Nuclear imaging in pulmonary medicine

14/1/11

- Nuclear medicine as a branch of medicine is relatively young

- Involves the administration of radiopharmaceuticals into the body and measuring the radioactive decay of these compunds by various instruments, which is then converted into digital images

- Different from conventional radiology in that there is no external radiation which is passed through the body

- Commonly used nuclear medicine techniques in pulmonary medicine include ventilation-perfusion scanning(V/Q scan) and positron emissision tomography – CT fusion(PET-CT)

PET-CT

- PET (positron emission tomography) is the fastest growing imaging technique worldwide
- It was first started in the 1970s
- PET-CT fusion was put into clinical practice in 1998
- Images the uptake and distribution of radiolabelled glucose in the body
- PET alone is a functional imaging technique while the addition of CT to it makes PET-CT both a functional and structural imaging technique

Basic principles

PET is based on two principles:

1. The widespread distribution of 18 fluoro-2-deoxy-D-glucose (FDG) which is a glucose analogue and is taken up in almost every cell in the body

   – Within the cell the FDG is phosphorylated and is trapped → allowing it to be effectively measured by PET

   – FDG has a half life of 110 min

2. The radioactive decay of the positron rich fluoride

Unstable isotopes(18 F) undergo radioactive nuclear decay

↓

Emission of positrons (positively charged particles with the same mass as electrons)

↓

Positrons travel through the surrounding tissues and are annihilated by collision with a corresponding electron

↓

Leads to creation of two 511 keV photons travelling in opposite directions; called as coincidence annihillation

↓

Thousands of these annihilations are measured by the PET scanner

↓

Scintillation detector absorbs photons and converts them into optical light; Photomultiplier tube converts this into digital signals

↓

Recorded on a computer

- PET images obtained are fused with CT images
- Rationale
  1. Precise localisation of lesions discovered on PET within an antomical reference frame
  2. CT data allows for correction for photon emission by the human body
  3. Use of CT acquisition data makes PET 25 – 30 % faster than PET alone
  4. Also results in more efficient use of the radiopharmaceutical

  CT adds specificity to PET

Standardized uptake value (SUV) – is used to quantify FDG uptake

$$SUV = \frac{\text{Tissue activity concentration}}{\text{Injected activity/Patient mass}}$$

Use in clinical pulmonary medicine

1. Mediastinal lesions
2. Lung pathology

Mediastinal lesions

- CECT has a major role in characterising mediastinal pathology
- PET-CT can provide additional diagnostic information
- Main role is for staging and follow up of malignant mediastinal tumours
- PET/CT with unenhanced CT is unable to help distinguish contiguity of tumor and mediastinum from the direct invasion of the walls of mediastinal structures

Malignant lesions show increased uptake On PET as compared to benign lesions
However, overlap may still occur

CT may help in further narrowing the diagnosis

Lung Pathology

1. Solitary pulmonary nodules(SPN)

- PET-CT is more accurate and specific than CT alone for characterizing SPNs

- Useful in SPN > 8mm

- In a patient with low clinical probability of malignancy, a negative PET-CT has a high negative predictive value

- Low – intermediate risk lesions which are metabolically inactive can be followed up radiologically

- Positive PET-CT in clinically low probability states requires biopsy for confirmation as some benign disorders also show uptake

- In patients with high clinical probability of malignancy direct biopsy is useful

- SUV > 2.5 is highly suspicious of malignancy

- False negatives
  - Well differentiated adenoCA
  - Carcinoid tumours
  - Bronchoalveolar carcinoma

2. Staging of non small cell lung cancer

- PET-CT is emerging as a standard pre operative assessment tool
- More sensitive than CT for staging and for differentiating malignancy from benign lung lesions such as post-obstructive atelectasis
- Also more sensitive and accurate in identifying metastasis
- May provide additional information in 40% of cases

3. Follow up of treated lung cancer

- PET-CT is useful in following up patients treated with surgery/radiotherapy, especially in presence of distorted anatomy because of treatment
- Differentiates post treatment fibrosis and scarring from recurrent disease

4. Radiation therapy planning

- Treatment changes as a result of using PET-CT
  - Prevention of inappropriate radiation therapy
  - Change in intent – curative vs palliative
  - Change in radiation dose
  - Change in radiation volume
- Use of PET-CT in radiation planning resulted in a 15 – 60% increase or decrease in treatment volumes

5. Assessment of response to therapy

- PET-CT helps in detecting an early response to therapy
- PERCIST criteria:
  - PET-CT is performed 6 – 8 wks after chemotherapy and 8 – 12 wks after radiotherapy
  - Complete disappearance of metabolic uptake → Complete metabolic response
  - Reduction of > 30% in SUV → partial metabolic response
  - Reduction in SUV of < 30% → stable disease
  - Appearance of new FDG avid lesions or increase in SUV > 30% → progressive disease

Ventilation – perfusion scan

- Normally functioning lung demonstrates homogeneous patterns of ventilation and perfusion

- The pathologic conditions affecting ventilation and perfusion may be divided into four functional categories:

1. **Vascular occlusive state**
   - Ventilation is preserved in presence of perfusion defects → V/Q mismatch
   - PTE, pulmonary vasculitis, extrinsic compression of vessels

2. Consolidative state

- Two components
    1. Alveolar collapse and atelectasis
    2. Leakage of fluid into airspace secondary to capillary damgae
- Will show matched V/Q defects
- Infections, inflammatory disorders, pulmonary infarction, atelectasis

3. Obstructive state

- Airway obstruction occurs from either narrowing and/or closure of small airways or loss of structural support, excessive bronchial secretions, bronchial spasm, mucosal edema, or foreign bodies

- Decrease in alveolar P_{O_2} → constriction in precapillary arterioles →redistribution of blood to better ventilated alveoli

- Matched V/Q defects

- Asthma, COPD, bronchiectasis

4. Restrictive state

- Hyperventilation may occur secondary to increased ventilatory drive

- Might lead to increased ventilation relative to perfusion → V/Q mismatch

Techniques

❑ all images are taken by either gamma camera or SPECT

A. Ventilation scan

- Performed using either radiolabelled gas or radiolabelled aerosol

- Always performed prior to perfusion scan because the photon energy of Xe133 is less than Tc99m used for perfusion study

- Materials used
  - Xenon 133
  - Xenon 127
  - Krypton 81m
  - 99m Tc DTPA aerosols
    - Technegas
    - Pertechnegas

- Patients breathes into a face mask or mouthpiece with nose clipped

- Images are taken at various times after administration of Xe 133 (or other isotope)
  1. First breath/ breath hold – after deep inspiration and breath holding
  2. Equilibrium – after normal tidal breathing for at least 4 min
  3. Washout images – taken as the radioisotope is vented to the atmosphere

- Abnormalities on the breath-hold and equilibrium images are areas of decreased 133 Xe accumulation
- Abnormalities on the washout phase are determined by asymmetry of the washout images
- Focal areas of retained activity represent regional air trapping

- Radiolabelled aerosols (99m Tc DTPA) are also used ; they are administerd as a nebulised solution → easy to administer and better patient cooperation

- May lead to deposition of radioactive isotopes in the central airways

- Newer agents (technegas and pertechnegas) are ultrafine aerosols which are less prone to deposition

2. Perfusion scan

- Intravenous injection of radiolabelled pharmaceutical
- Distributed according to regional blood flow

- Tracers used
  - 99m Tc MAA (macro aggregated albumin)
  - 99m Tc Human serum albumin
- Approximately 5mCi is injected
- Particles block the the precapillary arterioles – only 0.1% are blocked

- Eight views are obtained → anterior, posterior, left and right posterior and anterior obliques, and right and left lateral

Use in various pulmonary disorders

1. **Pulmonary thromboembolism (PTE)**
   - Approximate prevalence in patients referred for VQ scan is 33%
   - Diagnostic criteria for PTE were proposed in a study published in JAMA in 1990 as the PIOPED (Prospective Investigation Of Pulmonary Embolism Diagnosis) criteria

   - **PIOPED II study** → large multicenter study evaluating the accuracy of multidetector CTA in patients with suspected acute pulmonary embolism
   - computed tomographic venography (CTV) and a validated clinical assessment (the Wells score) were also evaluated

- the sensitivity was 83% and the specificity was 96% for CT angiography

- In a follow up analysis the sensitivity and specificity of V/Q scanning was studied
- High probability for pulmonary embolism → PTE present
- Normal or very low probability → PTE absent
- Low or intermediate probability → non diagnostic of PTE

- The sensitivity of PTE present scan finding was 78%
- The specificity of PTE absent scan finding was 98%

Categorization of defects

- Small : < 25% of average pulmonary segment
- Moderate : 25 to 75% of segment
- Large : >75% of segment.

Diagnostic criteria (PIOPED II)

1. High probability
2. Intermediate probability
3. Low probability
4. Very low probability
5. Normal

HIGH PROBABILITY

- \> 2 large defects with no abnormalities in ventilation or x-ray or defects in ventilation and x-ray smaller than Qdefect

- \> 2 moderate + 1 large m ismatched Q defects.

- \> 4 moderate mismatched Q defects.

INTERMEDIATE PROBABILITY

- 1 moderate
- 1 large or 2 moderate
- 1 large and 1 moderate
- 3 moderate mismatched Q defects
- Triple match in lower lobe
- Multiple perfusion defects with associated x-ray opacities.

LOW PROBABILITY

- A single matched V/Q defect
- More than three small segmental lesions
- Moderate-sized pleural effusion (greater than costophrenic angle but less than one third of pleural cavity with no other perfusion defect in either lung)
- Marked heterogeneous perfusion

VERY LOW PROBABILITY

- Q defects smaller than x-ray lesion
- 1-3 small perfusion defects
- Non segmental lesion (prominent lesion, cardiomegaly, elevated diaphragm)
- Stripe sign
- Pleural effusion at least $1/3^{rd}$ of the pleural cavity with no other defect in either lung.
- Triple match in middle or upper zone.

NORMAL

- No perfusion defect. Perfusion scan must outline the shape of the lungs seen on chest radiograph, which could be abnormal (e.g., scoliosis).

- The **typical finding of PTE** → large, wedge-shaped, peripheral perfusion defects in areas that have normal ventilation and that are normal on plain radiographs

- The larger the number of these defects, the more likely the patient has pulmonary embolism

PE MIMICS

- Chronic PE
- Other causes of embolism (septic,drug abuse, fat)
- Bronchogenic carcinoma
- Mediastinal or hilar adenopathy (with obstruction of pulmonary artery)
- Hypoplasia or aplasia of pulmonary artery
- Vasculitis

CHRONIC PTE

- Defects persisting for more than 3 m are likely to remain unresolved
- Most frequent cause for false positive interpretation in case of acute PE
- CTEPH is a entity where recurrent PE leads to development of pulmonary hypertension and dilatation of right sided chambers
- VQ scan shows multiple segmental mismatched perfusion defects indistinguishable from high probability scans in acute PE.
- The combination of plain radiography suggesting pulmonary hypertension and VQ scan with multiple perfusion defects is diagnostic of CTEPH

PISAPED CRITERIA

- Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis (PISAPED)

- Combines clinical probability, CXR and Q scan data

- Q scans classified as
  1. Normal
  2. Near-normal
  3. Abnormal compatible with PE (PE+: single or multiple wedge-shaped Q defects)
  4. Abnormal not compatible with PE (PE+: Q defects other than wedge-shaped

- Definitive diagnosis was established in 84% of patients

- Sensitivity → 92%
- Specificity → 87%

- PE+ with 'very likely' clinical presentation → 99% PPV
- PE+ with 'possible' clinical presentation → 92% PPV
- PE- with 'unlikely' clinical presentation → 97% NPV

Current role of V/Q scan

- Useful in
  1. Renal failure
  2. Contrast allergy
  3. Obesity
  4. Females – use of CT angiography has been linked to increased risk of breast cancer; the radiation exposure from a V/Q scan is 5% of that of a CT angiogram
  5. Claustrophobia

2. Assessment prior to lung resection

- FEV1 > 2 l or > 60% of predicted value → pneumonectomy
- FEV1 > 1.5 l or > 40% of predicted value → lobectomy

- Regional quantitation of ventilation and perfusion are obtained preoperatively.
- Percentage contribution of the region to be resected is subtracted from the total lung function.
- The preoperative FEV_1 multiplied by the percentage of lung remaining after resection gives the predicted post operative FEV_1.

3. Emphysema

- V/Q scans used to evaluate ventilation before and after lung volume reduction surgery

4. Hepatopulmonary syndrome

- Used to quantify shunt

5. Inflammatory lung diseases

- Lung epithelial permeability is evaluated by studying the clearance of inhaled Tc 99m DTPA aerosol from the lungs
- Normal clearance rules out inflammation in the lung (50 – 80 min)
- Rapid clearance is seen in
  - ARDS
  - Hyaline membrane disease
  - IPF
  - Sarcoidosis
  - Inhalational lung injury
  - Active smokers

Take home message

1. PET-CT is finding increasing use in staging of NSCLC, in post operative and post RT follow up, in recurrent lung cancer and in evaluation of solitary and multiple pulmonary nodules.

2. False negative results can occur with well differentiated adenocarcinoma, carcinoid tumours and bronchoalveolar carcinomas.

3. Overlap of benign with malignant disorders can occur.

4. V/Q scans have a role in females, renal failure and contrast allergy.

5. Use of new criteria and techniques reduces the number of indeterminate results.