Rationale Of A Pivotal Randomized Trial Comparing Aspiration Thrombectomy Vs Medical Therapy For Intermediate High Risk Pulmonary Embolism

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Disclosures:
In the past 12 months, my spouse or myself have engaged in financial relationships as follows:

• **Advisory Board**: Boston Scientific, Medtronic
• **Consultant**: Penumbra, Neptune Medical, Bard Vascular, Cordis, Biosense Webster, Abbott Vascular, Becton Dickinson, Surmodics
• **Speakers Bureau**: Abbott Vascular
• **Research Support**
  • Philips Healthcare, Spectranetics, Terumo, Boston Scientific, INARI, Penumbra, Ethicon, Walk Vascular, Vesper, Black Swan
• **Equity Shareholder**: Imperative Vascular, Summa Vascular, Innova Vascular, Thrombolex
Vacuum-Assisted Thrombectomy of Massive Pulmonary Embolism

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Aspiration Thrombectomy for Treatment of Acute Massive and Submassive Pulmonary Embolism: Initial Single-Center Prospective Experience

Juan José Ciambi-Dopazo, MD, Juan María Romeu-Prieto, MD, Marcelino Sánchez-Casado, MD, PhD, Beatriz Romerosa, MD, Alfonso Canabal, MD, PhD, María Luisa Rodríguez-Blanco, MD, and Carlos Lanciego, MD, PhD

Aspiration Thrombectomy for the Management of Submassive Pulmonary Embolism: A Single-Center Experience

Ramsey Al-Hakim, MD, Alok Bhatt, MD, and James F. Benenati, MD
EXTRACT-PE: Study Rationale

- Single arm aspiration thrombectomy studies reported improvements in RV/LV ratio and reduction in thrombolytic usage, while maintaining low MAE rates\(^3\)

Indigo Aspiration System for Treatment of Pulmonary Embolism

Results of the EXTRACT-PE Trial

Akhilesh K. Sista, MD, James M. Horowitz, MD, Victor F. Tapson, MD, Michael Rosenberg, MD, Mahir D. Elder, MD, Brian J. Schiro, MD, Suhail Dohad, MD, Nancy E. Amoroso, MD, David J. Dexter, MD, Christopher T. Loh, MD, Daniel A. Leung, MD, Bruce Kirke Bieneman, MD, Paul E. Perkowsk, MD, Michael L. Chuang, MD, James F. Benenati, MD, on behalf of EXTRACT-PE Investigators

Single Arm Catheter Directed Therapy IDE Studies:
Less than 500 patients

- Comparable change in RV/LV ratio for different treatment modalities
- UACDT requires longer treatment time, increased hospital length of stay and is associated with higher percent of major bleeding compared to mechanical thrombectomy

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment Modality</th>
<th>Primary Efficacy (Change in RV/LV ratio)</th>
<th>Primary Safety</th>
<th>Major Bleeding</th>
<th>All-Cause Mortality (30 days)</th>
<th>Device Time</th>
<th>Hospital Length of Stay (Days ± SDI)</th>
<th>Pulmonary Embolism (PE) Recurrence Rate (30 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEATTLE II (N=150)</td>
<td>EkoSonic Endovascular System</td>
<td>24%&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>10%</td>
<td>2.7%</td>
<td>12-24 hrs</td>
<td>8.8 ± 5</td>
<td>n/a</td>
</tr>
<tr>
<td>FLARE&lt;sup&gt;6&lt;/sup&gt; (N=106)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Inari Medical FlowTriever</td>
<td>25.1%</td>
<td></td>
<td>3.8%</td>
<td>1.0%</td>
<td>57 min (mean)</td>
<td>4.1 ± 3.5</td>
<td>1.9%</td>
</tr>
<tr>
<td>EXTRACT-PE&lt;sup&gt;7&lt;/sup&gt; (N=119)</td>
<td>Penumbra Indigo System</td>
<td>27.3%</td>
<td></td>
<td>1.7%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.7%</td>
<td>37 min (median)</td>
<td>3.7 ± 2.5</td>
<td>0%</td>
</tr>
<tr>
<td>RESCUE&lt;sup&gt;8&lt;/sup&gt; (N=109)</td>
<td>Bashir Endovascular Catheter</td>
<td>33.3%&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>0.92%</td>
<td>0.92%</td>
<td>5 hrs</td>
<td>2.88 ± 1.6</td>
<td>0%</td>
</tr>
</tbody>
</table>

- <sup>a</sup> 2 Patients were removed from the intention-to-treat population because of treatment with adjunctive thrombolytic therapy at index procedure. Denominators for all analyses exclude these 2 patients, who were analyzed separately.
- <sup>b</sup> Percent reduction calculated for subjects that had CT scan completed within 48 ± 6 hrs
- <sup>c</sup> 2 patients experienced 3 events ( groin access site bleeding, hemoptysis, death due to sustained ventricular tachycardia post-procedure).
- <sup>d</sup> Definitions of major bleeding differed for each trial. Please refer to the specific publications for further information.
Objective: evaluate real-world long-term functional outcomes, safety, and performance of the Indigo Aspiration System for the treatment of PE

Up to 55 Global sites

600 patients

Patient centric endpoints | QoL & functional

Long-term follow-up to 1 year

Interim analysis of N=87 through 90-day follow-up
Study Flow

- **Baseline visit**
- **Procedure (Day 0)**
- **Postprocedure (48 h ± 6 h)**
- **Discharge**
- **90-day follow-up (±14 d)**
- **365-day follow-up (±45 d)**

Incidence of device-related serious adverse events (SAEs)

RV/LV ratio & composite major adverse events (primary endpoints)

30-day mortality & symptomatic PE recurrence

Functional & quality of life assessments
### Periprocedural Characteristics

#### PE Risk Classification

- **5.7%** (5/87): Submassive/Intermediate Risk
- **94.3%** (82/87): Massive/High Risk

#### Periprocedural characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Interim analysis (N = 87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periprocedural data, median [IQR] or % (n)</td>
<td></td>
</tr>
<tr>
<td>Symptom onset to admission time, h(^a)</td>
<td>27 [12-93]</td>
</tr>
<tr>
<td>Symptom onset to puncture time, h</td>
<td>62 [31-111]</td>
</tr>
<tr>
<td>Thrombectomy procedure time, min(^b)</td>
<td>34 [21-47](^c)</td>
</tr>
<tr>
<td>ICU length of stay after procedure, d(^d)</td>
<td>1 [0-2](^c)</td>
</tr>
<tr>
<td>No ICU stay required</td>
<td>36.8% (32)</td>
</tr>
<tr>
<td>Hospital length of stay after procedure, d</td>
<td>5 [4-7]</td>
</tr>
</tbody>
</table>

\(^a\)Participants admitted before symptom onset were imputed to an admission time of 0.

\(^b\)First Indigo device insertion to last Indigo device removal. \(^c\)N=85.

\(^d\)Participants indicated as not admitted to the ICU were imputed to length of stay as 0 days.
## Safety

<table>
<thead>
<tr>
<th>Primary and secondary safety endpoints, % (n)</th>
<th>Interim analysis (N = 87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major adverse events within 48 h (composite)</td>
<td>2.3% (2)</td>
</tr>
<tr>
<td>Major bleeding within 48 h&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.3% (2)</td>
</tr>
<tr>
<td>Device-related death within 48 h&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Device-related clinical deterioration within 48 h&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.1% (1)</td>
</tr>
<tr>
<td>Device-related cardiac injury within 48 h&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Device-related pulmonary vascular injury within 48 h&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.1% (1)</td>
</tr>
<tr>
<td>Device-related serious adverse events&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.1% (1)</td>
</tr>
<tr>
<td>Any-cause mortality within 30 d&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Recurrent PE within 30 d&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.1% (1)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Per independent medical reviewer.  
<sup>b</sup>Per independent medical reviewer else principal investigator.  
<sup>c</sup>Per principal investigator.
RV/LV Ratio & sPAP

Mean Change in RV/LV Ratio
(CTA else ECHO)

Mean Change in Systolic Pulmonary Artery Pressure (sPAP)

Change calculated by using matched imaging modality pairs (n = 77)
Change calculated by using paired data (n = 80)
Quality of Life Outcomes at 90 Days

Mean Change in EQ VAS
(Visual Analog Scale)

<table>
<thead>
<tr>
<th></th>
<th>Discharge</th>
<th>90 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>55.2</td>
<td>79.2</td>
</tr>
</tbody>
</table>

Change calculated by using paired data (n = 70)

\( P < .001 \)

Median Change in Overall PE Quality of Life (PEmb-QoL)

<table>
<thead>
<tr>
<th></th>
<th>Discharge</th>
<th>90 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>36.7%</td>
<td>17.7%</td>
</tr>
</tbody>
</table>

Change calculated by using paired data (n = 77)

\( P < .001 \)

Increase: \( \Delta 23.9 \) MCID (chronic lung disease): 10-20%

Decrease: \( \Delta 19.0 \) MCID (PE): 15%

Extent of daily life affected by PE:

- Discharge: 36.7%
- 90 days: 17.7%

\textsuperscript{1}COPD 2005;2(1):105-110.
\textsuperscript{1}J Thromb Haemost 2018;16(12):2454-2461.
STRIKE-PE: Preliminary LIGHTNING FLASH (16fr) Data

Periprocedural data

- # of unique operators: 12
- Thrombectomy time, min\(^a\) (median): 25 min
- Bilateral treatment (mean): 93.3% (14/15)

\(^a\) First Indigo device insertion to last Indigo device removal

Outcomes

- RV/LV ratio change at 48hrs (mean): -0.56\(^a\)
- RV/LV ratio % reduction at 48hrs (mean): 36.5\(^a\)%
- Bleeding adverse events: 0% (0/15)
- Borg Dyspnea Scale % reduction pre-procedure to discharge (mean): 78\(^b\)%

\(^a\) N=14
\(^b\) N=13

Data as of 20APR2023 is preliminary, reported as is & undergoing data cleaning
Total of 17 cases have been completed, however data was only available for N=15
HOW CAN WE ADVANCE THE SCIENCE AND CREATE LEVEL ONE EVIDENCE FOR ASPIRATION THROMBECTOMY FOR ACUTE PULMONARY EMBOLISM?
A Prospective, Multicenter, Randomized Controlled Trial
Evaluating Anticoagulation Alone vs Anticoagulation plus Mechanical Aspiration with the Indigo® Aspiration System for the Treatment of Intermediate High Risk Pulmonary Embolism
In collaboration with PERT CONSORTIUM®
# Multidisciplinary Leadership

## Global PIs
- Rachel Rosovsky | *Hematology* | *MGH*
- Rob Lookstein | *Interventional Radiology* | *Mount Sinai (NY)*

## Steering Committee
- Ido Weinberg | *Vascular Medicine* | *MGH*
- Richard Channick | *Pulmonology* | *UCLA*
- John Moriarty | *Interventional Radiology* | *UCLA*
- Stavros Konstantinides | *Cardiology* | *University of Mainz, Germany*
- Sahil Parikh | *Interventional Cardiology* | *New York Presbyterian*
Objective: evaluate safety and efficacy in intermediate-high risk PE patients through a first of its kind comparison of mechanical aspiration thrombectomy to conservative management with anticoagulation alone.

Up to 20 sites

100 patients

Patient-centric endpoints | QoL & functional

90-day follow-up
STORM-PE Study Design & Objective

Intermediate-high risk patients

1:1 randomization

Indigo + AC vs AC Alone
Key Eligibility Criteria

Inclusion

▪ Clinical signs and symptoms consistent with acute PE with duration of 14 days or less
▪ Classification of intermediate high-risk PE as demonstrated by right ventricular dysfunction with RV/LV ratio ≥ 1.0 on CTPA and elevated cardiac biomarkers, including cardiac troponin, BNP, and/or NT-pro BNP above the upper limit of normal

Exclusion

▪ Administration of thrombolytic agents or glycoprotein IIb/IIIa receptor antagonist within 30 days prior to baseline imaging
▪ Hemodynamic instability
▪ Patients on ECMO
▪ National Early Warning Score 2 (NEWS2) ≥ 9
▪ Active cancer or cancer/tumor requiring active therapy (surgery, chemotherapy, targeted therapy, or radiation) in the previous 6 months or during the course of the trial (other than non-melanoma skin cancer) or tumor with caval invasion
Study Endpoints

Primary
- Change in RV/LV ratio at 48 hrs as assessed by CTPA

Secondary
- Major adverse events (MAEs) within 7 days: a composite of clinical deterioration requiring escalation of care, PE-related mortality, symptomatic recurrent PE, or major bleeding
- Functional outcomes through 90 days
- Quality of Life (QoL) through 90 days
- All-cause mortality within 90 days
- PE-related mortality within 90 days
- Symptomatic PE recurrence within 90 days
QoL & Functional Outcome Measures

- PEmb-QoL Questionnaire
- EQ-5D-5L Questionnaire & EQ-VAS
- 6MWT
- Borg Scale & mMRC for dyspnea
- NYHA Classification
- Post-VTE functional status scale (PVFS)
- Wearable Device Sub-study
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Intervention Comparison</th>
<th>Subjects</th>
<th>Site Information</th>
<th>Endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT-1:1</td>
<td>EKOS VS. ANTICOAG INTERMEDIATE HIGH</td>
<td>RCT 1:1 FLOWTRIEVER VS CDT INTERMEDIATE HIGH</td>
<td>406 SUBJECTS  65 GLOBAL SITES</td>
<td>MORTALITY ICH ISTH MAJOR BLEEDING CLINICAL DETERIORATION ICU LOS. (DISCHARGE)</td>
<td>(PE)-RELATED MORTALITY, CARDIORESPIRATORY DECOMPENSATION OR COLLAPSE, NONFATAL SYMPTOMATIC AND OBJECTIVELY CONFIRMED RECURRENTCE OF PE</td>
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<td></td>
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<td>PV02 AT 90 DAYS NYHA CLASSIFICATION AT ONE YEAR ISTH MAJOR BLEED AT 7 DAYS</td>
<td>RV/LV RATIO AT 48 HOURS (PE)-RELATED MORTALITY, CARDIORESPIRATORY DECOMPENSATION OR COLLAPSE, NONFATAL SYMPTOMATIC AND OBJECTIVELY CONFIRMED RECURRENTCE OF PE</td>
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<td>ALL-CAUSE MORTALITY BY 30 DAYS CLINICAL DETERIORATION AND/OR BAILOUT BY 30 DAYS ALL-CAUSE HOSPITAL READMISSION BY 30 DAYS DYSPNEA SCORE AT 48-HOUR VISIT</td>
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<td></td>
<td>12 MONTHS</td>
<td>30 DAY FOLLOW UP</td>
<td>12 MONTHS</td>
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</table>
Summary: STORM-PE

- First randomized, level 1 data comparing mechanical aspiration thrombectomy to anticoagulation alone
- Advance our understanding of best treatment options for intermediate high-risk PE patients
- Preliminary Flash data for STRIKE-PE is promising regarding efficacy and safety