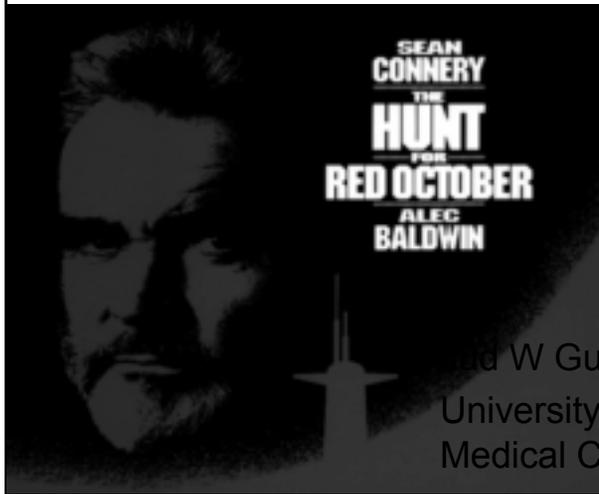


CT: Diagnosis of Pulmonary Embolism



David W Gurney MD FACR
University of Nebraska
Medical Center

The movie Hunt for Red October is about about a silent deadly submarine, a useful metaphor for the diagnosis of pulmonary embolus.

The Hunt for Red October

Find the clot!

CT finds the clot

PE is all about finding the clot. Examine the literature on PE and you'll find that the seminal papers all deal with finding the clot. In this lecture, we will review CT for diagnosing PE. CT visualizes the clot, and has rapidly emerged as an important clinical tool which will ultimately provide new insights into the natural history of this process.

Scope of Problem

3rd most common cause of death

90% survive initial embolus, but

2/3^{rds} not diagnosed

Pulmonary embolus is common and poorly diagnosed.

Common Undiagnosed Problem

Prevalence PE hospital patients	1%
Among deceased, diag unsuspected	70%
Prevalence autopsy	14%

How big is your hospital? 1% of those patients have pulmonary embolus.

Intensively studied

Medline search : pulmonary embolus

> 16,000 articles since 1966

> 1 article/day

Even though the world's literature is voluminous, I would assert that we know very little about the natural history of this disorder.

Landmark Investigations

Westermarck	1938	Roentgen diagnosis
Williams et al	1963	Angiography
Wagner	1964	Radioisotope scanning
UPET	1970	Treatment
Biello et al	1979	Probability classification
Hull et al	1983	Prospective Study
PIOPED	1990	Prospective Study
Remy-Jardin/Teigen et al	1992	CT Diagnosis

Nearly all landmark investigations deal with diagnosis.

Landmark Investigations

Westermarck	1938	Roentgen diagnosis
Williams et al	1963	Angiography
Wagner	1964	Fluoroscopic planning
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Hull et al	1980	Prospective Study
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Remy-Jardin/Teigen et al	1992	CT Diagnosis

**Treatment is known, the
difficulty in the past has
been the diagnosis**

Treatment is known and effective, the difficulty has been diagnosis.

Who's at risk

CHF
MI
Malignancy
Shock
Obesity
Pregnancy
Recent Surgery
Trauma
Bedridden

NBC correspondent
David Bloom dies
of blood clot while
covering Iraq war



This is a common list of predisposing conditions. Note that this encompasses a very large patient population.

Who's at risk

CHF

MI

Malignancy

In short, Any hospitalized patient

Obesity

Pregnancy

Recent Surgery

Trauma

Bedridden

Remember that prevalence is estimated at 1%.

Pathophysiology

Origin

Deep veins leg or pelvis

Embolization

Complete occlusion rare

Respiratory

Ventilation nonperfused lung

Hemodynamic

50% cross sectional area leads to right heart failure

Arising from the deep veins, complete occlusion is rare. Symptoms arise due to ventilation of nonperfused lung. Respiratory failure ensues when more than 50% of the capillary bed is occluded.

Problem, Who to Study?

Clinical suspicion

History & physical exam nonspecific

Silent embolism estimated in 40%

Moser Jama 1994

Clinicians have great difficulty in deciding who to test for pulmonary embolus. In fact, many patients don't have signs or symptoms.

History Not Helpful

Symptoms	PE (%)	No PE
Dyspnea	73	72
Pleuritic pain	66	59
Cough	37	36
Leg swelling	28	22
Leg pain	26	24
Hemoptysis	13	8

PIOPED Stein Chest 1991

When symptoms are present, patients are just as likely to have other diagnoses as have pulmonary embolus.

Physical Not Helpful

Signs	PE (%)	No PE
Tachypnea	70	68
Rales	51	40
Tachycardia	30	24
DVT	11	11

PIOPED Stein Chest 1991

The same is true for signs.

Often Wrong

Clinical assessment

Likelihood PE	Freq	Correct
80 - 100%	10%	68%
0 - 19	26	91
20 - 79	64	30

PIOPED Jama 1990

Clinicians are very uncertain as to who does or does not have pulmonary embolus.

Limited Help

Lab

D-dimer false negative 5-10%

Numerous lab tests have come and gone. The most recent candidate lacks the sensitivity to diagnose PE.

Not Helpful

Chest x-ray

	PE (%)	No PE
Atelectasis	68	48
Pl effusion	48	31
Elev diaph	24	19
Cardiomegaly	12	11
Pulm edema	4	13

10% Normal

PIOPED Stein Chest 1991

Chest x-ray is also unreliable, in fact 10% are normal.

Classic chest x-ray sign

	Sensitivity	Specificity	Likelihood ratio
Plump PA Fleischner sign	12%	82%	0.66
Oligemia Westermark Sign	11	92	1.75
Infarct Hamptom's Hump	22	82	1.20

PIOPED Worsley Radiology 1993

Classic chest x-ray signs are infrequent.

Not Helpful

Fleischner Sign

Notice that the likelihood ratio for the prominent pulmonary artery is less than 1.0. In Bayes theorem, this actually **decreases** the likelihood of PE. So much for this classic sign.



In fact, the Fleischner sign, the enlarged pulmonary artery due to the clot, actually decreases the probability of PE.

Problem 1: Sensitive but nonspecific

V/Q Scanning

100% sensitive

But,

Anything that will alter blood flow will cause an abnormal perfusion scan. The list of entities that interfere with blood flow is long. Pulmonary embolism does not occupy a unique position on this list.

V/Q scanning has been the traditional test for PE. The problem is not sensitivity but specificity.

Problem 2: Frequently Not Helpful

PIOPED

V/Q Classification	Freq (%)	PE	No PE
Normal	14	4	96
High Probability	13	88	12
Indeterminate/Low	73	29/12	71/88

Based on V/Q patterns, patients are classified into four categories. Unfortunately, most patients fall into the low - indeterminate category in which too much uncertainty exists.

Problem 3: Poor Agreement

Reader Agreement: V/Q

Scan Classification	Agreement
Normal	94%
High Probability	95%
Indeterminate/Low	70%

PIOPED JAMA 1990

In addition, the largest category has poor interobserver agreement.

However,

The main problem with V/Q scanning:
Don't see clot, only the secondary
effects of the clot

The main problem with V/Q scanning is that the test does not primarily visualize the clot, only the secondary effects of the clot. Historically, all tests that rely on secondary signs, such as hypotonic duodenography for pancreatic masses, have been abandoned as soon as a test modality became available that could depict the primary pathology.

Broken promises

For years, Nuc Med has promised
infarct avid agents

Alderson PO. Radiology State of the Art 164: 1987

Wellman HN. Sem Nucl Med 16: 1986

Time's up!

Nuclear medicine physicians have been unsuccessful in
developing in infarct avid agent.

It's the clot stupid

To paraphrase James Carville.

Multiple chances

Natural history embolic episode



Avg 8 emboli/episode (UPET data)

Although V/Q scanning has 100% sensitivity for embolic episode, many don't realize that the sensitivity is less for an individual clot

Sensitivity 83% completely occluding clot

Sensitivity 26% partially occluding clot, also

Angiograms have demonstrated clot in 10% normally perfused lobes,

There are multiple chances to make a diagnosis of PE in an embolic episode.

A deep venous clot fragments in the right ventricle, showering an average of 8 emboli to the lung. In older studies correlating angiograms with V/Q scans, V/Q scans were not 100% sensitive for individual emboli. The important point is that for an embolic episode there are multiple chances to make a diagnosis.

See the clot, but

Pulmonary Angiography

Invasive

Expensive

Tech expertise

Morbidity/Mortality low

Rarely done



The one traditional test that does depict the clot is pulmonary angiography. Various reasons have been given for the poor utilization, in any case this is a rarely performed test.

Problem 1: Gold?

Gold Standard or Fool's Gold

False negative rate small peripheral emboli 25%

Overall false negative rate 1-9%

Quinn AJR 1987

Pulmonary angiography is not perfect, especially for small subsegmental emboli.

Problem 2: Poor Agreement

Reader Agreement: Pulm Angio

Location	Agreement
Lobar	98%
Segmental	90%
Subsegmental	66%

PIOPED Stein circulation 1992

Similar to V/Q scans, reader agreement for subsegmental emboli is poor.

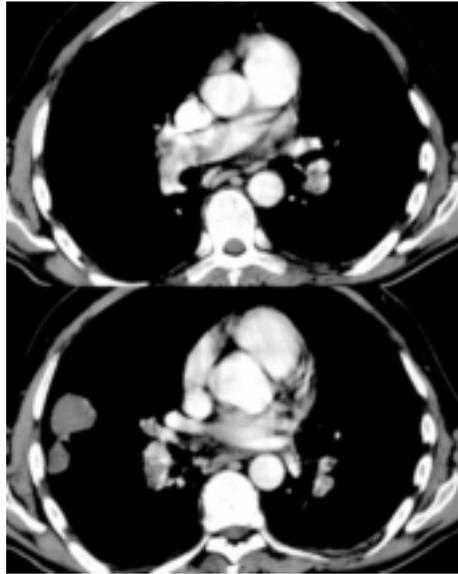
Problem 3: Frequently not done

Practice Pattern

...1982	...1995
600 suspected	650 suspected
V/Q scan	V/Q scan
434 (72%) unresolved	525 (81%) unresolved
Pulm Angio 50 (12%)	Pulm Angio 71 (14%)
Sustman AJR 1982	Henschke Chest 1995

Over the years little has changed in physician's practice patterns. Pulmonary angiography is a rarely utilized modality.

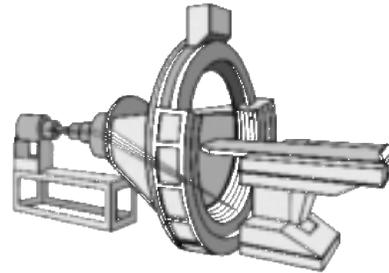
CT: The Clot!



CT pulmonary angiography is a new modality that primarily visualizes the clot

Technology Advance

Spiral or
Electron beam



Rapid acquisition

Technologic advances, either spiral CT or electron beam CT allows rapid acquisition during the contrast bolus through the pulmonary arteries.

Spiral Technique

Slice thickness 3 mm
Pitch 1.4
Reconstruction 1 mm
Delay 15-20 sec (Test bolus)
Diaphragm to Arch
Nonionic contrast: 3ml/sec
120 kV, 300 mA
FOV: width of chest

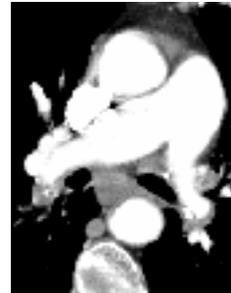


ROI should > 185 HU

The typical spiral technique utilizes thin collimation, scanning through the central pulmonary arteries. If the patients have difficult holding breath, start at the diaphragm and proceed cranially. The top most images are not as subject to respiratory motion artifact as are the basilar images. If the patient cannot hold breath, quiet breathing still results in diagnostic images in most patients.

Multislice Technique

Slice thickness 2.5 (8), 1.25 (16)
Table speed 15 mm
Reconstruction interval 1 mm
Delay 25
Entire chest
Nonionic contrast 3ml/sec
120 kV, 300 mA
FOV: width of chest
Scan time 12



ROI should > 185 HU

Multislice CT add the capability to do thinner slices and larger coverage. Timing of the contrast bolus is not as critical.

Combined venography

2% with have DVT and negative PA's
10 yrs ago - 30% of CT angio's positive
Now < 5%
Gondal dose
Not recommended

Richman J Thromb Haemost 2003

One can combine CT venography with angiography. In a multi-institutional study of 541 patients, DVT alone was found in 15%. CT, as compared to US, is as accurate as US in evaluating the deep venous system. However, over time, the rate of positive CT pulmonary angiograms has decreased as physicians have realized the inadequacy of their history and physical skills in detecting PE. As a result, the positive rate is now less than 5%. Because of the large gonadal dose with venography, I've chosen to discontinue the routine use of combined venography and pulmonary angiography.

Number emboli

Emboli/PT	Modality	Reference
8	Pulm Angio	UPET 1970
6.2	Spiral CT	Remy-Jardin 1992
6.8	Electron CT	Teigen 1993

Note the good concordance with the number of emboli detected as compared to historical studies of the number of emboli per embolic episode.

Spiral CT Results

Author	n	Entry	Sens %	Spec %
Remy-Jardin '92	42	PA	100	96
Teigen '93	86	Suspected	95	80
Goodman '94	20	Indet V/Q	64	89
Teigen '95	60	PA	71	97
Remy-Jardin '96	75	PA	91	78
Von Rossum '96	149	All	94	96
Ferretti '97	164		87	
Mayo '97	142	N US	89	98
Garg '98	26	All	66	100

Sens 88% Spec 95%

A large number of studies have been published. Entry criteria vary, from correlation with pulmonary angiography, clinical suspicion, indeterminate V/Q scans, or those with deep venous ultrasound. Combining all results, sensitivity and specificity are both high.

Reader Agreement: Spiral CT

Scan Classification	Agreement
Positive	98%
Negative	95%

Mayo Radiology 1997

In contrast to V/Q scans and pulmonary angiography, reader agreement is high for both positive and negative interpretations.

Technically Inadequate

Modality	Inadequate	Reference
Spiral CT	2%	Remy-Jardin '96
Pulmonary Angiography	3%	PIOPED '90

Most patients have diagnostic scans. The failure rate is similar to pulmonary angiography.

Subsegmental Embolus: Problem?

Sensitivity CT poor

25% had subsegmental embolus only

Goodman AJR 1995

Of some concern is the report that the sensitivity of CT is poor for subsegmental emboli.

Are subsegmental emboli important?

Lung removes small emboli

An important function of the normal lung is removal of small emboli. Lung backed-up by:

Dual blood supply

Triple oxygen supply

Exposed to entire venous circulation

One of the normal functions of the lung is to remove small emboli. The lung is ideally suited to this task. It has a large redundant capillary bed and a dual blood supply. The reservoir capacity of the venous system has the disadvantage of slow flow and tiny clots may form that are then removed by the lung.

Are subsegmental emboli important?

Do they occur normally?

In normal nonsmoking subjects

5% have subsegmental defects at V/Q
scanning

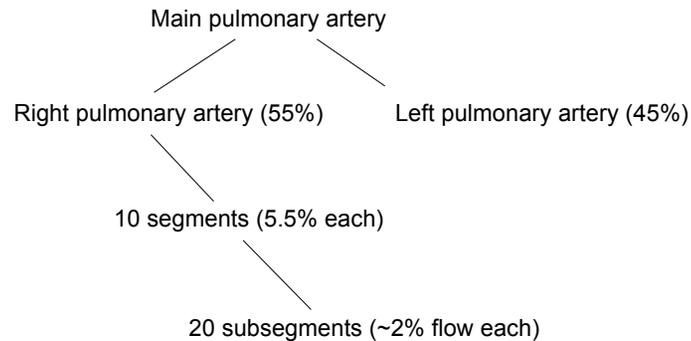
Tetalman Radiology 1973

Whether normal emboli occur is hard to document. In an older study of normal volunteers, 5% had subsegmental defects at V/Q scanning.

Are subsegmental emboli important?

Consequence of subsegmental embolus

Assume the following



What are the consequences of a single subsegmental embolus? Assuming an anatomic distribution of blood flow, and assuming a conservative 2 subsegments per segment. Each subsegment receives only 2% of the total blood flow.

Are subsegmental emboli important?

Consequence of subsegmental embolus

Is 2% a great loss?

Normal pulmonary reserve easily compensates for this loss. If missed, these clots may have little consequence.

Are subsegmental emboli important?

If Missed

Remember subsegmental emboli missed
at angio

Outcome negative pulmonary angio
Good: PIOPED 1 yr surveillance
PE in 4 (0.6%)

Stein Circ 1992

For example, certainly subsegmental emboli are missed at angiography, however the outcome of patients with normal pulmonary angiography is good.

Are subsegmental emboli important?

Subsegmental emboli frequency

PIOPED

6% had only subsegmental emboli (20/375)

In those, V/Q scan results

High Prob	1
Indeterminate	9
Low	10

Subsegmental emboli are not a common manifestation of an embolic episode. In the PIOPED study, only 6% of the patients had isolated subsegmental emboli. Note that if subsegmental emboli are important, V/Q scanning remains a poor testing modality.

Are subsegmental emboli important?

Subsegmental emboli

Therefore,

V/Q also not helpful and remember,

Angio has significant observer variability

Remember there is not a reliable test for subsegmental clots.

Are subsegmental emboli important?

Outcome Negative CT

1000 negative CT angiograms

3 month follow-up

11 (8 DVT, 3 PE)

< 1% incidence, 0.3% fatal

Swensen Mayo Clin Proc 2002

Similar to pulmonary angiography, the outcome of patients with negative CT pulmonary angiography is good.

Additional information

Alternative diagnosis

In those without PE

2/3rds additional info

Pneumonia

Cardiovascular disorders

Interstitial lung disease

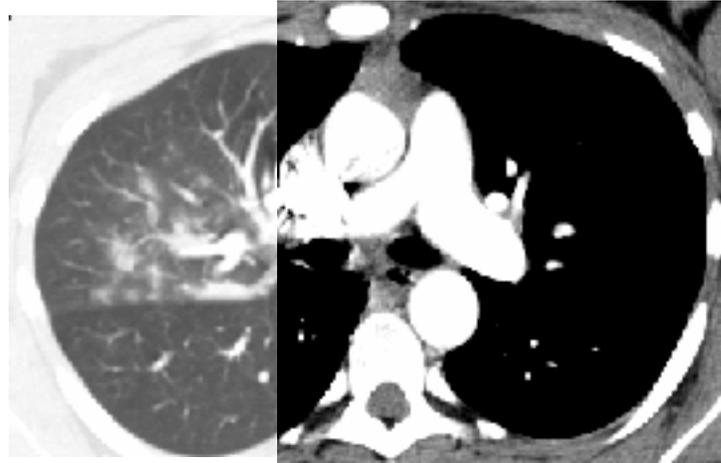
Malignancy

Pleural disease

Kim Radiology 1999

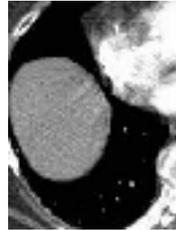
In contradistinction to V/Q scanning, CT add other information. Up to 2/3rds of patients have other diagnoses at CT which may be the cause of the patient's symptoms.

Additional information



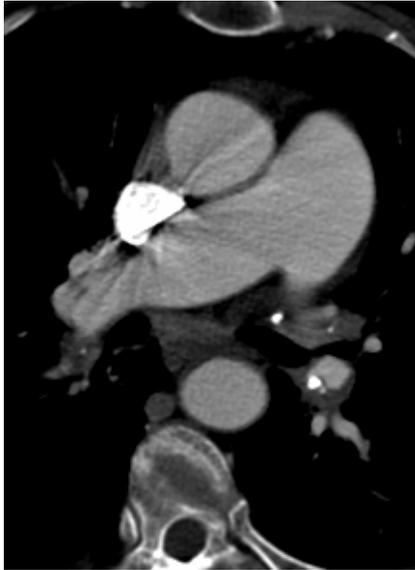
In this example, the CT angiogram was normal. Focal consolidation in the right upper lobe due to pneumonia was the cause of the symptoms.

Viewing

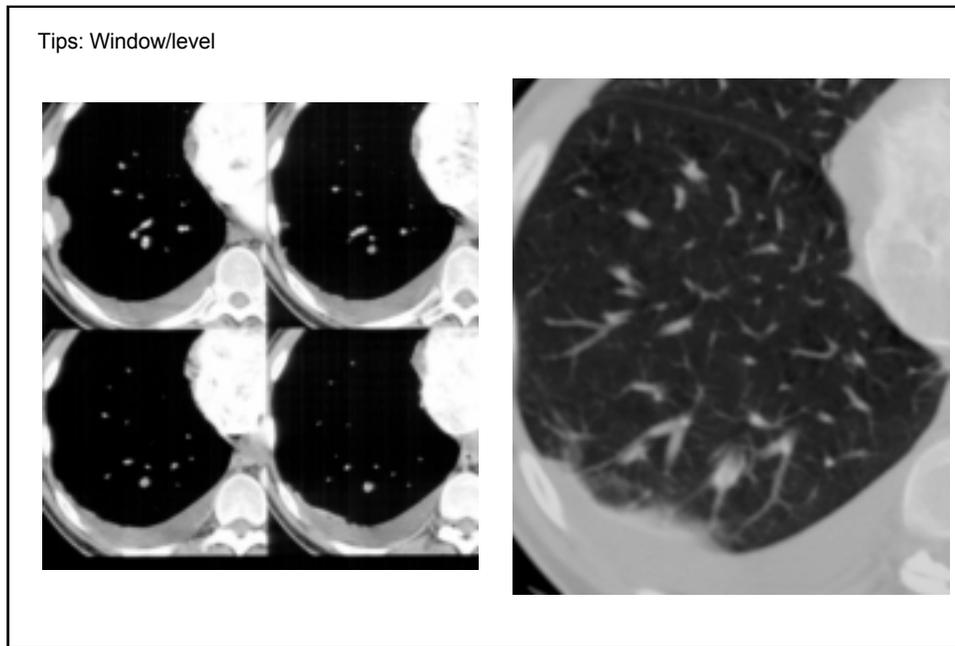


When reviewing CT angiogram studies, it is important to review the scan on a workstation and cine back and forth between sections. This greatly facilitates the visualization of small clots.

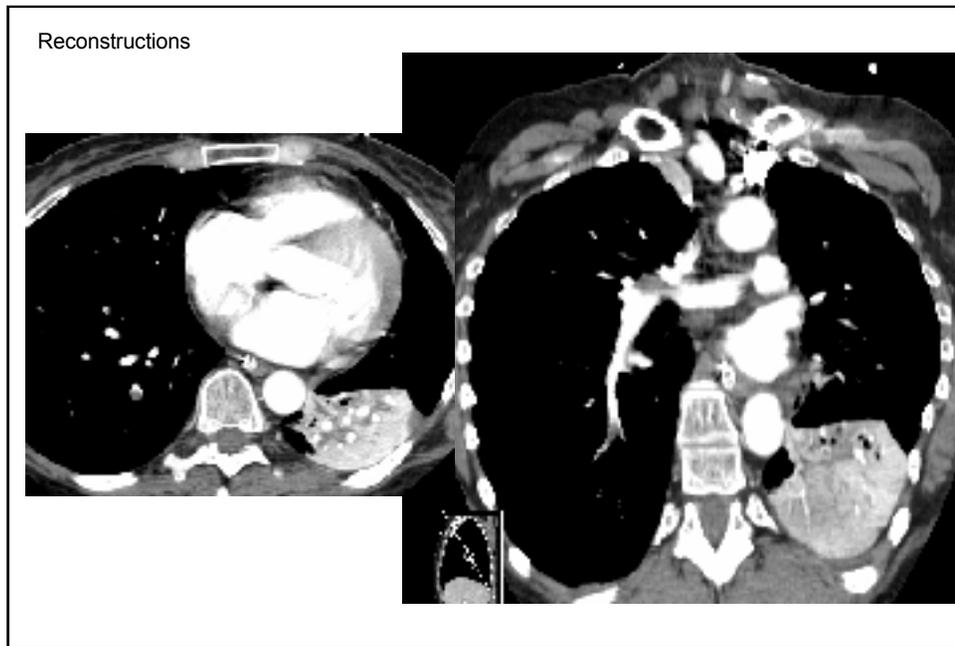
Tips: Window/level



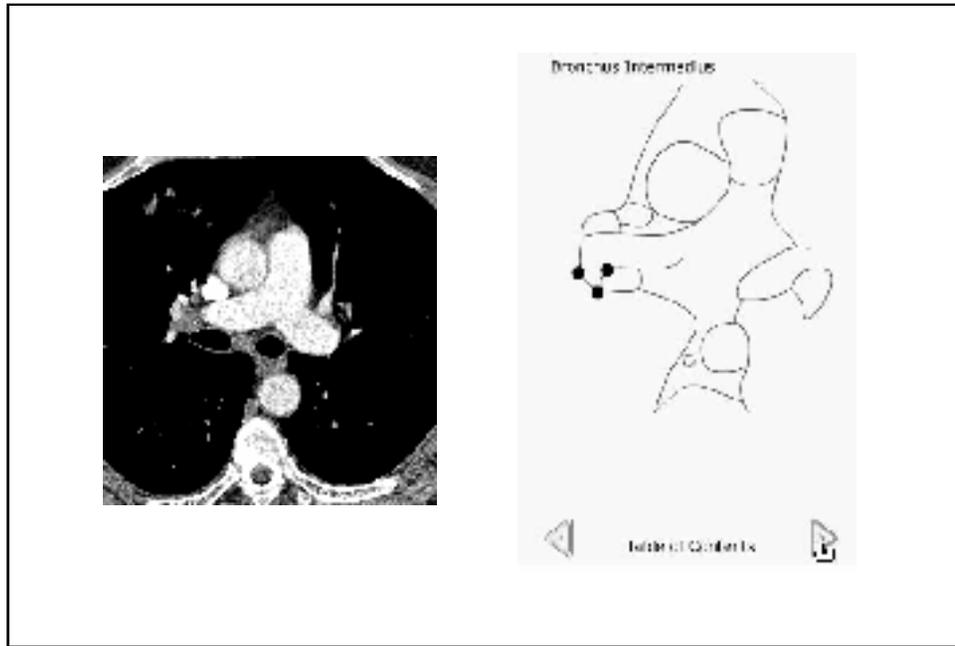
Various other window widths are also helpful. Here, the bone window better demonstrates the calcification in a chronic embolus.



Lung windows are valuable for small emboli. Here the clot is barely perceptible on the mediastinal windows but seen to better advantage on the lung windows.

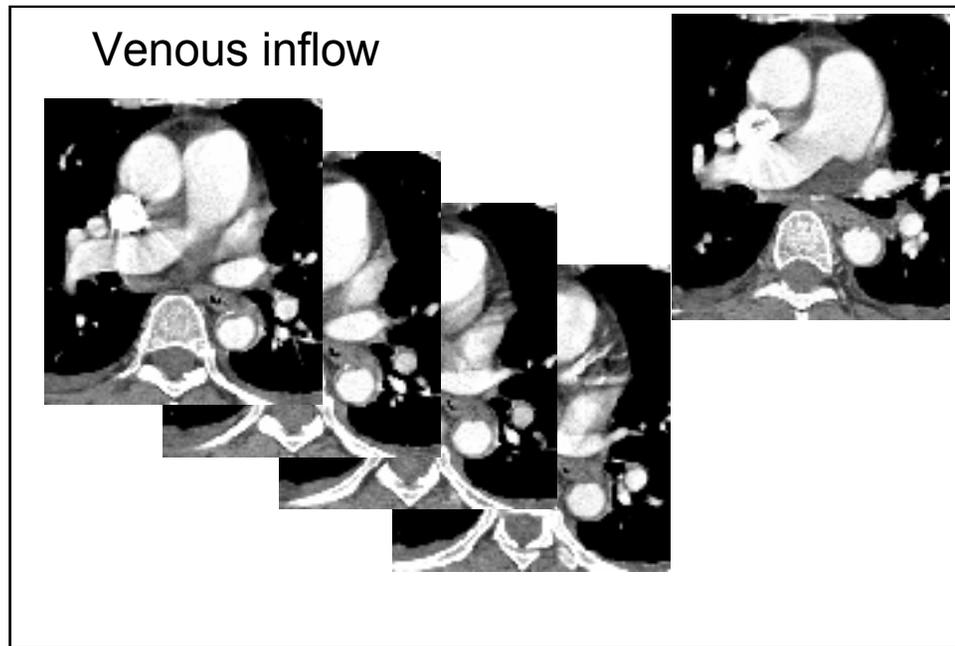


I find reconstructions less helpful, however, for oblique running arteries, particularly through the lingula or right middle lobe, reconstructions may be helpful. In this example, the subsegment embolus is seen to better advantage in an oblique coronal plane.



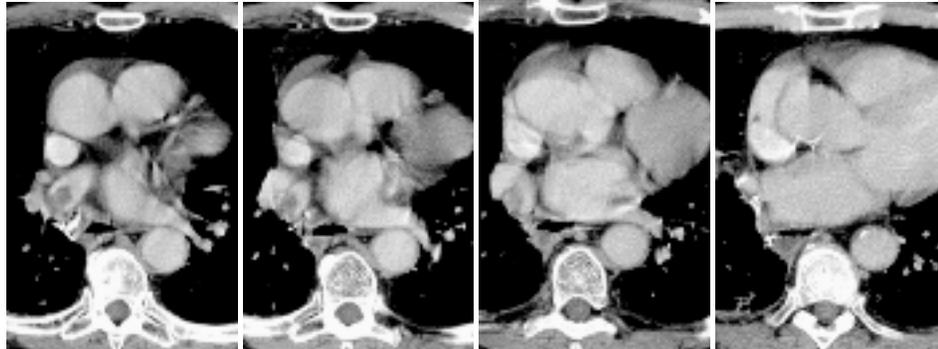
False positive clots are related to motion artifact, asymmetric filling or normal lymph nodes. It is helpful to have a handy chart showing the normal locations of lymph nodes within the hilum.





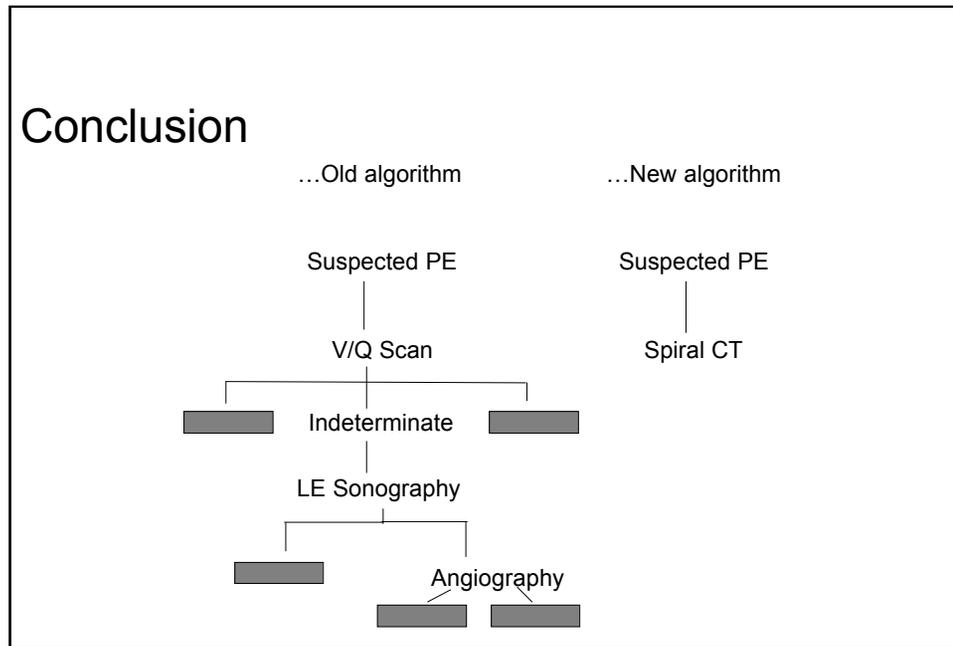
Occasionally, an unexplained drop in the concentration of contrast in the artery is mistaken for a pulmonary embolus as is seen here in the left lower lobe pulmonary artery. The decreased concentration of contrast is not as striking as that seen with pulmonary embolus and is homogenous throughout the cross section of the artery. Usually seen on only 1 or a most 2 contiguous slices, (as seen here). This is thought to be due to poor mixing of blood and contrast in the right ventricle. This is more often seen the faster the scanner, with the electron beam CT I've seen a completely unopacified main pulmonary artery surrounded by pre-and post slices with fully opacified blood. Contributing to this phenomenon is the patient valsalving rather than just holding their breath. The valsalva maneuver will decrease venous return through the SVC (contrasted blood) and increase the flow through the IVC (noncontrasted blood).

Plication defect



An unusual false positive is a plication defect due to the surgeon inverting the stump at the time of lobectomy.

Conclusion



CT angiography has emerged as a test with high sensitivity and specificity for the diagnosis of pulmonary embolus, For many it the initial and only test used for this diagnosis.