postoperative pulmonary edema is a life-threatening complication that develops 2-3 days after pulmonary resection, usually after pneumonectomy or lobectomy, although less common in the latter. Postpneumonectomy pulmonary edema is a clinical condition in which a patient experiences rapidly progressing dyspnea and hypoxemia and the remaining lung develops rapid infiltration, progressing to diffuse interstitial pulmonary edema, consolidation, and adult respiratory distress syndrome. The most common cause of the edema is overhydration from excessive fluid replacement during surgery. Other causes are acute myocardial infarction with left heart failure, decreased serum protein concentration or capillary injury from sepsis or prolonged inspiration of gases with a high oxygen concentration. The most frequent radiologic findings are similar to those in hydrostatic pulmonary edema without diffuse alveolar damage and include Kerley lines, peribronchial cuffing, and ill-defined vessels. (Fig. 14 on page 22) These findings have a tendency to disappear within a few days.

**Gossypiboma**

The term gossypiboma is used to describe a mass within the body that is composed of cotton matrix and most commonly refers to a retained surgical sponge. The pleural space is the most likely site for surgical swabs, but the swabs may become invaginated into the lung, mimicking an intrapulmonary lesion. Early in the postoperative period, gossypiboma may be confused at radiology with lung abscess, loculated empyema, complicated hematoma, or seroma.

**Esophagopleural Fistula**

Esophagopleural fistula is a devastating pathologic condition that occurs in 0.2%-1.0% of patients who undergo pneumonectomy. Patients with esophagopleural fistula represent a very heterogeneous group because the condition can result from at least three different mechanisms: surgically-caused injury, mediastinal cancer recurrence, and chronic infection. Large lesions appear during the immediate postoperative period. A diagnosis of esophagopleural fistula is obvious when food particles appear in the drainage fluid. Smaller leaks may lead to chronic empyema as they are harder to detect.

Esophagography can be used as an imaging modality (Fig. 15 on page 23). Standard and high-resolution CT are also useful in the diagnosis and management of esophagopleural fistula or of any tumor recurrence that creates a fistula at the bronchial stump.

**Radiation**
Injury to the lung is common after therapeutic irradiation of intrathoracic and chest wall malignancies.

Radiologic manifestations of radiation induced lung disease (RILD), including groundglass opacities or consolidation in the acute phase and traction bronchiectasis, volume loss, and consolidation in the late phase, are well described in the literature.

It is crucial to the radiologist to know of the expanded spectrum of these manifestations to provide an early diagnosis and, consequently, better treatment of patients after radiation therapy for intrathoracic malignancies.

Radiation pneumonitis and fibrosis are expected changes in the chest. Other more serious complications such as myocardial infarction, pericardial effusion, brachial plexus neuropathy, bone and soft tissue necrosis, fractures and radiation-induced malignancy may also occur.

**Radiation induced pneumonitis**

Radiation induced pneumonitis typically develops approximately 6-8 weeks after treatment with doses of 30-40 Gy and is a well known early expected effect of therapy that is related to total dose given. Radiation pneumonitis is most extensive 3-4 months following the end of therapy and eventually leads to radiation fibrosis. Fibrosis becomes a stable finding approximately 9-12 months after therapy and should remain relatively stable unless there is superimposed infection or recurrent tumor.

Radiation injury to the lungs does not follow anatomic boundaries. It has sharp, well defined areas of air space consolidation with borders that conform to the radiation portals, and this specific finding is the most valuable to the radiologist to correct diagnose a case of radiation induced pneumonitis (Fig. 16 on page 24). Less extensive radiation pneumonitis may present as patchy consolidation in the irradiated field and when the damage is very early or minimal in extent, manifests as indistinctness of the pulmonary vasculature (Fig. 17 on page 25).

Radiation fibrosis is generally seen in all patients who received therapeutic doses of radiation. Bronchiectatic changes may also be seen (Fig. 18 on page 26). Less obvious changes include minimal pleural thickening, slight elevation of the hila or minor fissure, slight medial retraction of pulmonary vessels, minimal tenting of elevation of a hemidiaphragm and minor blunting of cardiophrenic angles. Volume loss is typical. Therefore, on CT, radiation induced disease can appear as homogeneous consolidation, patchy consolidation, discrete consolidation or solid consolidation. Radiation induced fibrosis present, on CT, with: a) volume loss, b) linear scarring, c) chronic consolidation often with air-bronchograms, d) traction bronchiectasis, e) mediastinal shift, f) pleural thickening, and g) ipsilateral pleural effusion (Fig. 19 on page 27).
Recurrent disease should be suspected in irradiated lung if there is alteration in the stable contours of radiation fibrosis, failure of contracture of an area of radiation pneumonitis or filling in of ectactic bronchi.

**Radiation induced bone necrosis**

Changes in bone after radiotherapy follow a characteristic pattern. For diseases of the chest, these changes typically encompass the ribs, clavicle and shoulder. The first conventional radiographic sign of change is demineralization and osteopenia which develops approximately 12 months after therapy is completed and may be progressive. Small lytic areas in irradiated bone may be seen and may be difficult to distinguish from metastatic disease. (Fig. 20 on page 28) Spontaneous fractures, aseptic necrosis and bony resorption may also occur within the radiation field.

**Chemotherapy**

Classic chemotherapy agents inhibit cell division and target rapidly proliferating cells. Newer molecular targeted therapies are directed at specific molecules responsible for regulating cell activities, and the onset and presentation of their toxicities may therefore differ.

**Pulmonary infiltrates**

Pulmonary infiltrates are the most common radiologic manifestation of both classic and new targeted chemotherapy toxicities. Toxicity from the classic chemotherapy agents typically results in bilateral interstitial infiltrates presenting with progressive dyspnea. The radiologist should be aware that some pulmonary toxicities can be asymptomatic. These pulmonary infiltrates should not be mistaken for tumor progression.

Pulmonary infiltrates that develop in patients undergoing chemotherapy can result from progression of disease, infection and inflammation caused by chemotherapy toxicity. Knowledge about which chemotherapy agents are more likely to cause pulmonary toxicity may aid in judging the most likely cause. Chemotherapy-induced lung injury can manifest early as infiltrates, pulmonary edema, hypersensitivity reaction, or pleural effusions. Pulmonary toxicity of some of the older standard chemotherapy agents can be dose dependent-seen at high cumulative doses, as in the case of bleomycin and carmustine. Of the standard agents, bleomycin and methotrexate are most often associated with pulmonary toxicity. Several radiologic patterns of pulmonary toxicity have been associated with bleomycin, including cryptogenic organizing pneumonia (Fig. 26 on page 34), eosinophilic hypersensitivity (Fig. 27 on page 35), and,
most commonly, interstitial pneumonitis, which may progress into fibrosis. Methotrexate pulmonary toxicity typically presents within the 1st year of therapy with bilateral interstitial and alveolar infiltrates and pleural effusions, is often accompanied by fever and peripheral eosinophilia, and does not progress to fibrosis if the medication is stopped. There are other drugs that can produce similar changes in the lungs, although the extensive description of those is beyond the scope of this work.

Four radiologic patterns have been described on CT scans: (a) a nonspecific area with ground-glass attenuation (Fig. 22 on page 30 and Fig. 23 on page 31), (b) multifocal areas of airspace consolidation, (c) patchy distribution of ground-glass attenuation accompanied by interlobular septal thickening (Fig. 25 on page 33), and (d) extensive bilateral ground-glass attenuation or airspace consolidations with traction bronchiectasis (Fig. 24 on page 32). The most common pattern is a nonspecific area of ground-glass attenuation, and the pattern associated with the highest mortality rate is extensive bilateral ground-glass airspace consolidation, thought to represent diffuse alveolar damage.

**Pulmonary haemorrhage**

Major and fatal hemoptysis can occur in patients treated with bevacizumab for non-small cell lung cancer, reported in about 5% of patients. Tumour necrosis and cavitation were found as potential risk factors for pulmonary haemorrhage. So much that a squamous histologic appearance is a risk factor for pulmonary haemorrhage, becoming an exclusion criterion for bevacizumab therapy. (Fig. 21 on page 29)
Fig. 1: Lung cancer located in the left hilum (arrow), with multiple micronodules in the superior left lobe, corresponding to hematogenous spread.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 2:** The patient depicted in Fig.1 underwent a left pneumectomy. Notice the mediastinal shift to the left, where no lung parenchyma is seen.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 3:** The arrow points to the right oblique fissure in its normal location. In a normal situation, there should be a similar structure on the left side (the left oblique fissure). This patient had a left superior lobectomy.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
Fig. 4: The chest radiographs depicted here were obtained one day apart, being the right one the most recent. On the right, a "white lung" is seen. It was related to a hemothorax that developed in just 24 hours.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT

Fig. 5: Hyperdense material in the pleural cavity (arrow). When aspirated, the pleural fluid had a considerable amount of blood.
Fig. 6: There is a moderate hemothorax on the right, where there is evidence of contrast material (arrow). This image is diagnostic of a leak between a blood vessel and the pleural cavity.
Fig. 7: Tension pneumothorax on the left, with mediastinal shift to the right.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 8:** Pneumomediastium caused by a bronchial leak. This type of fistula can happen between a bronchial structure and the pleural cavity, leading to a bronchopleural fistula.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
Fig. 9: Empyema after left pneumectomy - There is fluid in the remanescent pleural cavity, with thick borders and some enhance following contrast administration.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 10:** Empyema after right pneumectomy - There is fluid in the remanescent pleural cavity, with thick borders and some enhance following contrast administration. Notice the volume loss of the right hemithorax, with elevation of the diaphragm (there is a considerate amount of liver parenchyma seen in this image)

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 11:** Empyema - Some signs that should be reported: 1 - Mediastinal shift to the right (loss of volume on the right hemithorax, following a lower lobe resection) 2 - Fluid in the right pleural cavity, with enhancing thick borders, corresponding to an empyema. 3 - Consolidation of some areas of lung parenchyma in contact with the empyema.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
Fig. 12: Area of ground-glass density, mainly in a central location, sparing the subpleural space. This patient had aspirated his vomit the previous night, leading to a aspiration pneumonia.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 13:** Necrotizing pneumonia after middle lobe resection. Note the cavitation where the middle lobe originally was, as well as some ill-defined nodules in the right lower lobe, due to inflammatory changes.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 14:** Pulmonary edema - Ground-glass areas in a predominantly central location, sparing some subpleural ones, with large vessels. Cardiomegaly.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 15:** Esophago-pleural fistula. After swallowing a barium meal, it opacifies a rather visible esophago-pleural fistula.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
Fig. 16: Radiation pneumonitis - interstitial thickening, mainly in posteromedial location on the right lung, with straight borders, not following any anatomical one.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
Fig. 17: Small lung nodule, ill-defined, caused by previous radiotherapy (arrow). Note some interstitial thickening in the vicinity of that nodule.
Fig. 18: Fibrotic changes after radiation therapy. This area shows yet again straight borders with bronchiectasis.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
Fig. 19: Radiation pneumonitis - interstitial thickening with straight borders, not following any anatomical one. Small focal collection of pleural effusion (dotted dash).

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 20:** Permeative lytic pattern on the first three ribs on the right (arrows), related to osteoradionecrosis. There is also a sclerotic mass on the anterior border of the second rib of residual nature (dotted arrow). The bottom image was obtained using a MIP algorithm.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 21:** Alveolar hemorrhage. Widespread ground glass opacification in a central position, sparing the subpleural space.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
Fig. 22: Area of ground-glass opacification in a emphysematous lung.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 23:** Single area of ground-glass opacification in the left lower lobe, with some associated atelectasis.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 24:** Diffuse pulmonary fibrosis with bronchiectasis.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
Fig. 25: Diffuse and patchy distribution of ground-glass attenuation.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 26:** Organizing cryptogenic pneumonia with area of groundglass opacification (arrow) and atoll's sign (dotted arrow) - ground glass opacification surrounded by a denser rim.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
**Fig. 27:** Eosinophilic hypersensitivity pneumonia - Wide areas of groundglass opacification in a mosaic appearance.

© Medical Imaging Department, Faculty of Medicine, University Hospital of Coimbra - Coimbra/PT
Conclusion

With the continuous advance of treatment options for lung and breast cancer and the improved survivability of patients, the radiologist must be able to tell disease recurrence from iatrogenic changes.
References


