2015 VQ Scans: SPECT and SPECT/CT

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DISCLOSURE STATEMENT

I have no relevant financial relationships with commercial interests to disclose.
Learning Objectives

1. Understand the probability vs outcome-based interpretation schemes for VQ scans.

2. Compare the rationale for VQ planar, SPECT and Q-SPECT/CT.
Pre-test
What is an advantage of the PISAPED approach over the PIOPED criteria?

A. Increased specificity
B. Increased accuracy
C. Decreased sensitivity
D. Decreased non-diagnostic
• What is the recommended ventilation agent for VQ SPECT?

A. $^{133}$ Xenon
B. $^{99m}$Tc DTPA
C. Technegas
D. $^{81m}$ Krypton
• Compared to planar imaging, VQ SPECT has decreased

A. Sensitivity
B. Specificity
C. Positive predictive value
D. Inter-observer variability
What interpretation criteria is recommended for VQ SPECT CT?

A. Modified PIOPED II
B. PISA-PED
C. EANM (European Association of NM)
D. No established criteria
What is the major concern that controversies over the solitary sub-segmental clot has raised?

A. Decreased treatment
B. Decreased detection
C. Increased accuracy
D. Increased diagnosis
2015 VQ Scans: SPECT and SPECT CT
Format

1. Review interpretation schemes
   - PIOPED, PISAPED

2. Probability vs outcome reporting
   - Outcome reporting concerns

3. Planar vs SPECT vs SPECT CT
   - VQ SPECT issues in US

4. The small clot dilemma
Venous Thromboembolism

• DVT
• PE

• PE Issues:
  1) Interpretation criteria
  2) VQ SPECT
PE

- PE: life-threatening; 70% fatal PE undiagnosed before death

- > 90% PE have DVT

- 30-50% DVT will have PE
PE

- US estimate: > 650,000/yr; > 50,000 die

- UnRx PE: 18 - 38% die*

- Rx PE:
  - 25% die w/in 1 yr (co-morbid factors)
  - now: 2 - 10% die from PE
  - 1% chronic PE (pulmonary HTN)

* If unstable, 58% die
PE

• 90% multiple, > 85% bilateral
• lower > upper lobes

• Normal perfusion = negates anticoagulation, good prognosis

• abnormal VQ does NOT make the diagnosis
Scan Interpretation Criteria
Basic Principle

• Why diagnose PE? Pt survived.

• **Treat and prevent the potentially fatal PE**

• PE recurrence
  – Untreated: 25%
  – Treated: 8%
Interpretation Schemes

• US: PIOPED I & II, mod PIOPED I (probabilities)
  – survey 15/18 acad sites*; 1 hybrid

• Europe/Canada/Australia: modified PIOPED II (Q scan/CXR) and PISAPED (outcomes)

* 2013: PE present, PE absent & few non-dx; 2/18 sites
PIOPED I (1990)

- Multi-site prospective (> 900)
- S/S of VQ scan
- VQ & pulm angio c/w clinical outcomes
- Dev categ & criteria for prob of acute PE, later modified (1993)*
- Prevalence: 33% (68% inpt)

* Mod PIOPED I: One segmental MM (low → intermed)
PIOPED I: Major Problems

1. Only 28% definitive diagnosis
   • 72% inconclusive, 44% intermediate

2. Low probability had unacceptable high frequency of PE

3. High probability had a low sensitivity (41%)
PIOPED II (2006)

- Multi-site prospective (> 800)
- Assess efficacy of CTA-CTV in acute PE & evaluate “very low prob” VQ
- Composite reference: VQ, CTA, CTV/USN, DSA
- S/S: 83%/96%; NPV 95%, PPV 86%
- Prevalence: 23% (11% inpt)

* PPV and NPV are useful when considering the clinical value of a test. They are dependent on the prevalence of the disease in the population of interest.
CTA

- 1990’s to 2000’s déc # VQ scans
  - high # of “non-diagnostic” VQ
  - inc # CTA in PE

- 2015: CTA procedure of choice in PE: reported PE +/-PE -
  - propose VQ “outcomes” report like CT
Modified PIOPED II

• 2 versions:
  – VQ & CXR
  – Q scan & CXR

• Reporting:
  – VQ: High, nondx, very low, normal
  – Q: PE present, PE absent, nondx
Modified PIOPED II

• VQ
  • **High**: 2 or > VQ MM
  • **V Low**: nonseg, Q<CXR, triple M-mid/upper, 1-3 small, 2 or > M w/o CXR, stripe sign, lg effusion
  • **Normal**: no defects
  • **NonDx**: All others

• Q scan
  • **PE(+)**: 2 or > Q/CXR MM
  • **PE(-)**: nonseg, Q<CXR, 1 match mid/upper, 1-3 small, “stripe sign”, one large effusion
  • **NonDx**: All others
Very Low Probability (<10%)

- Non-segmental defect
- Q < CXR abnormality
- 1-3 small segmental defects
- 1 triple match (V:Q:CXR) mid to upper lung
- “Stripe sign”
- Solitary large effusion
- >= 2 VQ match w/ normal CXR
Mod PIOPED II

• 2008 Sostman *
• Retrospective analysis of PIOPED II pts using VQ scans
• 74% classified as PE+/PE-

PISAPED* (1995)

- Clinical prob + CXR + Q scan
  - 176 pt; prevalence 35%; 1° inpt
  - Clinical assessment must be good

- PE present, PE absent, non-Dx
  - 37/176 PE+; 69/176 abnormal
  - S/S: 89%/92%; PPV 95%; NPV 81%; accuracy 90%

* Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis
PISAPED

- **PE present:** >= 1 wedged shaped Q defect (shape is important)
- **PE absent:** non-wedged shaped Q defect
  - Contour defect by enlarged heart, mediastinum or diaphragm; near normal or normal Q
- **Non-diagnostic:** Cannot classify as PE+ or PE-

* 2011 SNMMI Practice Guideline For Lung Scintigraphy
PISAPED Critique

1. ¼ abn but PE(-): no angio or F/U
2. ½ abn: no angio (contraindications)
3. PE(+): not all had angio
4. No angios on normal/near normal
5. Same reviewer for clinical assessment & scan interpretation (clinical bias)
2008 Comparative Trial*

- Mod PD II (Q/CXR) vs PISAPED
- 2/2 readers; prevalence: 19% (19/889)
- Nondx: mod PD II 21%; PISAPED 0%
- If exclude nondx, S/S
  - mod PD II: 85%/93% (omit 21% nondx)
  - PISA: 80%/97%
- PISAPED = Mod PD II (Q only) & PD II, but less non-Dx studies

2011 SNMMI Practice Guideline for Lung Scintigraphic
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<thead>
<tr>
<th>Interpretation Schemes*</th>
<th>PIOPED I</th>
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Gottschalk

• “A very low probability interpretation of a VQ scan is as reliable as CTA in excluding PE when the clinical probability is low or moderate.”
38 yo male with shortness of breath.

What is the interpretation by PIOPED II, Mod PIOPED II & PISAPED?
Normal ventilation
One large segmental mismatch
One large segmental mismatch

- Mod PIOPED I & II: Intermediate
- Mod PIOPED II (V/Q): Non-diagnostic
- Mod PIOPED II (Q): Non-diagn
- PISAPED: PE present
# Imaging Acute PE*

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<th>Method</th>
<th>Sens</th>
<th>Spec</th>
<th>Non-Dx</th>
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<td>85%</td>
<td>93%</td>
<td>21-27%</td>
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<td>Mod PD II Q</td>
<td>77%</td>
<td>98%</td>
<td>No low &amp; intermed</td>
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<td>93-97%</td>
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UHS last 100 VQ scans

- 57 quantitative VQ (lung transplant)
- 43 for PE (PIOPED II)
- Definitive diagnosis: 32 (74%)
- Indeterminate: 11 (26%)
Gestalt Interpretation*

- “Experienced NM physicians may provide a more accurate interpretation than is provided by the listed criteria.”

* 2011 SNMMI Practice Guideline For Lung Scintigraphy
How should VQ scans be reported?

- Probability?
- Outcomes?
  - PE present, PE absent
PE+/PE- Reporting Concerns (US)

1) Probability reporting: understood by readers and clinicians.

2) PISAPED: small w concerning limitations
   - no large multi-site prosp trial: diverse pt pop & dis, satisf outcomes, wide range of readers
   - reproduce results; McClean* 238 pt; unable

3) Identify wedge vs non-wedge defects. Not easy.

PE+/PE- Reporting Concerns

4) Essentially a binary reporting system, highly dependent on pretest probability

- PIOPED II discordant pretest prob/report
- high prob: low pretest
  - PPV VQ 56%
  - PPV CTA 58%
- low prob: pretest low 4% risk
  intermediate 10% risk
  high 35% risk
23 yo F @ 23 wk IUP. Acute on chronic dyspnea.

Over last 2 days, CXR, USN for DVT & (-) chest CT neg. Echo: Mild RV↑, PA 50 mmHg

VQ requested. Rad resident refusing, pt w/o dyspnea now. Team unsure.
Normal ventilation
>2 large segmental VQ mismatches
Normal CXR
• High probability for acute PE
• High clinical suspicion: PPV 97%
• Discordant: PPV 56%
A *Trinary* Reporting System

- **Freeman (2011) Montefiore Medical Ctr**
- Retrosp, 6 month, 664 pt
- PE present* (High prob): 8.4%
- PE absent (normal, v low, low): 88.1%
- Non-diagnostic (intermed): 3.5%
- FN 1.14%

* One moderate defect w/ (-) CXR: high prob; PPV 86% but 100% w/ high clinical
PE+/PE- Reporting Concerns

5) Litigation

- “PE present” – NO PE and severe complication or death

- “PE absent” – NO anticoagulate, die from PE

To SPECT or NOT to SPECT

Will this help with scan interpretation?
US vs Europe/Australia/Canada

1. Ventilation agents
   - US: $^{133}\text{Xe}$, $^{99m}\text{Tc}$ DTPA*, $^{99m}\text{Tc}$ SC
   - EAC: Technegas, $^{99m}\text{Tc}$ DTPA, Krypton**

2. V scan
   - US: often
   - EAC: VQ SPECT vs Q

* Not FDA approved for ventilation studies
** $^{133}\text{Xe}$ limited availability
US vs Europe/Australia/Canada

3. Modality
   - US: planar
   - EAC: SPECT*

4. Interpretation
   - US: probabilities (PIOPED)
   - EAC: outcomes (PISAPED)

• European Assoc of NM “VQ SPECT should be the preferred modality whenever possible”
No major US advocate for SPECT

1. Planar vs SPECT vs SPECT CT
2. Ideal ventilation agent
3. SPECT interpretation
4. Will outcome change?
No major US advocate for SPECT

1. Planar vs SPECT vs SPECT CT
2. Ideal ventilation agent
3. SPECT interpretation
4. Will outcome change?
Planar vs SPECT

- No major prospective trial (SPECT vs CT)
- **Planar**: 1970s, L Freeman “VQ planar has stood the test of time”

- **SPECT**: Inc contrast resolution → inc diagnostic value; ↑ S/S, ↓ indeterminate (3%), accuracy* 94% c/w CT
  - ↑ intra-observer reproducibility**: Planar 91%; SPECT 94%
  - ↑ inter-observer**: Planar 79%; SPECT 88%

*2012 L Freeman “deals with accuracy rather than outcome”
Reinartz et al. (2004)*

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<th>SPECT</th>
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<td>93%</td>
<td>81%</td>
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SPECT: Higher sensitivity  
CT: Higher specificity  
Similar accuracy  

Reinartz et al (2004)*

<table>
<thead>
<tr>
<th></th>
<th>SPECT</th>
<th>CT</th>
<th>Planar</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>97%</td>
<td>86%</td>
<td>76%</td>
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<tr>
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SPECT: Higher sensitivity  
CT: Higher specificity  
Similar accuracy  

22 yo F h/o VSD & pulm stenosis repair with SOB.

CXR & Vent: normal 1 mod defect
Non-segmental defect: L hilum

No PE w/ SPECT vs Intermediate probability w/ planar
Planar vs SPECT*

• SPECT > Planar
  – sensitivity, specificity, accuracy, ability to localize defects (RLL medial basal)

• SPECT < Planar
  – inter-observer variability, non-diagnostic exams

* No hallmark study like PIOPED
VQ SPECT vs SPECT CT*

• Sensitivity 97% equal

• Specificity
  – SPECT 88%; SPECT CT 100%

• Non-diagnostic
  – SPECT 5%, SPECT CT 0%

<table>
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<tr>
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<th>VQ SPECT</th>
<th>VQ SPECT/CT</th>
<th>CTA</th>
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<tr>
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<tr>
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81 patients

Gutte et al* (Denmark)

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81 patients

# Radiation Exposure

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<th><strong>SPECT CT</strong></th>
<th><strong>CTPA</strong></th>
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<tr>
<td>Body</td>
<td>2.5 mSv</td>
<td>8-20 mSv</td>
</tr>
<tr>
<td>Breast</td>
<td>0.3-1 mSv</td>
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# Radiation Exposure

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No major US advocate for SPECT

1. Planar vs SPECT vs SPECT CT
2. Ideal ventilation agent
3. SPECT interpretation
4. Will outcome change?
Ventilation Agents

• VQ SPECT: needs a superior ventilation agent

• Technegas (Australia): ideal agent, ultrafine Tc-labeled carbon; not in US

• $^{99m}$Tc DTPA: “very satisfactory”

• Krypton: $$$
Which ventilation agent?

- 158 facilities surveyed
- 78/158 responded (49%)
- $^{99m}\text{Tc DTPA}$ 58%
- $^{133}\text{Xe}$ 42%
- $^{99m}\text{Tc}$ sulfur colloid (SPECT)
- $^{99m}\text{Tc}$ PYP

M Tulchinsky (Penn State) 2014 survey (2015 MWM)
Which ventilation agent?

- 158 facilities surveyed
- 78/158 responded (49%)

- $^{99m}$Tc DTPA  58%
- $^{133}$Xe  42%
- $^{99m}$Tc sulfur colloid (SPECT)
- $^{99m}$Tc PYP

M Tulchinsky (Penn State) 2014 survey (2015 MWM)
Normal VQ SPECT (SC)

Courtesy M Graham, MD. PhD U of Iowa
No major US advocate for SPECT

1. Planar vs SPECT vs SPECT CT
2. Ideal ventilation agent
3. SPECT interpretation
4. Will outcome change?
SPECT

- V/Q viewed in axial, sagittal, coronal
- Can generate **planar-like** images (2 methods)*, 20-30 min
  1) Angular summed: blurred images, harder to read than true planar
  2) Re-projected planar
- Need CXR
- False neg with non-occlusive clot

* VQ ratio, quotient images
Planar & Planar-like images

True

Angular summed

Reprojected

Note: advocating SPECT, but viewing in “planar-like” images

EANM* Recommended Reporting

1. No PE
   - Normal Q, nonseg MM, matched or reverse MM VQ defects

2. PE present
   - 1 seg VQ MM or 2 subseg VQ MM

3. Non-diagnostic for PE
   - multiple VQ abnormalities not typical for any disease

*European Association of Nuclear Medicine
** Criteria proposed but NOT validated w/ a gold standard
EANM

• 1-3% solitary subseg VQ defect is nondx, per EANM is “No PE”

• EANM* (not SPECT CT)
  - > 3000 VQ SPECT using EANM rec
  - NPV 97-99%
  - S/S 96-99% and 91-98%
  - nondx 1-3%

SPECT/SPECT CT Reporting

• Criteria for reporting is not established
• PIOPED categories based on planar imaging. Translate to SPECT/SPECT CT?
• No multi-site comparison w/ planar
• VQ SPECT ↑ specificity, ↓ false + than with only Q
• Many experts report: PE +, PE -, non-diag
Barriers to SPECT Imaging

- Familiarity with planar imaging
- Unfamiliarity with 3D lung imaging
- Need for a good ventilation agent
- How to report VQ SPECT*
- Changes in workflow
- Lack of perceived need to change

* Various criteria used to call PE(+) on SPECT
Q SPECT CT

How many have used?

Routinely?
Q SPECT CT

I recently converted for indeterminate cases with a normal CXR.
Reviewing a journal article

- Used Q SPECT CT for indeterminate CTA and VQ scans
- 49 CTA: VQ scans focused in CT area of indeterminate concern
  - 25 diagnostic (1 Q SPECT nondx)
  - 24 VQ nondx
- 182 VQ: 9 nondx
- Overall non-diagnostic: 4.9%
Reviewing a journal article

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67 yo man with dyspnea, ESLD CIN, coagulopathy.
NGT (no V)

“Stripe sign?”

LPO RPO
LLL anterior & lateral basal, superior seg
LLL superior segment
3 segmental Q defects without CT abnormality: Acute PE
3 segmental Q defects without CT abnormality: Acute PE

Which interpretation criteria?

Gestalt
Q SPECT CT

• Chest x-ray must be relatively normal

78 yo F with increasing shortness of breath.
Normal ventilation.
Indeterminate for acute PE
No major US advocate for SPECT

1. Planar vs SPECT vs SPECT CT
2. Ideal ventilation agent
3. SPECT interpretation
4. Will outcome change?
Subsegmental Emboli: the Solitary Small Clot

- Improved technology, inc PE diagnosis, but **NO change in recurrence or death**
- **Problem**: Clinical signif of a small clot
- Cath pulm angio (CPA) & planar VQ
  - long hx: CPA & planar NPV 99-100%
  - **miss small clots** (CPA, VQ, CTA)

* JAMA over diagnosis of PE. No change outcome.
What to Do with the Small Clot?
The Small Clot

- L Freeman: advocates “outcomes” over “accuracy” in diagnosing & managing PE
- “Planar is good enough” – Freeman

- More reports: the small PE does not need treatment in healthy people
- “…most such thrombi do not need to be treated & therefore do not need to be detected”
The Small Clot

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- More reports: the small PE does not need treatment in healthy people
- “…most such thrombi do not need to be treated & therefore do not need to be detected”
L Goodman (Wisconsin)*

- “Healthy patients often pass clots from the legs to the lungs, which are trapped by the lung capillary bed and lysed by intrinsic fibrinolysis protecting the systemic circulation”

- Peripheral veins do not (DVT)
- Rationale for aggressive RX for DVT

* Radiology 2005
In the Past

• PE treated: readily anticoagulate*
• A solitary small clot? Unknown (didn’t see)
• Autopsy: 51-90% old or recent PE, most not fatal
  – Healthy accident victims who died immediately: 20% with macroscopic PE
• Meta-analysis (23 studies): CTA (-)
  – 4657 pt, no Rx, 3 mo VTE 1.4%, fatal PE 0.51%
• NO studies for unRx subsegmental clot

* Solitary small clot not an issue
One 1994 study

- Nielsen (Denmark)
- RCT, 87 outpt with +DVT (venography)
- No PE symptoms, 49% occult PE
- ½ anticoagulated (44 pt); ½ anti-inflam (43 pt)
- 3 months: 19 pt each group progressed in DVT or PE
- No deaths from VTE. 1 anticoagulated pt died
- NO DIFFERENCE in RX vs NO RX

Stein* PIOPED I untreated PE

- 20/376 unRx PE (initially neg angio)
- 1 pt (5%) died from PE; 1 pt nonfatal PE
- All pt < 3 seg MM VQ defects (60% Rx pt)
  - lower clot burden
- UnRx & Rx pt grouped to size of VQ defects: no difference in outcomes

- “Mild untreated PE”- lower mortality from recurrent PE than prior overt PE

2015 MWM

• **Freeman:** Trinary reporting system
• >10,000 pt
• FN 1%
• **CT 2x > PE dx w/o change in outcome**
• > 3000 VQ and 1799 CT: PE(+)
  – VQ 6-9%
  – CT 14%
Is Treatment Justified?

- Outpt + adequate cardiopulmonary reserve + one small clot = NO treat

- Risk of RX (warfarin)

<table>
<thead>
<tr>
<th>months</th>
<th>major bleed*</th>
<th>die</th>
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</thead>
<tbody>
<tr>
<td>3</td>
<td>3%</td>
<td>0.5%</td>
</tr>
<tr>
<td>12</td>
<td>1%</td>
<td>7%</td>
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- Pt on long term Rx, 10% of major bleeds are fatal
- Fang et al Circulation 2013; 128: A12186 “1 yr mortality in warfarin-treated patients with PE was nearly 10%.” (EMR of 4 sites 2004-2010)
Anticoagulation: strongly consider

1. Inadequate cardiopulmonary reserve
2. Coexisting acute DVT
3. Recurrent small PE possibly from thrombophilia to prevent chronic PE and pulmonary hypertension
Take Home: What to do

• A small clot w/o DVT

• Need to know if the risk of fatal PE > risk of major anticoagulation complication to include death.
Final comments on Planar.... and SPECT.... and SPECT CT?
Planar vs SPECT in US

1. VQ planar: “*good enough*” withstanding the “*test of time*” – L Freeman

2. No ideal ventilation agent or reporting

3. L Freeman* on VQ SPECT
   - advantage: ease of interpreting studies
   - Same FN (VQ/SPECT/CT): same outcomes
   - Over DX & RX clinical inconsequential clot

* Freeman LM et al Semin Nucl Med 2012. 42:3-10
What about SPECT CT?

Q SPECT CT for indeterminate CTA or VQ.

CTA: indeterminate region
VQ: normal CXR
SUMMARY

• Interpretation schemes:
  – PIOPED: probabilities – clinical familiarity
  – Mod PIOPED II (Q only) & PISAPED: outcomes – no large trials

• wedge vs non-wedge shaped defects
  – can be a challenge
SUMMARY

- Binary reporting needs clinical input
- Litigation
- VQ planar: has stood the “test of time”
- VQ SPECT: no ventilation agent or reporting criteria (US)
- Q SPECT CT: indetermin CTA or VQ
- Concern for over diagnosis & treatment of the small clot: outcome over accuracy
Post-test
What is an advantage of the PISAPED approach over the PIOPED criteria?

A. Increased specificity
B. Increased accuracy
C. Decreased sensitivity
D. Decreased non-diagnostic
What is an advantage of the PISAPED approach over the PIOPED criteria?

A. Increased specificity
B. Increased accuracy
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Decreased non-diagnostic exams

- The advantages of the PISAPED approach over PIOPED are:
  
  1. Virtually eliminating the non-diagnostic exams
  2. Increased sensitivity (PIOPED I 41%; PISAPED 86%) with only a slight decrease in accuracy (PIOPED 97%; PISAPED 94%).

What is the recommended ventilation agent for VQ SPECT?

A. $^{133}$ Xenon
B. $^{99m}$Tc DTPA
C. Technegas
D. $^{81m}$ Krypton
• What is the recommended ventilation agent for VQ SPECT?

A. $^{133}$ Xenon
B. $^{99m}$Tc DTPA
C. Technegas
Technegas

- Technegas is “better than the best liquid aerosol.”
- $^{133}$Xe is a dynamic acquisition and not amendable to SPECT imaging.
- $^{99m}$Tc DTPA aerosol has deposition problems and not FDA approved.
- $^{81m}$Kr has limited access and is costly.

SAM # 3

• Compared to planar imaging, VQ SPECT has decreased

A. Sensitivity
B. Specificity
C. Positive predictive value
D. Inter-observer variability
• Compared to planar imaging, VQ SPECT has decreased
  A. Sensitivity
  B. Specificity
  C. Positive predictive value
  D. Inter-observer variability
Inter-observer variability

• VQ SPECT has both decreased intra-observer (planar 91%, SPECT 94%) and inter-observer (planar 79%, SPECT 88%) variability.

What interpretation criteria is recommended for VQ SPECT CT?

A. Modified PIOPED II
B. PISA-PED
C. EANM (European Association of NM)
D. No established criteria
What interpretation criteria is recommended for VQ SPECT CT?

A. Modified PIOPED II
B. PISA-PED
C. EANM (European Association of NM)
D. No established criteria
No established criteria

- Criteria for VQ SPECT CT has not been established.

- There are no multi-site comparative trials with planar imaging.
What is the major concern that controversies over the solitary sub-segmental clot has raised?

A. Decreased treatment
B. Decreased detection
C. Increased accuracy
D. Increased diagnosis
SAM # 5

• What is the major concern that controversies over the solitary sub-segmental clot has raised?

A. Decreased treatment
B. Decreased detection
C. Increased accuracy
D. Increased diagnosis
Increased diagnosis

• Concern is in over diagnosis and over treatment of PE.

• Since the advent of CT, there has been an increase in PE diagnosis without change in overall outcome.

• Concern has been raised over the over diagnosis of the clinically inconsequential clot.
References


Questions?