

Sub-segmental PE – To Treat or not to Treat



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Disclosures

- Consultant for / research support from
 - Astellas
 - Bayer
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 - GE Healthcare
 - Guerbet
 - Medrad
 - Siemens Healthcare

OUTLINE

- I. Background/ Definitions
- II. Diagnosis of subsegmental PE (SSPE)
- III. Clinical Significance
- IV. Management/ Controversies



Background

- Traditionally, all PEs are treated in the same manner with anticoagulation independently of size, number and location of thrombi
- MD-CTPA increases the visualization of peripheral arteries => increased detection rate of small PEs

Do they all need to be treated ?

Isolated Sub Segmental PE

- Sub-segmental artery = artery derived directly from a segmental division (4th generation and further)
- Defect limited to sub-segmental arteries



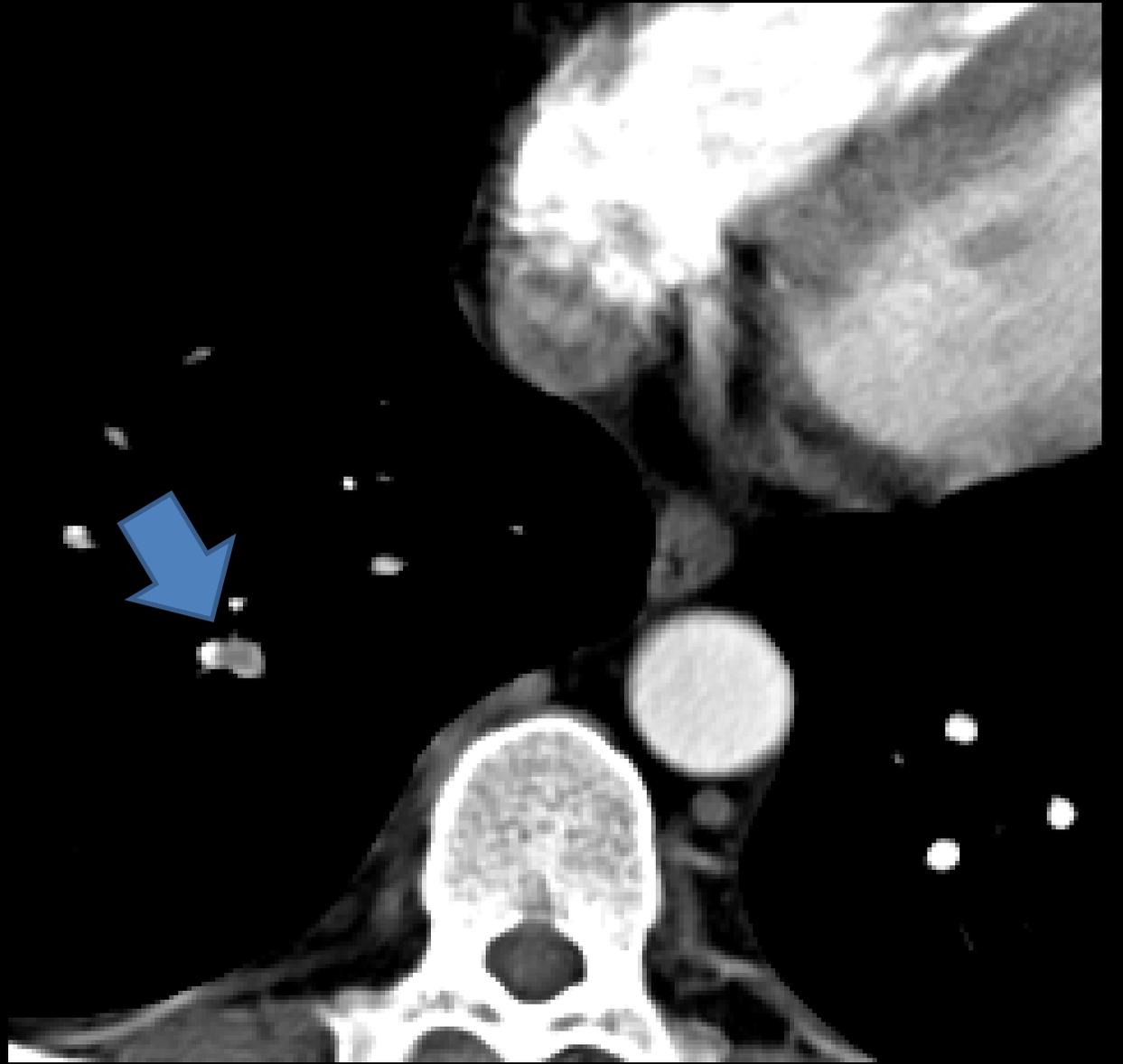
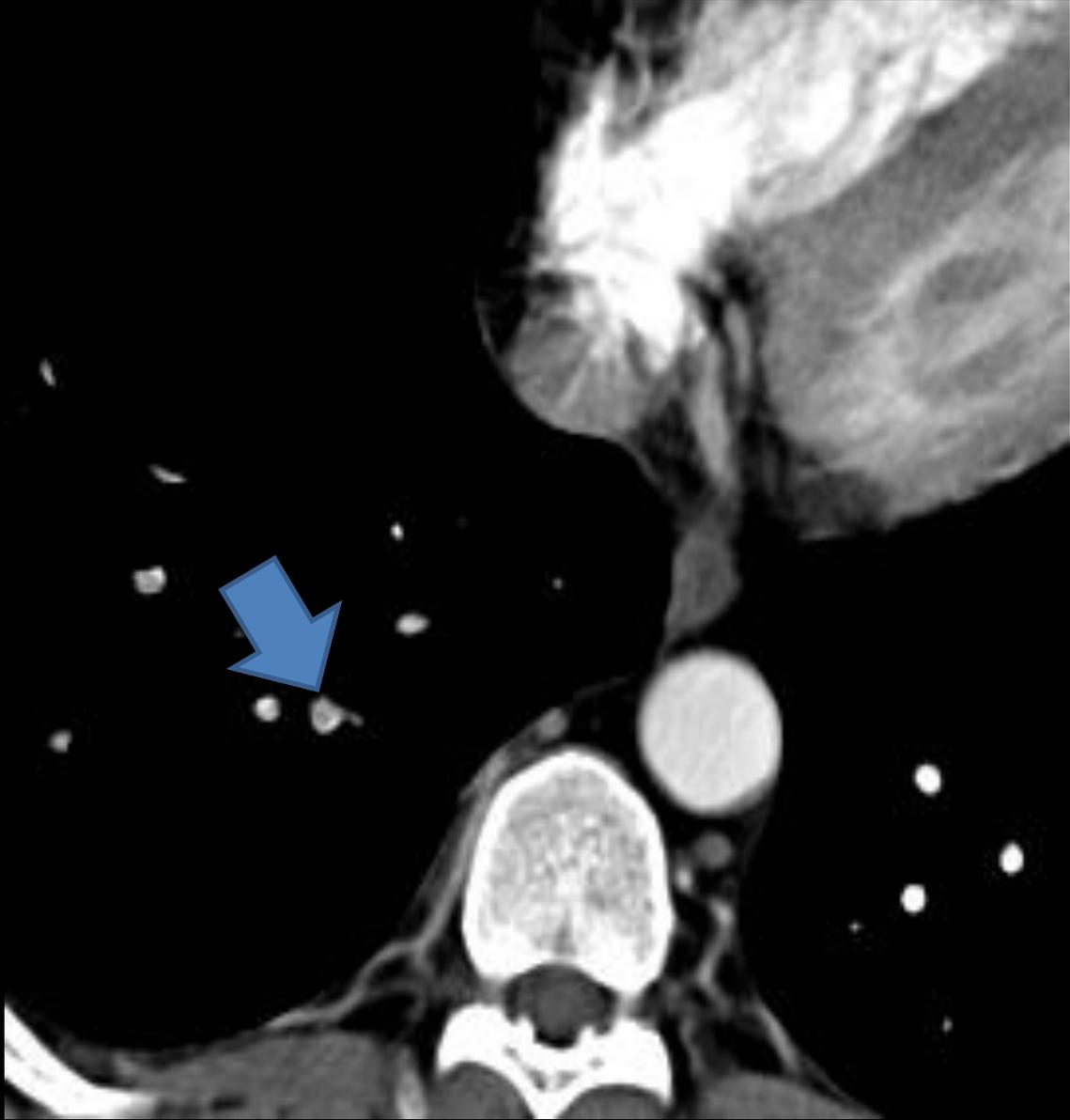
Schoepf et al., Circulation 2004

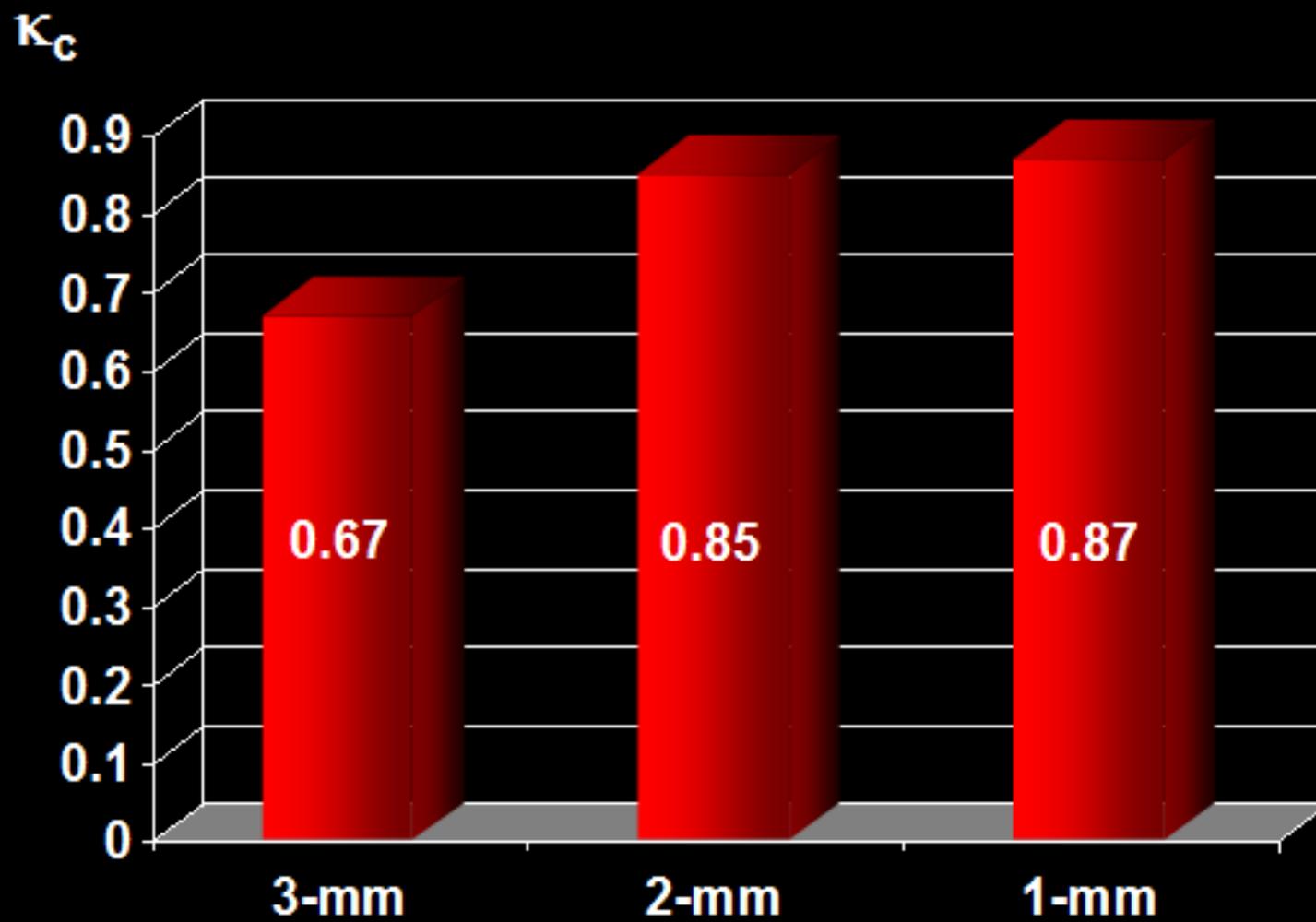
Jackson and Huber nomenclature [14]	Boyden nomenclature [12]		subsegmental arteries
	Segments	segmental arteries	
right upper lobe			
apical	S1	RA1	RA1a RA1b
anterior	S2	RA2	RA2a RA2b
posterior	S3	RA3	RA3a RA3b
Right middle lobe			
lateral	S4	RA4	RA4a RA4b
medial	S5	RA5	RA5a RA5b
right lower lobe			
apical	S6	RA6	RA6a+b RA6c
medial basal	S7	RA7	RA7a RA7b
anterior basal	S8	RA8	RA8a RA8b
lateral basal	S9	RA9	RA9a RA9b
posterior basal	S10	RA10	RA10a RA10b
left upper lobe			
apicoposterior	S1+3	LA1	LA1a LA1b LA3a LA3b
anterior	S2	LA2	LA2a LA2b
lower division			
superior lingula	S4	LA4	LA4a LA4b
inferior lingula	S5	LA5	LA5a LA5b
left lower lobe			
apical	S6	LA6	LA6a+b LA6c
arteromedial basal	S7+8	LA7+8	LA7a LA7b LA8a LA8b
lateral basal	S9	LA9	LA9a LA9b
posterior	S10	LA10	LA10a LA10b

Diagnosis

Spiral CT – Gold Standard

- MDCT pulmonary angiography is now the gold standard for PE diagnosis
- Thin sections increase diagnostic accuracy of SSPE





Schoepf et al., *Radiology* 2002

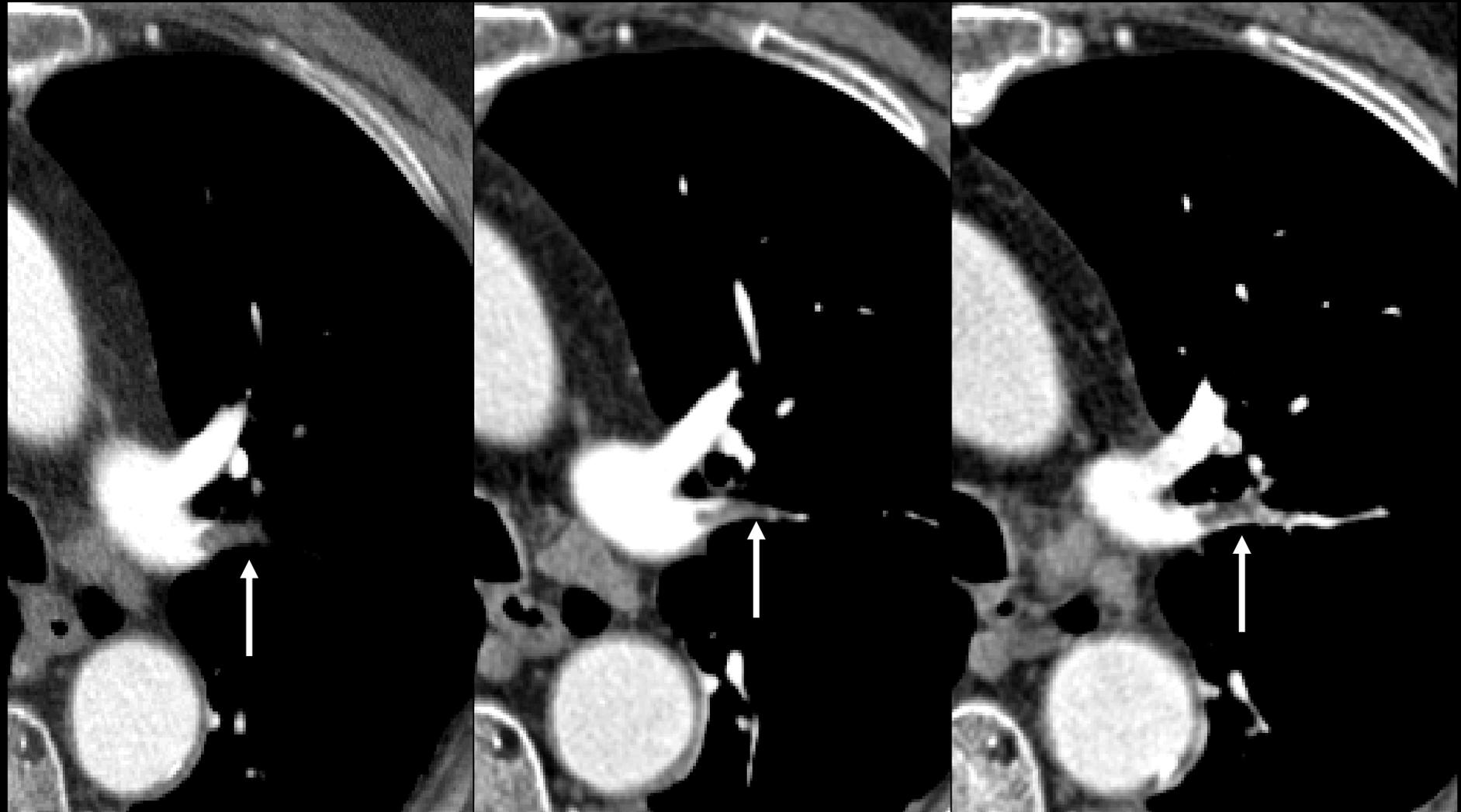
Author	Journal	Modality	Slice	Segmental	Subsegmental
Remy-Jardin	Radiology	SCT	3-mm	85 %	37 %
Remy-Jardin	Radiology	SCT	2-mm	93 %	61 %
Schoepf	Radiology	SCT	3-mm	84 %	72 %
Schoepf	Radiology	EBCT	3-mm	93 %	78 %
Ghaye	Radiology	4SLCT	3-mm	NA	84 %
Ghaye	Radiology	4SLCT	1-mm	NA	94 %
Schoepf	Radiology	4SLCT	3-mm	NA	86 %
Schoepf	Radiology	4SLCT	2-mm	NA	93 %
Schoepf	Radiology	4SLCT	1-mm	NA	97 %
Herzog	RSNA	16SLCT	0.7-mm	100%	99 %

Herzog RSNA 16SLCT 0.7-mm 100% 99 %

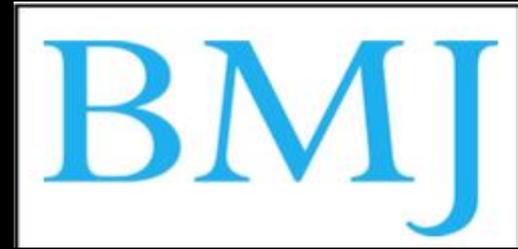
3 mm

2 mm

1 mm



When a test is too good: how CT pulmonary angiograms find pulmonary emboli that do not need to be found



From 2001-2008: 14-fold increase in use of CTPA



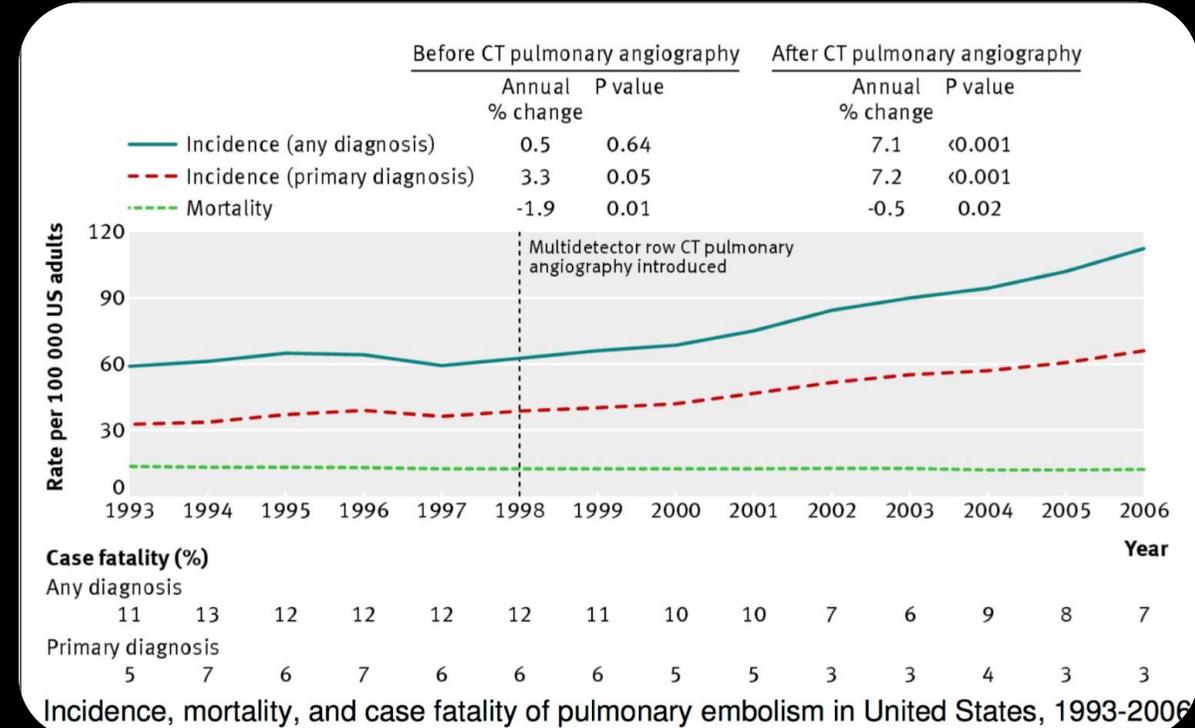
80% increase in PE diagnosis

BUT

NO change in age adjusted mortality



Increase in diagnosis rate of low severity disease



Wiener RS et al. When a test is too good: how CT pulmonary angiograms find pulmonary emboli that do not need to be found. *BMJ* 2013

Symptomatic subsegmental pulmonary embolism: what is the next step?

Table 1 Rate of SSPE diagnosis and 3-month risk of VTE in patients with and without PE according to the number of CTPA detectors

	SDCT	All MDCT	MDCT 4 detectors	MDCT 16 detectors	MDCT 64 detectors
Rate of SSPE diagnosis					
No. of patients with PE	1123	1534	461	207	100
Proportion of SSPE, % (95% CI)	4.7 (2.5–7.6)	9.4 (5.5–14.2)	7.1 (3.8–11.3)	6.9 (0.7–23.3)	15.0 (7.7–24.1)
3-month risk of VTE					
No. of patients without PE	1943	2982	547	424	239
3-month risk, % (95% CI)	0.9 (0.4–1.4)	1.1 (0.7–1.4)	1.4 (0.7–2.7)	0.6 (0.1–1.6)	0.8 (0.1–3.0)

CI, confidence intervals; CTPA, computed tomography pulmonary angiography; MDCT, multi-detector computed tomography; SDCT, single-detector computed tomographic pulmonary angiography; SSPE, subsegmental pulmonary embolism.

Increase in proportion of SSPE detected with more advanced CT technology

Qualitative analysis: percentage of lobes with central vascular enhancement score ≥ 3 and percentage of lobes with peripheral vascular enhancement score = 5 at 80 kVp and 140 kVp imaging.

	CVE score ≥ 3			PVE score = 5		
	80 kVp	140 kVp	p value	80 kVp	140 kVp	p value
CTPA (n = 100)	100%	86%	p < 0.0001	92%	53%	p < 0.0001
RT (n = 98)	100%	78%	p < 0.0001	89%	26%	p < 0.0001
RC (n = 47)	100%	90%	p < 0.0001	84%	16%	p = 0.028

Note: CVE = central vascular enhancement; PVE = peripheral vascular enhancement; CTPA = CT pulmonary angiography; RT = routine chest CT study; RC = reduced contrast volume CT pulmonary angiography.

Lower kV further increases peripheral vascular visibility

Is it really PE ?

Multidetector Computed Tomography (MDCT) in the Diagnosis of Pulmonary Embolism: Interobserver Agreement among Radiologists with Varied Levels of Experience

ACTA
RADIOLOGICA

Table 3. Agreement between each observer as compared with the consensus reading on the most proximal level of PE estimated for each level separately

	Main pulmonary and lobar Agreement, % (κ)		Segmental Agreement, % (κ)		Subsegmental Agreement, % (κ)	
	R	L	R	L	R	L
Observer 1	91 (0.86)	90 (0.91)	78 (0.69)	92 (0.8)	71 (0.56)	94 (0.89)
Observer 2	98 (0.88)	88 (0.8)	78 (0.76)	83 (0.5)	28 (0.4)	33 (0.43)
Observer 3	98 (0.86)	95 (0.85)	78 (0.73)	69 (0.55)	0 (0.0)	19 (0.28)
Observer 4	84 (0.68)	91 (0.82)	56 (0.4)	88 (0.64)	29 (0.32)	13 (0.16)

Kappa values (κ) indicate agreement with consensus reading. Observers 1 and 2 were board-certified radiologists, whereas 3 and 4 were trainees with 2 years' experience. R: right; L: left.

The inter-observer agreement was lowest for SSPE with a mean k of 0.38

Ghanima et al. Multidetector computed tomography (MDCT) in the diagnosis of pulmonary embolism: interobserver agreement among radiologists with varied levels of experience. *Acta Radiologica* 2007

Is it really PE ?

Difference in interpretation of computed tomography pulmonary angiography diagnosis of subsegmental thrombosis in patients with suspected pulmonary embolism¹



The thoracic radiologist agreed with 51% of SSPE diagnosis

11% of SSPE were reinterpreted as negative

"Given the uncertainty around SSPE management, studies positive for SSPE should be reviewed by an expert thoracic radiologist"

Table 1 Index and thoracic radiologist's interpretations of the most proximal filling defect detected on CTPA

	Index interpretation				Total
	Lobar	Segmental	Subsegmental	Normal	
Thoracic radiologist's interpretation					
Lobar	0	2	26	0	28
Segmental	0	0	36	0	36
Subsegmental	0	0	8	4	12
Normal	0	0	0	4	4
Total	0	2	70	4	76

Overdiagnosis of Pulmonary Embolism by Pulmonary CT Angiography

TABLE I: Comparison of Contrast Enhancement, Patient Age, and Pulmonary Embolism (PE) Location in All and Discordant Pulmonary CT Angiography Examinations Reported as Positive for PE by the Original Radiologist

Variable	All Cases	Discordant Cases
Total	174 (100)	45 (25.9)
Patient age (y), mean (range)	64 (17–99)	60 (23–91)
Single-vessel PE	67 (38.5)	31 (46.2)
Multiple-vessel PEs	107 (61.5)	14 (13.1)
Mean quality of contrast enhancement (HU)	327.0	291.3 ^a
Pulmonary trunk PE	6 (3.4)	0 (0)
Main pulmonary artery PE	28 (16.1)	1 (4.0)
Lobar pulmonary artery PE	37 (21.3)	6 (16.2)
Segmental pulmonary artery PE	71 (40.8)	19 (26.8)
Subsegmental pulmonary artery PE	32 (18.4)	19 (59.4)

59.4% of SSPE were reinterpreted as negative

Hutchinson et al. **Overdiagnosis of Pulmonary Embolism by Pulmonary CT Angiography**. *American Journal of Roentgenology* 2015

Clinical Significance

Subsegmental pulmonary embolism: A narrative review☆

Table 1

Three months follow-up of patients with subsegmental pulmonary embolism.

Study		F/U (months)	Proportion of SSPE among positive CTPA %	SSPE not treated/total SSPE	VTE <i>n</i>	All-cause mortality <i>n</i>	Death due to VTE <i>n</i>
Musset et al. (2002)	SDCT	3	3.3	9/12	0	0	0
Perrier et al. (2005)	MDCT 16	3	1.0	1/2	0	0	0
Eyer et al. (2005)	MDCT 8, 16	3	15.4	25/67	0	5	0
Donato et al. (2010)	MDCT 64	3	7.9	21/92	0	0	0
Pena et al. (2012)	MDCT 64	3	9.6	18/70	0	N/A	0
Mehta et al. (2014)	MDCT	3	N/A	12/32	0	1	0
Goy et al. (2015)	MDCT 16	3	15.0	30/73	0	N/A	0

Small retrospective studies show no recurrent VTE in patients with SSPE left untreated

Symptomatic subsegmental pulmonary embolism: what is the next step?

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CI, confidence intervals; CTPA, computed tomography pulmonary angiography; MDCT, multi-detector computed tomography; SDCT, single-detector computed tomographic pulmonary angiography; SSPE, subsegmental pulmonary embolism.

Increase in proportion of SSPE detected with more advanced CT technology

No increase in the 3 month risk of VTE



To Treat ?

Or Not To
Treat ?

That is the
Question



Data is still controversial



Not to treat

No Fooling Around: Direct Visualization of Pulmonary Embolism¹

Radiology

Removing small asymptomatic emboli is a normal function of the lung
These may be part of normal existence and may remain unrecognized
except after CT or biopsy

Not to treat

Diagnosis and Management of Isolated Subsegmental Pulmonary Embolism: Review and Assessment of the Options

CLINICAL AND APPLIED THROMBOSIS/HEMOSTASIS

Table 2. Treatment With Anticoagulants Compared With No Treatment of Isolated Subsegmental Pulmonary Embolism

References	Method	Recurrent PE With Anticoagulants (%)	Fatal PE With Anticoagulants (%)	Major Bleed With Anticoagulants (%)	Recurrent PE, No Treatment (%)	Fatal PE, No Treatment (%)	DVT Excluded (%; Method)	Follow-up (months)
Eyer et al ²³	8-, 16-detector CTA	0/40 (0)	0/40 (0)		0/20 (0)	0/20 (0)	20/20 (100; CTV)	3
Schultz et al ³⁸	16-detector CTA				0/10 (0) ^a	0/10 (0) ^a	10/10 (100; CTV)	3
Donato et al ²⁴	16-, 64-detector CTA	1/69 (1.4)	0/69 (0)	5/69 (7)	0/21 (0)	0/21 (0)	19-20/21 (90-95; US)	3
Cha et al ¹⁴	16-, 64-detector CTA	0/12 (0) ^b	0/12 (0) ^b		0/7 (0) ^b	0/7 (0) ^b		
Engelke et al ³⁹	4-, 16-detector CTA			4/49 (8)		0/47 (0) ^c	12/47 (34; US/venography)	1

7% risk of major bleeding in patients with SSBPE treated with anticoagulation (1.3% fatal)

No 3 months recurrence of PE or fatal recurrence => patients with SSPE could do without treatment

Stein PD et al. **Diagnosis and management of isolated subsegmental pulmonary embolism: review and assessment of the options.** *Clinical and Applied Thrombosis/Hemostasis* 2012

Withholding treatment is reasonable if:

- (1) pulmonary–respiratory reserve is good;
- (2) no evidence of deep venous thrombosis (DVT) on serial testing;
- (3) major risk factor for PE was transient and no longer present;
- (4) no history of central venous catheterization or atrial fibrillation; and
- (5) willingness to return for serial venous ultrasound.

To Treat

Risk profile and clinical outcome of symptomatic subsegmental acute pulmonary embolism

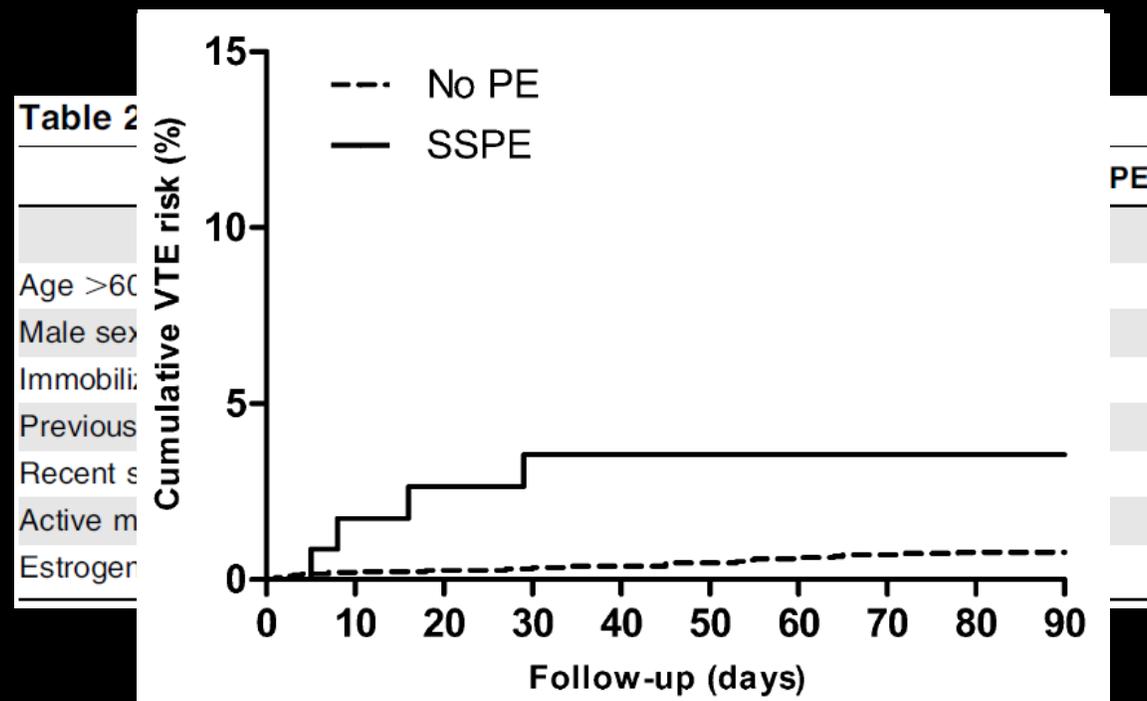


SSPE and proximal PE share a similar risk profile

SSPE and proximal PE share a similar clinical course

Recurrent VTE and mortality are higher with SSPE

Patients with a similar risk profile for PE should be treated for SSPE

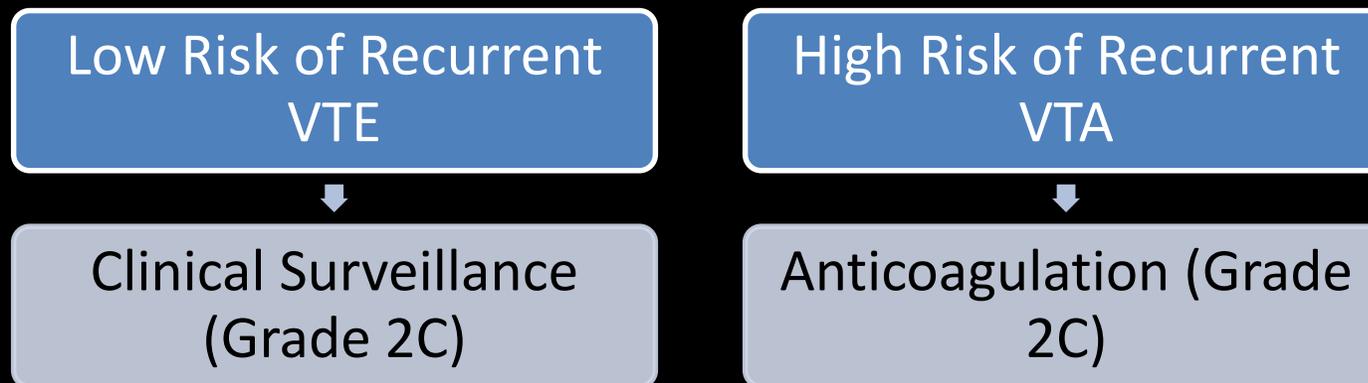


Den Exter PL et al. Risk profile and clinical outcome of symptomatic subsegmental acute pulmonary embolism. *Blood* 2012

To Treat



SSPE but NO DVT



Risk of recurrent VTE	Definition
Low	Patients without cancer
Intermediate	Local or recently resected cancer
High	Advanced/Distal metastatic cancer

To Treat

Management of venous thromboembolic diseases and the role of thrombophilia testing: summary of NICE guidance

thebmj

SSPE should not be discriminated from PE from proximal arteries

Chong LY et al. Management of venous thromboembolic diseases and the role of thrombophilia testing: summary of NICE guidance. *BMJ* 2012

Recommends to make a decision on an individual basis for initiating anti-coagulant therapy, with respect to the clinical situation and bleeding risk

Anticoagulant treatment for subsegmental pulmonary embolism (Review)



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Library**

Trusted evidence.
Informed decisions.
Better health.

“There is no evidence from randomized controlled trials to assess the effectiveness and safety of anticoagulation therapy versus no intervention in patients with isolated subsegmental pulmonary embolism (S SPE) or incidental SSPE, therefore we can not draw any conclusions regarding implications for practice”

Future Research

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

A Study to Evaluate the Safety of Withholding Anticoagulation in Patients With Subsegmental PE Who Have a Negative Serial Bilateral Lower Extremity Ultrasound (SSPE)

This study is currently recruiting participants. (see [Contacts and Locations](#))

Verified February 2015 by Ottawa Hospital Research Institute

Sponsor:

Ottawa Hospital Research Institute

Information provided by (Responsible Party):

Marc Carrier, MD, Ottawa Hospital Research Institute

ClinicalTrials.gov Identifier:

NCT01455818

First received: October 18, 2011

Last updated: February 4, 2015

Last verified: February 2015

[History of Changes](#)

Results are expected in 2017

Summary

- The prevalence of SSPE is increasing with the advances in CT technology
- Studies with suspected SSPE should be reviewed by an expert thoracic radiologist
- The question of whether isolated SSPE should be treated remains controversial
- More prospective trials are required
- Meanwhile the decision should be based on an individual basis weighing risk and benefit



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Thank
You!!!