State of the Art Multimodal Monitoring

Baptist Neurological Institute

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Disclosures

I have no financial relationships to disclose with makers of the products here discussed.

Outline

I Brief Overview ICP monitoring.

II Microdialysis

III Brief Overview about brain tissue oxygen monitoring $P_{bt}O_2$(licox)

IV Near Infrared Spectroscopy (NIRS)

V Quantitative EEG

Monitoring the Brain in Coma

- Black box
- No reliable exam
- Need to determine if the tissue is in crisis

Secondary Brain Insults

- **Decreased substrate delivery**

– Hypotension

- Vasospasm

– Hypoxia

- **Aggravate hemorrhage or edema**

– Hypertension

- **Cellular toxicity**

– Hyperglycemia

Increased metabolism

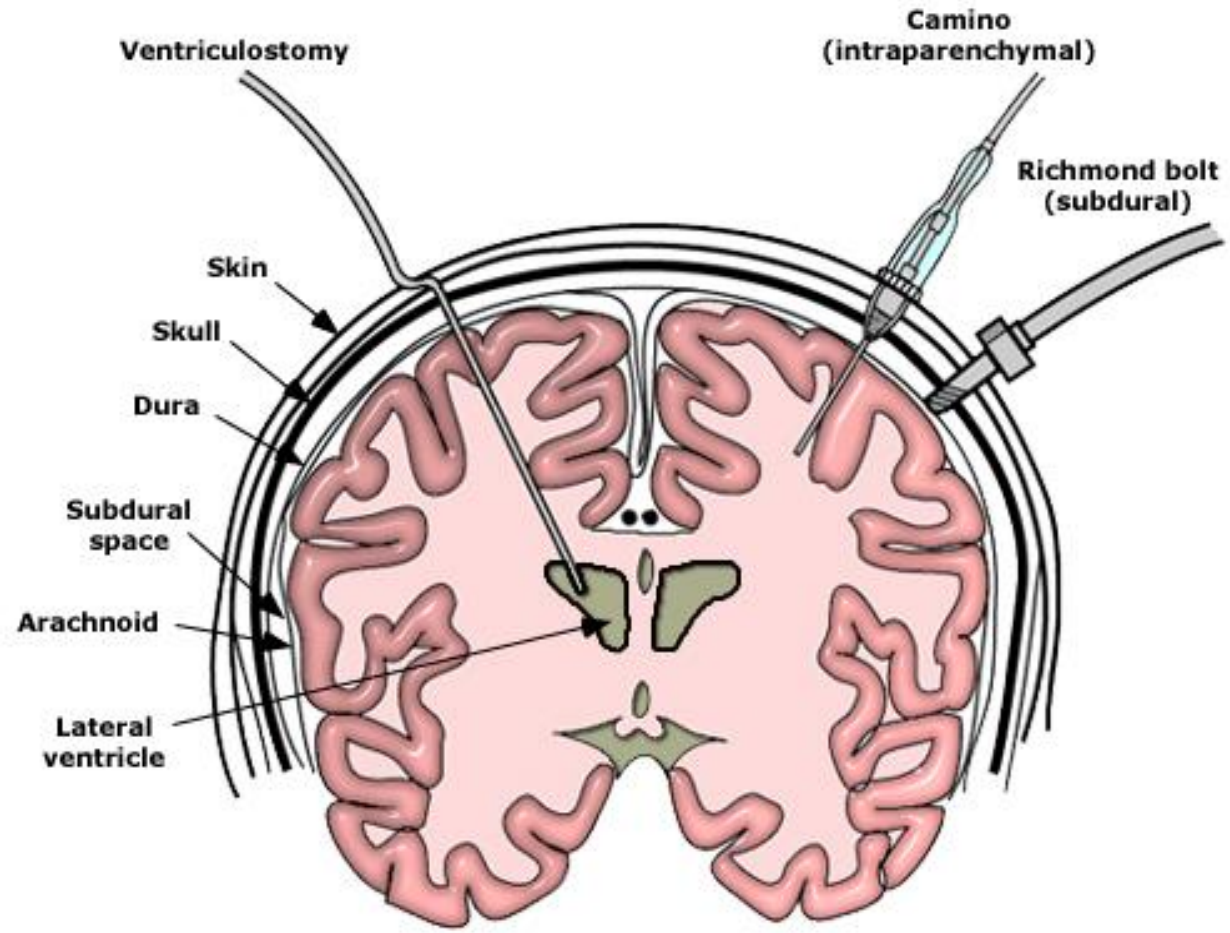
– Fever

– Seizures

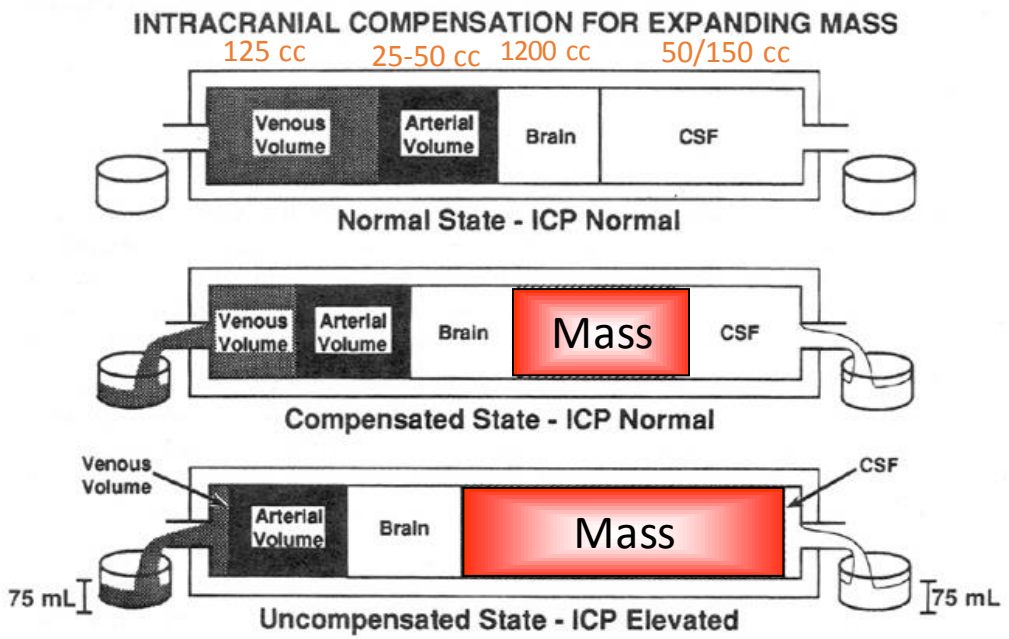
Limitations of the GCS & NIHSS

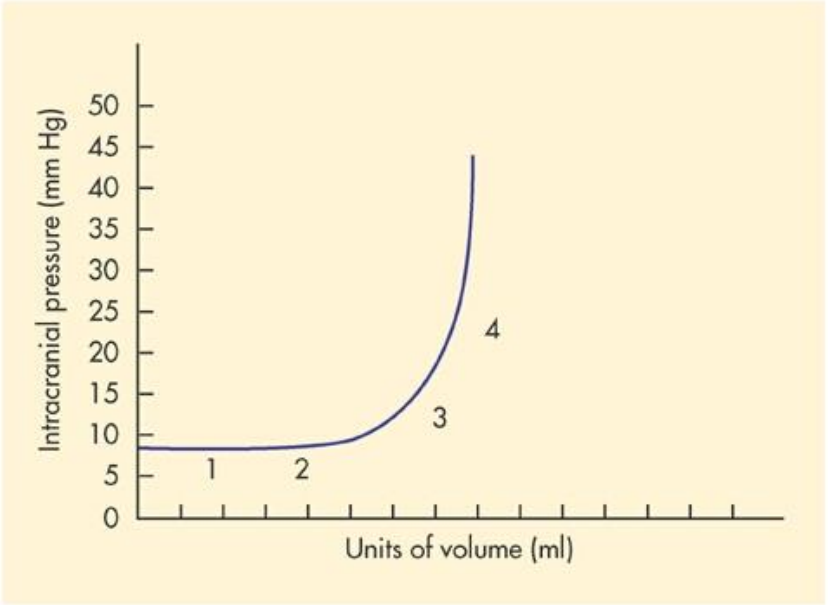
- Does not directly assess *brainstem function*
- Does not evaluate alterations in *respiratory pattern*
- *Verbal component* cannot be tested in comatose or intubated patients
- *Underestimates* LOC, especially in dominant hemisphere lesions

ICP monitors



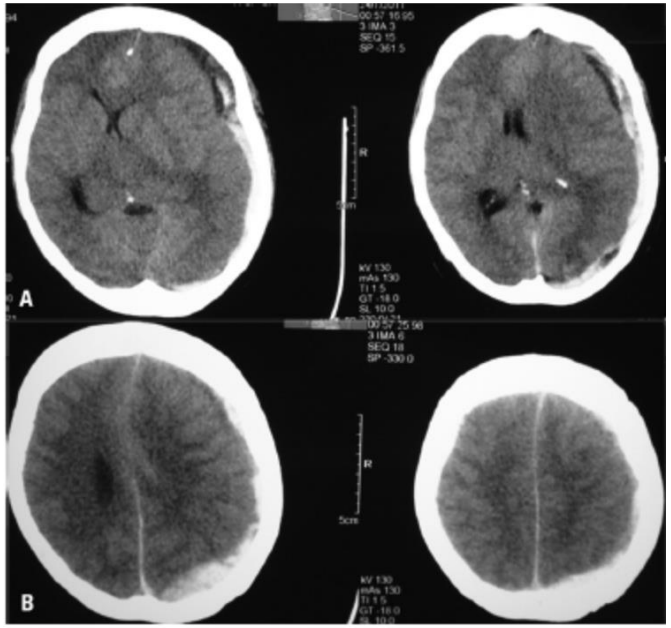
Monroe-Kellie Doctrine cont'd

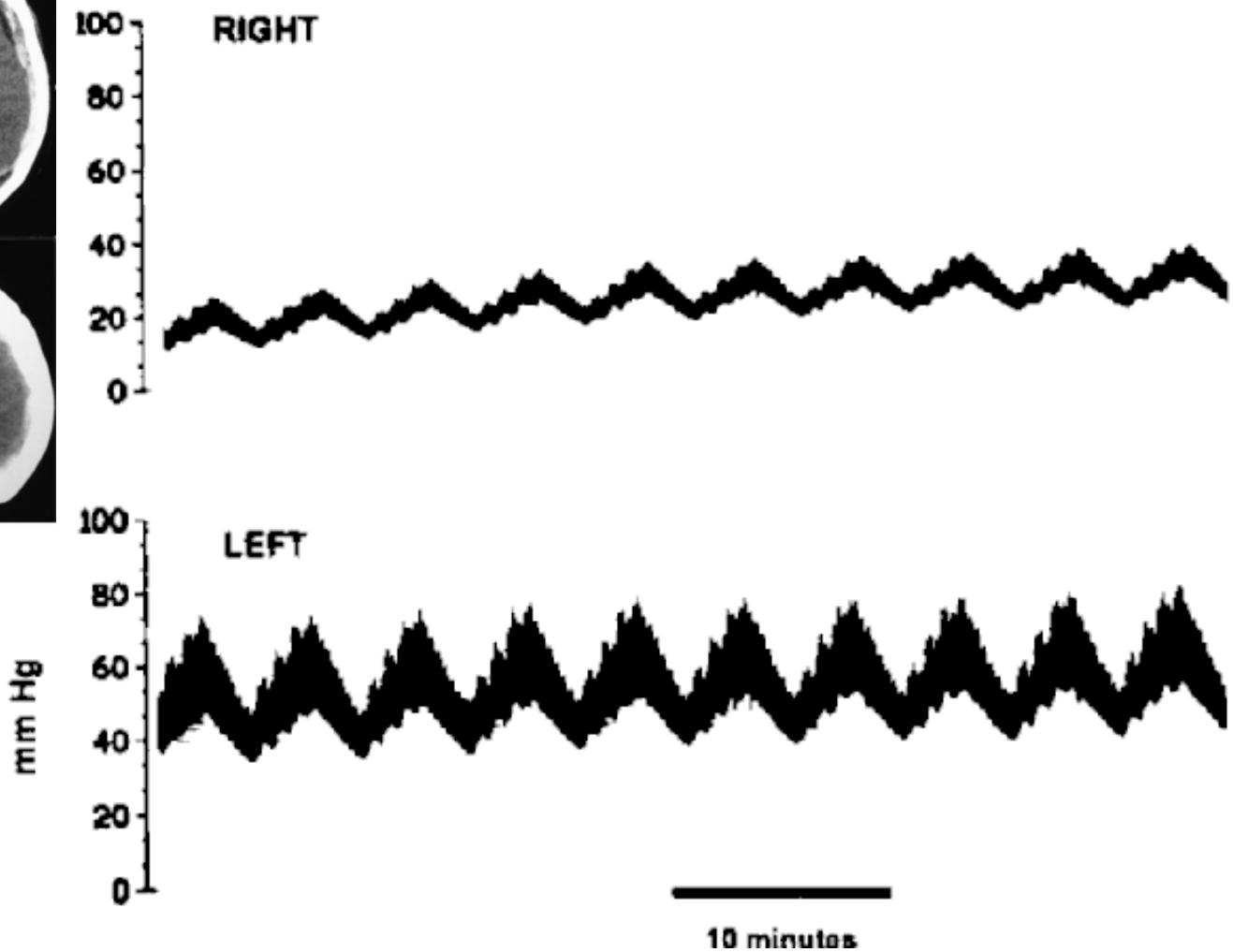




Interhemispheric supratentorial intracranial pressure gradients in head-injured patients: are they clinically important?

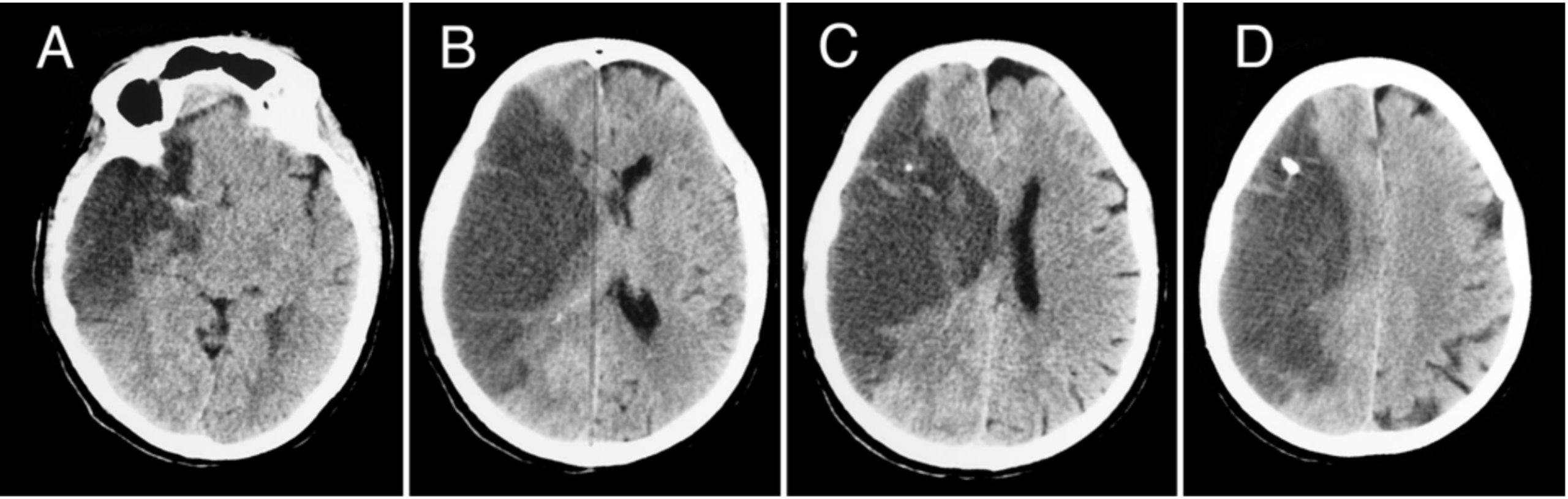
JUAN SAHUQUILLO, M.D., PH.D., MARIA-ANTONIA POCA, M.D., MERCEDES ARRIBAS, R.N., ANGEL GARNACHO, M.D., PH.D., AND ENRIQUE RUBIO, M.D., PH.D.





Subdural
13 mm Shift
Left to right

Monitoring intracranial pressure in patients with malignant middle cerebral artery infarction: is it useful?



Patients with a malignant MCA infarction may show **ICP values < 20 mm** Hg despite **marked MLS (> 5 mm)**, large brain infarctions, and **neurological deterioration (pupillary abnormalities)** indicating **uncal herniation.** Consequently, ICP monitoring cannot substitute for strict clinical and neuroradiological follow-up in these patients.

J Neurosurg 112:648–657, 2010

BEST-TRIP Trial

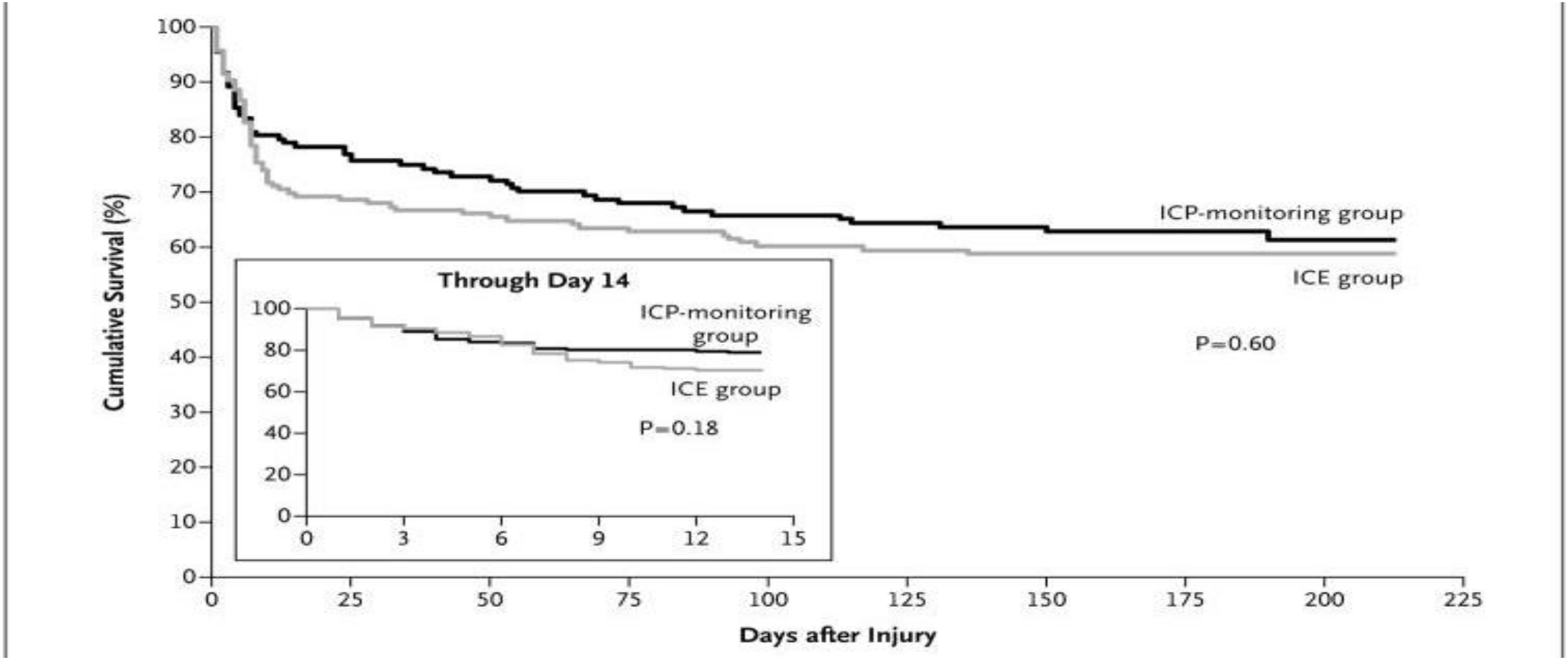
- Multicenter RCT *(Chesnut et al)* in which 324 patients with severe TBI were randomized to

A) ICP/CPP monitoring group and

B) Imaging and clinical examination group

Primary outcome: composite of survival time, impaired consciousness, and functional status at 3 months and 6 months and neuropsychological status at 6 months

Kaplan Meier survival plot



BEST-TRIP Trial results

Composite score: 56 in the pressure-monitoring group vs. 53 in the imaging-clinical examination group (NS)

Six-month mortality was 39% in the pressure-monitoring group and 41% in the imaging-clinical examination group (NS)

So is monitoring unnecessary or suboptimal???

neurocritical care society Neurocrit Care (2012) 17:49–57
DOI 10.1007/s12028-012-9708-y

ORIGINAL ARTICLE

Early Cerebral Metabolic Crisis After TBI Influences Outcome Despite Adequate Hemodynamic Resuscitation

Nathan R. Stein · David L. McArthur · Maria Etchepare · Paul M. Vespa

Hemodynamic Monitoring vs Metabolic Neuronal Monitoring

Does Hemodynamic resuscitation improve neuronal metabolic profile?

Table 1 Incidence and duration of metabolic crisis in the first 72 h post injury

Parameter	% Patients (*n*)	Mean duration (h)
Glucose < 0.8 mmol/L	76.3 (58/76)	38.0 ± 21.5
LPR > 25	93.4 (71/76)	44.9 ± 23.8
Metabolic crisis	73.7 (56/76)	33.5 ± 22.8

Metabolic crisis (MC) persists despite adequate hemodynamic resuscitation.

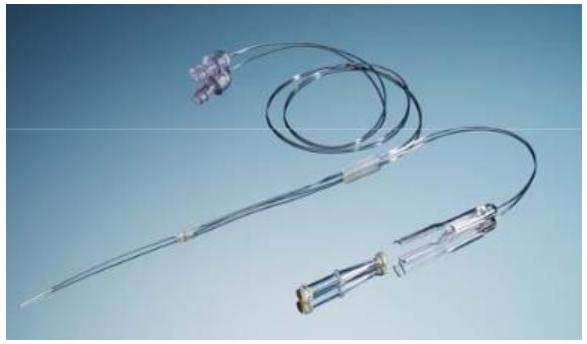
For every 12 h spent in MC the odds of having a poor outcome is more than doubled.

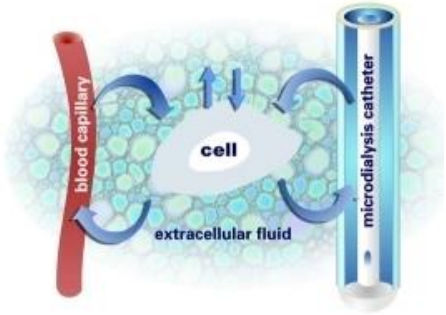
Stein, Neurocritical care 2013

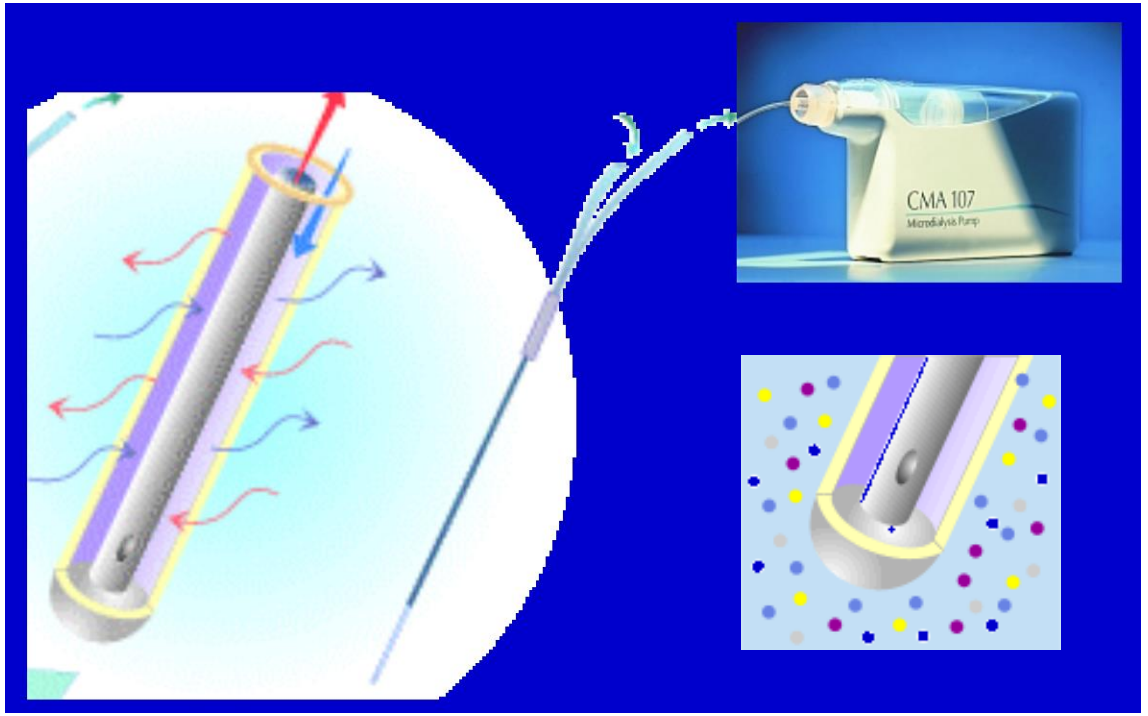
- Markers of metabolic distress in the brain compartment appears to be distinct from that of the systemic circulation, with traditional hemodynamic and oxygenation goals likely underestimating the requirements of the injured brain.

Systemic Resuscitation $\neq$ **Cerebral Resuscitation.**

Cerebral Microdialysis

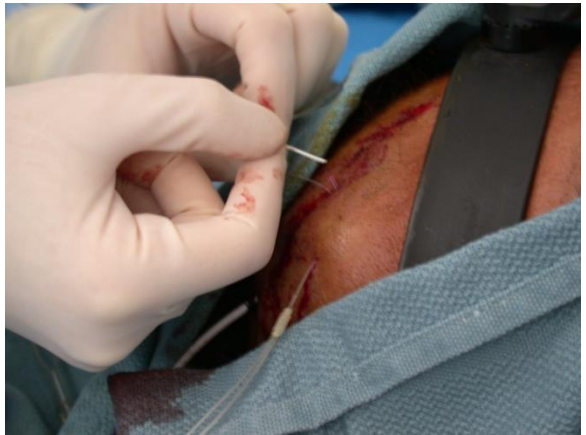


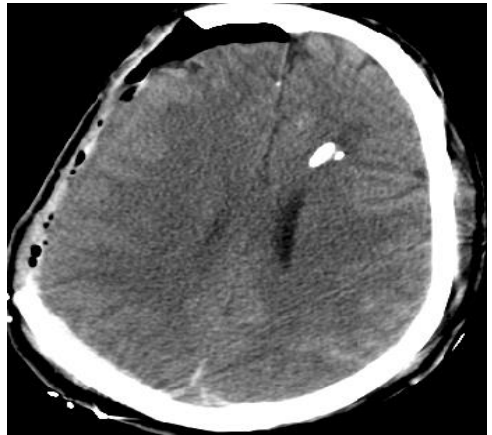




Brain Tissue Oxygenation:
Microdialysis

- Perfusion system:
  - Uses osmotic gradients method
  - Flexible
  - Membrane sizes: 6kDA – 90kDA
  - Measures local tissue metabolite levels





Normal Values

Table 1: Normal reference values for brain cerebral microdialysis from normal appearing human brain tissue

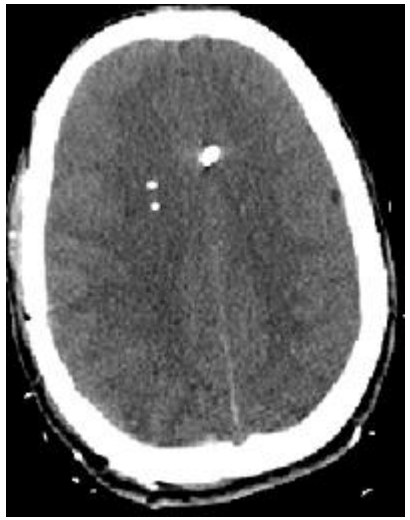
Perfusion Rate	**Glucose** (mmol/L)	**Lactate** (mmol/L)	**Pyruvate** (µmol/L)	**LPR**	**Glycerol** (µmol/L)	**Urea** (mmol/L)	**Glutamate** (µmol/L)
0.3 µL/min	1.7 ± 0.9	2.9 ± 0.9	166 ± 47	23 ± 4	82 ± 44	4.4 ± 1.7	5 ± 10
1.0 µL/min	0.9 ± 0.6	1.4 ± 0.9	103 ± 50	21 ± 6	42 ± 29	2.5 ± 1.3	5 ± 10
2.0 µL/min	0.45 ± 0.61	0.7 ± 0.7	26 ± 19	15 ± 5	30 ± 43	2.5 ± 1.4	2.5 ± 4.7

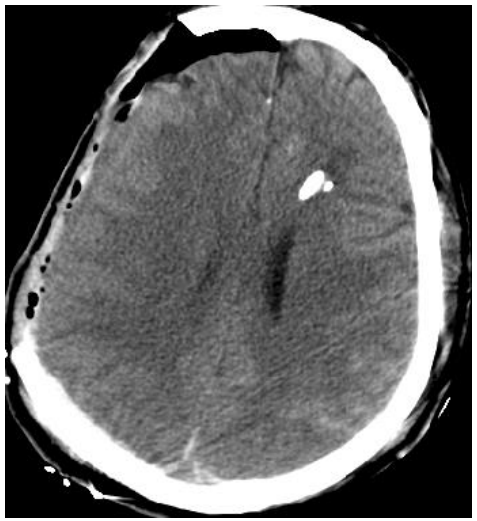
Adapted from Hillered 1990, Reinstrup et al 2000 and Vespa et al 2007

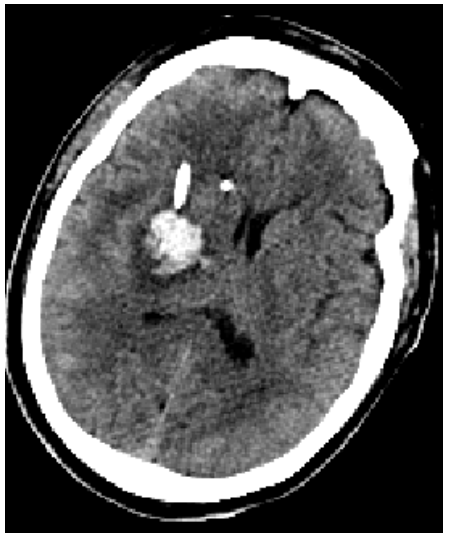
Table 2: Reference values for brain microdialysis during brain ischemia

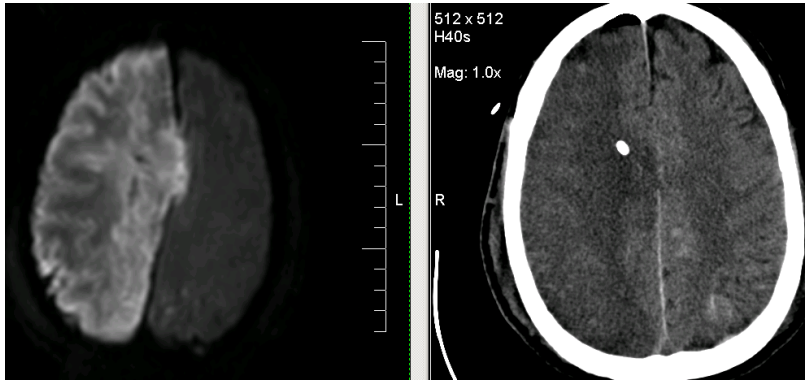
Perfusion Rate	**Glucose** (mmol/L)	**Lactate** (mmol/L)	**Pyruvate** (µmol/L)	**LPR**	**Glycerol** (µmol/L)	**Urea** (mmol/L)	**Glutamate** (µmol/L)
0.3 µL/min	↓ 0.6 ± 0.5	↑ 4.1 ± 0.9	↓ 60 ± 47	↑ 40 ± 8	↑ 40 ± 44	4.4 ± 1.7	↑ 10 ± 10

Adapted from Persson 1992; Vespa 1998





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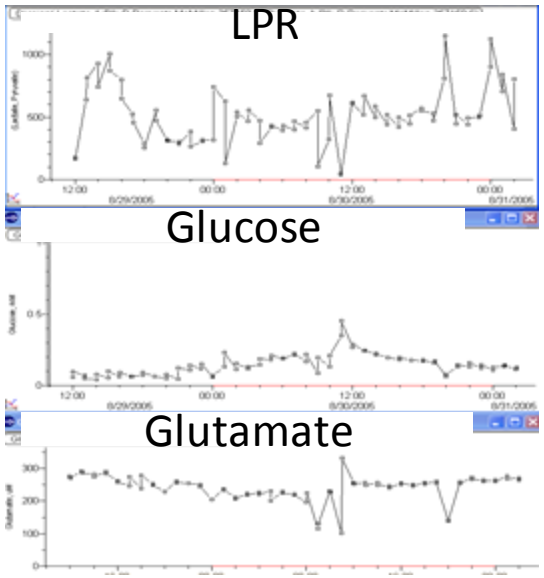
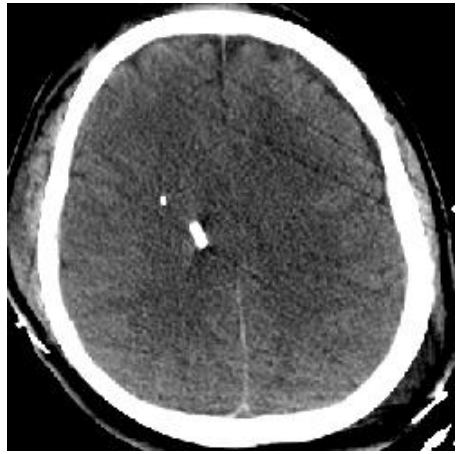
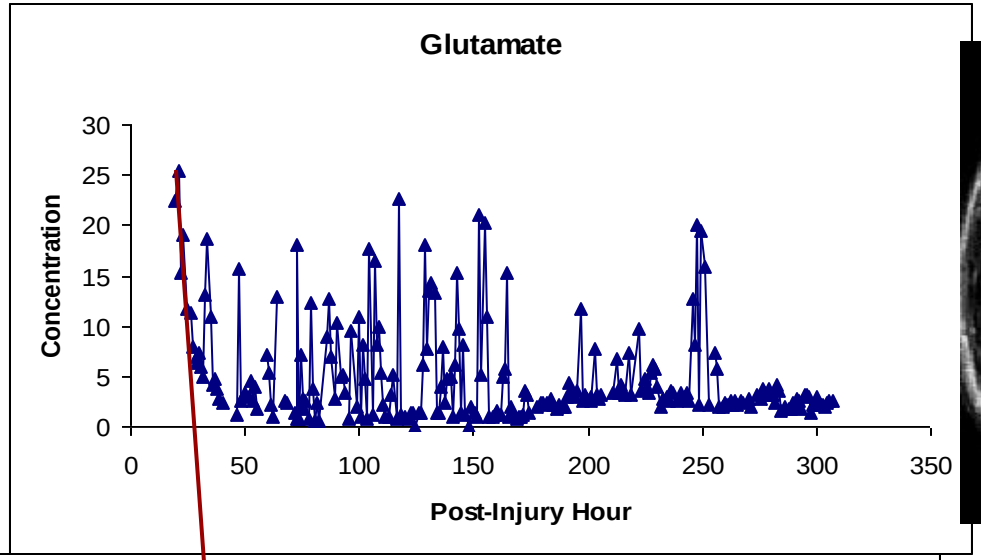
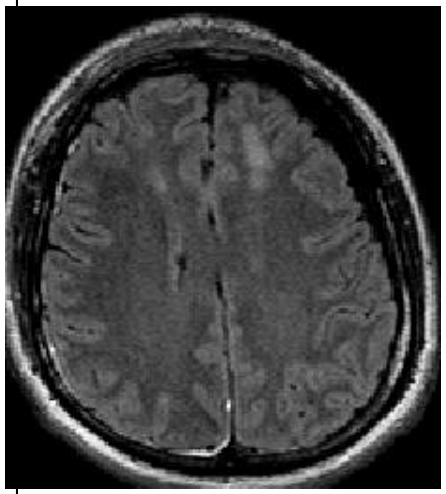
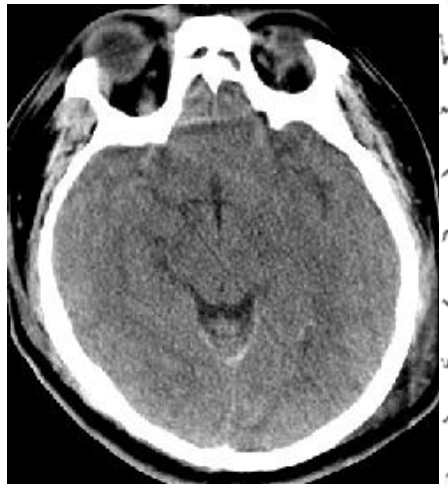

LPR
Glucose
Glutamate

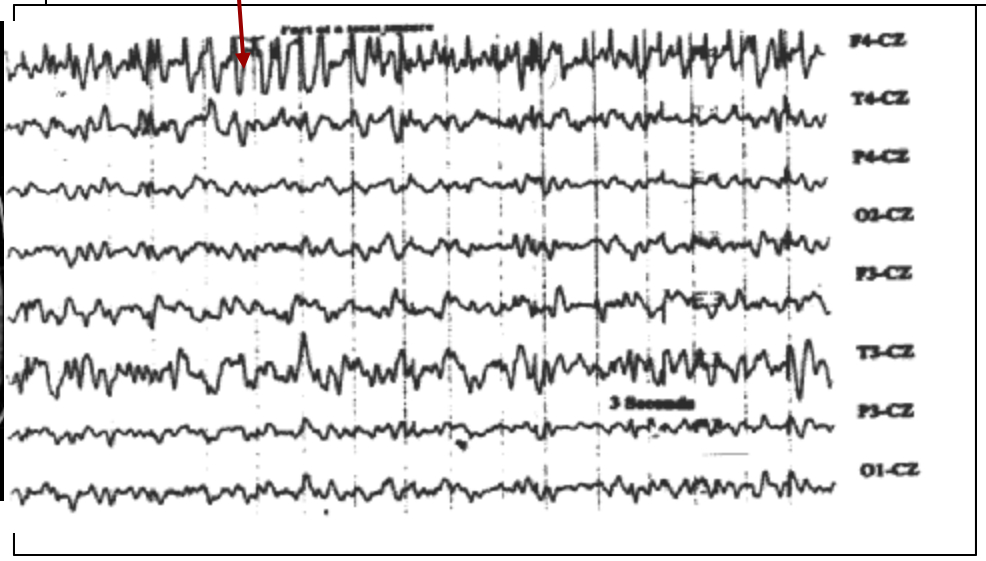
Periodic spikes in glutamate, LPR and EEG seizures

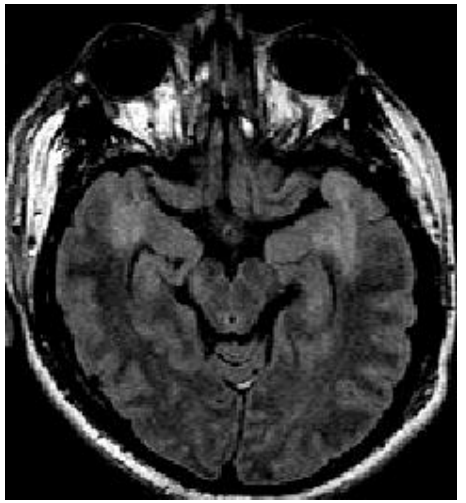




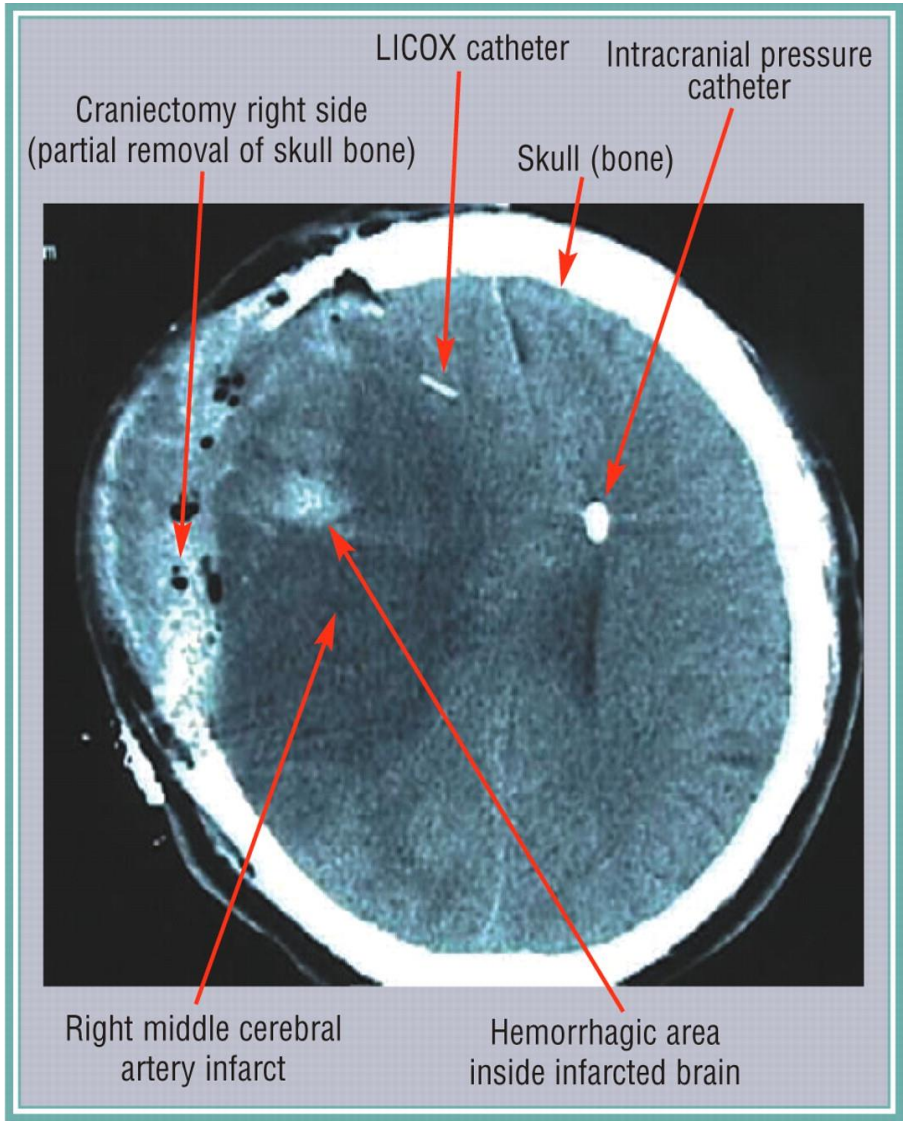


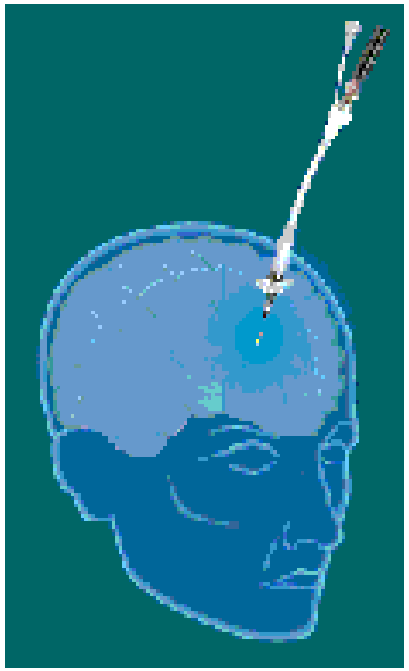






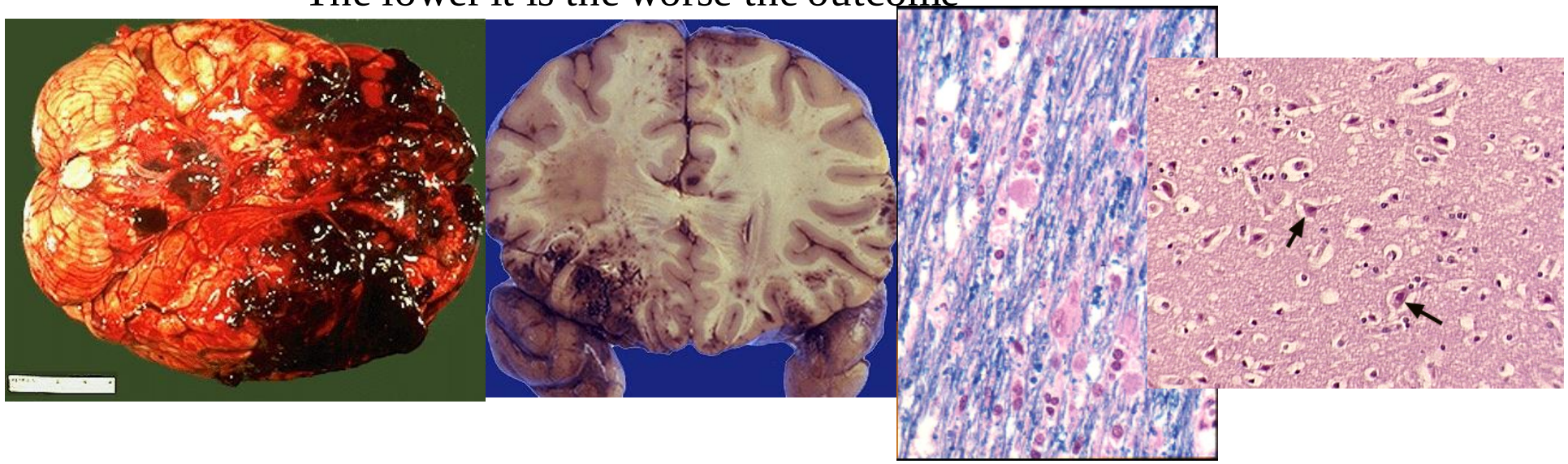
Brain Tissue Oxygenation Monitoring





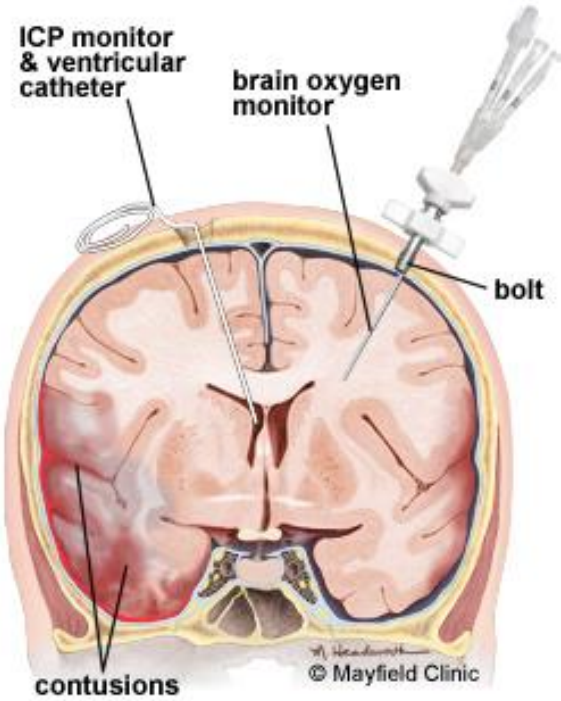
Rationale for Monitoring Brain Oximetry

- Fundamental concern about O2 delivery to the brain stems from:
  - Brain is 2% body weight, but consumes 20% of O2
  - Graham et al autopsy series showing brain ischemia after trauma
  - CMRO2 correlates with outcome
  - The lower it is the worse the outcome



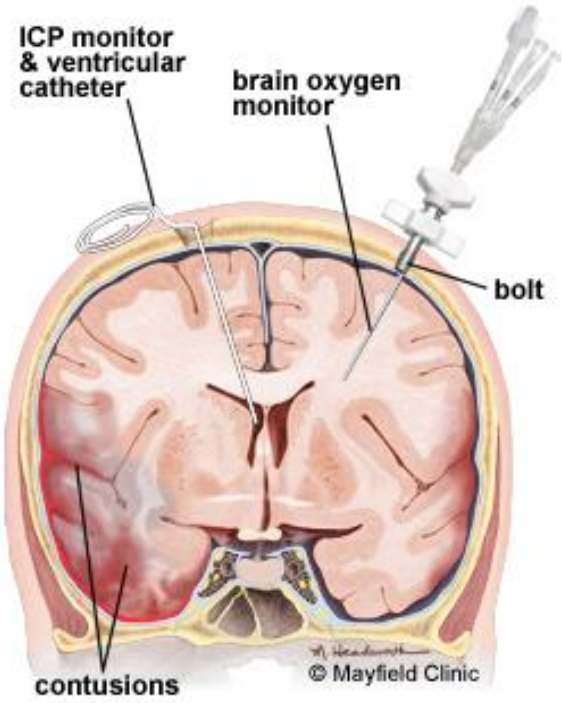
Graham DI, J Neurol Neurosurg Psychiatry. 1989

How Does It Work?



- Probe covered by an O_2 permeable membrane
- O_2 diffuses from brain through membrane
- Inside probe is an electrolyte solution
- O_2 changes the charge of the solution
- Charge is carried through cables to the external Licox computer and displayed

Brain Tissue Oximetry



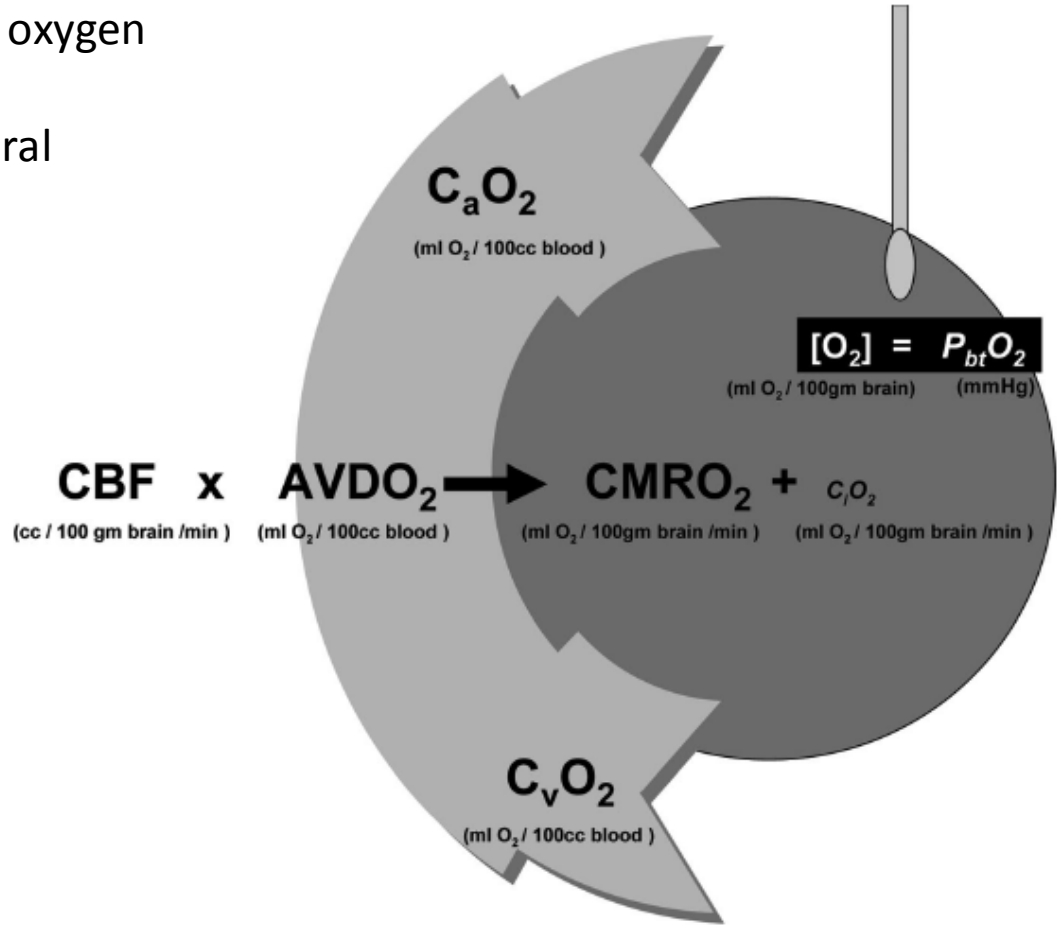
- Local brain tissue oxygenation + brain temp.
- 2.5 cm deep to pial surface, PbtO2 in 3 cm radius
- Location: non-dominant frontal in diffuse TBI, SAH
- Normal 37-48 mmHg
- Risk of Bad clinical outcome:
  - $P_{bt}O_2$ < 15mmHg for 30 minutes (critical brain hypoxia)
  - $P_{bt}O_2$ < 10mmHg for 10 minutes (severe brain hypoxia)
- $P_{bt}O_2$ <5mmHG- High Mortality
- $P_{bt}O_2$ <2mmHg-Neuronal Death

Bardt T, Acta Neurochirugica 1998
Hoffman WE, Surg Neurol 1996

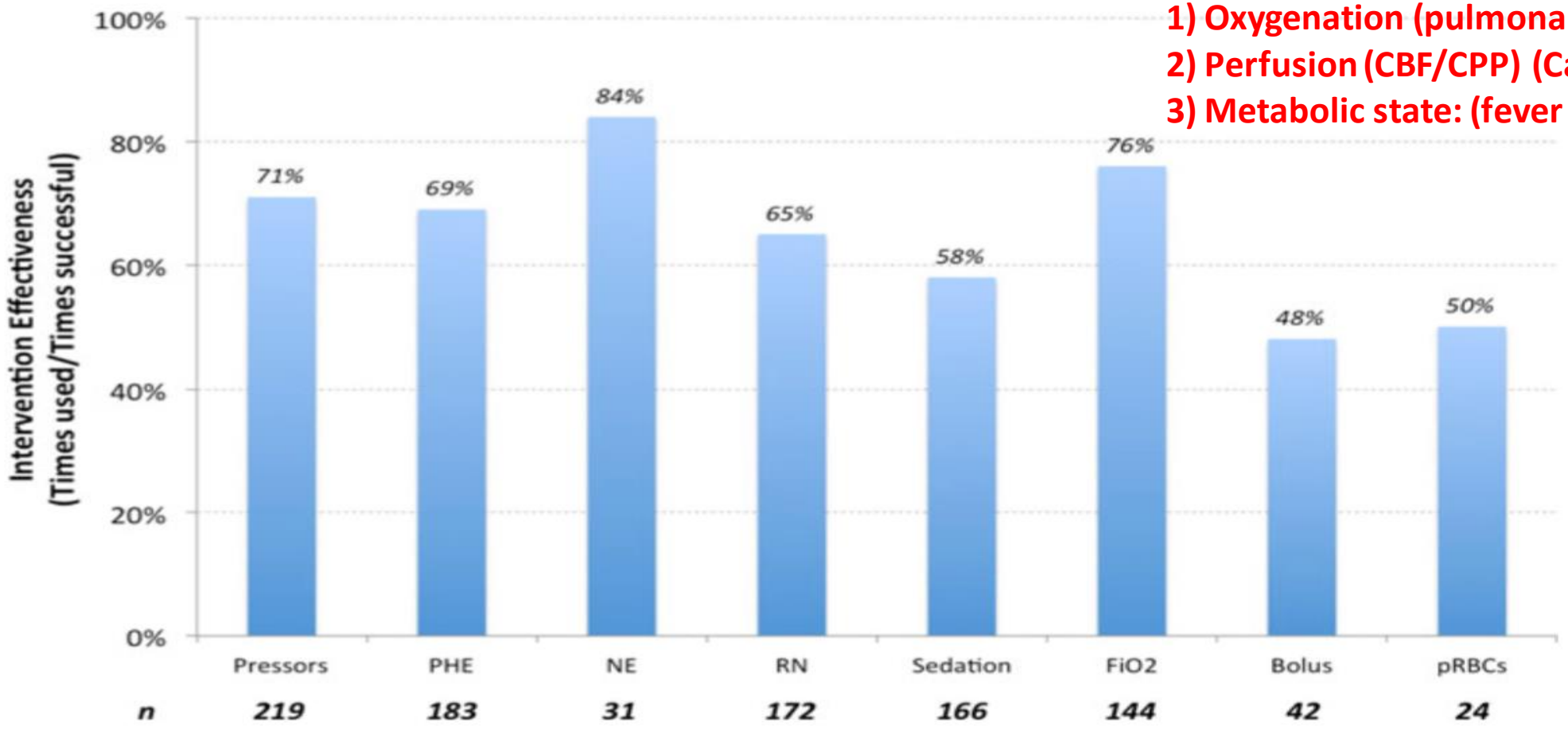
What is PbtO2 measuring?

1) The balance between regional oxygen delivery and cellular oxygen consumption
2) Oxygen diffusion rather than total oxygen delivery or cerebral oxygen metabolism
3) Oxygen that accumulates in brain tissue.

1) Oxygenation (pulmonary system)
2) Perfusion (CBF/CPP) (Cardiovascular system)
3) Metabolic state: (fever and seizure)



Medical Management of compromised Brain Oxygen Recordings in SAH



1) Oxygenation (pulmonary system)
2) Perfusion (CBF/CPP) (Cardiovascular system)
3) Metabolic state: (fever and seizure)

Bohman LE Neurocritical care 2013

Does the use of PtiO2 improve outcome? YES

Reduced mortality rate in patients with severe traumatic brain injury treated with brain tissue oxygen monitoring

MICHAEL F. STIEFEL, M.D., PH.D., ALEJANDRO SPIOTTA, M.D., VINCENT H. GRACIAS, M.D., ALICIA M. GARUFFE, M.S.N., OSCAR GUILLAMONDEGUI, M.D., EILEEN MALONEY-WILENSKY, M.S.N., STEPHANIE BLOOM, M.S.N., M. SEAN GRADY, M.D., AND PETER D. LEROUX, M.D.

Case controlled prospective study using PtiO2

n = 28 pts with ICP + PtiO2

n = 25 historical control patients with ICP only

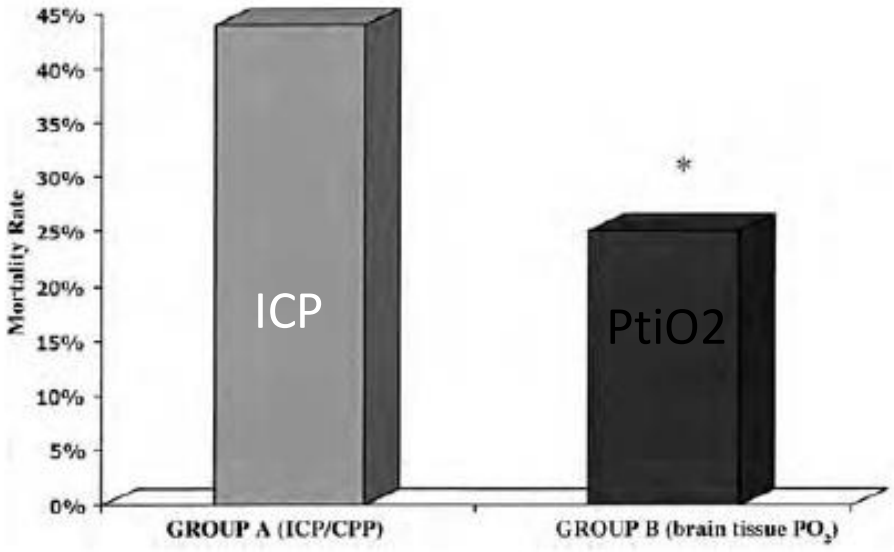
Stiefel et al JNS p 805-811

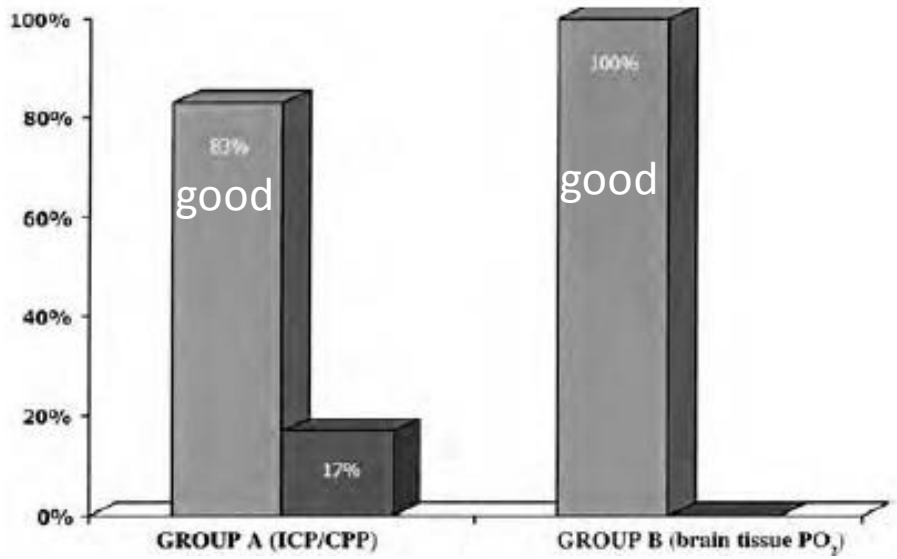
Steifel et al 2005

Monitored physiological variables among 53 patients who underwent ICP/CPP–based therapy or combined ICP/CCP and brain tissue PO_2–based therapy

Monitored Variable	Group A	Group B	p Value
ICP monitor (days per patient)	ICP only	ICP + PtiO2	0.09
mean daily ICP (mm Hg)	15.22 ± 4.21	17.00 ± 7.36	0.34
mean max daily ICP (mm Hg)	21.52 ± 6.9	25.5 ± 9.5	0.16
no. of ICP episodes >20 mm Hg	5.30 ± 7.65	14.05 ± 22.85	0.43
mean daily CPP (mm Hg)	72.93 ± 8.76	72.90 ± 6.19	0.44
mean min daily CPP (mm Hg)	56.3 ± 9.6	57.7 ± 7.1	0.63
no. of CPP episodes <60 mm Hg	3.82 ± 4.97	8.00 ± 13.18	0.46

Steifel et al 2005 outcome data





Patients who died had

- more frequent PtiO2 < 15
- longer durations of PtiO2 < 25

Non-invasive Techniques

- Near infrared spectroscopy
- Oxygen positron emission tomography
- Functional MRI

Near Infrared Spectroscopy NIRS

- Found to penetrate tissues 1977
- Used for brain oxygenation in 1985
- FDA approved 1993
- Skull can be penetrated by NIR light with λ of 700-1300 uM.

NIRS

Depth of penetration is proportional to distance between light source and detector max is about 5 cm

Typical depth into brain is 1.7 cm

Spatial Resolution is about 1 cm x 1.7 column

85% of signal comes from brain, 15% from other tissues (skin, bone)

Estimates Regional brain tissue oxygenation

Normal: 60-80%, Hypoxia-ischemia <45%, Hyperemia > 80%

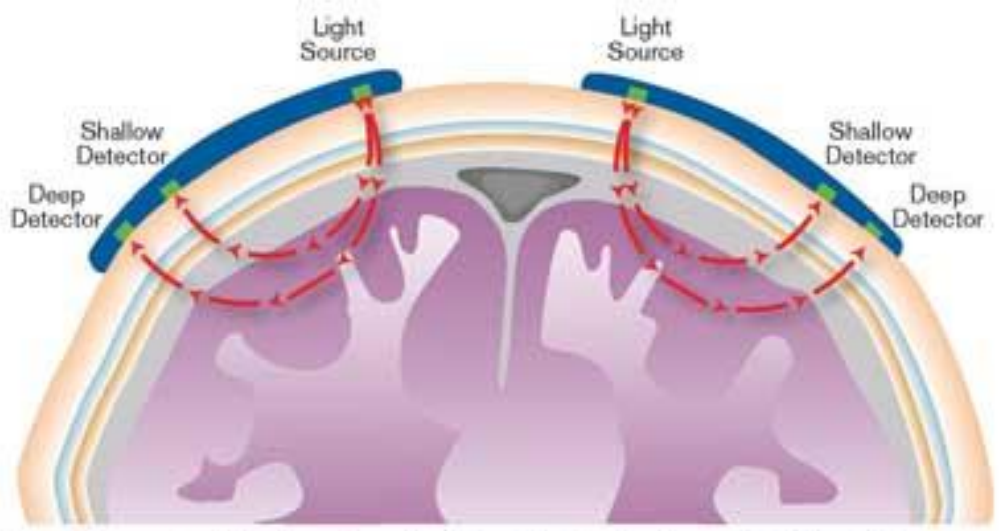
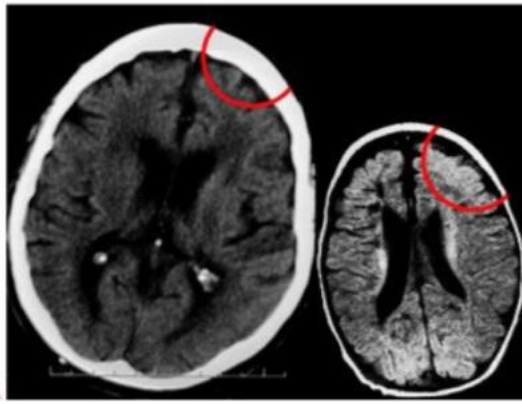


Figure 1: Diagram of cerebral oximetry illustrating a deep and shallow photo detector paired with each light source.

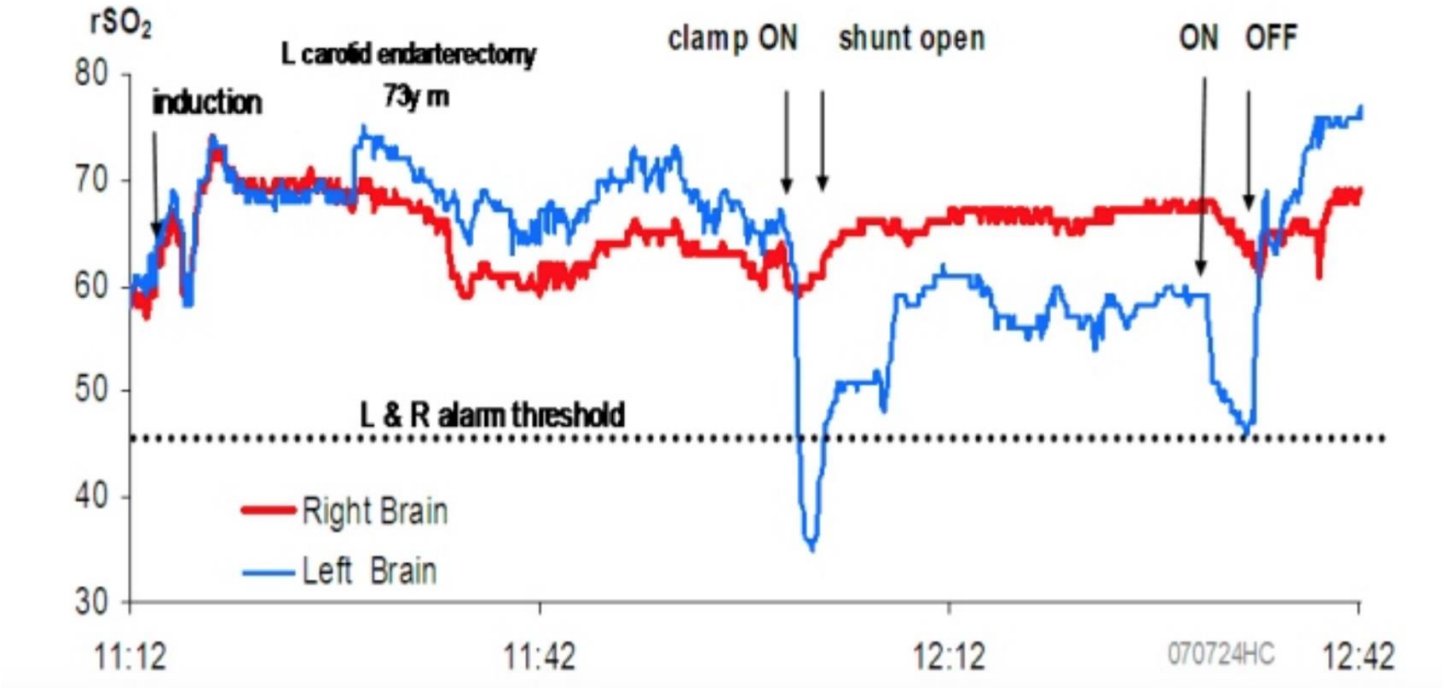


Use of NIRS

- Extensive use in CEA
- Extensive use in cardiac bypass surgery
- Limited use in Cardiac Arrest
- Limited use in adult TBI
- Extensive use in neonatal brain injury

NIRS in CEA

Figure 14: Cerebral Hyperperfusion

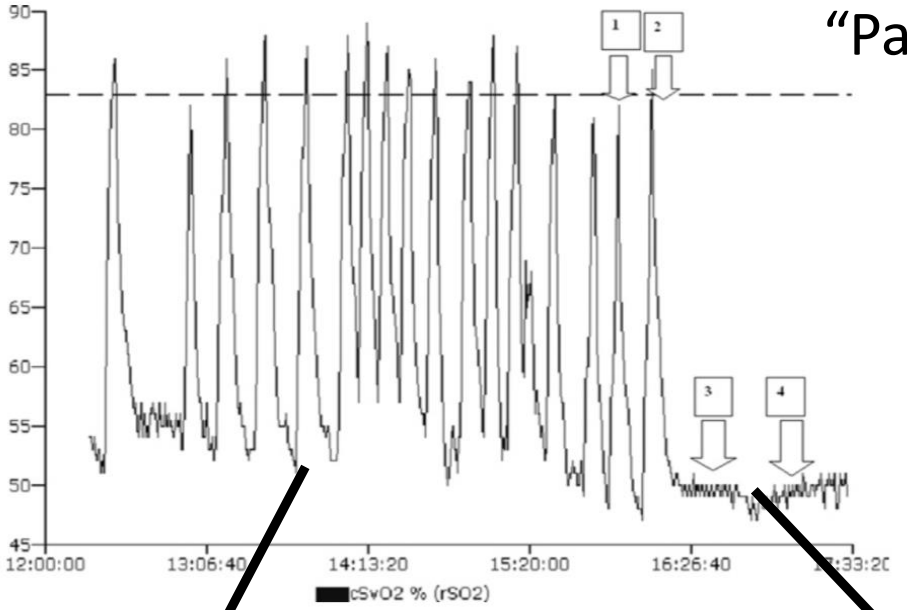


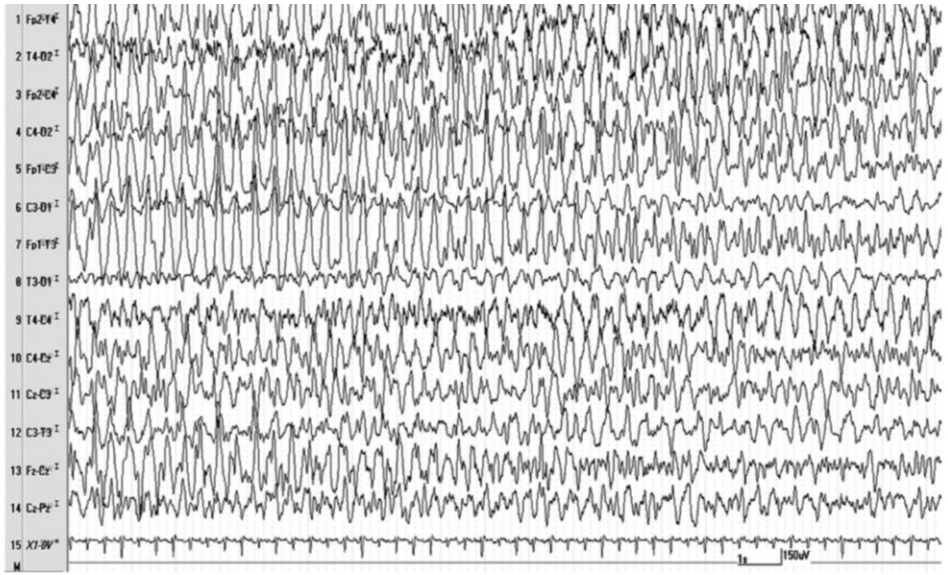
- In CEA, rSO2 desat > 12% / <45% is correlated highest risk of stroke with carotid clamping
- Useful post CEA, 10% increase in cerebral oximetry reading post CEA = 10 fold increase in risk of hyperperfusion syndrome.

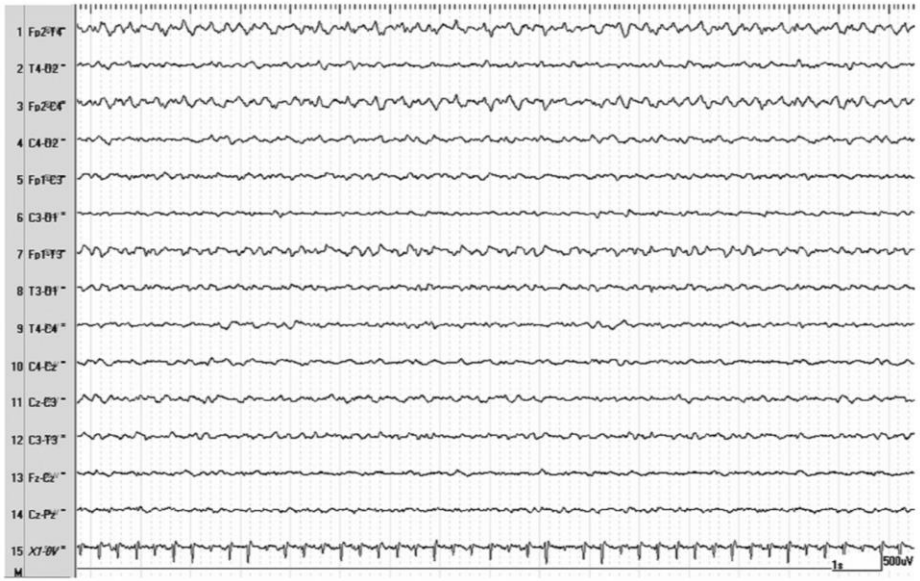
1. Murkin JM et al 2007

NIRS in Status Epilepticus

"Pathologic Peaks"



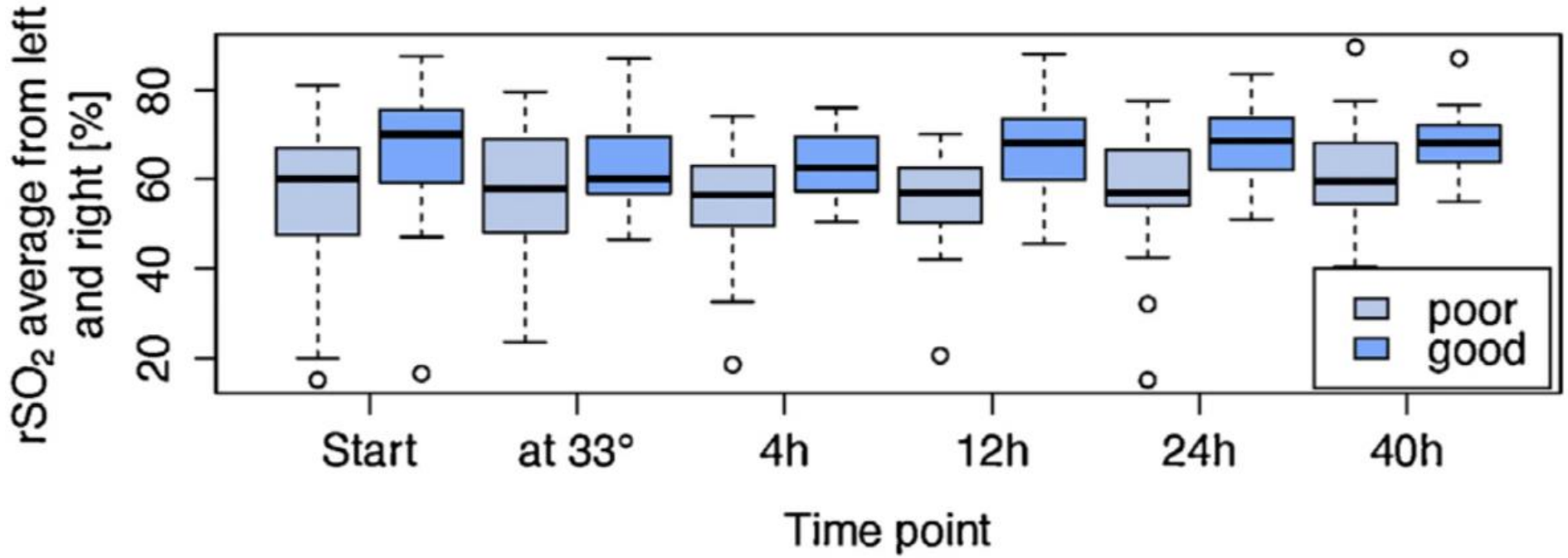




Giorni 668-671 et al 2009

Regional cerebral oxygen saturation after cardiac arrest in 60 patients—A prospective outcome study

C. Storm [a,*], C. Leithner [b], A. Krannich [c], A. Wutzler [d], C.J. Ploner [b], L. Trenkmann [a], S. von Rheinbarben [a], T. Schroeder [a], F. Luckenbach [a], J. Nee [a]



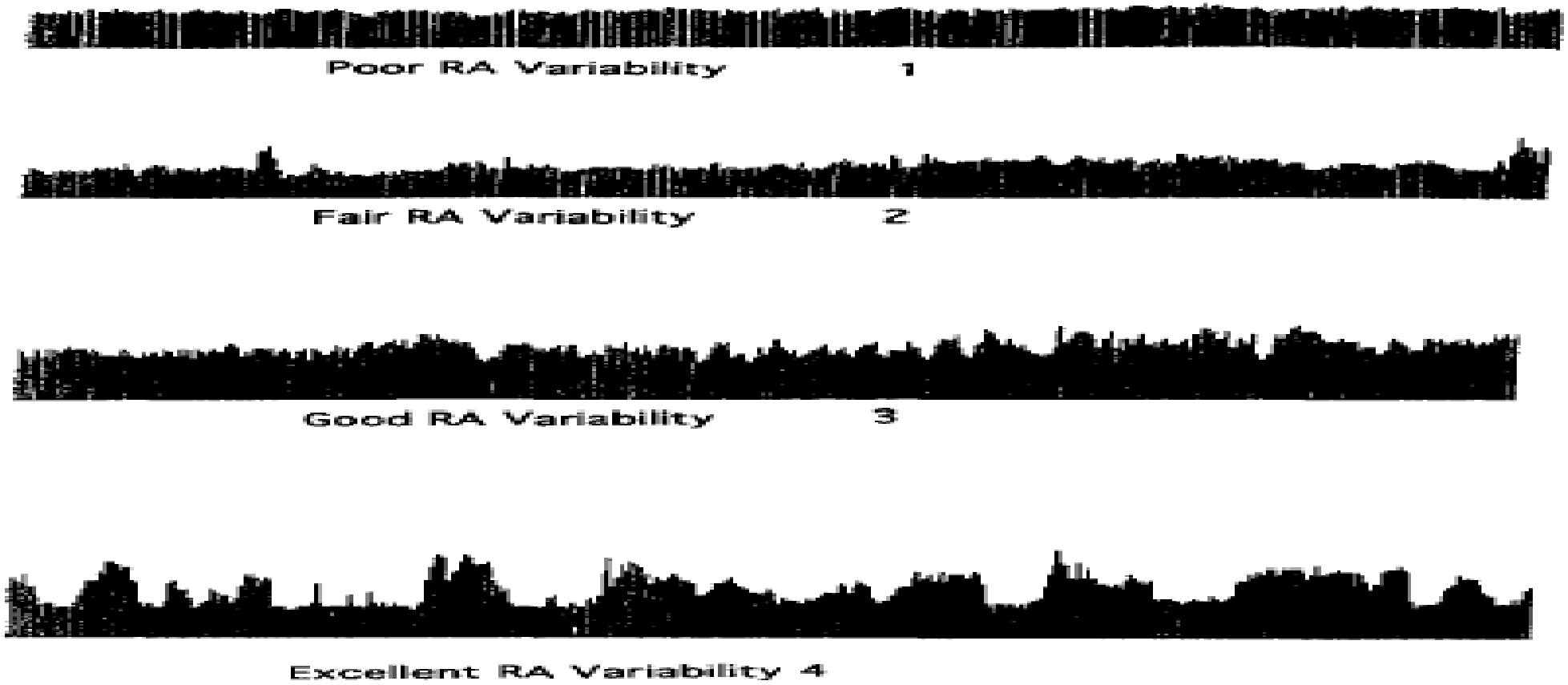
Continuous- Spectral EEG

- 94 comatose patients with severe TBI and cEEG monitoring: 22% had seizures (52% non-convulsive): *Vespa et al 2010*
- 21% incidence of seizures in patients with deep ICH; 28% lobar, 26% overall (*Vespa et al, 2006)*
- (50/402)12 % of SAH patients had seizures. 100 % were nonconvulsive seizures with a mean duration of 6 hours. (De Marchis et al, 2016)
- ***For each hour that a SAH patient spend in nonconvulsive status, there is a deterimental gain equivalent to 2 years for both cognitive and functional outcomes.***
- It no longer acceptable to make the ICU team aware of electrographic seizures many hours after the occurrence.

Quantitative EEG detects ischemia by trending changes in fast frequencies

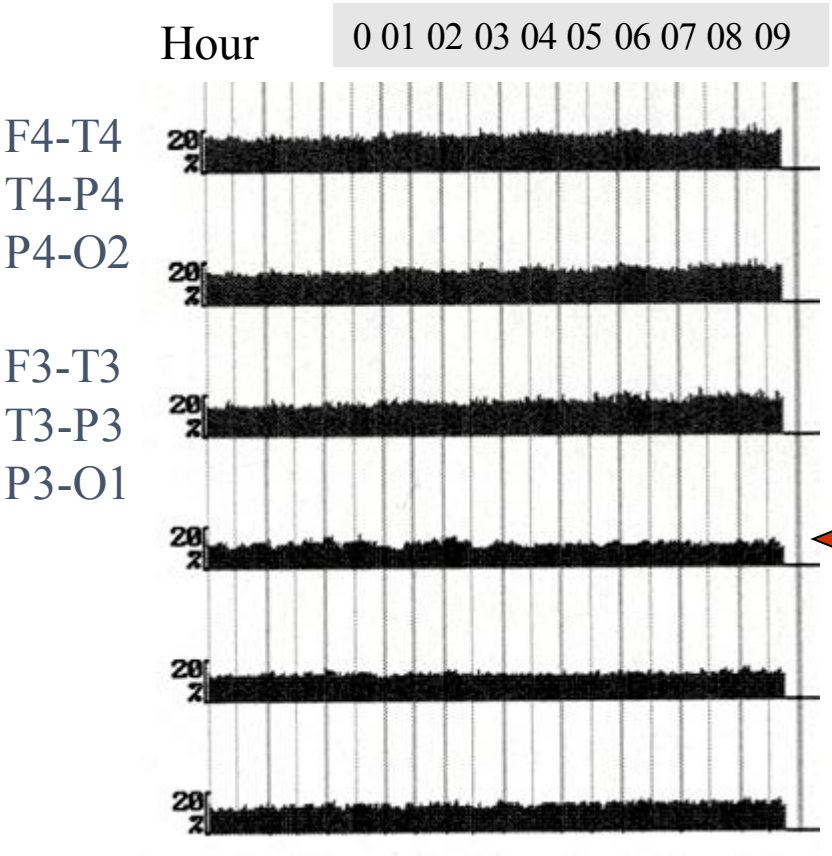
Strong Correlation between percent alpha variability and regional CBF in the acute and chronic strokes (Ingvar et al. 1976, Nuwer 1987 et al)

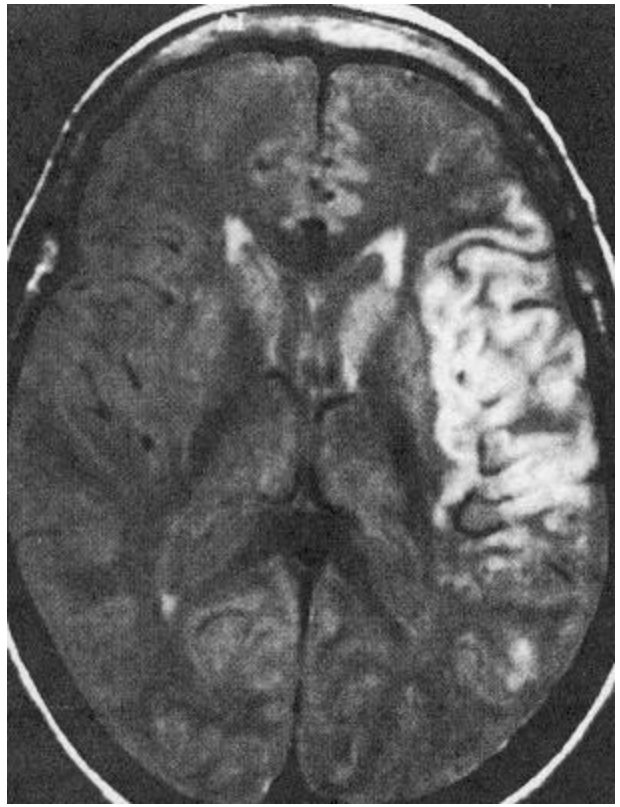
- Percent alpha trend (8-13 Hz)
- Variability of 8 hour trend (PAV)



Vespa et al 1997

Left Percent Alpha power is less, and PAV is worse. Left MCA Stroke





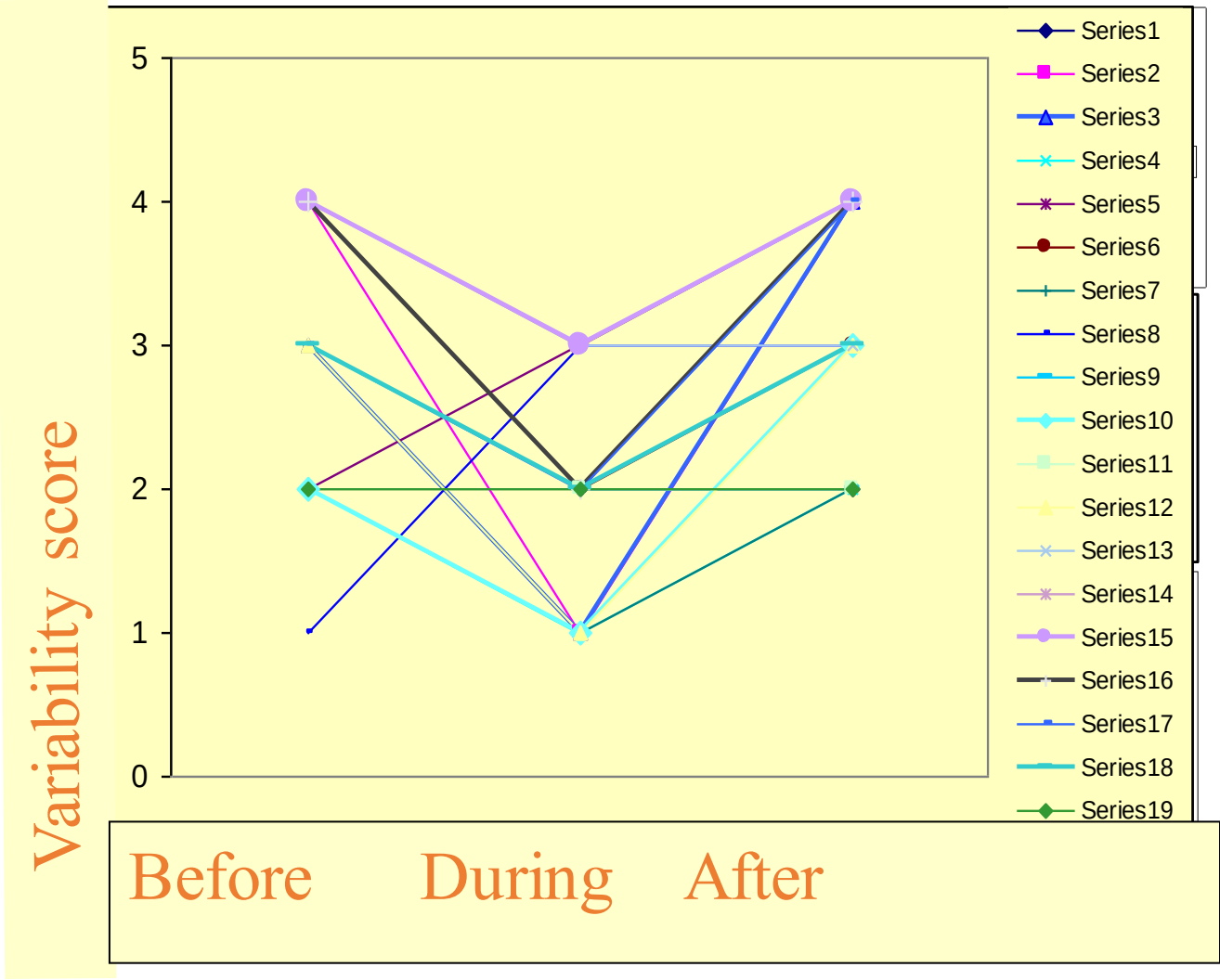
Early Detection of Vasospasm after SAH

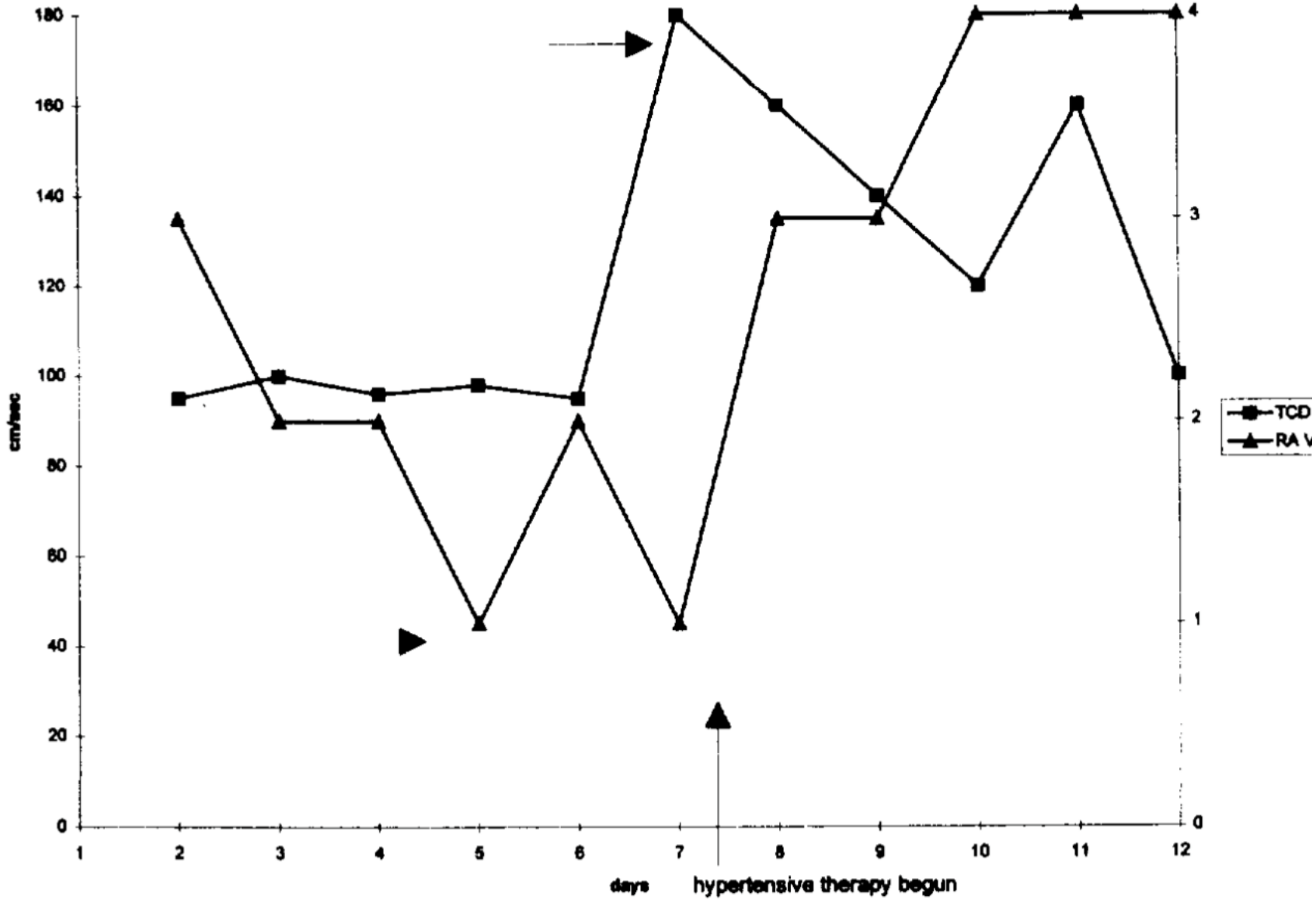
Vespa et. al. 1997 J Clin Neurophys 103:607-615

Prospective study
19 pts with confirmed vasospasm-→ simultaneous decrease in PAV.

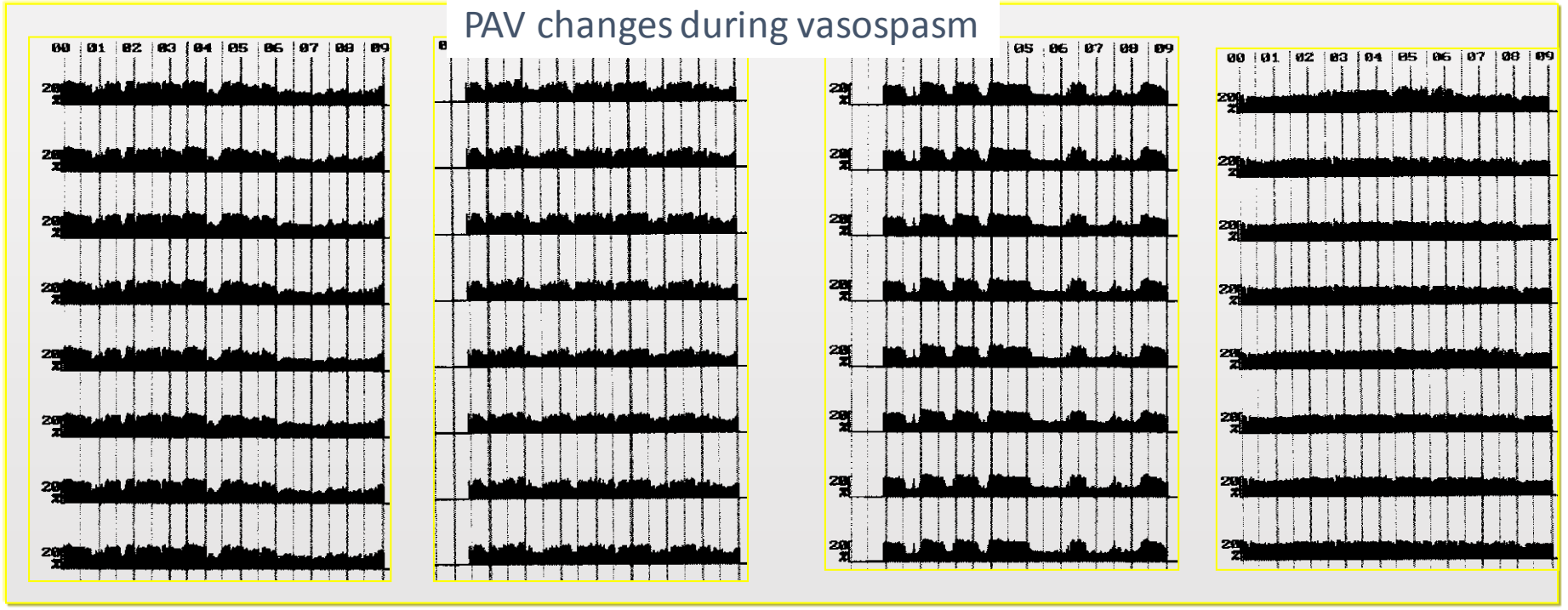
10/14 had decreased RA variability at least 2 days prior to TCD

4/14 had same-day changes of RA variability and TCD.

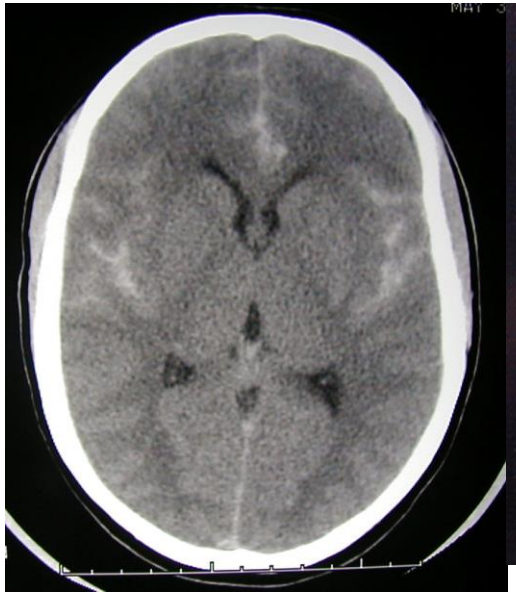


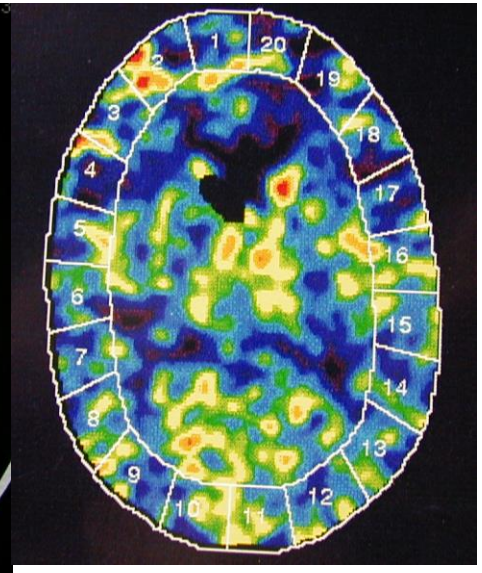

180
160
140
120
100
80
60
40
20
0
cm/sec
4
3
2
1
0
TCD
RA V
1
2
3
4
5
6
7
8
9
10
11
12
days
hypertensive therapy begun

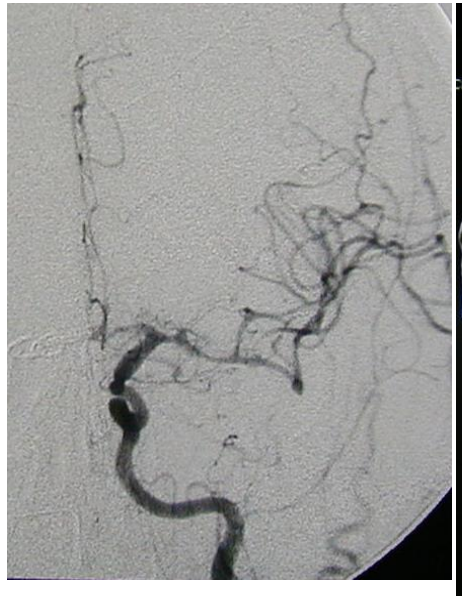
PAV changes during vasospasm

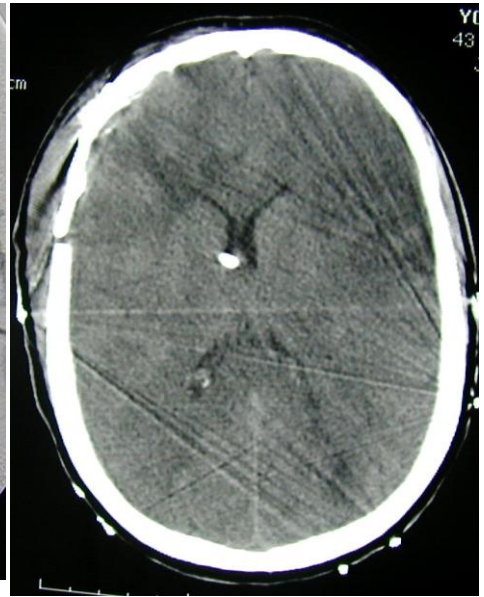


Vasospasm | Hypertensive & Hypervolemic | Papaverine | Infarction

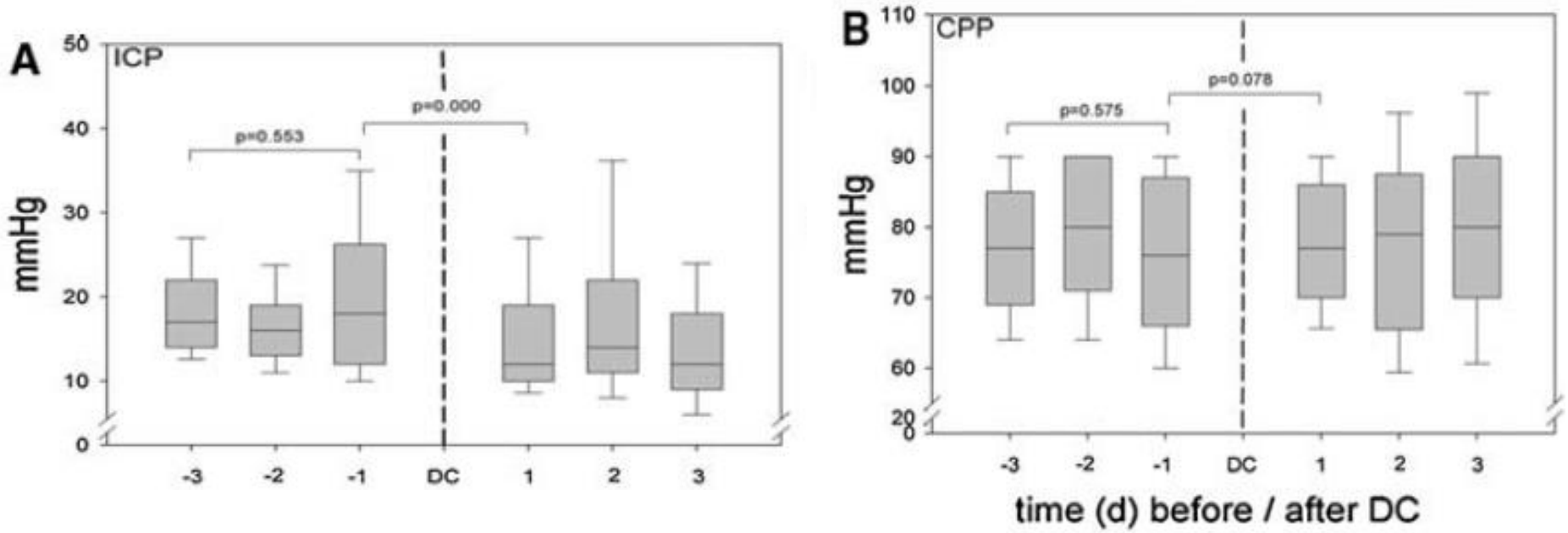








Decompressive Craniectomy in Aneurysmal Subarachnoid Hemorrhage: Relation to Cerebral Perfusion Pressure and Metabolism



- From day 1–3 before DC the L/P ratio increased

L/P ratio surpassed the defined thresholds of cerebral crisis 40 h (25–48) before onset of refractory intracranial hypertension, which occurred 4.2 h (1–10) before surgery.

Nagel, Neurocrit Care 2012