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How Nuclear Medicine Can Help Diagnose Chronic Thromboembolic Pulmonary Hypertension

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Disclosure Information

Timothy Morris, MD

- This presentation was supported financially by Bayer Pharmaceuticals.
- I have served as a consultant for Bayer.
- There are no other relevant financial relationship to disclose.
- I will not discuss the off label use and/or investigational use in my presentation:



D.T.*

- 70 yo man
- Chief complaint: dyspnea on exertion

*Identifying information was altered to comply with HIPPA requirements.



D.T. (continued)

Seven years ago (in New York)

- DVT and PE
 - Saddle embolus
 - No identified “provoking factor”
 - Rx’d “thrombolytics and heparin”
- Long term Rx with warfarin



D.T. (continued)

Two years ago (after a flight to Russia)

- DVT “recurrence”
 - CUS = “clot” in right femoral vein
 - Rx’d enoxaparin



D.T. (continued)

Last year (in Florida)

- Chest pain
 - Large “saddle embolus”
 - “extensive thrombus in the left pulmonary artery and the right pulmonary artery”
 - Rx’d tPA and heparin
 - Discharged on enoxaparin



D.T. (continued)

Three months ago

- Continued, progressive dyspnea on exertion
- Referred to UCSD Medical Center



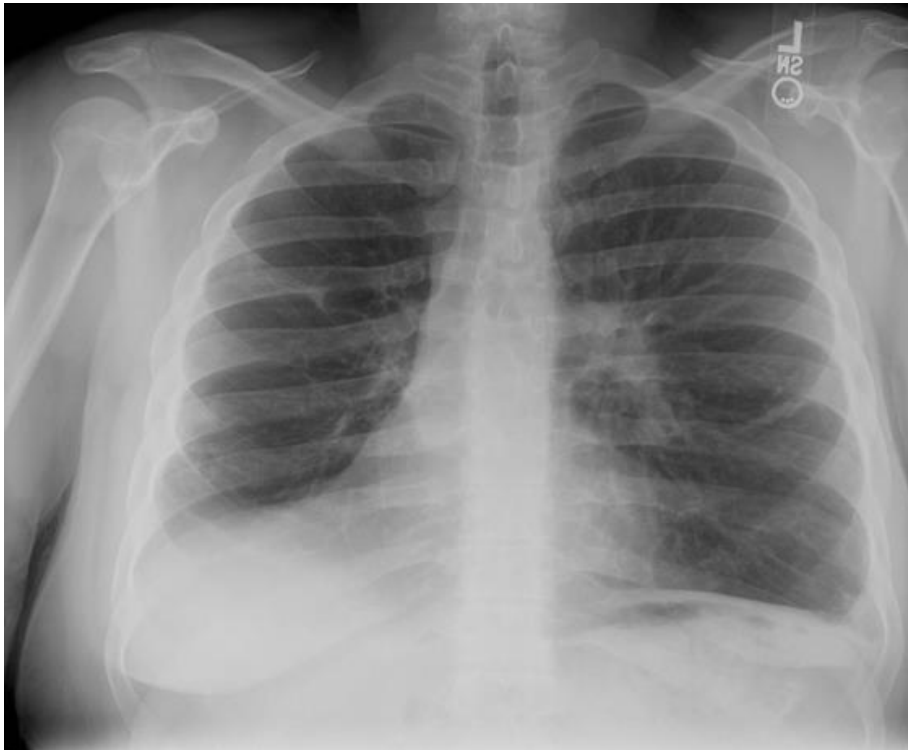
Evaluation at UCSD

- BP 90/64 HR 84 RR 16
- Well developed man
- Lungs clear
- Heart RRR
- Loud P2
- Pleural rub (right side)





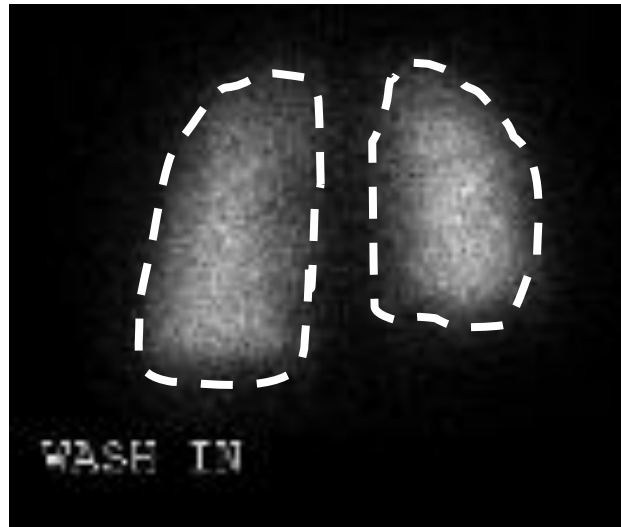
CXR



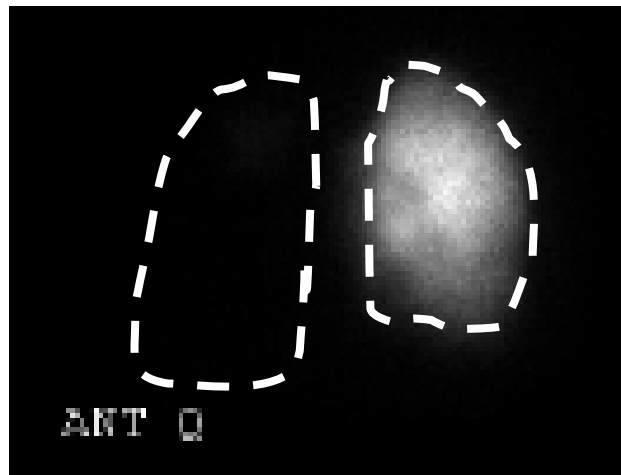


V/Q scan

Anterior
Ventilation Scan

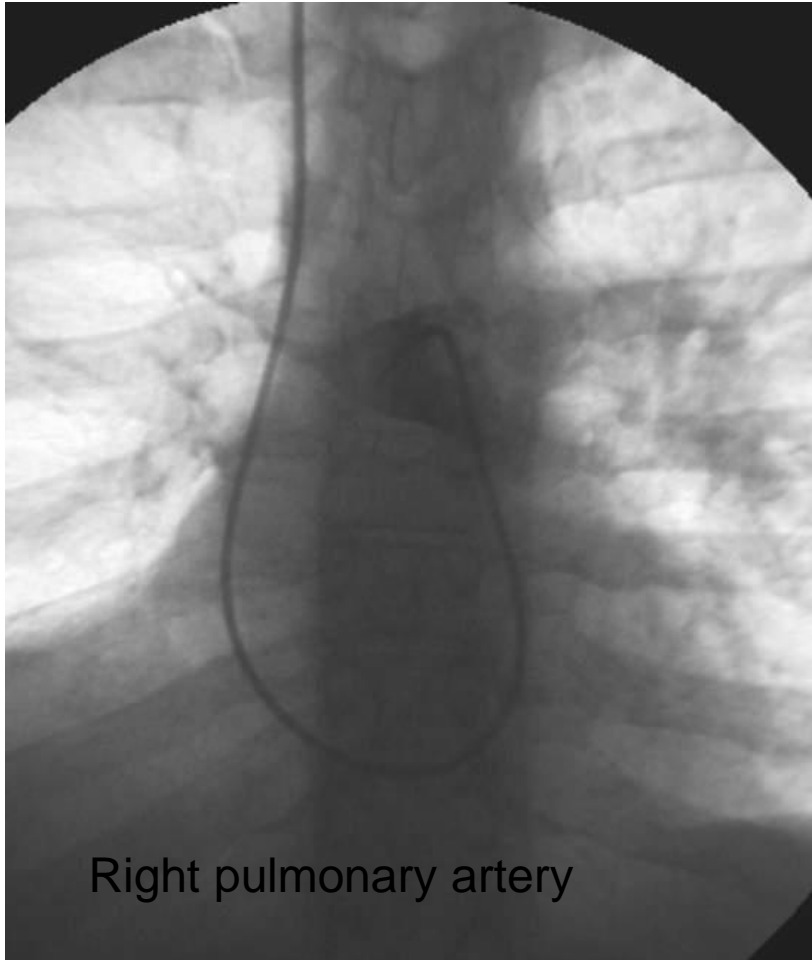


Anterior
Perfusion Scan

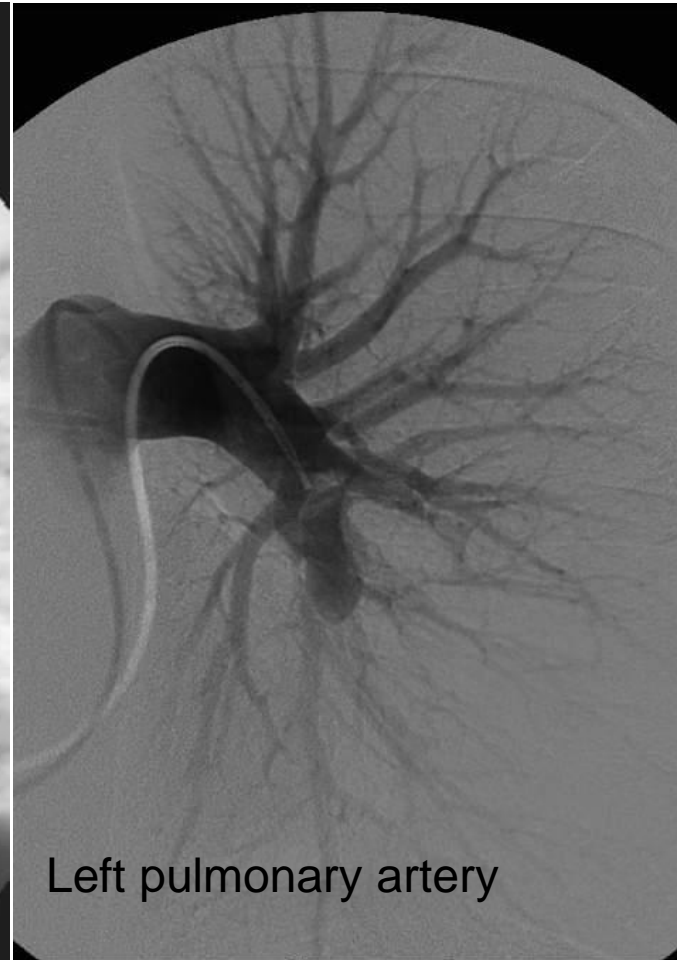




PAgram



Right pulmonary artery



Left pulmonary artery

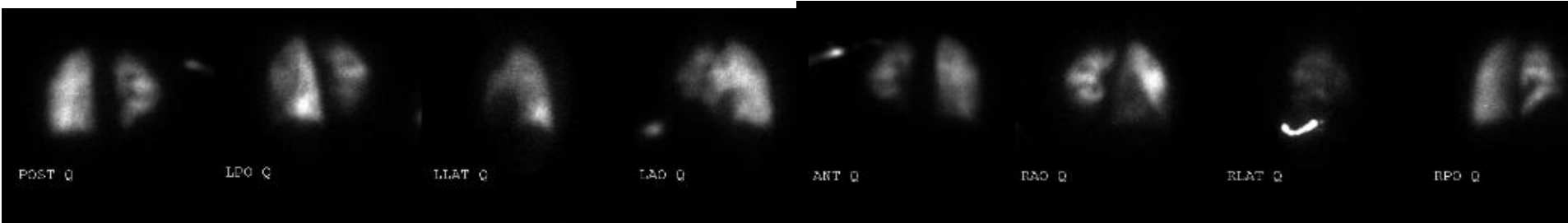


Pre-op and Post-op Q Scans

Pre-op

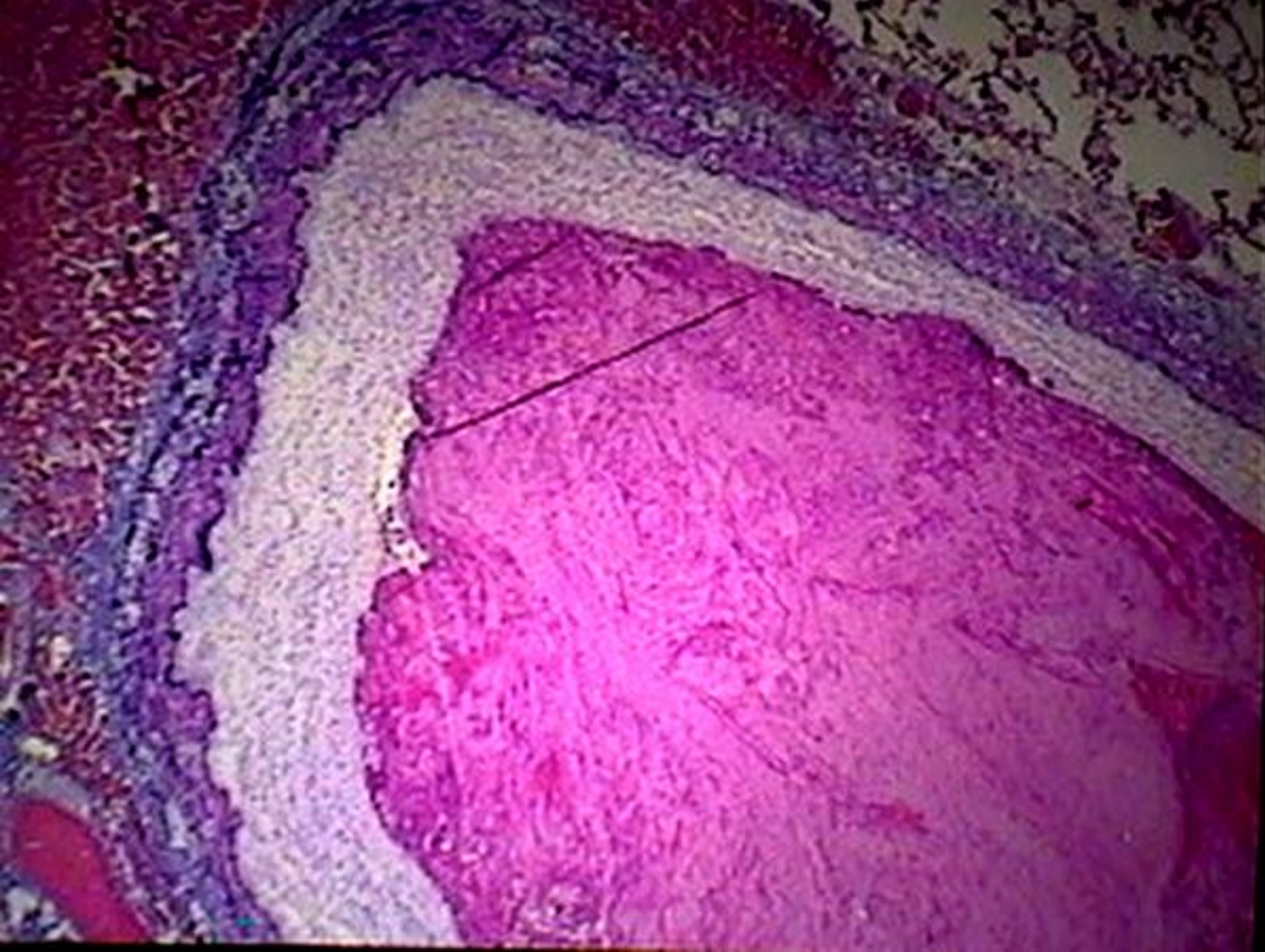


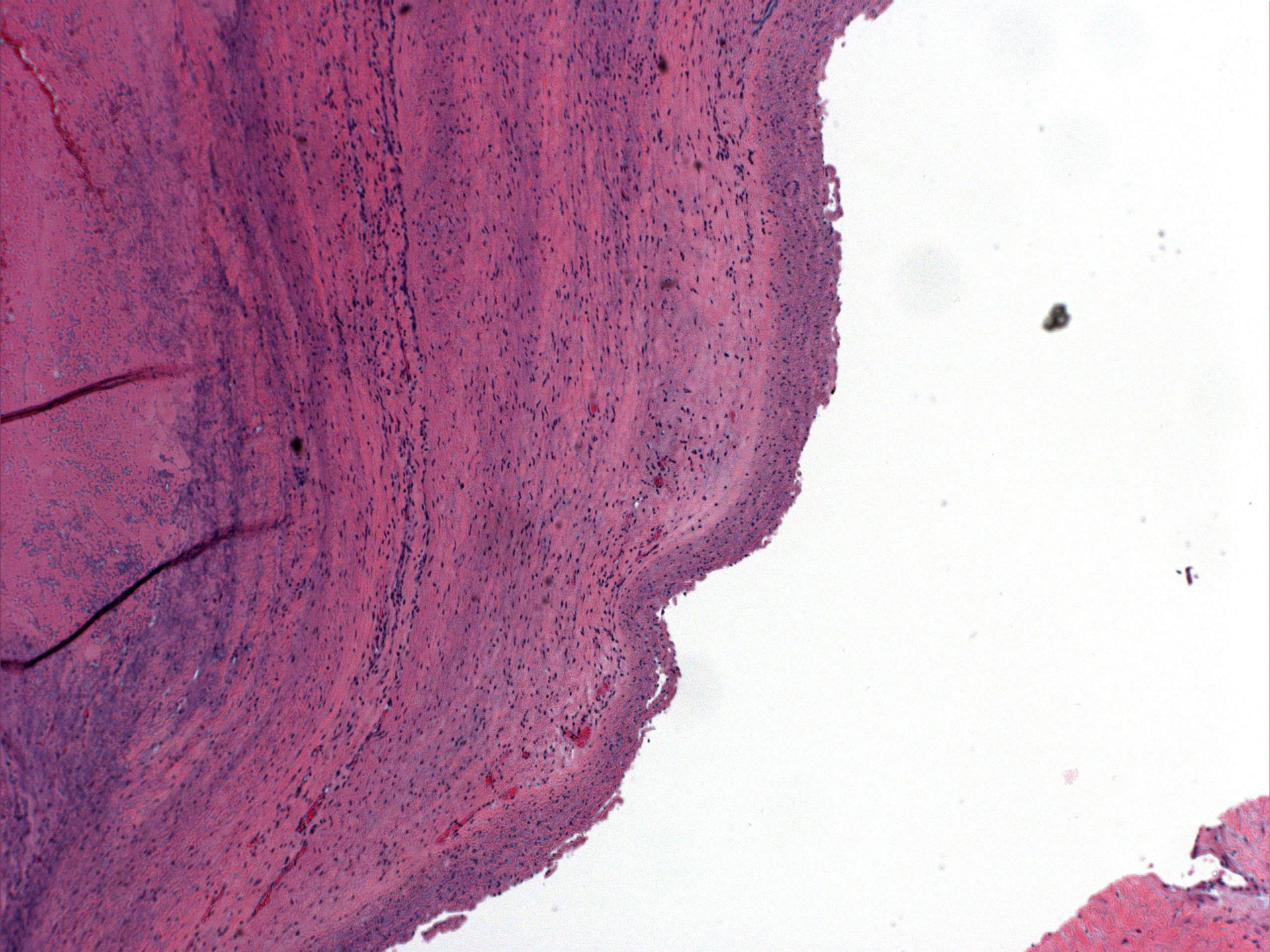
Post-op

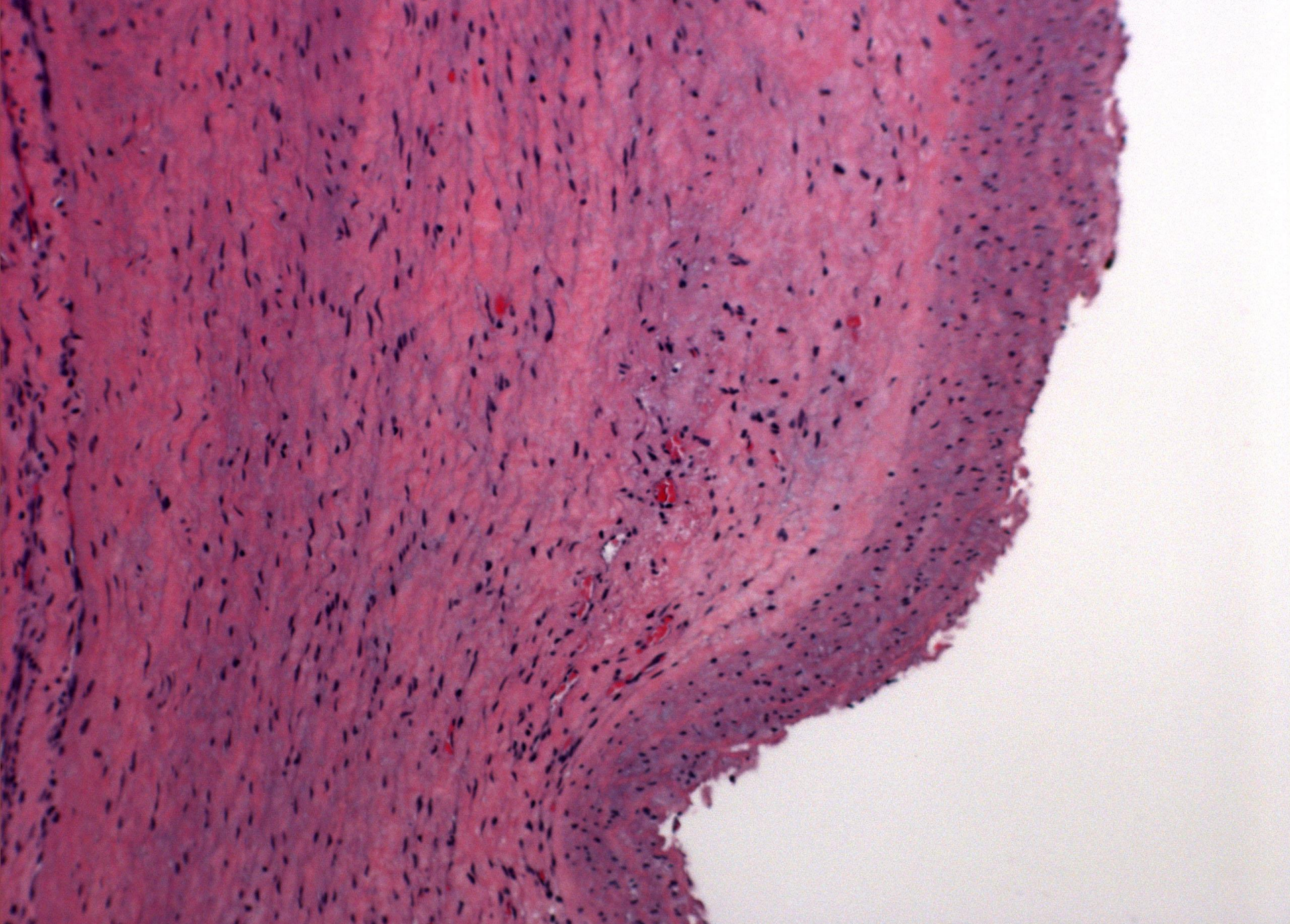


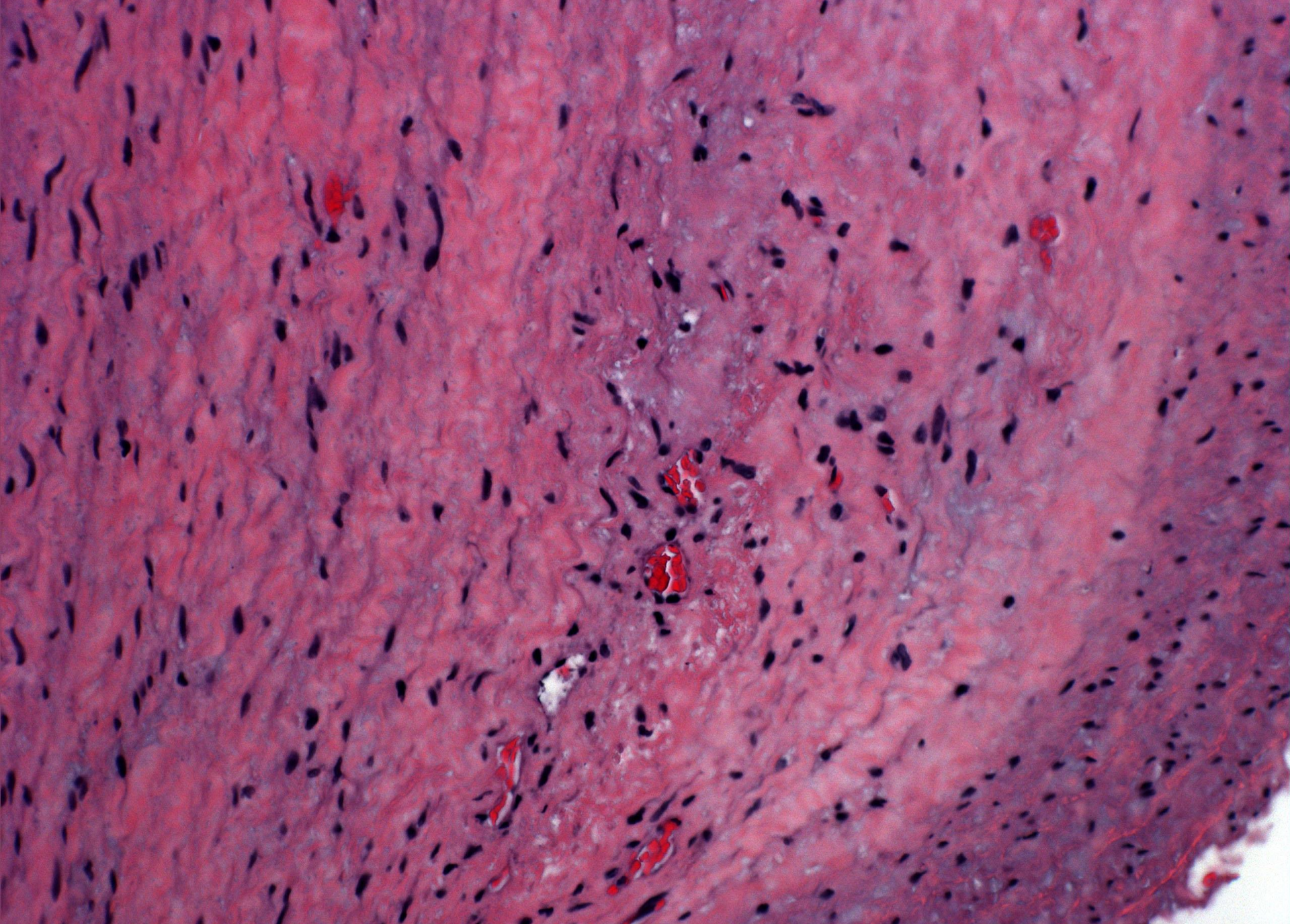
Chronic Thrombo-embolic Pulmonary Hypertension





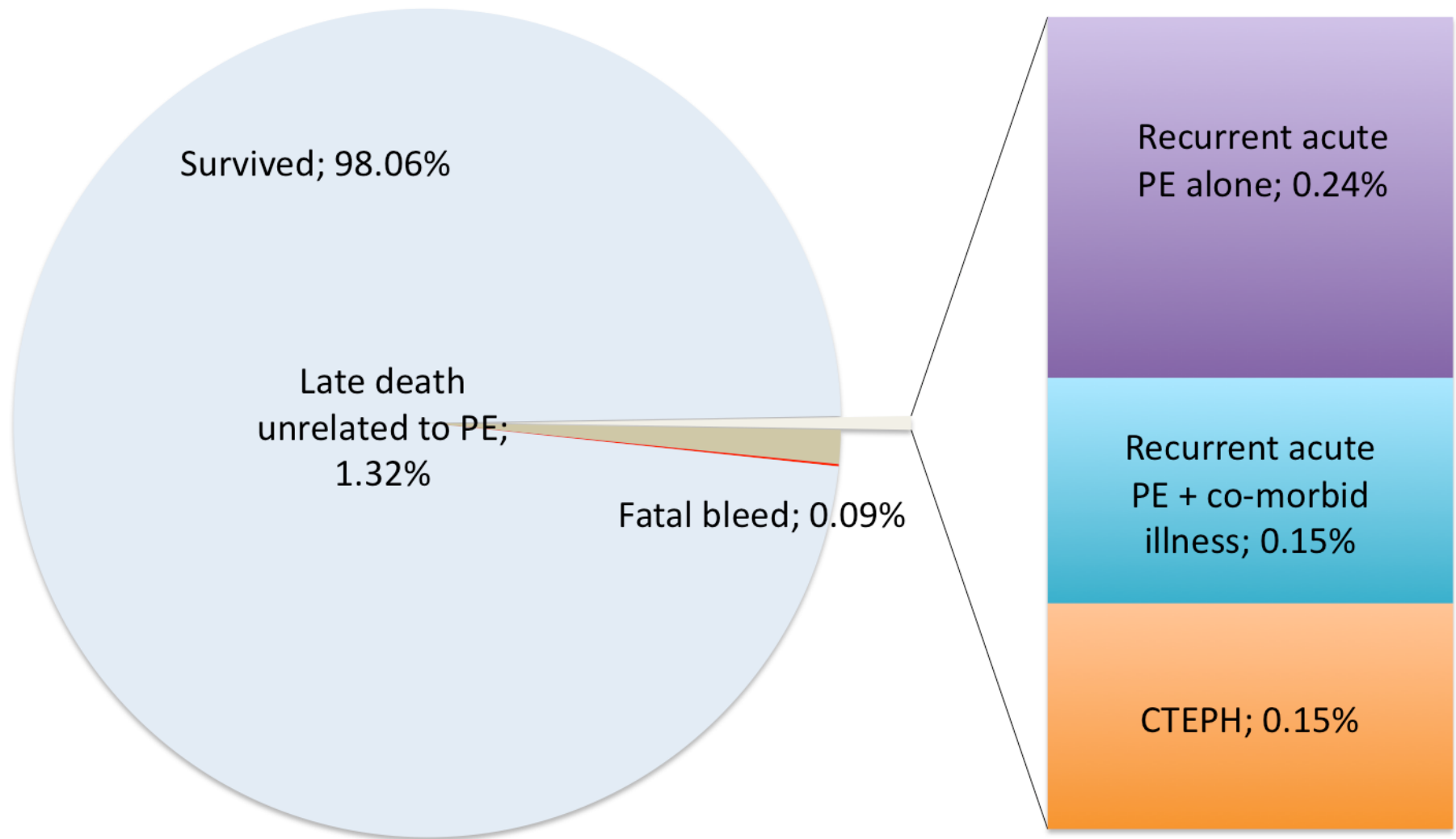








Causes of Death > 1 month after Acute PE



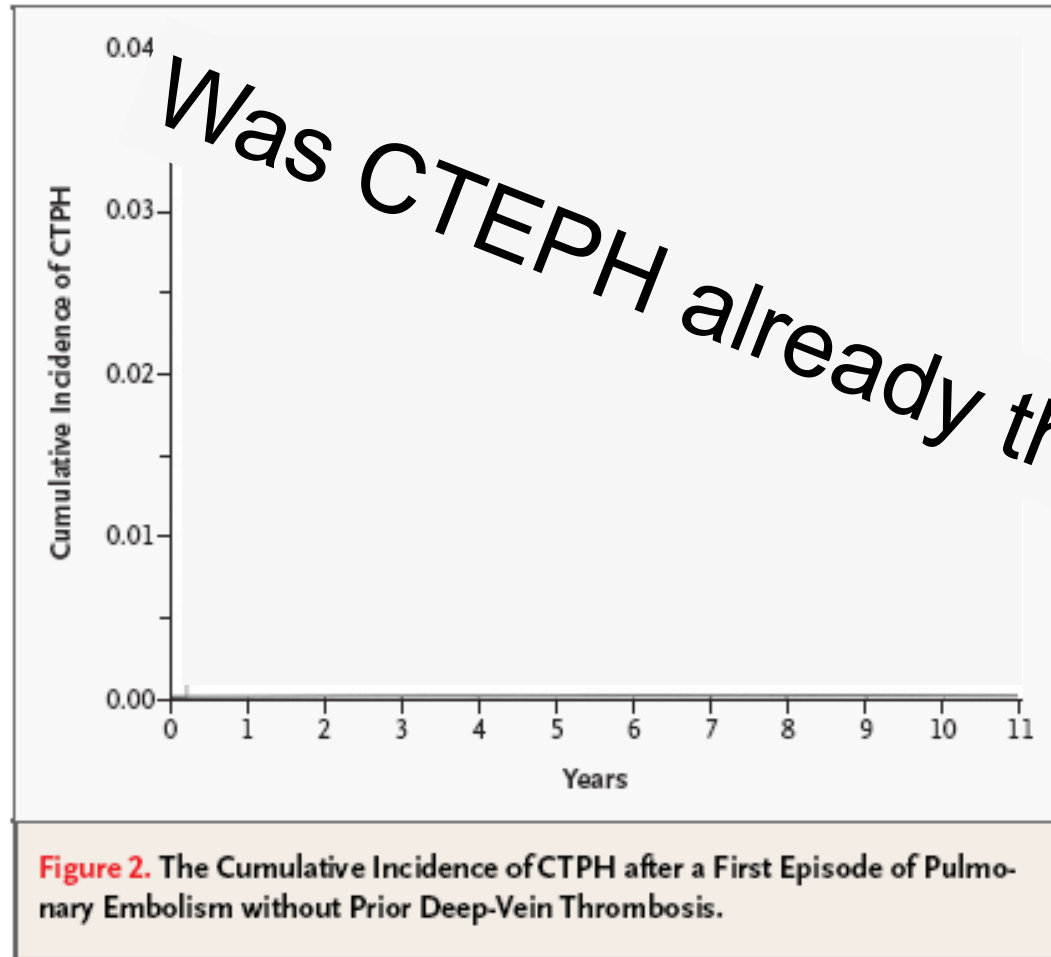


CTEPH after Acute PE

Reference	n	Follow-up (months)	CTEPH Incidence
Pengo (2004)	223	94.3	3.8%
Miniati (2006)	320	25.2	1.3%
Becattini (2006)	259	46	0.8%
Klok (2010)	866	34	0.57%
Poli (2010)	239	36	0.4%
Surie (2010)	110	36	2.7%



CTEPH Diagnosis After Acute PE





Risk factors for CTEPH

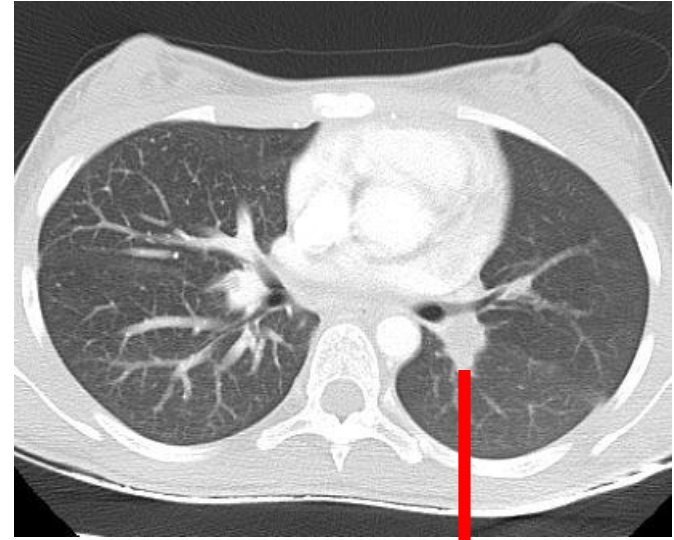
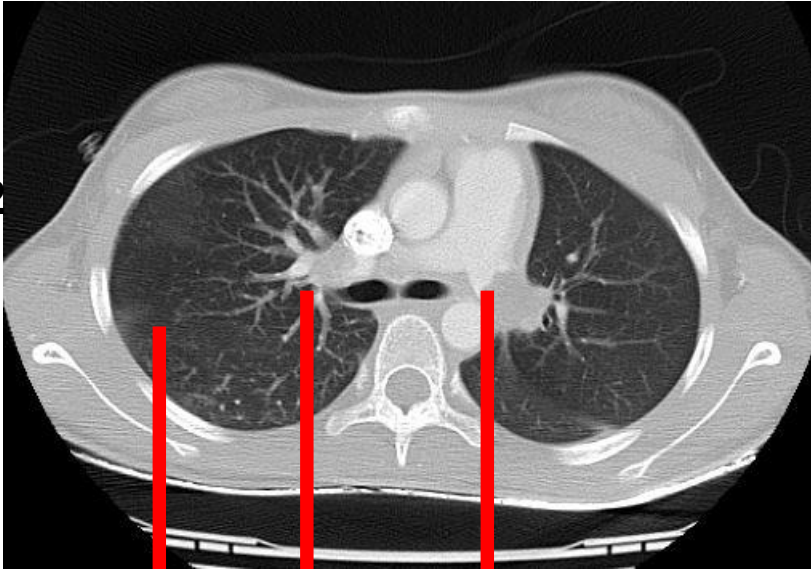
Was CTEPH already there?

	Points for score
Unprovoked PE	
Known hypothyroidism	
Symptom onset > 2 weeks before PE diagnosis	+ 3
Right ventricular dysfunction on CT or echocardiography	+ 2
Known diabetes mellitus	- 3
Thrombolytic therapy or embolectomy	- 3

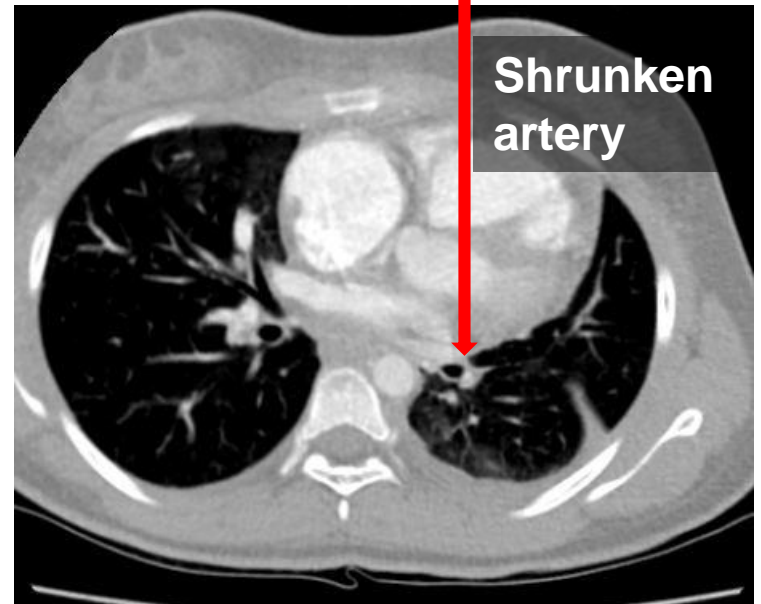
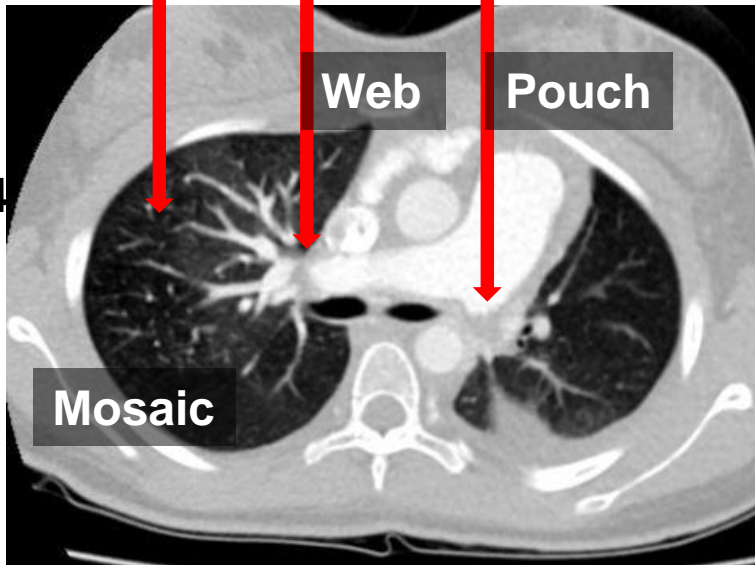
1. Klok FA, Dzikowska-Diduch O, Kostrubiec M, Vliegen HW, Pruszczyk P, Hasenfuss G, et al. Derivation of a clinical prediction score for chronic thromboembolic pulmonary hypertension after acute pulmonary embolism. J Thromb Haemost 2016;14(1):121-128.

CTEPH can be mistaken for Acute PE

Oct 2012



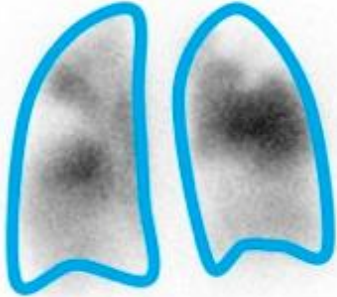
Mar 2014





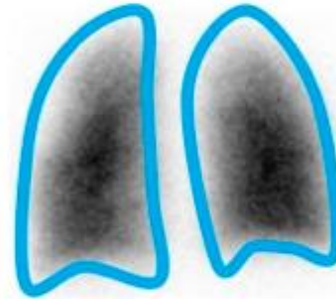
Recovery of Perfusion after Acute PE

Perfusion upon Presentation



34%
Defect

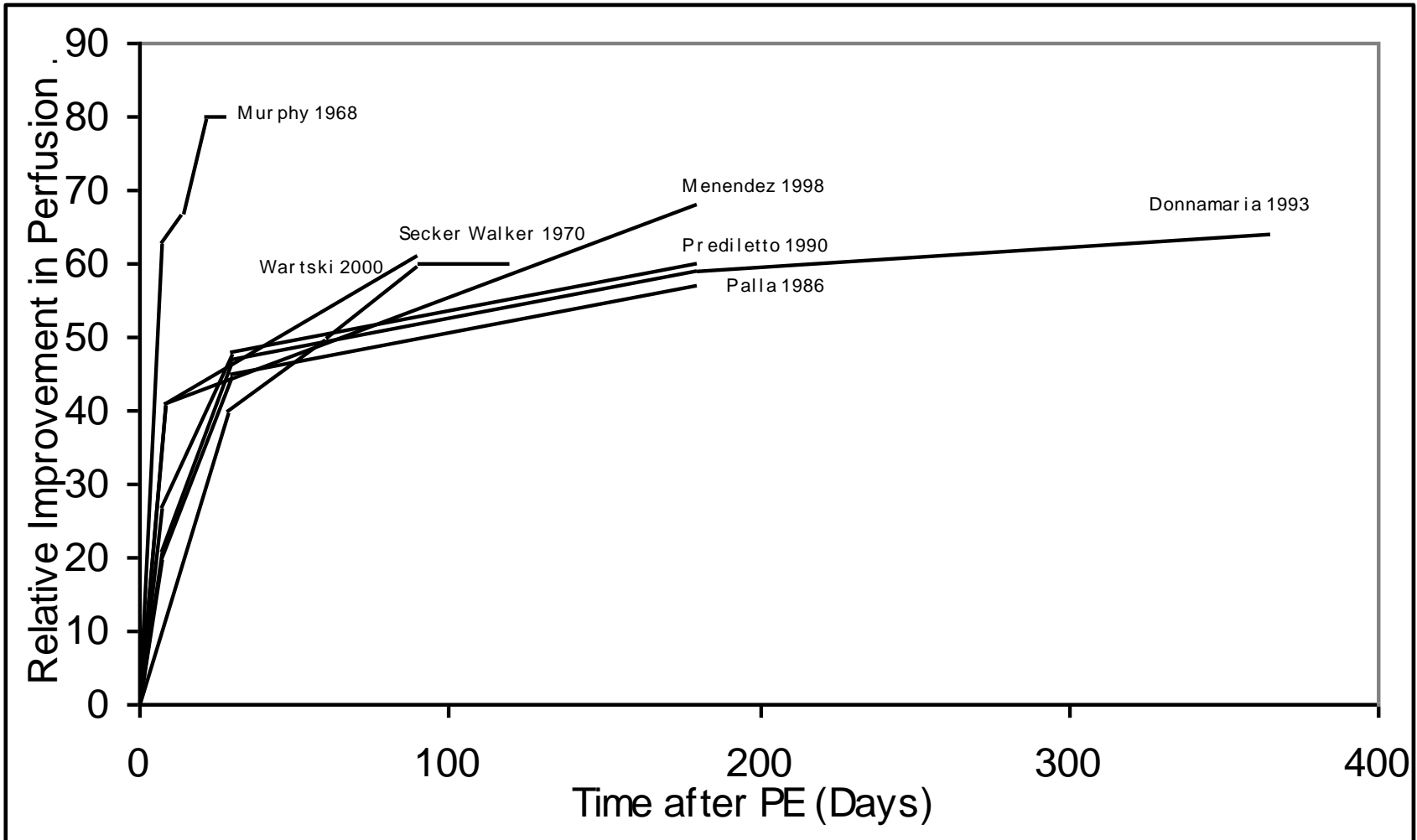
Perfusion after 6 months



0%
Defect

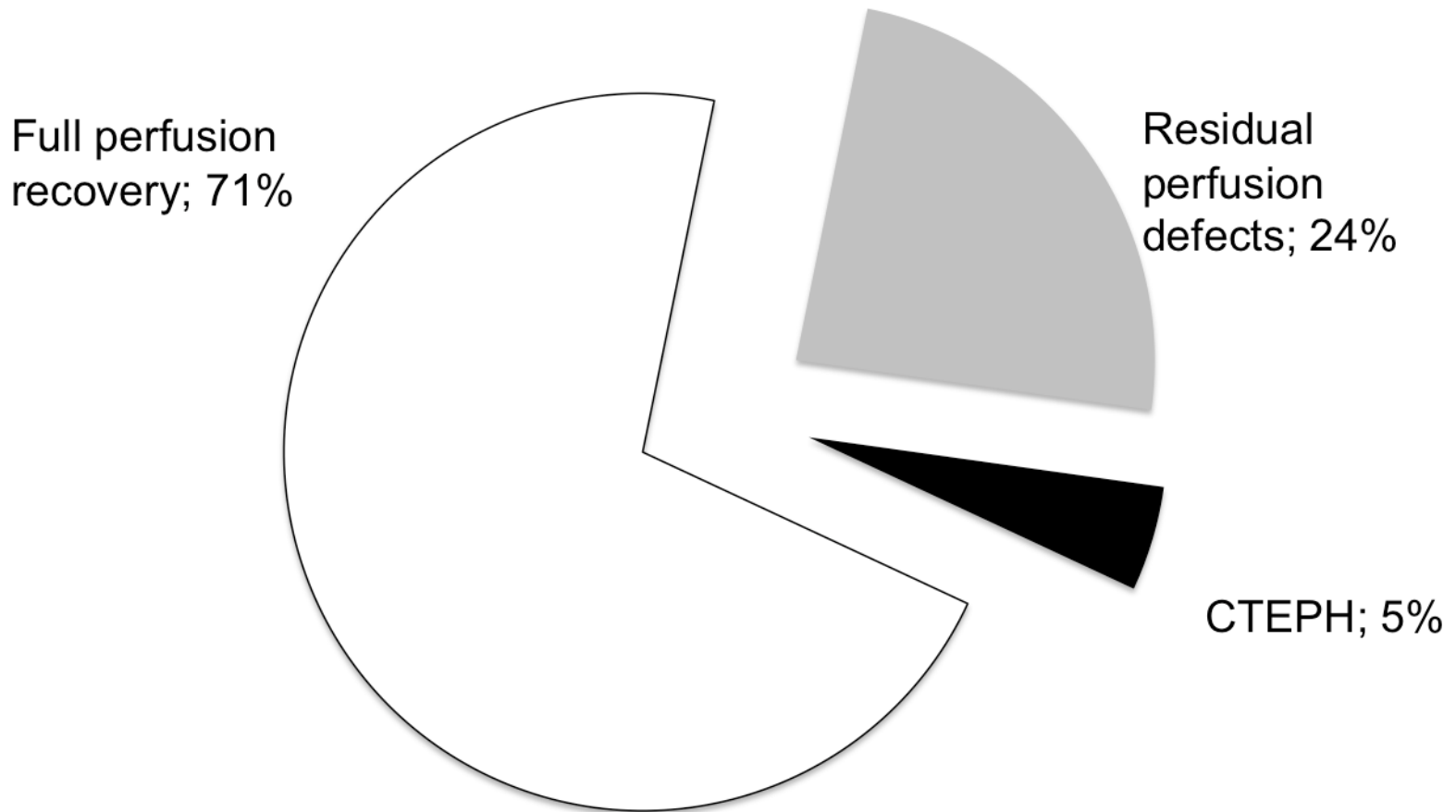


Improvement Relative to Initial Perfusion Defect





Frequency of Residual Defects Post-PE





Clinical Consequences of Residual Q Defects

- More dyspnea
- Lower 6 min walk distance
- Higher PAP
- More CTEPH



Clinical points

- CTEPH may be present at the time of PE diagnosis.
- Many people do not recover lung perfusion after acute PE



Scintigraphic VQ scanning is useful

- After acute PE
- When CTEPH is suspected

Computed Tomographic Pulmonary Angiography vs Ventilation-Perfusion Lung Scanning in Patients With Suspected Pulmonary Embolism

A Randomized Controlled Trial

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Michael J. Kovacs, MD

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Chris Skedgel, MSc

Keith O'Rourke, PhD

Philip S. Wells, MD

PULMONARY EMBOLISM IS A COMMON and serious medical condition leading to the hospitalization or death of more than 250 000 people in the United States each year.¹ It is the third leading cause of cardiovascular mortality and is estimated to result in 5% to 10% of all deaths in US hospitals.² Despite the potentially lethal nature of this condition, pulmonary embolism remains one of the most difficult conditions to

Context Ventilation-perfusion (\dot{V}/\dot{Q}) lung scanning and computed tomographic pulmonary angiography (CTPA) are widely used imaging procedures for the evaluation of patients with suspected pulmonary embolism. Ventilation-perfusion scanning has been largely replaced by CTPA in many centers despite limited comparative formal evaluations and concerns about CTPA's low sensitivity (ie, chance of missing clinically important pulmonary emboli).

Objectives To determine whether CTPA may be relied upon as a safe alternative to \dot{V}/\dot{Q} scanning as the initial pulmonary imaging procedure for excluding the diagnosis of pulmonary embolism in acutely symptomatic patients.

Design, Setting, and Participants Randomized, single-blinded noninferiority clinical trial performed at 4 Canadian and 1 US tertiary care centers between May 2001 and April 2005 and involving 1417 patients considered likely to have acute pulmonary embolism based on a Wells clinical model score of 4.5 or greater or a positive D-dimer assay result.

Intervention Patients were randomized to undergo either \dot{V}/\dot{Q} scanning or CTPA. Patients in whom pulmonary embolism was considered excluded did not receive antithrombotic therapy and were followed up for a 3-month period.

Main Outcome Measure The primary outcome was the subsequent development of symptomatic pulmonary embolism or proximal deep vein thrombosis in patients in whom pulmonary embolism had initially been excluded.

Results Seven hundred one patients were randomized to CTPA and 716 to \dot{V}/\dot{Q} scanning. Of these, 133 patients (19.2%) in the CTPA group vs 101 (14.2%) in the \dot{V}/\dot{Q} scan group were diagnosed as having pulmonary embolism in the initial evaluation period (difference, 5.0%; 95% confidence interval [CI], 1.1% to 8.9%) and were treated with anticoagulant therapy. Of those in whom pulmonary embolism was considered excluded, 2 of 561 patients (0.4%) randomized to CTPA vs 6 of 611 patients (1.0%) undergoing \dot{V}/\dot{Q} scanning developed venous thromboembolism in follow-up (difference, -0.6%; 95% CI, -1.6% to 0.3%) including one patient with fatal pulmonary embolism in the \dot{V}/\dot{Q} group.

Conclusions In this study, CTPA was not inferior to \dot{V}/\dot{Q} scanning in ruling out pulmonary embolism. However, significantly more patients were diagnosed with pulmonary embolism using the CTPA approach. Further research is required to determine whether all pulmonary emboli detected by CTPA should be managed with anticoagulant therapy.

Trial Registration isrctn.org Identifier: ISRCTN65486961

JAMA. 2007;298(23):2743-2753

www.jama.com



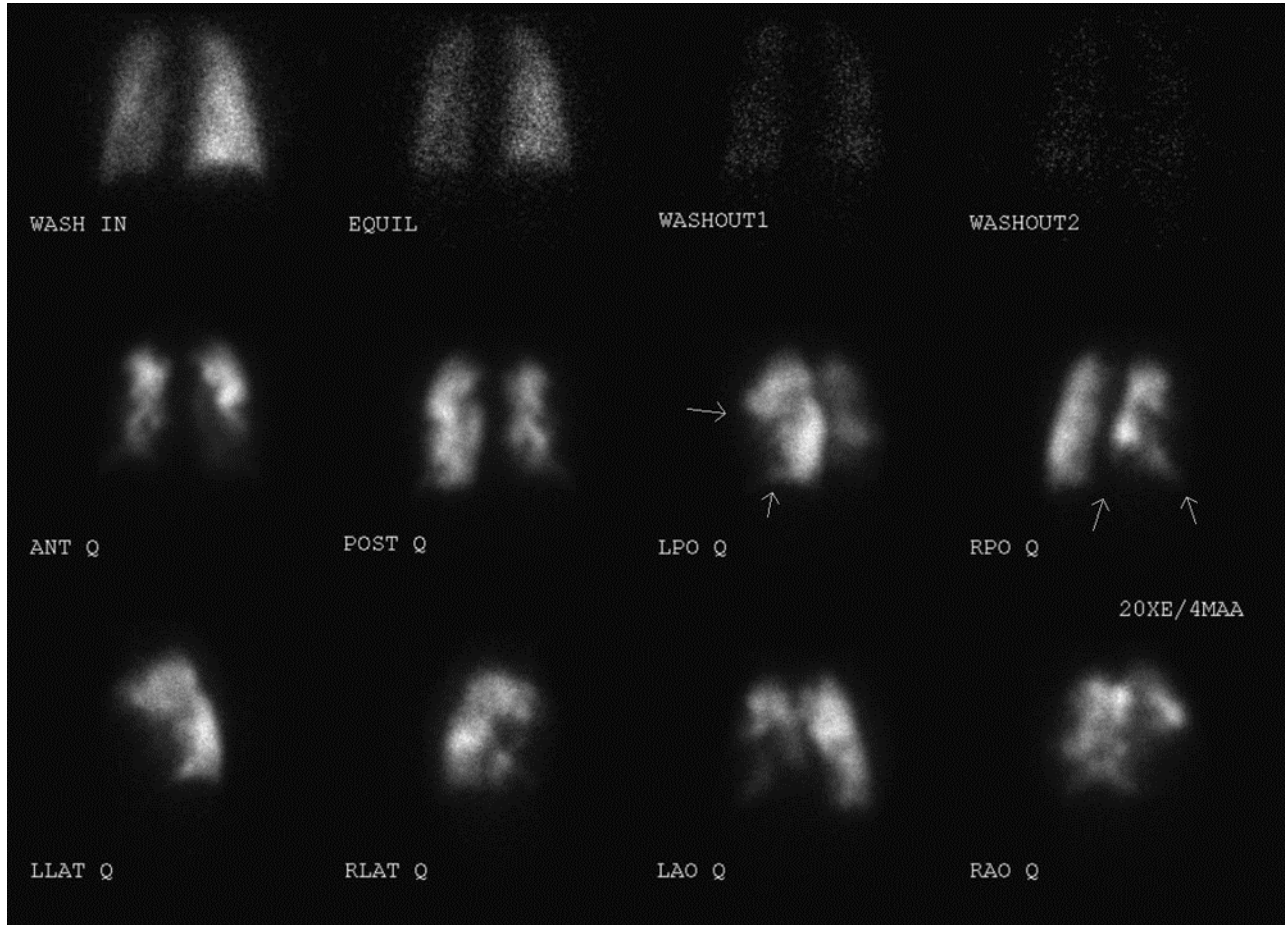
VQ is as sensitive as CTPA for Acute PE

	CTPA	V/Q
	(n = 561)	(n = 611)
PE total	2 (0.4)	4 (0.7)
Fatal PE	0	1 (0.2)
DVT	0	2 (0.3)
Total VTE ^b	2 (0.4)	6 (1.0)

1. Anderson DR, Kahn SR, Rodger MA, Kovacs MJ, Morris TA, Hirsch A, et al. Computed tomographic pulmonary angiography vs ventilation-perfusion lung scanning in patients with suspected pulmonary embolism: a randomized controlled trial. JAMA : the journal of the American Medical Association 2007;298(23):2743-2753.



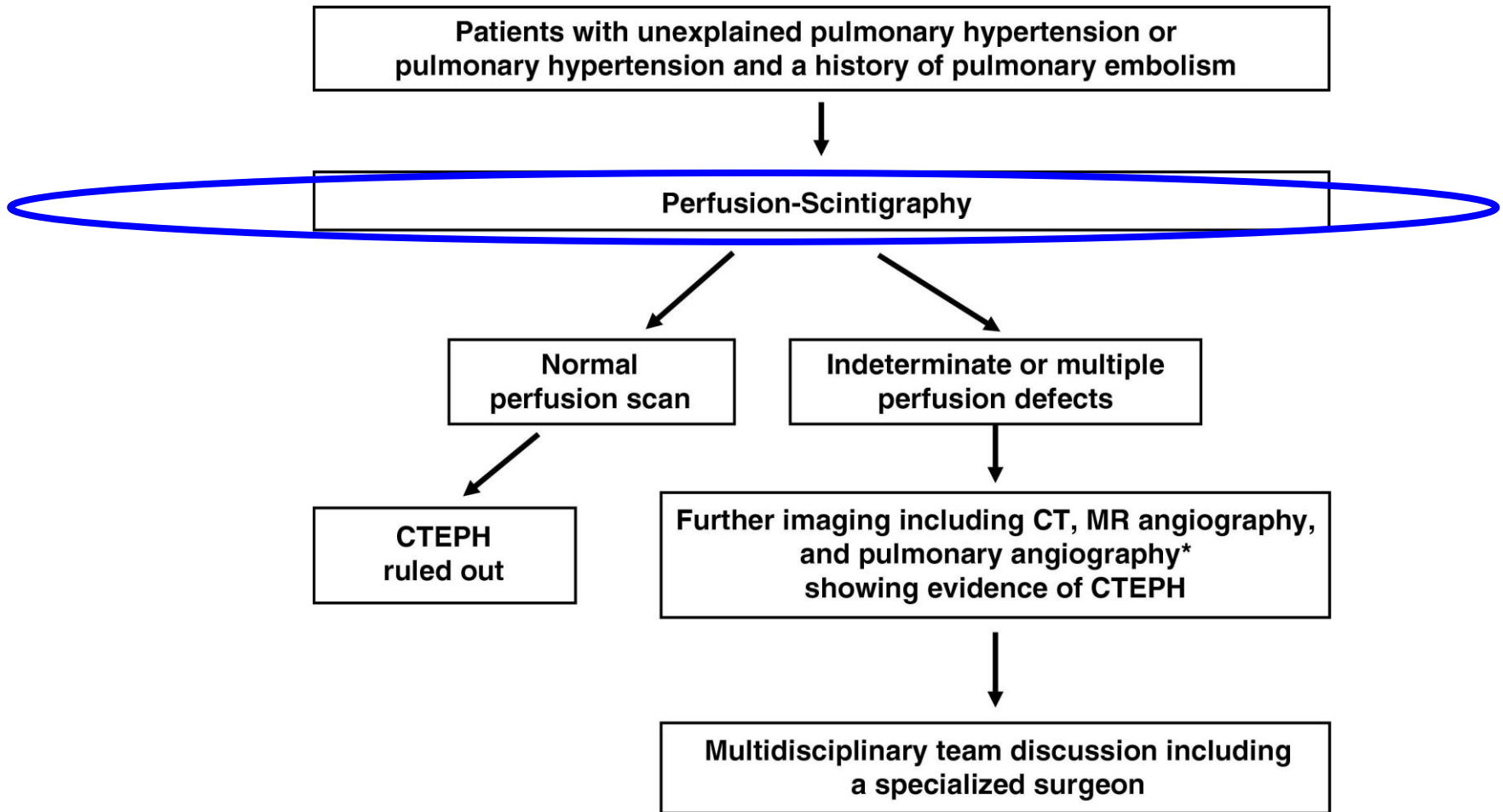
VQ is the best CTEPH screening test



Courtesy of Timothy Fernandes, MD, University of California, San Diego



General Diagnostic Approach



1. Hoepfer MM, Barbera JA, Channick RN, Hassoun PM, Lang IM, Manes A, et al. Diagnosis, assessment, and treatment of non-pulmonary arterial hypertension pulmonary hypertension. *Journal of the American College of Cardiology* 2009;54(1 Suppl):S85-96.



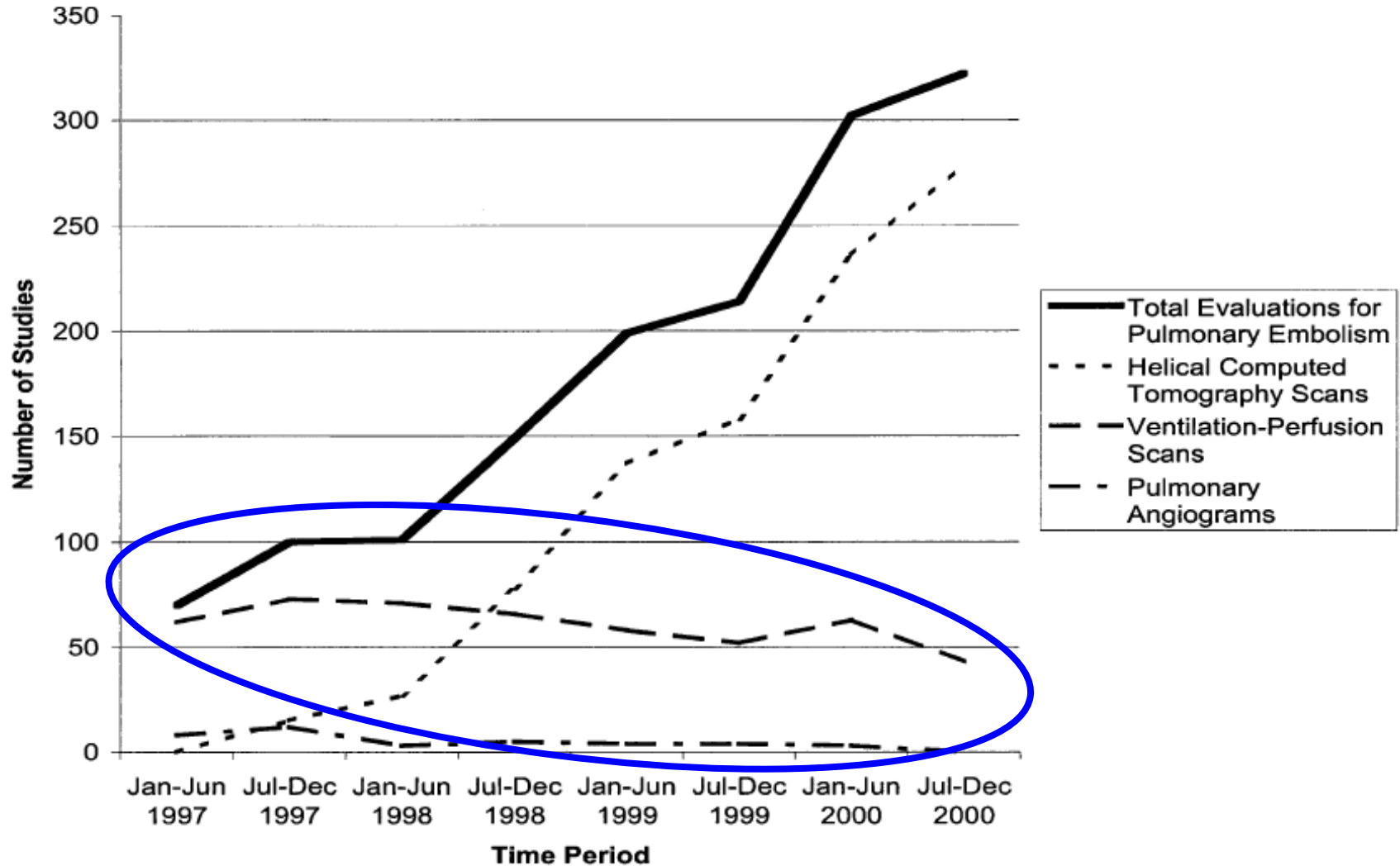
VQ vs CTPA for CTEPH

Indicator	Scintigraphy		CTPA
	V/Q (1)*	V/Q (2)†	
Sensitivity (%)	97.4	96.2	51.3
Specificity (%)	90	94.6	99.3
Accuracy (%)	92.5	95.2	82.8
NPV (%)	98.5	97.9	79.7
PPV (%)	83.5	90.3	97.6

1. Tunariu N, Gibbs SJ, Win Z, Gin-Sing W, Graham A, Gishen P, et al. Ventilation-perfusion scintigraphy is more sensitive than multidetector CTPA in detecting chronic thromboembolic pulmonary disease as a treatable cause of pulmonary hypertension. Journal of nuclear medicine : official publication, Society of Nuclear Medicine 2007;48(5):680-684.



VQ is less and less common



Trowbridge RL, Arazo PA, Gotway MB, Bailey RA, Auerbach AD. The effect of helical computed tomography on diagnostic and treatment strategies in patients with suspected pulmonary embolism. *Am J Med* 2004;116:84-90.



Feedback about VQ scans from cardiologist and pulmonologist

- “Nuclear medicine lung scans are not available in my hospital.”
 - During nights and weekends
 - Any time
- “Lung scans are too hard to read.”
- “Not enough experience in lung scans.”

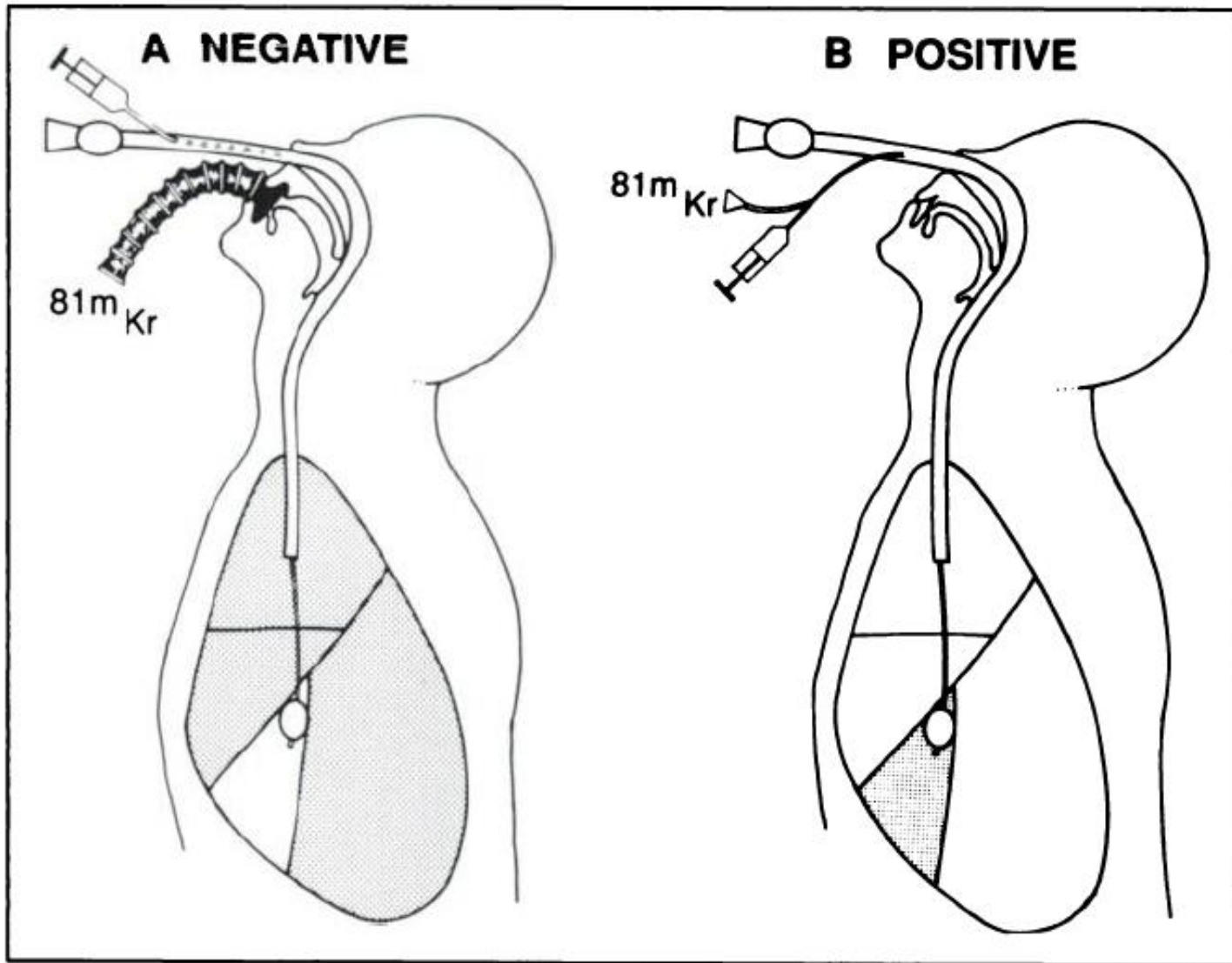


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Why is scintigraphy such a challenge for lung perfusion?



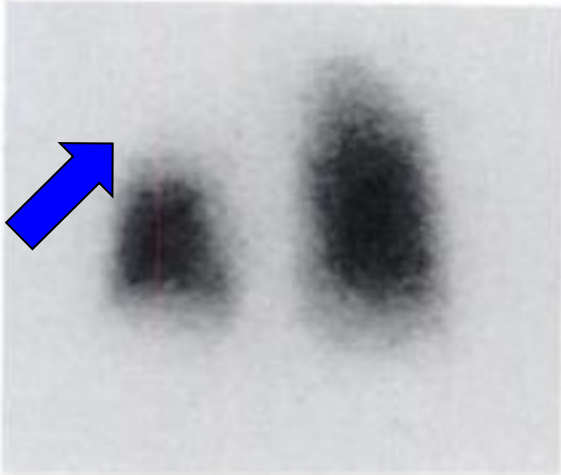
Experimental “segmental defect”



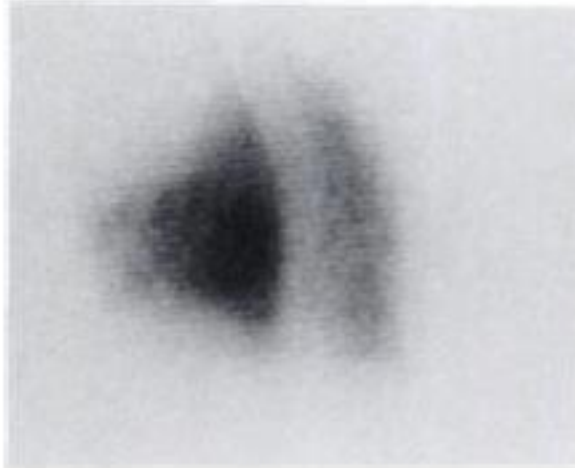
OCCLUSION



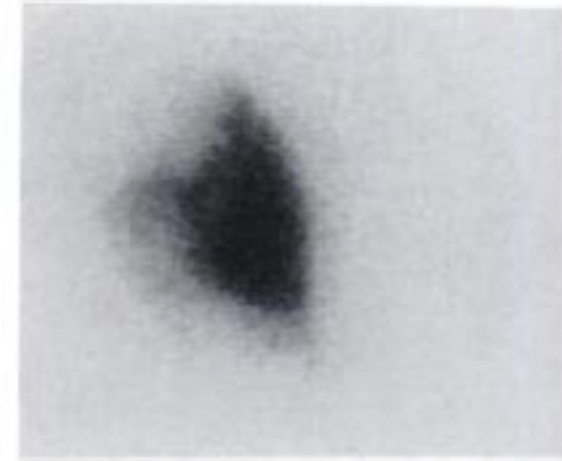
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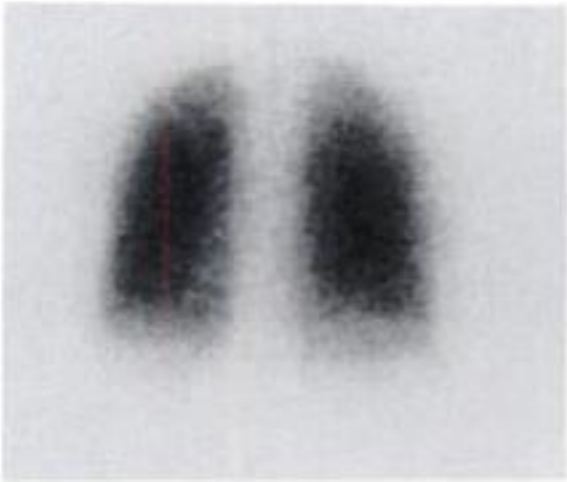
POST



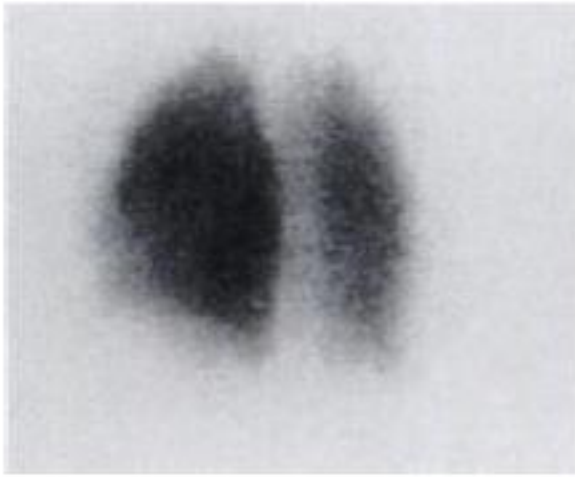
**LPO
CONTROL**



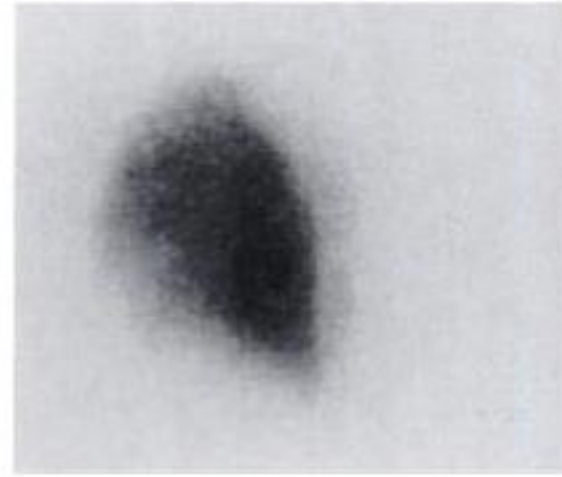
LLAT



POST



LPO



LLAT

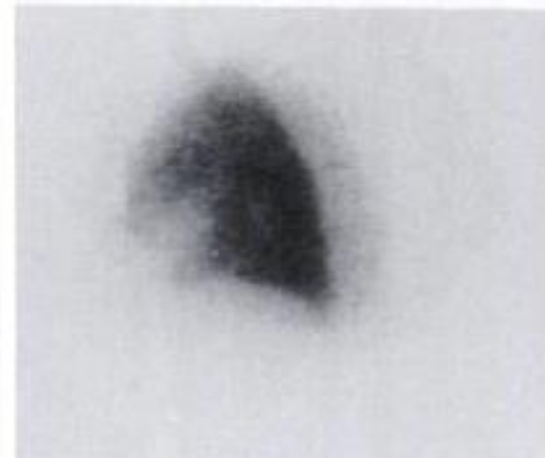
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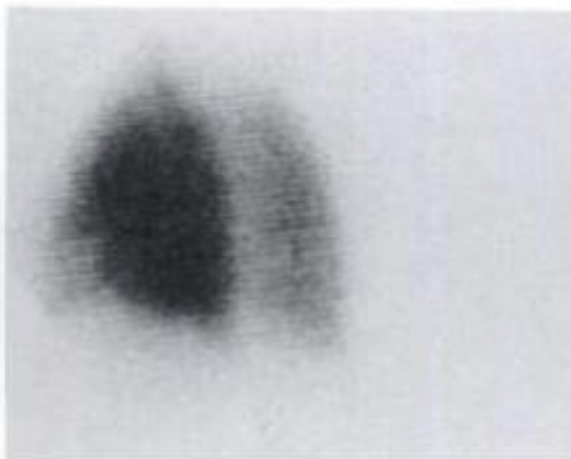
LPO
CONTROL



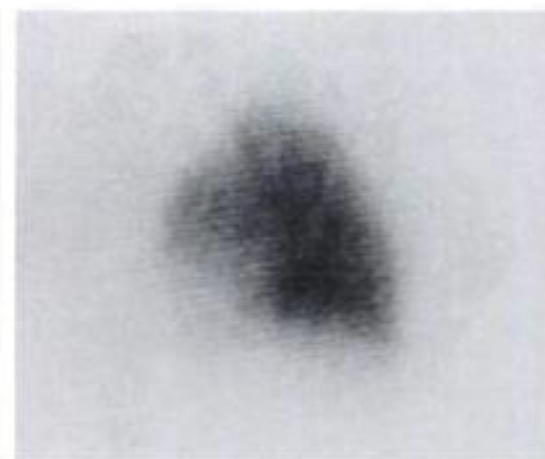
LLAT



POST



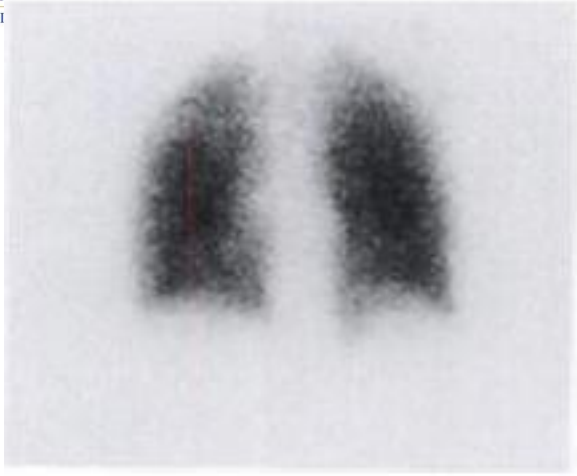
LPO



LLAT



OCCLUSION



POST

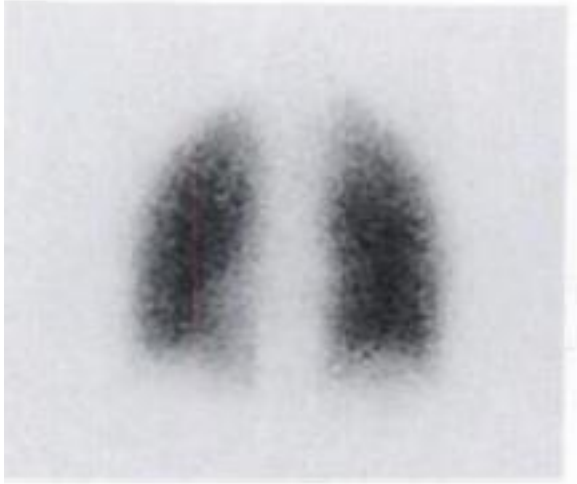


RPO



RLAT

CONTROL



POST



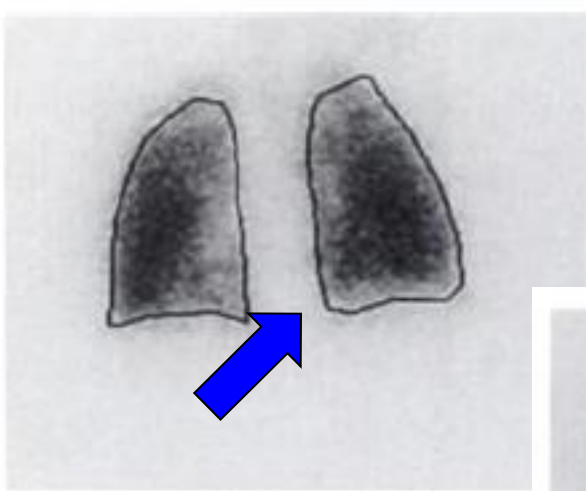
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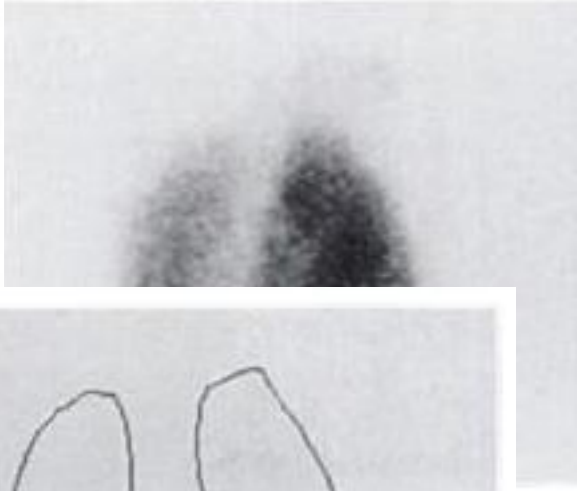
RLAT



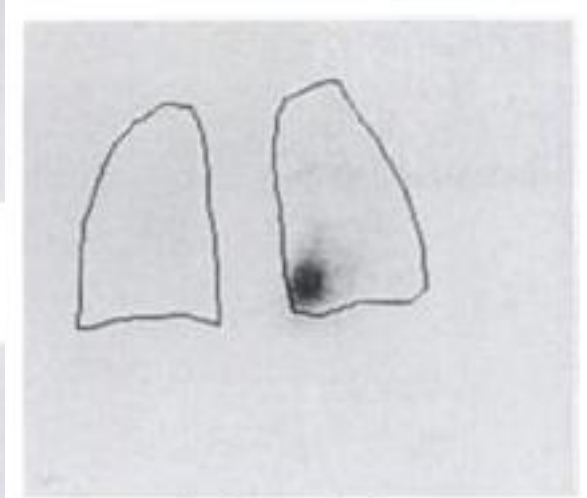
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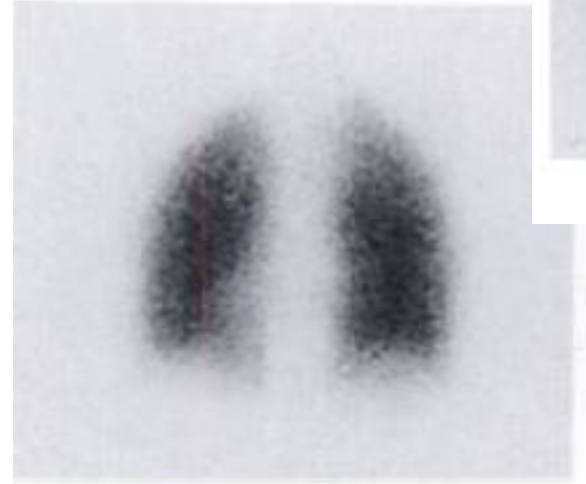
POST NEG



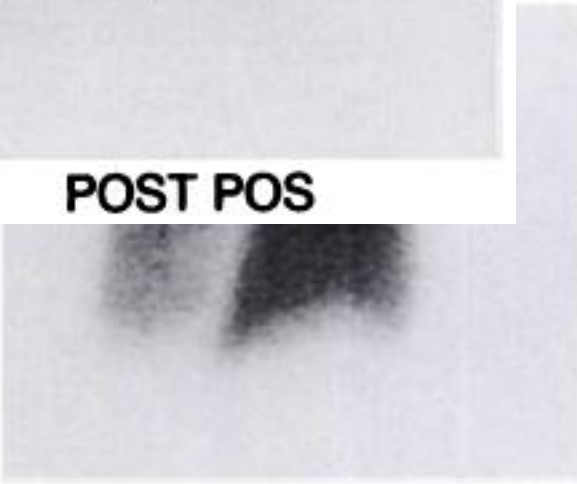
ANT



POST POS



POST



RPO



RLAT

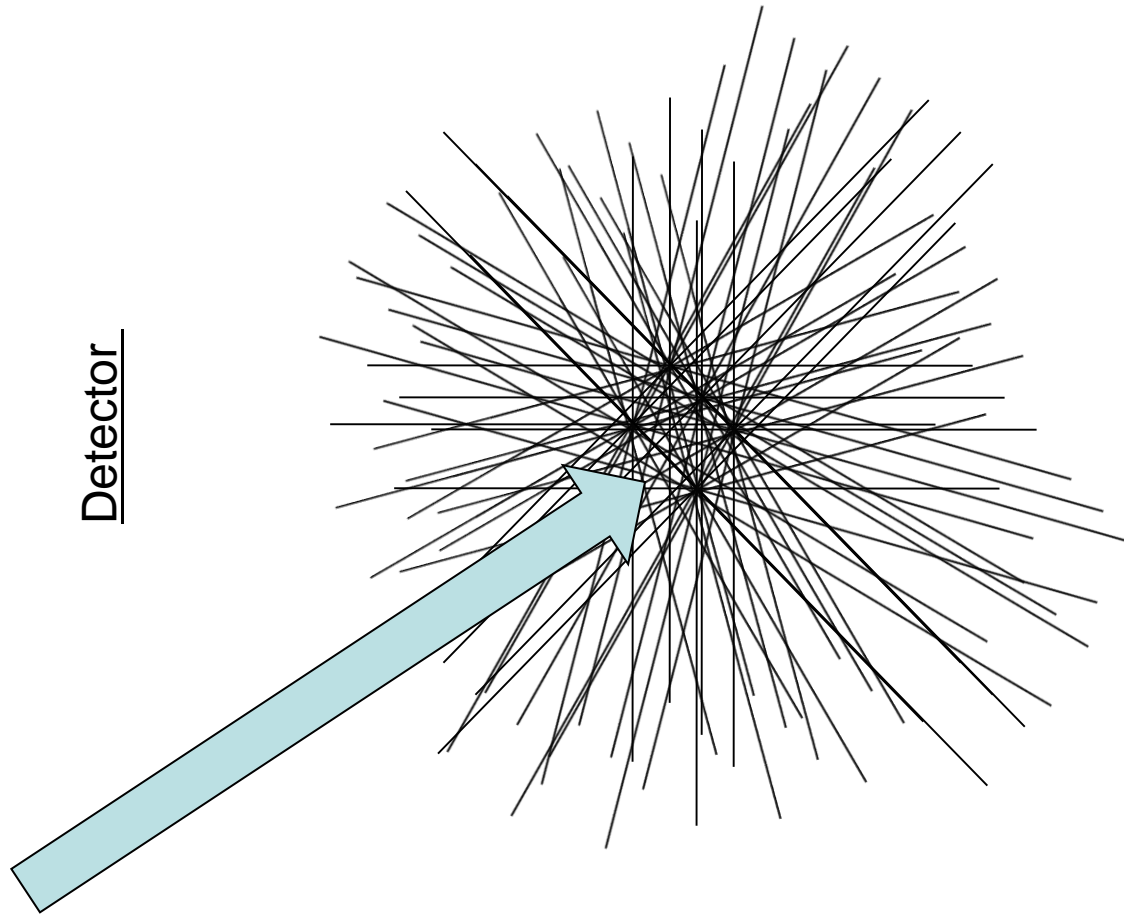


Views that demonstrated defects

	POST*	PO†	LAT‡
Left Upper Lobe			+
Apico-posterior		+	
Anterior	-		+
Lingula	-		+
Superior	-		+
Inferior	-		+
Left Lower Lobe		+	
Anterior	-		+
Apical		+	
Lateral	-	+	
Posterior		+	
Right Upper Lobe			+
Apical			+
Anterior		+	+
Posterior			
Right Middle Lobe			+
Medial		-	+
Lateral	-		+
Right Lower Lobe		+	
Medial	-	-	-
Anterior			+
Apical		+	
Lateral		+	
Posterior		+	

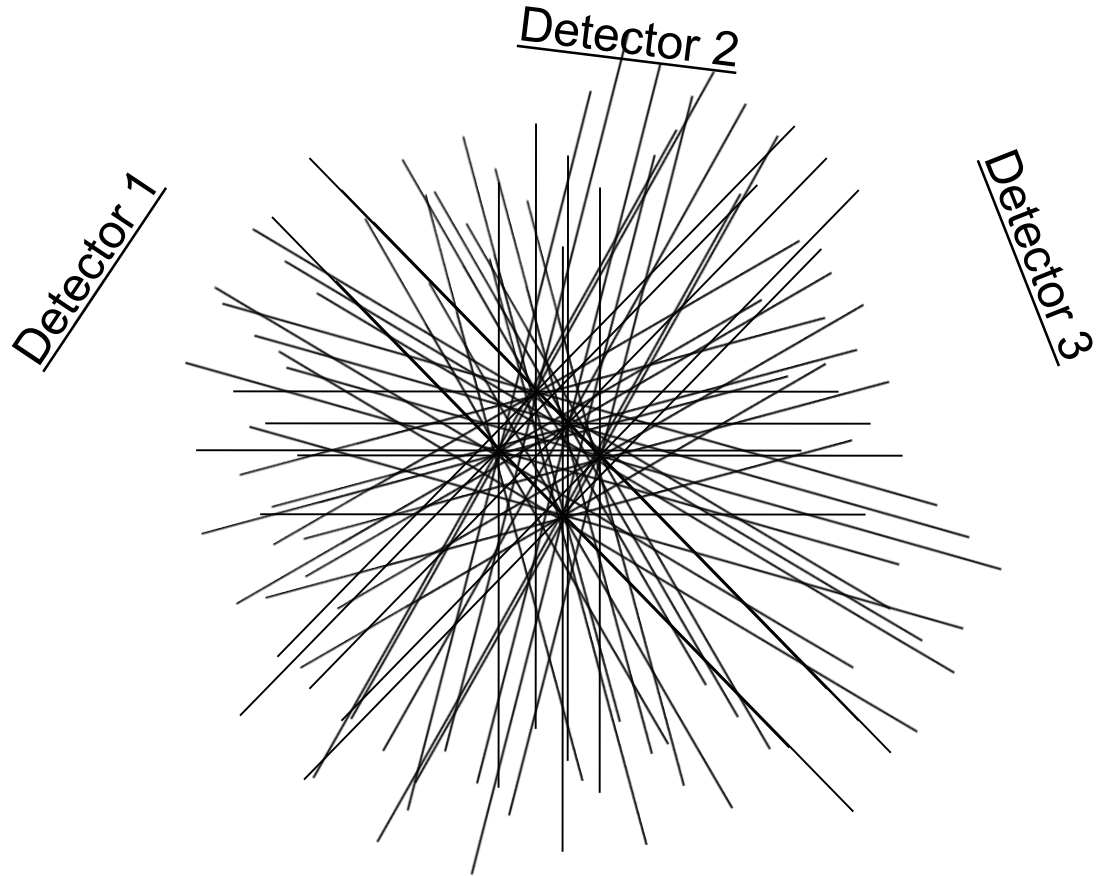


Planar Perfusion Scan



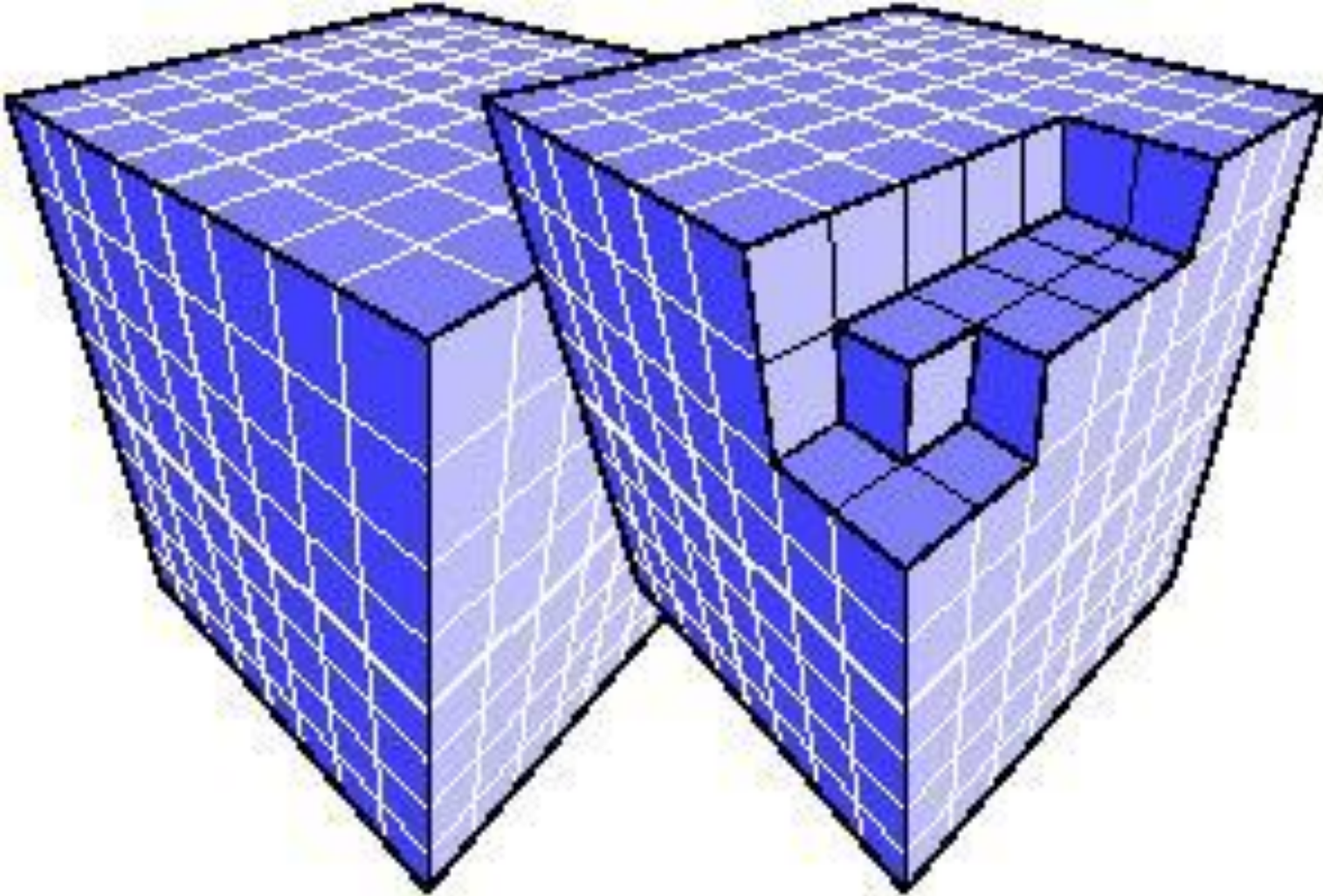


SPECT Data





SPECT “Voxel” Dataset



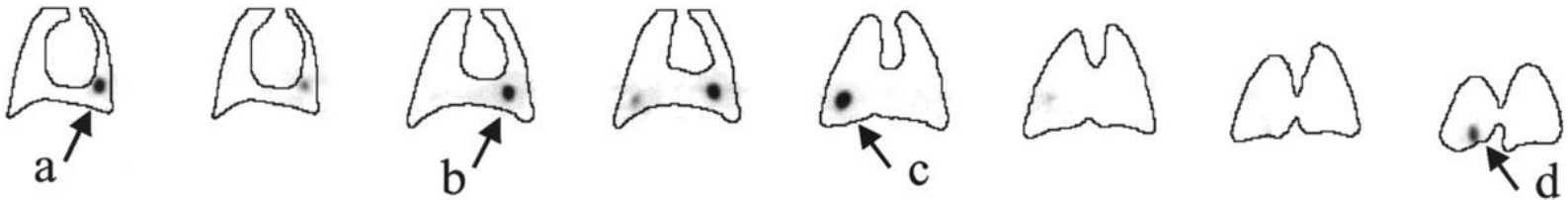


Where are the defects?

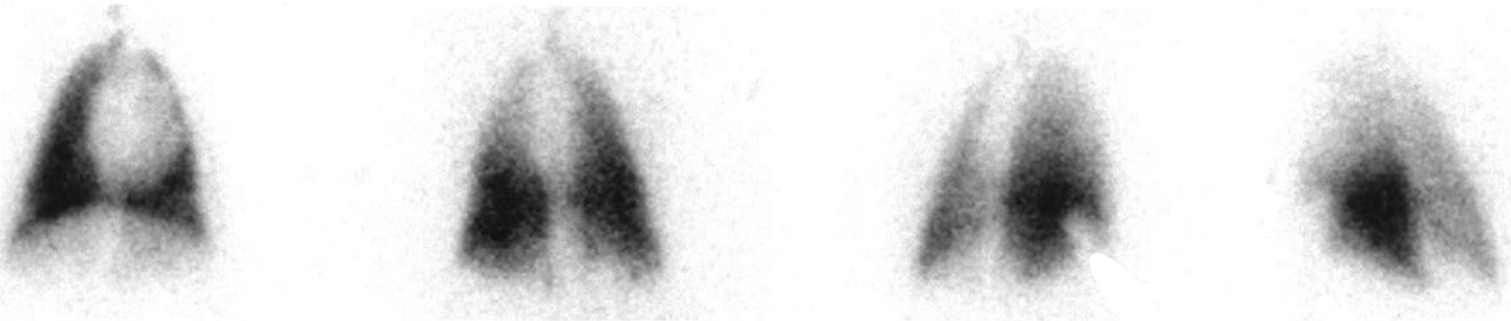
SPECT Q scan (coronal slices)



Emboli (coronal slices, front to back)



Planar Q scan



Anterior

Posterior

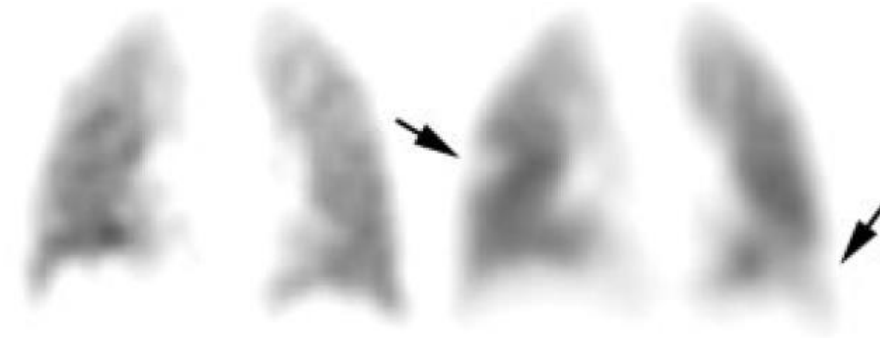
RPO

LPO

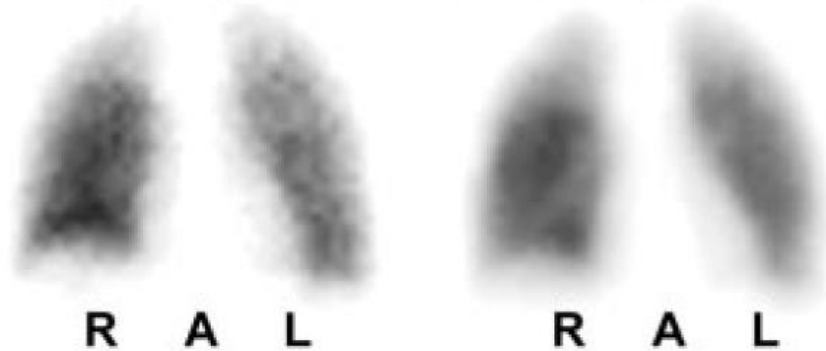


SPECT V/Q for Acute PE

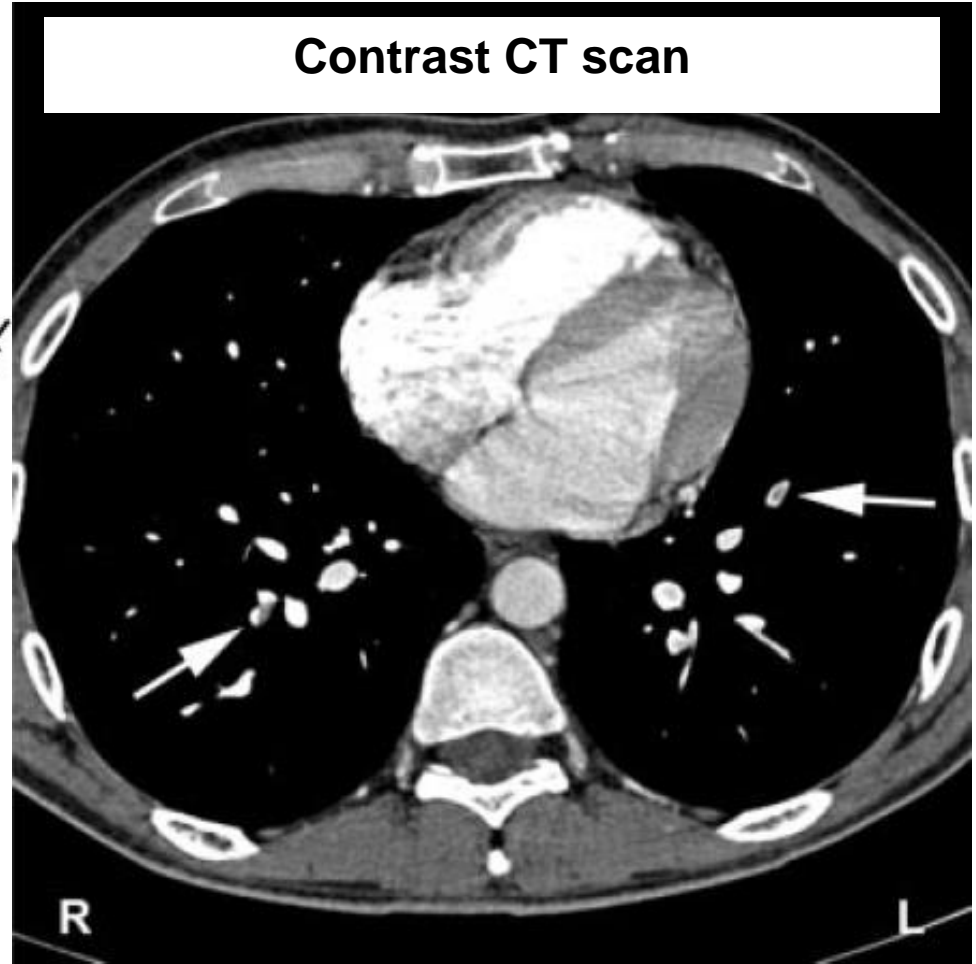
SPECT V/Q scan



planar V/Q scan



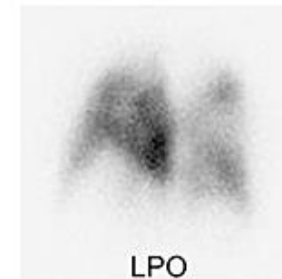
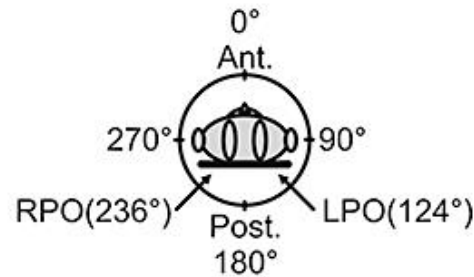
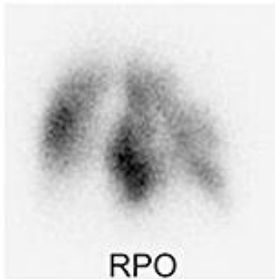
Contrast CT scan



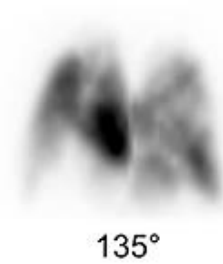
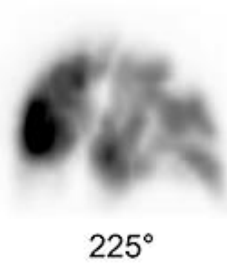


SPECT vs Planar VQ in CTEPH

Planar perfusion scans



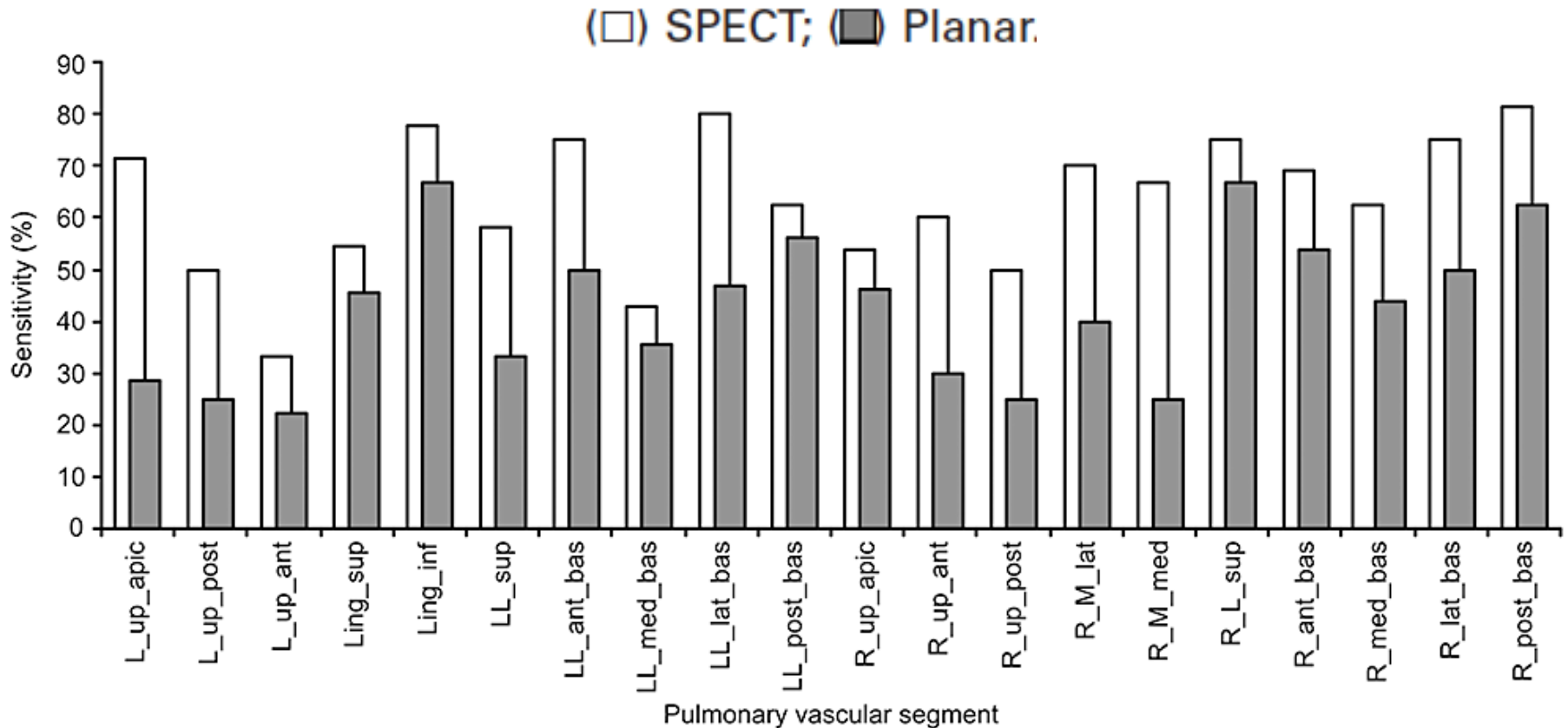
SPECT perfusion scans



1. Soler X, Hoh CK, Test VJ, Kerr KM, Marsh JJ, Morris TA. Single photon emission computed tomography in chronic thromboembolic pulmonary hypertension. *Respirology* 2011;16(1):131-137.



SPECT vs Planar VQ for CTEPH

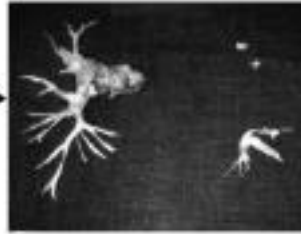


1. Soler X, Hoh CK, Test VJ, Kerr KM, Marsh JJ, Morris TA. Single photon emission computed tomography in chronic thromboembolic pulmonary hypertension. *Respirology* 2011;16(1):131-137.

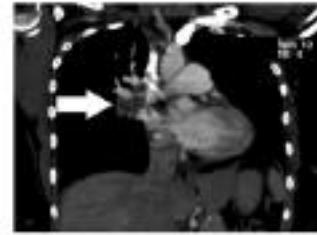
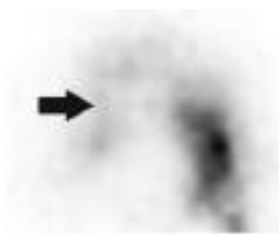


Planar VQ vs CT for CTEPH

Planar VQ



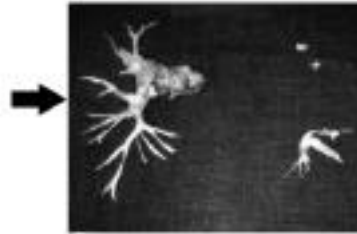
CT



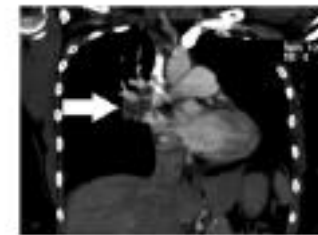
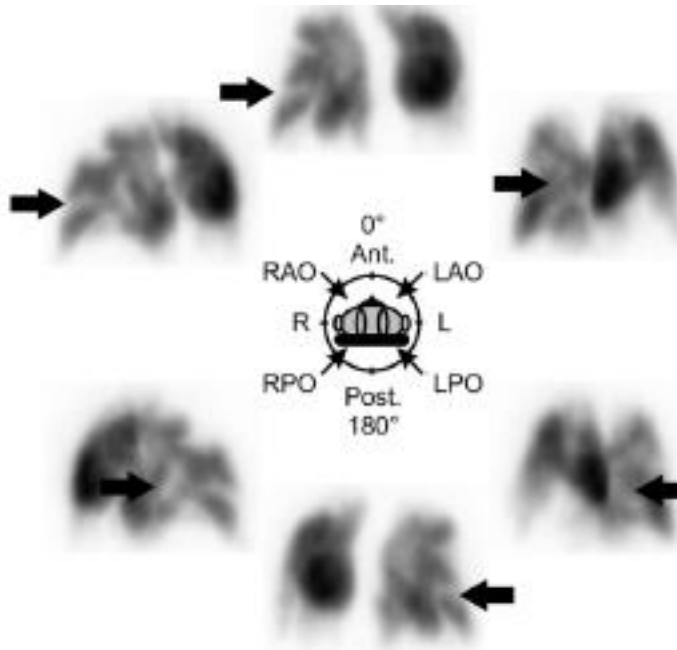
1. Soler X, Kerr KM, Marsh JJ, Renner JW, Hoh CK, Test VJ, et al. Pilot study comparing SPECT perfusion scintigraphy with CT pulmonary angiography in chronic thromboembolic pulmonary hypertension. *Respirology* 2012;17(1):180-184.

SPECT vs CT for CTEPH

SPECT



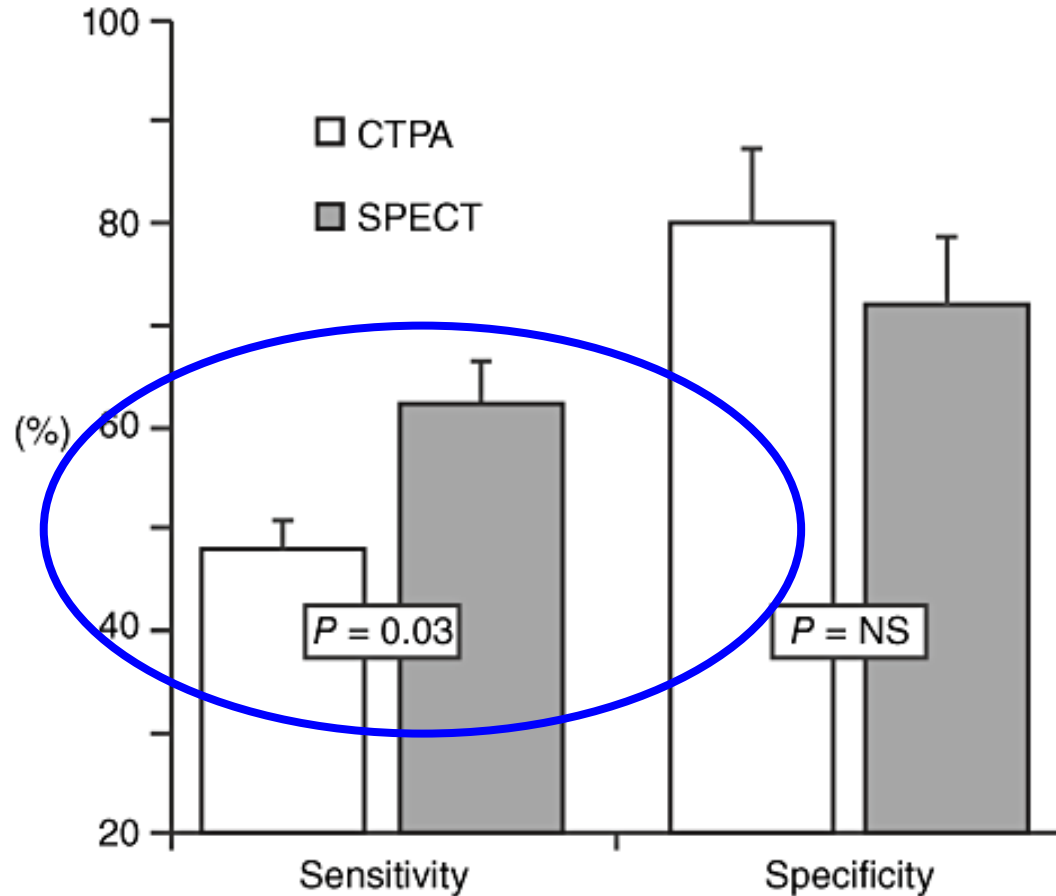
CT



1. Soler X, Kerr KM, Marsh JJ, Renner JW, Hoh CK, Test VJ, et al. Pilot study comparing SPECT perfusion scintigraphy with CT pulmonary angiography in chronic thromboembolic pulmonary hypertension. *Respirology* 2012;17(1):180-184.



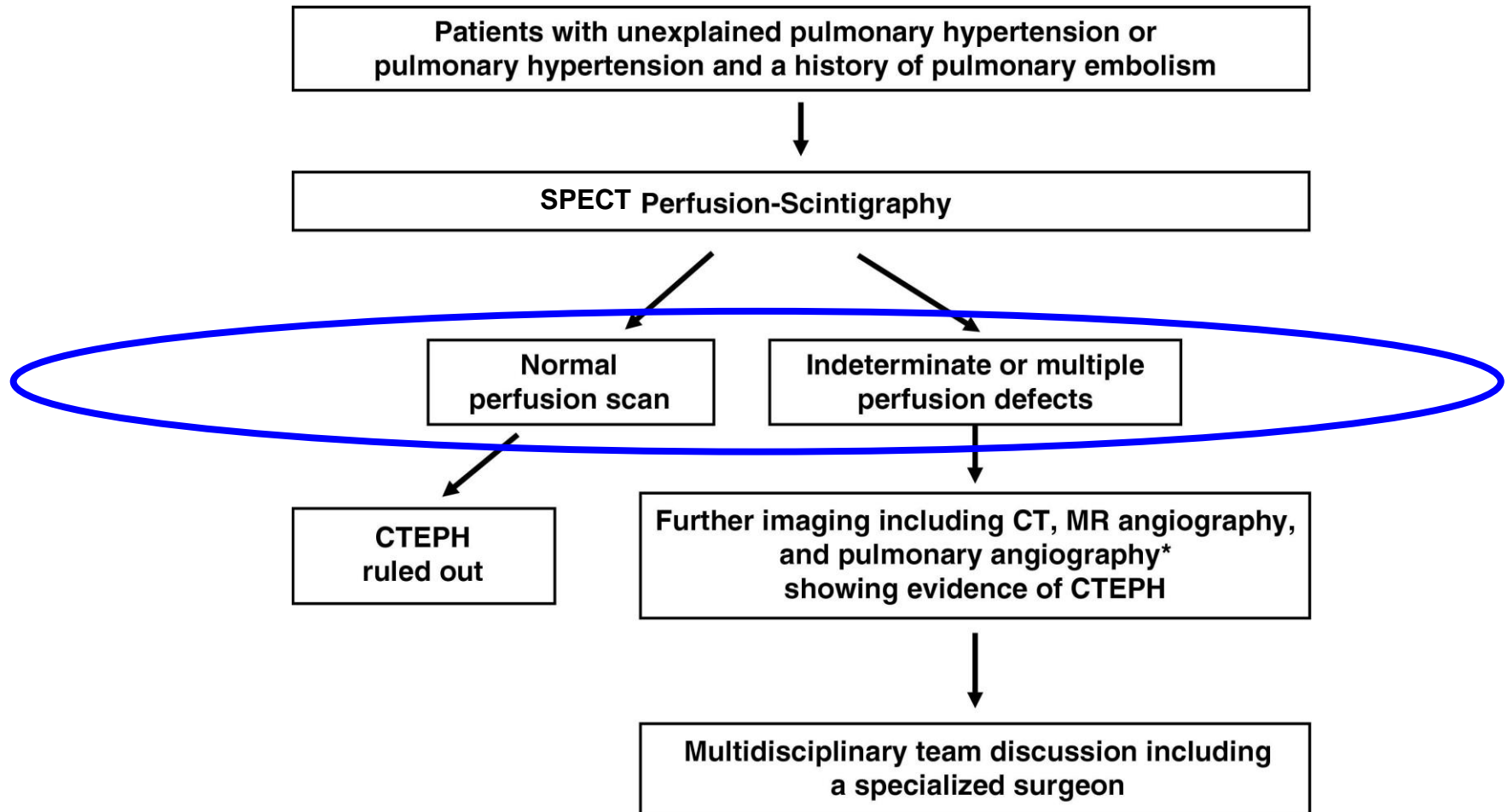
SPECT VQ vs CT for CTEPH



1. Soler X, Kerr KM, Marsh JJ, Renner JW, Hoh CK, Test VJ, et al. Pilot study comparing SPECT perfusion scintigraphy with CT pulmonary angiography in chronic thromboembolic pulmonary hypertension. *Respirology* 2012;17(1):180-184.



General Diagnostic Approach



1. Hoeper MM, Barbera JA, Channick RN, Hassoun PM, Lang IM, Manes A, et al. Diagnosis, assessment, and treatment of non-pulmonary arterial hypertension pulmonary hypertension. *Journal of the American College of Cardiology* 2009;54(1 Suppl):S85-96.



Echocardiogram

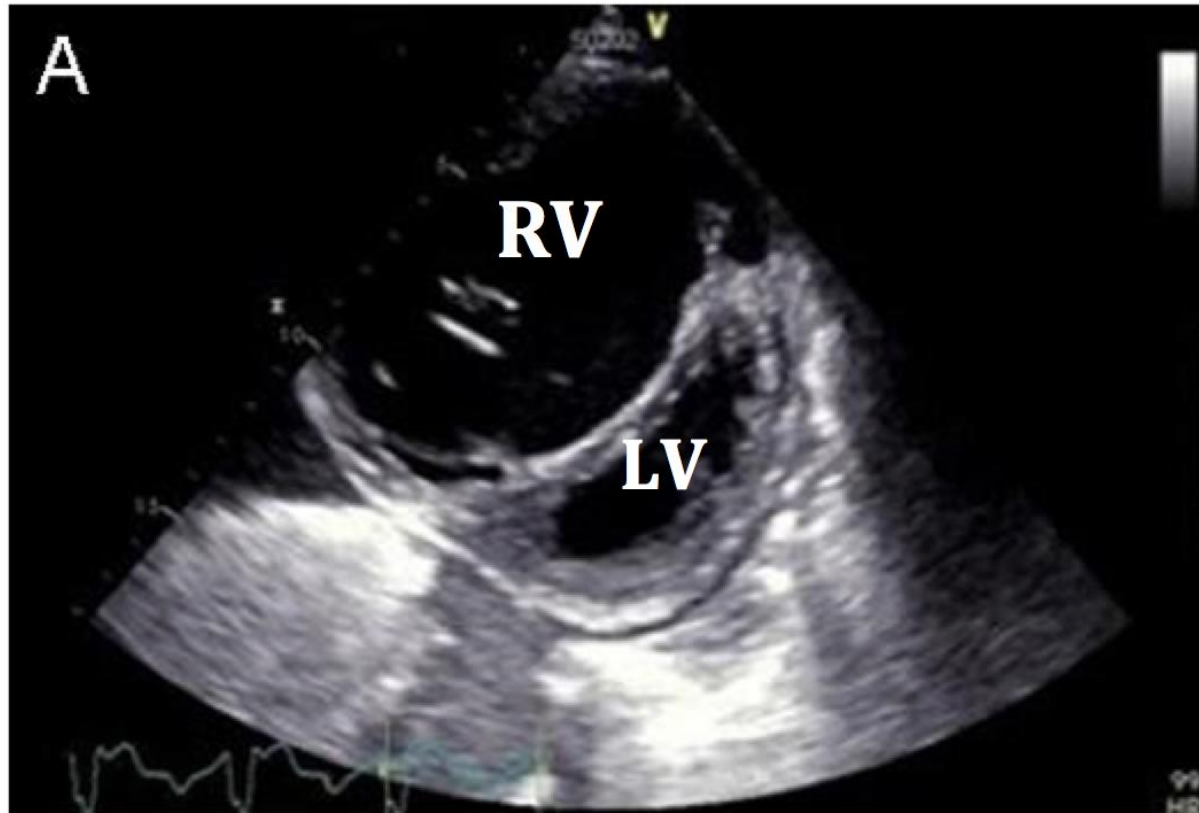
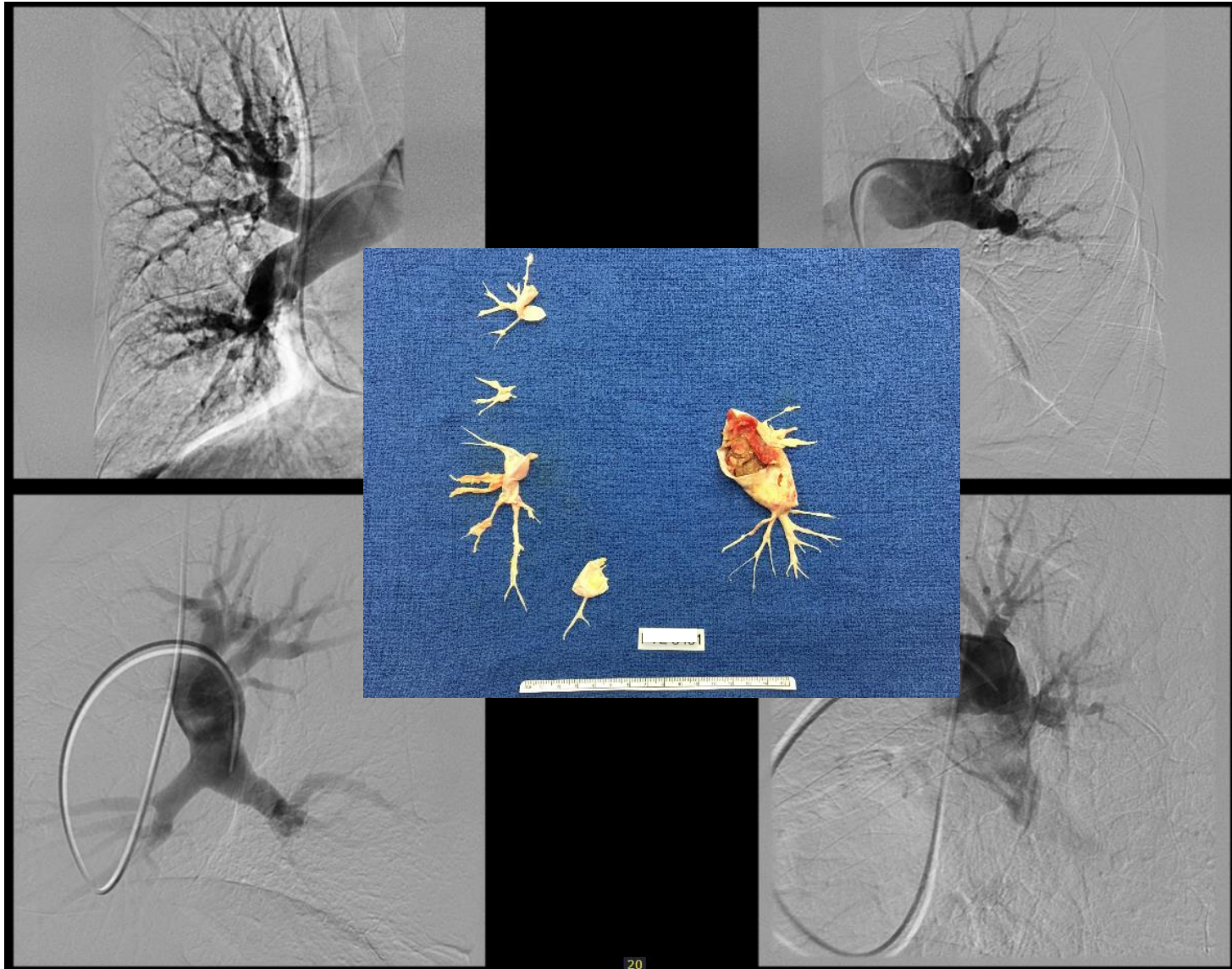


Figure 1. Parasternal short axis view of right ventricular dilation and interventricular septal shift

Courtesy of Victor Test, MD, Duke University Medical Center

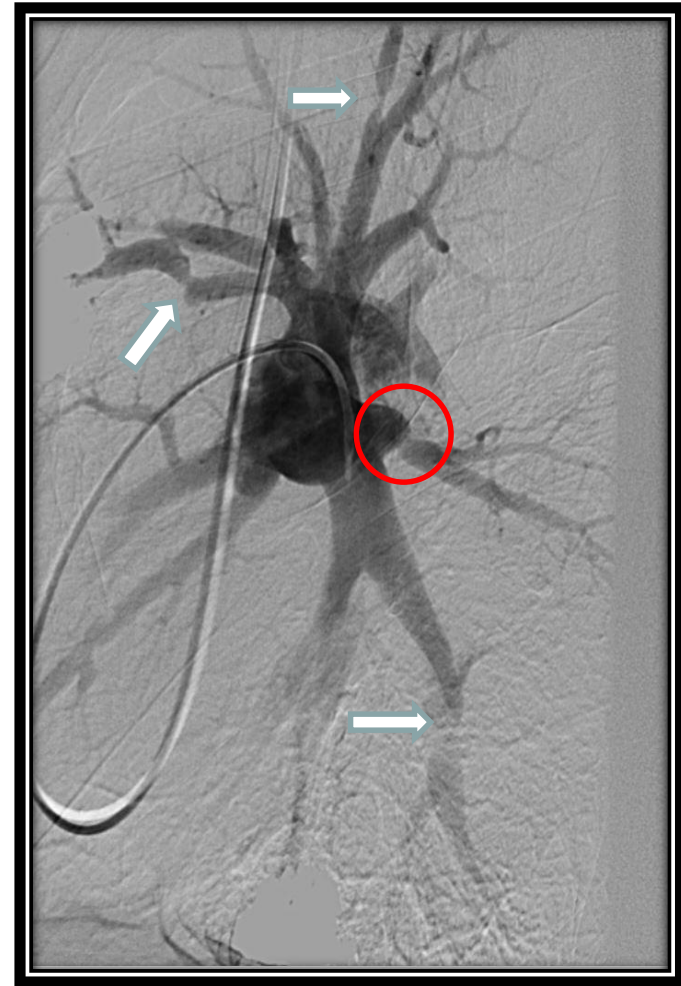
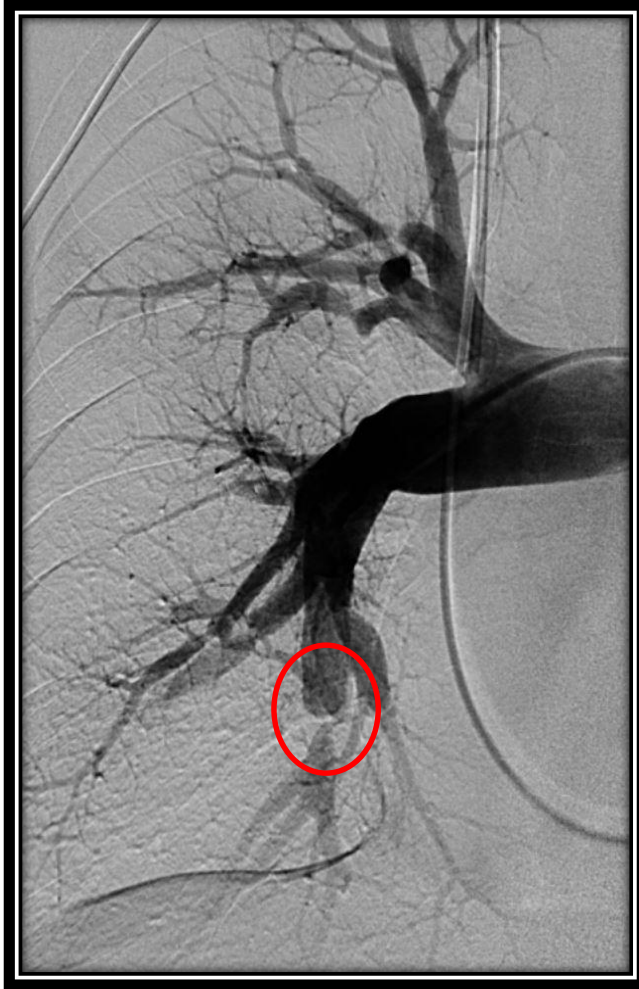


Pulmonary Angiogram: Gold Standard





CTEPH diagnosis by angiogram



Courtesy of William R. Auger, MD, University of California, San Diego

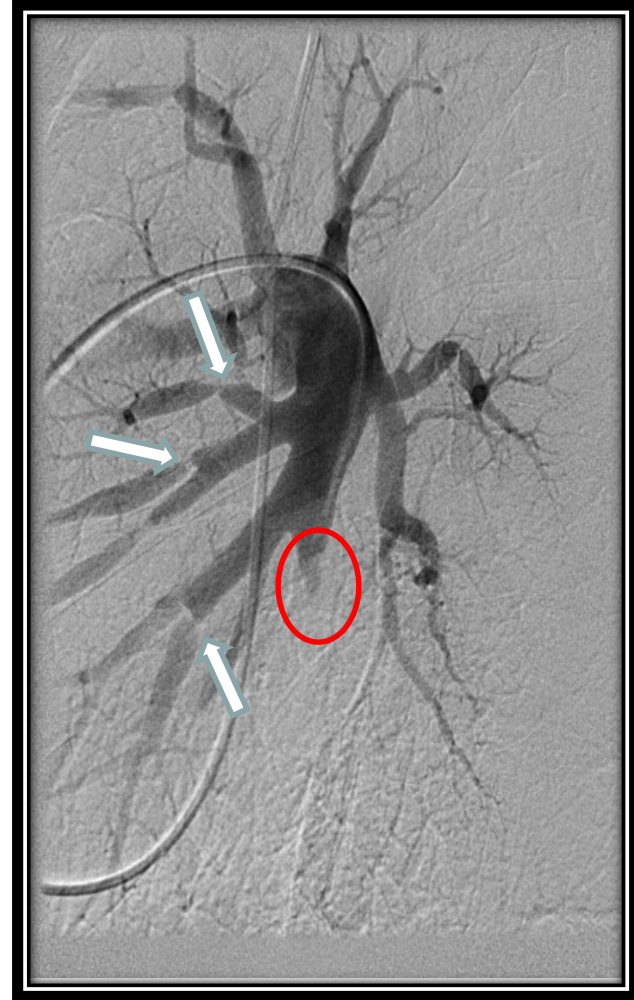


Pulmonary Angiogram: Mapping

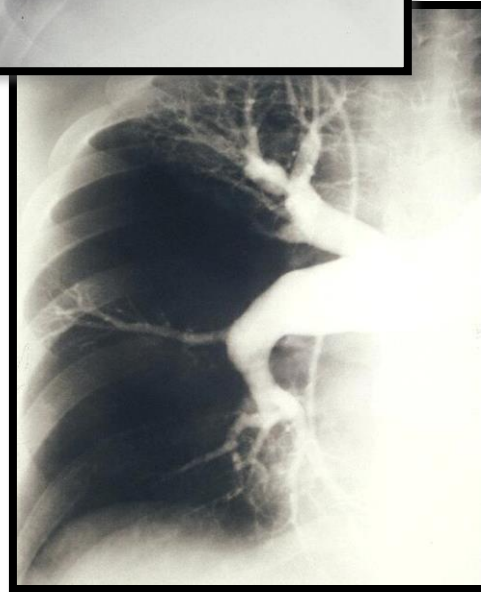
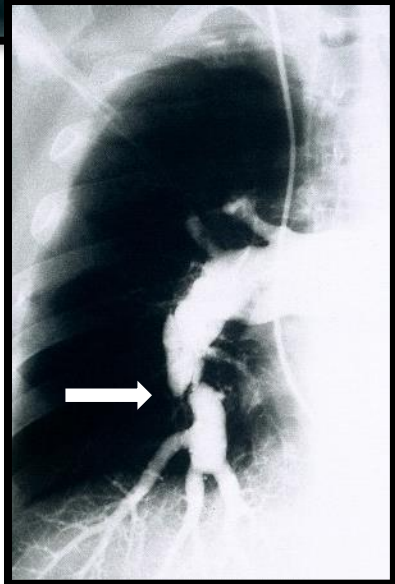
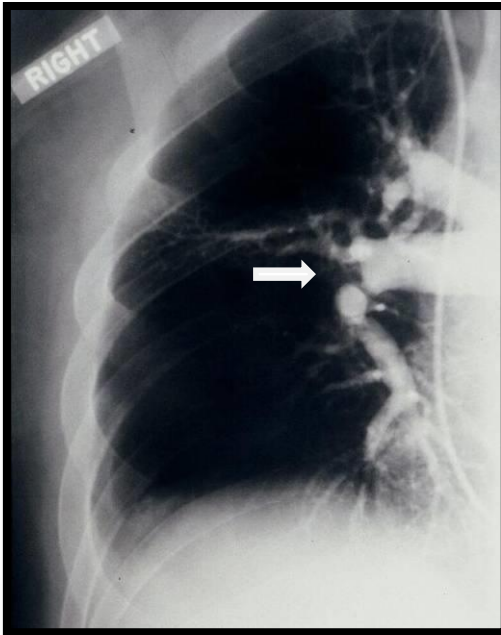
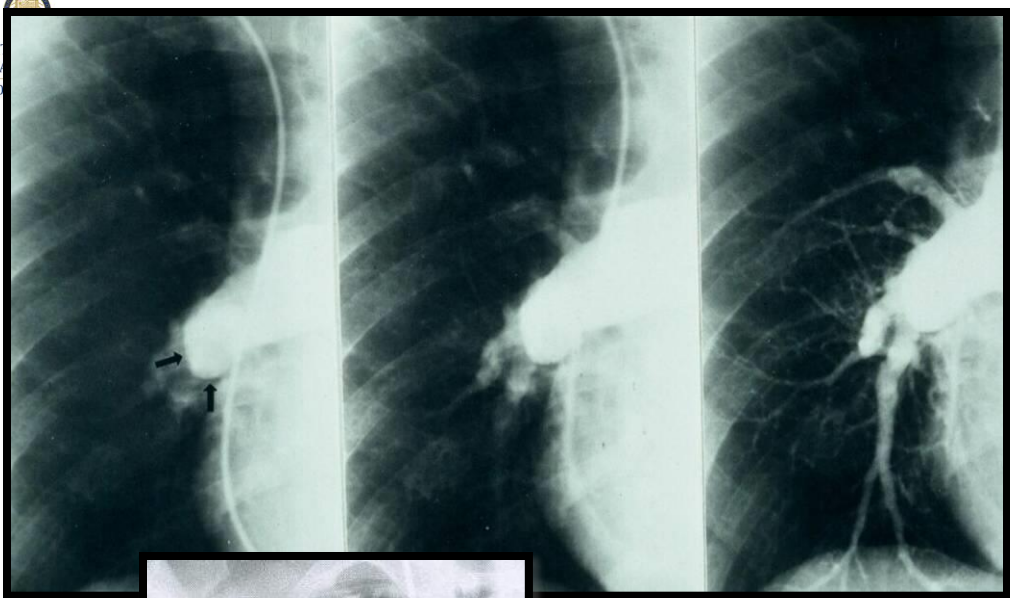
PA



LAT



Courtesy of William R. Auger, MD, University of California, San Diego



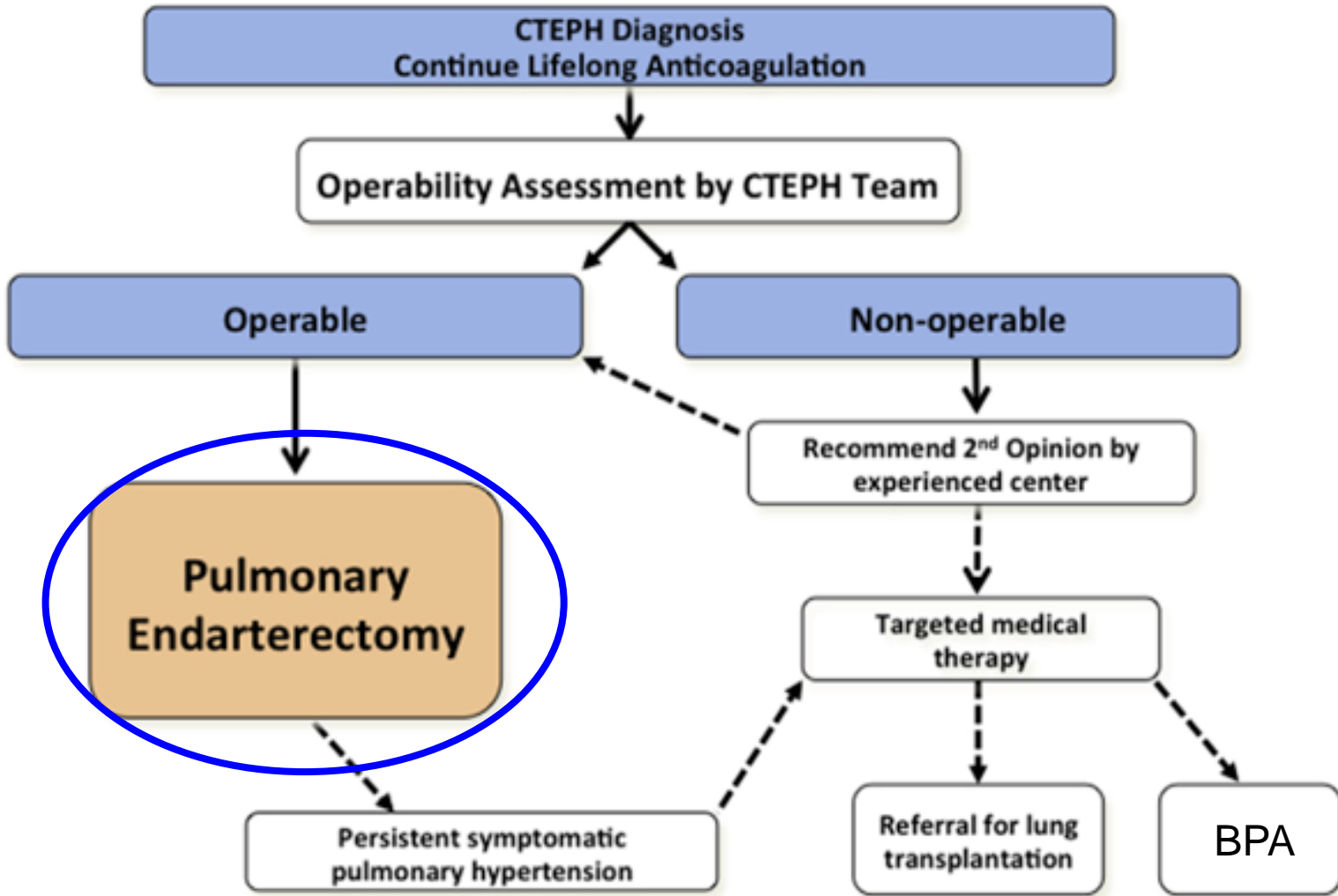
Courtesy of William R. Auger, MD, University of California, San Diego



CTEPH and Pulmonary Angiography

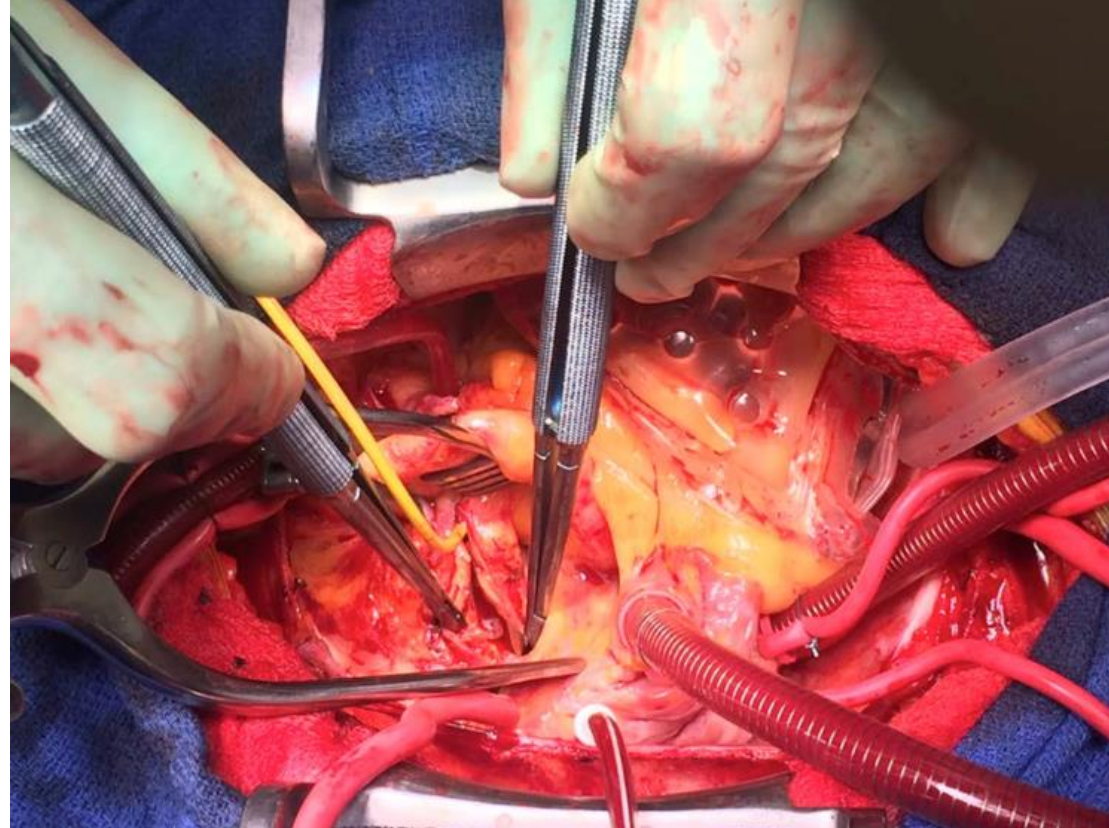
- Hemodynamic assessment at time of procedure
- Complete assessment process for surgical candidacy

CTEPH Treatment Guidelines



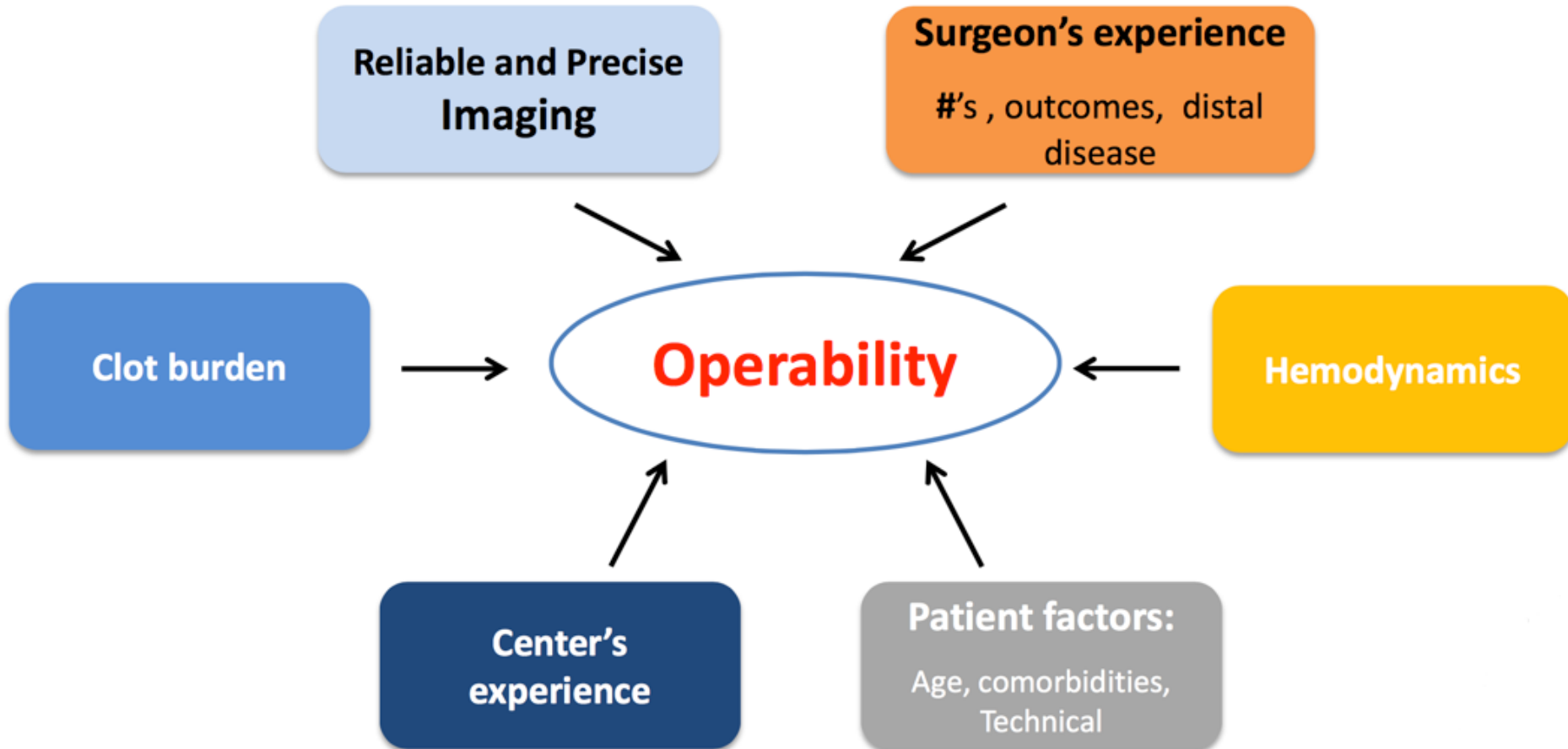


PTE: Tools and Technique



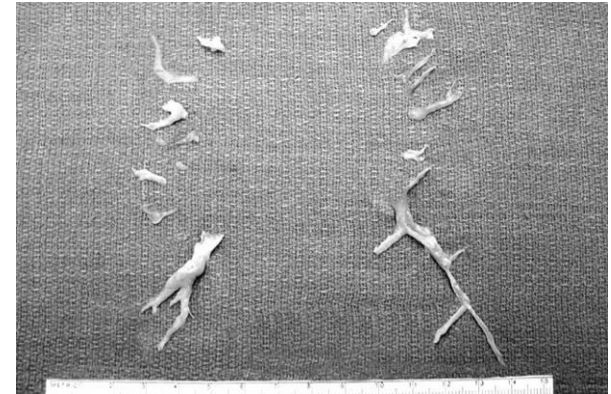
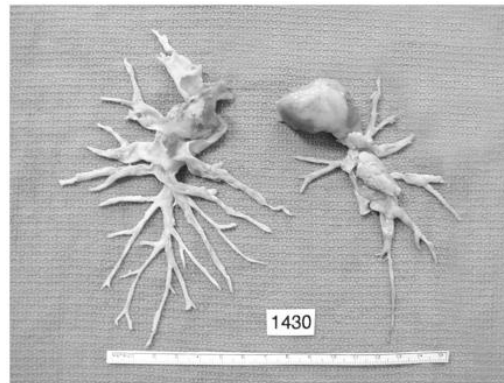


PTE Operability Assessment

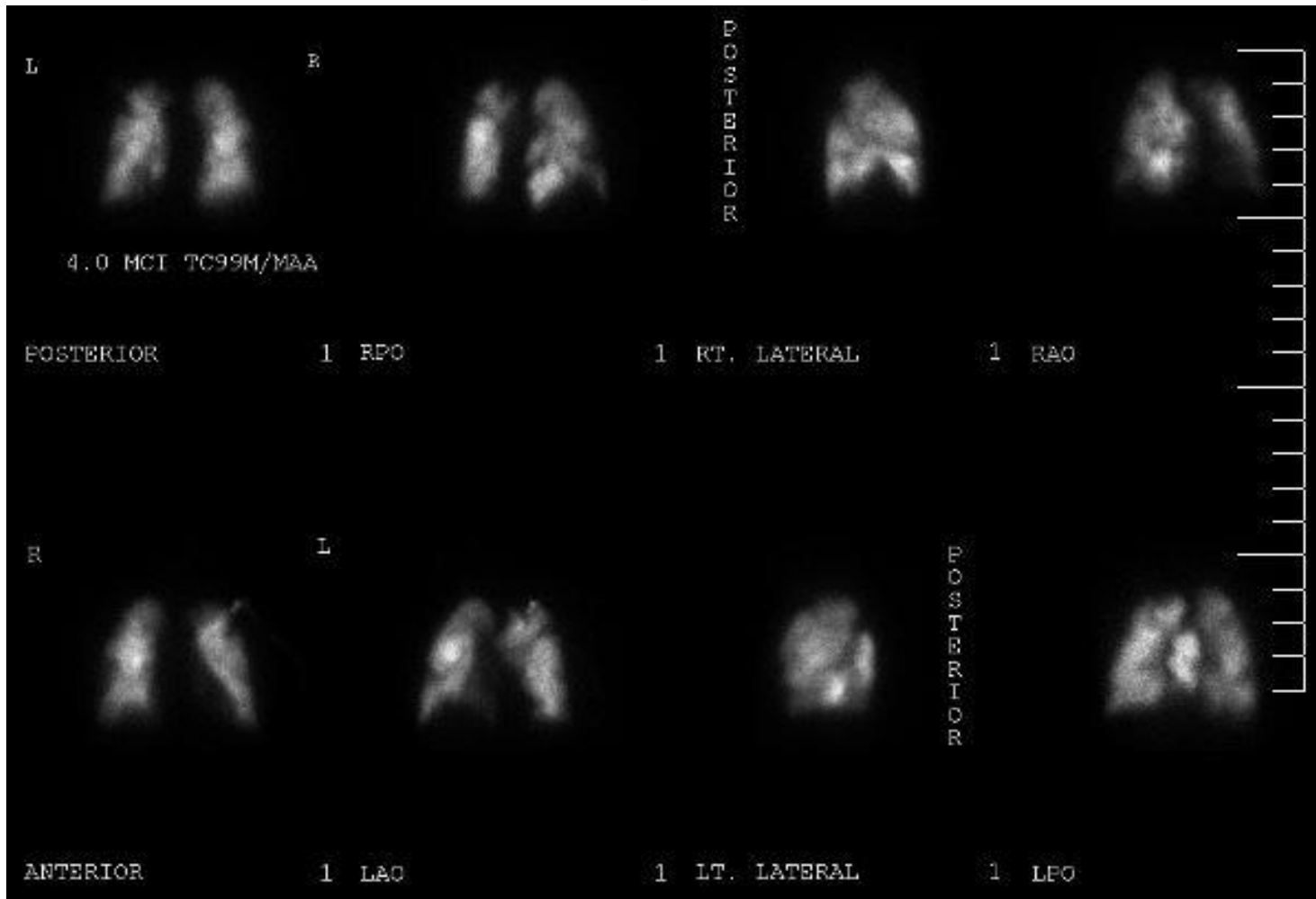




CTEPH: Pulmonary endarterectomy



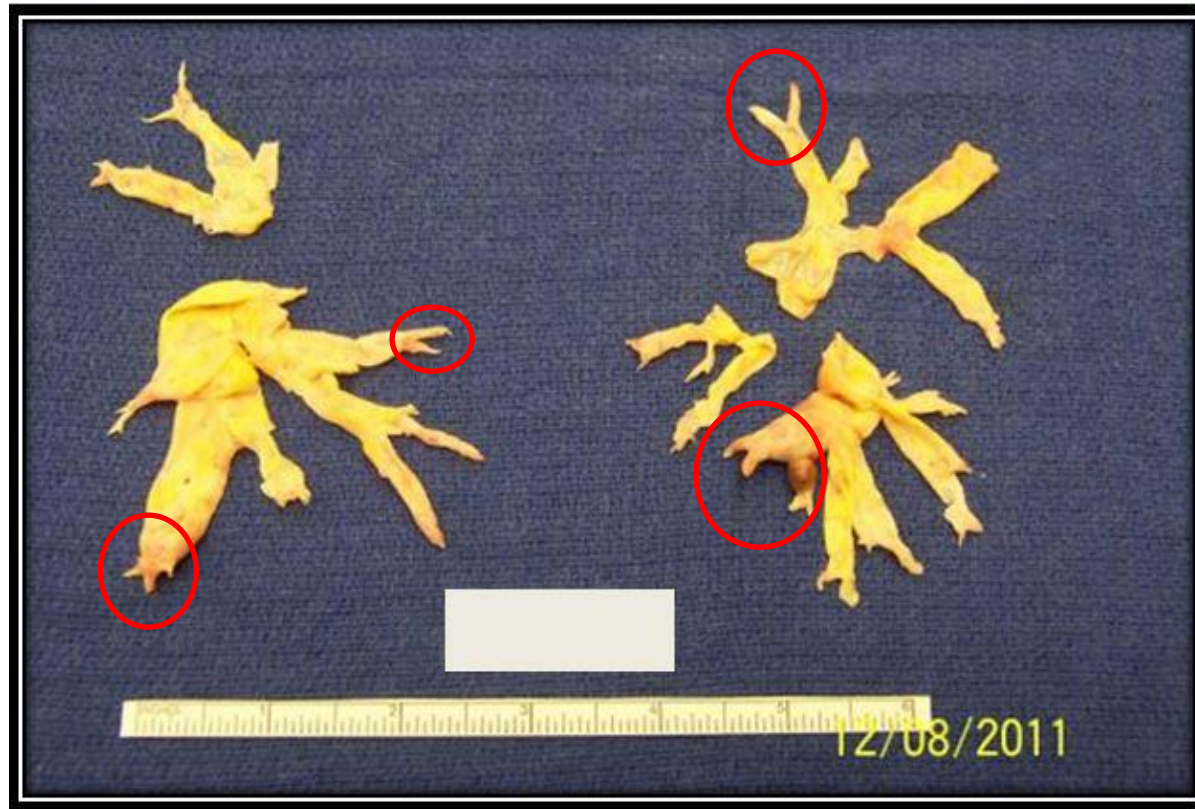
Even small perfusion defects can be important



Courtesy of William R. Auger, MD, University of California, San Diego



CTEPH specimen in “small defect” patient

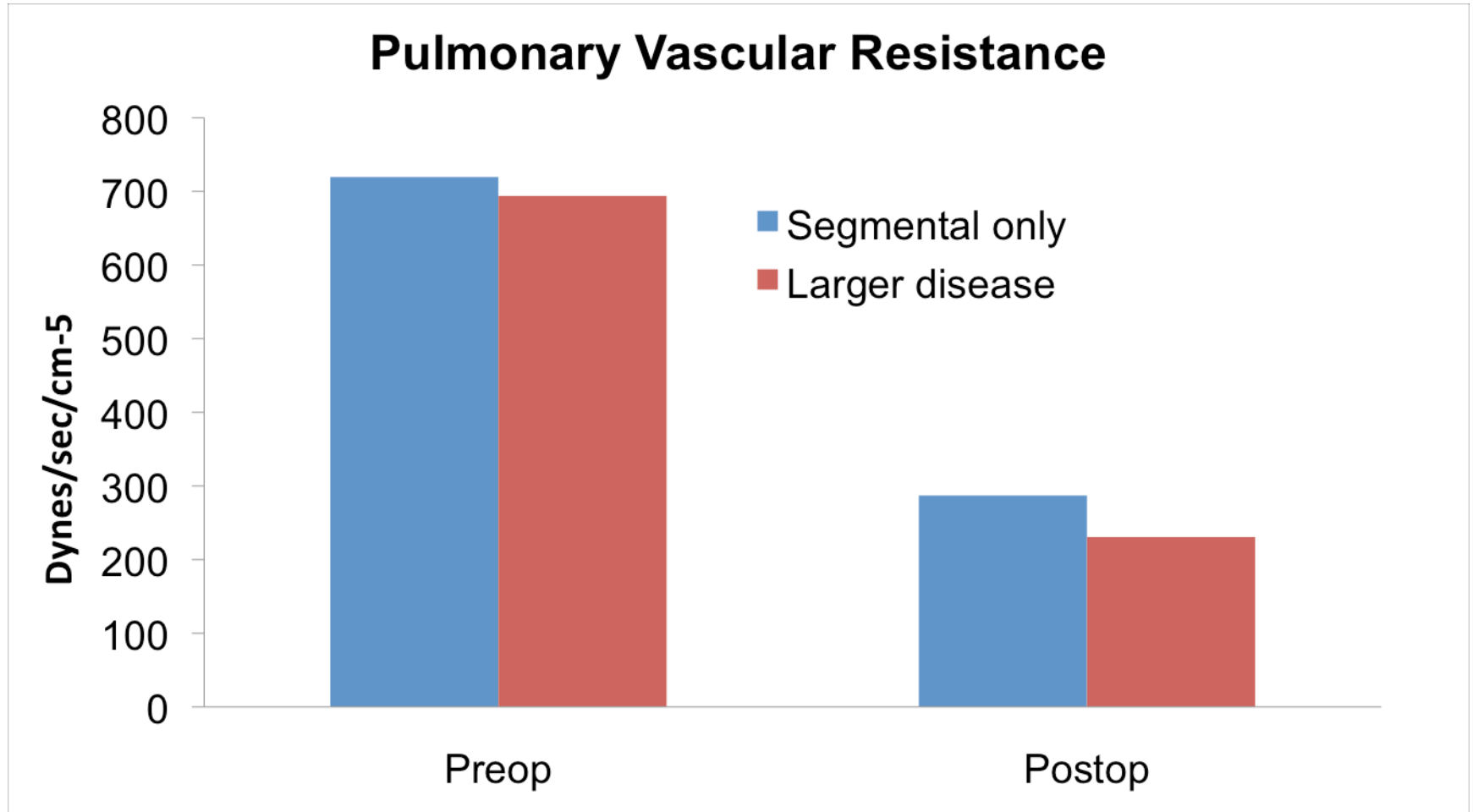


POSTOP: CVP 7 PAp 37/12 (21) CO 5.3 l/min PVR 211

Courtesy of William R. Auger, MD, University of California, San Diego

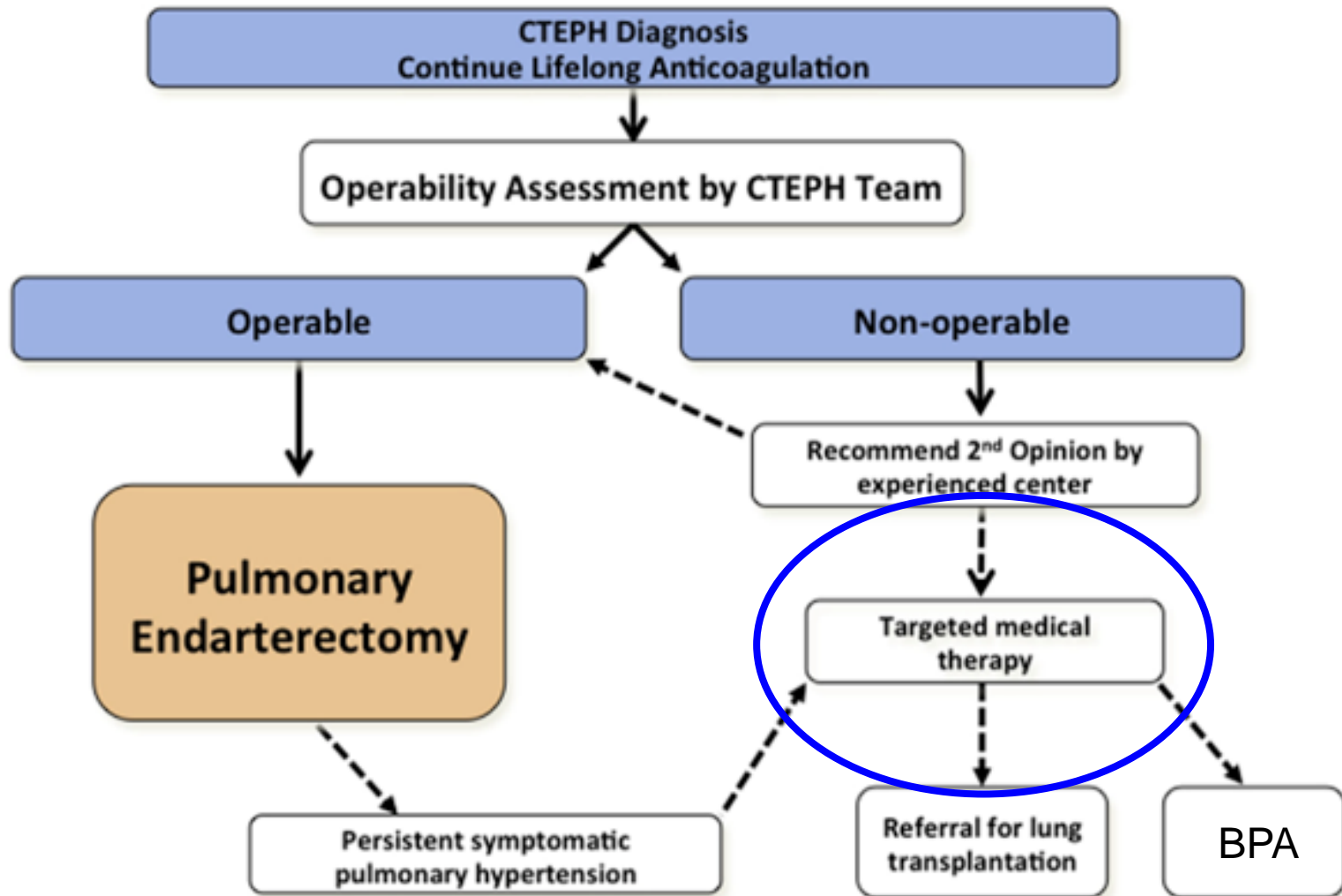


Hemodynamic Outcomes: Segmental level resection

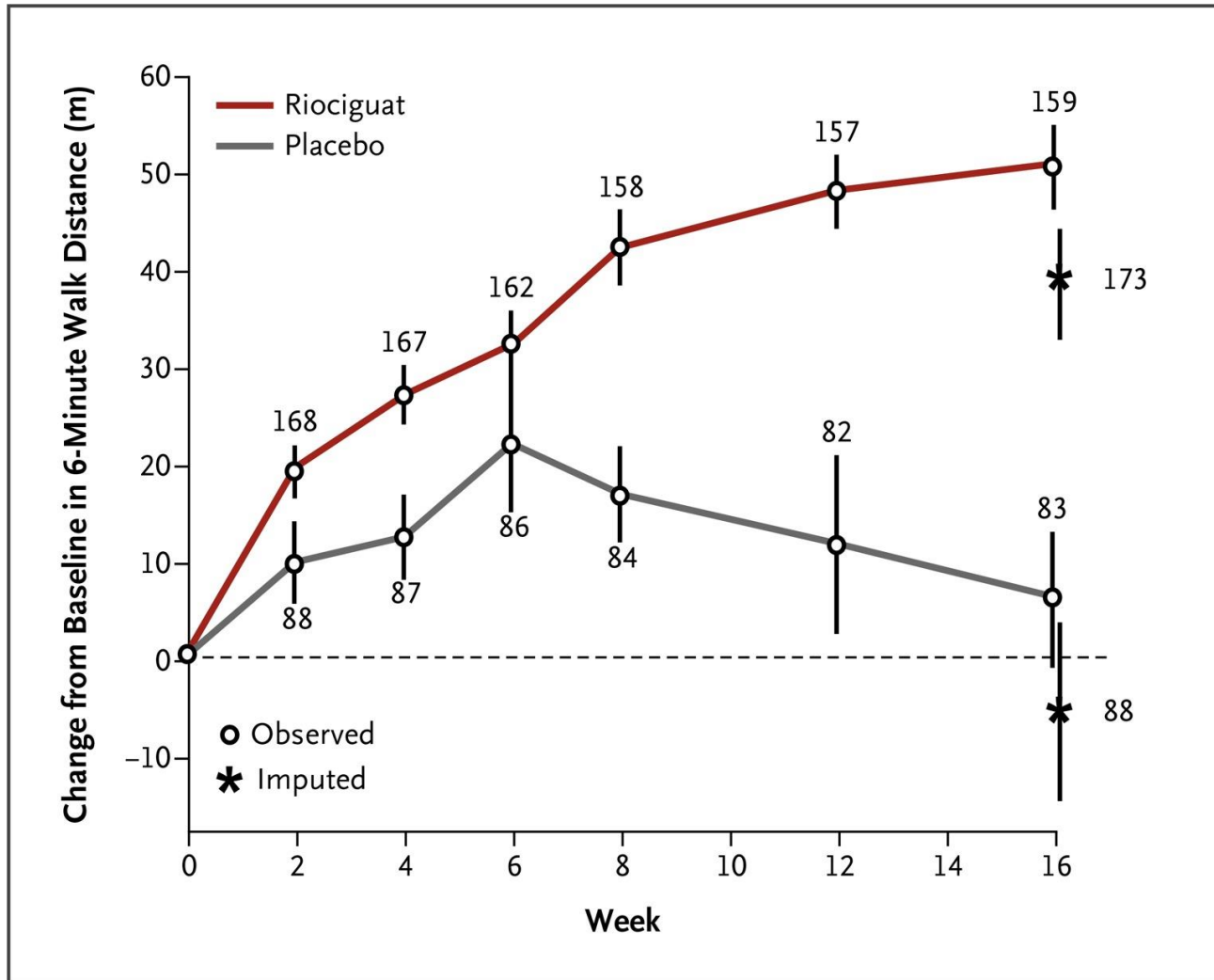


Courtesy of William R. Auger, MD, University of California, San Diego

CTEPH Treatment Guidelines



CHEST-1: Mean Change from Baseline in the 6-Minute Walk Distance with Riociguat



Ghofrani H-A et al. N Engl J Med 2013;369:319-329



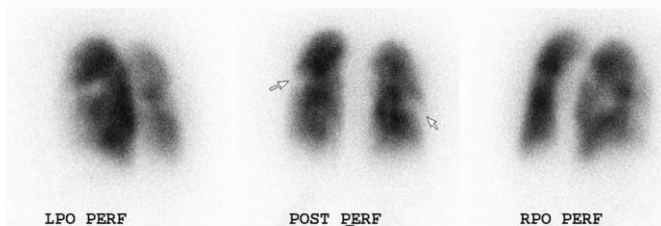
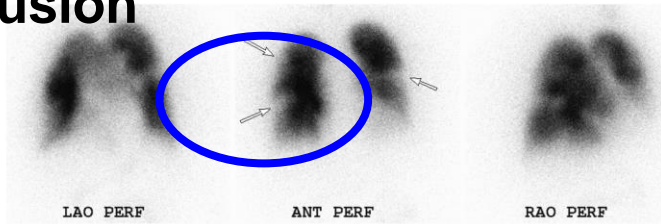
UNIVERSITY of CALIFORNIA
SAN DIEGO
SCHOOL OF MEDICINE

New nuclear medicine techniques for CTEPH?

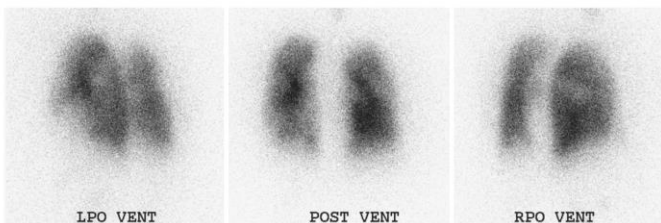
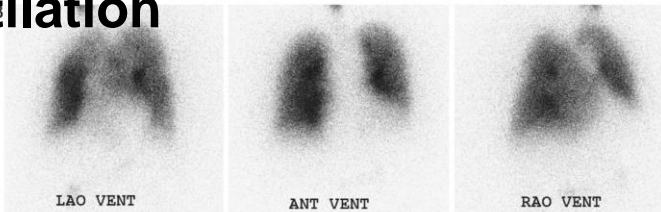


Planar V/Q

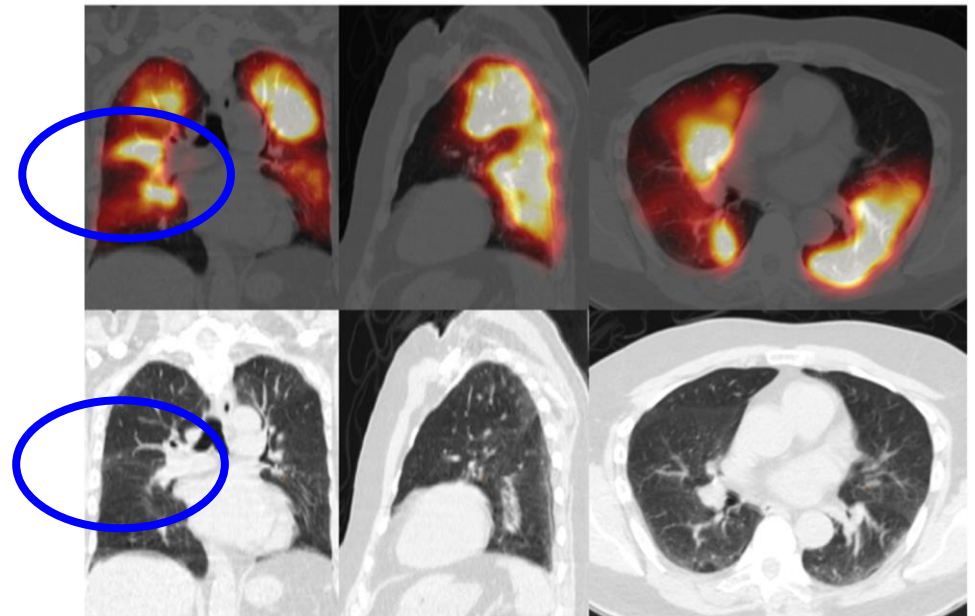
Perfusion



Ventilation



Q-SPECT/CT



1. Lu Y, Lorenzoni A, Fox JJ, Rademaker J, Vander Els N, Grewal RK, et al. Noncontrast perfusion single-photon emission CT/CT scanning: a new test for the expedited, high-accuracy diagnosis of acute pulmonary embolism. *Chest* 2014;145(5):1079-1088.



Feedback about VQ scans from cardiologist and pulmonologist

- “Nuclear medicine lung scans are not available in my hospital.”
 - During nights and weekends
 - Any time
- “Lung scans are too hard to read.”
- “Not enough experience in lung scans.”



Conclusions

- CTEPH should be considered in
 - “Acute PE” with signs of pulmonary hypertension
 - Post-PE dyspnea
 - Unexplained dyspnea.
- VQ scan is the best screening study for CTEPH
 - Respect small defects!
- SPECT may improve sensitivity
- Pulmonary angiography is the best definitive test
- Centers with expertise in CTEPH should assist in operability assessment