



STAIR 2013

Study Designs and Endpoints in Ongoing Endovascular Stroke Trials

Wade S. Smith, MD, PhD

Director UCSF Neurovascular Service
Daryl R. Gress Professor of Neurocritical Care and Stroke

Disclosures

- IA t-PA is not labeled for clinical use
- NIH
 - U10 NS058931 - NETT
- Consultant:
 - Stryker
- DSMB
 - HCRI, NIH

Wade S. Smith, MD, PhD

Director UCSF Neurovascular Service

Daryl R. Gress Professor of Neurocritical Care and Stroke

Ongoing Trials

| Trial | Status | Design | Design | PI |
|------------|----------------|---------------|--|-------------------------------|
| CRISP | Recruiting | Observational | Prospective Cohort, Observational | M. Lanssberg |
| SWISS | Recruiting | Observational | IV t-PA or IAT within 6 hours, consecutively treated | M. Arnold, K Nedeltechew |
| PRIISM2 | Not recruiting | Observational | Mindframe device, consecutive registry | M. Soderman |
| ENDOSTROKE | Recruiting | Observational | Outcome of patients treated with mechanical embolectomy | O. Singer |
| ESCAPE | Recruiting | Randomized | Randomized Emb vs. Medical Tx | M. Hill |
| THERAPY | Recruiting | Randomized | IV t-PA vs IV t-PA + IA Penumbra | J Mocco, P. Khatri, O Saaidat |
| REVASCAT | Recruiting | Randomized | Randomized, prospective, Solitaire vs. medical therapy | M Ribo |
| WASSABI | Recruiting | Randomized | Randomized IV t-PA vs. IA therapy | E. Levy, T. Kass-Hout |
| MR CLEAN | Recruiting | Randomized | IA t-PA/Embolectomy vs. Medical Therapy; IV t-PA allowed | DWJ Dippel |
| BASICS | Recruiting | Randomized | Randomized between IV t-PA + IA tx vs. IV t-PA alone | W. Schonewille |
| SWIFT | | | Randomized IV t-pa vs. IV t-PA | |
| PRIME | | | | |

Randomized Trials

| Trial | Design | Image Selection | Window | Eligibility | Size | Enpt* |
|----------------|--|--|--|--------------------------|------|-----------------------|
| ESCAPE | Randomized Embolectomy vs. Medical Therapy (Iv t-PA ok) | CTA: ICA T/L, M1 or both M2s; ASPECTS > 5 & CTP criteria | < 12 h | NIHSS >= 6 | 250 | mRS = 0-2 |
| THERAPY | IV t-PA vs. IV t-PA + IA Penumbra Randomized, prospective, Solitaire vs. medical therapy (IV t-PA ok) | CTA/MRA: clot > 8 mm length | IV t-PA < 4.5 h, then Penumbra | NIHSS >= 8 or aphasic | 692 | mRS = 0-2 |
| REVASCA T | Randomized IV t-PA vs. IA therapy | CTA/MRA/DSA: ICA T/L or M1 | < 8 h | NIHSS > 5 | 690 | mRS shift analysis |
| WASSABI | IA t-PA/Embolectomy vs. Medical Therapy (IV t-PA ok) | CTP: Penumbra, ASPECTS >=7 | WOS < 24 h | NIHSS 8-22 | 90 | mRS |
| MR CLEAN | Randomized between IV t-PA + IA tx vs. IV t-PA alone | MRA/CTA/TCD/DSA: M1-2, A1-2 | < 6 h | NIHSS >=6 | 500 | mRS |
| BASICS | Randomized between IV t-PA + IA tx vs. IV t-PA alone | CTA/MRA: BA occlusion | < 6 h to IA treatment | NIHSS >=10 | 750 | mRS 0-3 |
| SWIFT PRIME | Randomized IV t-PA vs. IV t-PA and IA Solitaire | CTA/MRA & CTP or MRP criteria | IV t-PA < 4.5 h, then IA Solitaire start <1.5 h later | NIHSS 8-30 | 833 | mRS |

* - all endpoints are at 90 days post stroke

Randomized Trials

IMS-III- like design: 4/8

| Trial | Design | Image Selection | Window | Eligibility | Size | Enpt* |
|----------------|--|--|--|--------------------------|------|-----------------------|
| ESCAPE | Randomized Embolectomy vs. Medical Therapy (IV t-PA ok) | CTA: ICA T/L, M1 or both M2s; ASPECTS > 5 & CTP criteria | < 12 h | NIHSS >= 6 | 250 | mRS = 0-2 |
| THERAPY | IV t-PA vs. IV t-PA + IA Penumbra | CTA/MRA: clot > 8 mm length | IV t-PA < 4.5 h, then Penumbra | NIHSS >= 8 or aphasic | 692 | mRS = 0-2 |
| REVASCA T | Randomized, prospective, Solitaire vs. medical therapy (IV t-PA ok) | CTA/MRA/DSA: ICA T/L or M1 | < 8 h | NIHSS > 5 | 690 | mRS shift analysis |
| WASSABI | Randomized IV t-PA vs. IA therapy | CTP: Penumbra, ASPECTS >=7 | WOS < 24 h | NIHSS 8-22 | 90 | mRS |
| MR CLEAN | IA t-PA/Embolectomy vs. Medical Therapy (IV t-PA ok) | MRA/CTA/TCD/DSA: M1-2, A1-2 | < 6 h | NIHSS >=6 | 500 | mRS |
| BASICS | Randomized between IV t-PA + IA tx vs. IV t-PA alone | CTA/MRA: BA occlusion | < 6 h to IA treatment | NIHSS >=10 | 750 | mRS 0-3 |
| SWIFT PRIME | Randomized IV t-PA vs. IV t-PA and IA Solitaire | CTA/MRA & CTP or MRP criteria | IV t-PA < 4.5 h, then IA Solitaire start <1.5 h later | NIHSS 8-30 | 833 | mRS |
| | | | <4.5 h IV t-PA, then IA < 90 | | | |

* - all endpoints are at 90 days post stroke

Randomized Trials

IV t-PA is allowed in all, required in 5/8

| Trial | Design | Image Selection | Window | Eligibility | Size | Enpt* |
|-------------|---|--|---|-----------------------|------|--------------------|
| ESCAPE | Randomized Embolectomy vs. Medical Therapy (IV t-PA ok) | CTA: ICA T/L, M1 or both M2s; ASPECTS > 5 & CTP criteria | < 12 h | NIHSS >= 6 | 250 | mRS = 0-2 |
| THERAPY | IV t-PA vs. IV t-PA + IA Penumbra | CTA/MRA: clot > 8 mm length | IV t-PA < 4.5 h, then Penumbra | NIHSS >= 8 or aphasic | 692 | mRS = 0-2 |
| REVASCAT | Randomized, prospective, Solitaire vs. medical therapy (IV t-PA ok) | CTA/MRA/DSA: ICA T/L or M1 | < 8 h | NIHSS > 5 | 690 | mRS shift analysis |
| WASSABI | Randomized IV t-PA vs. IA therapy | CTP: Penumbra, ASPECTS >=7 | WOS < 24 h | NIHSS 8-22 | 90 | mRS |
| MR CLEAN | IA t-PA/Embolectomy vs. Medical Therapy (IV t-PA ok) | MRA/CTA/TCD/DSA: M1-2, A1-2 | < 6 h | NIHSS >=6 | 500 | mRS |
| BASICS | Randomized between IV t-PA + IA tx vs. IV t-PA alone | CTA/MRA: BA occlusion | < 6 h to IA treatment | NIHSS >=10 | 750 | mRS 0-3 |
| SWIFT PRIME | Randomized IV t-PA vs. IV t-PA and IA Solitaire | CTA/MRA & CTP or MRP criteria | IV t-PA < 4.5 h, then IA Solitaire start <1.5 h later | NIHSS 8-30 | 833 | mRS |
| | | | <4.5 h IV t-PA, then IA < 90 | | | |

* - all endpoints are at 90 days post stroke

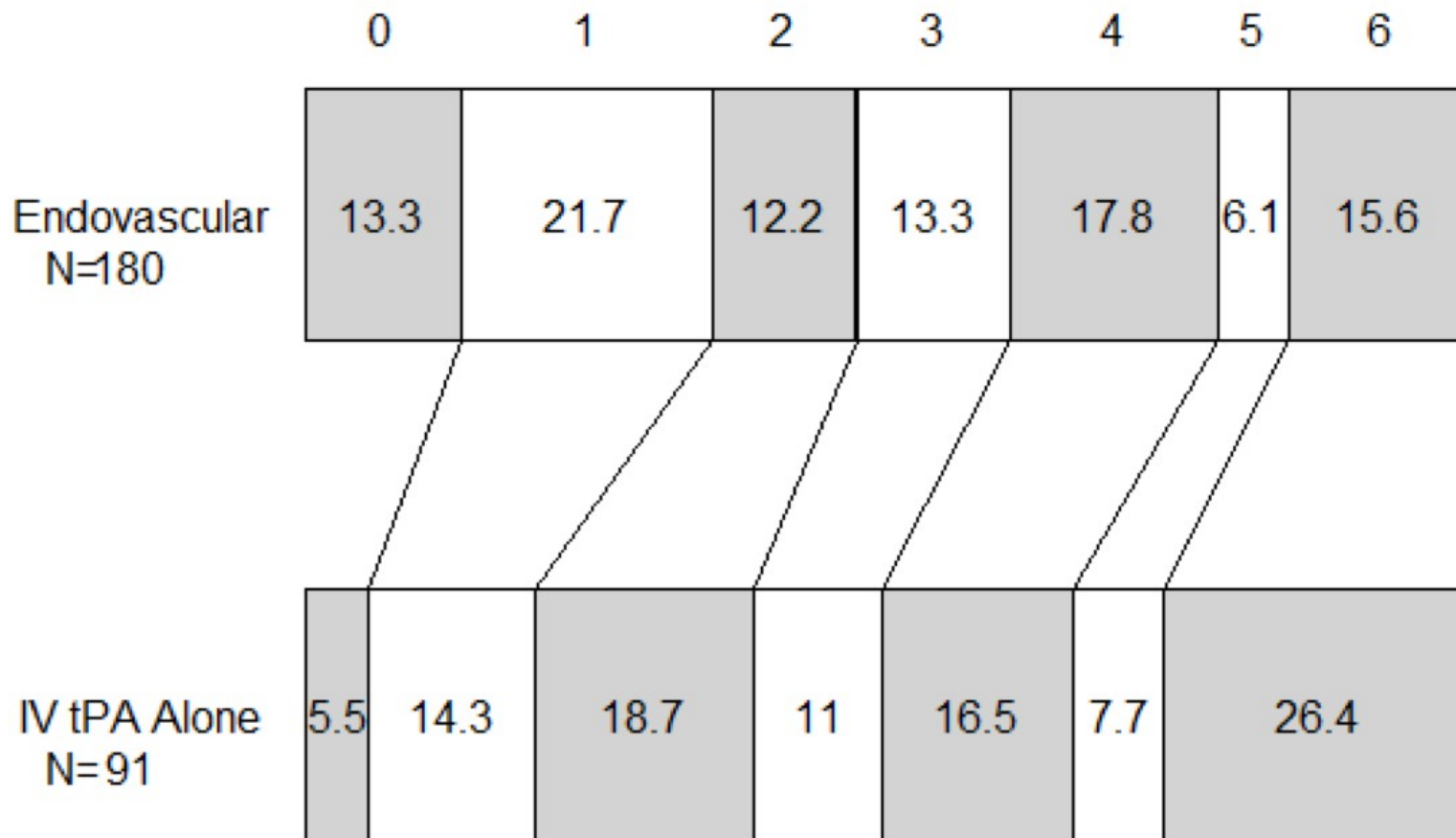
Randomized Trials

All 8 require CTA or MRA confirmation of LVO

| Trial | Design | Image Selection | Window | Eligibility | Size | Enpt* |
|-------------|---|--|---|-----------------------|------|--------------------|
| ESCAPE | Randomized Embolectomy vs. Medical Therapy (IV t-PA ok) | CTA: ICA T/L, M1 or both M2s; ASPECTS > 5 & CTP criteria | < 12 h | NIHSS >= 6 | 250 | mRS = 0-2 |
| THERAPY | IV t-PA vs. IV t-PA + IA Penumbra | CTA/MRA: clot > 8 mm length | IV t-PA < 4.5 h, then Penumbra | NIHSS >= 8 or aphasic | 692 | mRS = 0-2 |
| REVASCAT | Randomized, prospective, Solitaire vs. medical therapy (IV t-PA ok) | CTA/MRA/DSA: ICA T/L or M1 | < 8 h | NIHSS > 5 | 690 | mRS shift analysis |
| WASSABI | Randomized IV t-PA vs. IA therapy | CTP: Penumbra, ASPECTS >=7 | WOS < 24 h | NIHSS 8-22 | 90 | mRS |
| MR CLEAN | IA t-PA/Embolectomy vs. Medical Therapy (IV t-PA ok) | MRA/CTA/TCD/DSA: M1-2, A1-2 | < 6 h | NIHSS >=6 | 500 | mRS |
| BASICS | Randomized between IV t-PA + IA tx vs. IV t-PA alone | MRA/CTA/TCD/DSA: M1-2, A1-2 | < 6 h to IA treatment | NIHSS >=10 | 750 | mRS 0-3 |
| SWIFT PRIME | Randomized IV t-PA vs. IV t-PA and IA Solitaire | CTA/MRA & CTP or MRP criteria | IV t-PA < 4.5 h, then IA Solitaire start <1.5 h later | NIHSS 8-30 | 833 | mRS |
| | | | <4.5 h IV t-PA, then IA < 90 | | | |

* - all endpoints are at 90 days post stroke

90-Day mRS Distribution, Baseline CTA Occlusion Present



van Elteren test p-value 0.0114



Randomized Trials

Perfusion selection required in 3/8

| Trial | Design | Image Selection Window | Eligibility | Size | Enpt* | |
|-------------|---|--|---|-----------------------|-------|--------------------|
| ESCAPE | Randomized Embolectomy vs. Medical Therapy (IV t-PA ok) | CTA: ICA T/L, M1 or both M2s; ASPECTS > 5 & CTP criteria | < 12 h | NIHSS >= 6 | 250 | mRS = 0-2 |
| THERAPY | IV t-PA vs. IV t-PA + IA Penumbra | CTA/MRA: clot > 8 mm length | IV t-PA < 4.5 h, then Penumbra | NIHSS >= 8 or aphasic | 692 | mRS = 0-2 |
| REVASCA | Randomized, prospective, Solitaire vs. medical therapy (IV t-PA ok) | CTA/MRA/DSA: ICA T/L or M1 | < 8 h | NIHSS > 5 | 690 | mRS shift analysis |
| WASSABI | Randomized IV t-PA vs. IA therapy | CTP: Penumbra, ASPECTS >=7 | WOS < 24 h | NIHSS 8-22 | 90 | mRS |
| MR CLEAN | IA t-PA/Embolectomy vs. Medical Therapy (IV t-PA ok) | MRA/CTA/TCD/DSA: M1-2, A1-2 | < 6 h | NIHSS >=6 | 500 | mRS |
| BASICS | Randomized between IV t-PA + IA tx vs. IV t-PA alone | CTA/MRA: BA occlusion | < 6 h to IA treatment | NIHSS >=10 | 750 | mRS 0-3 |
| SWIFT PRIME | Randomized IV t-PA vs. IV t-PA and IA Solitaire | CTA/MRA & CTP or MRP criteria | IV t-PA < 4.5 h, then IA Solitaire start <1.5 h later | NIHSS 8-30 | 833 | mRS |

* - all endpoints are at 90 days post stroke

Randomized Trials

Window ranges up to 24 hours, 3/8 < 4.5 hrs

| Trial | Design | Image Selection | Window | Eligibility | Size | Enpt* |
|-------------|---|--|---|-----------------------|------|--------------------|
| ESCAPE | Randomized Embolectomy vs. Medical Therapy (IV t-PA ok) | CTA: ICA T/L, M1 or both M2s; ASPECTS > 5 & CTP criteria | < 12 h | NIHSS >= 6 | 250 | mRS = 0-2 |
| THERAPY | IV t-PA vs. IV t-PA + IA Penumbra | CTA/MRA: clot > 8 mm length | IV t-PA < 4.5 h, then Penumbra | NIHSS >= 8 or aphasic | 692 | mRS = 0-2 |
| REVASCA T | Randomized, prospective, Solitaire vs. medical therapy (IV t-PA ok) | CTA/MRA/DSA: ICA T/L or M1 | < 8 h | NIHSS > 5 | 690 | mRS shift analysis |
| WASSABI | Randomized IV t-PA vs. IA therapy | CTP: Penumbra, ASPECTS >=7 | WOS < 24 h | NIHSS 8-22 | 90 | mRS |
| MR CLEAN | IA t-PA/Embolectomy vs. Medical Therapy (IV t-PA ok) | MRA/CTA/TCD/DSA: M1-2, A1-2 | < 6 h | NIHSS >=6 | 500 | mRS |
| BASICS | Randomized between IV t-PA + IA tx vs. IV t-PA alone | CTA/MRA: BA occlusion | < 6 h to IA treatment | NIHSS >=10 | 750 | mRS 0-3 |
| SWIFT PRIME | Randomized IV t-PA vs. IV t-PA and IA Solitaire | CTA/MRA & CTP or MRP criteria | IV t-PA < 4.5 h, then IA Solitaire start <1.5 h later | NIHSS 8-30 | 833 | mRS |

* - all endpoints are at 90 days post stroke

Randomized Trials

Six of 8 have no upper limit to NIHSS

| Trial | Design | Image Selection | Window | Eligibility | Size | Enpt* |
|-------------|---|--|---|-----------------------|------|--------------------|
| ESCAPE | Randomized Embolectomy vs. Medical Therapy (IV t-PA ok) | CTA: ICA T/L, M1 or both M2s; ASPECTS > 5 & CTP criteria | < 12 h | NIHSS >= 6 | 250 | mRS = 0-2 |
| THERAPY | IV t-PA vs. IV t-PA + IA Penumbra | CTA/MRA: clot > 8 mm length | IV t-PA < 4.5 h, then Penumbra | NIHSS >= 8 or aphasic | 692 | mRS = 0-2 |
| REVASCA T | Randomized, prospective, Solitaire vs. medical therapy (IV t-PA ok) | CTA/MRA/DSA: ICA T/L or M1 | < 8 h | NIHSS > 5 | 690 | mRS shift analysis |
| WASSABI | Randomized IV t-PA vs. IA therapy | CTP: Penumbra, ASPECTS >=7 | WOS < 24 h | NIHSS 8-22 | 90 | mRS |
| MR CLEAN | IA t-PA/Embolectomy vs. Medical Therapy (IV t-PA ok) | MRA/CTA/TCD/DSA: M1-2, A1-2 | < 6 h | NIHSS >=6 | 500 | mRS |
| BASICS | Randomized between IV t-PA + IA tx vs. IV t-PA alone | CTA/MRA: BA occlusion | < 6 h to IA treatment | NIHSS >=10 | 750 | mRS 0-3 |
| SWIFT PRIME | Randomized IV t-PA vs. IV t-PA and IA Solitaire | CTA/MRA & CTP or MRP criteria | IV t-PA < 4.5 h, then IA Solitaire start <1.5 h later | NIHSS 8-30 | 833 | mRS |

* - all endpoints are at 90 days post stroke

Study Design and Endpoints

in ongoing endovascular Trials

- 8 planned or ongoing randomized prospective trials; totals 3,805 patients
- All allow or require IV t-PA
- All require CTA or MRA unlike IMS-III and SYNTHESIS
- IMS-III design in 50% but include LVO imaging requirement
- Perfusion imaging required in 3/8 trials
- mRS is primary outcome for all trials but may have different ranges

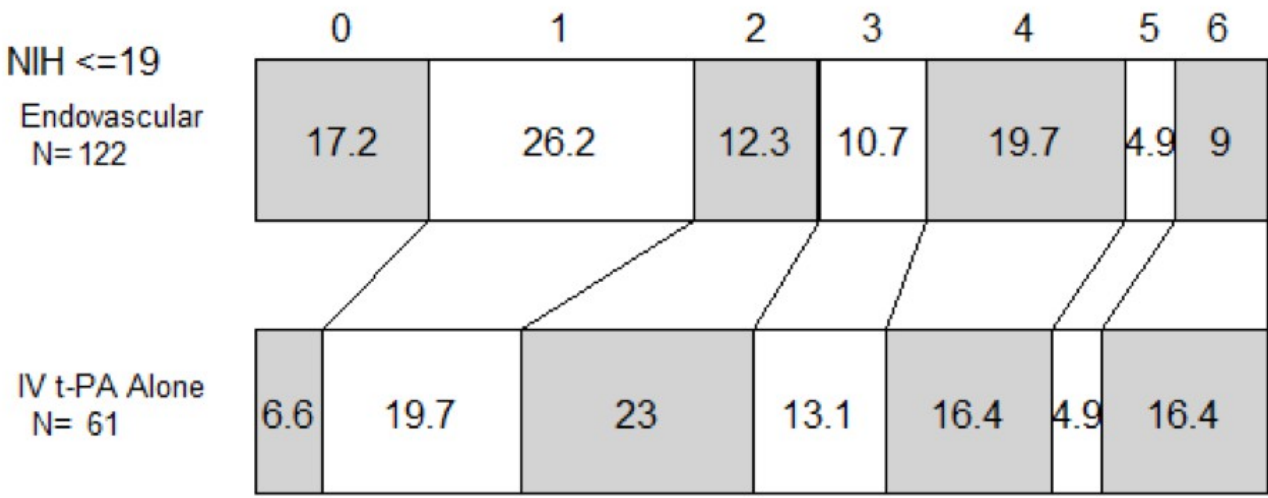
Study Design and Endpoints

in ongoing endovascular Trials

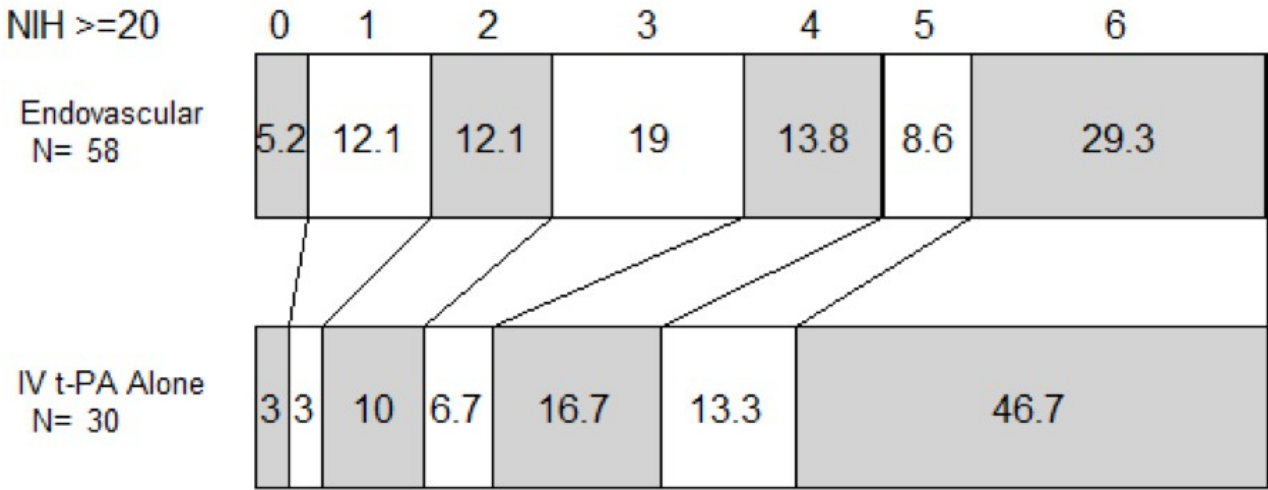
Concerns

- Allowance of relatively low NIHSS
- No strong emphasis on time to IA treatment

90-Day mRS, Baseline CTA Occl Present, by Severity Strata



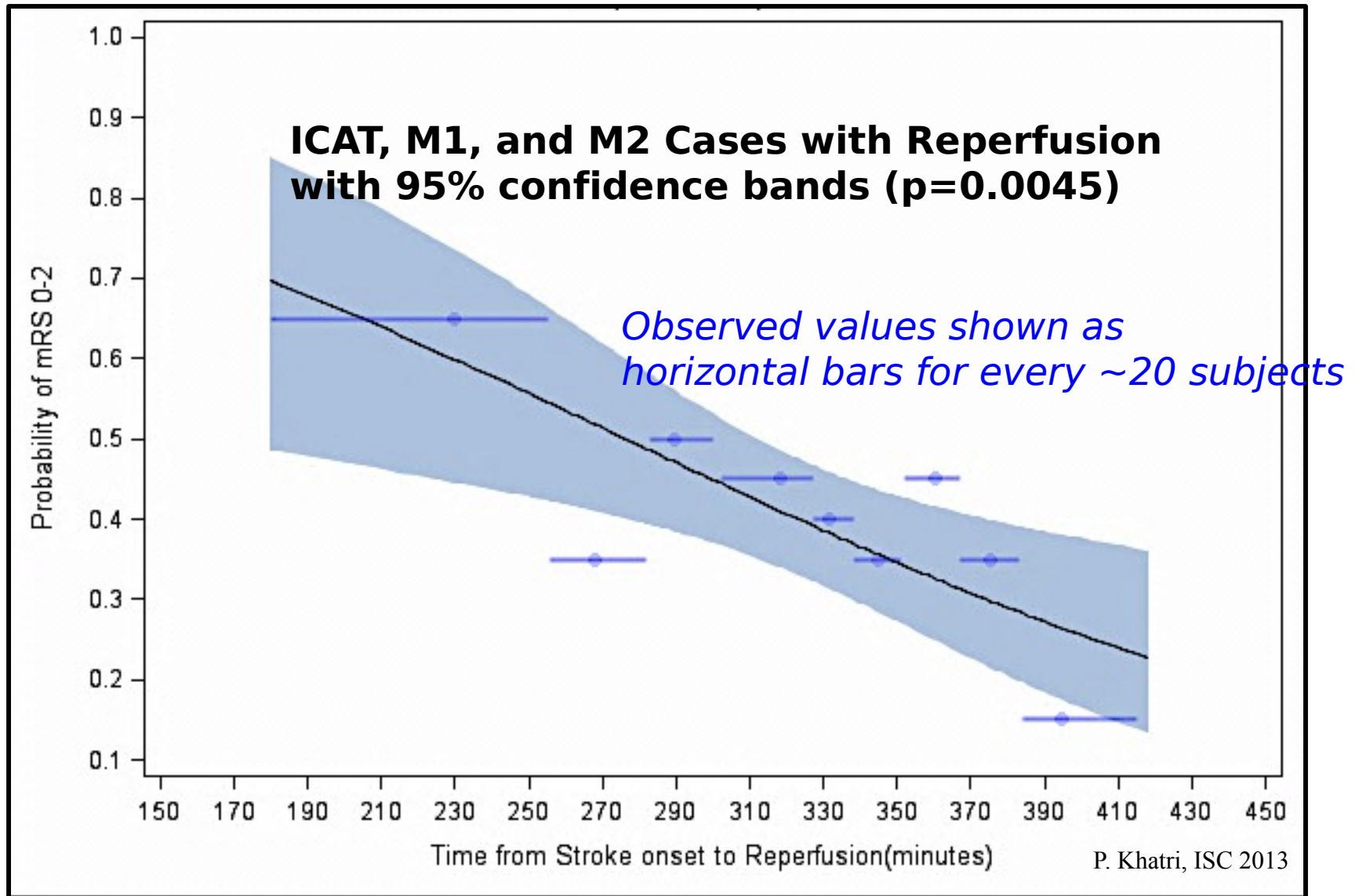
P= 0.0648

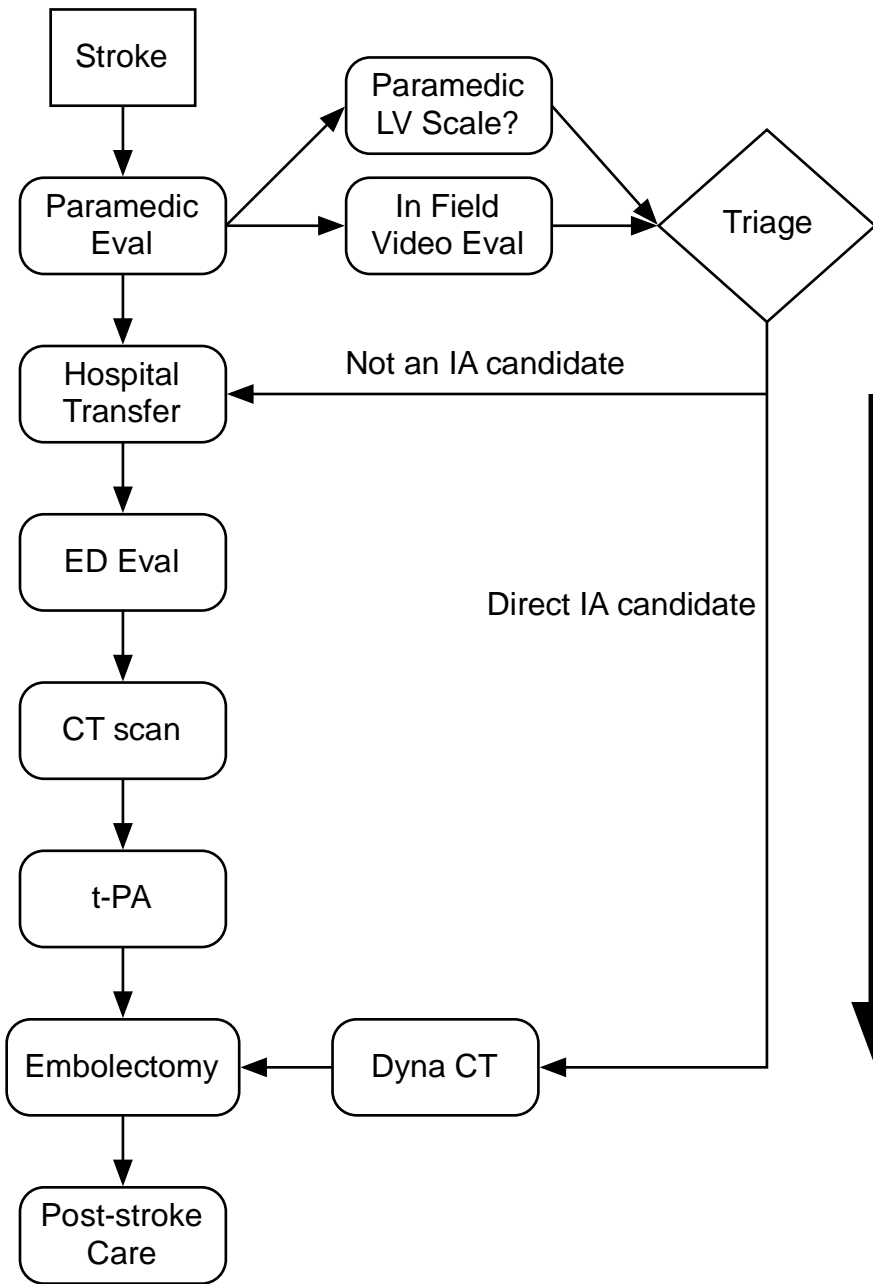


P= 0.0330

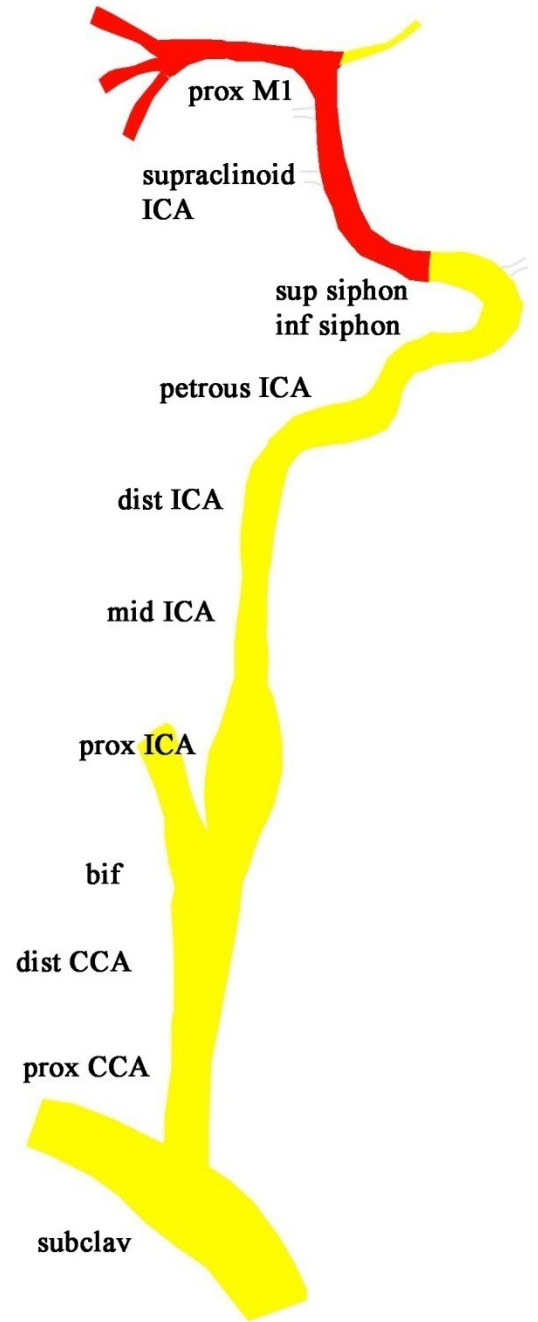


Time to Reperfusion and Good Clinical Outcome Observed Vs Predicted.





1.5 hours



Study Design and Endpoints in ongoing endovascular Trials

Concerns

- Allowance of relatively low NIHSS
- No strong emphasis on time to IA treatment

