The Coaxia Neuroflo Device for Penumbra Augmentation During Acute Stroke

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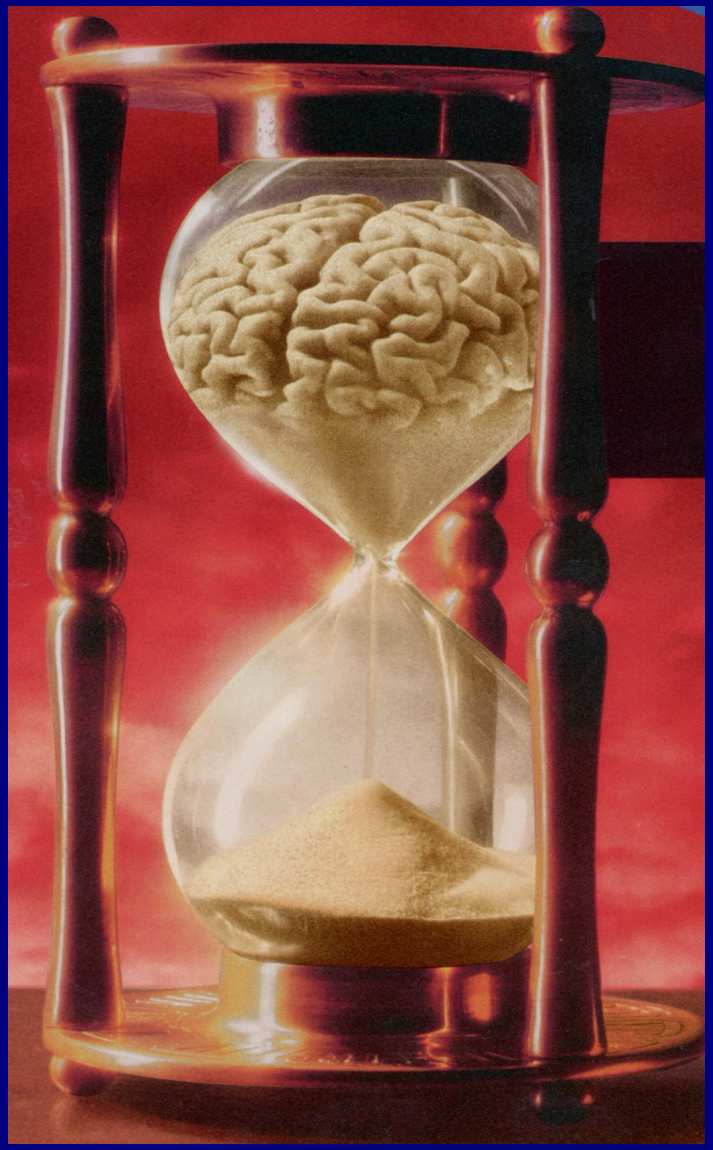
Presenter Disclosure Information

Name: Mark Reisman, M.D.

Within the past 12 months, the presenter or their spouse/partner have had the financial interest/arrangement or affiliation with the organization listed below.

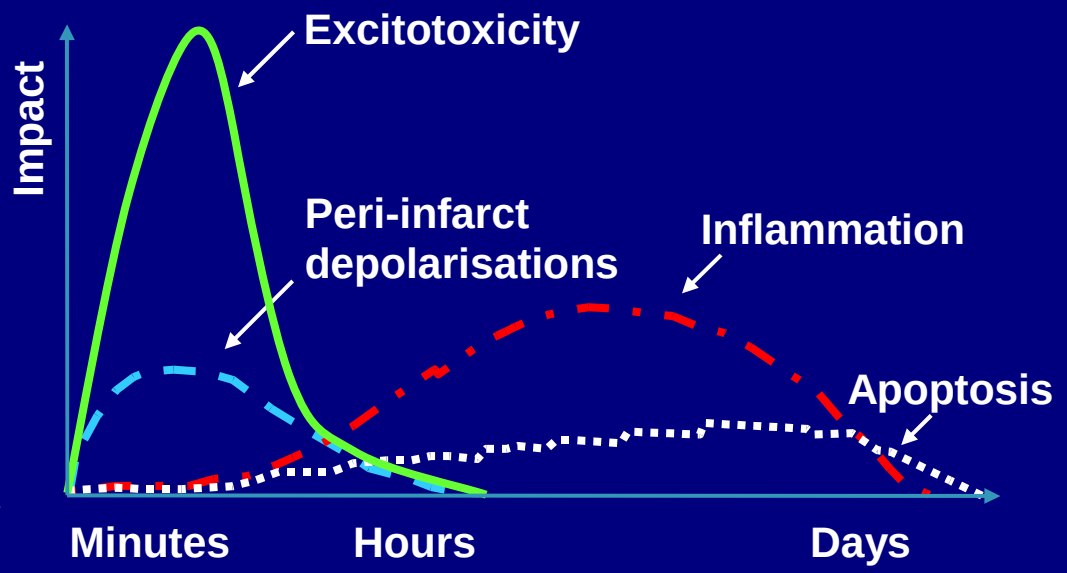
Nothing To Disclose



Time is Brain !

Acute Stroke Treatment

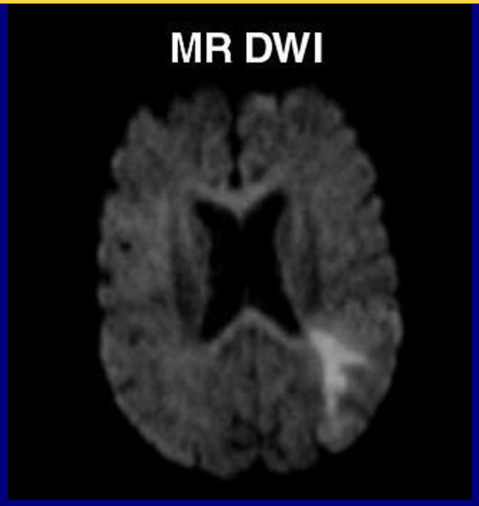
- ***Recanalization:***
  - **Thrombolytics, Antithrombotic**
  - **Mechanical, Laser, Ultrasound**
- ***Neuroprotectors:***
  - **Anti-excitotoxic**
  - **Anti-inflammatory**
  - **Anti-apoptotic**
- ***Manipulation of:***
  - **Temperature**
  - **Blood pressure**
  - **Oxygen levels**
  - **Haemodynamics/rheology**



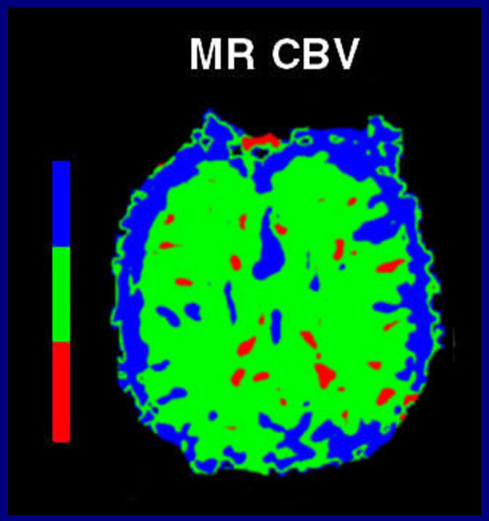
Dirnagl et al. Trends Neurosci 1999

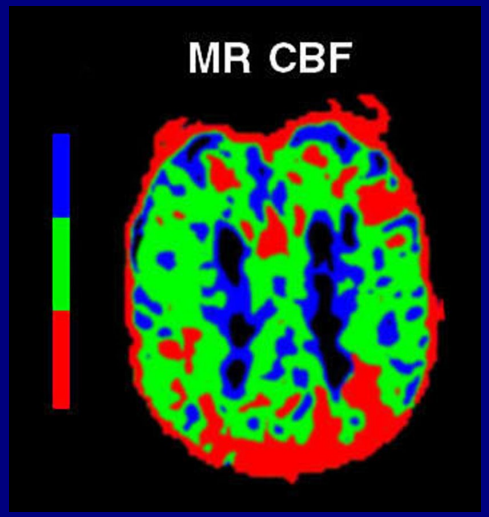
The MRI Approach

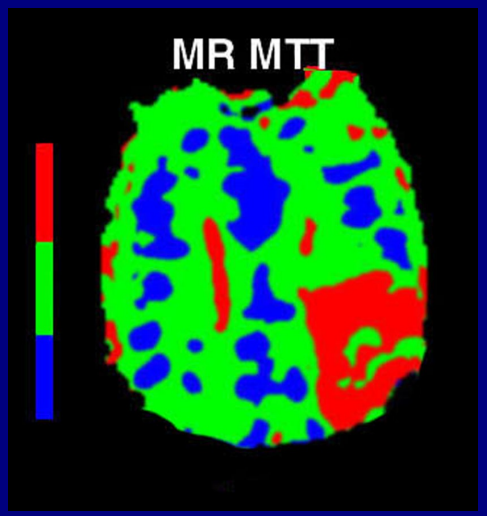
DWI abnormality = infarct



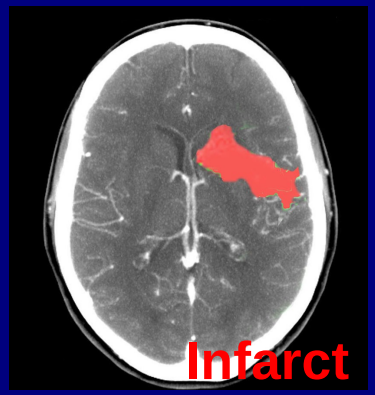
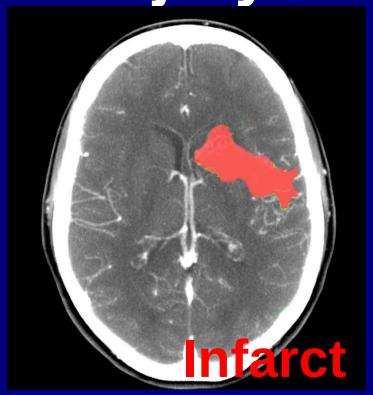
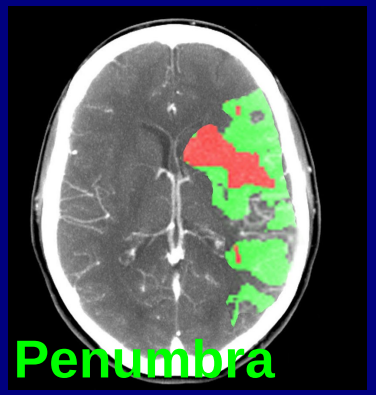
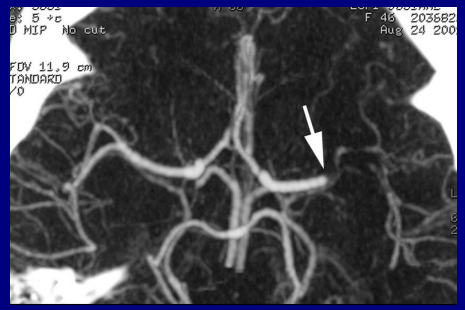
DWI/PWI mismatch = penumbra



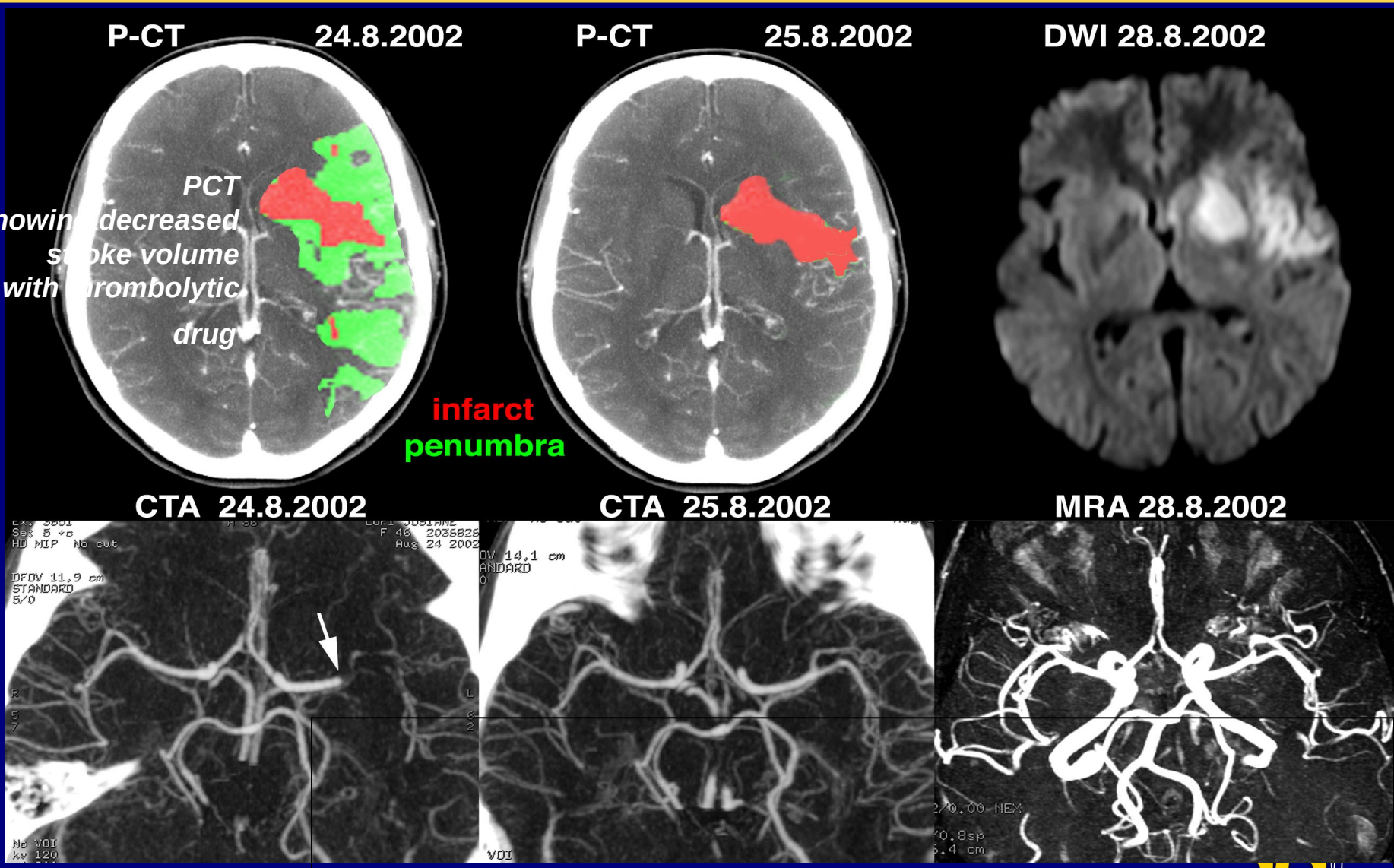




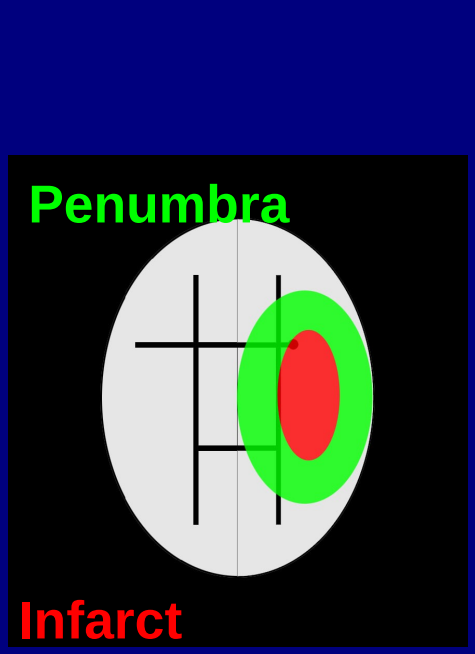
The NCT/PCT/CTA Approach

NCT/PCT	PCT	PCT	CTA
Hemorrhage	**Ischemic Injury**	**Perfusion Status**	**Vessel Status**
			
	Sensitive, Early Detection Quantified	rCBF rCBV MTT TTP	Large Vessel Intracranial & Extracranial Occlusions

Surrogate Marker for Drug Effect

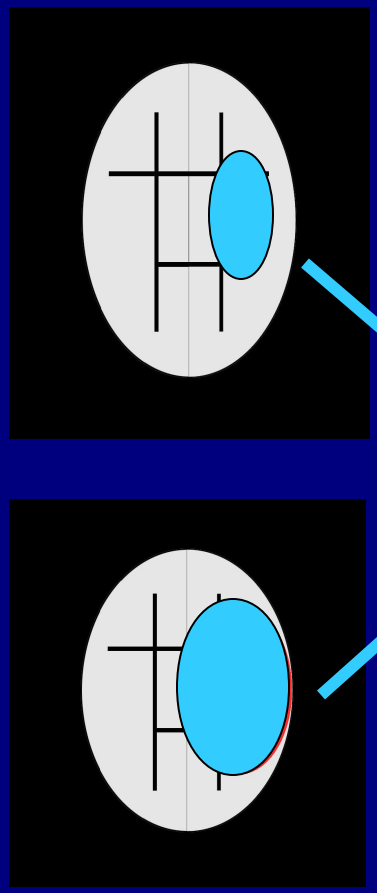


Goal of treatment



Successful treatment

Unsuccessful treatment



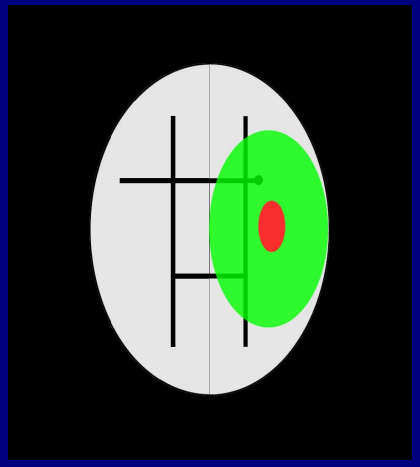
Final Stroke Size

$$\text{Success} = \frac{\text{Penumbra} - (\text{Final Stroke Size} - \text{Infarct})}{\text{Penumbra}}$$

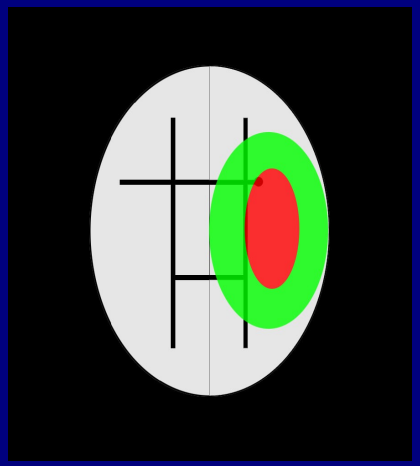
Penumbra / Infarct Ratio

Lausanne Stroke Index =

$$\frac{\text{Pénombre}}{\text{Pénombre + Infarctus}}$$



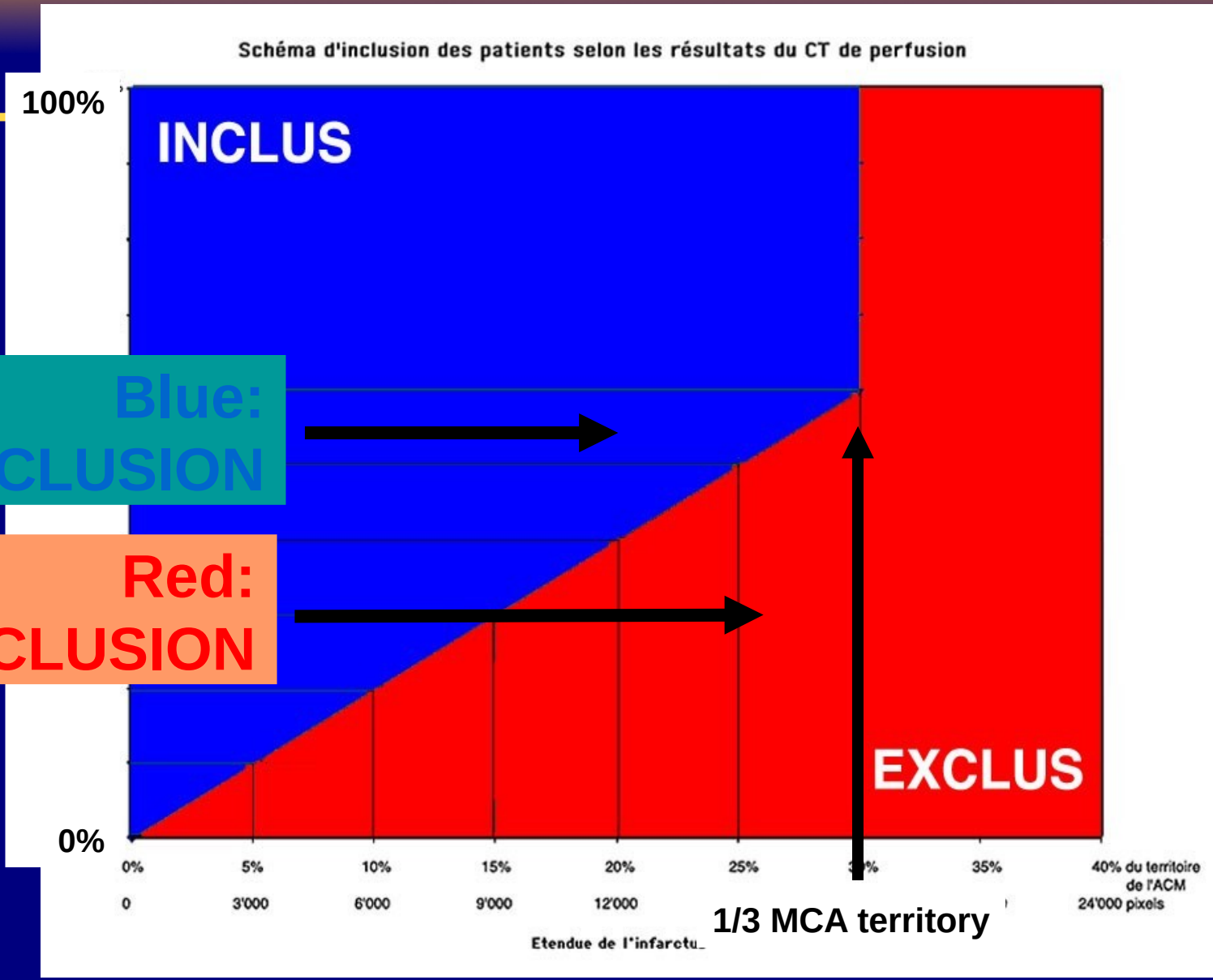
Favourable prognosis:
High LSI
→
considerable improvement of NIHSS



Unfavourable prognosis:
Low LSI
→
no improvement of NIHSS

Annals of Neurology 2002;51:417-432

Stroke Index



Blue: INCLUSION

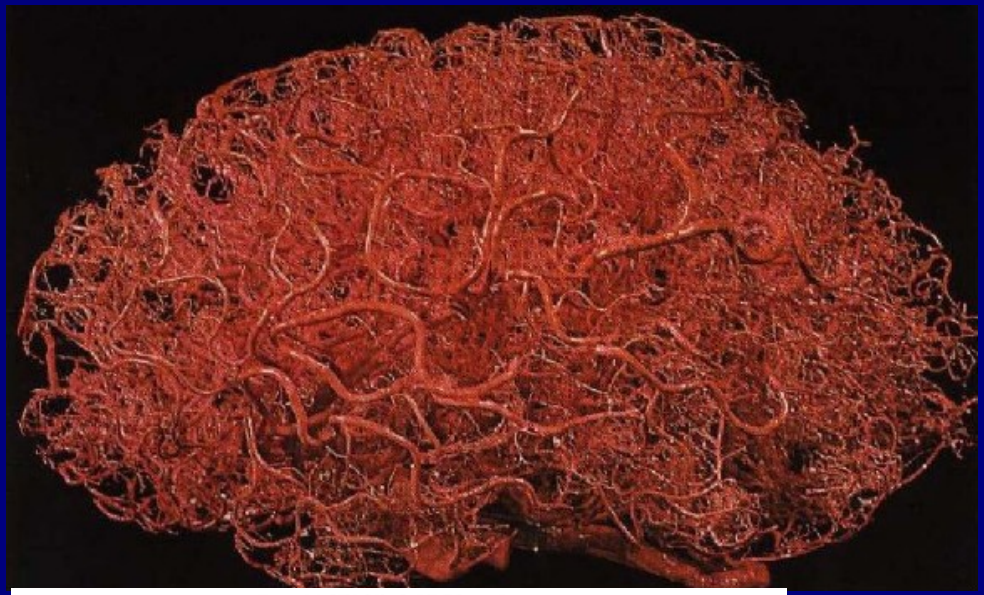
Red: EXCLUSION

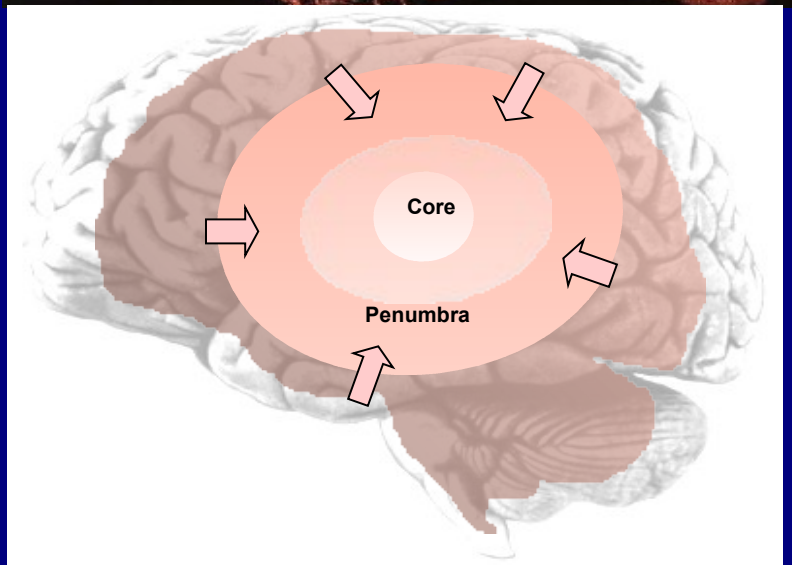
1/3 MCA territory

Infarct Size

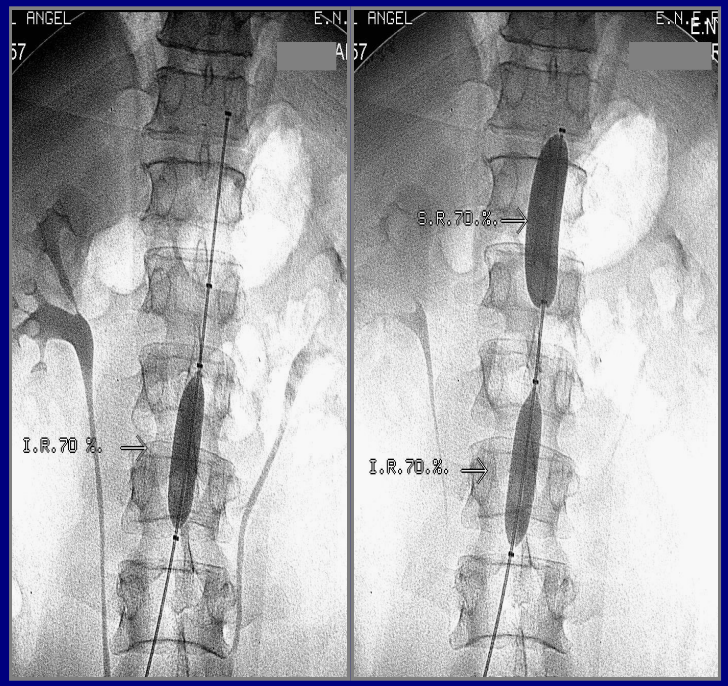
A New Approach to Treating Cerebral Ischemia

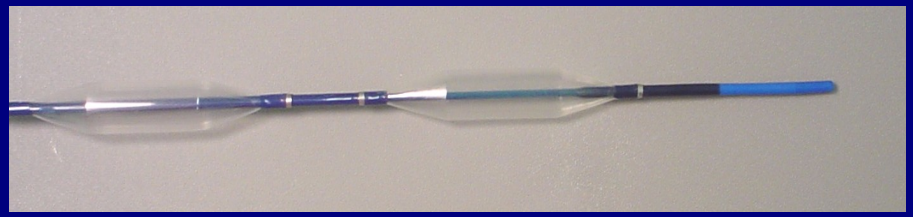
- Globally increase cerebral perfusion via partial occlusion of descending aorta
- Utilize extensive cerebral collateral network
- Add volume and flow to the cerebral vasculature without systemic side effects
- Salvage ‘at risk’ tissue immediately (penumbra)
- Minimize risk of hemorrhagic conversion
- No intracranial access required





The Method: Partial Aortic Occlusion with NeuroFlo™





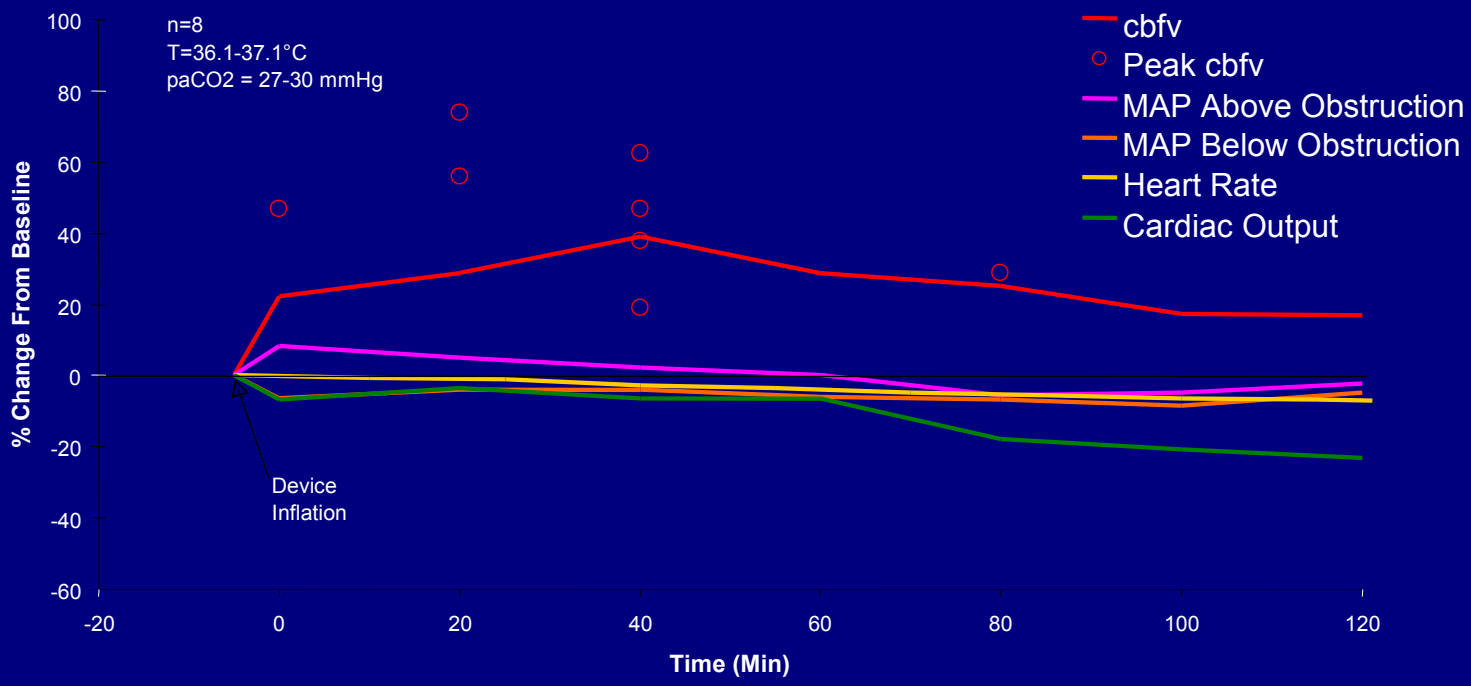
- Temporary, partial occlusion of descending aorta increases flow to carotids
- Dual balloon aortic catheter
- 9 Fr sheath; femoral access
- Balloons advanced to supra- and infra-renal
- Balloons sequentially inflated to 70% luminal occlusion
- 45 minute inflation/treatment

<u>DESIGN / BENEFITS</u>

- Dual balloons and pressure measurements create stable, controllable occlusion
- Cerebral perfusion increases 30% and persists beyond balloon deflation
- Unique, supra- & infra-renal design preserves renal perfusion

Pre-Clinical Proof of Concept: Hemodynamics / Flow

Swine Hemodynamics at 70% occlusion; n=8

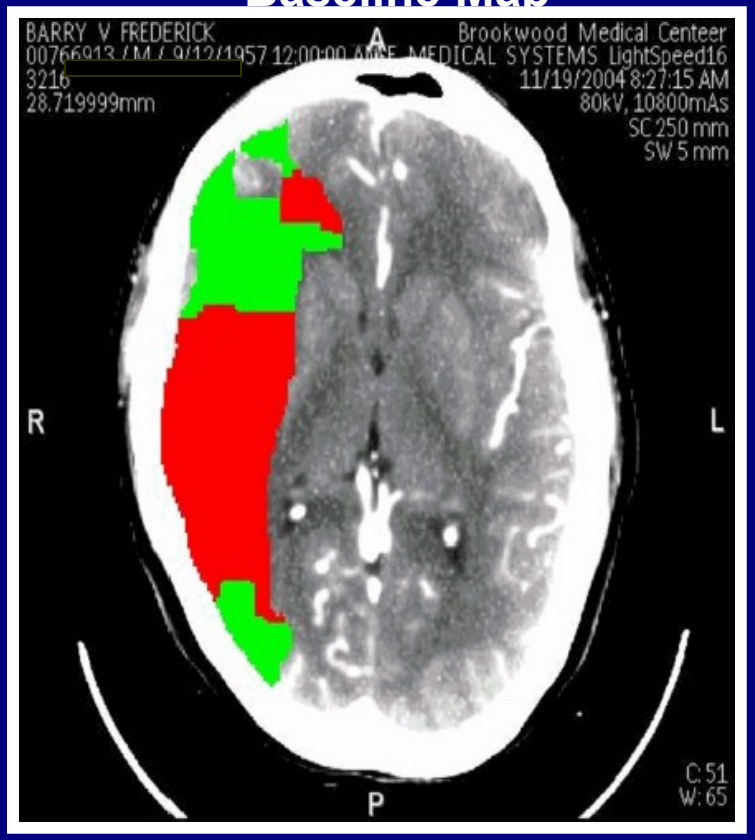


- CBFV increases average >30%
- Minimal systemic effect on MAP, HR and CO

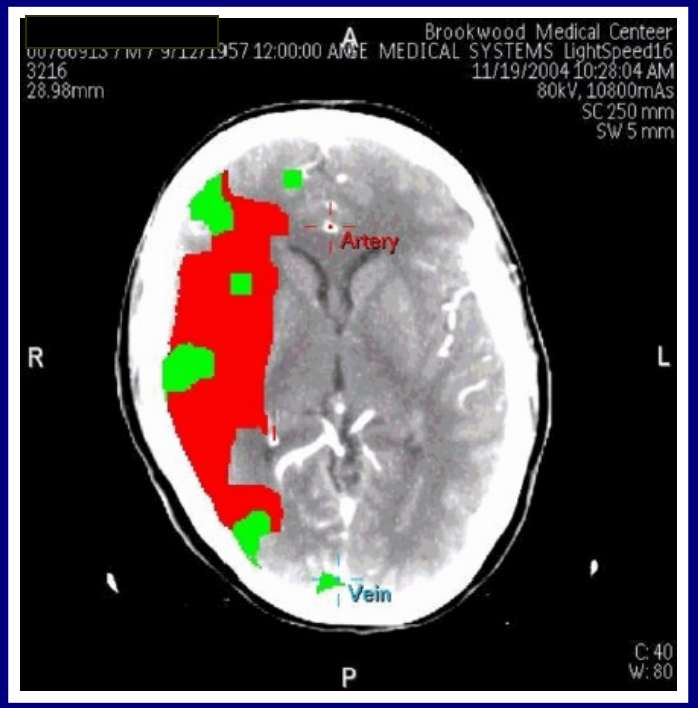
Natural Progression of Infarct in Stroke

CoAxia Non-treatment Patient Example (010-007)

Baseline Map

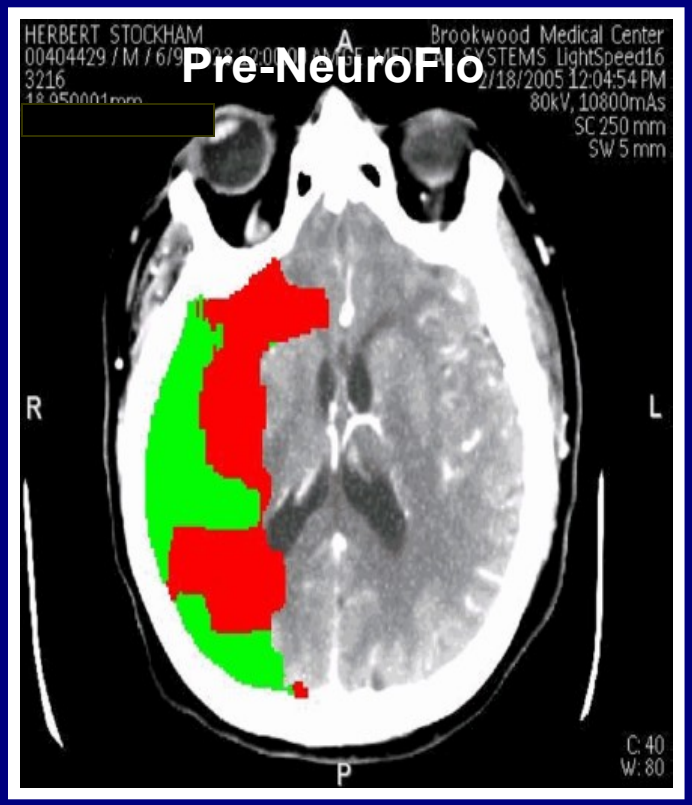


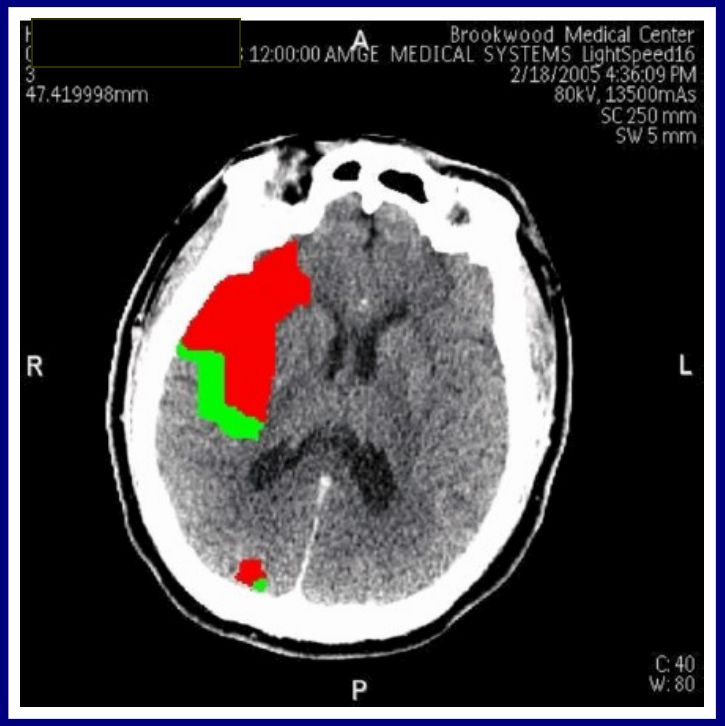
Follow-up Map



% Change of summary map (Baseline vs Follow-up)		
Total area	**"At risk"**	**"Infarct"**
- 5%	**- 50%**	**+ 22%**

NeuroFlo Effect on Stroke Patient





% Change of summary maps (Pre vs Post-NeuroFlo)		
Total area	**"At risk"**	**"Infarct"**
- 54%	**- 78%**	**- 37%**
"At risk" penumbra resolves to normal		

Clinical History

- Pre-Clinical Studies
  - Rat, canine, porcine models; various studies
  - Validated perfusion increase w/o systemic effects; optimized design
- Phase I Stroke (focus on safety)
  - Conservative, incremental balloon inflation
  - 9 US and European centers; 17 patients
- Phase II Stroke (focus on outcome / perfusion)
  - Several minute inflation to target occlusion
  - 5 US centers; 12 patients
- Phase I Vasospasm (focus on safety and outcome)
  - Single center (Buenos Aires)
  - Treatment evolved during the study; 24 patient

Human Feasibility Summary: Ischemic Stroke

		Total Treatment (n=29)
Baseline	Median NIHSS baseline	9.0
	Mean time to treat (hrs)	7.6 ± 2.2
	NIHSS reduction ≥ 3 peri-procedural	61% (17/28*)
24 hours	NIHSS reduction ≥ 3 or resolution (24 hr)	62% (16/26**)
	NIHSS 0-2 (24 hr)	27% (7/26**)
	Median NIHSS (24 hr)	5.0
30 days	Median NIHSS 30 days	5.0
	% reduction in median NIHSS	44%
	mRs ≤ 1 30 days	37% (10/27***)

*1 patient sedated peri-procedurally

** 2 patients sedated plus 1 missing data point at 24 hrs

*** 2 patients died (unrelated to procedure)

Human Feasibility Summary: Cerebral Vasospasm

Peri-procedural Neurological Improvement	Baseline NIHSS	10
	Mean NIHSS reduction	-3.4
	NIHSS reduction ≥ 2	71%
	NIHSS reduction ≥ 4	43%
Perfusion Augmentation	TCD	82%
	Angiogram	67%
30 Day Neurological Improvement	NIHSS ≤ 2	13/16 (81%)
	Modified Rankin ≤ 2	9/10 (90%)

Adverse Events

Type of events	# patients (%)
No adverse events	9/29 (31%)
Only non-serious events	12/29 (41%)
Serious, non-fatal events	6/29 (21%)
Deaths	2/29 (7%)

All events adjudicated by Safety Review Committee:

No deaths considered to be device- or procedure-related

1 serious AE considered procedure-related (groin hematoma)

8 non-serious AEs considered procedure-related:

- 5 groin bleed / hematoma
- 1 allergic reaction
- 1 vaso-vagal reaction
- 1 mild neurologic deterioration

Feasibility Results Have Led to Pivotal Trial

SENTIS Stroke Trial

- Pivotal, randomized trial for ischemic stroke is FDA approved and ongoing
- NeuroFlo vs. medical management
- Up to10 hours post symptom onset
- 90 day neurological recovery as primary endpoint
  - pre and post Tx perfusion imaging data – secondary endpoint
- 40 sites
  - 25 currently in process; seeking up to 15 additional sites

Conclusion

- An interventional treatment for stroke victims beyond the 3 hour tPA window (up to 24 hours if penumbra?)
- Wide availability due to ease of use and early data on safety
- Role for interventional cardiology in acute stroke

We hope to have more data and acute outcomes to present at TCT 2006