

Acute Stroke Intervention State of the Art

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Conflicts

**No financial Interest
in Any Drugs or
Devices in my
presentation**

Time Window for Treatment

- **0-3 IV therapy**
- **0-6 IA therapy**
- **0-8 mechanical revascularization**

Loosely based on cerebral perfusion data in primates

FIBRINOLYTICS (INTRAVENOUS)

tPA for acute ischemic stroke. NINDS trial

624 patients with ischemic stroke within 3 hours

Intravenous tPA (0.9 mg/kg)

vs

placebo

Follow-up
3 months

tPA

placebo

Improvement at 24 h

47%

39%

Favorable outcome at
3 m (Rankin scale)

42%

27%

Intracerebral hemorrhage

6.4%

0.6%

Death at 3 m

17%

21%

**Patient treated with IV tPA had
a relative 30% greater
likelihood of having minor or
no deficit at 3 months
based on Rankin score
true for all subgroups**

Role for IV tPA

0-3 hours

NIHSS < 12

**less severe strokes that
present early after onset**

Ultrasound-enhanced systemic thrombolysis for acute ischemic stroke

Alexandrov et al NEJM 2004

- **2 MHz TCD focused on occluded intracranial vessel**
- **126 patients with acute stroke two groups ultrasound vs placebo**
- **Complete recanalization or dramatic clinical recovery within two hours**
- **49% (31pts) vs 30% 19pts (p=0.03)**
- **42% vs 29% 3 month favorable outcome**
 - **(P=0.2)**

Microbubble tPA, TCD

Molina et al stroke Feb 2006

- 38 pts tPA TCD monitoring plus 3 doses of 2.5 g (400 mg/mL) of galactose-based MBs given at 2, 20, and 40 minutes after tPA bolus (MB group).
- Two-hour complete recanalization rate was significantly ($P=0.038$) higher in the TCD group
- **tPA/US/MB group (54.5%)**
- **tPA/US (40.8%)**
- **tPA (23.9%) groups.**

**3 – 20 % of
patients arrive
within a 3 hr
window**

FIBRINOLYTICS (INTRA-ARTERIAL)

Prolyse in Acute Cerebral Thromboembolism (PROACT) II

180 patients with occlusion of middle cerebral artery
within 6 hours of onset

Intraarterial Prourokinase (9mg)

vs

placebo

Follow-up

3 months

Prourokinase

Placebo

Recanalization

66%

18%

Hemorrhagic
transformation

10%

2%

Favorable outcome

40%

25%

**Treated patients had a
60% relative increase
in good or excellent
outcome
Rankin 0-2**

EMS BRIDGING TRIAL

- **53% recannalization in the IV/ IA tPA group**
- **28 % IA tPA alone**
- **No clear difference in outcome between the groups**

Minimize reperfusion hemorrhage



Qualitative

or

Quantitative

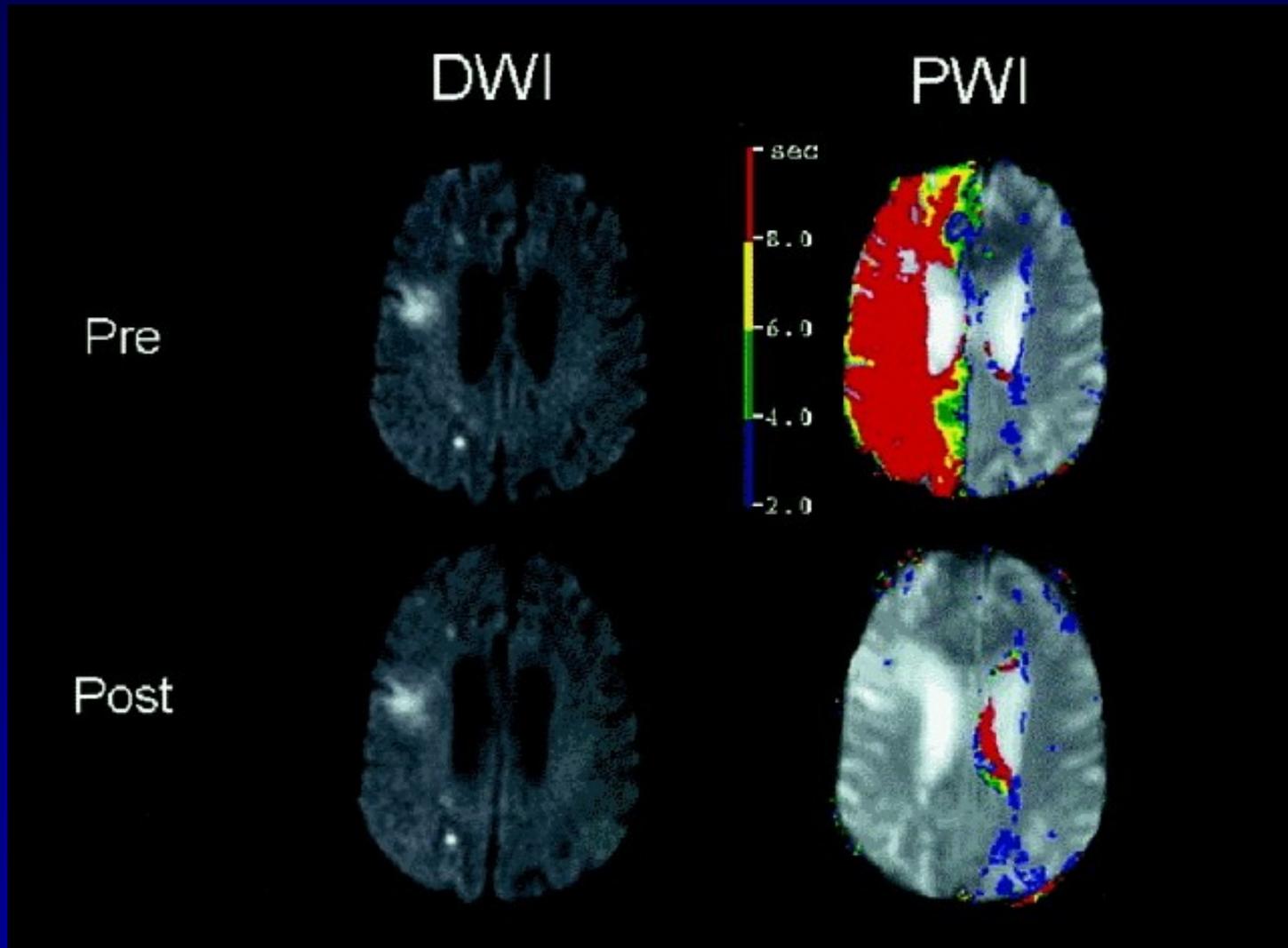
**test of brain tissue
viability**

PERFUSION IMAGING

MRI

**The apparent
diffusion coefficient
of water is decreased
in areas of ischemia**

MRI Diffusion/Perfusion



Magnetic Resonance

TIME

MOTION

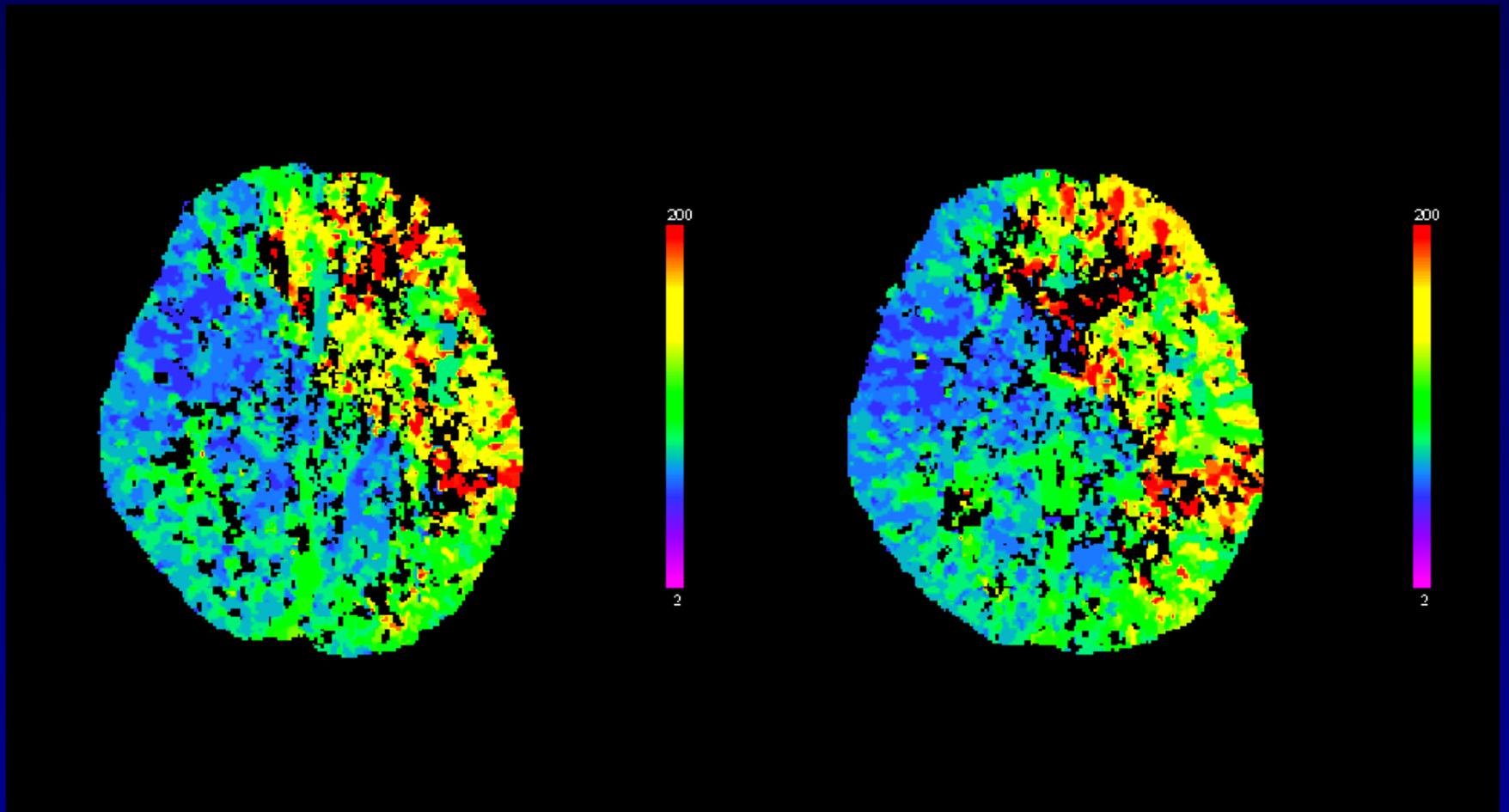
RESOLUTION

cerebellum and

brainstem

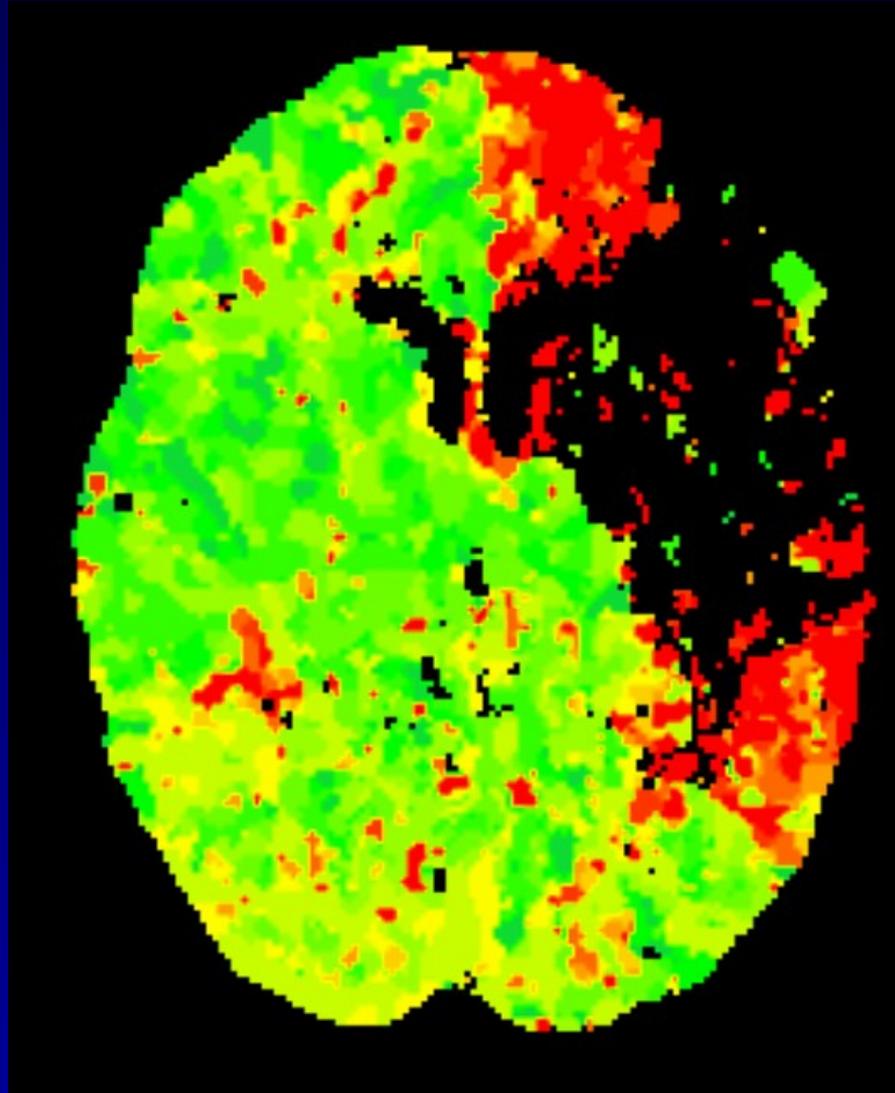
CT

Ischemic Penumbra



**Size of Infarct
Zone predictive of
Intracranial
Reperfusion
Hemorrhage**

Reperfusion Hemorrhage



Outcome Driven by Volume Ratio

Infarct volume

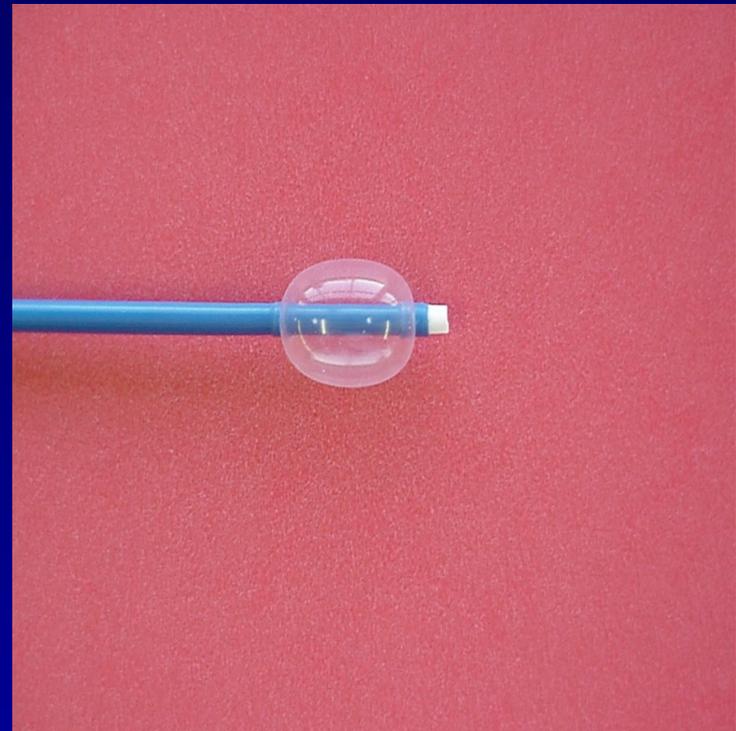
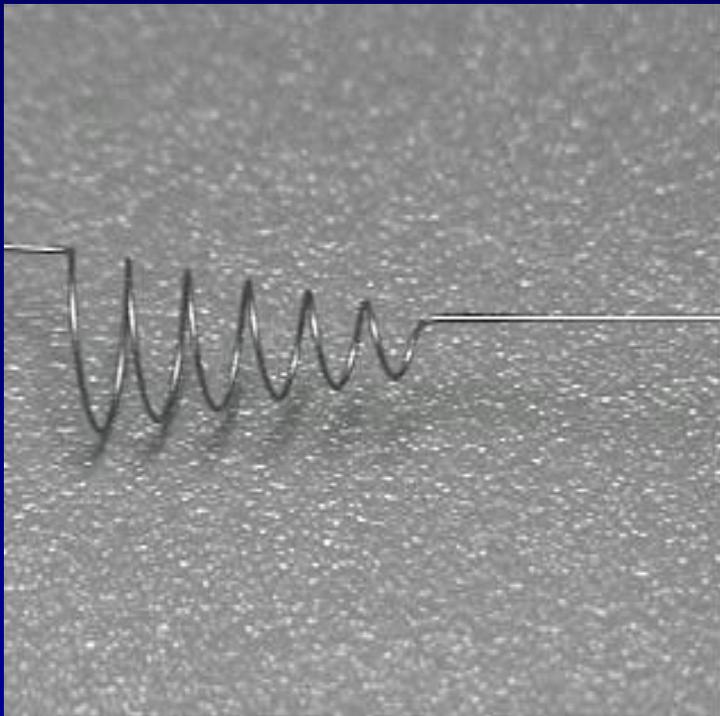
**Ischemic Penumbra
volume**

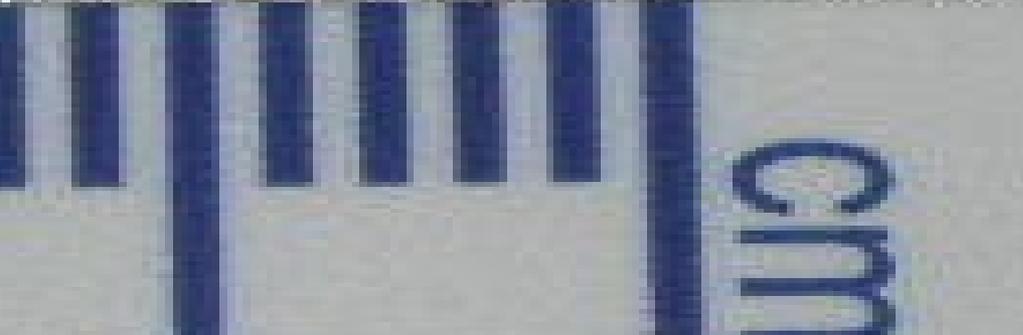
Mechanical Thrombolysis

Concentric Merci

Retriever

Thrombus Retriever X5

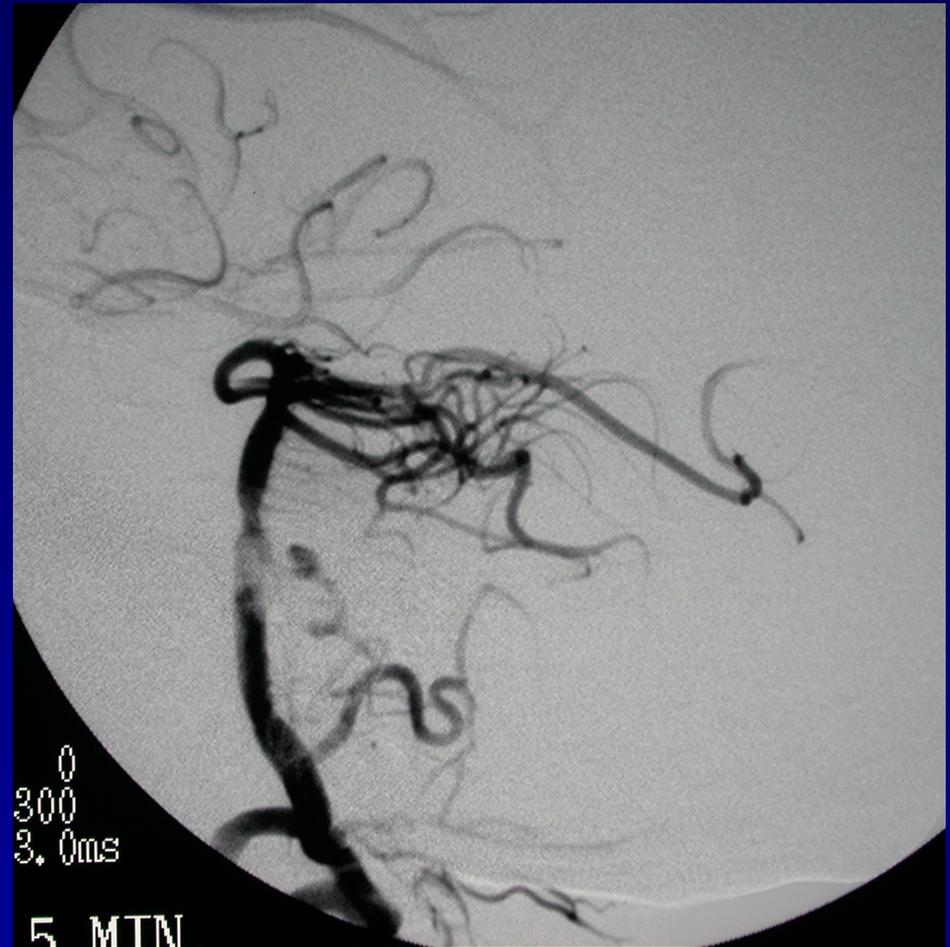
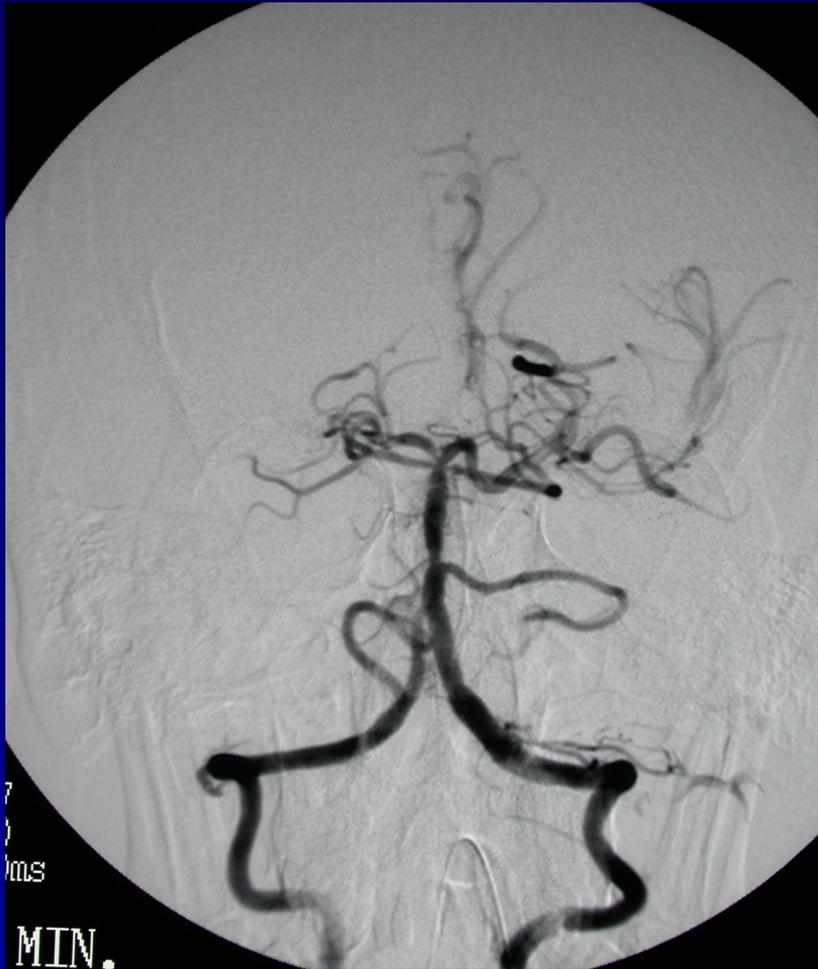




Basilar Occlusion 24 yr male NIHSS 16



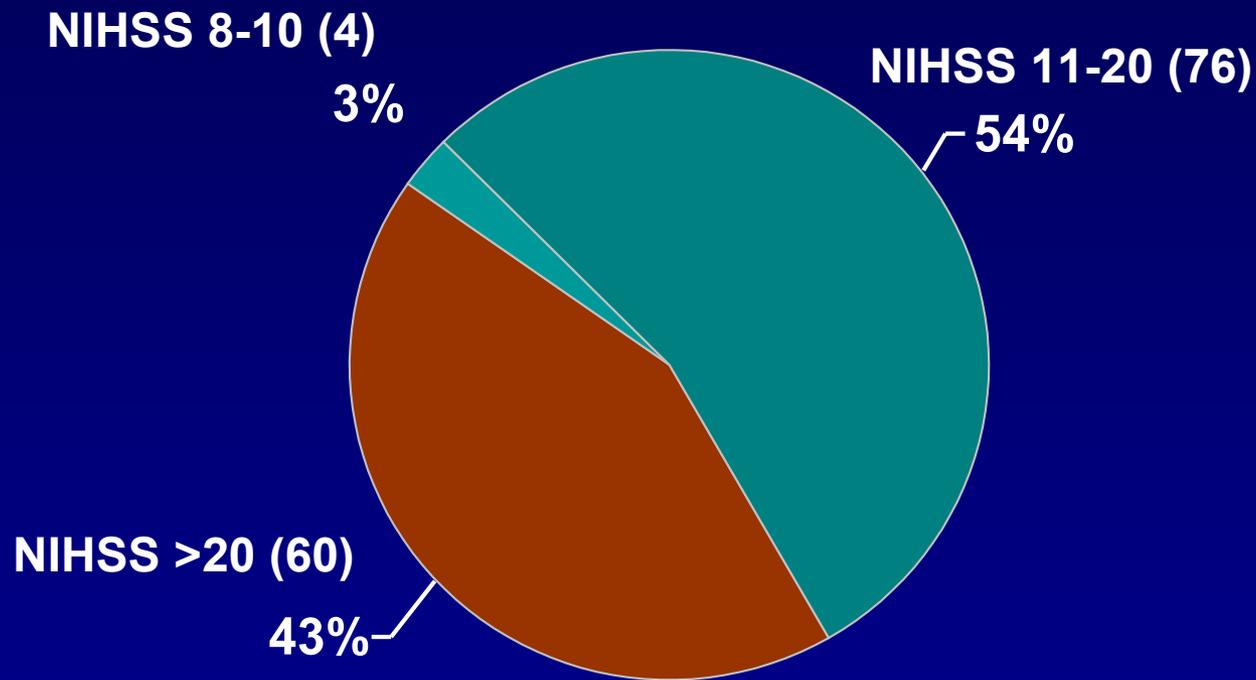
Basilar Occlusion



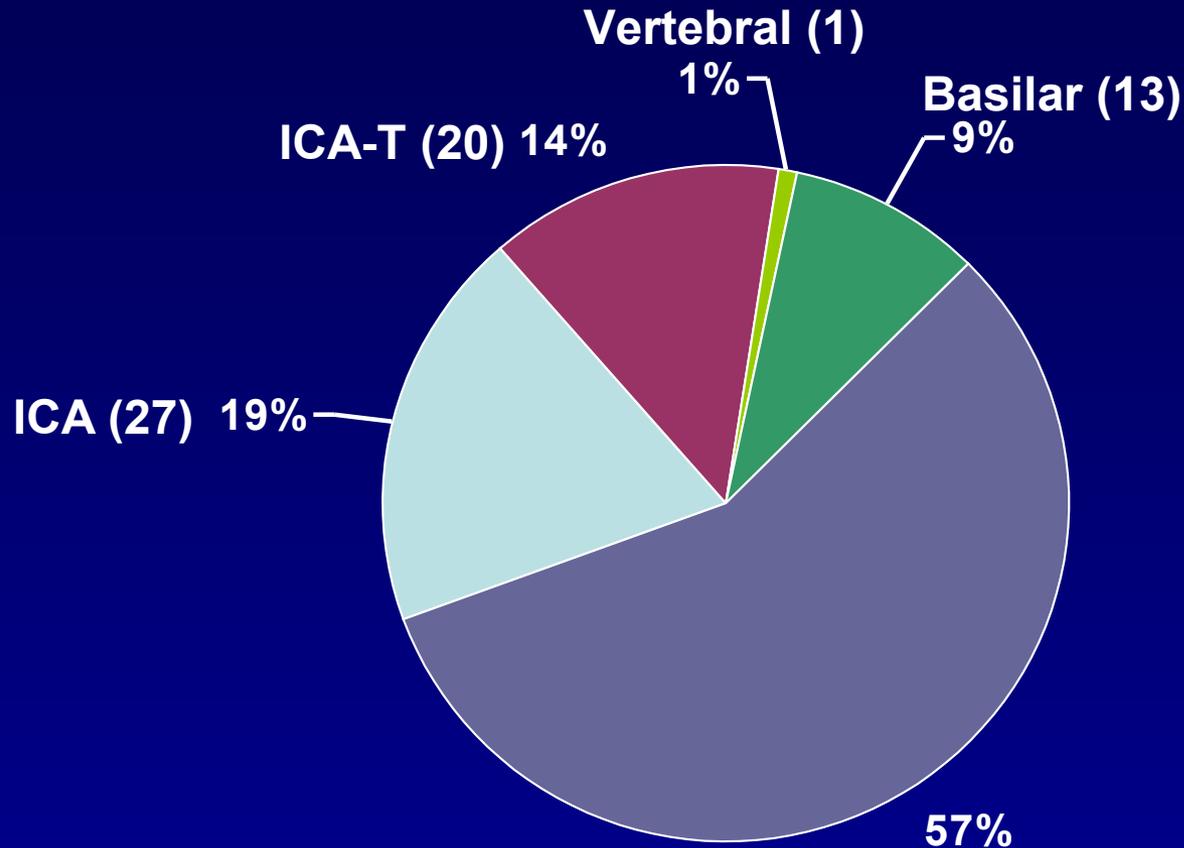
Merci Registry

- **141 patients**
- **46% female**
- **Mean Age 67**
- **Mean Baseline NIHSS 20**
- **Mean Treatment time approx 4 hrs**

Baseline NIH Stroke Scale (n=140*)



Occlusion Location (n=141)

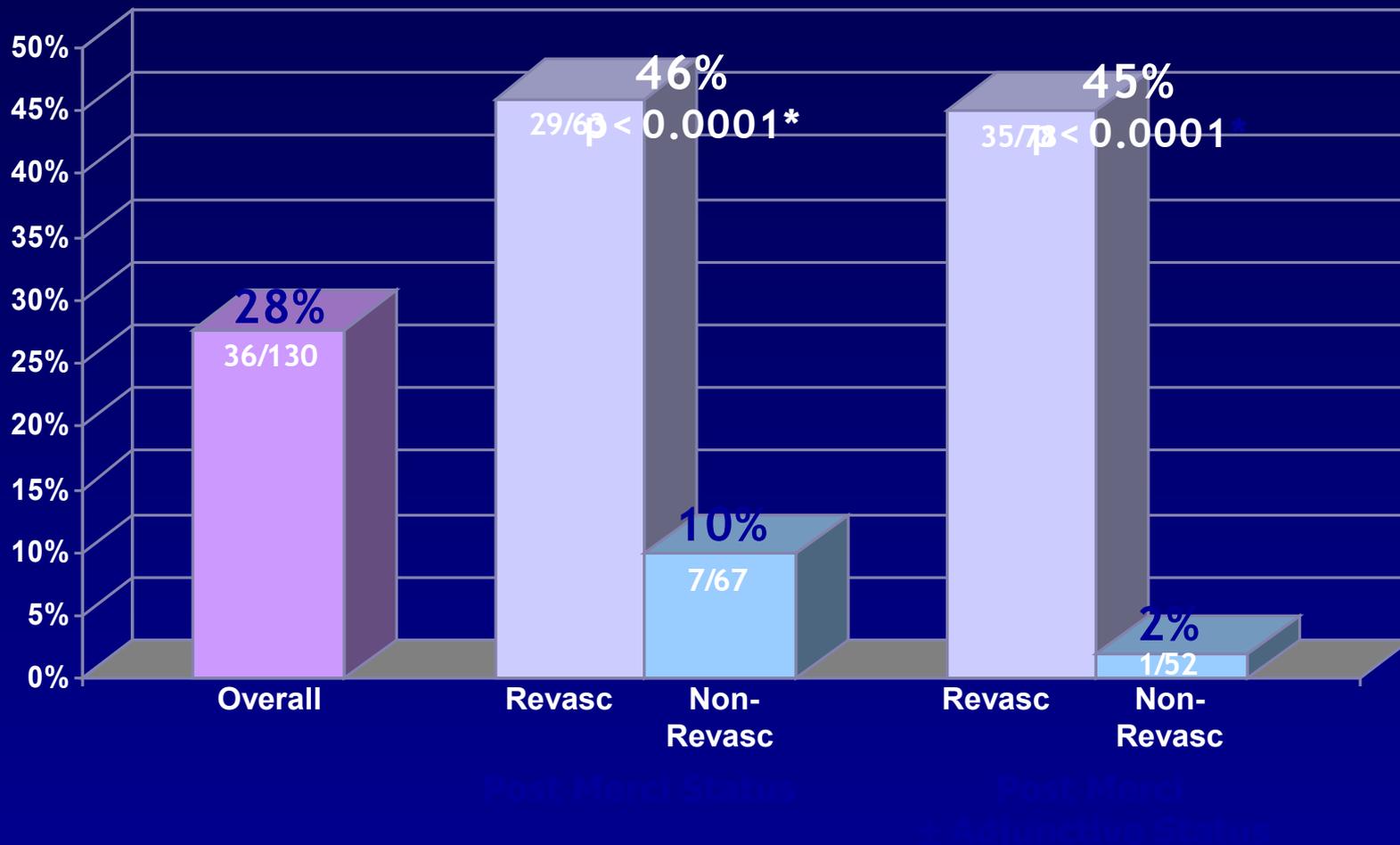


ICA (80)

MERCI TRIAL RECANALIZATION

- **Retriever alone** 48%
- **Retriever plus
adjunctive** 60%

Good Outcome (90-Day mRS ≤ 2) By Revascularization Status



Symptomatic ICH

MERCI 7.8%

PROACT II 10.8%

Self expanding intracranial stent

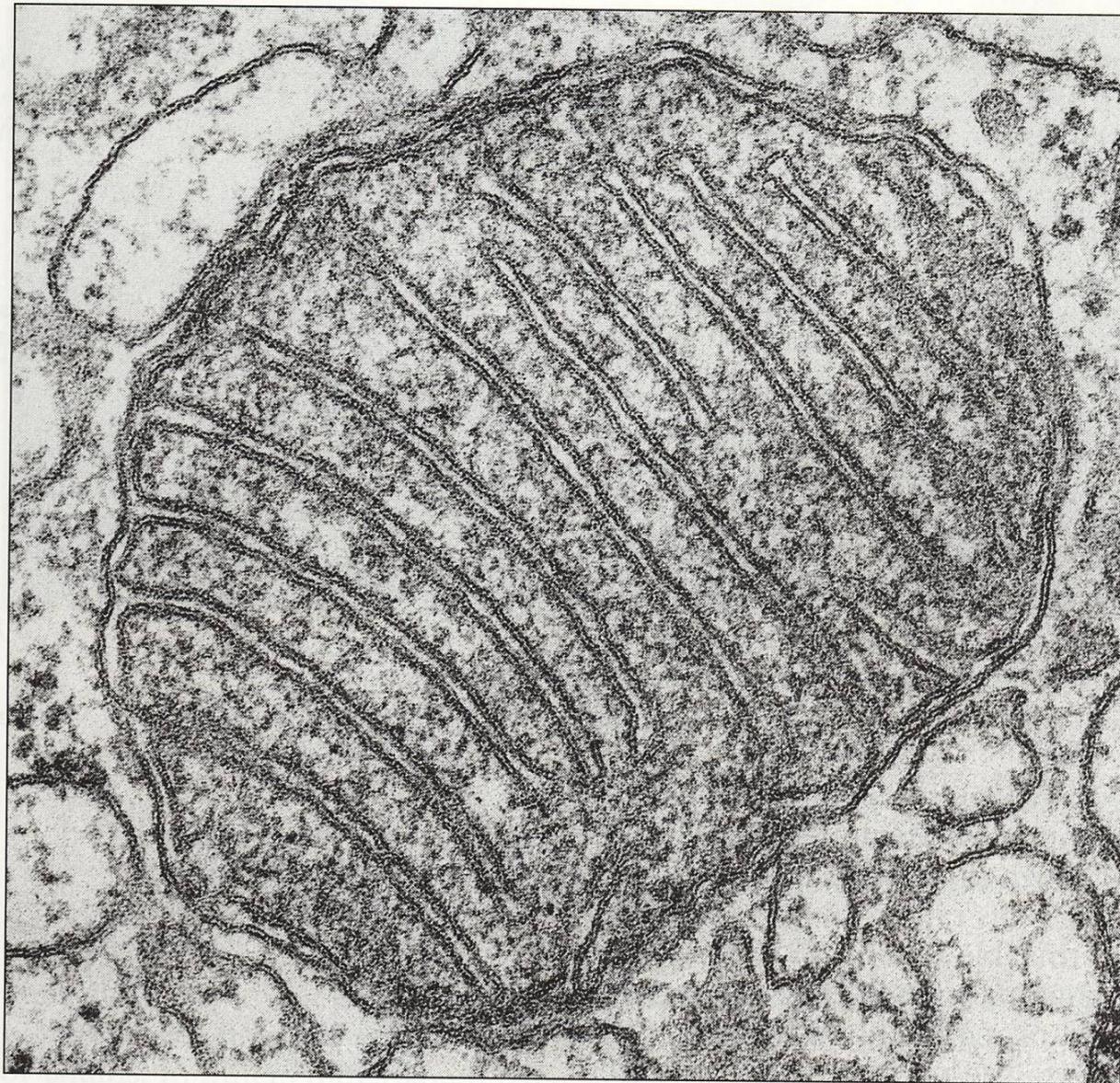
Levy et al Neurosurgery March 2006

- **Overall recanalization rate 79%**
 - (Thrombolysis in Cerebral Infarction Grade 2 or 3)
79%.
- **8 internal carotid artery terminus**
- **7 in the M1/M2 segment**
- **4 in the basilar artery.**
- **6 deaths**
- **NIHSS 16 (15-22)**
- **Survivors NIHSS 5 (2-11)**

**The Target for
Pharmacologic or
Mechanic Therapy
is the**

**Ischemic
Penumbra**

Mitochondria
Energy
generator of
the Cell



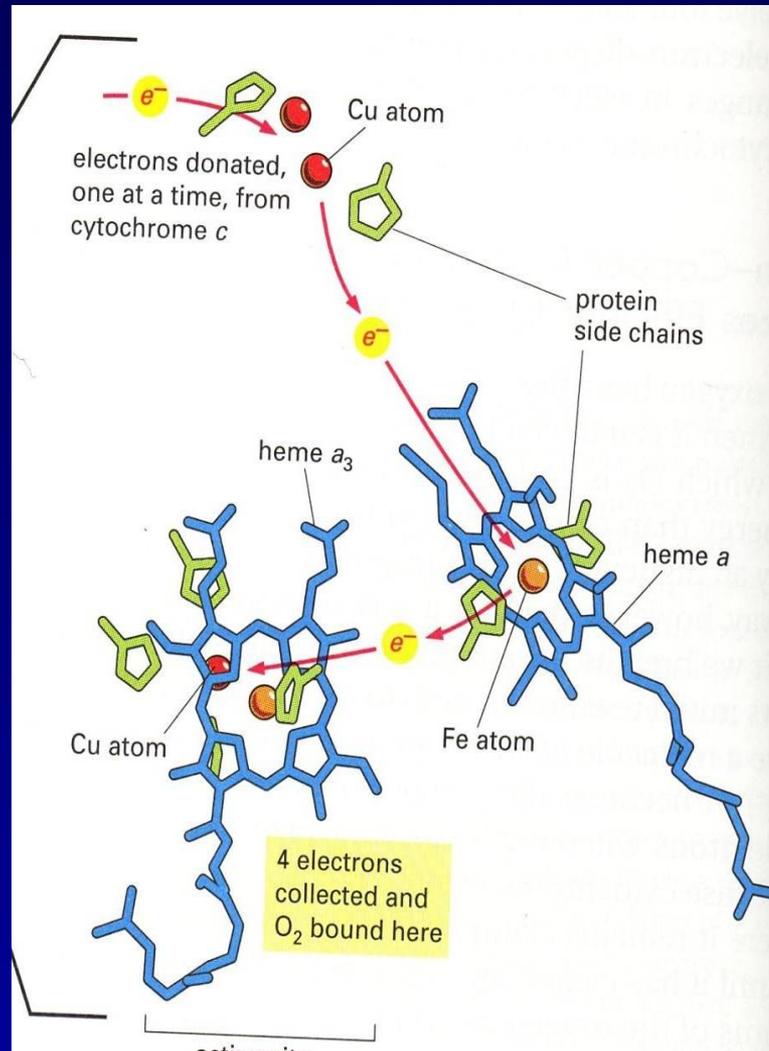
100 nm

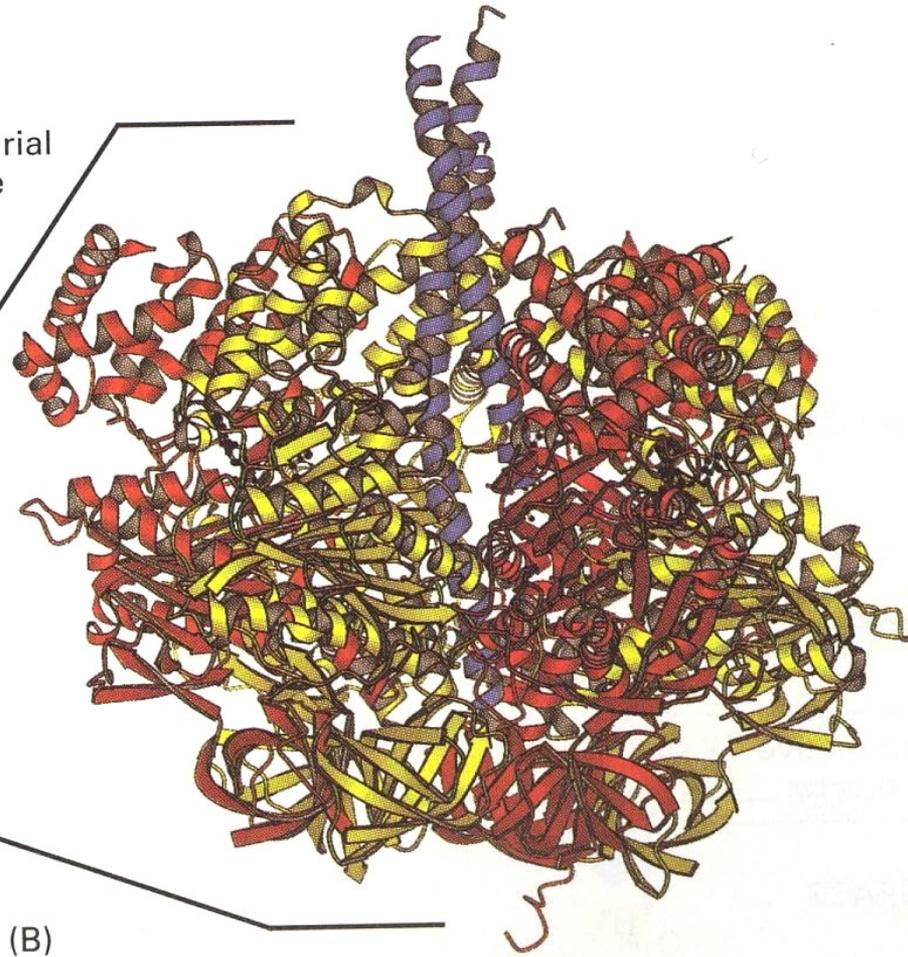
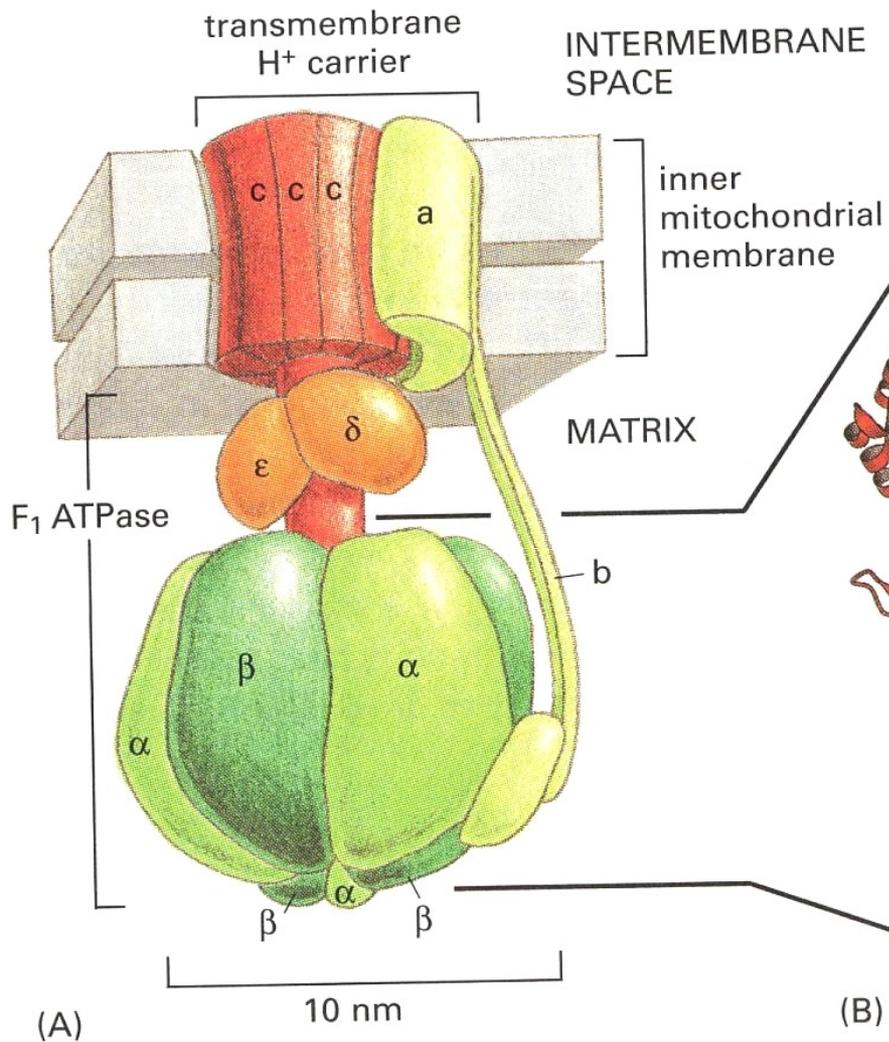
**Electrons come from burning
pyruvate**

**Energy from Electrons to
run the proton pump forming a
proton gradient**

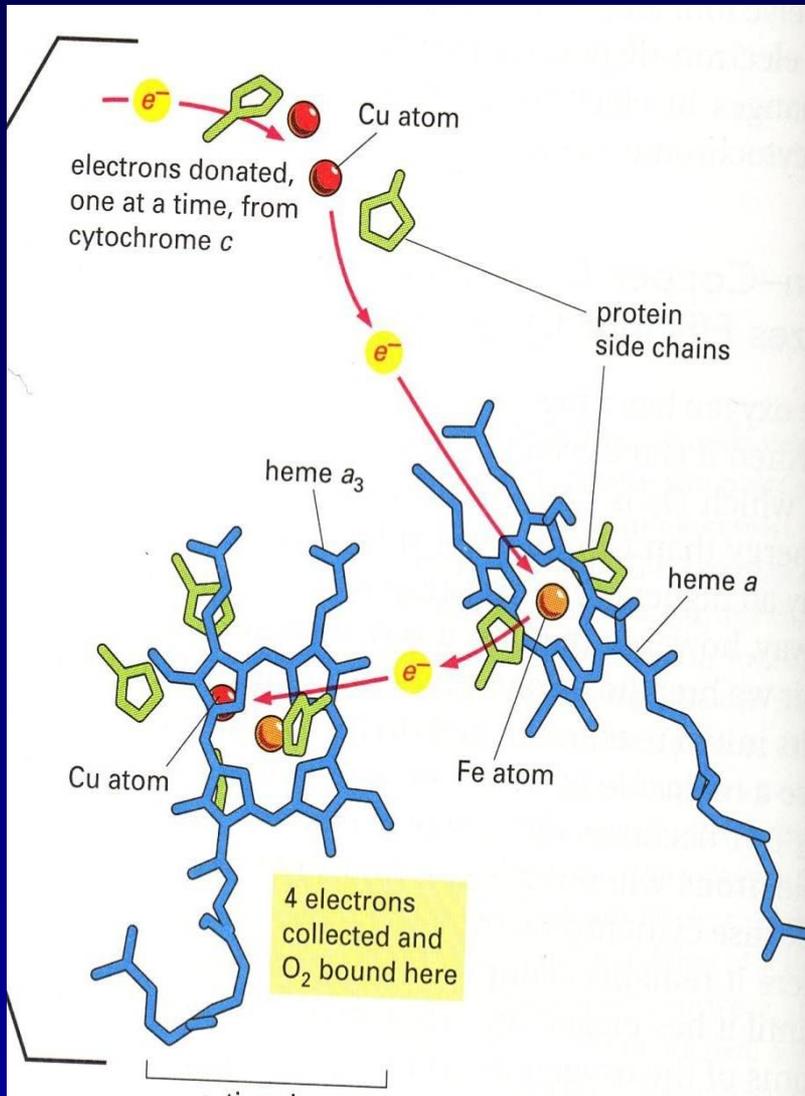
**protons flow back through ATP
synthetase and drives ADP to
ATP**

Energy storage cytochrome c





Cytochrome C



- **Copper Center in Cytochrome C has absorption spectra in the near infrared**
- **can we make Cytochrome C emit an electron with NIR irradiation**

**Switch Fuel
Sources
pyruvate
for an
Infared Photon**

**Phototherapy
in clinical trials
24 hr window**

**Stroke
Intervention is
Expensive**

**Original DRG
non interventional
stroke
approximately
\$6000**

DRG 559

IV thrombolysis

\$11,500

**mechanical
thrombolysis
DRG 1 and DRG 559
\$22,000**

Acuity of patient Mix

Conclusion

**Perfusion Imaging
should guide all
stroke intervention**

**To help minimize
symptomatic ICH**

Thank You

