Moderate Pulmonary Embolism Treated with Thrombolysis (MOPETT) Trial

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Disclosures

- MS: Consultant to Covidien

Pulmonary Embolism

- >100,000 annual deaths
- Third leading cause of cardiovascular mortality
- Most common preventable cause of death

- **Thrombolysis has been used for massive PE**
- **Hemodynamic instability and shock**
- **5% of PEs qualify for standard dose**
- **Concern about major bleeding and ICH**
- **ICH 2-6%**
- **Major bleeding 6-20%**

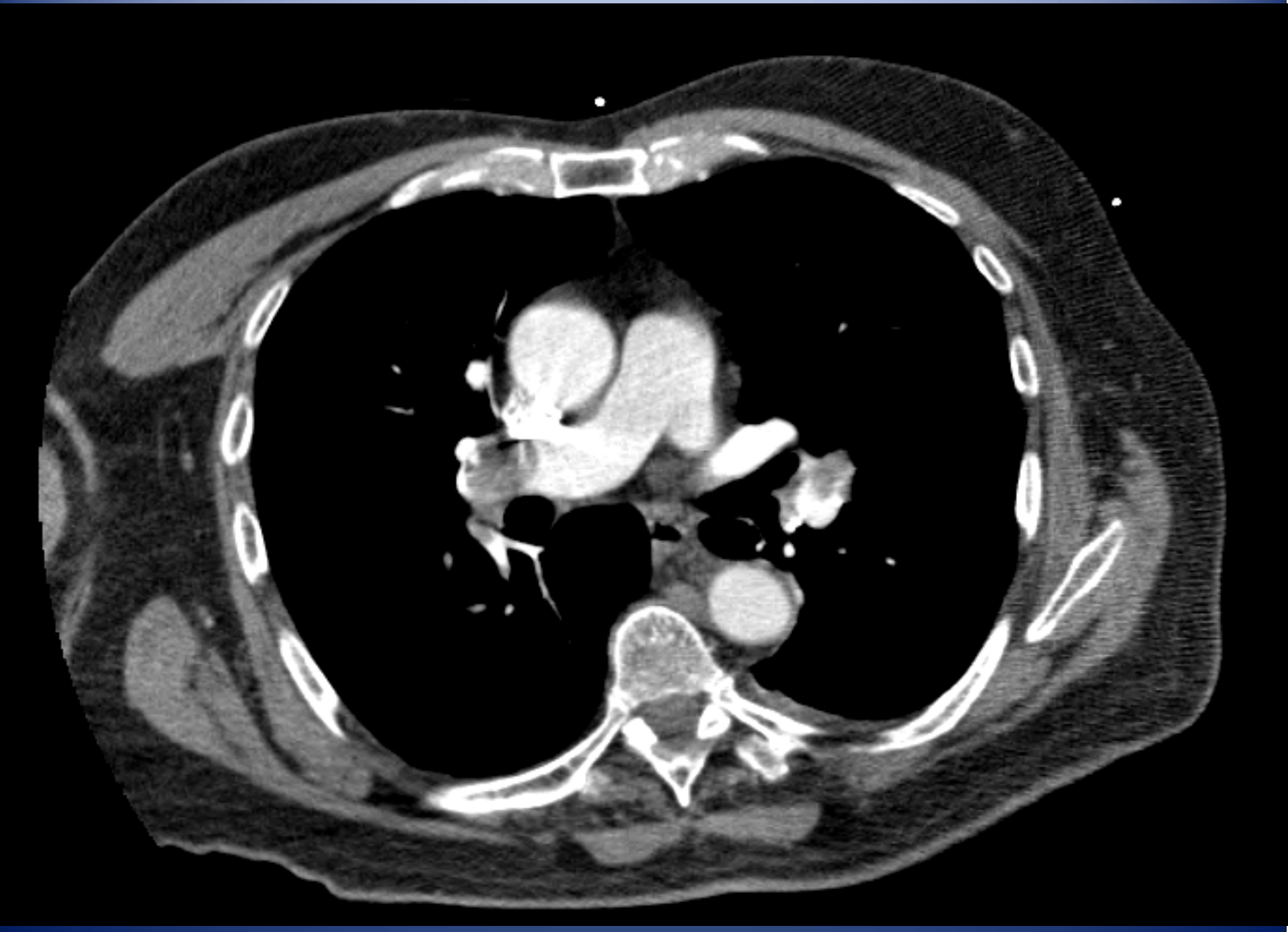
- **Standard dose t-PA 100mg in 2 hrs**
- **Hesitancy of practitioners to use t-PA when patient is hemodynamically stable**
- **Unresolved issue of concomitant parenteral anticoagulation with t-PA**

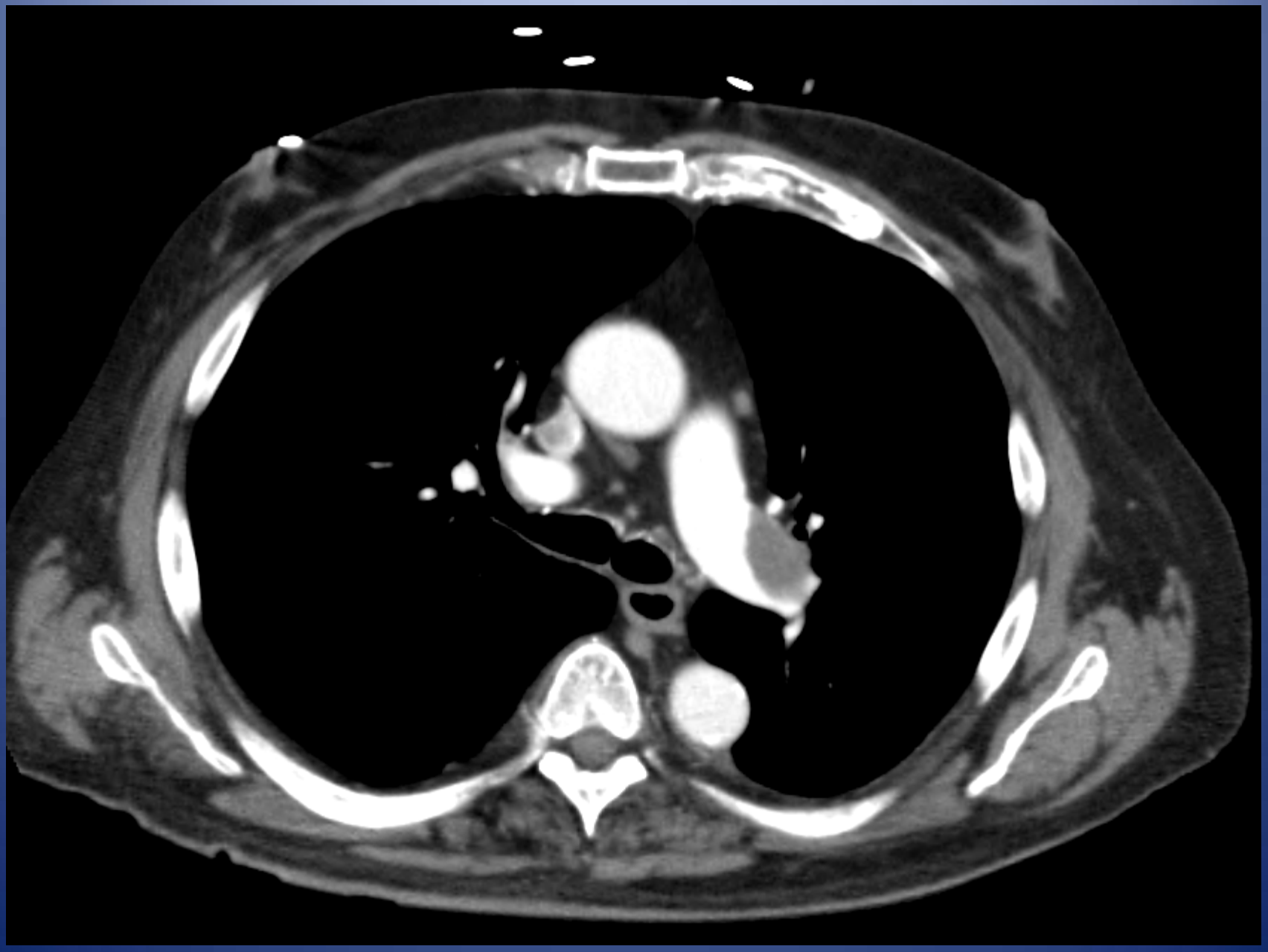
“SAFE DOSE t-PA” ?

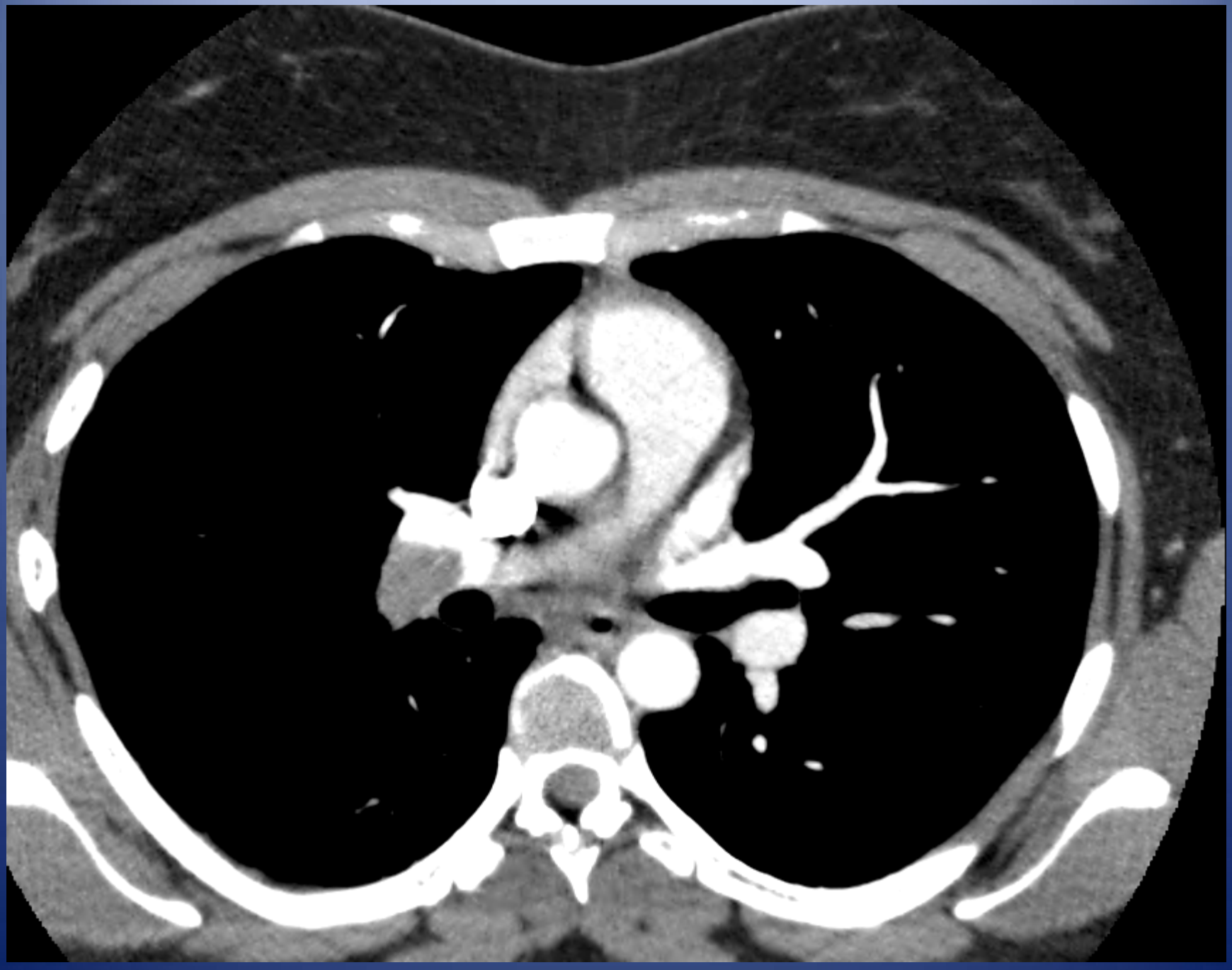
“ SAFER DOSE t-PA” ?

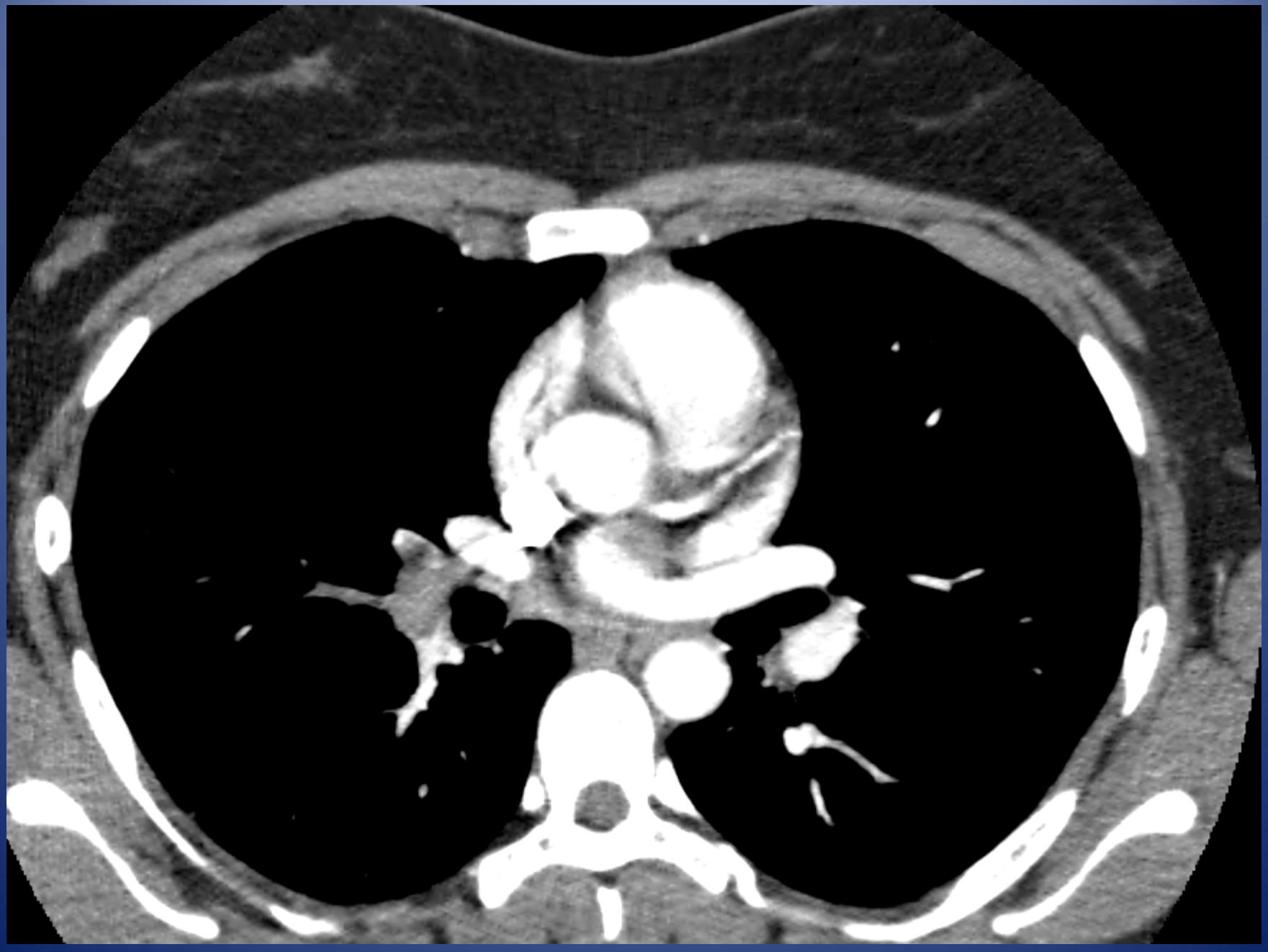
Rational for Efficacy of “ Safe dose” thrombolysis

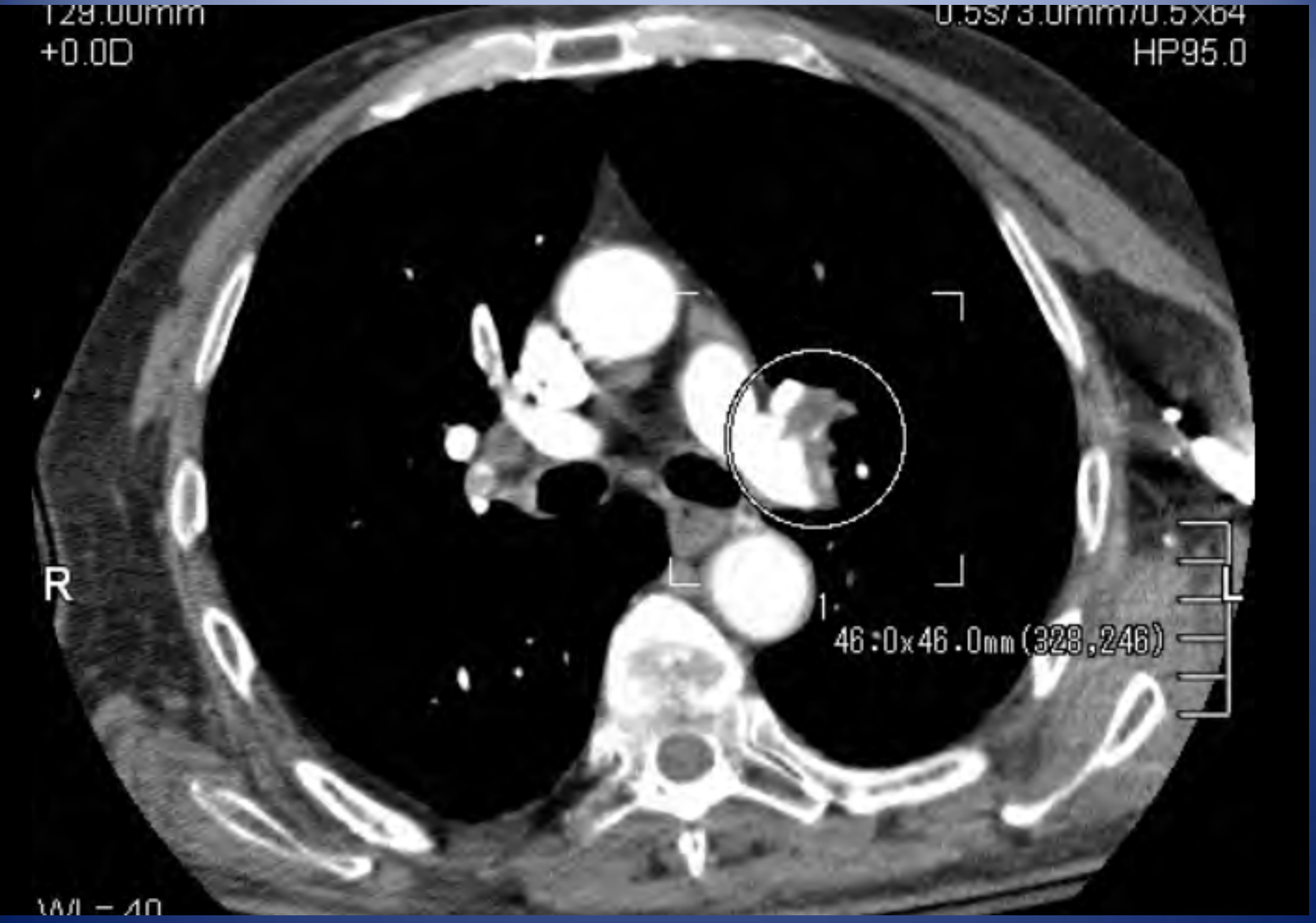
- Thromboembolus in pulmonary arterial circulation is exquisitely sensitive to lysis
- Lungs= point of convergence of venous circulation
- Pulmonary blood flow= Entire CO
- Almost all t-PA molecules converge in lungs
- Different than in thromboembolic CVA and acute MI
- Brain 15% of CO; Heart 5%; hence same dose should not necessarily apply







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HP95.0
R
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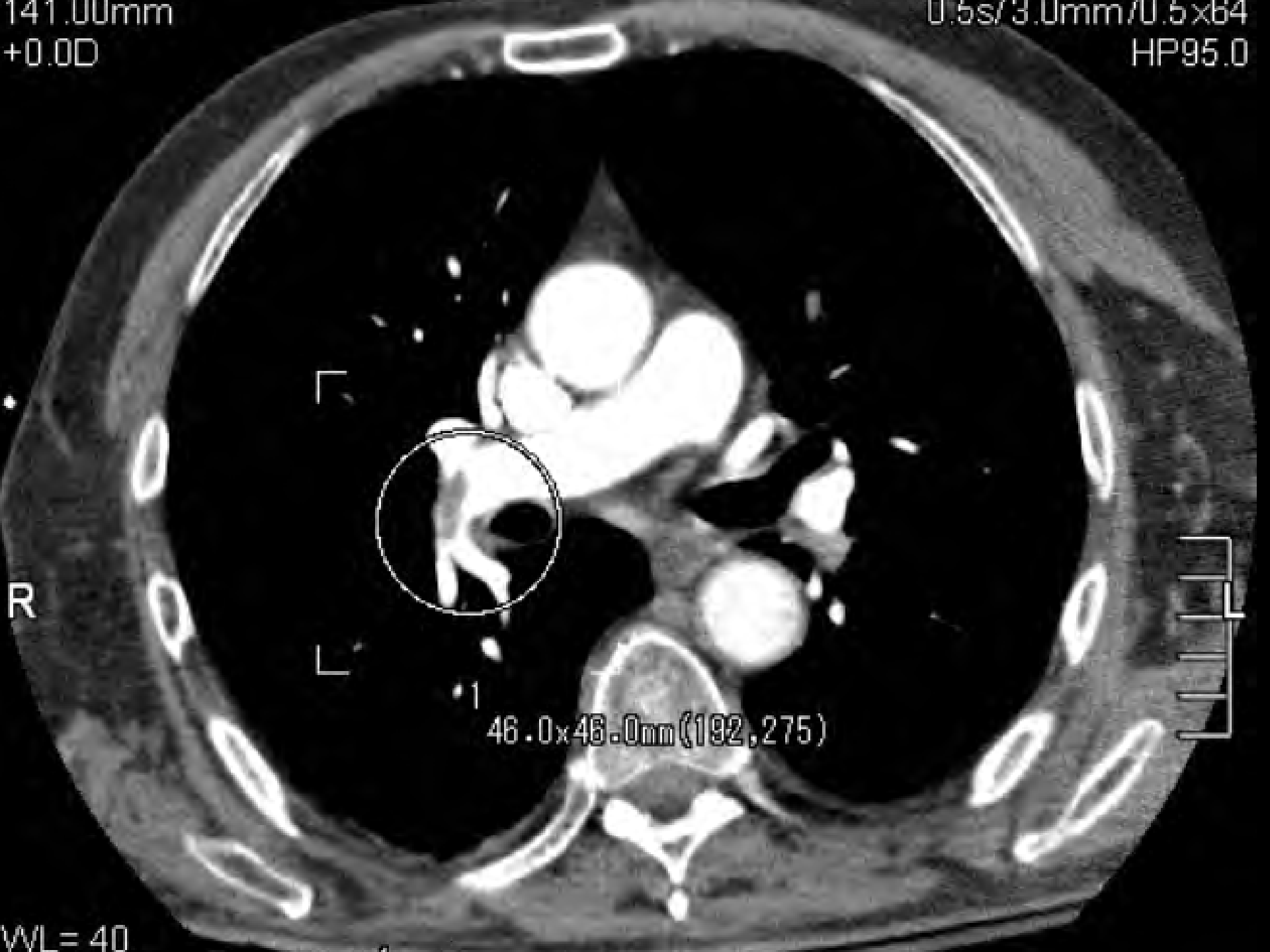
46.0x46.0mm (328,246)
WL = 40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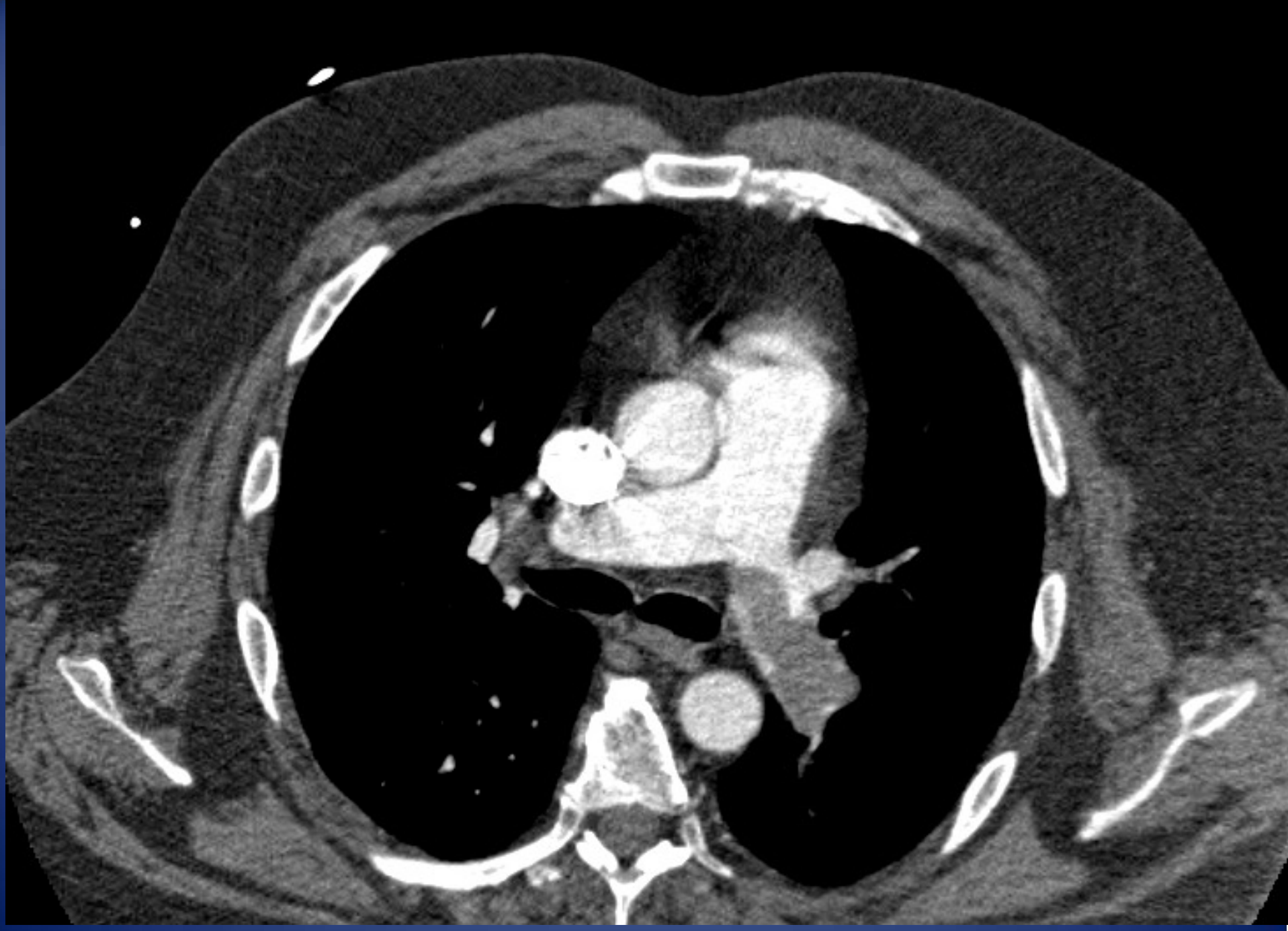
WL= 40



MOPETT Trial

121 Patients

TT= 61

CG= 60

F/U= 28±5 m

58

56

Primary Endpoints

1) Pulmonary HTN

2) Recurrent PE+ Pulmonary HTN

Secondary Endpoints

- **In-Hospital Bleeding**
- **Duration of Hospitalization**

Inclusion criteria

- PE + 2 of the following:
  - Chest Pain
  - Tachypnea > 22 RPM
  - Tachycardia resting HR>90 BPM
  - Dyspnea
  - JVP > 12 cmH20
  - Cough
  - Oxygen desaturation

Evaluation of Troponin I and BNP

Echocardiographic features

- **PASP> 40 mmHg**
- **RV hypokinesia**
- **RV enlargement**

Exclusion Criteria

- BP≥200/100
- Surgery , major trauma in preceding 2 weeks
- Brain mass
- ICH, SDH , neurologic surgery within preceding 1 year
- GI bleeding requiring transfusion in preceding 2 m
- Need for full dose thrombolysis

“Safe Dose” t-PA

- For ≥ 50Kg = 10mg in 1 min followed by 40 mg in 2 hr
- For < 50 Kg = 0.5mg/Kg total dose : 10 mg in 1 min followed by remainder in 2 hr

	FG n= 61	CG N=60	p Value
Male	28 (46)	27(45)	0.92
Age	58±9	59±10	0.56
Weight	84±14	83±13	0.68
Previous or concomitant disease- n (%)			
Hypertension	32 (52)	31 (52)	0.93
Diabetes mellitus	23 (38)	25 (40)	0.66
Cardiovascular	35 (57)	37 (62)	0.80
Hypercholesterolemia	27 (33)	25 (30)	0.77
Pulmonary	22 (36)	25 (42)	0.53
Renal	8 (13)	9 (15)	0.77
Current smoker	12 (20)	15 (25)	0.48
Unprovoked PE	28 (46)	27 (45)	0.92
Estrogen therapy	6 (10)	7 (12)	0.75
Cancer			
Active	8 (13)	9 (15)	0.77
History	3 (5)	3 (5)	0.98
Known prothrombotic state	6 (10)	5 (8)	0.77
Previous VTE	13 (21)	12 (20)	0.86
Concomitant DVT	35 (57)	33 (55)	0.79

Concomitant Anticoagulation TG

- Enoxaparin (80%) : 1mg/Kg/SQ (not to exceed 80 mg for initial dose)

- Heparin (20%) Bolus = 70 U /Kg, and not to exceed 6000U

  Maintenance 10 U/Kg/ Hr while tPA being infused (not to exceed 1000U/Hr)

  1 hr after termination of t-PA increased to 18 U/Kg/Hr

Adjusted to PTT 1.5-2 X baseline

LABORATORY	6:45 MST	19:50 MST	13:05 MST	4:00 MST	14:03 MST	5:25
Basos				1		
Neut#				6.5		
Lymph#				4.2 H		
Mono#				0.7		
Eos#				0.2		
Baso#				0.1		
GENERAL COAGULATION						
PT	22.2 H			21.5 'H		17.2 H
INR	2.0 *H			1.9 *H		1.4 *H
APTT	64 *H	>200 *C	55 *H	144 *C		76 *H

		0.8 L				0.8 L	
		0.6				0.6	
		0.3				0.2	
		0.0				0.1	
COAGULAT							
	51 * H	127 * C	>200 * C	42 * H	130 * C	77 * H	183

Intense fluctuations in PTT with "standard heparin protocols"

Anticoagulation CG

- **Enoxaparin (80%) : 1mg/Kg/SQ BID**
- **Heparin (20%) Bolus = 80 U /Kg followed by 18 U/Kg/Hr**
- **Warfarin started on admission**

- **66% had BNP or Trop I elevation**
- **RV enlargement 12/61(20%) and 14/60 (23%)**
- **RV hypokinesia 3/61(4.9%) and 4/60(6.6%)**

	TG	CG	p Value
Initial PASPmm Hg	50±6	51±7	0.40
Change within 48 hours	- 16±3	-5±2	<0.001
PASP at 6 m	31±6	49±8	<0.001
PASP at final F/U	28±5	43±6	<0.001

Primary Endpoints

	TG N= 58	CG N=56	p Value
Pulmonary HTN at 28 m	**9 (16)**	**32 (57)**	**p<0.001**
Pulmonary HTN + recurrent PE at 28 m	**9 (16)**	**35 (63)**	**p<0.001**

Pulmonary HTN= PASP> 40 mmHg

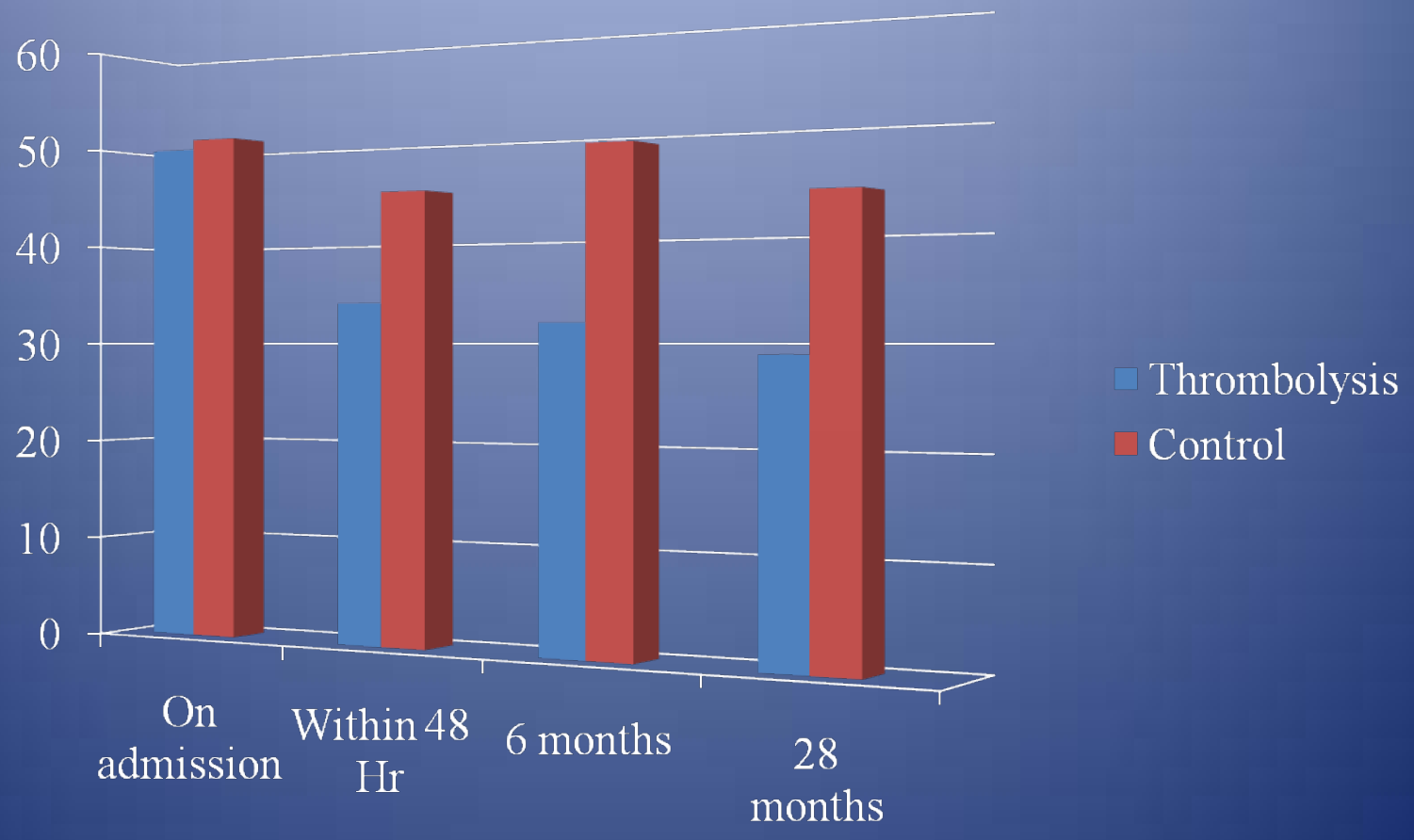
Secondary Endpoints

	TG N= 61	CG N=60	p Value
Recurrent PE	0	3 (5)	0.077
Mortality	1(1.6)	3 (5)	0.301
PE + Mortality	1 (1.6)	6 (10)	0.0489
Hospital Stay	2.2±0.5	4.9±0.8	<0.001
In-hospital Bleeding	0	0	-

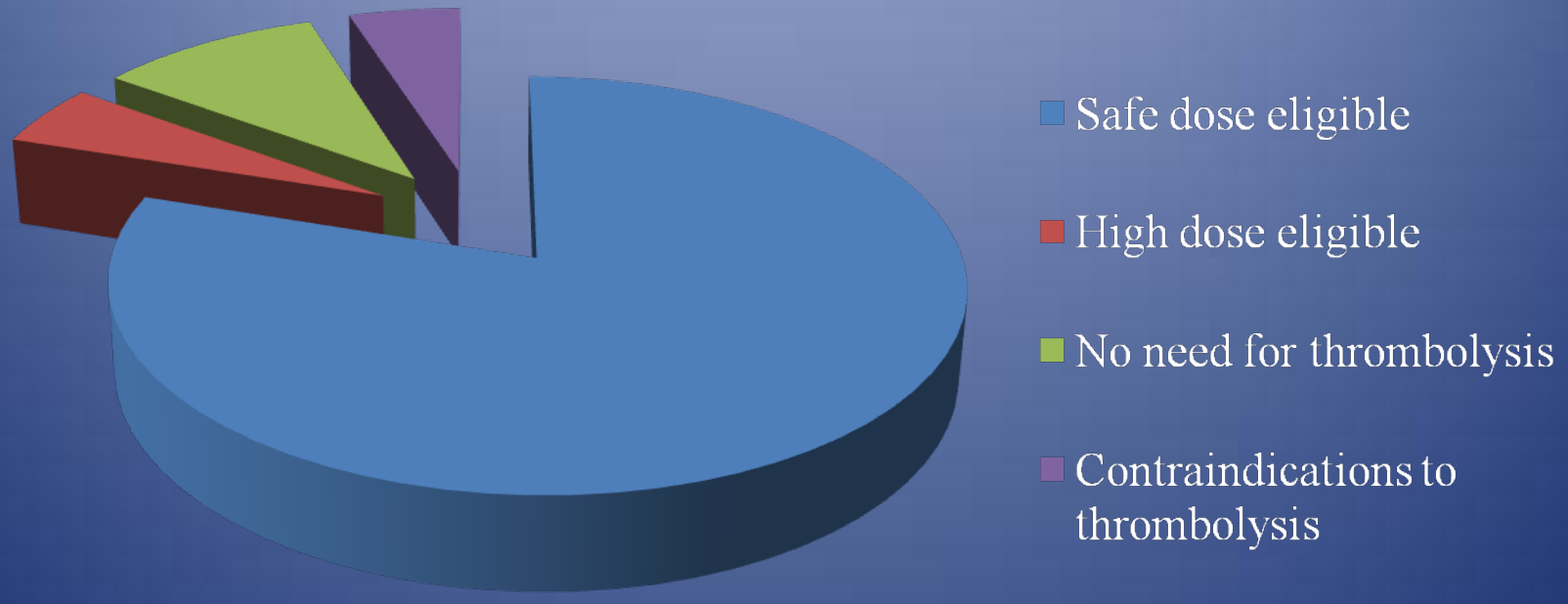
Thrombolysis serving as a "pulmonary stress test"

- Patients with infarction would develop worsening or new onset chest pain
- Ambulatory within 24 hr

Changes in PASP (mmHg)



Eligibility For Thrombolysis



Conclusions

- Low dose thrombolysis is safe and effective in moderate PE
- Rapid reduction in PA pressures
- Reduction of Pul HTN & recurrent PE at 28 m
- No bleeding/ ICH
- Earlier hospital Discharge : (pulmonary “stress test”)
- Trend in reduction of recurrent PE and possibly mortality
- Importance of dose modification for concomitant anticoagulants

HAPPY NOWRUZ