**Ventilation-Perfusion Scintigraphy:**

Trinary Versus Probabilistic Interpretation and SPECT Versus Planar Imaging

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SCIENTIFIC PROGRAM

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**Is CTA always the method of choice for diagnosing PE?**

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**CT – An increasing source of radiation exposure**

- 60 million CT exams done in 2002
- BEIR VII says 10 mSv associated with a lifetime risk of 1 in 1000 for developing a solid CA or leukemia.
- If CT gives a dose of 10 mSv or more, that is 60,000 new cancers
- They estimate this could be the cause of 1.5% to 2% of US cancer cases


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**Exposure is expressed in mGy [aka RADs].**

10 mGy = 1 RAD

Absorbed dose is expressed in mSv [aka REMs]

10 mSv = 1 REM.

At the energies of the gammas we are talking about there is no difference, i.e 1 mGy = 1 mSv.
Soaring use of CT worries physicians

- From the BOSTON GLOBE  11-26-2007.
- CT usage is soaring -- 63 million in 2005, up 43 million from 1995
- Dr. D. Bor, Chief of Med. at Cambrige Health Alliance, sends memo to 150 docs, “do not over use CT – e.g. automatic CT to dx kidney stones, consider ultrasound.
- There is particular concern in pts. getting multiple CT scans
- Note this is from the lay press.

Soaring use of CT worries physicians

Alternative strategies to CT*

- BEIR VII says low dose is less then 100 mSv
- BEIR VII recent study of Japanese A-bomb survivors in lowest dose group have increased incidence of cancer. The mean whole body exposure is 29 mSv equiv., the mean organ equiv dose is 34 mSv. There is no safe threshold.
- Leukemia, thyroid, and breast most common Ca.
- Latency 10-20 years for breast.
- And, 100 mSv causes Cancer in 1 in 100.

Radiation Exposure of V/Q Scintigraphy vs. MDCTA

The bottom line is that the radiation exposure to the breasts of women in the child bearing age group from MDCTA is somewhere between 65-250 times greater than that from V/Q scintigraphy. Most quotes are in the 70-100 X range.

Additionally, the estimated radiation exposure from a standard 2 view mammogram is associated with 3-4.4 mSv which makes the MDCTA radiation dose approximately 10-20 times greater.

Why Diagnosis of PE is Critically Important? The Answer from the 1970s:


Total PE Incidence 630,000

Survival > 1 hr 563,000 (89%)

Death in 1 hr 67,000 (11%)

Diagnosis missed 400,000 (71%)

Diagnosis made, treatment started 163,000 (29%)
V/Q Lung Scintigraphy for PE

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Diagnosis of PE

- Challenge in daily clinical practice
  - Clinical signs and symptoms lack sensitivity and specificity
  - No simple, non-invasive, accurate, widely available, single diagnostic test
- Important not to misdiagnose patients with suspected VTE
  - False-negative: high mortality of untreated PE
  - False-positive: duration and risks of anticoagulant therapy
- As a result
  - Low threshold for clinical suspicion
  - Low proportion of patients with confirmed VTE

What’s the Main Diagnostic Challenge in the 21st Century Western (US) Medical Practice?

Is the Low Prevalence the Western Medicine’s Problem?

Clinical Probability
Clinical Decision Rules

Why?

Leadership

Because they can … and we did nothing to object, prevent or reverse it.

If you like to object effectively, drop me an email at Mark.Tulchinsky@gmail.com

Wells’ score for PE

- History of DVT or PE
- History of immobilization or surgery (<4 weeks)
- Cancer
- An alternative diagnosis is less likely
- Hemoptysis
- Unilateral leg pain
- Low O2; intermediate 2-4; high: ≥ 5

Likely ≤ 4; likely > 4

Revised Geneva score

- Age + 65 years
- History of DVT or PE
- Surgery or fracture (<1 month)
- Cancer
- Unilateral leg pain
- Hemoptysis
- Heart rate > 94
- 75 - 94 mins
- ≥ 95 mins
- Pain at calf palpation and swelling

 unlikely ≤ 4; likely > 4
V/Q Lung Scintigraphy for PE

**D-Dimer**

- **D-Dimer**
  - Fibrin degradation products
  - Measured through a simple, cheap, fast, blood test
  - Highly sensitive to the presence of a blood clot
    - Positive in almost all patients with DVT or PE
    - Low likelihood of VTE if negative
  - Not specific
    - Positive in many other conditions than VTE (infection, surgery, cancer, pregnancy, elderly, etc.)
    - If positive, doesn’t mean that there is an active clot

**Diagnostic Tests for PE**

- Gold-standard test for PE: pulmonary angiography ()
  - Invasive (mortality related to the test 1%)
  - Expensive
- Risk of thromboembolic event following a negative pulmonary angiography ≈ 2%
  - Used to validate diagnostic strategies
  - A diagnostic strategy is considered to safely exclude the diagnosis if the 3-month risk of recurrent VTE doesn’t exceed 3%

**V/Q (Ventilation/Quotient) Imaging**

- Classic PE would have no perfusion
- Classic PE should have normal ventilation
- Classic PE mostly happens in textbooks
- PE may occur in a previously diseased lung – CXR opacities - poorly ventilated and/or perfused – CTPA should be favored, but if no opacities – V/Q should be favored
- PE may cause hypoxic bronchospasm, decreasing local ventilation
- PE may cause hemorrhage, decreasing local ventilation (Hampton’s hump)

**Ventilation Agents**

- 133Xenon gas
- 127Xenon gas
- 81mKrypton gas
- 99mTc DTPA aerosol
- 99mTc Technegas (not available in USA)

**Advantages of Xenon Gas**

- Offers “Single breath” image, equilibrium image and washout phases of ventilation
- Washout identifies areas of air trapping in obstructive airway conditions.
- Washout is the most sensitive part of the test for airway disease
- 3 minutes is the minimum of re-breathing at equilibrium to produce diagnostic washout study
V/Q Lung Scintigraphy for PE

- S.B. EQ.
- Wash-out
- RT LAT POST
- LT LAT LAO
- RPO LPO
- ANT RAO

"Re-Vent" with Xe-133
- Tc on Tc RT LAT
- Tc on Xe
- Xe on Xe
- S.B. EQ.

Xe-133 in COPD

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Perfusion in COPD

VENTILATION AGENTS

Xenon-133

CHARACTERISTIC

- Energy (keV): 81
- Pulmonary Radiation Dose: High (8)
- Spatial Resolution: Poor
- Sensitivity for COPD: Excellent
- Portability: None
- Disposal: Trap + Neg Pressure
- Cost: Low

Disadvantages of Xenon Gas

- Poor energy for imaging, significant internal attenuation (Xe-133)
- Requires significant patient cooperation
- Adds significant dead space and resistance to breathing
- Requires a low pressure room and trapping system
- Cannot be done on ventilator patients
- Long half life when room is contaminated. Xenon sits in a layer on the floor

Disadvantages of Xenon Gas (continued)

- Not always available on call
- Not portable
- Hypoxic patient may have to breathe room air for several minutes
- Can only obtain single projection first breath images, however, can be repeated in desired view ("re-vent")

VENTILATION AGENTS

Tc-99m DTPA Aerosol

CHARACTERISTIC

- Energy (keV): 140
- Pulmonary Radiation Dose: Low
- Spatial Resolution: Good
- Sensitivity for COPD: Good
- Portability: Good
- Disposal: Easy
- Cost: Low

Advantages of Aerosols

- Patient is maintained on high flow oxygen throughout the study
- No resistance to breathing
- Minimal dead space
- No patient cooperation required
  - Works with tidal breathing
  - Easily inserted in line with a respirator. Allows ventilation of a respirator dependent patient without contaminating the respirator
- No gas trapping equipment required
- Does not require a negative pressure room
V/Q Lung Scintigraphy for PE

Contraindications and Warnings: Perfusion Lung Imaging

- Contraindication
  - Severe Pulmonary Artery Hypertension (which in our facility means systolic PA pressure > 69 mm Hg)
  - Allergy to albumin products

- Warnings
  - Known Right to Left Shunt
  - Pregnancy

Right to Left Shunt – This is What It Looks Like

Shunt % = \( \frac{\text{Total body cts-lung cts}}{\text{Total body cts}} \times 100 \)

Advantages of Aerosols (Continued)

- Portable, can actually be taken to the ward
- Always available
- Competitively priced
- Able to obtain ventilation images in the same projections as perfusion images for direct comparison
- Fewer studies failed
- The patient is not ventilated during the images. Ventilation is complete prior to imaging in most cases.

Disadvantages of Aerosols

- Not a true gas, provides only first breath equivalent images
- No equilibrium or washout phases

Note: Use of Tc-99m-DTPA for Ventilation studies is “off-label” use!

VENTILATION AGENTS ⁸¹ᵐKrypton

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>⁸¹ᵐKrypton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (keV)</td>
<td>176 &amp; 192</td>
</tr>
<tr>
<td>Pulmonary Radiation Dose</td>
<td>Low</td>
</tr>
<tr>
<td>Spatial Resolution</td>
<td>Good</td>
</tr>
<tr>
<td>Sensitivity for COPD</td>
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<td>Disposal</td>
<td>Easy</td>
</tr>
<tr>
<td>Cost</td>
<td>High</td>
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</tbody>
</table>

Advantages of ⁸¹ᵐKrypton Gas

- Short half life (13 s.) permits re-imaging the patient almost immediately
- The energy level would permit post perfusion ventilation
- First breath equivalent images can be obtained in the same projections as perfusion images
- Because of short half life there are no contamination problems
Disadvantages of $^{81m}$Krypton Gas

- Relatively Expensive
- Short half life rubidium generator (4.5 hours)
- Images must be obtained while patient is being ventilated
- Limited availability, patients must be scheduled in advance. No availability for after hours studies.

VENTILATION AGENTS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>$^{127}$Xenon</th>
</tr>
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<tbody>
<tr>
<td>Energy (keV)</td>
<td>203</td>
</tr>
<tr>
<td>Pulmonary Radiation Dose</td>
<td>Moderate</td>
</tr>
<tr>
<td>Spatial Resolution</td>
<td>Fair</td>
</tr>
<tr>
<td>Sensitivity for COPD</td>
<td>Excellent</td>
</tr>
<tr>
<td>Portability</td>
<td>None</td>
</tr>
<tr>
<td>Disposal</td>
<td>Trap, Pressure</td>
</tr>
<tr>
<td>Cost</td>
<td>Moderate</td>
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</tbody>
</table>

VENTILATION TECHNIQUE (PSU/HMC)

- $^{99m}$Tc DTPA Aerosol
- 30-50 mCi in Nebulizer
- 0.8 to 1 mCi to patient
- LEAP or LEHR Collimator
- Patient supine with back to camera
- Aerosolize until 100 K/60 seconds
- Imaging Matrix 256 x 256 W
- Eight Views: Anterior, then every 45°
- If count rate below 50 K/min, re-aerosolize

Perfusion Technique (PSU/HMC)

- $^{99m}$Tc MAA, 6 mCi
- Approximately 250-500 K particles
- >90% of particles 10-90 micron range (Mean, 20-40 micron)
- Approximately 0.1% to 0.2% of Pulmonary capillary bed is embolized
- Inject supine
- Do Not draw blood back into syringe
- Image for 1 minute (minimum) or longer if 1000K counts are not achieved in 1 minute

Causes of Perfusion Defects on Lung Scans

- Pulmonary Embolus
- Bulla or Cyst
- Localized Hypoxia (Asthma, Bronchitis)
- Surgery
- Pleural Effusion
- Tumor
- Metastasis
- Hilar Adenopathy

Causes of Perfusion Defects on Lung Scans

- Pulmonary artery atresia/hypoplasia
- Fibrosing Mediastinitis
- Radiation Therapy
- Pneumonia
- Pulmonary Edema
- Atelectasis
- Pleural Fibrosis
- Vasculitis
Perfusion Technique (Cont.) (PSU/HMC)

- Imaging Matrix 256 x 256 W
- Eight View Study: Anterior, then every 45° (Posterior, both Laterals, all four Oblique views)
- Must override ventilation counts at least 5 or 6 to one (preferably more)
- Must reduce particle load to 120K (not radioactivity) in presence of pulmonary hypertension (<70 mm Hg, systolic)

Defect Sizing Rules

- Small (subsegmental): <25% of an anatomic segment
- Moderate: ≥ 25% but <75% of a segment
- Large: ≥ 75% of a segment (Arithmetic equivalent: 2 moderate = 1 large)
- Nonsegmental: rounded or irregular defect which is not wedge shaped and does not correspond to an anatomic segment. Such a defect expected to cross segmental boundaries

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“Matching” Rules

- Perfusion defect can be compared to either CXR or ventilation study
- Perfusion defect substantially larger than ventilation abnormality or CXR density is considered “mismatched”
- Equal or greater ventilation or CXR abnormality compared to perfusion defect constitutes "matched"

Segmental Lung Schema

- Upper Lobe: Apical, Posterior, Anterior
- Lower Lobe: Superior, Posterior Basal, Lateral Basal, Anterior Basal
- Middle Lobe (right): Lateral, Medial
- Lingula (left): Superior, Inferior

72 y/o male with prior PE on treatment

What’s Wrong with this Picture?
Where is the Tc-99m-MAA Dose? “The Needle-in-Haystack Problem”

Images of The Injection Site: “The Needle-in-Haystack Problem”

The residual activity in the syringe was about 500 µCi. But ... the needle was discarded before the post calibration assay.

The needle was retrieved and activity in it was 5.5 mCi. What happened is Tc-99m-MAA clumped and stuck/wedged in the needle of syringe. The clumped Tc-99m-MAA is porous; hence, it allows the liquid to go through it.

Repeat Perfusion Scan Following 6 mCi Tc-99m-MAA Injection

SPECT-CT

Normal V/Q

- Perfusion image is exactly the shape of the lungs as seen on chest X-ray
- No perfusion defects

Very Low Probability V/Q

- ≤ 3 small perfusion defects with normal chest X-ray
- Perfusion defects that are explained by anatomical variants, such as decreased activity over the prominent aortic arch, or in the enlarged cardiac impression, etc.
V/Q Lung Scintigraphy for PE

Low Probability Lung Scan (Revised PIOPED)
- Nonsegmental perfusion defects, regardless of number, ventilation, or chest X-ray findings
- Perfusion defect substantially smaller than CXR density, regardless of ventilation
- Any number of small (subsegmental) perfusion defects, normal chest X-ray
- V/Q matches, provided CXR is unremarkable and some lung has normal perfusion

High Probability Lung Scan (Revised PIOPED)
- ≥ 2 large V/Q mismatches or the arithmetic equivalent in moderate or large and moderate

Indeterminate Lung Scan (Revised PIOPED)
- Single V/Q match
- Anything not covered by low or high probability categories (< 2 segmental mismatches)
- Single moderate and up to 1.5 large equivalents in mismatched perfusion defects with normal chest X-Ray.
- Any collection of matched defects with abnormal enough perfusion that the study would be high probability if ventilation were normal.

Probabilistic Vs. Trinary Interpretation of V/Q Scan

<table>
<thead>
<tr>
<th>Probabilistic, Such as PIOPED</th>
<th>Trinary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal, very low</td>
<td>Negative for PE</td>
</tr>
<tr>
<td>High (includes single large MM)</td>
<td>Positive for PE</td>
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<tr>
<td>Indeterminate/Intermediate</td>
<td>Inconclusive Test</td>
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Confusing for clinicians Clear for clinicians

V/Q Lung Scintigraphy for PE

**Practical PE Algorithm**

- **Basics:**
  - As compared to PECT, V/Q scan radiation exposure is 4 times less overall, 100 times less to the breast, but 10 times more to the fetus.
  - V/Q is often inconclusive in patients with abnormal CXR, but they do not degrade accuracy of CTPA.
- **Practical Algorithm:**
  - CXR normal or minimally abnormal = V/Q
  - CXR is abnormal = CTPA
  - Females, V/Q will have much less breast exposure.
  - Pregnant females = CTPA, if contrast allergy do low dose Q only NO “V” (tracer ends up in the bladder).
  - Abnormal renal function or contrast allergy = V/Q.

**Current diagnostic strategies – V/Q**

- **Clinical probability**
  - Wells’ score
  - Abbreviations: Neg. = negative, US = ultrasound

- **Current diagnostic strategies – V/Q**
  - Clinical probability
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**Screening for V/Q**

- Does the patient have CXR in past 24 hrs?
- Are there major opacities?
- Does the patient have pulmonary hypertension (history, CXR, ECG, ECHO)?
- Does the patient have R-to-L shunt?
- Is the patient pregnant or potentially pregnant?

**Current diagnostic strategies – V/Q**

- Positive DD or high clinical probability: CUS (93)
- Negative V/Q scan (27)
- Negative, V/Q (49) No PE
- Positive (54) PE
- Low, Clin prob (14)
- Intermediate, Clin prob (7)
- High, Clin prob (46)
- Normal, 35
- Interim, Clin prob (21)
- High, Clin prob (54)
- Positive US (54)
- CUS (93) PE (17)

**Current diagnostic strategies – V/Q**

- Clinical probability
  - Wells’ score

- **Likely**
  - V/Q
  - Normal, Inconclusive, High prob

- **Unlikely**
  - D-Dimer
  - Negative, Positive

- **No PE**
  - US
  - Negative, Positive

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  - Negative, Positive
Pregnancy and V/Q

- A threshold dose of 50 mGy is required for induction of deterministic effects, none of the potential hazards such as fetal death, malformation or mental retardation are a specific risk with the low exposures of ionizing radiation used in diagnostic imaging.

Case of Shortness of Breath

CLINICAL HISTORY: The patient was admitted with complaints of shortness of breath. There is a significant A-a gradient, respiratory alkalosis and hypoxia. Evaluate for pulmonary embolism.

Estimated fetal and maternal radiation doses from different techniques using in the investigation of suspected pulmonary embolic disease in pregnancy:

<table>
<thead>
<tr>
<th>Type of investigation</th>
<th>Estimated radiation dose (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal</td>
<td>Maternal</td>
</tr>
<tr>
<td>Ventilation scintigraphy</td>
<td>0.2-0.6</td>
</tr>
<tr>
<td>Single-section</td>
<td>0.060</td>
</tr>
<tr>
<td>Multi-section</td>
<td>0.37-0.36</td>
</tr>
<tr>
<td>CT thorax</td>
<td>0.01-0.02</td>
</tr>
<tr>
<td>CT angiography</td>
<td>5.3</td>
</tr>
<tr>
<td>Pulmonary angiography</td>
<td>At least 0.5</td>
</tr>
</tbody>
</table>

Fetal doses may be underestimated (figures represent estimated anterior doses).
Causes of Unilateral Decreased Perfusion

- Pulmonary Agenesis or stenosis
- Swyer James Syndrome
- Saddle Embolus
- Pneumothorax
- Large Effusions
- Mediastinal Fibrosis (Histoplasmosis)
- Tumor

Caveat

- A single large perfusion defect consisting of several contiguous segments (with either normal or abnormal ventilation) has a significant likelihood of being due to hilar tumor.

Congestive Heart Failure

- Enlarged Cardiac Defect (obliterating lingula)
- Fissure Sign (effusion in fissures)
- Rounded Posterior Gutters or Basilar Defects (effusion in posterior gutters)
- Redistribution of Flow to Upper Lobes
- Patchy “Checker Board” perfusion (interstitial edema)
- Focal Non-segmental Defects (alveolar edema)

Shortness of Breath

- Patient with known CHF now complains of worsened shortness of breath.
**Diffuse Abnormality on CXR**

- More than 75% of patients with diffuse opacity consistent with pulmonary edema have normal or near-normal perfusion on V/Q

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**Asthmatic Patient with Increasing Shortness of Breath**

**CLINICAL HISTORY:** History of asthma and increasing shortness of breath for the past three days. PO2 on room air of 32 with PO2 in the 90's on 02 by nasal cannula. Evaluate for pulmonary embolism.

**CXR:** There is a focus of decreased aeration in the right middle lobe which may represent an infectious infiltrate versus a focal area of atelectasis. A more linear horizontal opacity in the left upper lobe likely represents atelectasis. The left hemidiaphragm is elevated.
Planar V/Q Limitations

- Overlap of segments
- Difficult to estimate defect size
- Cannot visualize deep structures
  - Medial basal segment of RLL
- Significant inter-observer variability

Increased use of CTPA over V/Q is mostly responsible for higher PE detection. Additional PE that CTPA detected DID NOT reduce PE-associated deaths! Therefore, additional PE detected by CTPA was NOT clinically consequential.


Like CT is Superior to CXR, SPECT is Superior to Planar V/Q

SPECT of computerised model of PE

- Phantom study
  - Developed from CT, cadaveric lung
  - 18 segmental defects, 47 subsegmental defects

- Results
  - Sensitivity: planar 77% SPECT 97%
  - Accuracy of defect size: planar 51% SPECT 97%
LUNG SPECT

83 patients

Technegas 485MBq
Tc99m MAA 265MBq

Ventilation Perfusion
Kx8cm Simultaneously (15mins)
Tc99m MAA 150MBq

Sensitivity 76% 87%
Specificity 68% 91%
Accuracy 81% 94%

Raisans et al., JNM, 2004, vol. 56, 1591-1598

Large Defect Detected on Both
Small Detected Only on SPECT

Defects Detected on SPECT (TP)
Planar was Negative

Equal Quality When Airspace is Normal
Technegas Better DTPA in COPD

Inter/intraobserver variability

114 patients

Intraobserver reproducibility
Interobserver reproducibility
Specificity

Planar 91% 79% 78%
SPECT 94% 88% 96%

Collect, NM Comm, 2002

Intermediate probability

- Modified PIOPED criteria
  - Low 82%, Intermediate 4%, high 14%
  - (PIOPED: 39% Intermediate)

- RNSH 4%
- Copenhagen (Guttm) 5%

Colbhus, NM Comm, 1997 (Freeno)
V/Q Lung Scintigraphy for PE

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SPECT - literature

- Limited but consistent
  - Improved sensitivity (Stieg, Amerio, Meguid, et al)
    - 81-100%
  - Increased specificity (Koerner, Ada, Coelho, et al)
    - 81-85%
  - Decreases the number of intermediate results (Rosenstiel, Chabbert)
    - >5%
  - Very high NPV (Laibov, Am J Med Com press, 1997)
    - 98.5%
  - Reduces the inter-observer variability (Stieg, Coelho, Graf)
    - ~5%

SPECT Showed More Defects

- 7 Perfusion Defects

PICTURE

Reporting Criteria

- Positive for PE
  - More than 1 large segmental or > 2 moderate subsegments mismatches that are distributed in a vascular pattern
- Negative for PE
  - Normal perfusion
  - Matched defects
  - Non-segmental defects
- Non-diagnostic (“Indeterminate”)

Royal North Shore Hospital
(Sydney, Australia)

RNSH 3D lung atlas

Ant Post RPO RAO
V/Q Lung Scintigraphy for PE

Acquisition + processing requirements

- What is required?
  - Camera – multhead
    - 6-12 mins
  - Computing
    - OSEM
  - Counts
    - Ventilation
      - 30-50MBq DTPA or Technegas
    - Perfusion
      - 100-220MBq Tc99m MAA
      - 20mins, 1.2-2mSv

1. New methods of display
   e.g. V/Q Quotient

2. Positive (very!) Study

3. Image fusion
   combine SPECT + CTPA

Central Pulmonary Emboli

Possible filling defect
- poor contrast enhancement

Mark Tulchinsky, MD, FACNM
Planar V/Q result is better understood by clinicians when Trinary criteria used.
CTPA finds more thrombi, but additional findings are not clinically relevant.
SPECT V/Q finds more thrombi and easier to interpret than planar, but the advantage may not be clinically relevant.

Selective use of SPECT V/Q in challenging planar findings recommended.