7:30–8:00 AM Coffee and Pastries—Grand Assembly

Cases of the Day

***Moderator:* Melissa L. Rosado de Christenson, MD**

7:30–7:45 AM Case of the Day
Satinder P. Singh, MD

7:45–8:00 AM Case of the Day
Ana M. Salazar, MD

Airways

***Moderator:* Ann N. C. Leung, MD**

8:00–8:20 AM Diseases of the Trachea
Wallace T. Miller, Jr, MD

8:20–8:40 AM Bronchitis, Bronchiectasis, and Bronchiolitis: The Role of Imaging
Rosita M. Shah, MD

8:40–9:10 AM CT of Small Airways Diseases
Gordon Gamsu, MD

9:10–9:30 AM Emphysema in Infants and Children
Kook Sang Oh, MD

9:30–9:50 AM Imaging of Airways: Role of Multidetector CT
David P. Naidich, MD

9:50–10:05 AM Panel Discussion and Questions

10:05–10:20 AM Break

Image Storage, Transfer, and Manipulation

***Moderator:* Philip A. Templeton, MD**

10:20–10:40 AM Computer-aided Diagnosis for Chest Radiology
Heber M. MacMahon, MD

10:40–11:00 AM The Pitfalls in the Interpretation of Temporal Subtraction for Chest Radiographs
Takeshi Johkoh, MD, PhD

11:00–11:20 AM Multimodal Image Registration in Thoracic Imaging
Suzanne L. Aquino, MD

11:20–11:40 AM Practical PACS: What the "Experts" Won't Tell You
Eric M. Hart, MD

11:40 AM–Noon Panel Discussion and Questions (Selecting PACS, DR, and CR for your Practice. *Paul J. Chang, MD,* will join the panel.)

Noon–1:00 PM Lunch (on your own)

Infections

Moderator: **Sanford A. Rubin, MD**

1:00–1:20 PM — Bacterial Infections of the Lung
David S. Schwartz, MD

1:20–1:40 PM — Tuberculosis in the 21st Century
Sanford A. Rubin, MD

1:40–2:00 PM — Pulmonary Nontuberculous Mycobacterial Infection
H. Page McAdams, MD

2:00–2:20 PM — Pulmonary Infections in the Bone Marrow Transplant Patient
Ann N. C. Leung, MD

2:20–2:40 PM — Immune Restoration Disease in AIDS: What the Radiologist Needs to Know
Joel E. Fishman, MD, PhD

2:40–3:00 PM — Pulmonary Infections in AIDS: New Trends and Changing Patterns
Phillip M. Boiselle, MD

3:00–3:10 PM — Panel Discussion and Questions

3:10–3:25 PM — Break

Modality Updates

Moderator: **Charles S. White, MD**

3:25–3:45 PM — CT Fluoroscopy
Charles S. White, MD

3:45–4:05 PM — Radiation Dose Considerations in Chest CT
Ernest M. Scalzetti, MD

4:05–4:25 PM — Thoracic MRI Technique and Interpretation
Philip Costello, MD

4:25–4:45 PM — PET Scanning: Practical Applications and Pitfalls in the Thorax
Jo-Anne O. Shepard, MD

4:45–5:05 PM — Practical Nuclear Medicine for Thoracic Radiologists
Mayur M. Patel, MD

5:05–5:15 PM — Questions and Discussion

5:30–6:30 PM — **Unknown Case Session**
Moderator: **Robert D. Pugatch, MD**

Diseases of the Trachea

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Introduction

Tracheal diseases may be divided into three general categories: extrinsic compression or invasion of the trachea by mediastinal lesions, intrinsic tracheal abnormalities and foreign bodies. Intrinsic and extrinsic lesions may be subdivided into malignant and non-malignant causes. In general, malignant causes are more common among adult patients and non-malignant causes among pediatric patients. Although many abnormalities may be detected by careful observation of the tracheal air column on the chest radiograph, CT will most often provide improved detection and characterization of diseases of the central airways. We will review these sequentially.

I. Extrinsic Causes of Central Airway Obstruction

The most common cause of extrinsic tracheal compression are mediastinal and pulmonary neoplasms. In children, vascular anomalies such as double aortic arch may lead to airway compromise. Rarely, mediastinal infections and other disorders will result in tracheal narrowing.

A. Nontracheal Neoplasms Which May Cause Tracheal Obstruction

The most common extrinsic mass to narrow the trachea and result in upper airway obstruction is the multinodular goiter. Most often when there is narrowing, the patient has accommodated to the disorder and has no clinical symptoms. Therefore, morphologic narrowing of the trachea by a multinodular goiter, except in extreme cases, should not raise alarm unless it is associated with significant clinical symptoms and physiologic, i.e. PFT, evidence of upper airway obstruction.

Hodgkin's and non-Hodgkin's lymphomas may, when large, compress and narrow the trachea, and produce respiratory impairment due to obstruction.

Thyroid, esophageal and bronchogenic carcinoma may invade the trachea and produce respiratory obstruction, but this is an uncommon manifestation of these common tumors. With macroscopic invasion, imaging will demonstrate a large extrinsic mass originating in the thyroid, lung or esophagus, adjacent to the trachea with direct extension of tumor through the tracheal wall and into the tracheal lumen. This is most problematic in the case of esophageal carcinoma because of the incidence of tracheoesophageal fistulae, a complication which may lead to repeated aspiration of esophageal and gastric contents. In some instances, radiation therapy will sterilize a previous esophageal mass, resulting in a new tracheoesophageal fistula.

B. Extrinsic Compression by Vascular Rings

Vascular rings are an important cause of obstructive airways disease in children. In general, the ring must effectively encircle the trachea, or trachea and esophagus, to produce sufficient constriction to cause symptoms. Symptoms include respiratory compromise, stridor and/or recurrent pneumonia, or symptoms of esophageal obstruction, dysphagia, regurgitation or poor feeding. The vascular rings most likely to cause airways obstruction are: double aortic arch, right arch with an aberrant left subclavian, and pulmonary sling.

Double aortic arch, as the name implies, represents failure of involution of the embryologic right aortic arch. Thus, the ascending aorta anteriorly divides into two arches, which coalesce into the descending aorta posteriorly. The trachea and esophagus travel through this complete vascular ring, which can constrict the trachea and esophagus and produce obstruction.

In-patients with a right aortic arch, an aberrant left subclavian may arise from the descending aorta and ascends to the left arm behind the trachea and esophagus. The ring is completed by the ligamentum arteriosum, which connects the left subclavian artery with the pulmonary artery. Once again, the ring surrounds and can constrict the aorta and esophagus.

Pulmonary sling occurs when the left pulmonary artery arises aberrantly from the right pulmonary artery and travels back to the left lung between the esophagus and trachea. Thus, the right and left pulmonary arteries encircle the trachea and can result in respiratory obstruction. Many infants with pulmonary sling will also have complete tracheal rings. In this entity, the tracheal rings are circular rather than "U" shaped and completely surround the trachea. This may result in a congenital tracheal stenosis. This combination of a pulmonary sling and complete tracheal rings has been called the "ring-sling" complex.

Double aortic arch and aberrant left subclavian may produce a posterior indentation on the trachea on lateral chest radiographs, and will characteristically produce a posterior indentation on the esophagus following barium swallow. Pulmonary sling will cause a posterior impression on the trachea on chest radiographs and barium swallows and an anterior impression on the esophagus on barium swallows. MRI and CT scans will directly demonstrate the aberrant vessels.

Nearly all symptomatic vascular rings will have one or more radiographic abnormalities on either the PA or lateral chest radiograph. Findings on the lateral radiograph included retrotracheal opacity, anterior bowing of the trachea, and tracheal narrowing. Findings on the PA radiograph included right aortic arch, distal tracheal indentation and right descending aorta. Recognition of these findings in a child with stridor, recurrent pneumonia or dysphagia should prompt further evaluation with barium swallow CT or MRI to confirm the presence of a vascular ring.

C. Mediastinal Infections Which Produce Large Airway Stenosis

Fibrosing or sclerosing mediastinitis is a rare condition characterized by progressive mediastinal fibrosis with compression and often constriction of a variety of mediastinal structures. It is most often the long-term complication of previous histoplasma infection. Why some individuals develop fibrosing mediastinitis after histoplasma infection and others do not is unclear. However when it occurs, there is an excessive production of fibrous tissue, which over decades can produce stenosis or occlusion of regional structures. An idiosyncratic hypersensitivity reaction to the presence of organisms or associated degenerated materials is the most commonly suggested mechanism for this disorder.

The most common chest radiographic manifestation is superior mediastinal widening, often with a lobulated appearance, resembling extensive mediastinal adenopathy. Calcification within the mass may be radiographically apparent in some cases. In some cases, the mediastinum may appear normal but secondary effects on the lung implicate the presence of mediastinal disease, including pulmonary edema from pulmonary venous obstruction, pulmonary infarction from pulmonary arterial or venous obstruction, and atelectasis from airways obstruction.

The characteristic CT appearance of fibrosing mediastinitis is of an infiltrating calcified mediastinal mass. This calcification characteristically appears as ill-defined sheets. Narrowing of the tracheobronchial tree and pulmonary infiltrates are also frequent findings.

Other granulomatous infections, which involve mediastinal lymph nodes, may produce tracheobronchial strictures, most commonly tuberculosis. These can produce focal tracheal narrowing and result in respiratory impairment.

II. Foreign Bodies

Foreign bodies are a rare cause of obstructive lung disease and are seen most commonly in children. These are most often due to aspirated foodstuffs, especially small round or oval foods such as peas and peanuts. Children may aspirate small toys, and adults may aspirate oral appliances such as denture fragments. Children who aspirate will most often be otherwise of normal health, however, adults will often have predisposing conditions associated with airway compromise especially neurologic disorders and alcohol abuse. Foreign body aspiration will most often present as acute respiratory compromise, however, in some cases it may present as recurrent episodes of pneumonia.

Chest radiographs may demonstrate lobar atelectasis, complete lung collapse, or air trapping, and may reveal the foreign body, when radio-opaque. CT will also demonstrate the secondary abnormalities of airways obstruction, and will directly demonstrate the endobronchial foreign material in most cases.

III. Intrinsic Causes of Central Airways Obstruction

A. Focal Tracheal Narrowing Which May Cause Airway Obstruction

Focal tracheal strictures can be subdivided into two general categories of disease: neoplastic causes and non-neoplastic causes.

1. Tracheal and Central Bronchial Neoplasms

Primary tumors of the trachea are quite rare. Approximately one half to three quarters of tracheal tumors are malignant, most commonly squamous cell carcinoma and adenoid cystic carcinoma. However, the majority of tracheal tumors in infants and children are benign.

The most common presenting symptom of patients with intrinsic tracheal tumors is dyspnea at rest or with exertion in approximately 80% of cases. The tracheal lumen must be narrowed by one third of the normal diameter for symptoms of dyspnea to occur. This airway narrowing may be clinically recognized as stridor, a whistling sound heard on inspiration. Cough is also commonly present in patients with tracheal tumors. Hemoptysis may be present in as many as 20% of patients. Most of these will have squamous cell carcinoma. Recurrent pneumonia, changes in voice related to invasion of the recurrent laryngeal nerve or direct extension in to the larynx and dysphagia from invasion of the esophagus are infrequent symptoms encountered in patients with tracheal neoplasms.

a. Benign Neoplasms of the Trachea

As noted previously, benign neoplasms of the trachea are more commonly encountered in children. They most often comprise laryngeal papilloma, nerve sheath tumors: neurofibromas and neurilemmomas, hemangiomas, pleomorphic adenomas and chondromas.

Papillomas represent a branching or lobulated tumor composed of a fibrovascular stalk and surrounding epithelium and come in two clinical and etiologic scenarios: multiple and solitary.

The multiple form of airway papilloma is referred to as juvenile laryngotracheal papillomatosis. This is an uncommon neoplastic growth secondary to infection with human papilloma virus types 6 and 11 but is the most common benign tracheal neoplasm. There is an association with maternal genital warts and the development of laryngeal papillomas in children and therefore the etiology of this disorder may be transmission via oropharyngeal aspiration at the time of birth. Most often papilloma will be present in the larynx of infants and young children, and in the majority of cases will remain localized or spontaneously resolve. Tracheobronchial involvement may occur in as many as 20% of cases. Papillomatosis results in multiple polypoid mucosal masses. Radiographic manifestations include polypoid intraluminal masses, atelectasis and obstructive pneumonitis. Involvement of distal airways can produce pulmonary nodules which when present are frequently cavitary.

Solitary papilloma of the tracheobronchial tree is less common than the multiple form and characteristically occur in middle aged men. This differing epidemiology suggests that these tumors may have a different pathogenesis from juvenile laryngotracheal papillomatosis. Solitary papillomas are usually small, 5 mm. to 15 mm. in diameter, intraluminal masses that most commonly occur in the lobar and segmental bronchi and produce atelectasis and obstructive pneumonitis on chest radiographs. Tracheal locations have been reported.

Pleomorphic adenoma is the most common benign bronchial gland tumor to affect the trachea. It consists of an epithelial component that forms small cyst like or gland like structures and a myoepithelial component.

Tumors of nerve origin may be found and are derived from paratracheal neural bundles, which travel longitudinally with the trachea. Most commonly, these tumors are neurofibromas and neurilemmomas. They will appear as broad based, well-defined masses centered on the tracheal wall, an appearance which indicates their origin from submucosal tissue.

Tracheal hemangiomas are encountered in young infants and may increase in size in the first few weeks of life but then spontaneously regress and disappear over the subsequent few years. This pattern parallels that of cutaneous hemangioma. The tumor may arise directly from the tracheal wall or extend into the trachea from a larger mediastinal mass.

Chondroma is the most common tumor of the mesenchymal tissue of the trachea. A benign neoplasm, there is a 4:1 male preponderance. Unlike most other benign tumors of the trachea, this is more commonly encountered in adults than children. It will appear as a well-defined polypoid mass extending into the tracheal lumen. It will often have regions of calcification detectable by CT imaging, a potential clue to the diagnosis. The only other tracheal tumors likely to have radiographically identifiable calcification are hamartomas and chondrosarcomas.

Other benign mesenchymal tumors may be encountered within the trachea including fibromas, leiomyomas, lipomas, fibrous histiocytomas and hamartomas.

b. Malignant Neoplasms of the Trachea

Squamous cell carcinoma accounts for approximately 50% of all tracheal tumors. Other bronchogenic carcinomas including adenocarcinoma, small cell carcinoma, and adenosquamous carcinoma have been reported but are rare. Most patients with bronchogenic carcinomas of the trachea will have an extensive smoking history. Direct extension of tumor into the mediastinal soft tissues has been found in approximately one third of patients and cervical lymph node metastasis has been found in approximately one third of patients. Survival is poor.

Adenoid cystic and mucoepidermoid carcinomas are low grade malignant neoplasms of the minor salivary glands and mucous secreting cells of the major airways. Adenoid cystic carcinomas account for approximately one third of all tracheal malignancies. Patients most often present with dyspnea, in their

40's and 50's. Chest radiographs may demonstrate a hemispheric or lobulated mass projecting into the lumen of the trachea. CT scans or MRI exams will reveal that there is nearly always extension of tumor into the surrounding mediastinal soft tissues. Adenoid cystic carcinoma has a predilection for longitudinal spread along the nerve sheaths traveling underneath the tracheal cartilage rings. Thus tumor may appear as a focal mass with extensive longitudinal thickening of the tracheal wall and is an important imaging clue to the diagnosis of adenoid cystic carcinoma. It is important for the radiologist to recognize this longitudinal extension, which may be unrecognized or underestimated on CT scans. It is also important to alert the surgeon to the longitudinal extension of tumor, a significant problem for surgical therapy because it may require a more extensive resection of the trachea than is technically feasible.

Mucoepidermoid carcinoma represents approximately one percent of tracheal malignancies. Most mucoepidermoid carcinomas arise in the main and lobar bronchi with a small minority originating in the trachea. Characteristically, the tumor will be discovered in patients, in their 30's and 40's, and will present with cough, hemoptysis, wheeze and/or recurrent pneumonia. Unlike adenoid cystic carcinoma, the tumor is usually confined to the bronchial wall and does not spread into adjacent pulmonary or mediastinal tissues.

Carcinoid tumor, a neuroendocrine carcinoma, is derived from Kutchitzky cells, part of the epithelium of the central airways. They are the third most common tracheal carcinoma and may account for as many as 5% of primary tracheal malignancies. When this occurs, they may result in proximal airway obstruction with the usual symptoms of tracheal masses such as dyspnea, cough and wheezing or stridor. Carcinoid tumors have a variable malignant potential. This risk of metastasis can be estimated by pathologists, based on the extent of mitosis, nuclear and cellular pleomorphism of the tumor and presence of necrosis. The presence of lymph node metastasis indicates a bad prognosis and therefore requires more extensive surgical resection. Atypical carcinoid tumors, those with higher malignant potential, account for approximately 10% of all carcinoids. When involving the trachea, carcinoid tumors will appear as a smooth, well-defined sessile mass projecting into the lumen of the trachea. Gross pathologists have noted that in most carcinoids, the majority of the tumor is extraluminal, with only a small portion projecting into the lumen of the airway, a manifestation which has resulted in the term "iceberg tumor".

Tracheal malignancies other than bronchogenic carcinoma, adenoid cystic carcinoma, mucoepidermoid carcinoma and carcinoid tumors account for approximately 7% of all tracheal tumors. These include soft tissue sarcomas such as chondrosarcomas, fibrosarcomas and rhabdomyosarcomas. These are derived from the soft tissue elements of the tracheal wall and are exceedingly rare. Hematogenous metastasis to the trachea is exceedingly rare. The most likely sources of hematogenous metastasis to the trachea are melanomas, breast carcinomas and malignancies of the genitourinary tract. These will usually appear as a polypoid soft-tissue mass projecting into the tracheal lumen.

2. Post Intubation or Post Tracheostomy Stricture

Tracheal stenosis as a complication of intubation or tracheostomy is among the most common causes of chronic upper airway obstruction. As many as 5% of patients with prolonged endotracheal intubation will experience stridor at the time of extubation with approximately 1% of patients developing permanent fibrotic stricture. Many of these post intubation strictures will be roentgenographically visible and yet will be clinically insignificant. Increasing the size of the endotracheal tube or tracheostomy tube and increasing the inflating pressure of the balloon both increase the severity of resultant strictures. At the stoma of a tracheostomy, strictures may preferentially affect the anterior surface of the trachea. In cross section the trachea resembles a peaked roof or A-shaped stricture. Tracheomalacia and airway obstruction due to tracheal collapse may also result from prolonged intubation.

3. Strictures due to Inhalational Burns

Thermal injury to the tracheal mucosa is a rare cause of tracheal fibrosis. As much as one third of patients with severe burn injuries will result in thermal injury to the central airways, however, less than 1% of burn victims will develop clinically significant post-burn stenosis. Inhalational burns are most frequently seen in those with facial burns and those with extensive burns to the body. Characteristically, the extent of tissue damage is most severe in the proximal trachea just below the vocal cords and progressively decreases in the more distal trachea.

4. Laryngotracheal Bronchitis (Croup)

Laryngotracheal bronchitis, more commonly known as croup, is an acute viral respiratory illness commonly seen in young children, usually less than 4 years of age. This is the most common cause of acute obstructive airways disease in children. Viral infections known to cause croup in order of frequency are: parainfluenza virus, respiratory syncytial virus (RSV), adenovirus, influenza A and B viruses. These organisms produce mucosal and submucosal edema throughout the tracheobronchial tree. However, the mucosa approximately 1 centimeter below the larynx is only loosely attached predisposing this site to critical narrowing due to edema. This edema results in the loss of the normal lateral convexities of the subglottic trachea and results in the characteristic inverted "V" appearance of the proximal trachea as seen on frontal chest and neck radiographs. Typically, patients will present with stridor and a barking cough after several days of fever and rhinitis.

5. Idiopathic Subglottic Stenosis

In rare instances, a short segment stenosis of the trachea may be found without antecedent history of trauma, infection, inhalation injury, intubation, or systemic disorder known to produce tracheal stenosis. This characteristically occurs in women who present with progressive dyspnea on exertion and wheezing. The stenosis is most often 2-3 cm. in length and present in the proximal trachea, just distal to the larynx. Circumferential fibrosis is present without destruction of the tracheal cartilages. Radiographs may demonstrate a focal area of narrowing in the cervical trachea. CT will confirm the stenosis and may demonstrate focal wall thickening.

B. Diffuse Tracheal Wall Abnormalities Which May Cause Airway Obstruction

Diffuse disorders of the trachea are rare phenomena. However, these are important entities for radiologists to be aware of because CT scanning can play an important role in their diagnosis. These disorders produce obstructive lung disease, in most cases, because they result in diffuse narrowing of the trachea, or because the airway wall collapses during inspiration. They fall into several classes of disease: 1) Tracheomalacia. 2) systemic, inflammatory conditions which may affect the trachea such as relapsing polychondritis, Wegener's granulomatosis and Crohn's disease, 3) infiltrative disease, which may affect the trachea such as amyloidosis and 4) idiopathic abnormalities of the tracheal wall such as tracheopathia osteochondroplastica and tracheomegaly (Mune Kuhns disease). The CT appearance of these diseases are in some ways different from one another and may help in distinguishing between the various causes of diffuse tracheal narrowing. Each entity will be reviewed and their salient CT features are outlined in Table 1.

1. Tracheomalacia and Bronchomalacia

Tracheomalacia and bronchomalacia are descriptive terms indicating weakness of the walls of the trachea and bronchi and their supporting structures. There is a rare congenital form of the disease due to deficiency of cartilage. However the majority of cases are a result of degeneration of the tracheal cartilages due to chronic inflammation. The loss of cartilaginous integrity results in tracheal collapse during inspiration. The most common etiology of tracheomalacia is extended endotracheal intubation or tracheostomy. However, chronic obstructive pulmonary disease, trauma, recurrent infection and polychondritis are other potential etiologies. Chest radiographs may demonstrate narrowing of the trachea, which may be focal or diffuse. CT will confirm the luminal narrowing and will show the tracheal wall to have normal or near normal thickness. Greater than 50% collapse of the trachea on expiratory images in comparison to inspiratory images has been promoted as an indicator of tracheomalacia on CT scans.

2. Relapsing Polychondritis

Relapsing polychondritis is an idiopathic autoimmune inflammatory condition of cartilage which results in destruction of cartilaginous structures throughout the body, most commonly the ear lobes and the nose but also including the ribs, tracheobronchial tree and peripheral joints. The diagnosis is made on the basis of recurrent inflammation of two or more cartilaginous sites. Some of the more prominent abnormalities include tracheal collapse, and deformity and flaccidity of the nose and ears, and joint and anterior rib pain. Chondrolysis can lead to severe arthritis. Respiratory complications have accounted for 50% of reported deaths. Fixed narrowing of the trachea and central bronchi may be demonstrated on chest radiographs but will be demonstrated to better advantage on CT or MRI imaging. CT will confirm the airway narrowing and will demonstrate extensive thickening of the tracheal wall without calcification. The absence of calcification is an important diagnostic feature separating relapsing polychondritis from some other diffuse tracheal disorders that can be recognized on imaging.

3. Wegener's Granulomatosis

Wegener's granulomatosis is an autoimmune granulomatous vasculitis with predilection for involvement of the lungs, kidneys and upper and lower respiratory tract. It typically affects patients in their 30's to 50's, and is without sex predominance. The etiology remains uncertain. Thoracic involvement

Table 1

Diffuse Disorders of the Tracheal Wall

Disease	**caliber**	**wall thickness**	**Ca++**	**extrathoracic findings**
Tracheomalacia	decr	-	-	-
Relapsing polychondritis	decr	+++	-	+++
Wegener's granulomatosis	decr	+++	-	++
Crohn's disease	decr	+++	_	+++
Amyloidosis	decr	+++	++	++
Tracheopathia osteochondroplastica	decr	+++	+++	-
Tracheomegaly	incr	-	-	-

most common appears as one or multiple pulmonary nodules or as diffuse alveolar hemorrhage. Tracheobronchial involvement is uncommon and when present is usually a late manifestation of disease. It will often be difficult to recognize the tracheobronchial involvement by chest radiographs although focal and diffuse tracheal narrowing may be demonstrated. Tracheal and bronchial wall thickening and luminal narrowing may be detected by CT, most commonly in the subglottic trachea.

4. Ulcerative Colitis

Although exceedingly rare, tracheobronchitis is one of the many extraintestinal manifestations of ulcerative colitis. Airway disease may predominantly involve the large airways and produce diffuse irregular narrowing and bronchiectasis or predominantly small airway narrowing and result in bronchiolitis obliterans. CT scans may demonstrate diffuse irregular thickening of the tracheal wall without calcification, which results in diffuse luminal narrowing.

5. Amyloidosis

Amyloidosis, a disorder of abnormal protein deposition, may have wide ranging systemic effects in nearly all organ systems including renal disease, CNS vascular disorders, bone lesions, and pulmonary masses. Thoracic involvement by amyloidosis may take one of several anatomic patterns of involvement: 1) tracheobronchial, 2) nodular parenchymal and 3) diffuse interstitial forms. Although these anatomic patterns may overlap, in most cases, there is a predominant site of involvement. Tracheobronchial involvement most commonly results in diffuse or multifocal, submucosal infiltrates which produce apparent tracheal wall thickening and tracheal narrowing. Less commonly it will produce a single submucosal mass like lesion. Calcification or ossification may occur although is less common than calcification in tracheopathia osteochondroplastica.

6. Tracheobronchopathia Osteochondroplastica

Tracheobronchopathia osteochondroplastica is a rare idiopathic disorder of the trachea resulting in bony metaplasia of the submucosal tissues of the trachea. This disorder is most commonly seen in elderly men and may often be clinically silent. Patients may occasionally complain of dyspnea, hoarseness, cough, wheezing or hemoptysis. The bony metaplasia is virtually always confined to the tissues adjacent to the tracheal cartilages, leaving the membranous trachea normal.

Radiographic abnormalities are confined to the trachea and proximal bronchi, which demonstrate diffuse luminal narrowing, which may have a nodular character. CT will also reveal diffuse narrowing and will easily demonstrate calcified nodules, which protrude into the tracheal lumen. CT will also demonstrate wall thickening adjacent to the cartilages with sparing of the membranous portion of the trachea.

7. Tracheobronchomegaly

Tracheobronchomegaly, or Mounier-Kuhns syndrome, is the only diffuse abnormality of the trachea resulting in increased luminal diameter. This condition is of unknown pathogenesis. Pathologically both the cartilaginous and membranous portions of the trachea are affected with resultant thin, atrophied muscular and elastic tissues. This causes increased compliance of the central airways resulting in abnormal flaccidity and easy collapsibility of the central airways. Patients may develop dyspnea because the abnormal increased compliance of the trachea prevents normal efficient transfer of air. Patients will characteristically have a cough with a whooping sound, which is caused by motion of the floppy trachea. Patients may also develop recurrent pneumonias as a result of impaired cough mechanics.

Chest radiographs will show marked dilatation of the sagittal and coronal diameters of the trachea. Careful inspection will also show a corrugated appearance of the anterior trachea due to redundant mucosa protruding between the cartilaginous rings. This appearance is often best appreciated on the lateral view. CT will confirm dilatation of the trachea and will usually show central bronchial dilatation or bronchiectasis. Airway wall thickness is usually normal.

IV. Conclusions

Tracheal obstruction is a rare cause of obstructive lung disease. However, when pulmonary function testing suggests a central cause for obstruction, imaging may play an important role in the diagnosis. Many causes of central airway obstruction may be distinguished by their imaging features, especially those demonstrated on CT or MRI imaging.

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Bronchitis, Bronchiectasis, and Bronchiolitis: The Role of Imaging

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Objectives

1. define optimal imaging technique in suspected airway disease
2. recognize imaging differences between patients with and without airway disease
3. define the role of expiratory CT in the assessment of airway disease
4. correlate imaging findings with functional parameters

Optimizing Airway Visualization

The detection and diagnosis of airway diseases has been facilitated by HRCT techniques which allow for spatial resolution on the order of 0.2-0.3mm. This same number corresponds to the wall thickness of 2mm airways, which by physiologic parameters are defined as the small airways. In disease states, imaging of more peripheral small airways, including the terminal bronchioles(normal diameter 0.7mm, wall thickness 0.1mm) becomes feasible.

Optimal imaging is dependant on narrow collimation and appropriate window settings and can be significantly aided by the use of expiratory scanning.

At slice thickness of 1.0-1.5mm, bronchiectasis is diagnosed with sensitivity of 97-98% and specificity of 93-99%.(1,2) If slice thickness is increased to 3mm, sensitivity and specificity drop to 84 and 82%.(3) The effect of electronic windowing can likewise be dramatic. While a level of –450HU is considered most accurate for assessing true bronchial diameter and wall thickening, the images may be 'too dark' for assessment of other parenchymal abnormalities, and a level of –700 is often preferred. Further reduction in window levels may significantly reduce specificity, contributing to apparent wall thickening and blurring.

Expiratory scanning, combined with standard HRCT imaging, may assist detection of early airway disease by demonstrating air trapping. On expiratory scanning, normal lung parenchyma demonstrates homogeneous increase in density(84-372HU, mean 200HU) and reduced volume.(4) Air trapping is recognized by areas of geographic (lobular) lucency, preserved volume and normal architecture. In the majority of cases, air trapping is accompanied by other parenchymal abnormalities of airway disease. Areas of lucency due to air trapping will display reduced vessel size, likely reflecting reflex vasoconstriction due to local hypoxemia.

Diagnosis in Airway Disease

The utility of imaging in the assessment of airway disease is dependent on accurate differentiation between normal and abnormal airways, early detection of and high diagnostic accuracy in disease states, and significant correlation with functional parameters.

Normal vs Abnormal

Some overlap exists between imaging findings in healthy individuals and patients with airway disease, such that degree of the 'abnormality' may be more important than the presence of the finding itself. Mosaic attenuation patterns and expiratory air trapping have been recognized in 21-52% of healthy subjects, shown to increase in frequency with advancing age.(4,5) The degree of air trapping may be important, with segmental air trapping demonstrated more frequently in asthmatics compared to healthy subjects and with healthy subjects demonstrating an air trapping area of < 25%.(6) Bronchial wall thickening was a better indicator of airway disease when comparing asthmatics and healthy subjects, identified in 83% of patients with severe obstruction, 35-38% of asthmatics with normal PFT's or minimal impairment, and in only 4% of controls.(6)

Early Detection of Airway Disease

Expiratory scanning may aid early detection of airway disease by demonstrating air trapping in the absence of associated parenchymal abnormalities in up to 20% of patients. Furthermore, because HRCT permits detection of focal abnormalities compared with the more global representation of parenchymal abnormalities provided by PFT's, it has been suggested that expiratory scanning may be a more sensitive indicator of early disease, allowing visualization of morphologic abnormalities prior to a change in clinical parameters. In a study of patients with clinically suspected obstructive lung disease, expiratory air trapping was present in 51% of patients with severe obstruction, 72% of patients with small airway disease and in 4 of 10 patients with clinically suspected disease and normal PFT's, supporting the latter.(7)

Diagnosis in Airway Disease

With the addition of expiratory scanning, abnormalities at CT can be read with improved confidence and are more accurately differentiated from infiltrative parenchymal disease.

For the diagnosis of bronchiectasis, HRCT is considered equally accurate to bronchography and cross sectional distribution can be used to suggest etiology. Morphological features are also important, with cylindrical bronchiectasis most closely associated with obstruction and cystic bronchiectasis with a greater prevalence of positive P. aeruginosa cultures.(8)

Imaging abnormalities in pathologically confirmed small airway disease range from centrilobular opacities to mosaic attenuation patterns and air trapping. HRCT has been shown efficacious in the diagnosis of longstanding bronchiolitis obliterans, with reported sensitivity and specificity of 80-94%. Early disease may be more difficult to detect, with diagnostic accuracy of only 71% in one series.(9)

In the evaluation of hemoptysis, CT is a significant contributor, suggesting specific diagnoses in 50% of nondiagnostic bronchoscopies and providing staging information in cases of bronchogenic carcinoma.(10)

In the HIV-positive patient, airway abnormalities, including bronchial dilation and air trapping, can be detected prior to the onset of documented pulmonary infection. Patients with air trapping have also been shown to have significantly reduced FEV1 and FEF25-75 parameters, increasing in severity with longer duration of HIV seropositivity.(11)

Correlation with Functional Parameters

Inspiratory HRCT findings, including severity and extent of bronchiectasis, bronchial wall thickening and mucus plugging, demonstrate significant correlation with obstructive parameters. At expiratory scanning, significant inverse correlations between air trapping and FEV1, FEV1/FVC and FEF25 have also been shown.(7,9)

Indications for Imaging in Airway Disease

The contributions of imaging in clinically suspected airway disease can be significant. Expiratory scanning in conjunction with standard inspiratory HRCT may readily explain obstructive PFT parameters by confirming large or small airway disease. The current literature also suggests that imaging, particularly expiratory scanning, may confirm clinically suspected airway disease when PFT's are still normal. Additionally, coexistent parenchymal disease or other pathology may be detected. In instances where tissue diagnosis is required, imaging can be utilized to guide open or bronchoscopic biopsies, noting the usual patchy distribution of abnormalities in airway disease.

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CT of Small Airways Diseases

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Small airways are by definition less than 2 mm in internal diameter.

The diagnosis of small airway disease is challenging for the clinician as well as the radiologist, as there are no pathognomonic clinical or functional features. The chest radiograph is normal or may show non-specific findings. HRCT scanning is currently the best imaging technique for assessment of diseases of the small airways. As the normal bronchioles measure less than 1 mm in diameter and have a wall thickness of less than 0.1 mm, they are below the limit of visibility on HRCT scans and thus are too small to be visualized. The bronchioles are centrilobular structures being clustered near the center of secondary pulmonary lobules. This accounts for the characteristic centrilobular (bronchocentric) distribution of bronchiolar abnormalities on HRCT scan.

HRCT Findings

The HRCT scan findings in patients with small airway diseases can be classified into 2 groups:

1) Thickening of bronchiolar walls, often with filling of dilated bronchioles with granulation tissue, mucus, granulomas, or pus results in a pattern of small centrilobular nodules and branching tubular structures. These abnormalities represent enlarged bronchioles coursing perpendicular and parallel to the CT plane of section. The association of both nodular and linear branching opacities give the "tree-in-bud" appearance. The centrilobular nodules may have either well-defined, regular-shaped margins, of soft tissue density, or have poorly-defined margins and appear as hazy ground-glass densities. Areas of consolidation or ground glass attenuation may be present reflecting inflammation associated with the bronchiolar inflammatory lesions, or focal areas of bronchopneumonia in case of acute infectious bronchiolitis. Whenever a "tree-in-bud" appearance is suspected, we do multiple HR slices through a representative region of the lung and perform MIP or 3D reconstructions to image the entire block of tissue.
2) Obstruction of the bronchiolar lumen results in hypoxia of the underventilated lung, reflex vasoconstriction and air-trapping. The combination of local vasoconstriction and air-trapping results in decreased vessel caliber and lung attenuation in the affected areas of the lung. There is associated blood flow redistribution to areas of normal lung that are therefore of higher than normal attenuation. These changes are usually patchy in distribution and result in adjacent areas of abnormal low attenuation lung and relatively overperfused higher attenuation normal lung. This combination is referred to as "mosaic perfusion." The mosaic perfusion CT pattern can be also caused by primary pulmonary arterial abnormalities, such as chronic pulmonary thromboembolism.In patients with small airway diseases, the regional differences in lung attenuation and lung perfusion are increased on expiratory scans due to air-trapping. Expiratory scans accentuate subtle differences between normal and abnormal lung that may be seen on inspiratory scan or may be demonstrated air-trapping even when the inspiratory scans are normal. We routinely perform three spaced end-expiratory scans in all patients with suspected airways disease.

Classification of Bronchiolitis

For the pathologist, small airway disease has the same connotation as bronchiolitis. The current pathological classification divides bronchiolitis into 2 main categories: cellular bronchiolitis and bronchiolitis obliterans.

Cellular Bronchiolitis is characterized by inflammatory cellular infiltrates that involve the lumen and/or the wall of bronchioles. It is seen in various infections including bacterial, viral, mycoplasma pneumonia, and invasive airway aspergillosis, and in association with many chronic larger airway diseases, such as bronchiectasis, asthma, and cystic fibrosis. It may also occur distal to any obstructive bronchial lesion. Other conditions may also feature a cellular bronchiolitis (respiratory bronchiolitis, hypersensitivity bronchiolitis, panbronchiolitis, and aspiration bronchiolitis).

HRCT findings consist predominantly of bronchocentric nodular and branching tubular opacities. Some nodules are larger, and ill-defined, reflecting extension of the inflammatory process to the adjacent peribronchiolar airspaces. Cellular bronchiolitis, depending on its cause, may improve with antibiotics or anti-inflammatory therapy or progress to bronchiolitis obliterans.

Bronchiolitis Obliterans has been a confusing term. Clinically, it refers to a syndrome of chronic airflow obstruction caused by pathologic changes in the small airways. Pathologically, bronchiolitis obliterans has been used to refer to two groups of lesions: **bronchiolitis obliterans with intraluminal polyps (BOOP) and obliterative bronchiolitis (BO). BOOP is sometimes referred to as cryptogenic organizing pneumonia (COP).**

In bronchiolitis obliterans with intraluminal polyps, histologically, polypoid endobronchial granulation tissue (composed of myxoid fibroblastic tissue) appears to float freely within a bronchial lumen or be only focally attached to the wall. In most cases, the fibroblastic proliferation is continuous with an organizing pneumonia in the more distal airspaces. When the two lesions are combined, the name **bronchiolitis obliterans with organizing pneumonia (BOOP)** is used. Bronchiolitis obliterans with intraluminal polyps is a common reparative reaction that occurs in a number of settings.

BO, on the other hand, does not have intraluminal polyps and is diagnosed pathologically by the obliteration of small airways. It is commonly found after inhalation injury, certain infections and transplantation.

BOOP: CT Findings

When organizing pneumonia is present, the main CT findings include unilateral or bilateral areas of ground-glass opacities and/or airspace consolidation. In over half the cases, the distribution of abnormalities is predominantly subpleural or peribronchial. Such distributions are also found when airspace consolidation takes the appearance of large nodular opacities with irregular margins, containing air-bronchograms associated with relatively broad subpleural and parenchyma bands. When organizing pneumonia is absent, the CT findings consist of centrilobular nodular opacities that may reflect the presence of intrabronchiolar granulation tissue polyps. Although many of the causes of bronchiolitis obliterans with intraluminal polyps are similar to those of constrictive bronchiolitis one rarely document the former evolving into the latter. The two may co-exist especially in patients with large airways disease.

(Obliterative) Constrictive Bronchiolitis (BO) is mainly characterized by concentric narrowing of the bronchioles caused by submucosal and peribronchiolar irreversible fibrosis. The lesions extend along the long axis of the airway, impairing collateral ventilation and causing an obstruction to airflow. It may be seen as the result of childhood viral infection, mycoplasma pneumonia or toxic fume inhalation, or in association with bronchiectasis, cystic fibrosis, and bronchopulmonary dysplasia. It is an uncommon pulmonary manifestation in patients with rheumatoid arthritis, particularly those treated with penicillamine. It is a manifestation of chronic graft versus host disease, following bone marrow transplantation, and as chronic rejection after heart-lung transplantation. It is rarely seen in inflammatory bowel disease. It has recently been described in association with pulmonary neuroendocrine cell hyperplasia, and as a result of ingestion of sauropus androgynous.

BO: CT Findings

The major HRCT findings include mosaic perfusion and air trapping. The obliterated bronchioles are not seen. Characteristically, the lesions appear patchy in distribution on both inspiratory and expiratory scans. In case of more global involvement of the small airways, the regional inhomogeneity in lung density is difficult to appreciate on inspiratory scans, and becomes visible only on expiratory scans. In patients with particularly severe and widespread involvement of the small airways, inspiratory scans demonstrate uniform decreased attenuation, and scans taken at end expiration may appear unremarkable. In these patients, the most striking features are paucity of pulmonary vessels, and lack of change of the cross section areas of the lung at comparable levels on inspiratory and expiratory scans. In such a situation, the distinction between constrictive bronchiolitis and panlobular emphysema may be difficult on the basis of CT appearances. Occasionally, lesions of constrictive bronchiolitis may be seen predominantly affecting one lung as in the Swyer James syndrome, a variant of constrictive bronchiolitis due to viral bronchiolitis occurring in childhood. HRCT usually shows lung hypoattenuation, bronchiectasis, and air-trapping. Most often similar changes are present in the other lung, but to a lesser extent.

The clinical course of constrictive bronchiolitis is highly variable. The majority of cases of postviral constrictive bronchiolitis are self limiting with no long-term consequences. In contrast, patients with constrictive bronchiolitis in association with rheumatoid arthritis and some patients developing constrictive bronchiolitis following heart-lung transplantation often have a more rapidly progressive disease with survival measured in months rather than in years.

Other Bronchiolitides

Follicular Bronchiolitis is a non-infectious lymphoid hyperplasia of the bronchus-associated lymphoid tissue. It is characterized histologically by the presence of hyperplastic lymphoid follicles with reactive germinal centers distributed along the bronchioles and, to a lesser extent, bronchi. Most cases are associated with connective tissue disease, particularly rheumatoid and Sjögren syndrome, immunodeficiency, or as a hypersensitivity reaction. A recent report described the HRCT findings in 12 patients with histologically proved follicular bronchiolitis. The cardinal CT feature consists of small centrilobular nodules variably associated with peribronchial nodules and areas of ground glass opacity.

Respiratory Bronchiolitis is a common incidental histologic finding in smokers. It is also referred to as smoker's bronchiolitis and sometimes as respiratory bronchiolitis interstitial lung disease. It involves mainly the respiratory bronchioles and is characterized by mild chronic inflammation of the respiratory bronchioles associated with prominent accumulation of pigmented macrophages in respiratory bronchioles and adjacent lung parenchyma. Rarely respiratory bronchiolitis may be sufficiently extensive in its involvement of lung tissue to cause mild interstitial lung disease.

The majority of patients with respiratory bronchiolitis are asymptomatic. Rarely, in heavy smokers, the condition may be severe enough to produce symptoms and lead to abnormalities on HRCT scans. The HRCT scans may show ill-defined small centrilobular opacities, sometimes associated with patchy areas of ground glass attenuation. These changes tend to have a predominantly upper lobe distribution. Linear bands expressing broad sheets of atelectasis or scarring may also be present in the lower lobes. If smoking is stopped, the changes show no further progression or resolve slowly.

Diffuse Panbronchiolitis is a condition of unknown etiology and an important cause of progressive obstructive lung disease in Japan and Korea that has only rarely been recognized in Europe and North America. It is characterized by a mononuclear cell inflammation of the respiratory bronchioles leading to lesions of constrictive bronchiolitis with secondary dilatation of proximal airways. In the early stage, the HRCT findings are small centrilobular nodular and tubular branching opacities, diffusely distributed in both lungs. In the later stages, the small opacities are connected to small ring or tubular images reflecting dilatation of terminal bronchioles, and decreased lung attenuation due to constrictive bronchiolitis appears in the periphery of the lungs. Although the majority of patients initially respond to erythromycin, the long-term prognosis is poor.

Diffuse Aspiration Bronchiolitis is a new entity characterized by a chronic inflammation of bronchioles induced by recurrent aspiration of foreign materials. In elderly patients, neurologic disorders and dementia are common associated disease. Oropharyngeal dysphagia is present in half of the patients. This entity however may occur in any patient with dysphagia, regardless of age. Clinical presentations are bronchorrhea, bronchospasm, wheezing and dyspnea, closely associated with oral food intake. Histological findings are chronic inflammation with a foreign body reaction in bronchioles. HRCT findings include disseminated small centrilobular linear branching opacities with a "tree-in-bud" appearance. Some patchy lobular areas of airspace consolidation may also be present.

Hypersensitivity Pneumonitis

Cellular bronchiolitis is frequently a major component of hypersensitivity pneumonitis. It accounts for the characteristic diffuse small ill-defined centrilobular nodules seen in patients with acute and subacute and hypersensitivity pneumonitis; hypersensitivity alveolitis shows areas of ground glass attenuation. It has been demonstrated recently that mosaic perfusion and expiratory air trapping is seen in the majority of patients with subacute or chronic hypersensitivity pneumonitis due to partial bronchiolar obstruction.

Conclusion

HRCT with selective use of MIP, 3D, and expiratory images is currently the best imaging technique for assessing small airway disease. It is the primary imaging modality for patients with suspected small airways disease (cough and dyspnea). In the majority of these patients CT provides clinically important information.

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Emphysema in Infants and Children

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Learning Objectives

At the completion of the course, the attendee will be able to:

1. Learn the difference between pediatric emphysema and adult emphysema.
2. Be able to differentiate different kinds of pediatric emphysema.
3. Be familiar with imaging approach and imaging characteristics.

There is a difference between pediatric emphysema and adult emphysema. Most of pediatric emphysema may not have irreversible alveolar epithelial destruction. Therefore, pediatric emphysema is defined as a condition that is characterized by enlargement of alveolar airspaces, resulting in more than a normal amount of air per unit volume of the lung (1). There are many factors that determine lung volume. They may work together or independently, including: (1) diameter of the airways, (2) number and size of alveoli, (3) elasticity of the lung tissue, (4) surfactant, and (5) compliance of the chest wall and diaphragm.

Obstructive emphysema is the most common emphysema in infants and children. Obstructive emphysema occurs when there is an incomplete airway obstruction, producing "incomplete ball valve" effect (2). A new equilibrium is quickly established between decreased expiratory flow and decreased inspiratory flow. But the affected lung remains emphysematous, and shows attenuated and stretched pulmonary arteries caused by hypoxic vasoconstriction, which is more evident on a chest CT than on a chest radiograph.

Congenital emphysema and compensatory emphysema are discussed. Air leak causing pulmonary interstitial emphysema or subpleural bleb is not "true" emphysema, but cannot be differentiated in many instances from emphysema.

Obstructive Emphysema

Narrowing of airway may be caused by intraluminal foreign body, intramural lesions, or extrinsic compression, and may result in "incomplete ball valve" effect and subsequent obstructive emphysema. Obstructive emphysema is manifested by increased size of the affected lung, hyperlucency and hypoxic vasoconstriction (3). The site of the obstruction determines bilateral, unilateral, lobar or localized emphysema.

The aspirated foreign body is the most frequent cause of obstructive emphysema. The aspirated foreign body usually lodges in either main stem bronchus with about equal frequency (4).

Other causes of obstructive emphysema include extrinsic compression, asthma, cystic fibrosis, tracheobronchial stenosis and/or malacia, congenital heart disease with left to right shunt (5), alpha-l-antitrypsin deficiency, Swyer-James (or MacLeod) syndrome, kyphoscoliosis, pectus excavatum deformity, and bronchial volvulus.

Congenital Emphysema

Congenital lobar emphysema is most common congenital emphysema. The affected emphysematous lobe is increased in size due to increased number of alveoli or an increase in both number and size of alveoli. The left upper lobe is most frequently involved (41%), followed by the right middle lobe (34%), and the right upper lobe (21%) (6). It rarely involves more than one lobe. Congenital lobar emphysema and bronchial atresia (7), hypoplastic emphysema show even distribution of emphysema in the affected lung while congenital cystic adenomatous malformation and cystic pulmonary sequestration show uneven distribution of emphysema. Congenital emphysema is also seen in association with Marfan's syndrome (8), cutis laxa, proteus syndrome, and neurofibromatosis.

Compensatory Emphysema

In compensatory emphysema, alveolar size is increased, but the pulmonary vascularity also increases in size proportionally. Therefore, the affected lung may not be hyperlucent.

Air Leak Mimicking Emphysema

(9, 10).

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Imaging of Airways: Role of Multidetector CT

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Friday

At the time of publication, no abstract was available.

Computer-aided Diagnosis for Chest Radiology

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Introduction

Visual detection of pulmonary abnormalities on screen-film radiographs is notoriously unreliable. Digital radiography can improve diagnostic accuracy due to its greater latitude, improved local contrast and more consistent image quality compared to screen-film systems. In addition to facilitating detection by traditional visual inspection of the image, digital imaging enables advanced techniques such as dual energy subtraction, temporal subtraction and automated nodule detection, which can improve diagnostic accuracy further, especially for subtle lesions such as early lung cancer.

Dual Energy Subtraction Chest Radiography

Dual energy subtraction radiography exploits the energy dependence of x-ray attenuation by different tissues. By subtracting the ribs and other bones from the image and displaying them separately, energy subtraction (ES) radiography can improve diagnostic accuracy. Two fundamentally different approaches have been used. One involves the use of sequential x-ray exposures in rapid succession, at different kVp settings. The second approach involves the use of a single exposure, which is recorded by two receptors separated by a filter. Each method has specific advantages and limitations. Existing storage phosphor based energy subtraction systems use a single exposure of two CR plates separated by a copper filter. Flat panel detector based systems will use sequential exposures of a single detector. With either approach, three PA images are produced: a standard image, a soft tissue image, and a bone image.

Energy subtraction images have been shown to be significantly superior for detection of pulmonary nodules compared to either screen-film, or standard digital radiographs. In our own experience, ES images have certain distinct advantages. Specifically, the soft tissue ES images clearly improve detectability of any focal soft tissue opacity that is partly or completely obscured by overlying bones. In some cases the soft tissue image can be helpful in characterizing a lesion by revealing its margins more completely than the standard image.

Energy Subtraction chest radiography can provide additional diagnostic information without additional radiation exposure, inconvenience, or discomfort to the patient. The proportion of cases in which ES images contribute important additional information will depend on the patient population, the types of pathology encountered, and the diagnostic accuracy of the individual reader. In some instances, use of ES can obviate the need for a CT scan by confirming the benign nature of lesion. In other instances, it can facilitate detection of pathology that would otherwise be overlooked.

Temporal Subtraction

Digital radiography allows various types of image enhancement to be performed, but techniques that improve the visibility of abnormal findings also tend to emphasize certain features of normal anatomy. Ideally, the visibility of pathological findings would be improved selectively, while normal anatomical structures would be suppressed. In the case of patients who have had a previous chest radiograph, an opportunity exists to enhance selectively areas of interval change, including regions with new or altered pathology, by using the previous radiographs as a subtraction mask. The temporal subtraction technique involves automated two-dimensional warping and registration of a previous with a current chest radiograph in order to produce a “difference image” in which unchanged areas appear as uniform grey while new opacities appear as isolated dark foci that stand out from the uniform background. Although the quality of the temporal subtraction image is affected by variations in patient positioning, this limitation can be partially overcome by the geometric warping that is performed.

In a controlled experiment, 11 observers interpreted 50 chest radiographs, including 29 lungs with new opacities, including nodules. Previous radiographs were provided for comparison in each case. The same cases were interpreted on a different occasion with the benefit of temporal subtraction images in addition to the current and previous radiographs. The observers as a group showed a substantial and highly significant improvement in diagnostic accuracy when temporal subtraction was used. Interestingly, the average interpretation time was reduced by 19% when temporal subtraction was used.

One of the unique advantages of temporal subtraction is that it can highlight areas of subtle change that may not appear obviously abnormal when viewed in isolation. Its ability to improve detection of a broad range of abnormalities, including nodules, infiltrative opacities, and even local pulmonary perfusion deficit alterations, are important advantages.

Although reproducible patient positioning improves the quality of temporal subtraction images, image warping techniques have been developed that reduce misregistration artifacts due to differences in projection. Because temporal subtraction enhances any type of pathologic change, its diagnostic benefits are complementary to other computer-aided diagnostic techniques, such as energy subtraction and computer-aided nodule detection. Temporal subtraction is being investigated in the setting of a lung cancer screening program in Japan.

Automated Lung Nodule Detection

Many potentially curable cancers, that are clearly visible in retrospect, are overlooked by radiologists. Failure of the radiologist to focus on the abnormality has been shown to be a contributing cause in such cases. The purpose of computer aided diagnosis (CAD) for nodule detection is to identify and indicate suspicious focal opacities on a radiograph that may represent cancer, in order to direct the radiologist's attention. A nodule detection program developed at the University of Chicago consists of 5 basic steps. The initial step involves a filtering operation that enhances nodular opacities in the image. A second filter is applied to the original image to suppress nodular opacities. From these two, a difference image is produced in which the complex anatomical background is minimized, while nodular structures are maximized. Next, multiple grade-level thresholding is performed based on the histogram of the difference image to identify "nodule candidates". The nodule candidates are then classified according to the threshold levels at which the nodule candidates are identified. Various image features are extracted from the difference image and the original image using region-growing techniques and edge gradient analysis to separate spurious from real nodules. The image features include contrast, effective diameter, degree of circularity or irregularity, and rates of change of the effective diameter and degrees of circularity and irregularity as gray-level thresholding is varied. Finally a rule-based analysis is applied to reduce the number of false positives.

In a large observer test performed at the Radiological Society of North America (RSNA) Meeting, 20 abnormal chest radiographs containing a nodule and 20 normals were included. One hundred forty six observers interpreted the cases on a computer workstation, first without, and then with the benefit of the nodule detection program. The results were evaluated using ROC analysis to determine the effect of the nodule detection program on diagnostic accuracy.

The detection accuracy achieved by individuals, on average, correlated with their experience and degree of specialization. Thus, chest radiologists achieve the highest accuracy, followed by other radiologists, radiology residents and non-radiologists. Detection accuracy improved significantly for each group when they used the CAD program. As with dual energy and temporal subtraction, radiology residents using the nodule detection CAD program had slightly (though not significantly) better accuracy than chest radiologists without the CAD program.

This nodule detection program has an average sensitivity of between 70% and 80% with an average of 1 - 2 false positives per radiograph. Although some obvious nodules are still missed by the program and though false positives are quite numerous, it is noteworthy that even experienced chest radiologists benefited from it in the observer test. Although the accuracy of the computer program alone is less than that of most radiologists, the errors of the program tend to differ from those of human observers. Consequently, the nodule detection program can increase the accuracy of even experienced radiologists.

Nodule Detection for CT Scans

Programs that analyze CT data to detect possible nodules are under intensive development, with a view to application in lung cancer screening programs, as well as in general radiological practice. Automated measurement of nodule volume and comparison on sequential scans are further goals of these research efforts.

Clinical Implementation of Computer-aided Diagnosis

A CAD system for mammography has been developed based on film digitization with a combination of hardcopy interpretation and softcopy CAD display. Although this approach may have certain niche applications for the chest (i.e., screening programs for cancer or industrial lung disease), it seems unlikely that a film-based system would be widely accepted. Particularly when so many hospitals are converting to digital image acquisition, it is logical to implement chest CAD in an all-digital workstation environment.

In a PACS, chest CAD programs can be applied to images as soon as they are acquired. The results can be stored as overlays that are available for immediate display at the workstation.

Dual energy subtraction is already available, and in routine clinical use. Temporal subtraction and nodule detection CAD are likely to become available during the next few years. As interpretation migrates from the traditional view box to the computer workstation, these diagnostic tools will likely be increasingly accepted and used by practicing radiologists, as a way to reduce errors and increase productivity.

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The Pitfalls in the Interpretation of Temporal Subtraction for Chest Radiographs

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In daily clinical practice, radiologists and physicians often compare present chest radiographs with previous ones of the same patients in order to detect interval changes such as newly developed pulmonary infiltration, tumor masses, pleural effusions, or changes in heart size. However, it is very difficult for us radiologists to identify subtle interval change, particularly lesions that involved overlap with anatomic structures such as ribs, vessels, heart, and diaphragm. Even established radiologists can miss important interval changes when they observe serial chest radiographs (1).

In cases with previous radiographs, subtraction of previous from current images can be useful to enhance any changes in local opacity. Therefore, recently a temporal subtraction scheme based on a nonlinear geometric warping technique has been developed (2-6). The process of temporal subtraction was as follows; 1) normalization of density and contrast images, 2) correction for lateral inclination by image rotation, 3) ribcage edge detection based on image profile analysis, 4) smoothing of low-resolution image using Gaussian filter (matrix size = 128 x 128), 5) lung segmentation using ribcage edge, 6) initial image matching: determination of global shift value using cross-correlation technique, 7) nonlinear image warping, and 8) image subtraction.

In an observer study, the detection accuracy of interval changes in chest radiographs was improved significantly by using temporal subtraction images (3). From our experience, in the detection of solitary pulmonary nodules, this temporal subtraction method can bring the promotion of the working efficiency for established chest radiologists and the improvement of the accuracy for general readers. In addition that, the temporal subtraction technique clearly improved the diagnostic accuracy for detection of ground-glass shadow on chest radiographs if observers have enough skills to evaluate the condition of films and the status of patients in exposure.

Of course, temporal subtraction is a promising tool for the follow-up studies of various pulmonary abnormalities by chest radiographs. Clinical chest radiographs are not usually reproducible in terms of patient positioning, x-ray projection, inspiration, and cardiac pulsation as well as pathology. It should be noted that misregistrations were caused by large amount of difference in x-ray projection, such as severe AP inclination or lotation, could not be completely accommodated with this method. It was found that poor correlation was generally obtained around regions which were difficult to match, because of (1) large lesions with interval changes, (2) location changes of device, (3) interval changes in the borders of the heart or the diaphragm, (4) changes in the borders of the heart or the diaphragm, (5) changes in the locations and angles of clavicles, and (6) regions with extremely low density. Therefore, in the application of temporal subtraction method for chest radiographs, pseudo abnormalities are often found in various situations. These pseudo abnormalities are due to either the difference of breath-hold level between previous and present films, inhomogeneous brightness of films, or the difference of exposure body position between previous and present films. In addition, there are some limitations of application of this method such as application to the follow-up of linear or reticular opacities because such abnormalities are often influenced the misregistration. It is very important for the correct interpretation of temporal subtraction images and the completing of robotic software to acknowledge these pseudo lesions and limitations on temporal subtraction images.

The aim of this presentation is twofold; the first one is to illustrate the pitfalls and limitations of temporal subtraction for chest radiographs and the second one is to propose the appropriate usage for this method.

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Disclosure Statement: This presentation was supported in part by a grant from Mitsubishi Space Softwear Co.

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Multimodal Image Registration in Thoracic Imaging

Suzanne L. Aquino, MD

This lecture will provide the following:

1. The background and basic premises of image registration
2. Review of registration algorithms and their limitations
3. Current state of applications to Thoracic imaging
4. Future directions of multimodal registration in Thoracic imaging

Multimodal Image Registration is the term applied to computer generated spatial matching and fusing of two or more images from different imaging modalities. The benefits are the combined sensitivity and specificity of complementary procedures which independently only provide anatomical accuracy or physiologic information. The result can be reflected in improved detection and localization of active or recurrent diseases. When fusing images over time this process can help assess pathologic and physiologic changes [1,2].

On a basic level this process involves a computer program that maps coordinates in one image to the correspondent coordinates in another image. Traditionally these coordinates were applied to the patient. In neuroradiology imaging an external frame and marker fiducials were placed on the patient's head as points for registration. Other techniques include the use of anatomic "internal" landmarks or surfaces of structures (i.e. brain surface) [2] or the matching of voxel properties i.e. image intensity values [3].

Algorithms for registration compute the best mapping transform based on a given matching strategy. Common transformations are rigid and affine. Rigid transformation is limited to translation and rotation to align datasets. The affine transformation includes translation, rotation, scale and shear. The shear would be applied to bring a rectangle into alignment with a parallelogram i.e. parallel lines are mapped to parallel lines. Shearing and scaling are also identified as "nonlinear registration" and are applied to overcome differences in geometric structures [3,4,5].

Registration of datasets can occur on a global (entire dataset involved) or local level and can be performed in multiple steps or series. For example the first series uses rigid transformation to align the objects on a global level and subsequent series involve refinement locally with affine transformations (including nonlinear warping). Most image registration used in clinical medicine today involves Neuroradiology and Neurosurgical planning. This domain (the brain) is suited to alignment with a rigid transformation because of the limitations in brain motion. Rigid transformation can be computed on a global basis using techniques such as the popular surface matching techniques [6].

Frontiers of multimodal image registration involve applications outside of neuroradiology imaging. Conventional linear registration is successful in fusing two datasets such as SPECT, FDG-PET, CT and MRI studies of the head. Monomodal registration, or registration of two studies from the same modality (CT to CT, cardiac SPECT to cardiac SPECT) is relatively straightforward as well. Fusion of two datasets from the same modality is facilitated by the ease of physical acquisition of datasets, simpler transformation models as well straightforward visual inspection of results. Registration of datasets from two different modalities is more challenging due to discrepancies in image resolution within datasets (matching points for registration are more difficult to identify), standard calibration of information, variations in patient positioning, and, in the thorax, respiratory variations and cardiac motion [5,7,8,9].

This lecture will encompass basic premises of image registration and provide a background on techniques available. We will review how this technique can be applied to Thoracic imaging for improved analysis of sequential scans obtained over time and specifically how this technique can enhance the interpretation of CT scans when fused with Nuclear Medicine PET studies in the assessment of tumor localization and activity.

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Practical PACS: What the "Experts" Won't Tell You

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Introduction and Objective

Most lectures on PACS concentrate on issues of hardware, software and computer connectivity. This lecture will focus on the human side of the PACS equation, and is intended to provide the non-PACS practitioner with practical tips about what to expect in the transition to a PACS environment. Topics will include reading room design, workstation set-up, ergonomics, reading patterns and clinical interaction.

Reading Room Design

The theoretical and real advantages of PACS implementation for the clinical radiologist are well documented. In practice, the migration from a film based environment to a PACS environment requires the dedication of a core of technical personnel responsible for hardware and software, and also of a core of well trained early clinical users, to guide their less computer-savvy or more change resistant colleagues through the early stages of the transition. Even with these change managers in place, the transition is highly anxiety provoking for many radiologists as it represents a fundamental shift in clinical performance and service provision. When coupled with unfamiliar equipment and poorly planned or executed workspaces, the changes may become overwhelming to some.

Light, or its absence, is the key to any PACS workspace. Fundamentally, current high-luminosity computer monitors are much less bright than light boxes. Strict attention must therefore be paid to the ambient light conditions in the PACS workspace in order to optimize image viewing conditions. Retrofitting of older spaces into PACS workspaces will typically require significant changes in overhead and task lighting, as well as attention to wall and floor covering colors and materials. Positioning of PACS workstations with respect to other computer units in the room, and also with respect to the door(s) in the workspace requires considerable thought, in order to prevent screen glare from a multitude of ambient light sources. The open or multi-station reading room common to some older departments becomes obsolete. In addition to light concerns, noise and heat issues may become important determinants of the number of workstations placed into any given reading room.

Workstation Setup

Workstations can be defined in terms of the resolution or the functionality they offer the user. A typical department will have several types of workstations in place, and these will vary in both resolution and functionality by intended user. The primary distinction is between "diagnostic" workstations (those used by radiologists for image interpretation and report generation), and "non-diagnostic" or "clinical" workstations (those used by technologists and clinicians for image review purposes other than primary diagnosis). Controversy exists as to the number of monitors that is "appropriate" for a workstation (1, 2, 4, or 8) as well as to the required resolution (1K vs. 2K) of those monitors.

In our practice, all diagnostic monitors have 2K resolution at high luminance, and the vast majority of our diagnostic workstations are 2-monitor set-ups. Most clinical or QA workstations offer 1 monitor and 1K resolution, at varying levels of luminance. In practical terms, each radiologist becomes comfortable with a workstation style after a few hours of trial and error. In our experience, most quickly abandon 4-monitor stations as they are typically more cumbersome to use and slower to load cases than 2-monitor stations. A few 4-monitor stations remain in our department, primarily used for MRI and fluoroscopy cases.

Ergonomics

Ergonomic issues in clinical PACS implementation have received scant attention to date. Ergonomic problems may be workstation related (inappropriate workstation table height, poor monitor luminance, poor keyboard or mouse functionality, etc.), or they may be workspace related (poor ambient noise or lighting control, inappropriate chairs, etc.), and will vary by institution. Some of this variance will be related to the amount of money spent on optimizing the workspace, and some to the level of electronic integration in the department, which determines the need for accessory equipment in an individual workspace.

In our experience, eyestrain, neck strain, carpal tunnel syndrome, and thumb arthritis are the most common repetitive use injuries that result from migration to an ergonomically sub-optimal PACS environment. While none of these has resulted in significant radiologist disability to date, all are potentially troublesome in the long term, and the major manufacturers will have to pay much greater attention to workstation and workspace ergonomics as more facilities implement PACS into their daily workflow.

Reading Patterns and Clinical Interactions

The most dramatic change in image interpretation patterns following PACS implementation occurs in cross-sectional imaging. Most "heavy-users" of PACS for CT and MRI interpretation rapidly migrate from a 12, 15, or 20 image film based "page" mode to a "cine" or "stack" mode for rapid, active image review, with the images typically displayed in a large field (2 or 4 image) format. Residents, who may still interpret film in other institutions, typically switch to a mixed "cine" and page mode. Projectional radiography is typically interpreted in a similar fashion as film, although usually with fewer displayed images per case. In the aggregate, case efficiency per radiologist typically decreases (sometimes dramatically) with initial PACS adoption, especially if the PACS archive is new and comparison must be made to filmed historical examinations. Efficiency improves dramatically as the user becomes more familiar with the PACS workstation, and especially as the PACS archive builds to include essentially all important comparison cases.

In our experience, significant changes in clinical interaction for projectional radiography and cross-sectional imaging occur following migration to PACS. First, there is an initial increase in consultations in all sections, as non-radiologist users get their introduction to PACS and need training in usage of the system. Next, there is a sustained, dramatic decrease in the number of clinical interactions for projectional radiography, despite an increase in the number of interpreted cases (because of essentially zero study loss). I refer to this as the "it's just a chest x-ray, anyone can read it" syndrome. Although some have advocated increased conferencing with the clinical services to overcome the decreased number of routine reading room clinical interactions, we have not found this to be effective. In our experience, many clinical services quickly become non-reliant on the radiologist for the interpretation of projectional radiographs.

At the same time, there is an increase in the number of consultations for cross-sectional imaging studies, related both to the increased number of cases reported (higher efficiency/throughput), and to the new ease of availability of the studies. Thus far, despite an apparent increase in clinical service fascination with cross-sectional imaging studies we have seen no decrease in reliance on the radiologist for interpretation of these studies.

Conclusion

There are a multitude of considerations that are a part of any PACS implementation decision. Most of these are technical or financial, and they can quickly overshadow the practical issues that are the concern of most clinical radiologists. Time spent optimizing some of these more practical concerns should help smooth the migration to PACS for many clinical practices.

Disclosure: Northwestern University Medical School and Northwestern Memorial Hospital have a PACS corporate R & D partnership with General Electric Medical Systems.

Bacterial Infections of the Lung

David S. Schwartz, MD

Objectives

1. Describe the host defenses in the prevention of bacterial pneumonia
2. Review the various forms of bacterial pneumonia (community-acquired, hospital-acquired, and ventilator-associated)
3. Describe the complications of bacterial pneumonia
4. Review the appearance of bacterial infections in the lung

Introduction

Pneumonia remains a significant cause of morbidity and mortality in the United States, with estimates of 2 million to 4 million cases each year. It is the sixth leading cause of death nationwide (approximately 60,000), and the most common lethal nosocomial infection, with the vast majority of deaths in the over-65 age group. An estimated 20 million patient-physician interactions each year are attributed to pneumonia.

While there may be other etiologies, bacteria are the most common cause of pneumonia in adults over the age of thirty. In children, viral pathogens are common, but these are less likely in immunocompetent adults. The most common viral pneumonias in adults are Influenza (usually A) occurring in epidemics, and the occasional case of varicella-zoster. Other causes are mycobacterial and fungal organisms. "Atypical pneumonia", usually associated with a better prognosis, has several etiologies, including intracellular organisms such as *Chlamydia pneumoniae* and *Mycoplasma pneumoniae.* Due to their clinical similarity with bacterial pneumonias, these are often included in a discussion of bacterial lung infections.

Host Defenses and the Development of Pneumonia

Most bacterial pneumonias arise from inhaling droplets small enough to reach the alveoli, or from aspirating secretions from the oropharynx or gastrointestinal tract. Hematogenous or lymphatic routes of infection are very uncommon. There is a normal host defense system that protects the lower respiratory system. As the airways branch (up to 20 times), airborne particles or droplets impact at the confluence of bronchi. These are then trapped in a layer of mucus, which is produced by the epithelial cells. Cilia produce an upward flow, returning these particles to the pharynx, where they are swallowed or expectorated. This flow is increased with a normal cough reflex, which prevents the accumulation of significant amounts of trapped material in the tracheo-bronchial tree.

If bacteria remain in the lower respiratory tract, alveolar macrophages may engulf and destroy them. If the organisms are too numerous or too virulent, the macrophages release a number of molecules that recruit neutrophils and initiate an inflammatory response. The airway mucosa may also produce a number of peptides that add to the inflammatory reaction. Humoral defenses, including the immunoglobulins (IgA and IgG), may also come into play.

Any abnormality that interferes with these defenses predisposes the patient to bacterial pneumonia. These include:

Agent	Result
Smoking Pollutants (SO_2, NO_2) Cigarette smoke	Altered ciliary function
Chronic obstructive pulmonary disease Cystic fibrosis Tracheotomy, intubation	Impairment of cough or clearance
Cystic fibrosis	Increased adherence of bacteria to the mucosal surface
IgG deficiency	Decreased humoral defense
IgA deficiency	Increased bacterial adherence to mucosa
Chronic malnutrition	Decreased cell-mediated immunity

The initial step in the development of pneumonia is usually colonization of the upper airway (including the oropharynx) or the stomach. There are a large number of causes, including poor oral hygiene, intubation or mechanical ventilation, as well as iatrogenic alteration of the gastric pH in ICU patients. When the organisms are aspirated (assuming a decreased host response or a large volume of organism), the bacteria adhere to the mucosa. As they invade the cells, there is an inflammatory reaction, with the production of exudate. If this is multifocal and centered on inflamed airways, the pattern is that of **bronchopneumonia**, with patchy consolidation and loss of volume. This may coalesce to produce more of a segmental appearance. With **lobar pneumonia**, extensive exudate forms, spreading across the segmental boundaries. This may involve part of a lobe, or the entire lobe. It may be multilobar or localized. Air bronchograms are typical, as the airways are not compromised in this disease. **Interstitial pneumonia** is not typical of bacterial infection, but it may be seen with *Mycoplasma pneumoniae*.

Community-Acquired Pneumonia (CAP)

Community-acquired pneumonia is suspected in the presence of at least two of the common symptoms: fever, cough, sputum production, dyspnea, sweats, hemoptysis, and chest pain. Consolidation, infiltration, or cavitation on chest radiograph is considered diagnostic. 20% of patients with CAP require hospitalization, most commonly those over the age of 50. The majority respond to outpatient therapy.

The common organisms include:

- *Streptococcus pneumoniae* (The most common etiology in adults >50)
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Staphylococcus aureus*
- *Legionella spp*.
- *Klebsiella pneumoniae* and other Gram-negative bacteria
- Anaerobic bacteria (oral flora)
- "Atypical pneumonia" -
  - *Mycoplasma pneumoniae*
  - *Chlamydia pneumoniae*

Risk factors for occurrence of pneumonia and increased severity of disease include:

- Chronic obstructive pulmonary disease
- >60 years of age
- Smoking
- Alcoholism
- Influenza outbreak (bacterial superinfection)
- Poor dental hygiene
- Intravenous drug use
- Immunosuppression

Hospital-Acquired Pneumonia (HAP): Nosocomial Infection

HAP refers to infections that develop after 48 hours of hospitalization. VAP (ventilator-associated pneumonia) has its onset during the first two days of mechanical ventilation. There is a high rate of mortality in patients with HAP, with an attributable mortality rate of 27-33%. The rate is as high as 75% in patients infected with particularly virulent organisms, such as *Pseudomonas aeruginosa* or *Acinetobacter*. The risk also increases with the severity of the underlying illness, inappropriate antibiotic therapy, and advanced age.

Diagnosis may be difficult, and the illness must be differentiated from other possible causes of fever and pulmonary infiltrates:

- Chemical aspiration without infection
- Atelectasis
- Pulmonary embolism
- Acute respiratory distress syndrome (ARDS)
- Pulmonary hemorrhage
- Lung contusion
- Infiltrative tumor
- Radiation pneumonitis
- Drug reaction
- Vasculitis
- Cardiogenic pulmonary edema

Complications of Pneumonia

- Abscess formation (*Klebsiella pneumoniae* and other gram-negative organisms, *Staphylococcus aureus*, aerobic and anaerobic streptococci, oral anaerobes such as *Bacteroides* and others)
- Parapneumonic effusion
- Empyema
- Organization
- Hematogenous dissemination of infection

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TB in the 21st Century

Sanford A. Rubin, MD

Tuberculosis (TB) is a disease that has undergone a dramatic change during the second half of the 20th century. In the early 1900's as many as 90% of adult city dwellers were found to have evidence of active or healed TB at autopsy. In 1900 TB caused one of five deaths among those aged 15 to 44 years, and in New York City 85% of children were infected with TB by age 14. Contrast the above figures with those given below:

1953 Case rate 53/100,000
1977 Case rate 14/100,000
Death rate 1.4/100,000
1977 30,000 new cases
1986 22,768 new cases (80% Pulmonary)

High School seniors with positive TB skin tests
1948 — 16.4%
1968 — 1.4%
1999 — ? (very low)

This marked decrease in the incidence of TB continued until 1985. It was due to a combination of better methods of diagnosis, isolation of infectious patients, and the development of effective therapy in the early 1950's that quickly renders patients noninfectious. The result has been closure of most TB hospitals and the following aftermath:

1. Medical students and residents are not as well trained in the diagnosis and treatment of TB as in previous years.
2. Fewer practicing physicians have a special interest in TB.
3. More TB cases are encountered in community hospitals by non-chest physicians.
4. Fewer children are infected leading to an increased incidence of primary TB in adults (± 20% of new cases). X-ray findings in adult primary TB often are not readily recognized even though the abnormalities are often typical of the disease; thus many cases of primary TB in adults are misdiagnosed.
5. Once diagnosed with TB, patients may be mismanaged by primary care physicians (including board-certified internists).

It should be remembered that TB is not evenly distributed throughout the population. The incidence of the disease is highest in lower socioeconomic groups, prisoners, residents of nursing homes, immigrants and refugees, and among health care workers. There also are a number of risk factors that are or may be associated with a higher incidence of TB including altered immunity, alcohol abuse, prior gastric surgery, diabetes, old age, pneumoconioses, and lung cancer. Since 1985 the incidence of TB has steadily increased, mainly due to the large number of cases in patients with AIDS.

The organism *Mycobacterium tuberculosis* is acquired by inhalation of contaminated droplets that have been coughed up by a patient with the disease.

The rate of development of postprimary TB from an old primary focus is approximately 1% per year in people with normal immunity. In people with deficient T-cell immunity (e.g. AIDS) it may be as high as 10% per year.

The radiographic features of primary TB in adults are listed below:

Primary TB (Adults)

Infiltrates	78%	25%	50%
Adenopathy	48%	10%	35%
Atelectasis	Rare	8%	18%
Pleural Effusion	38%	23%	24%
	Stead (1968)	Choyke (1983)	Woodring (1986)

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The changes of postprimary (reactivation, recrudescent) TB in adults are quite well known:

Postprimary TB

Infiltrates (Usual Upper Lobe Location)	87%	91%
Cavities	51%	45%
Endobronchial Spread	19%	21%
Pleural Effusion	--------	18%
	Hadlock (1980)	Woodring (1986)

Pulmonary TB in children may be of several varieties:

1. Primary
   a. Usual (Infiltrate and/or nodes)
   b. Miliary
   c. Mass or large infiltrate
   d. Effusion
   e. Atelectasis
2. Congenital (Neonatal)
   a. Disseminated
   b. Often fatal
3. Postprimary (Similar to adults)

In summary we may make a number of statements about the chest x-ray in pulmonary TB.

1. It is fairly sensitive.
2. It lacks specificity.
3. The changes are protean.
4. The findings may be unusual or may be altered by pre-existing disease.
5. Activity often cannot be accurately determined radiographically.
6. The features generally reflect the nature of the disease.

The consequences of delay in the diagnosis and treatment of TB include increased morbidity, increased mortality, and increased risk of infecting others. One must be aware of the widely variable appearance of the findings of TB. One should immediately become suspicious when the patient fits into any of the previously listed high-risk groups. Hopefully we can increase the rapidity and accuracy of the diagnosis of TB thus enabling prompt therapy and resulting in a decrease in the number of new cases.

Atypical Mycobacterial Infections

Pulmonary infections caused by atypical mycobacteria have become more common in recent years in the United States. The diagnosis often is overlooked because the findings may be subtle. Often the radiographic appearance may change slowly or not at all for long periods of time. The radiographic findings of atypical mycobacterial pulmonary infections are similar to those of TB in any given patient. The most common radiographic findings are one of more areas of clustered fibroproductive nodules that change very slowly. Cavities occur less commonly than in TB, and the walls of these cavities may be thin. Also, less inflammatory exudate may be present around these cavities. Pleural disease and bronchopleural fistulas may be seen.

Conventional and high resolution lung CT may show bronchiectasis in a significant number (approximately 50%) of these patients. The bronchiectasis tends to be more prevalent in the right middle lobe and lingula. The inflammatory nodules are much better seen on CT (especially high-resolution lung CT) than on conventional radiographs. Nodules that result from bronchogenic spread often result in the “tree-in-bud” appearance.

Infections caused by ***Mycobacterium avium complex*** **(MAC)**, also known as ***M avium-intracellulare***, are seen in three fairly well defined patient populations. Approximately 50% of patients with **MAC** infection have pre-existing lung disease such as other granulomatous diseases, obstructive lung disease, lung cancer, or bronchiectasis. A large number of patients with **MAC** infection have AIDS, or they have some other cause of deficient T-cell immunity. More recently recognized is a population of patients with **MAC** lung disease with previously normal lungs and normal immunity. This group is mostly Caucasian women over the age of 55. They frequently present with a chronic productive cough and weight loss, and they may have slowly progressive radiographic abnormalities. Response to treatment of these diseases is variable. ***M kansasii*** infection is much easier to treat than **MAC** infection. Early recognition of these diseases will allow earlier treatment and hopefully prevent the development of far-advanced disease.

Pulmonary Nontuberculous Mycobacterial Infection

H. Page McAdams, MD

Learning Objectives

1. To learn the most important causes of nontuberculous mycobacterial infection (NTMB) in the lungs.
2. To be able to describe the radiologic manifestations of the classic type of pulmonary NTMB infection.
3. To be able to describe the radiologic manifestations of the non-classical types of pulmonary NTMB infection.
4. To be able to describe the radiologic manifestations of the pulmonary NTMB infection in patients with AIDS.

Target Audience

All radiologists and clinicians involved in diagnosing or treating patients with known or suspected pulmonary NTMB infection.

Introduction

The nontuberculous mycobacteria (NTMB) are a ubiquitous group of organisms found throughout the environment that occasionally infect cervical lymph nodes, skin, soft tissues and lung. Pulmonary disease is increasing in prevalence and is most commonly caused by *Mycobacterium avium-intracellulare complex (MAIC)* and *Mycobacterium kansasii*, although *Mycobacterium xenopei*, *Mycobacterium fortuitum* and *Mycobacterium chelonei* are occasional pulmonary pathogens. Diagnosis of pulmonary NTMB infection can be difficult, but is facilitated by knowledge of the full spectrum of radiologic findings of this disorder.

Pathogenesis

NTMB are low-grade pathogens that occasionally cause infection after inhalation, ingestion or direct inoculation. Human to human transmission is rare and isolation of infected individuals is not required. Pulmonary infection is usually chronic and indolent, although severity depends on several factors including underlying lung disease and patient immune status. Pulmonary infections most commonly occur in patients over 50 years of age who have underlying lung disease or an immunologic disorder. Increased risk of NTMB infection also occurs in patients with rheumatoid arthritis, diabetes mellitus, alcoholism and nonpulmonary malignancies. In the last two decades *MAIC* has become an important pathogen in patients with AIDS.

Diagnosis

Diagnosis of pulmonary NTMB infection is often difficult. Sputum or bronchoalveolar lavage (BAL) fluid cultures can be falsely positive in patients with chronic lung disease and airway colonization and falsely negative in patients with noncavitary pulmonary infection. Intradermal skin testing for *M. avium-intracellulare, M. kansasii,* and *M. fortuitum* may be useful in distinguishing true infection from contamination or colonization, but clinical use is limited by cross-reaction between mycobacterial antigens. Infection can be confirmed by isolation of NTMB from transbronchial or open lung biopsy specimens. The diagnosis may also be made if sputum or BAL cultures are positive and there are associated appropriate clinical and radiologic findings (Table). Patients with AIDS are considered to have pulmonary NTMB infection if sputum or BAL cultures are positive, even if the chest radiograph is normal.

Clinical and Radiologic Manifestations

The clinical and radiologic manifestations of pulmonary NTMB infection can be divided into four groups: (1) classical infection, (2) non-classical infection, (3) nodules or masses in asymptomatic patients, and (4) infection in patients with AIDS.

(1) Classical Infection

This is the most common form of pulmonary NTMB infection. Affected patients are typically elderly caucasian men with underlying lung disease such as chronic obstructive pulmonary disease or pulmonary fibrosis. Systemic complaints such as weight loss, malaise and fever are common.

Classical NTMB infection typically manifests on chest radiographs with features that are similar to those of post-primary tuberculosis. The most common

Table: Diagnostic Criteria for Pulmonary NTMB Infection

(Official statement of the American Thoracic Scociety. Diagnosis and treatment of disease caused by nontuberculous mycobacterium. Am J Crit Care Med 1997;156:S1-25).

1. Clinical criteria
- a. Compatible signs/symptoms (cough, fatigue, weight loss, dyspnea)
- b. Reasonable exclusion of other diseases.

2. Radiologic criteria
- a. Chest radiographic abnormalities
  - i. Consolidation with or without nodules (persistent > 2 mo or progressive)
  - ii. Cavitation

iii. Multiple nodules alone
- b. HRCT abnormalities
  - i. Multiple small nodules
  - ii. Multifocal bronchiectasis with or without small lung nodules

3. Bacteriologic criteria
- a. Three sputum/bronchial wash cultures with negative AFB smear or two cultures and one positive AFB smear or
- b. Single bronchial wash with 2+, 3+, or 4+ positive culture* or positive culture with 2+, 3+, or 4+ AFB smear
- c. Tissue biopsy of lung
  - i. Any growth from biopsy of bronchopulmonary tissue
  - ii. Granuloma and/or AFB on lung biopsy with one or more positive cultures from sputum/bronchial wash

Note:
1. For a diagnosis of pulmonary disease, all three criteria (clinical, radiologic, bacteriologic) must be present except in patients with AIDS in whom the chest radiograph can be normal.
2. * In patients with AIDS, 1+ growth on culture of a single bronchial wash is sufficient except if the organism is MAIC which requires 2+ or more growth.

findings are heterogeneous linear and nodular opacities in the apical and posterior segments of the upper lobes. The degree of involvement varies from subtle segmental disease to extensive, bilateral multisegment disease. Cavitation is a common associated finding and cavities are typically small and thin-walled. Cavitation facilitates endobronchial spread of disease which manifests as unilateral or bilateral 5- to 15-mm centrilobular nodules.

Although pulmonary opacities can remain unchanged for many years, they more commonly progress slowly and are associated with progressive volume loss and scarring. Features that resemble healed primary tuberculosis, such as calcified pulmonary nodules or hilar nodes are, however, uncommon. Other uncommon findings include mass-like opacities resembling primary lung carcinoma (either in association with linear and nodular opacities or as an isolated finding), miliary disease, hilar and/or mediastinal lymphadenopathy and pleural effusions.

(2) Nonclassical Infection

This is the second largest group of patients with pulmonary NTMB infection. Affected patients are typically elderly caucasian women without underlying lung disease. Although these patients typically complain of chronic cough, systemic complaints are uncommon.

The radiologic manifestations of non-classical infection are characteristic and consist of mild to moderate bronchiectasis and multiple, 1- to 3-mm centrilobular nodules. Disease is usually isolated to, or most severe, in the lingula and middle lobe. Cavitation, ground glass opacities, volume loss and adenopathy are uncommon.

(3) Nodules in Asymptomatic Patients

Occasionally NTMB infection can manifest as solitary or multiple nodules which are usually incidentally detected in asymptomatic patients. The nodules are macroscopic granulomas and may represent the initial manifestation of pulmonary infection.

(4) NTMB Infection in Patients with AIDS

NTMB infection is generally associated with marked immunosuppression and usually occurs late in patients with AIDS (CD-4 count less than 50/mm^3). Although 15 to 24% of AIDS patients will develop disseminated extrathoracic disease, pulmonary infection is uncommon. Unlike other HIV-associated infections, NTMB pulmonary infection usually results from primary exposure and not reactivation of latent organisms.

The chest radiograph is often normal in many patients with *MAIC*-positive blood and sputum cultures. Mediastinal and hilar adenopathy are the most common findings. Small scattered alveolar and nodular opacities, miliary nodules and mass-like lesions occur only occasionally.

Summary

The most important clinico-radiologic manifestations of pulmonary NTMB infection may be summarized as follows:

1. *Classical NTMB infection*. Patients are usually elderly men who present with cough, weight loss and malaise. Radiologic findings are similar to those of post-primary tuberculosis: upper lobe heterogeneous opacities, cavitation and scarring.
2. *Non-classical NTMB infection*. Patients are usually elderly women without constitutional complaints. Radiologic findings are characteristic: bronchiectasis and centrilobular nodules isolated to, or most severe, in the middle lobe and lingula.
3. *NTMB infection in patients with AIDS*. Extrathoracic infection (blood, bone marrow, lymph nodes) occurs more frequently than intrathoracic disease. The chest radiograph is often normal in patients with NTMB infection. The most common intrathoracic abnormality is mediastinal or hilar adenopathy; small scattered pulmonary opacities can occasionally be seen.

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Pulmonary Infections in the Bone Marrow Transplant Patient

Ann N. Leung, MD

Objectives of Lecture

1. To review the typical time course of immunosuppression resulting from bone marrow transplantation.
2. To review the most common pulmonary pathogens that cause infection during specific periods in the post-transplantation course.
3. To review and illustrate radiologic findings of common pulmonary infections in the bone marrow transplant recipient.

I. Introduction

Bone marrow transplantation (BMT) is the intravenous infusion of hematopoietic progenitor cells to reestablish marrow function in a patient with damaged or defective bone marrow. BMT is currently the treatment of choice for many hematological malignancies and severe congenital or acquired disorders of the hematopoietic and immune systems. Allogeneic transplantation refers to the transfer of marrow from a donor into a recipient who is not an identical twin (syngeneic); autologous transplantation involves the use of the patient's own marrow to reestablish hematopoietic cell function.

Preparative regimens usually consisting of high-dose chemotherapy and total body irradiation are administered prior to BMT to eradicate the endogenous bone marrow and to achieve immunosuppression. After peripheral hematologic elements have reached a nadir, the donor marrow is infused. During the immediate peritransplant period, function of the absent bone marrow must be substituted by transfusional support of red blood cells and platelets. Neutropenia usually lasts a median of 2 to 3 weeks. Even after engraftment, patients will continue to suffer from profound immune impairment. Complete recovery of both cellular and humoral immune function does not occur until approximately one year after successful transplantation if graft versus host disease (GVHD) does not develop.

Pulmonary complications affect 40 - 60% of BMT patients and are a common cause of morbidity and mortality (1). More than 30% of BMT-related deaths are attributable to pulmonary disorders (2). In any individual patient, the risk and severity of complications will be modified by the following factors: 1) the type of underlying disease and associated pre-transplant therapy, 2) the type of transplantation (allogeneic, syngeneic or autologous), 3) the type of immunosuppressive therapy given to prevent or treat GVHD, 4) the presence and severity of GVHD, and 5) the presence of graft failure (3).

Infection is the most common complication that occurs in the BMT population. Because of the predictable course of transplantation induced-immune suppression and recovery, time lines have been established that focus the differential diagnosis on pathogens most likely to occur at sequential points in the transplantation process. Pulmonary infections may be classified as early or late, dependent on their time of onset, prior to or after 100 days post-transplantation.

II. Early Pulmonary Infections

In the first month after transplantation, neutropenia and damaged mucosal membranes are the predominant defects in host defense which predispose to bacterial and fungal infections. With engraftment and recovery of neutrophil count in the second and third months, viruses, particularly cytomegalovirus, play an increasingly important role in causing pulmonary complications.

A. Bacterial Infections

Bacterial infections may occur early during the neutropenic period or later, after engraftment but before full immune recovery. Bacteremias are common but because of the wide-spread use of broad-spectrum antibiotics for febrile episodes, bacterial pneumonias are rare. The institution of prophylactic non-absorbable antibiotics for gut decontamination has markedly decreased the incidence of gram-negative bacteremias.

B. Fungal Infections

Fungi account for 12 - 45% of post-BMT pneumonias and have emerged as a major cause of fatal infections (4, 5). The majority of fungal infections occur within the first 30 days after transplantation during the neutropenic period.

Aspergillus is the most common fungal pathogen reported to affect 0 - 20% of BMT recipients (4). Inhalation of the ubiquitous spores is believed to be the portal of entry. The radiologic patterns of disease closely reflect the pathogenesis of infection. In the early stages of the angioinvasive form of disease, a relatively well-circumscribed area of consolidation appears as the fungal infection spreads from small membranous and respiratory bronchiole lumens to the adjacent parenchyma; more extensive parenchymal opacification, sometimes in a characteristic wedge-shaped pattern, develops as the fungi invade adjacent vessels leading to thrombosis and hemorrhagic infarction. On CT, the angioinvasive stage manifests as a nodule surrounded by ground-glass attenuation (CT halo sign) representing the nidus of fungal infection and adjacent area of hemorrhagic infarction, respectively (6). In the recovery phase of infection, cavitation of the nodule will occur (air-crescent sign) usually coincident with clinical improvement and resolution of neutropenia.

Pulmonary candidiasis may develop via oropharyngeal aspiration or more commonly, via hematogenous dissemination. Chest radiographic findings may vary from unilateral, segmental or lobar consolidation to bilateral, diffuse homogeneous or patchy ill-defined opacities. On CT, the most characteristic finding is a nodular pattern of disease; nodules may be single or multiple and nodule size varies from 5 - 20 mm (7).

C. Viral Infections

Viral infections in the BMT population are a frequent occurrence and follow a predictable temporal pattern: herpes simplex (HSV) reactivation occurs in the immediate peritransplant period followed by cytomegalovirus (CMV) infection between days 30 and 120 and varicella zoster (VZV) reactivation between days 100 and 180 (8). HSV and VZV infections are usually limited to mucocutaneous involvement.

CMV infection occurs in 50 - 70% of allogeneic BMT recipients; approximately one-third of infected patients subsequently develop CMV pneumonia with a median time of onset of 50 - 60 days post-transplantation (1). CMV pneumonia is rare in autologous or syngeneic BMT patients; predisposing factors include prior CMV seropositivity, older age, and more severe grades of GVHD. Radiographically, findings are variable and range from a reticulonodular pattern to airspace consolidation that may be extensive and bilateral or lobar in distribution (9). Pleural effusions may be associated. The most common pattern on CT consists of multiple nodules 1 - 5 mm in size associated with areas of ground-glass attenuation (7).

D. Pneumocystis carinii Pneumonia

Pneumocystis carinii is the major protozoal pathogen in the BMT population. Since the institution of routine prophylaxis, the incidence of this infection has dropped sharply; currently, the majority of PCP infections develop in either non-compliant patients or patients in whom infection occurs prior to the institution of prophylaxis. The median time of disease onset is 2 months post-transplantation although cases have been reported as early as 2 weeks.

The radiographic manifestations of disease are dependent on the stage and severity of infection. In early stages, a diffuse, perihilar or reticulonodular pattern is present with associated ground-glass opacification. In later stages or more severe disease, homogeneous, bilateral consolidation may occur. On CT, the most characteristic finding of PCP is ground-glass attenuation. The distribution of ground-glass may be diffuse and homogeneous or geographic, with relatively normal secondary pulmonary lobules adjacent to diseased ones (10).

II. Late Pulmonary Infections

At 100 days post-transplantation, gradual improvement of both humoral and cellular immunity will continue until full recovery occurs at approximately one year. Except for VZV infections, autotransplants, syngeneic recipients, and allotransplants without GVHD experience relatively few late infections.

VZV is the single most frequent cause of late infections occurring in 25 - 40% of allotransplants and up to 28% of autotransplants. Infection is limited to the skin; associated pulmonary disease is uncommon.

Most other late infections occur in the setting of chronic GVHD, involve the respiratory tract, and are usually caused by encapsulated bacteria such as Streptococcus pneumoniae and Hemophilus influenzae or common respiratory viruses.

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Immune Restoration Disease in AIDS: What the Radiologist Needs to Know

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Objectives

1) To introduce the concept of immune restoration disease in AIDS.
2) To list the various thoracic and non-thoracic manifestations of this phenomenon.
3) To familiarize the audience with the radiological appearance of those types of immune restoration disease affecting the thorax.

Introduction

In the past few years, the treatment of AIDS has been revolutionized by the introduction of HAART (highly active antiretroviral therapy). In many patients, there has been a remarkable decrease in the incidence of opportunistic infections and some malignancies (especially Kaposi sarcoma), with a consequent sharp decline in mortality. Central to this improvement is the restoration of pathogen-specific immune responses once the proliferation of the HIV virus is brought under control. The specific functions recovered may not span the entire spectrum of original memory-type T cells and may leave "holes" of continued susceptibility. Nevertheless, with the increasing power of newer HAART regimens (including protease inhibitors, NRTI and NNRTI drugs, and others), it is hoped that immune system restoration will near completion.

As more and more patients were placed on HAART, it was observed that a number of individuals actually appeared to worsen clinically (and radiologically) after initiation of therapy. Some of these patients were being concurrently treated for known opportunistic infection while others had a history of previous infection; some had no known history. Worsening often involved fever, the development of lymphadenopathy, or organ-specific findings. A common feature to these patients was a very low (<100) CD4+ T-cell count before HAART, and most responded to HAART with at least a moderate increase in CD4+ count. Many of these patients improved without changes in therapy, but some required an interruption in HAART or addition of steroids to reduce inflammation. These observations have now been extended over a variety of organ systems; the term *immune restoration disease* encompasses this inflammatory process occurring at sites of preexistent or subclinical infection by opportunistic pathogens. By definition, these reactions occur within a short time period (a few days up to 6-8 weeks) after beginning HAART, and there should be no evidence of superimposed infections, drug resistance, or drug reaction. In the remainder of this abstract, I will enumerate the various settings in which this occurs and the radiographic manifestations (if any). It is important for the radiologist to recognize that, in this setting, radiographic worsening does not necessarily imply unsuspected infection or inappropriate therapy.

Mycobacterium avium Complex

Clinical restoration of cell-mediated immunity coupled with an inflammatory response was first described by French et al. in 1992, with the report that 27 (42%) of 64 patients who had been anergic to tuberculin prior to zidovudine (AZT) therapy subsequently developed a positive skin test response. Five patients also manifested an acute illness consisting of localized *Mycobacterium avium* complex infection, lymphadenopathy, and/or fever after one to two weeks of therapy. In 1998, five late-stage HIV-infected patients (CD4+ counts below 50) who were started on antiretroviral therapy with the protease inhibitor indinavir developed fever, leukocytosis, and generalized lymphadenopathy within three weeks of commencing therapy [16]. Nodal biopsy results demonstrated granulomatous inflammation with *Mycobacterium avium* complex infection. Evidence for immune restoration included increases in CD4+ counts, the presence of granulomatous features on biopsy specimens, and the vast preponderance of the "memory" CD4+ phenotype after treatment, suggesting an expansion of the CD4+ subset which had T-cell receptors to mycobacterial antigens resulting from the (previously subclinical) infection. Patients all improved after initiation of antimycobacterial therapy. It is now estimated that up to 5% of AIDS patients with low CD4+ counts will demonstrate this phenomenon. Lymphadenopathy may occur in the mediastinum or abdomen; peripheral adenopathy is less common. On CT, the nodes may be hypodense as is often seen in mycobacterial infections. Inflammatory abdominal masses can occur. In the chest, pulmonary consolidation and endobronchial granulomas have been reported. In this and other manifestations of immune restoration disease, pain is a common feature due to the lymph node swelling. Most authorities recommend continuing HAART if possible (to avoid HIV resistance), while adding anti-MAC therapy and steroids if necessary.

Tuberculosis

A type of immune restoration disease was first described in patients being treated for active TB in the 1950's, well before the era of AIDS. A transient worsening in either symptoms or signs of tuberculosis was described in small numbers of patients, usually occurring within one month after therapy is begun. New or worsened lymphadenopathy, fever, cerebral tuberculomas, and pleural effusions were termed "paradoxical responses". These transient findings were felt to be inflammatory responses due to improved host immunity as a result of antituberculous therapy.

In AIDS, where HAART causes an even more dramatic rise in immunity, these "paradoxical responses" have become much more common. In contrast to *M. avium*-related immune restoration disease, in which cultures often demonstrate the previously unsuspected organism, patients with tuberculosis who develop restoration disease are generally known to have active infection at the time of beginning HAART therapy. Thus anti-TB treatment has usually been given. We observed transient worsening on radiography in 14 (45%) of 31 AIDS patients with active TB after receiving antiretroviral therapy, including seven patients (23%) who showed severe worsening. Of 56 patients who were either HIV-negative or who did not receive antiretroviral therapy, only 11 showed worsening (p=.023), two of whom showed severe worsening (p=.009). AIDS patients in whom severe worsening occurred had a lower initial mean CD4+ cell count ($47/mm^3$) than other patients undergoing antiretroviral therapy ($145/mm^3$) (p=.024). Correlative evidence of a rise in cellular immunity was the conversion of PPD responses from anergic to positive in four patients with severe worsening.

Radiographically, a variety of manifestations may occur. In our seven cases of severe worsening, severely worsened pulmonary parenchymal disease was observed in four patients, hilar or mediastinal adenopathy in two patients, and pleural effusion in one patient. In four of the seven patients, the focus of radiographic worsening was in a previously normal region on the admission radiograph. Worsening was first noted between 1 and 5 weeks after initiation of antiretroviral therapy, with improvement occurring between 2 weeks and 3 months later. As with other forms of immune restoration disease, other causes of worsening, such as drug resistance, noncompliance, superimposed (new) infection, and drug reaction must be excluded. If they are, then treatment is as with *M. avium* conditions, with steroids used as necessary. Anti-TB and AIDS medications should not be discontinued unless absolutely necessary.

Other Manifestations of Immune Restoration Disease

Both thoracic and non-thoracic types of immune restoration phenomena after HAART therapy have been described. In the chest, a sarcoid-like disorder in two patients showed diffuse interstitial micronodular lesions, representing noncaseating granuloma in the absence of active infection. In another patient, hypersensitivity pneumonitis developed in a woman who kept pet birds, but only after beginning HAART. The chest radiographic pattern was similar in showing multiple granulomas. Removal of the birds from her home led to resolution.

Relapsing CMV retinitis was one of the first clinical scenarios of immune restoration disease. It is estimated that up to 50% of HIV patients with prior CMV retinitis will relapse after HAART. In the liver, hepatitis B and C infections can occur after HAART, either as worsening in previously known hepatitis or as the first sign of a preexisting subclinical infection (as with *M. avium*). Liver enzymes increase with hepatitis, levels of which must be carefully observed in patients who concomitantly take HAART due to potential adverse effects on liver function from those drugs. In the CNS, both mass lesions (tuberculomas) and cryptococcal meningitis have been described within a few weeks of HAART. Dermatological manifestations have included dermatomal herpes zoster eruptions as well as mucocutaneous herpes. Finally, autoimmune hyperthyroidism (Graves' disease) has been reported in three patients, although these have occurred 1-2 years after HAART.

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Pulmonary Infections in AIDS: New Trends and Changing Patterns

Phillip M. Boiselle, MD

In recent years, advances in our understanding of the molecular biology of the human immunodeficiency virus (HIV), along with the development of several promising therapeutic agents, has resulted in a new sense of optimism in the battle against the acquired immunodeficiency syndrome (AIDS). Not surprisingly, these advances have been accompanied by changes in the thoracic complications of AIDS.

This lecture provides an update on pulmonary infections in AIDS, with a special emphasis upon new trends and changing imaging features. The specific learning objectives of this lecture are as follows:

1. To review the spectrum of pulmonary infections that may complicate HIV infection and to describe their characteristic imaging findings.
2. To provide an update regarding new trends and changing patterns of pulmonary infections in HIV-positive patients.

Bacterial Infections

Bacterial infections, including infectious airways disease and pneumonia, have surpassed PCP as the most common cause of pulmonary infection in HIV-positive patients. Recurrent bacterial pneumonias are commonly observed early in HIV infection and are now included as an AIDS-defining illness. Early in HIV infection, most episodes occur secondary to *Streptococcus pneumoniae* and *Haemophilus influenzae*, the same organisms that commonly cause community-acquired pneumonia in the nonimmunosuppressed population. Radiographically, bacterial pneumonia usually presents as focal consolidation, in either a segmental or lobar distribution.

Pyogenic infectious airways diseases, including infectious bronchitis, bronchiolitis, and bronchiectasis, have been increasingly recognized in HIV-positive patients in recent years. Chest radiographs of patients with acute bacterial bronchitis may demonstrate bronchial wall thickening. Isolated small airways disease is particularly challenging to diagnose on conventional radiographics because abnormalities are often subtle and may mimic an interstitial pattern. In contrast, the high-resolution CT features of infectious bronchiolitis are quite characteristic and include small (3 mm) nodular and branching, Y- and V-shaped centrilobular opacities, which represent bronchioles that are impacted with inflammatory secretions. This pattern has been coined the “tree-in-bud” appearance. Although pyogenic infections are the most common cause of proliferative small airways disease in AIDS patients, viral and mycobacterial organisms are also important etiologies.

Interestingly, an increased prevalence of bronchiectasis has been described in association with HIV. In most cases, this is thought to occur as a complication of prior lung infections. However, bronchial dilation has also been described in HIV-positive patients without prior lung infections.

PCP

Despite a declining incidence secondary to improved prophylaxis, *Pneumocystis carinii* pneumonia (PCP) remains the most common cause of life-threatening pulmonary infection in HIV-positive patients. Advances in the prevention and treatment of PCP have been associated with an increased frequency of unusual manifestations and a trend toward more subtle radiographic presentations.

The classic chest radiographic presentation of PCP is a bilateral perihilar or diffuse symmetric interstitial pattern, which may be finely granular, reticular, or ground-glass in appearance. If left untreated, the parenchymal opacities may progress to airspace consolidation.

Importantly, the chest radiograph may be normal at the time of presentation in as many as 39 % of cases. CT, particularly high-resolution CT, is more sensitive than chest radiographs for detecting PCP, and thus may be helpful in evaluating symptomatic patients with normal or equivocal radiographic findings.

The classic high-resolution CT finding in PCP is extensive ground-glass attenuation, which corresponds to the presence of intra-alveolar exudate, consisting of fluid, organisms and debris. It is often distributed in a patchy or geographic fashion, with a predilection for the central, perihilar regions of the lungs.

Several features that were once considered unusual are now considered as typical manifestations. These features include cystic lung disease, spontaneous pneumothorax, and an upper lobe distribution of parenchymal opacities. In the past, these findings were described predominately in patients receiving aerosolized pentamidine prophylaxis. In recent years, however, these manifestations have been increasingly recognized outside of this setting, as aerosolized pentamidine has been largely replaced by more effective prophylactic agents, including trimethoprim-sulfamethoxazole and dapsone.

Tuberculosis

Pulmonary tuberculosis remains an important cause of pulmonary infection in the HIV-positive patient. Patients at particularly high risk for TB include intravenous drug abusers and patients from areas where TB is endemic. Reactivation TB is often one of the initial manifestations of HIV infection.

Radiographic manifestations vary depending upon the immune status of the patient. Early in HIV infection, when the CD4 count is >200/mm^3, the imaging features are typically those associated with reactivation TB, including parenchymal opacities with associated cavitation, often located within the apical, posterior, and superior segments of the lungs. In contrast, as the patient's immune level decreases, one will observe findings typically associated with primary TB, including consolidation and lymph node enlargement. This pattern is usually observed in patients with CD4 counts less than 200/mm^3, regardless of the actual mechanism (primary or reactivation) of infection. With regard to enlarged lymph nodes, they frequently demonstrate low-density centers and peripheral contrast enhancement.

In comparison to normal hosts, AIDS patients with TB are more likely to present with lymph node enlargement, diffuse lung disease, bronchogenic spread, miliary disease, and extrapulmonary disease. Such manifestations increase in frequency with increasing degrees of immune suppression. In the setting of severe immune suppression, a normal chest radiograph may be observed in a small minority of patients with active infection.

The "immune reconstitution syndrome" (a.k.a. "reversal syndrome") refers to an interesting phenomenon that may be observed in AIDS patients who are being treated for tuberculosis infection and are also receiving antiretroviral therapy. In the setting of immune restoration, such patients may demonstrate new or worsening lymph node enlargement, lung parenchymal disease, and/or pleural effusions, accompanied by onset of fever. Such paradoxical reactions are thought to be immunologically mediated by a heightened immune response. The diagnosis requires exclusion of other important causes, including noncompliance with therapy, drug resistance, other superimposed disease process, and drug reaction. Cultures for TB are invariably negative. Severely symptomatic patients may benefit from steroid therapy.

Atypical Mycobacterial Infections

Atypical mycobacterial infections in AIDS patients are usually secondary to *Mycobacterium avium-intracellulare* (MAI) and less commonly due to *M. kansasii*. Because MAC is a less virulent organism than *M. tuberculosis*, it is usually encountered in the setting of more advanced immunosuppression (CD4 < 50/mm^3).

Thoracic MAI involvement usually occurs in the setting of disseminated disease, with the gastrointestinal tract serving as the main entry site in most cases. Imaging findings in the lungs are variable and include multifocal patchy consolidation, ill-defined nodules, and cavities. Lymphadenopathy is frequently present, but is observed less frequently than in patients with TB. Importantly, a normal chest radiograph may be observed in roughly 20% of patients with documented pulmonary infection with MAI.

The "reversal syndrome" has also been recently described in association with MAI in HIV patients receiving highly active retroviral therapy. Affected patients present with an acute febrile reaction accompanied by new or enlarging lymphadenopathy.

Fungal Infections

Fungal infections are a relatively uncommon cause of pulmonary infection in AIDS patients. The most common fungal pathogen to involve the lungs in AIDS patients is *Cryptococcus neoformans*. Less common fungal infections include aspergillosis, histoplasmosis, blastomycosis, and coccidioidomycosis.

Pulmonary cryptococcal infection usually occurs in the setting of advanced immunosuppression (CD4 <100/mm^3). Imaging findings are nonspecific and include reticular or reticulonodular opacities, nodules, and foci of consolidation. Parenchymal abnormalities may be accompanied by lymph node enlargement and pleural effusion.

Viral Infections

Cytomegalovirus (CMV) is the most common viral pulmonary pathogen in AIDS patients. Although it is frequently recovered from the lungs, CMV is not considered a significant pathogen in most cases. CMV pneumonitis usually occurs in the setting of advanced immunosuppression (CD4 <100/mm^3).

The most common imaging features of CMV pneumonitis are ground glass opacities and alveolar consolidation, which may mimic PCP. Other imaging findings include nodules, masses, and small airways disease. The latter findings are not typically associated with PCP.

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CT Fluoroscopy

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Objectives

1) Describe the physical principles that permit "real-time" imaging with CT-fluoroscopy
2) Discuss the use of CT-fluoroscopy in the assisting percutaneous needle biopsy
3) Review the role of CT-fluoroscopy in guiding intrathoracic drainage procedures
4) Present data supporting the use of CT-fluoroscopy to assist performance of transbronchial needle aspiration

Introduction

Recent improvements in CT technology have led to the introduction of CT-continuous imaging, also known as real-time CT or CT-fluoroscopy. As compared to conventional guidance techniques, CT fluoroscopy may facilitate percutaneous needle and pleural drainage procedures. CT-fluoroscopy has also proved useful for a newer application, guidance of transbronchial biopsy.

CT-Fluoroscopy: Technical Specifications

CT-fluoroscopy was first introduced for clinical use in Japan in 1993. Fluoroscopic CT employs slipring technology and can be adapted for use with multislice CT[1,2]. Real-time visualization is accomplished with a fast parallel processor system that permits management of large quantities of data and allows for real-time reconstruction in a 256 X 256 matrix. After collection and processing of the first 360 degrees of data, each subsequent 60 degrees of data (0.17 sec) is added to the existing data and replaces the oldest 60 degrees of data. The first image is displayed 1.17 sec after initiation of CT-fluoroscopy. As a result of continuous updating, six images are displayed per second, each reflecting an accumulation of one second of data. The rapid updating of images imparts a real-time effect.

A control panel and monitor are located in the scanning room and can be moved freely to allow the radiologist, wearing a standard fluoroscopic lead apron for protection, to acquire and view CT images optimally without leaving the scanning room. The control panel allows selection of the laser light and adjustment of table position, height, and gantry angle. A button on the control panel or a foot-pedal identical to that used for routine fluoroscopy allows activation of real-time imaging.

Radiation dosimetry is an important consideration when using CT-fluoroscopy. Typical radiation dose factors are 80 - 120 kVp and 30 - 50 mA per second. Adjustments are made for the size of the patient and the area being imaged. In the lungs the high contrast between aerated lung and lung abnormalities may permit reduced dose parameters. A dedicated filter allows reduction of dose by 50% as compared to conventional CT. Absorbed skin dose using a body phantom approximates 20 cGy for an exposure of 50 seconds using 120 kVp and 50 mA.

Percutaneous Needle Aspiration

Standard CT is the most commonly used guidance technique for lung biopsy. It is safe and accurate. Sensitivity is greater than 90% for malignant lesions but is somewhat lower for benign nodules[3]. The main limitation of standard CT is the lack of real time visualization and the need for the biopsy team to exit the scanning room while the new needle position is documented. The use of CT-fluoroscopic guidance overcomes many of the limitations of conventional techniques.

Two operator approaches may be used to perform CT-fluoroscopic biopsy: real-time or interrupted real-time technique. With the real-time technique, the operator directly visualizes the procedure on the CT-fluoroscopic monitor while the needle is being advanced and during biopsy of the nodule itself. A needle-holder can be used to avoid exposure of the hand holding the needle to the primary radiation beam. The real-time technique allows coordination of table movement and patient respiration, permitting optimal visualization of the lesion.

The second basic approach to CT-fluoroscopic biopsy has been termed the interrupted real-time technique [4]. With the interrupted real-time technique, needle advancement and nodule biopsy are performed without direct visualization but are rapidly confirmed after each needle movement using a short duration of fluoroscopy, often while allowing the patient to remain in the gantry. When the needle tip is clearly identified within the nodule, aspiration is typically done blindly. Advantages of the interrupted real-time technique as compared to the real-time technique described previously include the increased distance of the operator from the primary beam and improved tactile sensation.

To date, the published clinical experience with the use of CT fluoroscopy to guide percutaneous needle biopsy is limited. Katada et al reported results of 60 CT fluoroscopic procedures in 57 patients, including 36 with CT guided intrathoracic procedures [2]. In their study, the target nodule was punctured on the first attempt in 83% of patients and the average number of passes for all nodules was 1.3. A diagnostic result was obtained in 32 (97%) of the 33 patients who underwent lung biopsy, including 17 malignant and 15 benign lesions. Mean procedure time was 54 minutes (range 24-139 minutes) with an average of 74 seconds of CT fluoroscopy time for each puncture. The authors reported 17 (47%) complications among the 36 thoracic procedures, including 16 pneumothoraces and one episode of hemoptysis. Katada et al concluded that the real-time capability of the CT-fluoroscopy permitted reduction in the number of needle punctures required to perform the biopsy and provided substantial overall advantages over standard CT [2].

The early experience at our institution with CT fluoroscopy to assist in the biopsy of small pulmonary nodules has also been promising[5]. We performed procedures on 17 patients with nodules less than or equal to 1.5 cm. In most cases, we used a coaxial biopsy technique and the interrupted real-time CT fluoroscopy method. Similar to standard CT, the needle tip was routinely identified by its characteristic low-density artifact. We established a diagnosis in 16 (94%) of the 17 lesions, including 11 malignant and 5 benign nodules. The mean number of passes was 2.5. The average fluoroscopic time for each puncture was 103 seconds. Good image quality was obtained using dose factors of 30 mA/120 kVp. Mean room time was 91.5 minutes. Complications in our series occurred in nine patients (53%), including eight with pneumothorax and one with hemoptysis. Two patients with pneumothoraces required chest tube drainage.

An important subjective advantage of CT fluoroscopy is the increased peace-of-mind that the rapid image display provides for the radiologist. The short time interval between movement of the needle and knowledge of its location and any complications can substantially decrease operator stress related with the procedure.

It is a subjective impression that CT-fluoroscopy allows biopsy to be performed more rapidly, particularly for small nodules. However, it is important to recognize that no study has directly compared the duration of procedures done with standard CT and CT fluoroscopy to ascertain if there is a decrease in procedure time with the latter. Likewise, other purported advantages of CT-fluoroscopic guidance have not yet been compared directly to standard CT.

Intrathoracic Drainage Procedures

Imaging guided chest drainage procedures can be used to guide treatment of simple or complicated pleural effusions, pneumothoraces or mediastinal fluid collections. Factors involved in the selection of the appropriate imaging modality for drainage of intrathoracic collections include the type of thoracic collection, patient condition and operator preference. In general, ultrasound is most useful for drainage of large free-flowing fluid collections. In contrast, complex fluid collections and air often cannot be distinguished from underlying aerated lung parenchyma by ultrasound and may require CT guidance. The real-time capability of CT fluoroscopy allows visualization of the safest approach to the fluid collection throughout the respiratory cycle, which is important in pre-procedure planning[6].

In our practice, pleural drainage is most often requested to treat parapneumonic effusions or empyema[6]. CT-fluoroscopy is used to plan the site of access to the pleural collection for optimal drainage and patient comfort. We have generally used the interrupted real-time technique because it minimizes exposure to the operator's hands. Using this technique, the needle is advanced in a stepwise manner with short applications of fluoroscopic CT to document the needle/catheter path. The radiologist stays in the CT suite and initiates CT fluoroscopy via the control panel. Either a trocar or modified Seldinger technique may be used to reach the pleural collection. Documentation of catheter placement with re-orientation, as necessary, is achieved with direct CT fluoroscopic observation. Complex, loculated fluid collections may necessitate multiple drainage catheters or intrapleural fibrinolytic therapy. Mediastinal fluid collections are drained in a manner similar to that described for pleural collections.

The technique for CT-fluoroscopic guided pneumothorax drainage is similar to that for drainage of pleural fluid collections. Smaller caliber chest tubes (8-10 French) are usually effective but a 12-14 French tube may be required for large pleural tears. CT fluoroscopy is particularly useful to guide catheter placement in complex, loculated pneumothoraces[6].

In our study of 20 patients who had a variety of pleural and mediastinal collections, we found CT-fluoroscopic assistance to be quite valuable, particularly in patients who were not compliant with breathing instructions and those with small or loculated collections[6]. The average procedure time in our case series was 32 minutes and the average CT fluoroscopic time was 143 sec.

Guidance of Transbronchial Needle Aspiration

Fiberoptic bronchoscopy with transbronchial needle aspiration (TBNA) is useful to sample mediastinal nodes and to diagnose central parenchymal lesions. Subcarinal and paratracheal lymph nodes are most accessible. One important disadvantage of TBNA as compared to surgical techniques is that the target node is not visible through the bronchoscope unless erosion of mucosa has occurred. The real-time capability of CT fluoroscopy is valuable in guiding TBNA[7]. Using CT fluoroscopy, each movement of the bronchoscope and needle can be verified quickly on the in-room monitor. CT fluoroscopy can also be used to guide TBNA for difficult lung lesions.

We have performed over 35 procedures using CT-fluoroscopic assisted TBNA, of which the first 27 have been analyzed[7]. Among the 27 procedures, 15 were performed for mediastinal nodes and 12 for lung nodules or areas of consolidation. The average lesion size was 1.9. Diagnoses included metastatic non-small cell cancer, small-cell cancer, invasive aspergillosis and pseudomonas. Overall, a correct diagnosis was obtained in 18 (75%) of 24 patients who had clinical or pathological follow-up. The mean total room time was just over one hour. The mean time from first to last use of the CT scanner was 49 minutes. The average duration of use of CT-fluoroscopy was 228 seconds. Using dose factors of 120 kVp and 30-50 mA, the approximate range of skin entrance doses for the procedures was 8-52 cGy. Malposition of the biopsy needle in the lung was easily observed on CT-fluoroscopy.

Our experience indicates that CT fluoroscopy may increase the diagnostic accuracy of inexperienced bronchoscopists by showing the precise location of the bronchoscopic needle in relation to the target lesion. By increasing confidence in needle placement, it may also encourage more experienced bronchoscopists to use a large gauge needle when necessary.

Miscellaneous Applications

The real-time guidance capability of CT-fluoroscopy may also be used for other thoracic procedures that are difficult to perform with non-fluoroscopic CT. For example, we have used CT fluoroscopy to evaluate the extent of a sinus tract in a patient with a draining cutaneous wound by observing the distribution of injected contrast in real-time. CT-fluoroscopy, because of its real-time capability, may be valuable to assess other dynamic processes such as tracheomalacia and sternal instability[4].

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Radiation Dose Considerations in Chest CT

Ernest M. Scalzetti, MD

Objectives

1. To appreciate why the radiation dose that patients receive during CT examinations is a growing concern.
2. To become acquainted with the concept of effective dose.
3. To appreciate the means at our disposal to change radiation dose.
4. To see how CT image quality is affected by dose reduction.

Computed tomography is the largest source of population exposure from diagnostic radiology in the USA. In the UK, CT scans account for ~ 4% of all diagnostic radiologic examinations but contribute ~ 40% of the total collective dose (1). In spite of this, radiation dose often is ignored in prescribing CT scanning protocols. For example, Paterson and co-workers found that adjustments to tube current were not being made in helical CT scans of children (2). Unlike in screen-film radiography, with digital radiographic systems like CT, there is no penalty for overexposure. There is only the further benefit of reduction in statistical image noise, or mottle. If radiation posed no risk for the patient, this would lead to a preference for larger doses. (3).

Radiation Dose Concepts

The concern over exposure to ionizing radiation encountered in CT arises from the stochastic processes of cancer induction and genetic effects. Exposures in CT are much too low to cause deterministic effects like epilation and erythema. In chest CT, our most appropriate concern is for cancer induction.

It is generally assumed that there is no threshold dose below which stochastic effects do not occur. It is also assumed for radiation doses in diagnostic imaging, that the likelihood of a stochastic effect increases with increasing dose.

Physical dose quantities (Gray, Rad) reflect energy implanted by the ionizing radiation. It is more useful to consider the “effective dose”, the mean dose to all of the irradiated organs and tissues, corrected for their radiosensitivity. Note that effective dose is greater in children than in adults. In fact, effective dose appears to vary continuously with patient size. (4)

Dose in Helical CT of the Chest

In single-slice helical CT, typical technique factors (120 kVp, 280 mA, 1 second scan time) result in effective doses of approximately 0.5 rem. Relative to PA and lateral chest radiographs, this dose is 2 orders of magnitude greater. “Low-dose” CT, performed by reducing tube current by 1 order of magnitude, results in a proportionate decrease in radiation dose.

Radiation doses encountered in multislice helical CT may be as much as 50% greater. (5).

Relationship between Dose and Image Quality with Changes in Tube Current

Of the image quality parameters (spatial resolution, temporal resolution and mottle), mottle is most intimately associated with radiation dose. It has been established that, above a threshold tube current (radiation dose), further increases in dose are attended by an imperceptible improvement in image mottle. (6) (7) As tube current is reduced below that threshold, there is steady decline in perceived image quality. This is the anticipated behavior of any digital radiographic or CT system, because image display has been divorced from image acquisition. In screen-film radiography one is penalized for overexposure by producing a blackened image. Overexposure in a digital system simply results in reduction of mottle and an increased radiation dose to the patient. In fact, it is not clear what the definition of overexposure is, in CT. It could be taken to mean that the patient has received a radiation dose beyond what would cause a perceptible improvement in mottle. Or it could be defined as a radiation dose that results in reduction of mottle beyond what is needed to achieve a desired level of diagnostic performance. The second definition is, of course, much more stringent.

If radiation doses are to be kept as low as reasonably achievable (ALARA), tube current should be adjusted to match the imaging task. It is well known that lung images are much more tolerant of dose reduction than mediastinal images. For lung cancer screening, S Itoh and co-workers found no loss of ability to detect 6 mm-diameter ground-glass nodules at a tube current of 20 mA. (8) An earlier study reached the same conclusion using conventional axial CT. (9)

Tube current should also be adjusted for patient size. As already noted, effective dose increases as patient size decreases (4). In fact, reduction of tube current alone may be insufficient to compensate for the increase in effective dose, in which case adjustment to kVp becomes a consideration. The relationship of kVp to radiation dose, however, is not linear, and changes in kVp also affect contrast resolution. (10)

Conclusion

There are two major issues. One is the impact of dose reduction on image quality, and the need to match the radiation dose to the imaging task. The other is the need to adjust the CT scanner's technique factors (tube current, and possibly tube potential as well) to maintain a comparable effective dose in patients of smaller size, particularly children.

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Thoracic MRI Technique and Interpretation

Philip Costello, MD, FACR, FRACR

This lecture will review the role of MRI in the evaluation of lung cancer, thoracic inlet evaluation, and mediastinal masses. Scan techniques and protocol design for specific disease processes will be discussed.

MR imaging of the thorax is used as a problem solving modality and almost always plays a secondary role to thoracic CT. MR examinations should only be performed after prior imaging studies have been reviewed so that appropriate pulse sequences, imaging planes, and section thickness are appropriately customized. The major advantages of MR include excellent soft tissue contrast, multiplanar imaging, and tissue characterization.

Significant limitations of MR in the thorax are related to physiological and cardiac motion artifacts and the inherent low proton density of normal lung limiting a detailed evaluation of pulmonary nodules and bronchial structures.

When establishing protocols there is a trade-off between the signal to noise ratio, field of view, slice thickness, and eventual spatial resolution.

Techniques to minimize physiological motion artifacts include cardiac gating, particularly when imaging the lower thorax. Phase encoding steps can be used to reduce respiratory motion artifacts or single breath-hold techniques employing fast multi-echo sequences.

T1 weighted spin echo sequences provide excellent anatomical detail of thoracic pathology. T1 weighted sequences are usually performed in the coronal and axial planes followed by T2 weighted axial images. Occasionally sagittal T2 weighted as well as coronal and sagittal T1 weighted images are employed for assessment of apical lung and peridiaphragmatic abnormalities. Gadolinium enhanced T1 weighted sequences are used in specific instances, particularly for mesothelioma evaluation, chest wall invasion, tumor recurrence versus radiation, pneumothorax, and for mediastinal mass characterization.

The differences in signal intensity of tissue depend upon their differences in proton density, T1, and T2 relaxation times. Increased water content also increases T1 and T2 relaxation times. High protein content lesions and paramagnetic substances (gadolinium or hemorrhage) decrease T1 with a variable effect on T2. Both fibrosis and connective tissue demonstrate short T2 times. As fat has high signal on both T1 and T2 weighted images, mediastinal and chest wall fat provide excellent contrast which enables differentiation of vessels, airways, and pathological processes.

Lung Cancer Evaluation

MR has an adjunctive role in the evaluation of stage III A versus stage III B disease. Mediastinal, pericardial, and chest wall invasion are better depicted on MR compared to CT. Direct chest wall invasion is much better appreciated by disruption of the thin layer of fat identified as high signal beneath the parietal pleura.

Superior sulcus tumors can particularly benefit from MRI examinations. As the brachial plexus, subclavian vessels, and bony structures can be involved by tumor growth and extension, MR is invaluable in the selection of appropriate candidates for surgical resection. A combination of coronal, sagittal, and axial images with surface coils define the anatomy of the brachial plexus. MR has an accuracy of 94% with surgical and clinical findings in comparison to CT which has an accuracy of 63% for tumor extent.

MR is useful in the evaluation of cysts with high protein fluid, as on CT these lesions may be interpreted as solid masses. T2 weighted images of such lesions have a uniform higher signal intensity than muscle, and gadolinium enhancement can demonstrate the lack of cyst enhancement. Neurogenic tumors typically have intermediate signal intensity on T1 weighted images and on T2 have high signal peripherally and low signal centrally. These tumors show marked enhancement with gadolinium, allowing accurate evaluation of intradural extension. Multiplanar imaging provides more precise longitudinal extension of tumor as well as extradural extension.

REFERENCE

MRI Clinics of North America. Vol. 8, No. 1, February 2000.

Friday

PROTOCOLS FOR THORACIC IMAGING

G. E. Signa 1.5 T (8.3v. software LX)

MEDIASTINAL MASS

	1	2	3	4	5	6
Comment				Dynamic	Dynamic	Dynamic
Coil Type	Body	Body	Body	Body	Body	Body
Pt Position					Optional	
Plane	Cor	Ax	Ax	Ax	Sag	Cor
Pulse Sequence	SSFSE	T1	SSFSE (T2)	FMPSPGR	FMPSPGR	FMPSPGR
Options		Cardiac* gated				
No Echoes	1		1			
Echo Train						
Center Frequency						
Flip Angle				75	75	75
TE1/TE2	60	Min	90	In Phase	In Phase	In Phase
TR		HR		150-220	150-220	150-220
Bandwidth				32	32	32
FOV (cm)	40	To Fit	To Fit	To Fit	To Fit	To Fit
Slice Thickness (mm)	5	5	5	5	5	5
Gap (mm)	1	1	1	1	1	1
Matrix 256X	128	192	128	128	128	128
NEX (averages)		2		1	1	1
Frequency Direction	S/I	R/L	R/L	R/L	R/L	R/L
Offset						
Gating, Breathing	Breath hold		Breath hold	Breath hold	Breath hold	Breath hold
GD-DTPA				Yes	Yes	Yes
Dynamic				Yes	Yes	Yes
No. of Slices						
Image Time						

BRACHIAL PLEXUS (Neurovascular coil-MedRad)

	1	2	3	4	5	
Comment						
Coil Type	Neck	Neck				
Pt Position						
Plane	Cor	Cor	Ax	Sag Split X2	Ax	
Pulse Sequence	SSFE	T1	FSE	T1	T1	
Options		NP/RC	NP Fat Sat	ST (R/L)	NP/RC/ST	
			FC		(S/I)	
No Echoes	1		1	1	1	
Echo Train			8			
Center Frequency						
Flip Angle						
TE1/TE2	90	Min Full	112	20	20	
TR		525	5000	400X2	500	
Bandwidth						
FOV (cm)	28	28	24	24	24	
Slice Thickness (mm)	5	5	4	5	5	
Gap (mm)	1	1	1	1	1	
Matrix 256X	192	192	192	192	192	
NEX (averages)		2	2	2	2	
Frequency Direction	S/I	S/I	R/L	S/I	R/L	
Offset						
Gating, Breathing	Yes					
GD-DTPA						
Dynamic						
No. of Slices			33		13	
Image Time	0:40	3:49	4:20	3:02	3:16	

PROTOCOLS FOR THORACIC IMAGING

G. E. Signa 1.5 T (8.3v. software LX)

CHEST MESOTHELIOMA

	1	2	3	4	5	6
Comment				Dynamic	Dynamic	Dynamic
Coil Type	Body	Body	Body	Body	Body	Body
Pt Position					Optional	
Plane	Cor	Ax	Ax	Ax	Sag	Cor
Pulse Sequence	SSFSE	T1	SSFSE (T2)	FMPSPGR	FMPSPGR	FMPSPGR
Options		RC/ST (S/I)				
No Echoes	1		1			
Echo Train						
Center Frequency						
Flip Angle				75	75	75
TE1/TE2	60	Min	90	In Phase	In Phase	In Phase
TR		HR		150-220	150-220	150-220
Bandwidth				32	32	32
FOV (cm)	40	To Fit	To Fit	To Fit	To Fit	To Fit
Slice Thickness (mm)	5	8	8	8	8	8
Gap (mm)	1	2	2	2	2	2
Matrix 256X	128	192	128	128	128	128
NEX (averages)		2		1	1	1
Frequency Direction	S/I	R/L	R/L	R/L	R/L	R/L
Offset						
Gating, Breathing	Breath hold		Breath hold	Breath hold	Breath hold	Breath hold
GD-DTPA				Yes	Yes	Yes
Dynamic				Yes	Yes	Yes
No. of Slices						
Image Time						

Abbreviations

SSFSE = Single short fast spin echo (T2)

FMPSPGR = Fast multiplanar spoiled gradient echo (with fat saturation)

RC = Respiratory compensated

Friday

MR in THORACIC IMAGING

- Lung Cancer
- Thoracic inlet / Pancoast tumors
- Mediastinal lesions
- Pleura / chest wall

MR IMAGING FOR LUNG CANCER

- Chest wall invasion
- Pleural involvement
- Mediastinal invasion
- Pericardial involvement
- Lymph nodes
- Metastases

Friday

CHEST WALL INVASION

- T1 invasion – similar intensity to tumor – Gd enhancement
- T2 high intensity
- Superior sulcus tumors
  - MR 94% accuracy
  - CT 63 % accuracy

CHEST WALL INVASION

- MRI more accurate than CT (94% vs. 63%)
- High resolution images with surface coils
- Identify effacement of the "bright" extrapleural fat line

PERICARDIAL INVASION

- Excellent delineation of the pericardium
- Differentiates adjacent tumor from pericardial invasion
- Identifies intracardial tumor

MEDIASTINAL INVASION

- T3 vs T4
- Excellent contrast between mediastinal fat, flowing blood, and tumor
- Identifies vascular encasement, compression, and invasion
- Depicts esophageal and airway involvement

METASTASES

- Adrenal mass
- MR - chemical shift
- Adenoma
  ↓ Signal on opposed phase vs in phase images

MAGNETIC RESONANCE IMAGING OF THE THORACIC INLET

- BRACHIAL PLEXUS
- SUPERIOR SULCUS OF THE LUNG
- TRACHEA
- THYROID

ANATOMY

- Formed by the union of ventral 1° divisions of C5-C8 & T1
- Upper trunk - 5^{th} & 6^{th} cervical nerves
- Middle trunk - 7^{th} cervical nerve
- Lower trunk - 8^{th} & T1 cervical nerves
- Roots (neck), trunks (supraclavicular region), cords (axilla)

SUPERIOR SULCUS TUMOR (PANCOAST)

- Bronchogenic carcinoma in extreme apex of lung
- Local invasion of surrounding structures
- Treatment – radiation ± lobectomy and chest wall resection

SUPERIOR SULCUS TUMOR (PANCOAST)

- Surgical contraindications –
  - Distant metastasis
  - Local invasion of mediastinum
  - Encasement of SCA
  - Invasion of vertebral body
  - Extensive invasion of brachial plexus

MEDIASTINAL MASSES

- Adjunct role to CT
  - Nature, location, extent
  - Cyst
  - Fat
    - Teratoma
    - Extramedullary hematopoiesis
  - Neurogenic tumors
  - Contrast allergies

MEDIASTINUM - CYSTIC LESIONS INDICATIONS FOR MRI

- Cystic content > simple serous fluid
- Posterior mediastinal lesions - meningocoeles

ANTERIOR MEDIASTINUM

- Thyroid
- Lymphatic malformations
- Hemangioma
- Thymoma
- Thymic cysts
- Germ cell tumors
- Teratoma & fat – fluid level

THYROID LESIONS

- Goiters exhibit high signal T2WT SE images
- Heterogeneity from Ca^{++}, hemorrhage
- MRI depicts relationship to airways, vessels

MEDIASTINUM - GERM CELL TUMORS

- MRI can differentiate fluid, fat, hemorrhage
- Multiplanar imaging in presurgical planning
- Cannot differentiate benign from malignant lesions

MIDDLE MEDIASTINUM

- Foregut cysts
  - Bronchogenic carcinoma
  - Esophageal duplication cyst
  - Neurenteric cysts
- Pericardial cysts

Friday

POSTERIOR MEDIASTINUM

- Neurogenic tumors - MR
  - Intraspinal extent
  - Spinal cord
  - Longitudinal spread
  - Extradural extension

SCHWANNOMA / NEUROFIBROMA

- T1 variable intensity
- T2 "target sign"
  - Bright peripherally
  - Low centrally - collagen
  - Uniform gadolinium enhancement

SYMPATHETIC GANGLIAL TUMORS

- T1 / T2 homogeneous; intermediate intensity
- Neuroblastomas
  - Invasive
  - Cystic
  - Heterogeneous

NEUROGENIC TUMORS: NEUROFIBROMA

- Target sign
- Very bright "cystic" T2 weighted images
- Mixed signal ? sarcoma

NEUROGENIC TUMORS: SCHWANNOMA

- Heterogeneous high SI on T2 weighted images

CASTLEMAN'S DISEASE

- Hyaline vascular / plasma cell
- Heterogeneous ↑ T1 signal
- Diffuse enhancement with Gd
- Flow voids – hypervascular nature

PET Scanning: Practical Applications and Pitfalls in the Thorax

Jo-Anne Shepard, MD

At the time of publication, no abstract was available.

Friday

Practical Nuclear Medicine for the Chest Radiologist

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Introduction

Radiologists are very familiar with the use of ventilation-perfusion imaging as a non-invasive screening test for pulmonary embolism. Recently, spiral CT has also been shown to be accurate in diagnosis of pulmonary embolism.[1,2,3]

The objective of this workshop is to familiarize the chest radiologist to various other radionuclide procedures available in diagnostic work up of non-thromboembolic pulmonary disorders.

Participation in this workshop will be beneficial to the general radiologists whose practice routinely involves interpretation of nuclear medicine procedures. The workshop is also intended to provide familiarity to these procedures for the academic chest radiologist who as a consultant at multidisciplinary conferences may be required to give opinion and make recommendation regarding best diagnostic work up.

Scintigraphic Localization Technique to Facilitate Operative Resections of Focal Rib Lesions

Bone scan directed biopsies are frequently performed by marking the skin corresponding to the site of increased radiopharmaceutical uptake. However, this technique is unreliable for rib biopsies since skin position may vary considerably with respiration and patient positioning on the operative table.

In this technique, a routine bone scan is obtained 2-3 hours following intravenous injection of approximately 20 mCi of Technetium 99m Methylene-diphosphonate. The lesion being localized is confirmed by increased uptake. Using a technetium point source and persistoscope image of the gamma camera, the lesion is localized superficially on the skin by a surgical marker. The skin is then prepped with betadine and topical anesthesia obtained using 2% Lidocaine. Under sterile precautions, a 25 gauge spinal needle is then used with direct pulpation to inject local anesthetic and approximately 0.1 to 0.3 cc of Methylene Blue into the rib periosteum. Chest radiographs are not routinely obtained post procedure to exclude a pneumothorax if the rib is easily palpable.

Skin marker aids in planning surgical incision and Methylene Blue in the rib periosteum allows positive intraoperative identification prior to resection. A specimen scan may be obtained to confirm the lesion has been resected. Methylene Blue also serves as a marker for histologic sectioning of the specimen.

Radiographically visible rib lesions can also be marked similarly under fluoroscopic visualization, a BB marker is placed on the skin corresponding to the rib lesion. Methylene Blue is then injected into the rib periosteum using the same technique.

Quantitative Pulmonary Perfusion Imaging

Quantitative pulmonary perfusion imaging (QPPI) is most frequently performed as preoperative or preradiation therapy evaluation in patients with lung cancer to predict post therapy FEV1.[4,5] QPPI is also used in preoperative assessment of patient prior to lung transplantation and lung volume reduction surgery for emphysema.[6]

In evaluation of lung cancer patients, QPPI is primarily beneficial for patients who have borderline pulmonary function tests. The post therapy function is predicted by multiplying the preoperative FEV1 by the percent relative perfusion of the lung that is expected to remain post operatively. The predicted post operative FEV1 of at least 800 ml/min is desired for patient to tolerate early weaning extubation following surgery.

QPPI can be easily performed with a standard gamma camera which are now readily available in all nuclear medicine departments. The exam is digitally acquired on either 128x128x8 or 256x256x8 matrix and quantitative analysis is performed by drawing region of interests over both lungs.

Although quantitative ventilation is often simultaneously performed, it is less reliable.

Inflammatory Diseases of the Lung

Gallium scintigraphy of the lung is beneficial in early evaluation of opportunistic pulmonary infections in immuno-compromised patients. Approximately two-thirds of AIDS patients manifest initially with P. carinii pneumonia.[7] Gallium scintigraphy has high severity for P. carinii pneumonia but application is limited due to low specificity. Gallium imaging is most useful in patients in whom there is a high clinical index of suspicion, in spite of negative chest radiograph. A negative gallium scan is reliable and should prompt further work-up for etiologies other than PCP.

Gallium scanning is used to evaluate activity for variety of interstitial inflammatory lung disorders. The exact mechanism for uptake is not known, but Gallium is demonstrated to accumulate in association with macrophages. The intensity and distribution of uptake is useful in characterizing the interstitial process and also acts as a marker of activity. In addition to assessing disease activity, Gallium scanning is helpful for monitoring progression and response to therapy particularly in patients with pulmonary sarcoidosis.[8]

Gallium imaging has been demonstrated to be a sensitive test for amiodarone related pulmonary toxicity.[9] Amiodarone is a commonly used antiarrhythmic agent that can result in drug hypersensitivity in up to 10% of patients. Due to significant mortality associated with this side effect, early and reliable diagnosis may be confirmed with Gallium scintigraphy, particularly since radiographic manifestations are non-specific.

Aerosol scanning is also used to depict increased capillary membrane permeability in active pulmonary inflammatory conditions. This application has limited usefulness since quantitative measurement of clearance rate of aerosol from lungs is hastened in smokers.

Pulmonary Tumor Imaging

Gallium 67 scanning is beneficial for staging of lymphomas at time of diagnosis. Double dose, delayed imaging protocols with SPECT imaging are routinely used to follow response to chemotherapy.[10,11] Gallium activity is helpful in distinguishing persistent disease from residual scar tissue and is complementary to CT scanning.

Somatostatin scanning has recently become available and may aid in diagnosis of pulmonary carcinoid tumor.

Positron-emission tomography (PET) is used to image glucose metabolism and is promising in a wide range of pulmonary oncologic applications.[12] Role of PET for evaluation of solitary pulmonary nodule and in staging of lung carcinoma will be demonstrated with clinical examples.

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