



VII CONGRESSO ANEU

CONTROVERSIE IN NEUROLOGIA
D'EMERGENZA E URGENZA

29 SETTEMBRE
1 OTTOBRE 2022

ROMA

**Stroke da
occlusione vaso
maggiore come
trattare?**

**Trombectomia
diretta**

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Azienda Policlinico Umberto I

UTN

Roma

European Stroke Organisation (ESO)–European Society for Minimally Invasive Neurological Therapy (ESMINT) expedited recommendation on indication for intravenous thrombolysis before mechanical thrombectomy in patients with acute ischemic stroke and anterior circulation large vessel occlusion

Evidence-based recommendation

For patients directly admitted to a thrombectomy-capable center for an acute ischemic stroke (≤ 4.5 hours of symptom onset) with anterior circulation large vessel occlusion and who are eligible for both treatments, we recommend intravenous thrombolysis plus mechanical thrombectomy over mechanical thrombectomy alone.

Both treatments should be performed as early as possible after hospital arrival. Mechanical thrombectomy should not prevent the initiation of intravenous thrombolysis, and intravenous thrombolysis should not delay mechanical thrombectomy.

Quality of evidence: Moderate ⊕⊕⊕

Strength of recommendation: Strong ↑↑

- 1) DIRECT-MT
- 2) DEVT
- 3) SKIP
- 4) MR CLEAN NO IV
- 5) SWIFT-DIRECT
- 6) DIRECT-SAFE

2331 pts

Medscape

**'Case Closed': Bridging
Thrombolysis Remains 'Gold
Standard' in Stroke
Thrombectomy**



Concerns regarding iv thrombolysis

- Potential procedural delays
- Clot fragmentation and distal clot migration precluding eligibility for MT
- Haemorrhagic complications
- Costs

Advantages

- Bridging IV thrombolysis may lyse distal thrombi
- Favorably alter clot properties to facilitate retrieval, leading to higher first-pass effect and successful reperfusion rates

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Potential procedural delays in real world

- Controllo dei valori pressori (<185/110 mmHg)
- Iperglicemia (goal <180-200 mg/dL)
- Necessità di sottoporre il paziente a radiografie per sospette fratture (femore, bacino etc)
- Problemi logistici

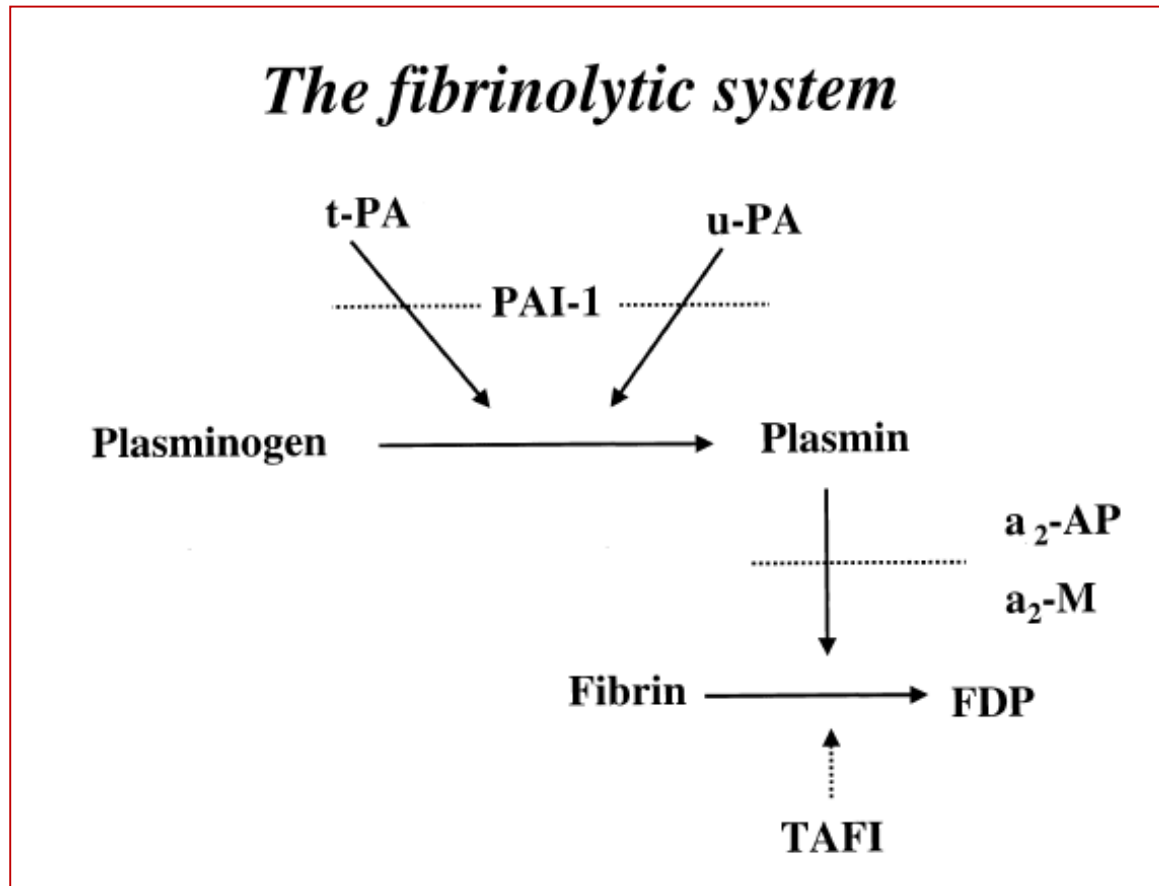


Concerns regarding iv thrombolysis

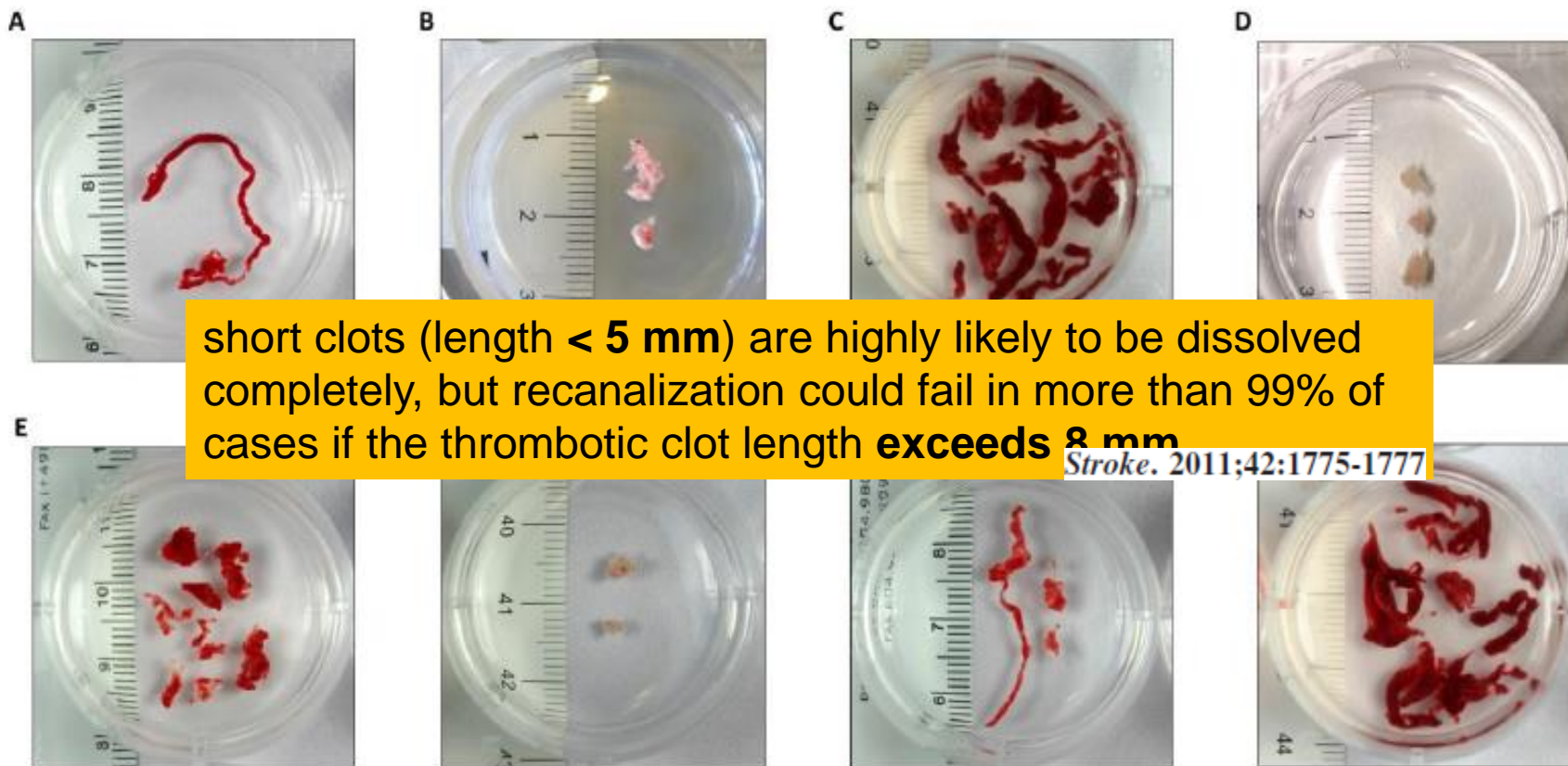
- Potential procedural delays
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Fibrinolysis:



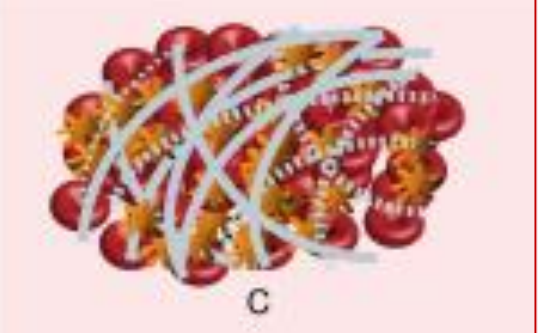

tPA sensitivity is associated with fibrin clot architecture
in the thrombus

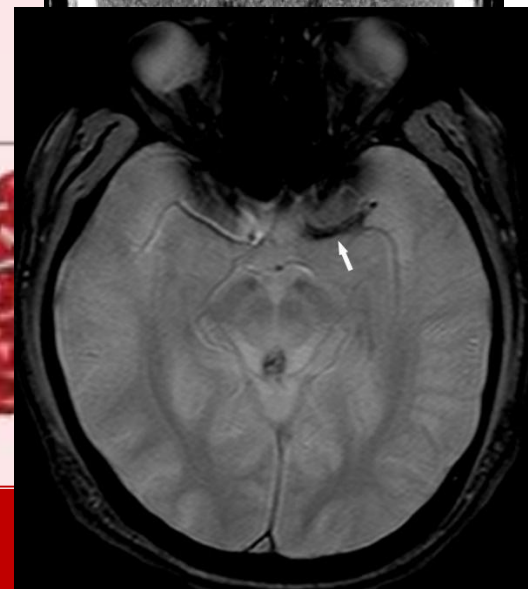


Macroscopic pictures of thrombi retrieved from stroke patients



Clot composition

	Fibrin-rich	RBC-rich
Mechanical thrombectomy	 <p>A</p>	 <p>B</p>
Thrombolysis	 <p>C</p>	 <p>D</p>

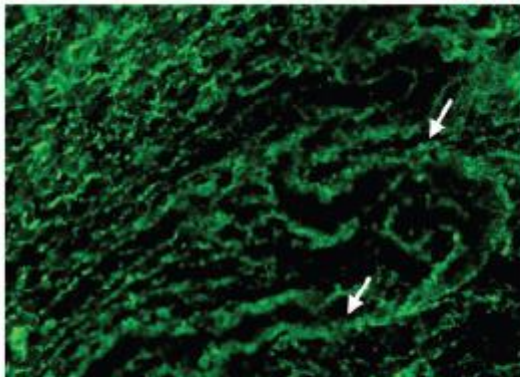


- Cardioembolic cause
- Stable and late phase thrombosis
- VWF

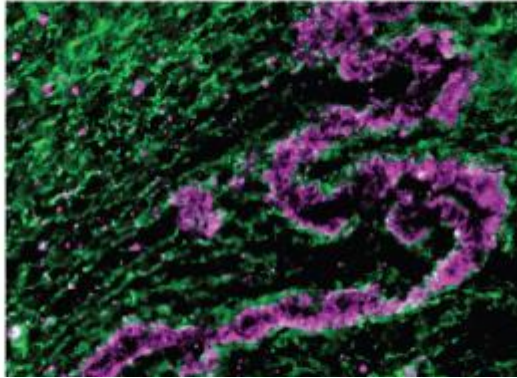
- Non-cardioembolic thrombi
- Hyperdense MCA sign
- Thrombus migration
- Early phase
- Inflammatory T cells and monocytes

D

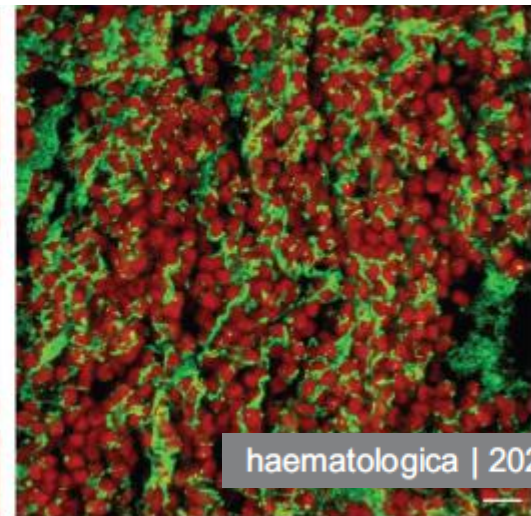
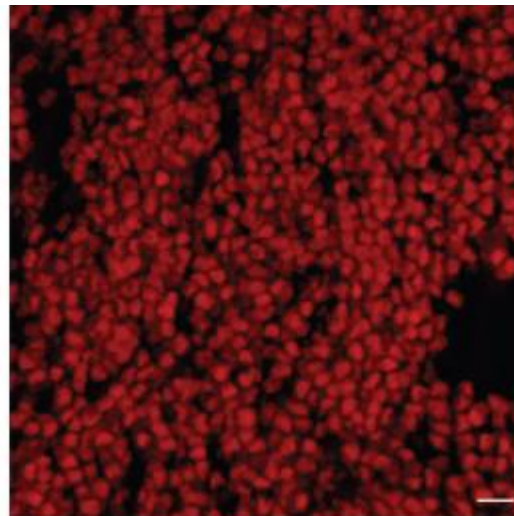
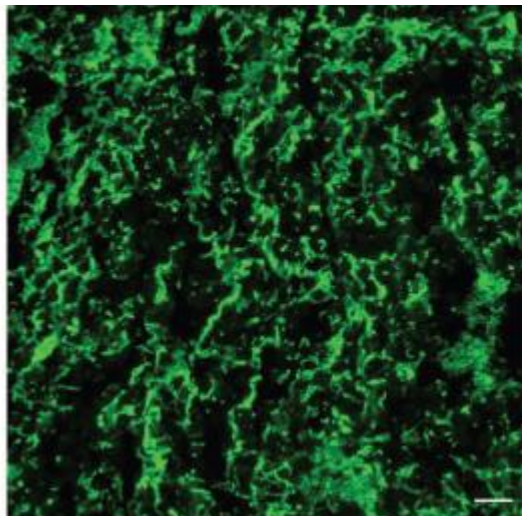
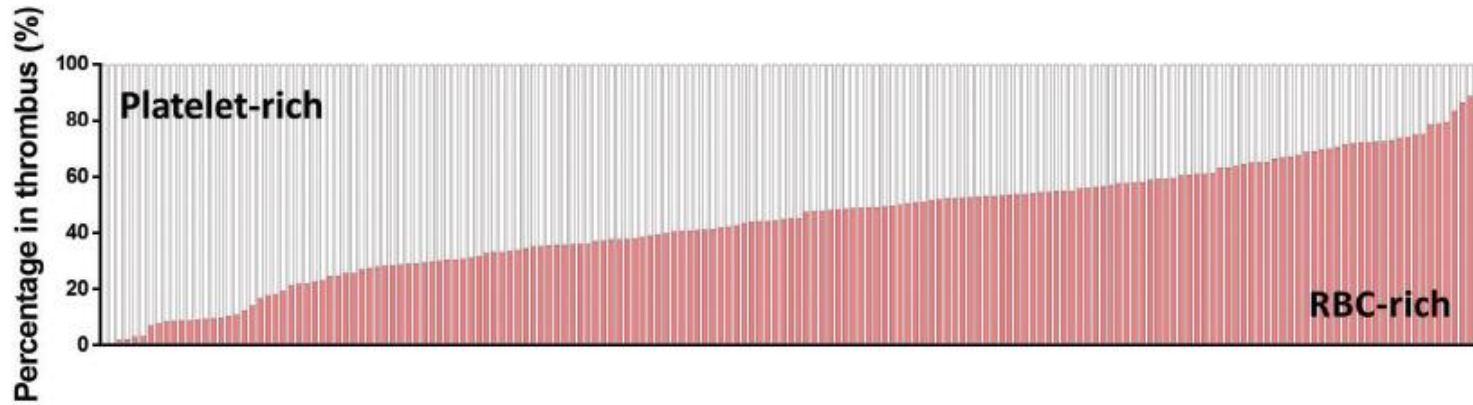
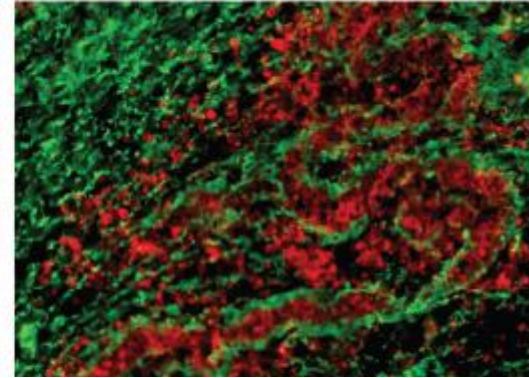
Fibrin(ogen)

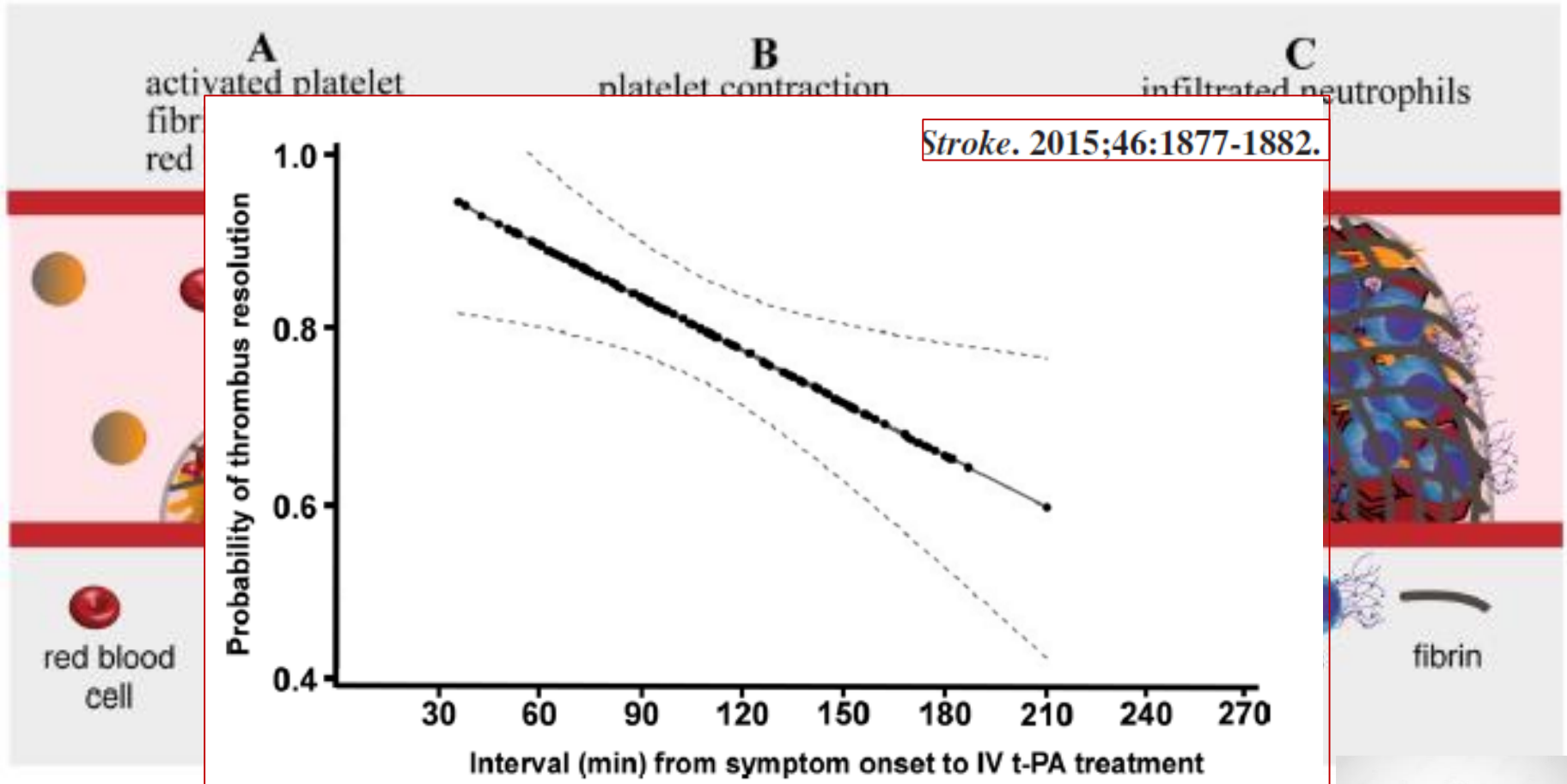


Fibrin(ogen); VWF



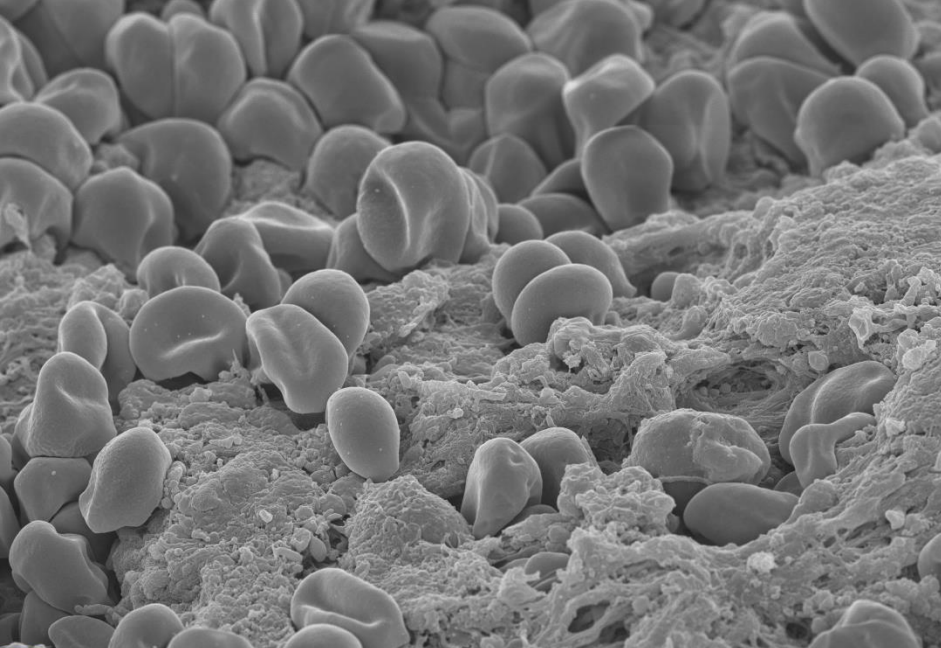
Fibrin(ogen); Platelets



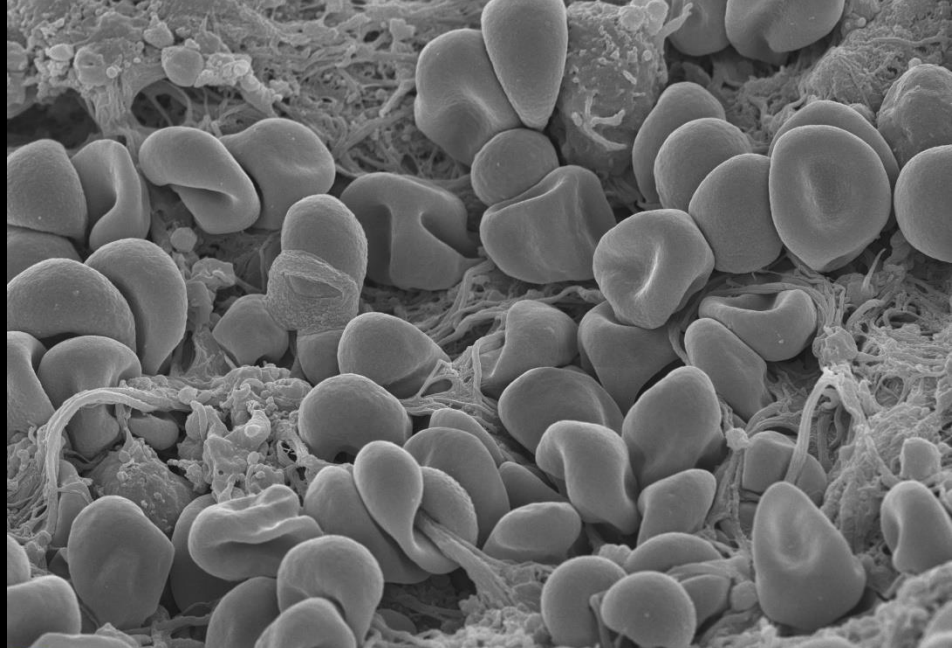


Time lost is penumbra lost
«Time lost is clot resolution lost»

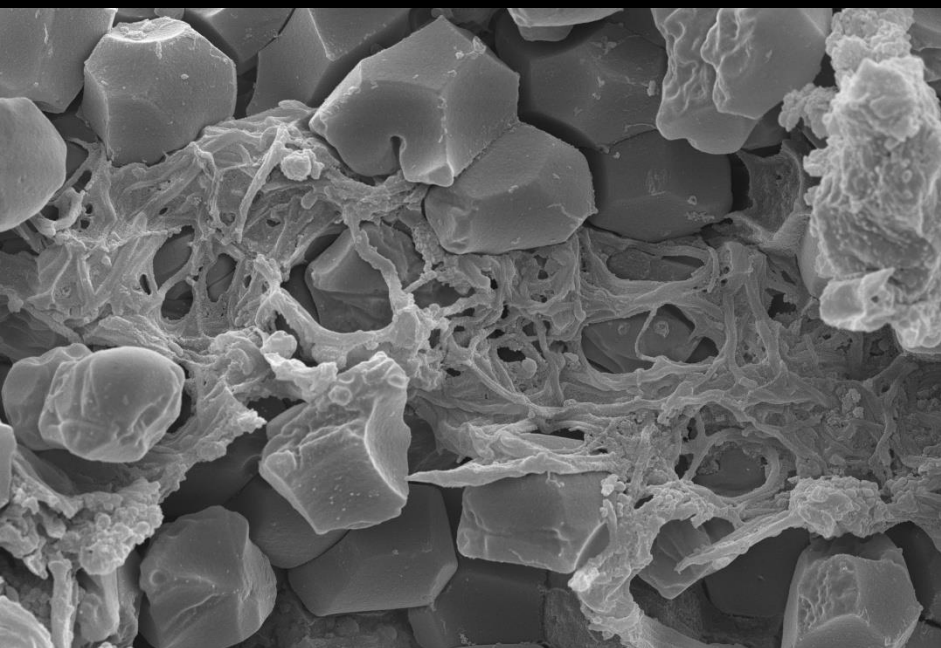




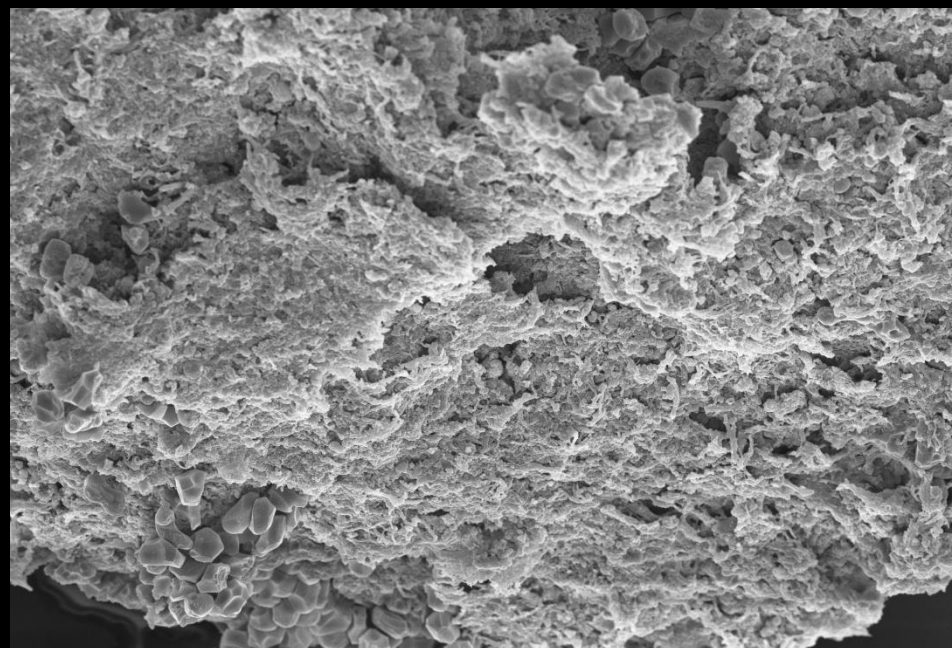
ZEISS Mag = 6.50 K X 3 μ m WD = 3.5 mm EHT = 10.00 kV Signal A = InLens Date: 16 Feb 2022 Time: 9:54:35
I Probe = 128 pA System Vacuum = 1.27e-05 mbar
GeminiSEM 450-8216010131 Noise Reduction = Line Int. Busy ESB Grid Is = 347 V Column Mode = High Resolution



ZEISS Mag = 7.75 K X 2 μ m WD = 3.6 mm EHT = 10.00 kV Signal A = InLens Date: 16 Feb 2022 Time: 10:03:03
I Probe = 128 pA System Vacuum = 9.73e-06 mbar
GeminiSEM 450-8216010131 Noise Reduction = Line Int. Busy ESB Grid Is = 347 V Column Mode = High Resolution



ZEISS Mag = 10.05 K X 2 μ m WD = 3.9 mm EHT = 10.00 kV Signal A = InLens Date: 16 Feb 2022 Time: 11:05:15
I Probe = 128 pA System Vacuum = 7.33e-06 mbar
GeminiSEM 450-8216010131 Noise Reduction = Line Int. Busy ESB Grid Is = 347 V Column Mode = High Resolution

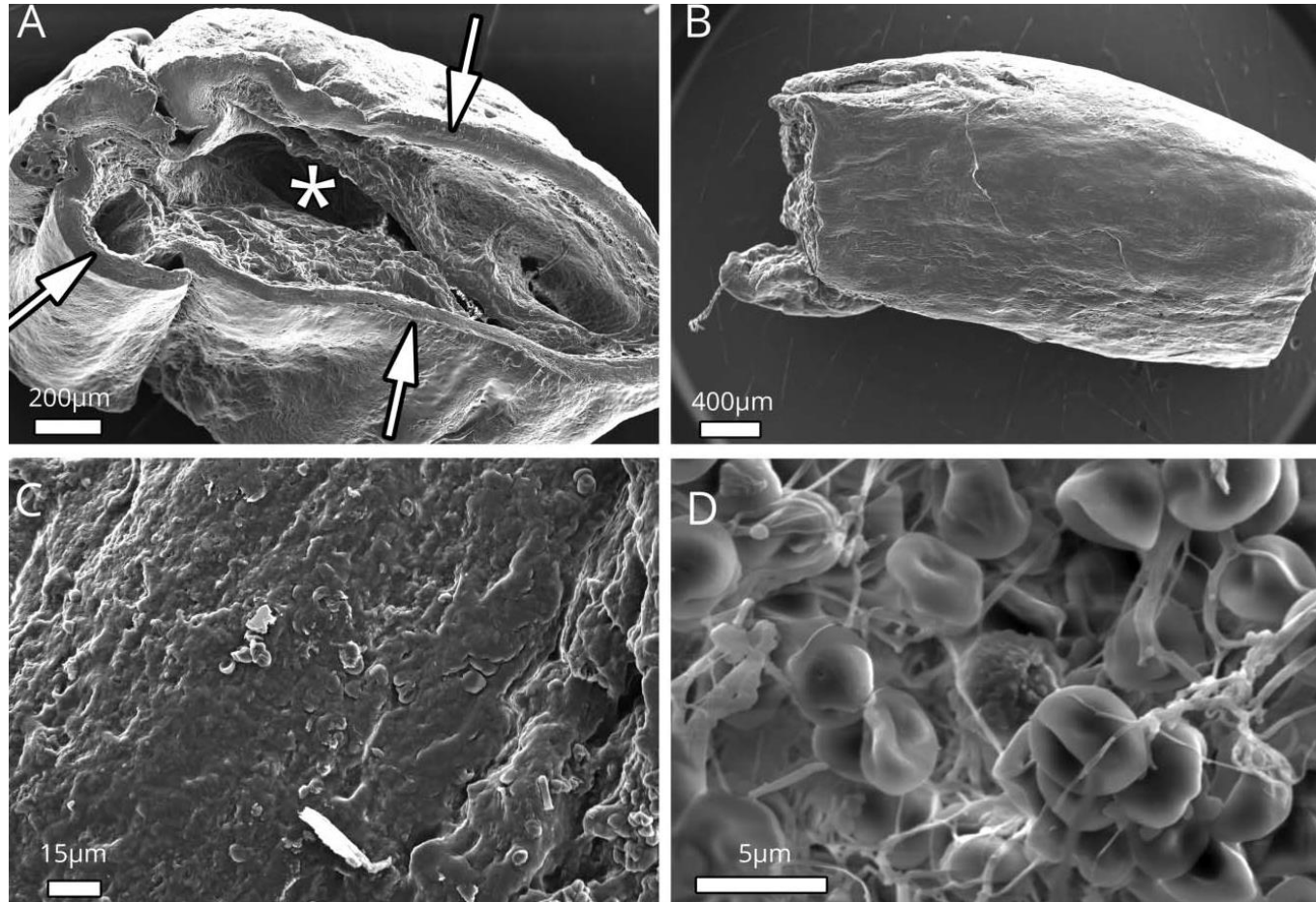


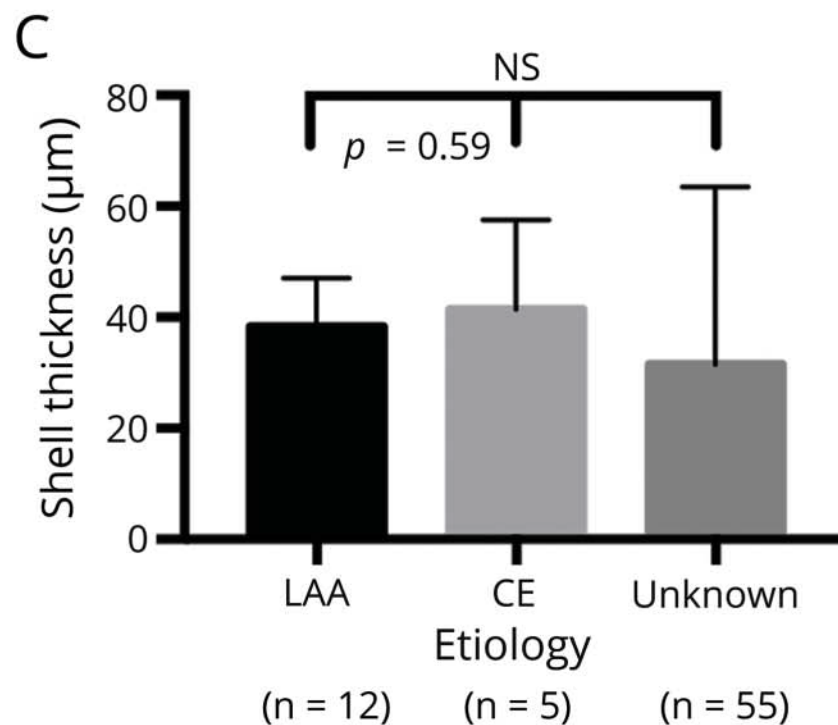
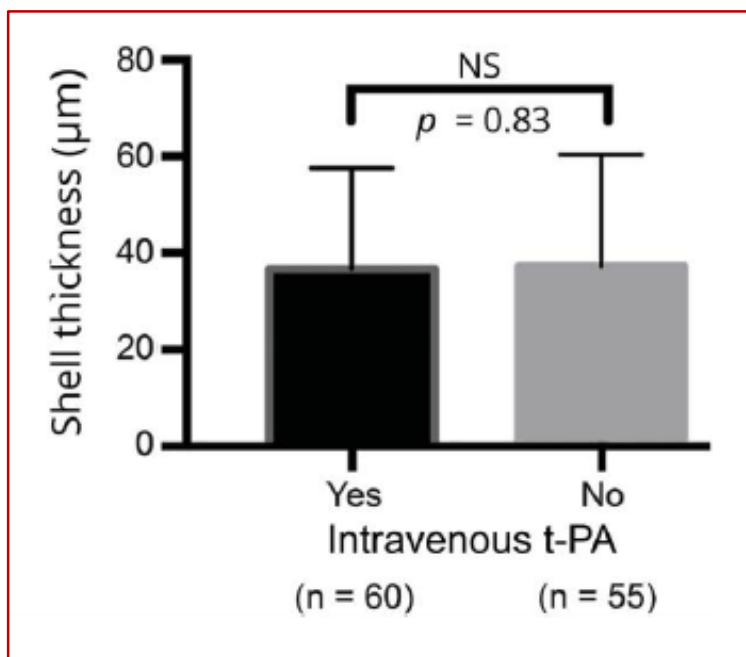
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I Probe = 128 pA System Vacuum = 7.28e-06 mbar
GeminiSEM 450-8216010131 Noise Reduction = Line Int. Busy ESB Grid Is = 347 V Column Mode = High Resolution

Advantages

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- Favorably alter clot properties to facilitate retrieval, leading to higher first-pass effect and successful reperfusion rates

Acute ischemic stroke thrombi have an outer shell that impairs fibrinolysis





Acute treatment

Histologically analyzed (n = 199)

IV tPA

49 (97/196)

Symptom to tPA time, min

152 (122-185)

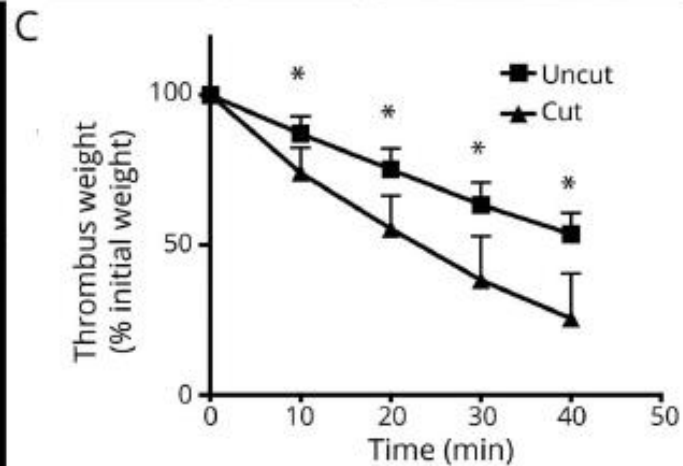
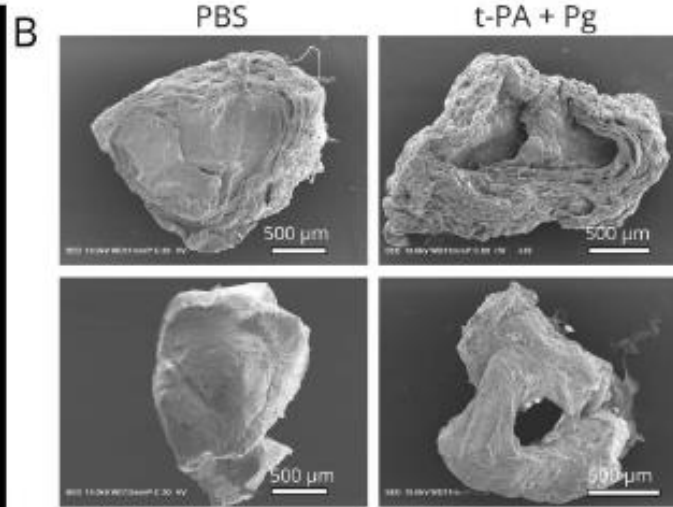
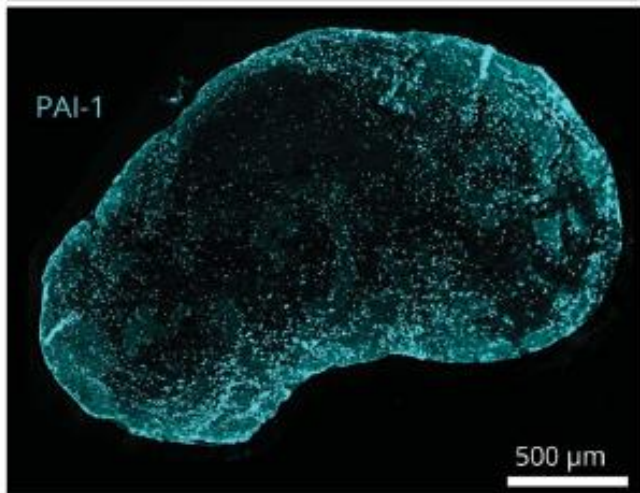
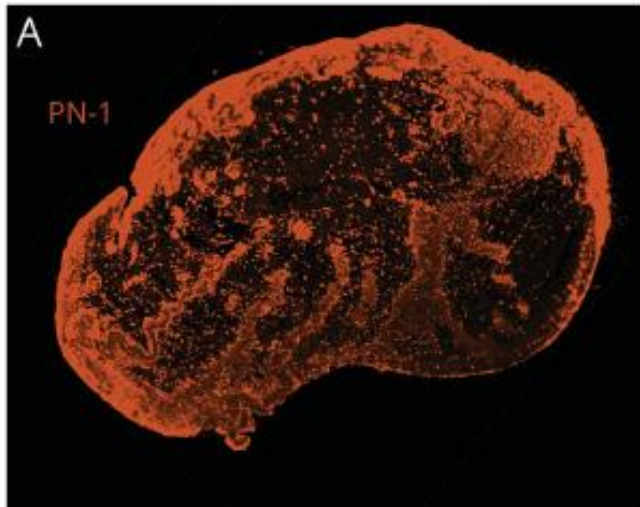
tPA to puncture time, min

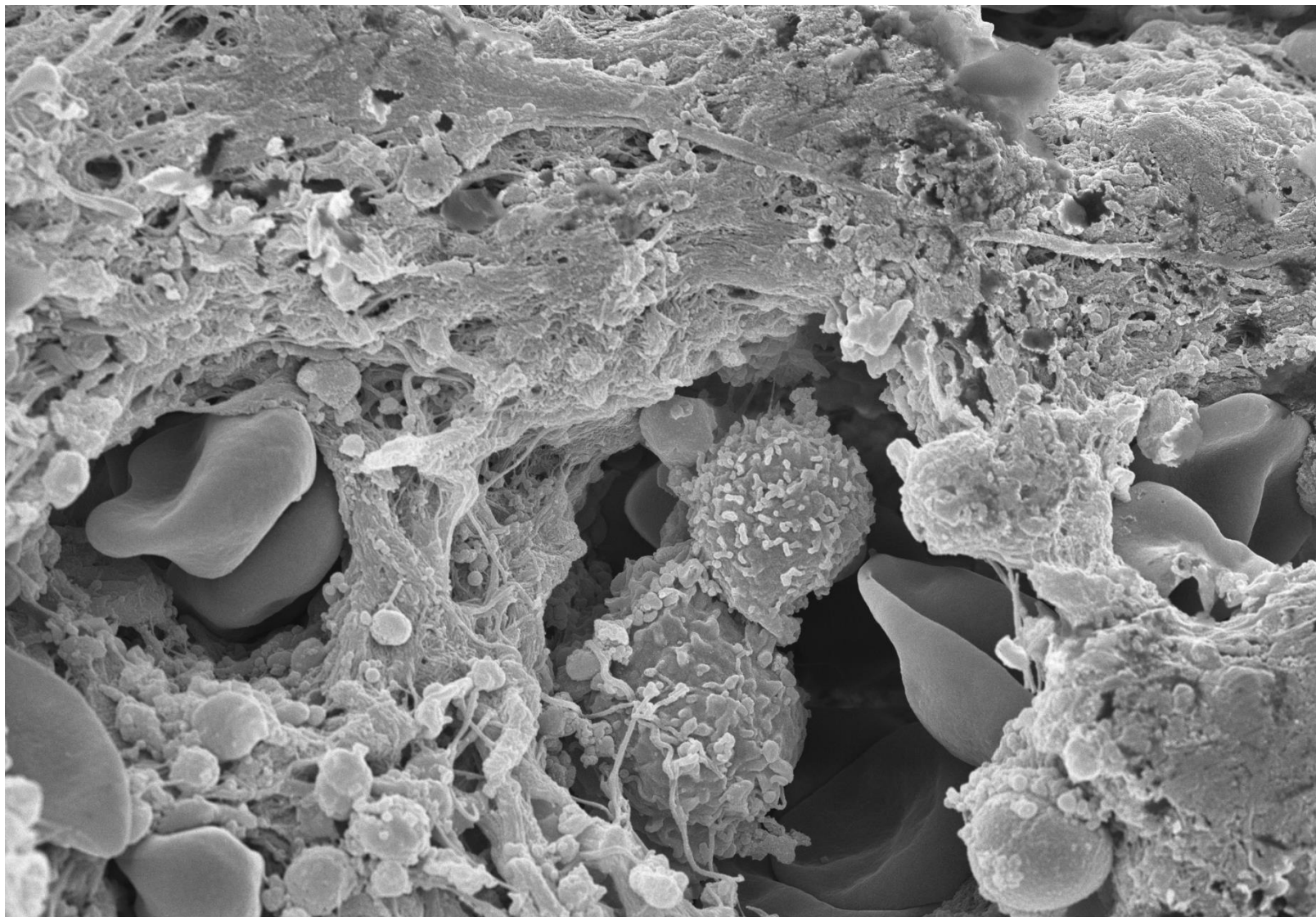
93 (60-117)

Symptom to recanalization time, min

297 (243-374)

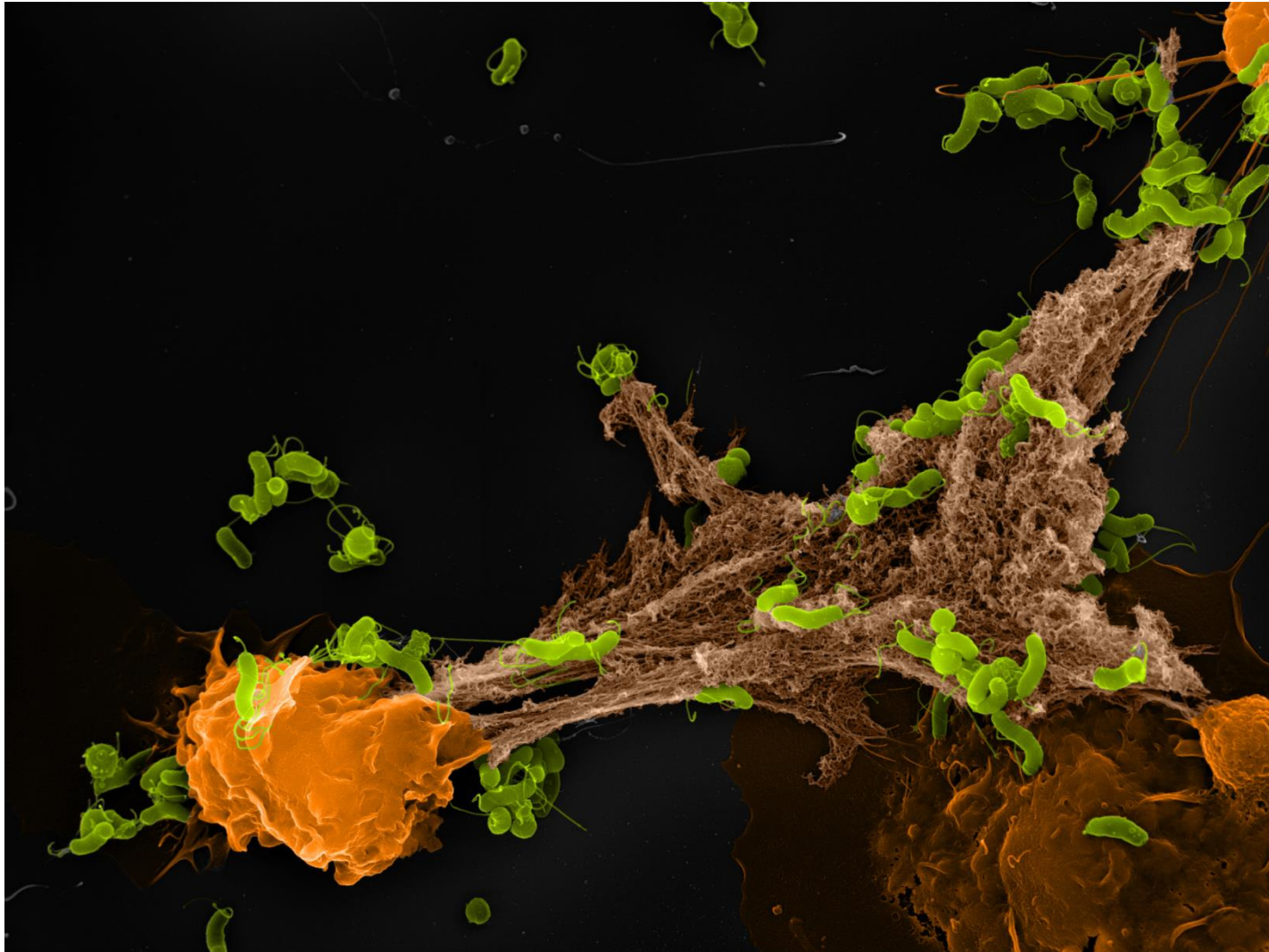
The thrombus outer shell is more resistant to tPA than the thrombus core



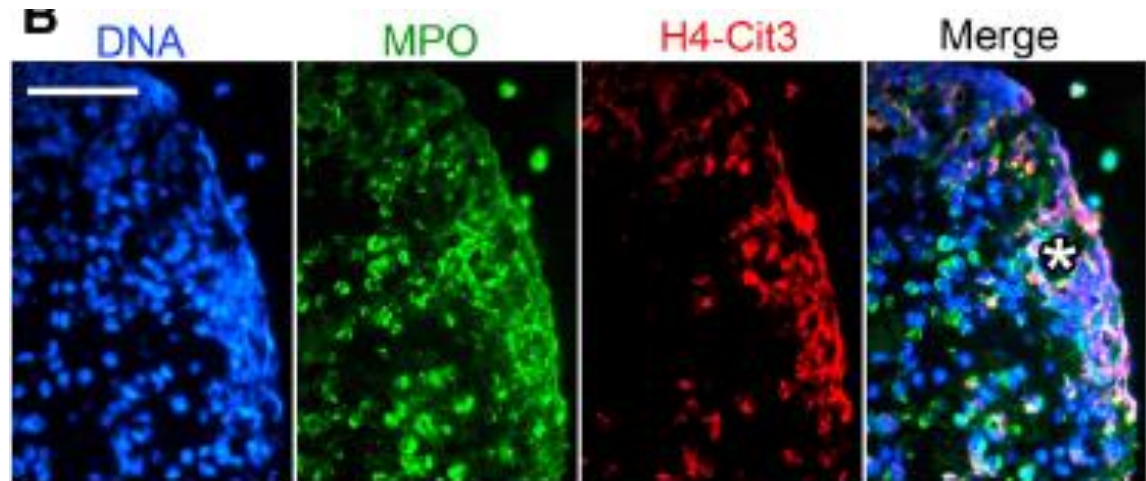
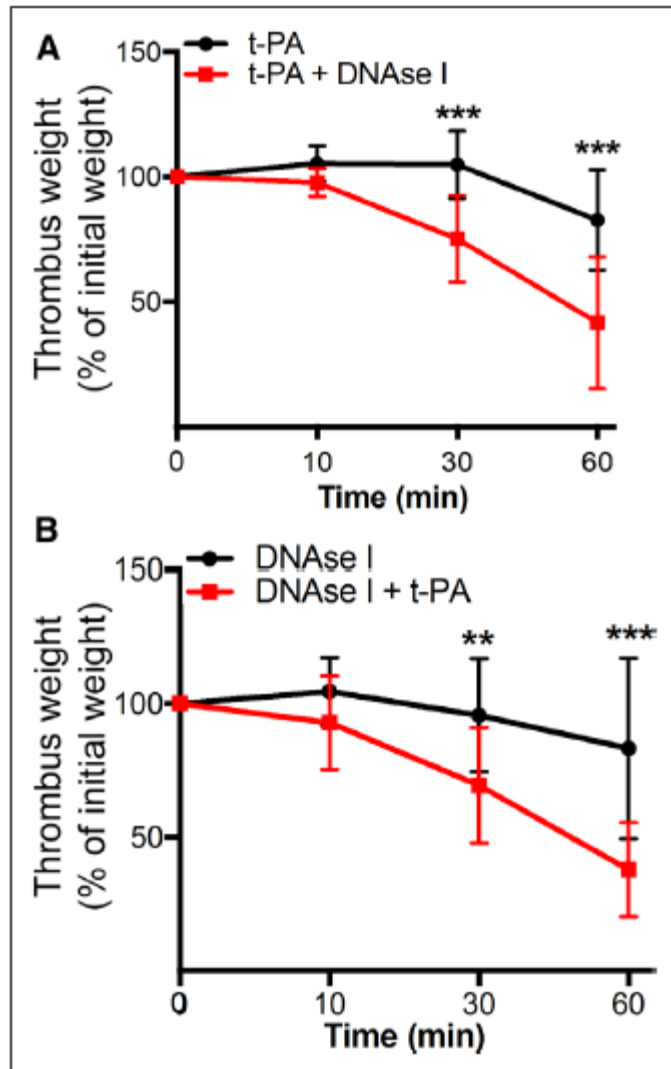


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Neutrophil extracellular traps (NETs)



Thrombus Neutrophil Extracellular Traps Content Impair tPA-Induced Thrombolysis in Acute Ischemic Stroke

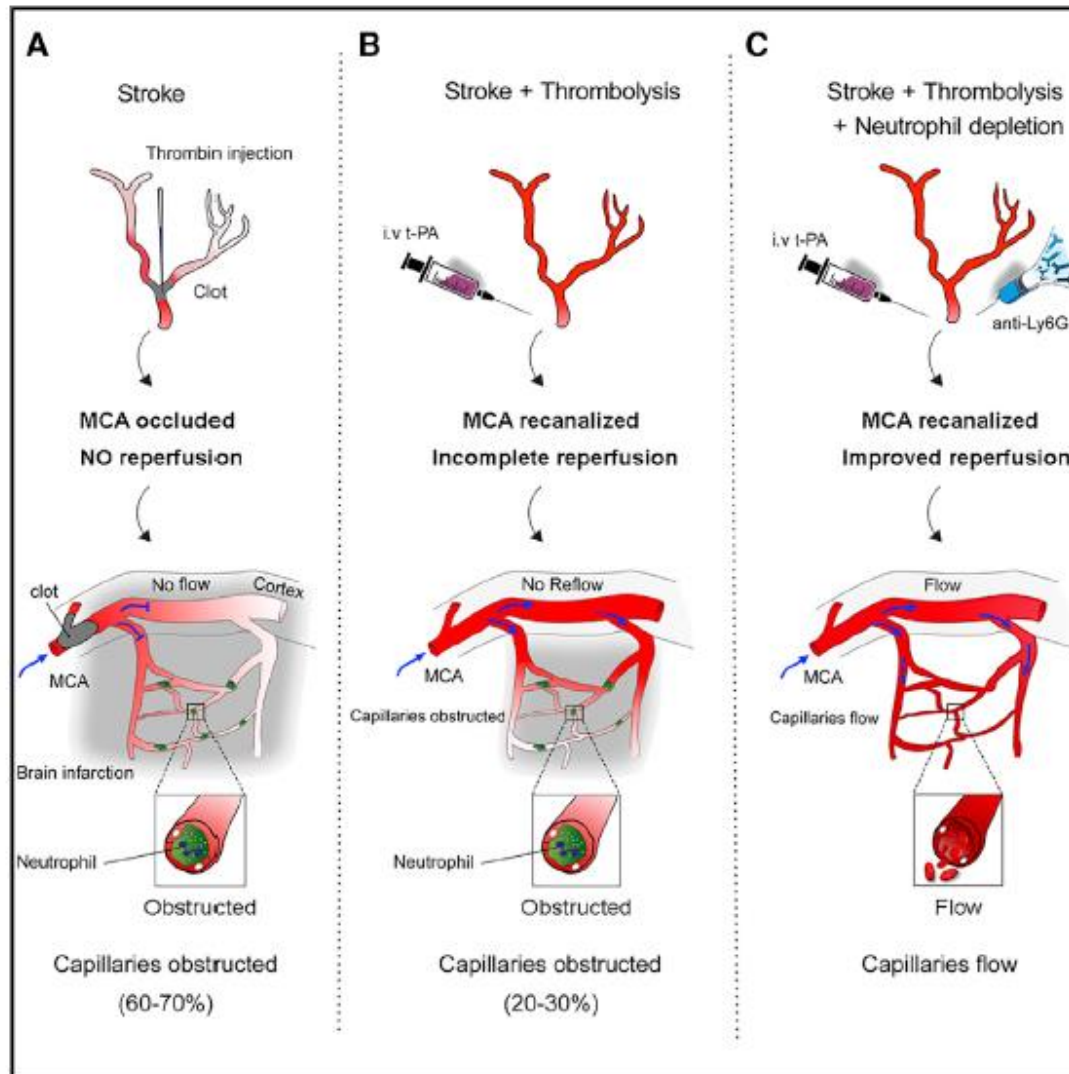


DNase 1 potentiates tPA-induced thrombolysis ex vivo.

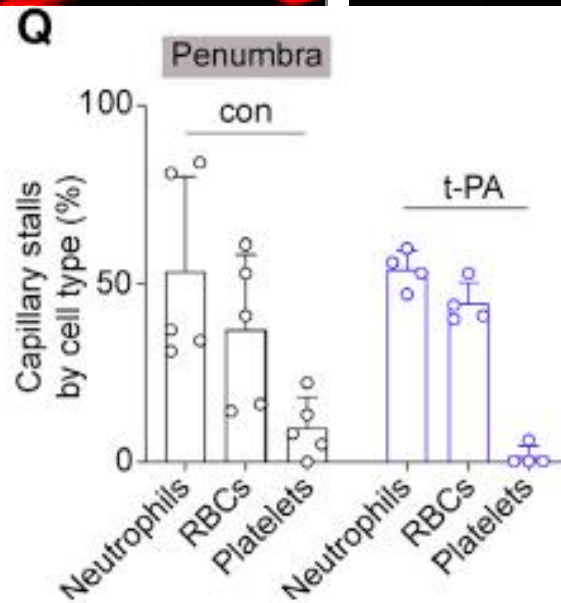
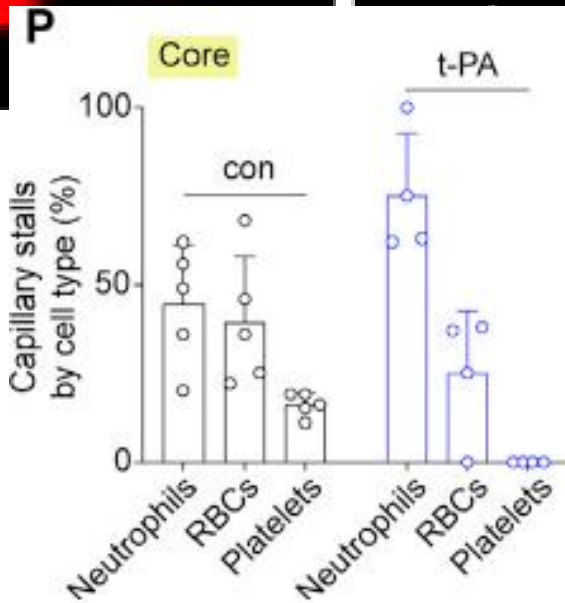
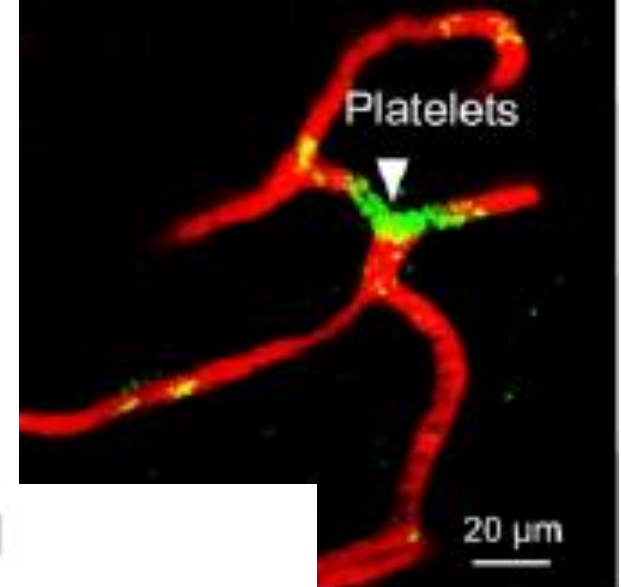
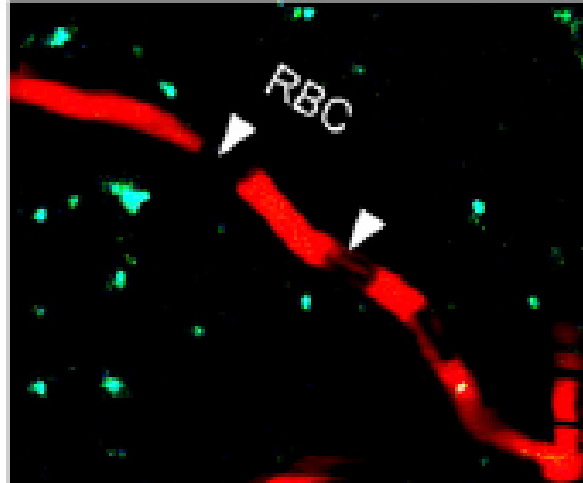
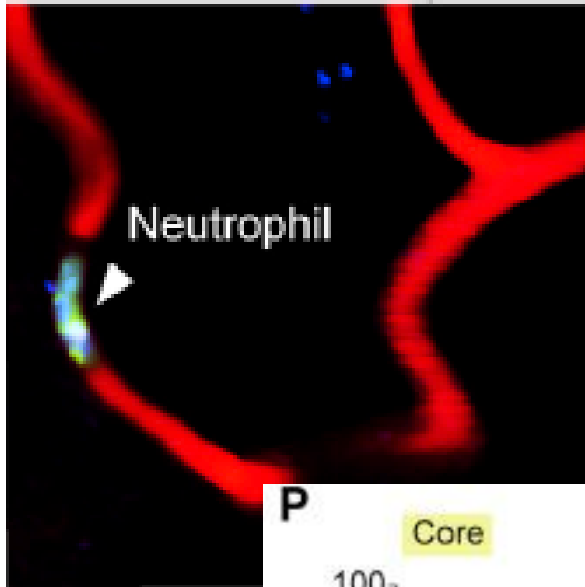
Advantages

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Neutrophils Obstructing Brain Capillaries Are a Major Cause of No-Reflow in Ischemic Stroke



Capillaries remain stalled after recanalization of the MCA

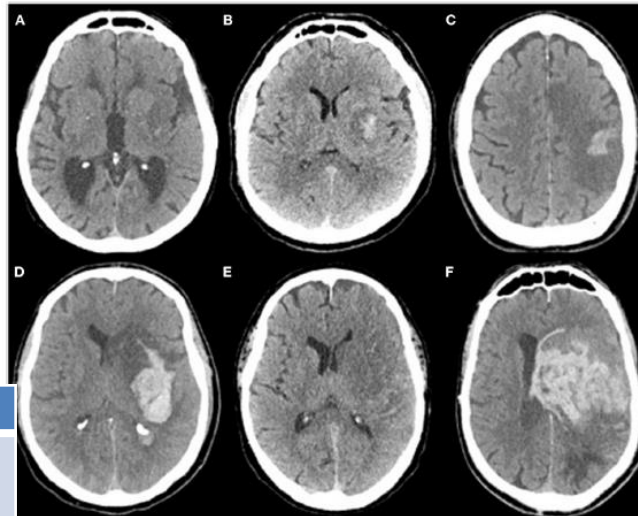


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- **Haemorrhagic complications**
- Costs

Intracranial Bleeding After Reperfusion Therapy in Acute Ischemic Stroke

Guillaume Charbonnier^{1,2,3*}, Louise Bonnet¹, Alessandra Biondi^{2,4} and Thierry Moulin^{1,3,4}



RISK FACTORS FROM RCT	STUDY POPULATION	ODDS RATIO
IV Thrombolysis (0.9 mg/Kg) vs placebo	Any IS	9.9 – 10.7
MT within 6 h	LVO	OR 1.06
FBG decrease	Any IS treated by IVT	1.92
BBB permeability	IS treated by IVT or MT	45.4
BBB disruption after MT	IS treated by MT	25.3
10 microbleeds on MRI	Any IS treated by IVT	5.55
Procedure time (MT)	IS treated by MT	1.43 per 30 min



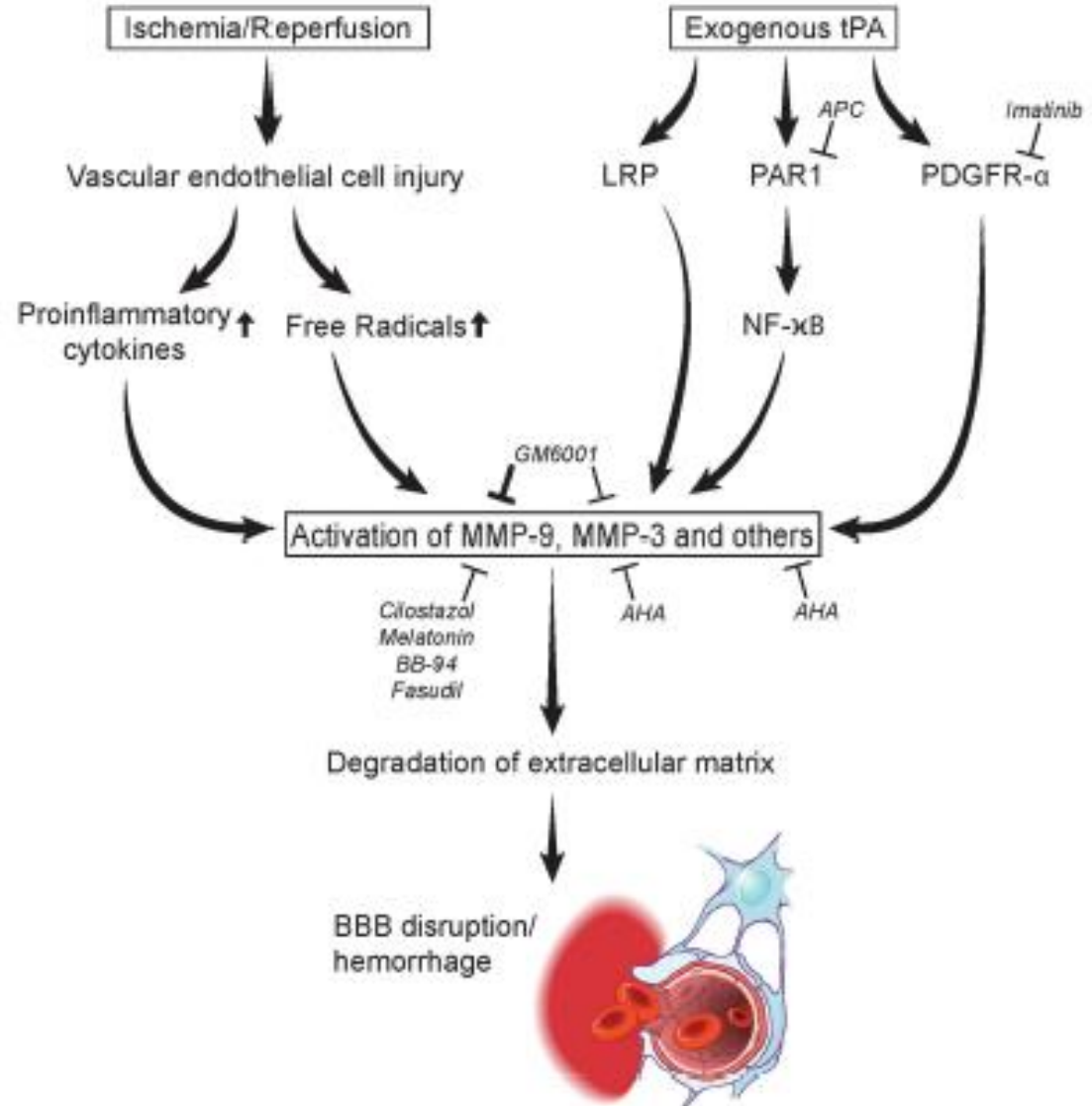
Matrix metalloproteinases and blood-brain barrier disruption in acute ischemic stroke

Shaheen E. Lakhan^{1,2*}, Annette Kirchgessner^{1,3}, Deborah Tepper² and Aidan Leonard¹

¹ Biosciences Department, Global Neuroscience Initiative Foundation, Beverly Hills, CA, USA

² Neurological Institute, Cleveland Clinic, Cleveland, OH, USA

³ School of Health and Medical Sciences, Seton Hall University, South Or



Subgroup metaanalysis:

Early ischemic signs on imaging

Pts at increased risk for hemorrhagic complications

Patients with a high clot burden



Bridging sì!

ma... Skip rTPA se («Mothership»):

- La fibrinolisi può ritardare la trombectomia
- Pz fragile a rischio di sanguinamenti
- Situazioni borderline
- Segni di ischemia estesa precoce alla Tc basale
- Occlusione di sifone, T carotideo

In futuro, bridging con nuovi farmaci trombolitici (anti-GPVI, DNAase I, etc)

