Prospective Multicenter Trial of Pharmaco-mechanical Catheter-Directed Thrombolysis with the Bashir Endovascular Catheter for Acute Pulmonary Embolism

The RESCUE Study

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On Behalf of RESCUE Investigators

Funding support: NHLBI – SBIR, Commonwealth of Pennsylvania Department of Heath and Thrombolex Inc.

Disclosure Statement of Financial Interest

I, Riyaz Bashir MD have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Co-Inventor

Faculty disclosure information can be found on the app

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Grant/Research Support	Thrombolex Inc.
Consulting Fees/Honoraria	Thrombolex Inc.
Major Stock Shareholder/Equity	Thrombolex Inc.
Royalty Income	Thrombolex Inc.
Ownership/Founder	Thrombolex Inc.
Intellectual Property Rights	Thrombolex Inc.
Other Financial Benefit	Thrombolex Inc.

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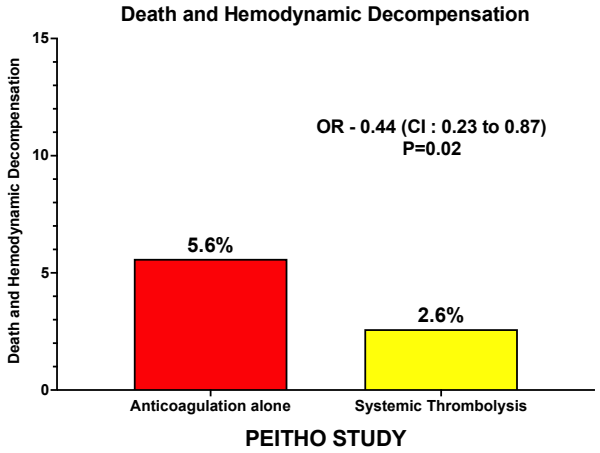
Study Rationale

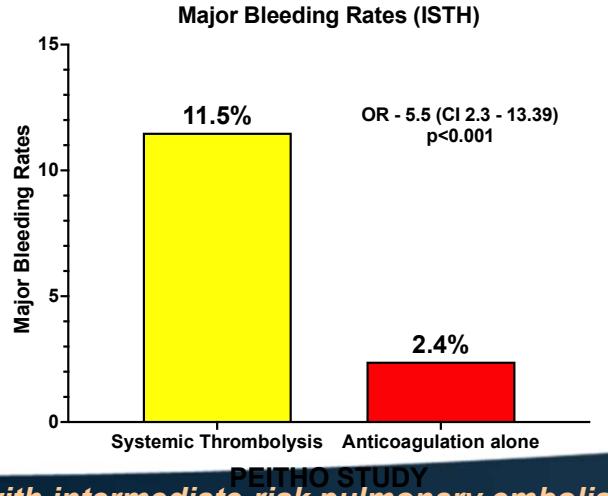
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

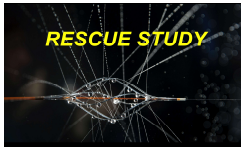
Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism

Improve the safety and efficacy by delivering a small dose of thrombolytic within the thrombus with a device designed for use in large vessels (pulmonary arteries).





**Meyer G,. Fibrinolysis for patients with intermediate-risk pulmonary embolism. N Engl J Med 2014;370:1402-11.*

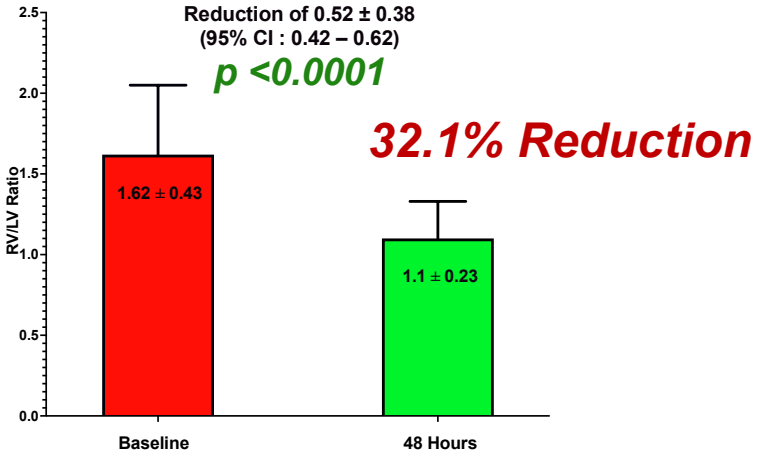


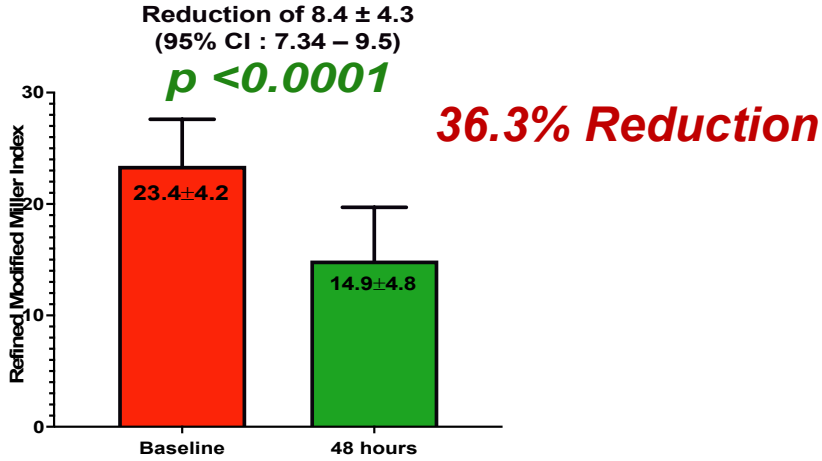
Circulation: Cardiovascular Interventions

Circ Cardiovasc Interv. 2021;13:e009611. DOI: 10.1161/CIRCINTERVENTIONS.120.009611 January 2021

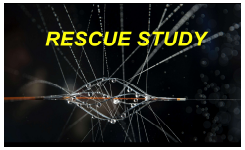
ORIGINAL ARTICLE

First-in-Human Study to Assess the Safety and Feasibility of the Bashir Endovascular Catheter for the Treatment of Acute Intermediate-Risk Pulmonary Embolism





First-in-Human study of Pharmaco-mechanical Catheter-Directed Thrombolysis (PM-CDT) with Bashir Endovascular Catheter has shown promising early results.

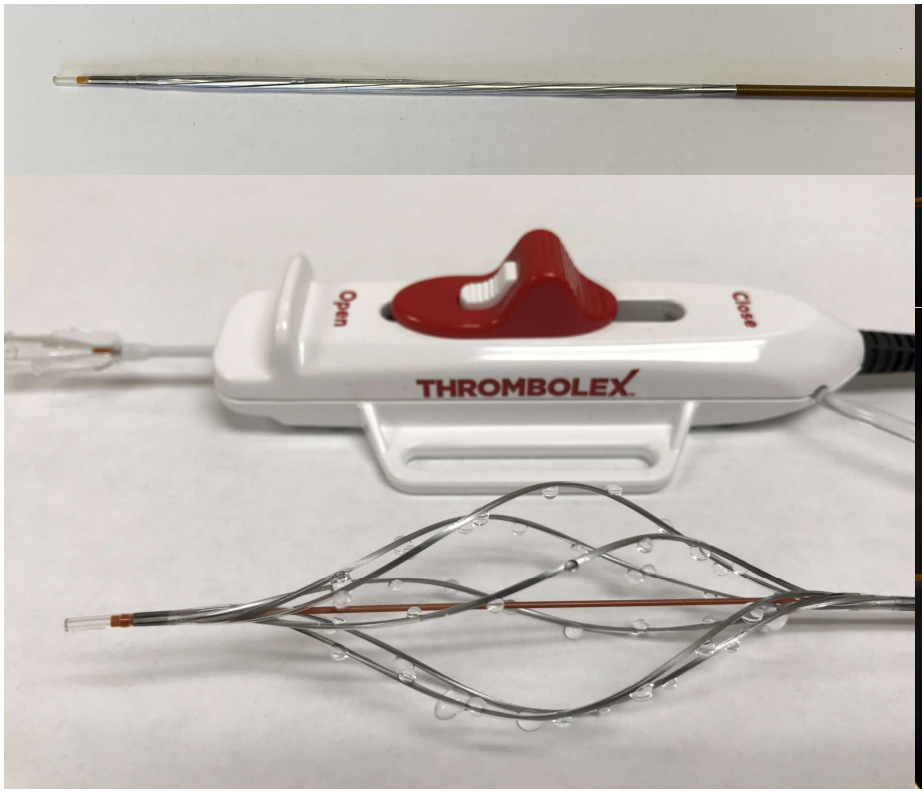


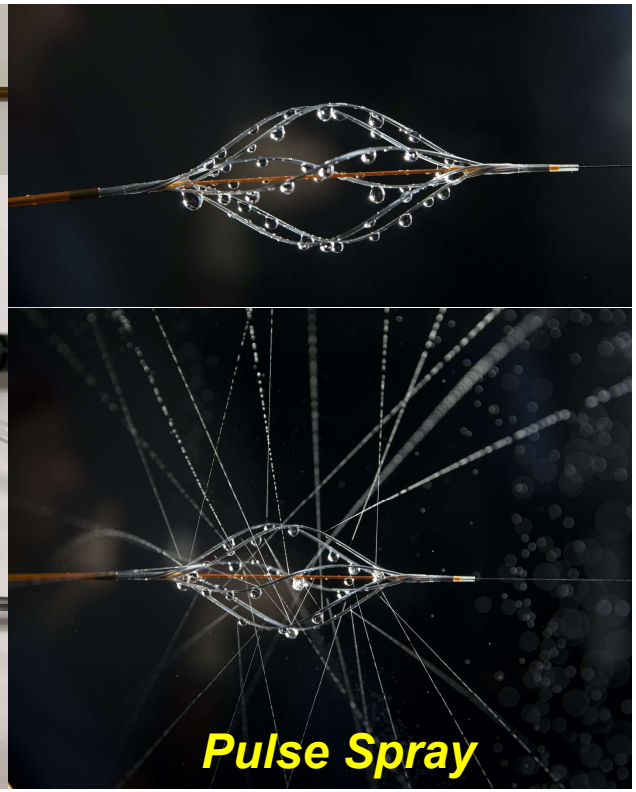
Study Objective

Assess safety and efficacy of Pharmaco-Mechanical Catheter-directed thrombolysis (PMCDT) using the Bashir Endovascular Catheter in patients with intermediate-risk acute pulmonary embolism.

- **Design**: Multicenter, prospective Single arm clinical trial

Pharmaco-Mechanical Catheter Directed Thrombolysis with Bashir Endovascular Catheter





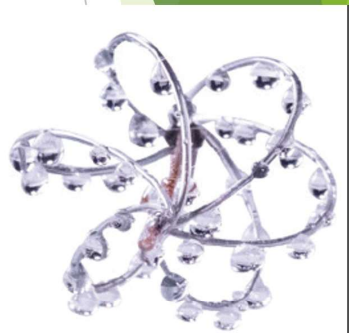
The Bashir Endovascular Catheter is not yet cleared for the treatment of Pulmonary Embolism

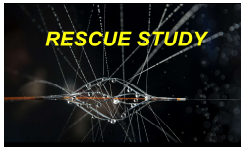
Potential Advantages of the Bashir Endovascular Catheter

- Wider cross-sectional distribution
- Prompt restoration of Blood flow
- Continuous monitoring of PA pressures
- Low profile - 7F compatible
- Ease of use
- No blood loss

Potential Implications:

- Reduced duration of therapy
- Reduced dose of thrombolytics
- Reduced Major bleeding rates
- Greater efficacy

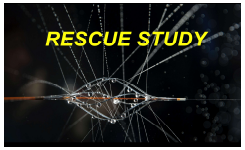




METHODS - Key Eligibility Criteria

- Inclusion Criteria
  1. 18 years to ≤ 75 years of age;
  2. PE symptom duration ≤ 14 days
  3. Filling defect in at least one main or lobar pulmonary artery
  4. RV/LV end diastolic diameter ratio ≥ 0.9

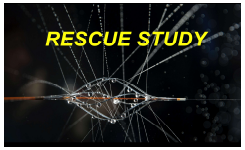
- Exclusion Criteria
  1. Active COVID 19 within last two months.
  2. CVA or TIA within one (1) year
  3. Head trauma, active intracranial or intraspinal disease
  4. Active bleeding
  5. Intracranial condition(s) that may increase the risk of bleeding



METHODS - Primary End-points

- Primary efficacy end-point:
  - Reduction in CTA derived RV/LV ratio at 48 hours from the baseline.

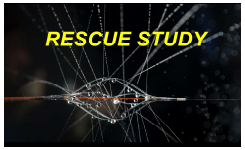
- Primary safety end-point:
  - Major bleeding and device related adverse events at 72 hours



METHODS

Secondary Efficacy End-point
PA obstruction reduction at 48 hours

Refined Modified Miller Index *as measured on CTA within 48 hours after the completion of the r-tPA infusion compared to baseline as evaluated by core lab.*

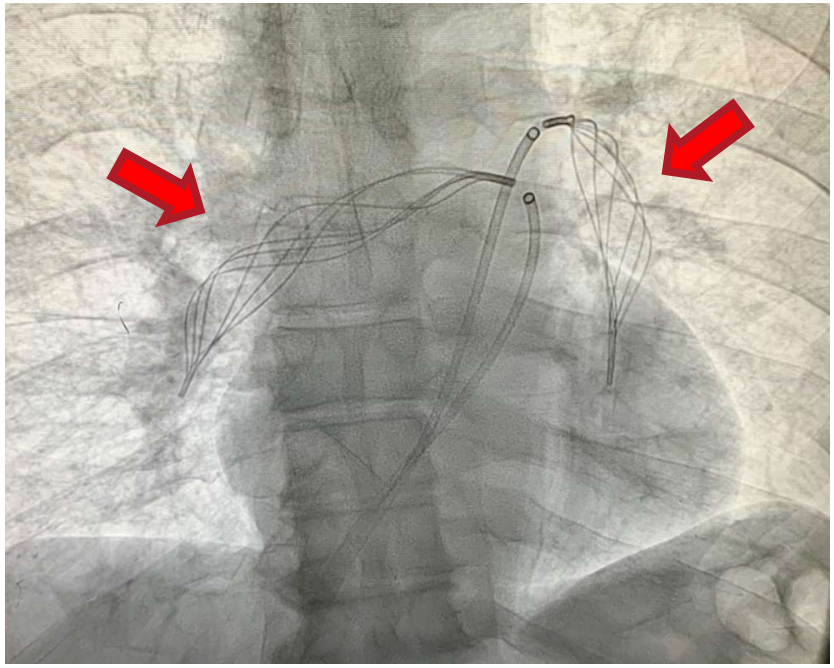


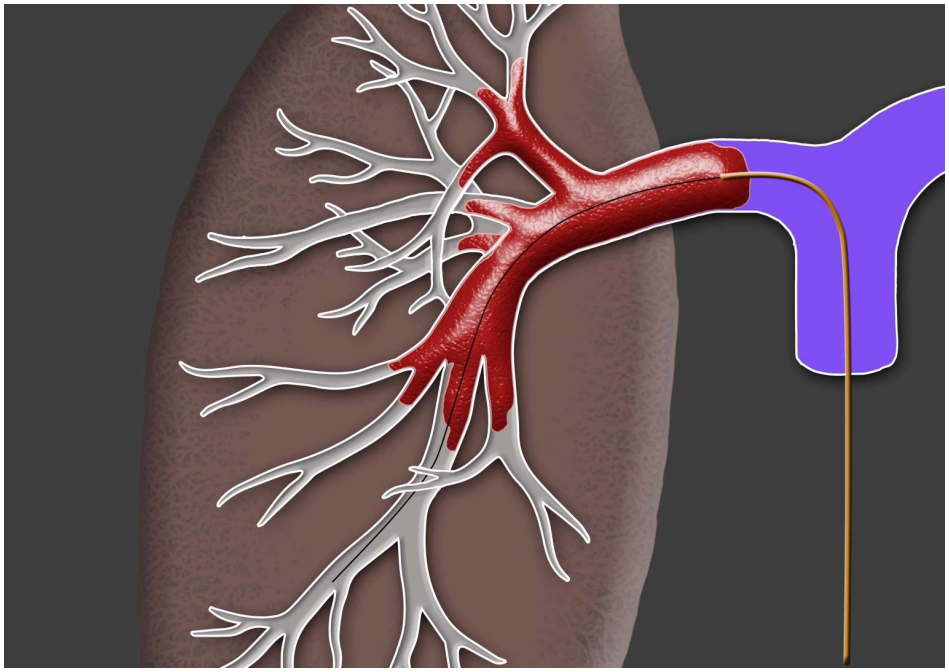
METHODS
Secondary Safety End-points

- Device related adverse events.
- All-cause mortality at 30-day follow-up.
- SAEs through 30-day follow-up.
- Recurrent PE through 30-day follow-up.

All end-points are adjudicated by the DSMB/CEC Committee

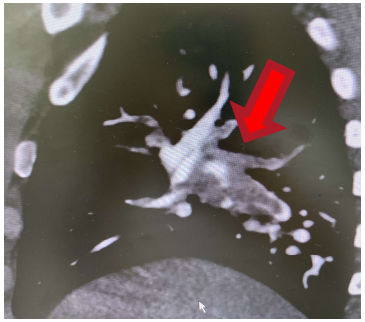
Rescue protocol



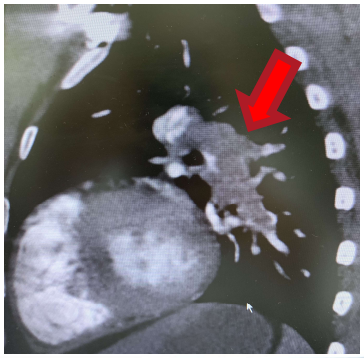


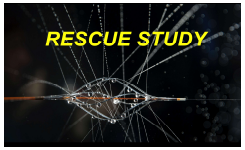
Unilateral PE – Total 7 mgs of rt-PA with Single device (2mgs pulse Spray and 5mgs over 5 hours)
Bilateral PE – Total 14 mgs of rt-PA with two devices (2 mgs pulse Spray and 5 mgs infusion into each PA over 5 hours)

Pulmonary Angiogram Post PM-CDT



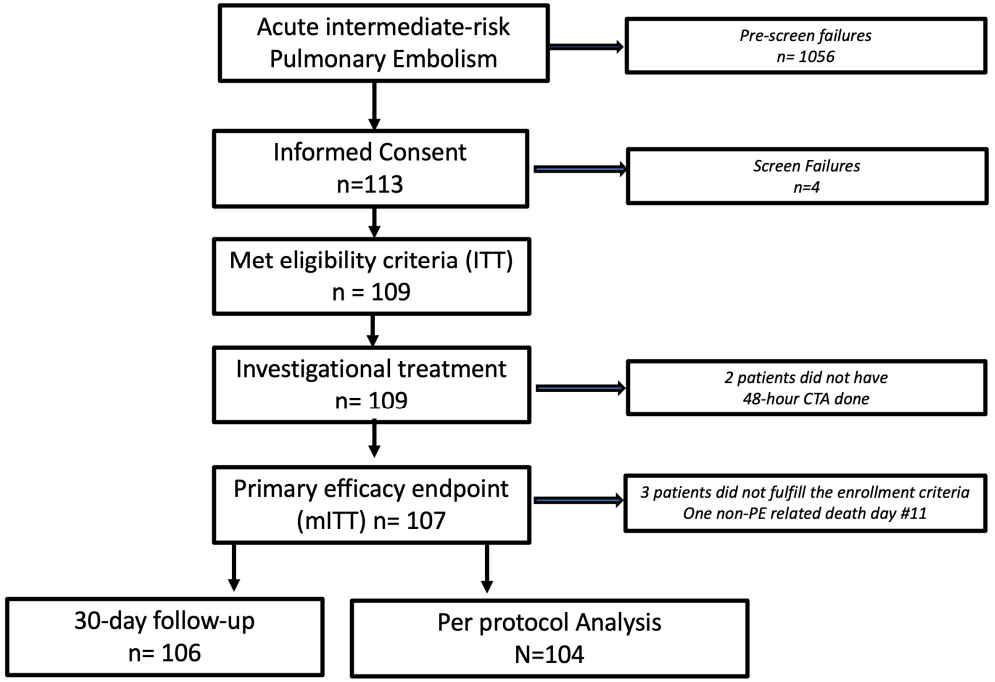
CTA
Pre PM-CDT

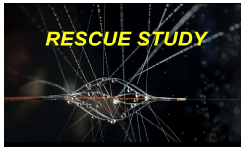




RESULTS

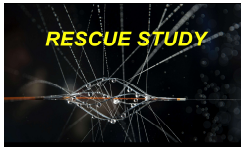
- A total of 109 patients
- 18 U.S. sites
- October 2020 to May 2022





Baseline Characteristics

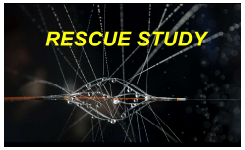
Characteristics (N=109)	Mean ± SD
Age (years)	57 ± 13.3
Body mass index (kg/m^2)	33.3 ± 6.05
Male Female	67 (61.5%) 42(38.5%)
Caucasian/Non-Hispanic African American Hispanic Other	64 (58.7%) 32 (29.4%) 10 (9.2%) 3 (2.8%)
BNP Troponin	1101 ± 1950 pg/ml 0.52 ± 2.1 ng/ml
History of Cancer	17 (15.6%)
Diabetes mellitus	27 (24.7%)
Previous DVT	28 (25.7%)
History of Pulmonary Embolism	15 (13.8%)



Pulmonary Embolism Characteristics

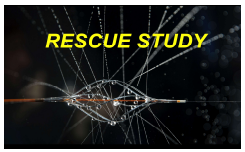
Characteristics (N=109)	*N (%)*
Unilateral Pulmonary Embolism Bilateral Pulmonary Embolism	**7 (6.4%)** **102 (93.6%)**
Elevated Troponin or BNP	**98/109 (89.9%)**
Elevated Troponin	**78/109 (66.1%)**
Elevated BNP	**78/105(74.3%)**
Negative Biomarkers	**69/109(8.3%)**

90% patients had both elevated biomarkers as well as right ventricular dilatation



RESULTS: Procedural Characteristics

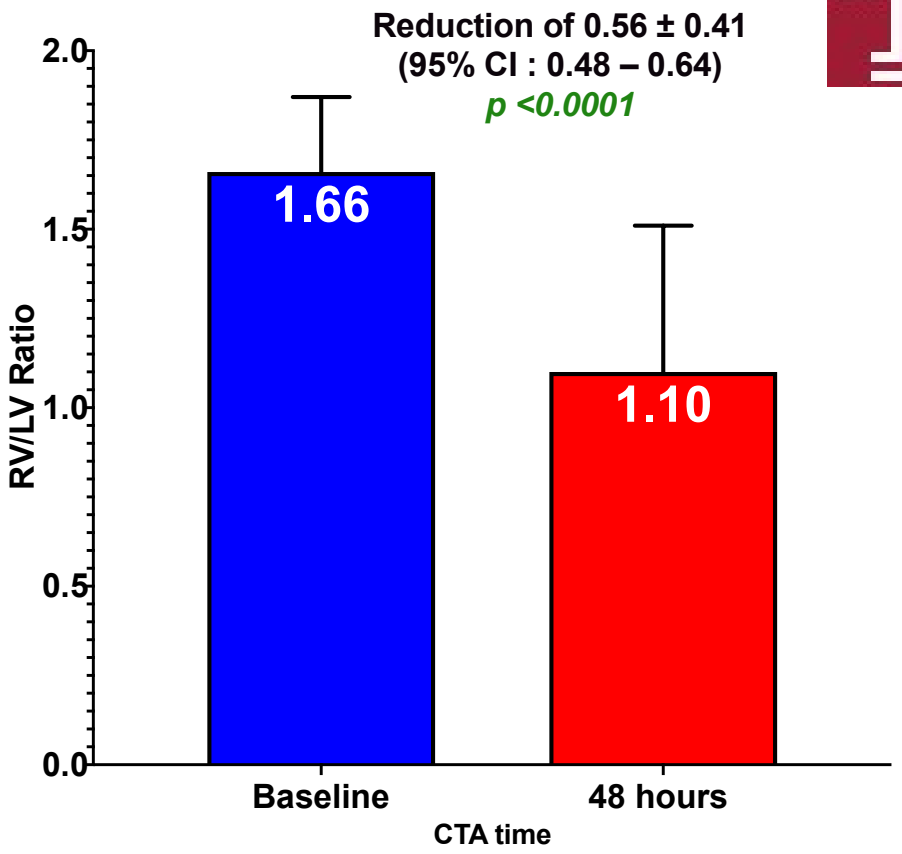
Characteristics (N=109)	
Total dose of rt-PA, mg	
Unilateral PE (Pulse spray + infusion)	7 (2+5)
Bilateral PE (Pulse spray + infusion)	14 (4+10)
Total procedure time in minutes (Median ± SD)	64.2±28.8
Catheter placement time in minutes (Median ± SD)	15±14
No. of devices per patient	
1	7 (6.4%)
2	103 (93.6%)
Completed r-tPA infusion (N=61)	109 (100%)

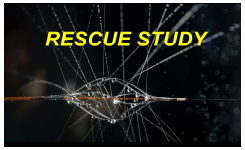


RESULTS

Primary Efficacy Outcome - RV/LV Ratio

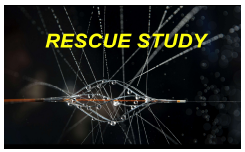
33.3 % Reduction



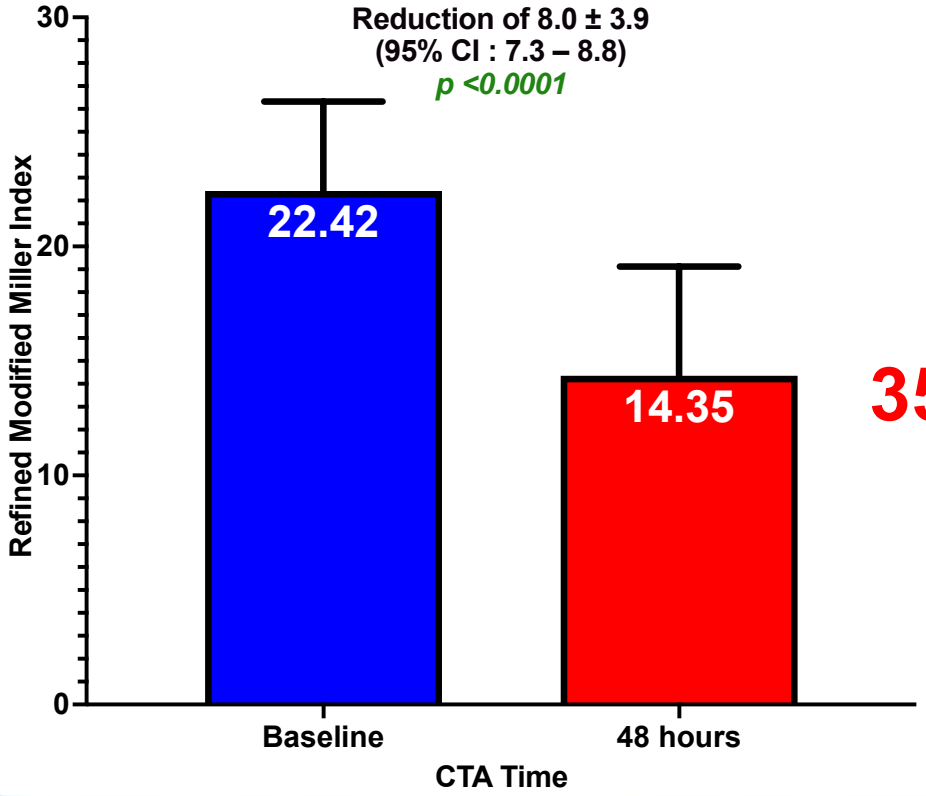


RESULTS: Primary Safety Outcomes

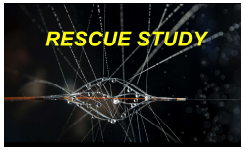
Outcomes	n (%)
Procedural Success (n=109)	109 (100%)
Major Bleeding within 72 hours (ISTH) (n=109)	1 (0.9%)
Major Device related adverse events (n=109)	1(0.9%)



Pulmonary Artery Obstructive Index Reduction
*Refined Modified Miller Index (*Core Lab.)



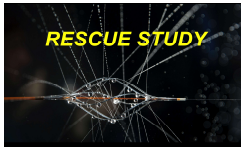
35.9% Reduction



RESULTS : Secondary Outcomes

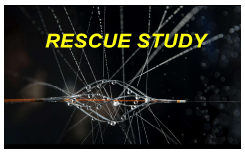
Outcomes	N (%)
Clinically Relevant Non-Major bleeding (n=109)	1 (0.92%)
Non major procedure related AE ‡(n=109)	2 (1.8%)
Recurrent PE through 30-day follow-up (n=104)	0 (0%)
SAEs through 30-day follow up (n=104)	7 (6.7%)
All-cause mortality at 30 days (n=104)	1 (0.92%)
Intracranial Hemorrhage	0 (0%)
Median Hospital Length of stay in days ± SD (n=109)	2.88 ± 1.6

‡epistaxis, non-access site hematoma with anemia



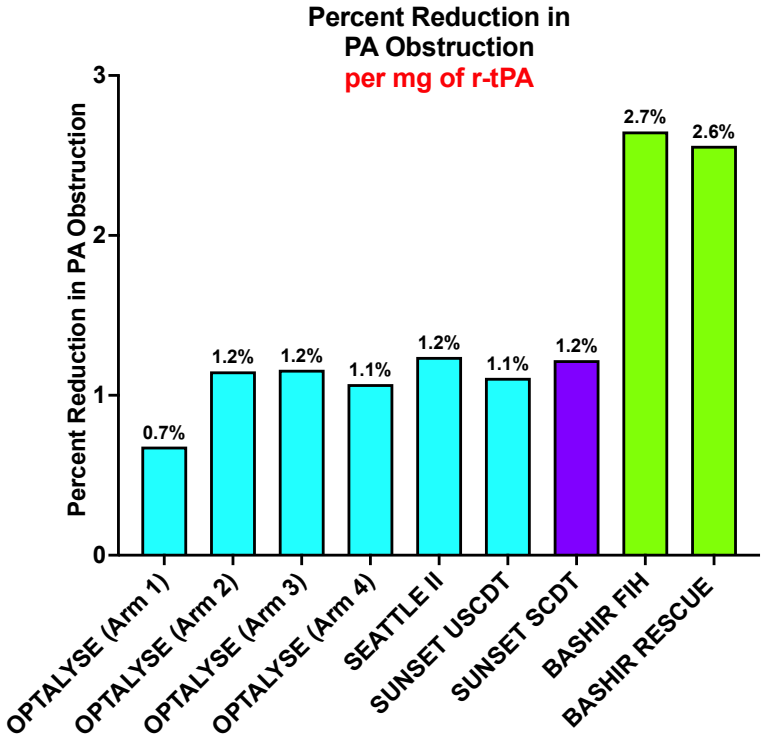
Hemodynamics at 5 hours

Outcomes	Baseline mean ± SD	Post PM-CDT mean ± SD	Difference mean ± SD	p-value
Systolic PA pressure, mmHg (n=93)	49.53 ± 13.39	43.74 ± 13.51	5.94± 10.69	<0.0001
Cardiac output, L/min (n=98)	4.81 ± 1.43	5.31 ± 1.59	0.49± 1.59	0.0029
Cardiac index, L/min per m^2 (n=98)	2.29 ± 0.60	2.47 ± 0.71	0.19± 0.76	0.0156



DISCUSSION

Thrombolytic Efficiency (Core Lab. Data)



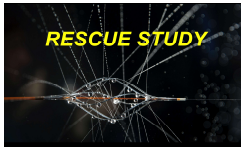
Ekosonic CDT

Standard CDT

Bashir Endovascular Catheter

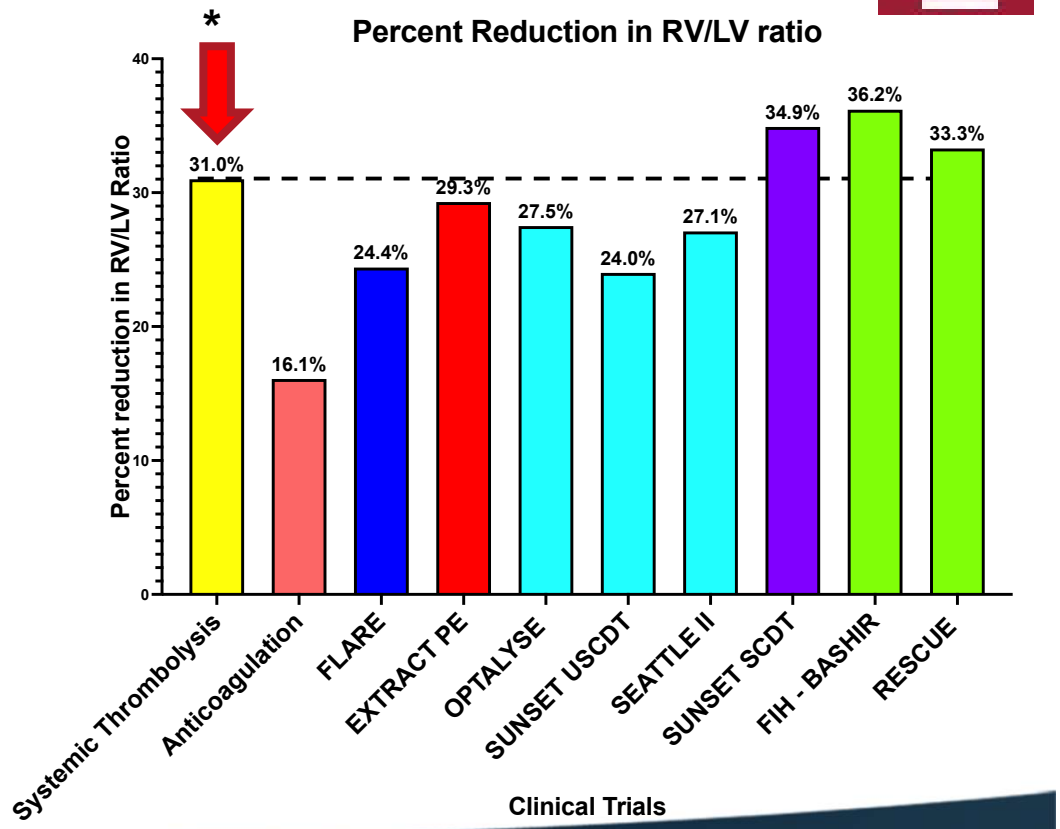
CRF TCT

The thrombolytic efficiency of one mg of r-tPA is higher with PM CDT

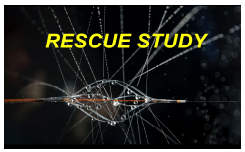


DISCUSSION

Reduction in RV/LV Ratio parallels that seen with systemic thrombolysis

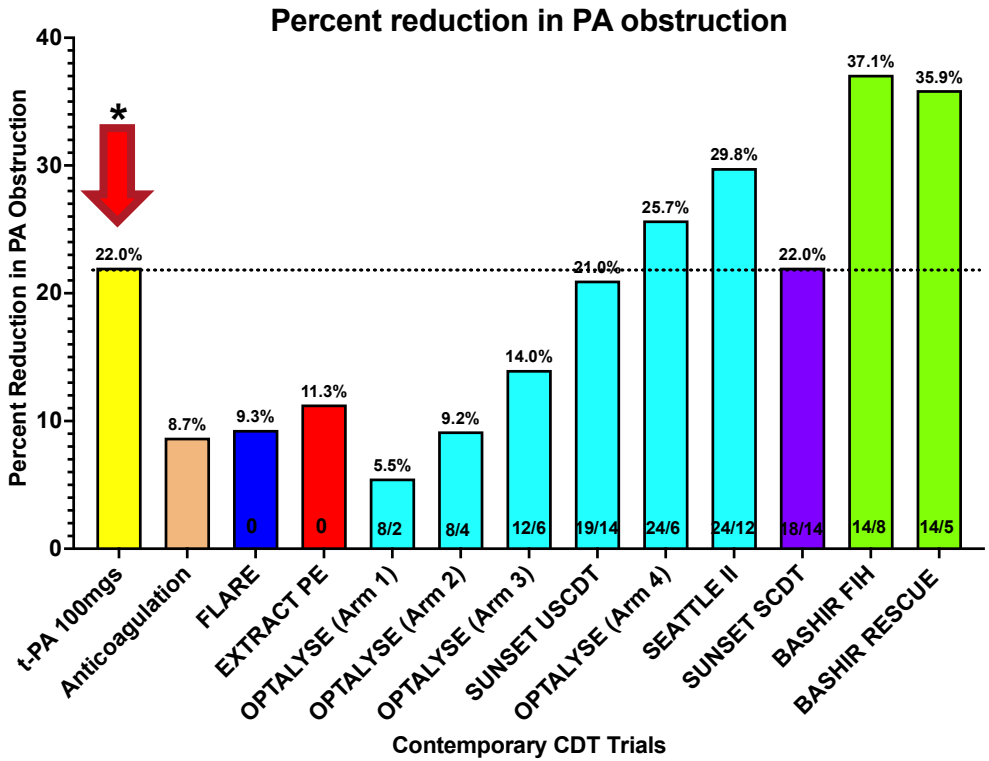


*Fasullo S, Am J Med Sci 2011;341:33-9.

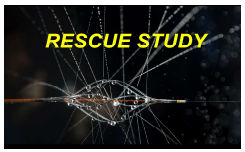


DISCUSSION

Reduction in Pulmonary Artery Obstruction parallels that seen with systemic thrombolysis



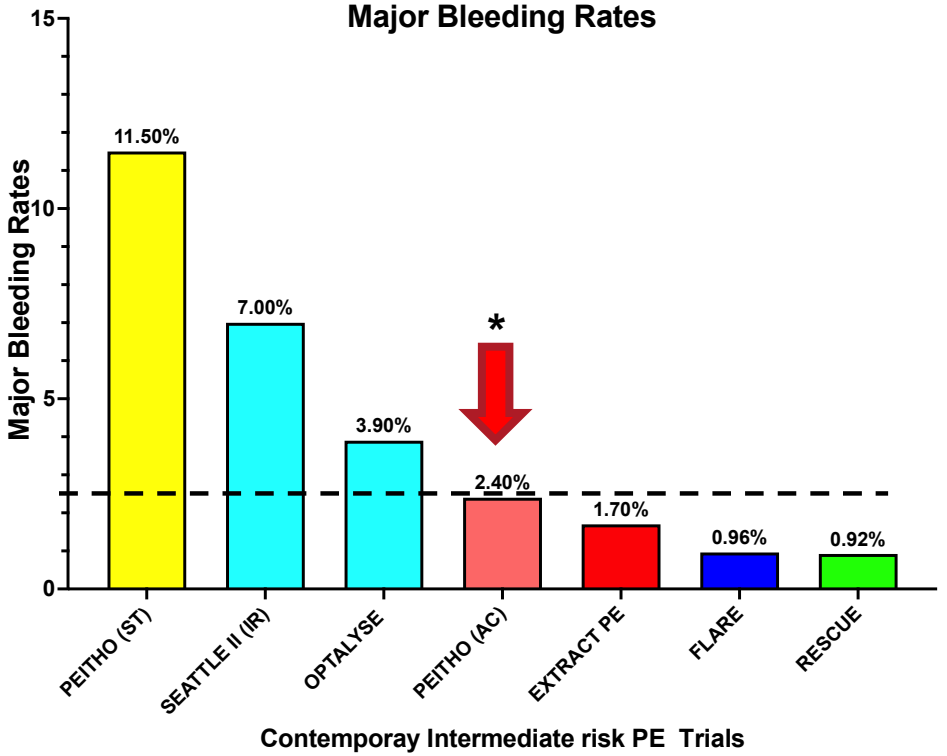
*Goldhaber, et al. Chest, vol. 106, no. 3, Sept. 1994



DISCUSSION

Safety

Major Bleeding rates with PM-CDT parallels that seen with anticoagulation alone



CRF TCT

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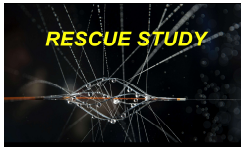
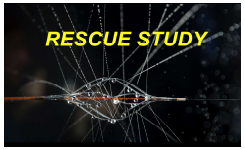


Conclusion

The RESCUE trial showed that PMCDT with the Bashir Endovascular Catheter met its primary efficacy and safety endpoints and demonstrated:

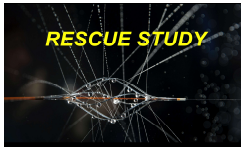
- Reduction in RV/LV ratio by **33.3%** at 48 hours ($p<0.0001$)
- Reduction in PA obstruction index by **35.9%** at 48 hours ($p<0.0001$)
- There were ***fewer than 1% major bleeding or device related adverse events***



Future perspective

- RCT to compare PM-CDT with:
  - Anticoagulation in Intermediate-risk PE patients
  - Systemic thrombolytics in high-risk PE patients.

- PE-TRACT and Hi PEITHO trials will inform us about longer term clinical and functional outcomes

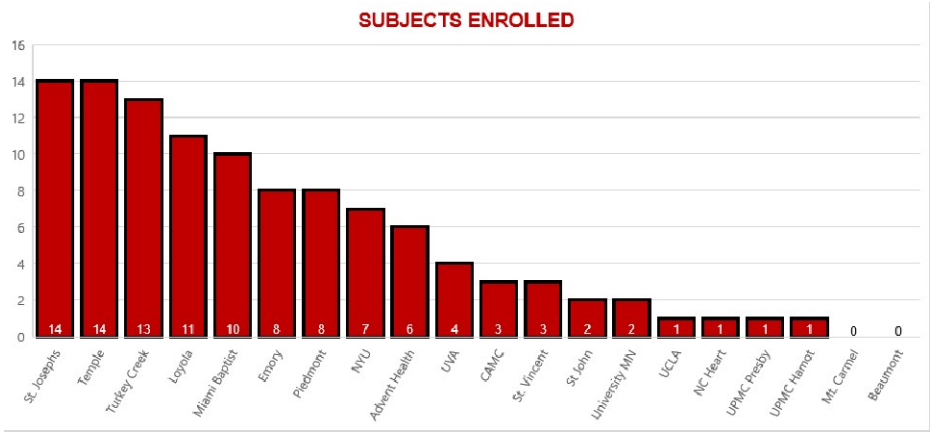


RESCUE STUDY

Management team

- Steering Committee
  - Dr Akhilesh Sista (National Co-PI)
  - Dr Kenneth Rosenfield (National Co-PI)
  - Dr Anthony Comerota
- DSMB/CEC
  - Dr Gregory Piazza (Chairperson)
  - Dr Raghu Kolluri
  - Dr Robert Lookstein
  - Dr Melissa S. Martinson (Statistician)

Enrollment by sites



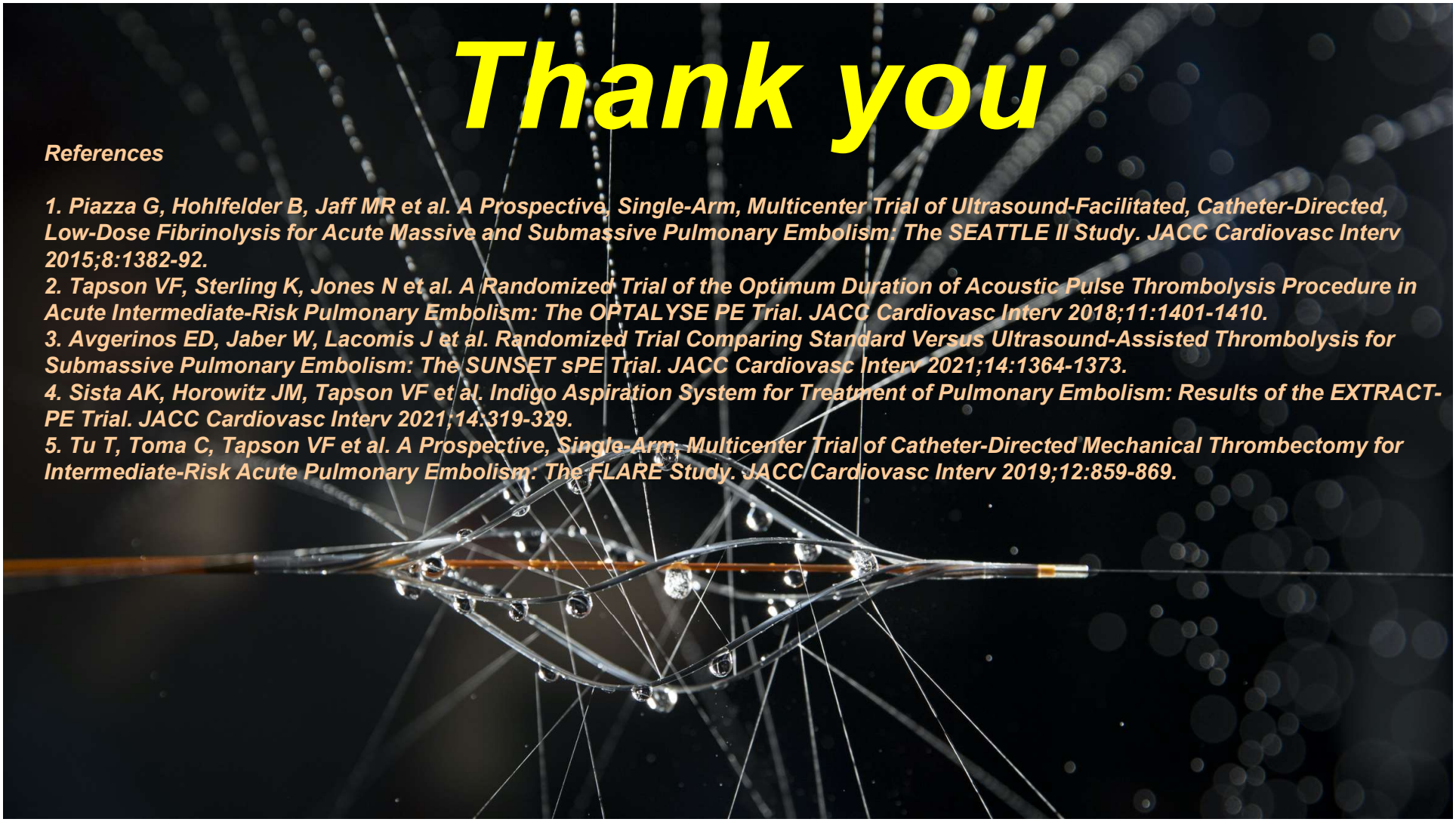
Imaging Core lab

NAMSA/Syntactx Inc. New York NY

Clinical Research Organization

Eminence Inc.

CRF TCT



Thank you

References

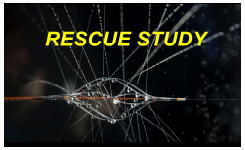
1. Piazza G, Hohlfelder B, Jaff MR et al. A Prospective, Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Catheter-Directed, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism: The SEATTLE II Study. JACC Cardiovasc Interv 2015;8:1382-92.

2. Tapson VF, Sterling K, Jones N et al. A Randomized Trial of the Optimum Duration of Acoustic Pulse Thrombolysis Procedure in Acute Intermediate-Risk Pulmonary Embolism: The OPTALYSE PE Trial. JACC Cardiovasc Interv 2018;11:1401-1410.

3. Avgerinos ED, Jaber W, Lacomis J et al. Randomized Trial Comparing Standard Versus Ultrasound-Assisted Thrombolysis for Submassive Pulmonary Embolism: The SUNSET sPE Trial. JACC Cardiovasc Interv 2021;14:1364-1373.

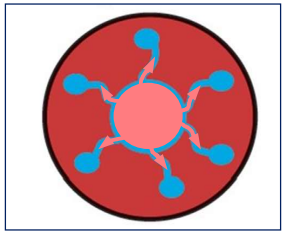
4. Sista AK, Horowitz JM, Tapson VF et al. Indigo Aspiration System for Treatment of Pulmonary Embolism: Results of the EXTRACT-PE Trial. JACC Cardiovasc Interv 2021;14:319-329.

5. Tu T, Toma C, Tapson VF et al. A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism: The FLARE Study. JACC Cardiovasc Interv 2019;12:859-869.



Synergistic Effect Of Endogenous And Exogenous Fibrinolysis

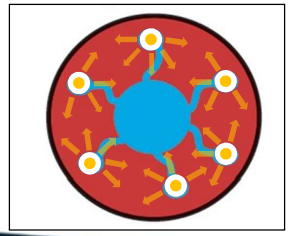
Rapid flow restoration
Endogenous



Luminal filling and blood velocity

Endogenous lytic activity[1,2]

Multichannel infusion
Exogenous

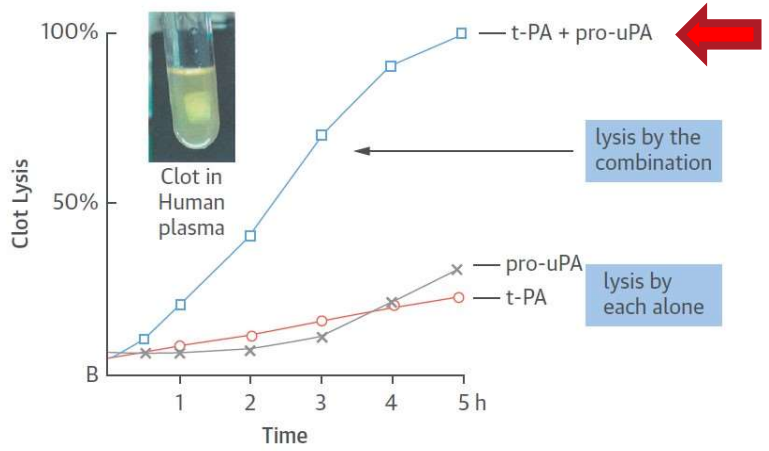


Exposure of fibrin receptors to t-PA

Exogenous lytic activity

Synergistic effect demonstrated in an in vitro model[3]

FIGURE 1 Synergistic Clot Lysis by t-PA and Pro-uPA In Vitro



Gurewich. J Am Coll Cardiol. 2016 Nov 8;68(19):2099-2106