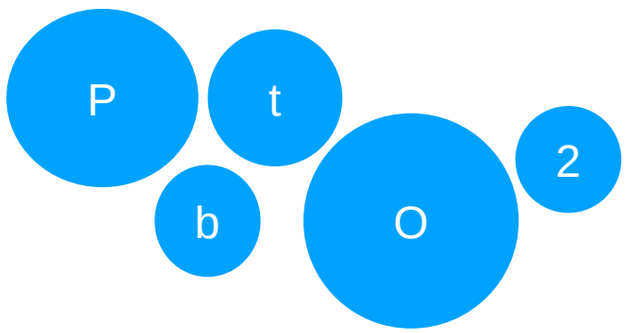
Brain Oxygenation Monitoring
…..what can we learn?

13th October 2018
ANZICS /ACCCN Intensive Care ASM
Adelaide

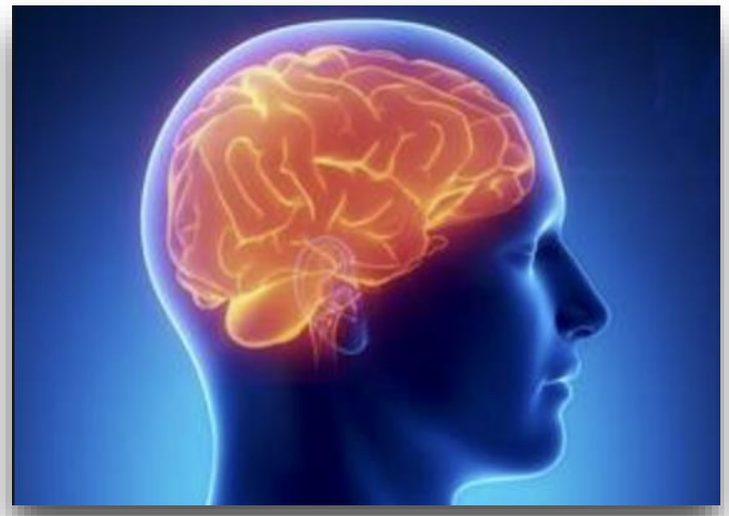


Dr Anusha Ganeshalingham
Paediatric Intensivist
Starship Children's Hospital
New Zealand

Traumatic Brain Injury

- Leading cause of death & disability
  - Primary injury occurs at impact
  - Acute management of severe TBI (GCS ≤ 8)
    - ‘Neurocritical Care’
      - Address intracranial mass lesions
      - Minimising secondary brain injury

Secondary Brain Injury



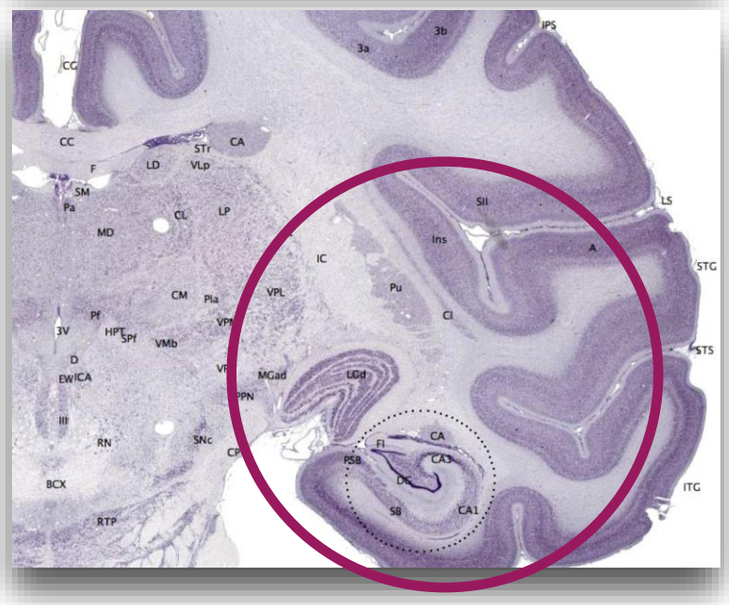


Table 2
TCDB data: Outcome by secondary insult at time of arrival at TCDB hospital ER for non-mutually exclusive insults

Secondary Insults	Number of Patients	Percentage of Total Patients	Outcome Percentage		
			Good or Moderate	Severe or Vegetative	Dead
Total cases	699*	100.0	42.9	20.5	36.6
Neither	456	65.2	51.1	21.9	27.0
Hypoxia	130	18.6	29.2	20.8	50.0
Hypotension	165	23.6	19.4	15.8	64.8
Both	52	7.4	5.8	19.2	75.0

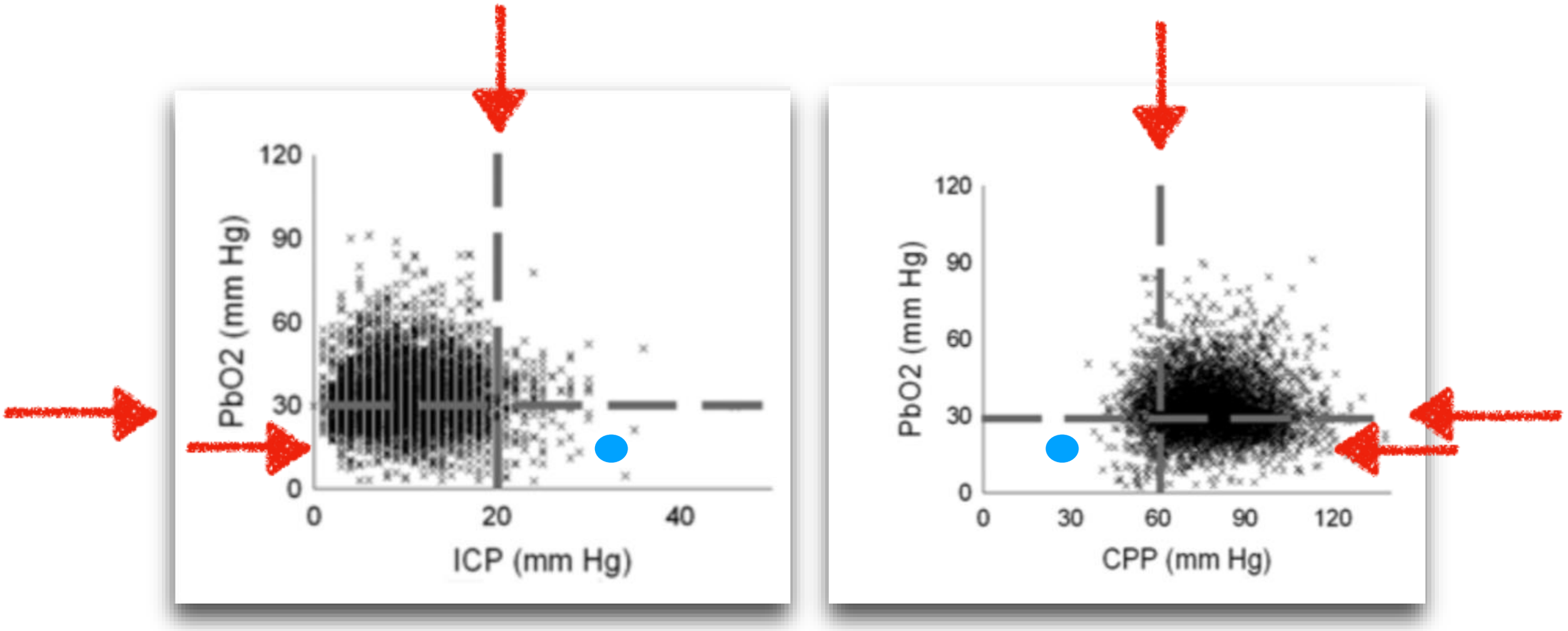
Hypoxia = $Pao_2 < 60$ mm Hg; hypotension = SBP < 90 mm Hg.
* The total number of patients is 699 instead of 717 because of missing admission data on blood pressure or arterial blood gas values in 18 patients.

CPP = MAP - ICP

[1]Chestnut R et al. The role of secondary brain injury in determining outcome from severe head injury. J of Trauma 1993; 34(2):216-222

Current Monitoring

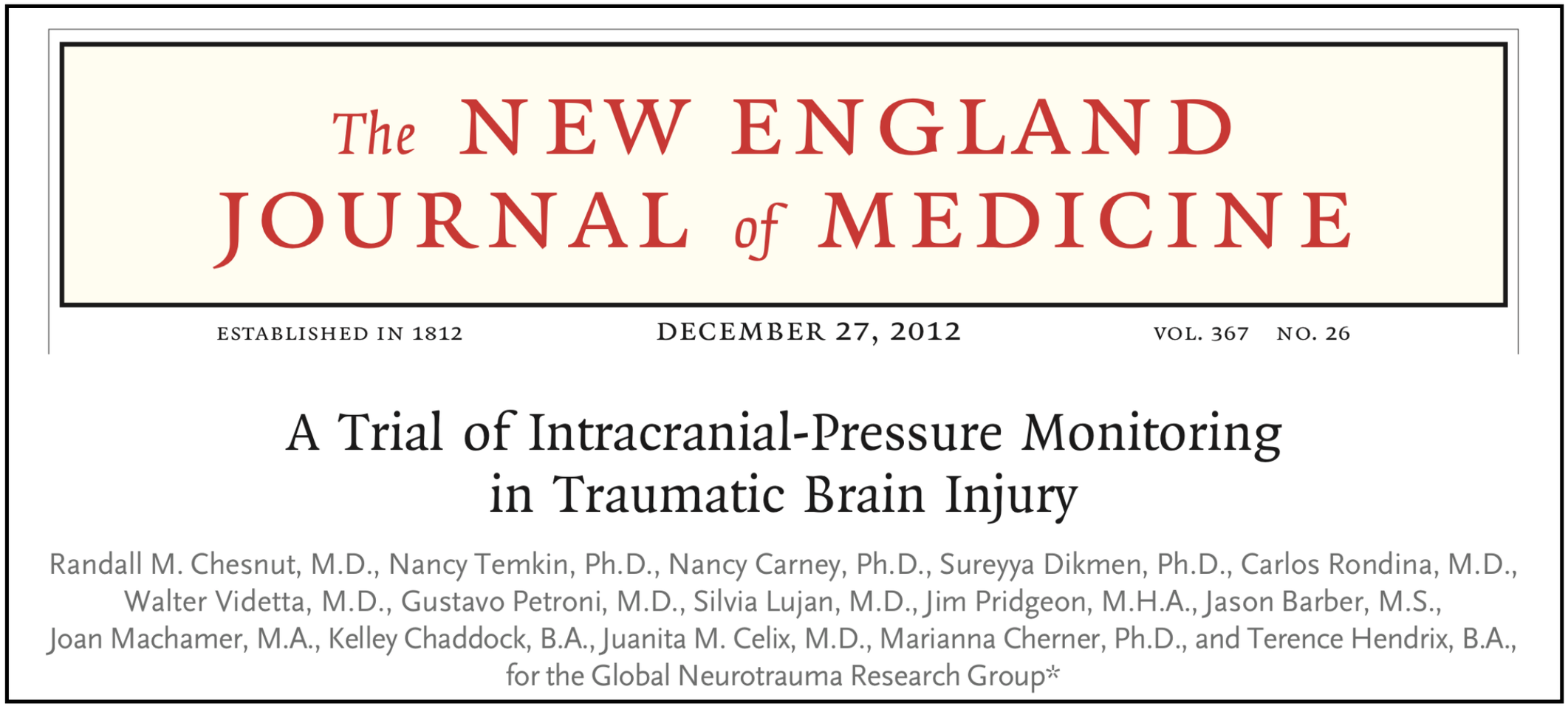
Brain tissue hypoxia can occur in the setting of a normal ICP (< 20 mmHg) and adequate CPP (> 60 mmHg)



Stippler et al. Brain tissue oxygen monitoring after severe traumatic brain injury in children: relationship to outcome and association with other clinical parameters. J Neurosurg Pediatrics 2012; 10:383-391.

Current Monitoring

There is insufficient evidence that ICP-guided management protocols improve outcomes



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 27, 2012 VOL. 367 NO. 26

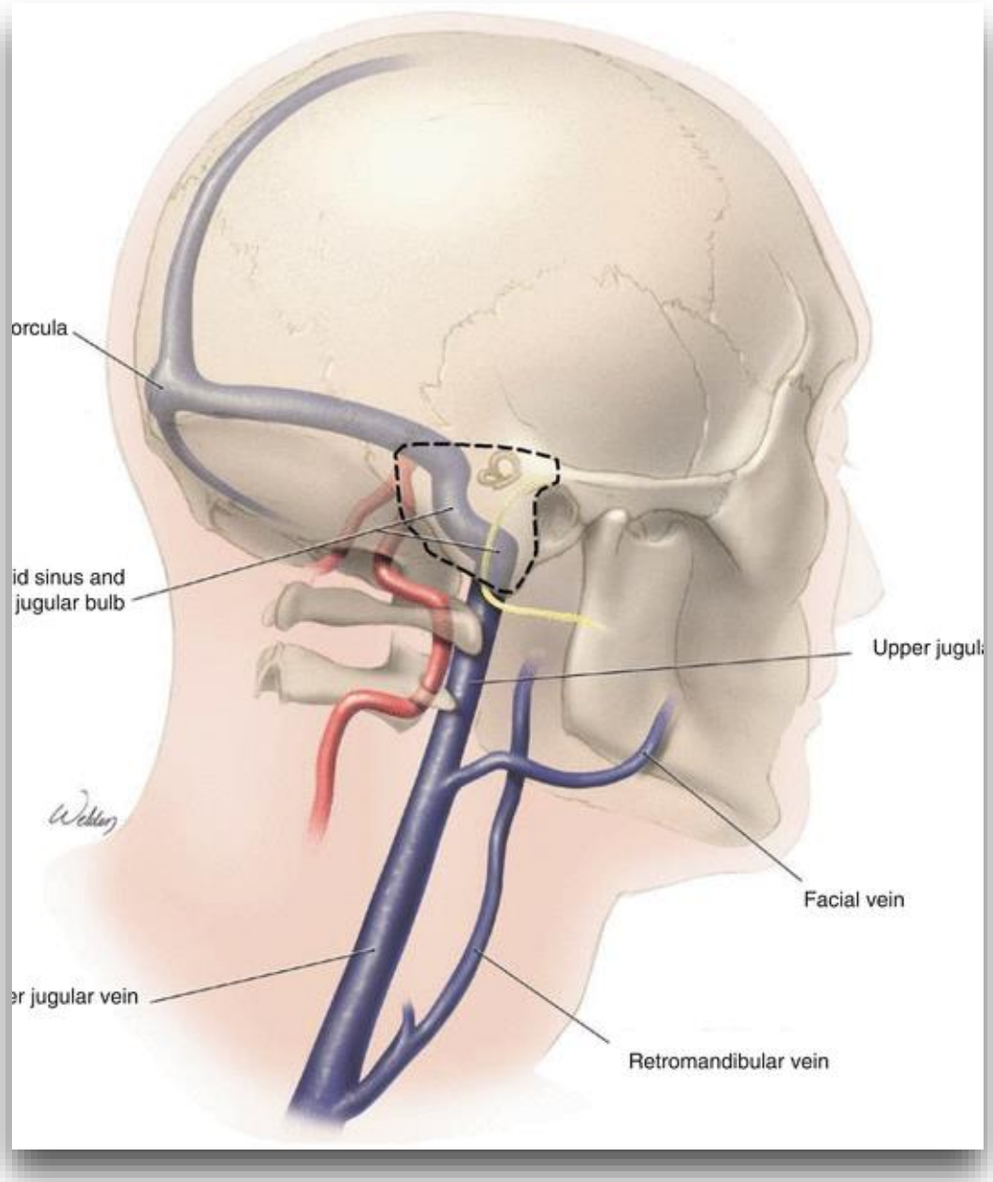
A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury

Randall M. Chesnut, M.D., Nancy Temkin, Ph.D., Nancy Carney, Ph.D., Sureyya Dikmen, Ph.D., Carlos Rondina, M.D., Walter Videtta, M.D., Gustavo Petroni, M.D., Silvia Lujan, M.D., Jim Pridgeon, M.H.A., Jason Barber, M.S., Joan Machamer, M.A., Kelley Chaddock, B.A., Juanita M. Celix, M.D., Marianna Cherner, Ph.D., and Terence Hendrix, B.A., for the Global Neurotrauma Research Group*

NEJM 2012; 367(26)

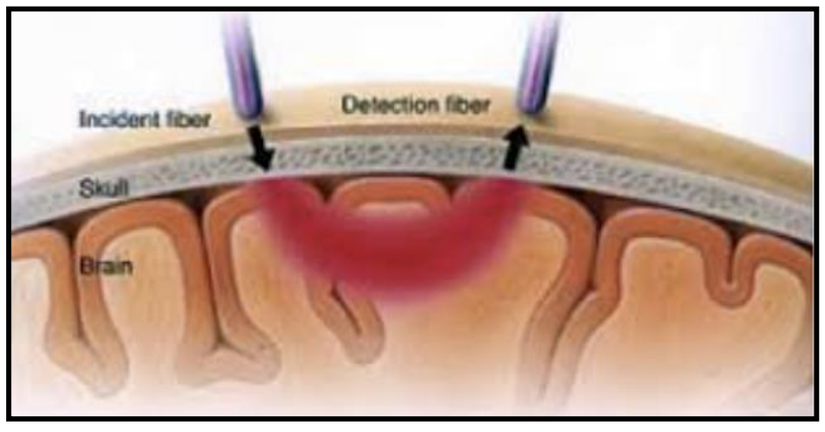
Cerebral Hypoxia

Jugular Venous Oxygen Saturations



- Global measure
- Continuous bedside tool
- Invasive
- Complications
    1. Line thrombosis
    2. Carotid artery puncture
    3. Pneumothorax
    4. Nerve injury

Near Infrared Spectroscopy



- Regional measure
- Non-invasive, continuous, bedside
- Threshold <45% for 3 hours
- Cardiac surgery
- You don’t need a pulse….

ORIGINAL ARTICLE

Near-infrared spectroscopy in vegetables and humans

An observational study

Ronald A. Kahn and Anelechi Anyanwu

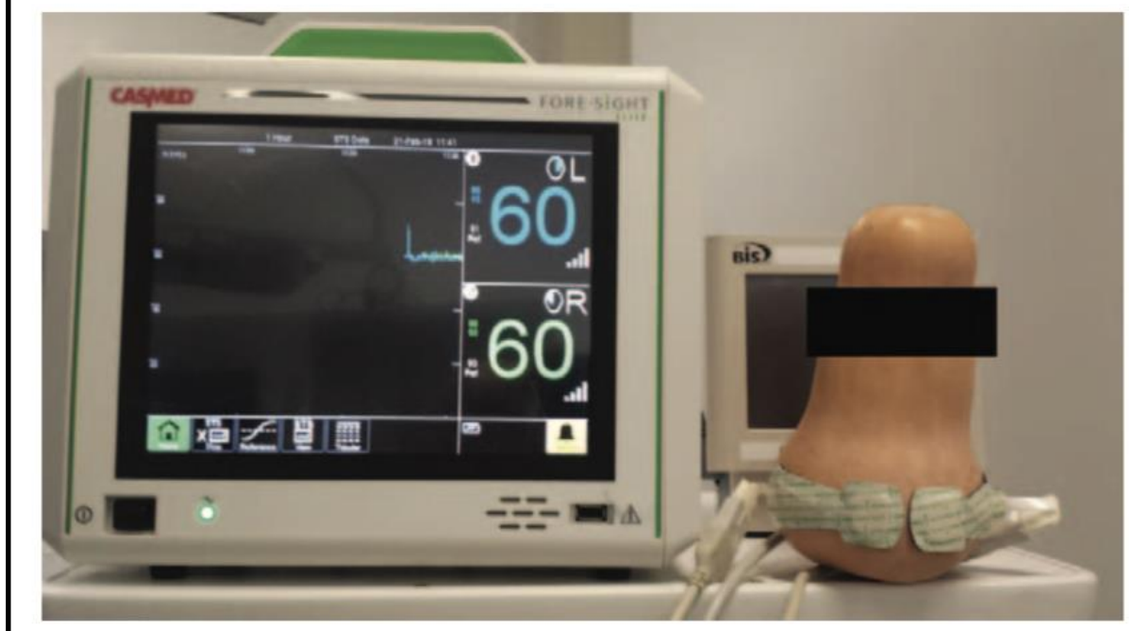


Table 2 Near-infrared-spectroscopy-derived oximetric values

	Oximetry (%)
Control	71 (68 to 74)[a]
Butternut squash	63 (62 to 64)
Yam	64 (63 to 65)
Yellow zucchini	75 (74 to 76)[a]

No evidence that intervening on NIRS findings improves outcomes

Brain Tissue Oxygen Tension

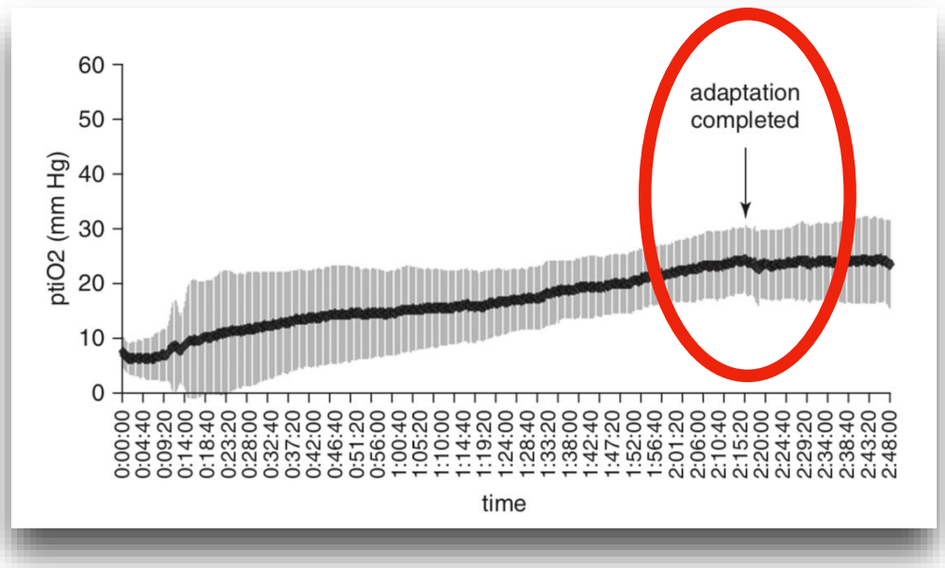
What are the components?

- Double-lumen catheter (one burr hole)
  - 1st: Temperature & parenchymal ICP
  - 2nd: Brain tissue oxygen tension
  - Separate catheter for EVD

- O_2 challenge to check probe function
  - Increase FiO_2 to 1.0

What are the limitations?

- Limitations
  - Focal measure (7-15 mm^2)
  - Adaptation time (average 2 hours[2])
  - Slight drift towards lower $PbtO_2$ with time
- Complications are rarely reported



2

[1]Okonkwo et al. Brain Oxygen Optimization in Severe Traumatic Brain Injury Phase-II. CCM 201745:1907-1914

[2]Pennings et al. PbtO2 in Awake Patients during Functional Neurosurgery: Assessment of Normal Values 2008. J of Neurotrauma 25: 1173-1177

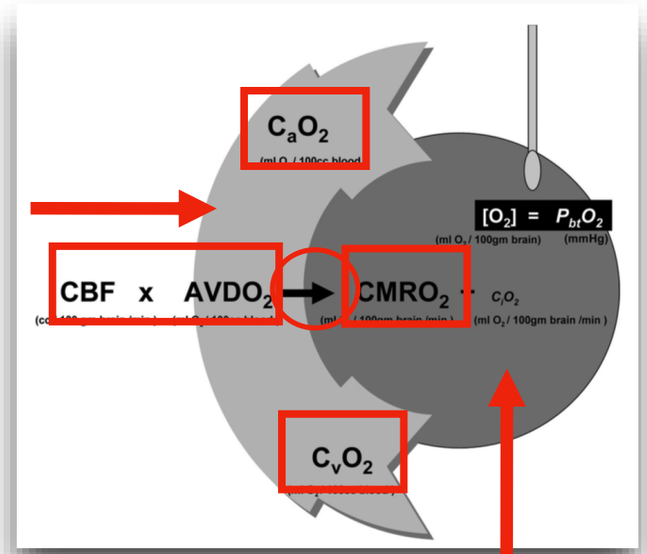
[3]Adamides et al. Focal cerebral oxygenation and neurological outcome with or without brain tissue oxygen guided therapy. 2009 Act Neurochir 151: 1399-1409

What does the number represent?

- Is it:-
  1. Total oxygen delivery?
  2. Local cerebral blood flow?
  3. Cerebral oxygen metabolism?
  4. CaO_2 or CvO_2 or $AVDO_2$?
  5. Balance between O_2 delivery & O_2 metabolism?
  6. Diffusion of dissolved plasma oxygen?

What does the number represent?

- Fick Principal - Kety and Schmidt
  - CBF x $AVDO_2$
  - i.e. CBF x (CaO_2 - CvO_2)

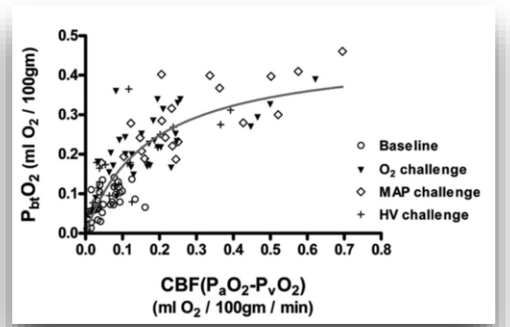


[1]

- CBF x
  - CaO_2 = (SaO_2 x 1.34 x Hb) - (PaO_2 x 0.003)
  - CvO_2 = (SaO_2 x 1.34 x Hb) - (PvO_2 x 0.003)

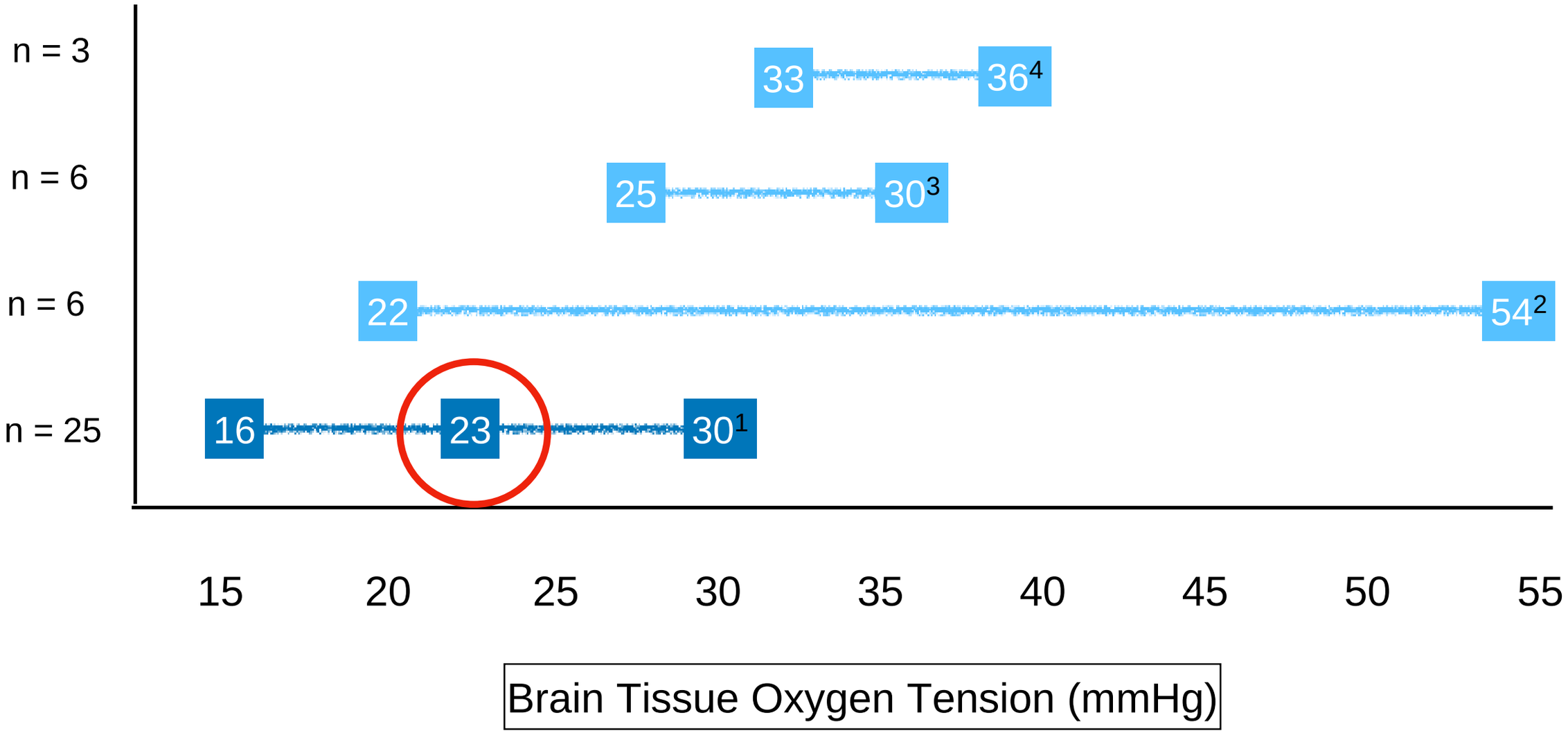
- CBF x dissolved plasma oxygen

r^2= 0.86



[1]Rosenthal et al. PbtO2 is more indicative of O2 diffusion than O2 delivery, CCM 2008; 36(6): 1917-1923

What is normal brain PbtO2?



[1]Pennings et al. PbtO2 in awake patients during functional neurosurgery: The assessment of normal values. J Neurotrauma 2008; 25: 1173-1177.
[2]Hoffman et al.Brain Tissue Oxygen, CO2 and pH in Neurosurgical Patients at risk. Anesth Analg 1996;82:582-6.
[3]Maas et al, Monitoring cerebral oxygenation. Acta Neurochir Suppl (Wien) 1993; 59:50-57.
[4]Assad et al. Measurement of local PO2 of the brain cortex non cases of tumours. Adv Neurosurg 1984;12:263-6.

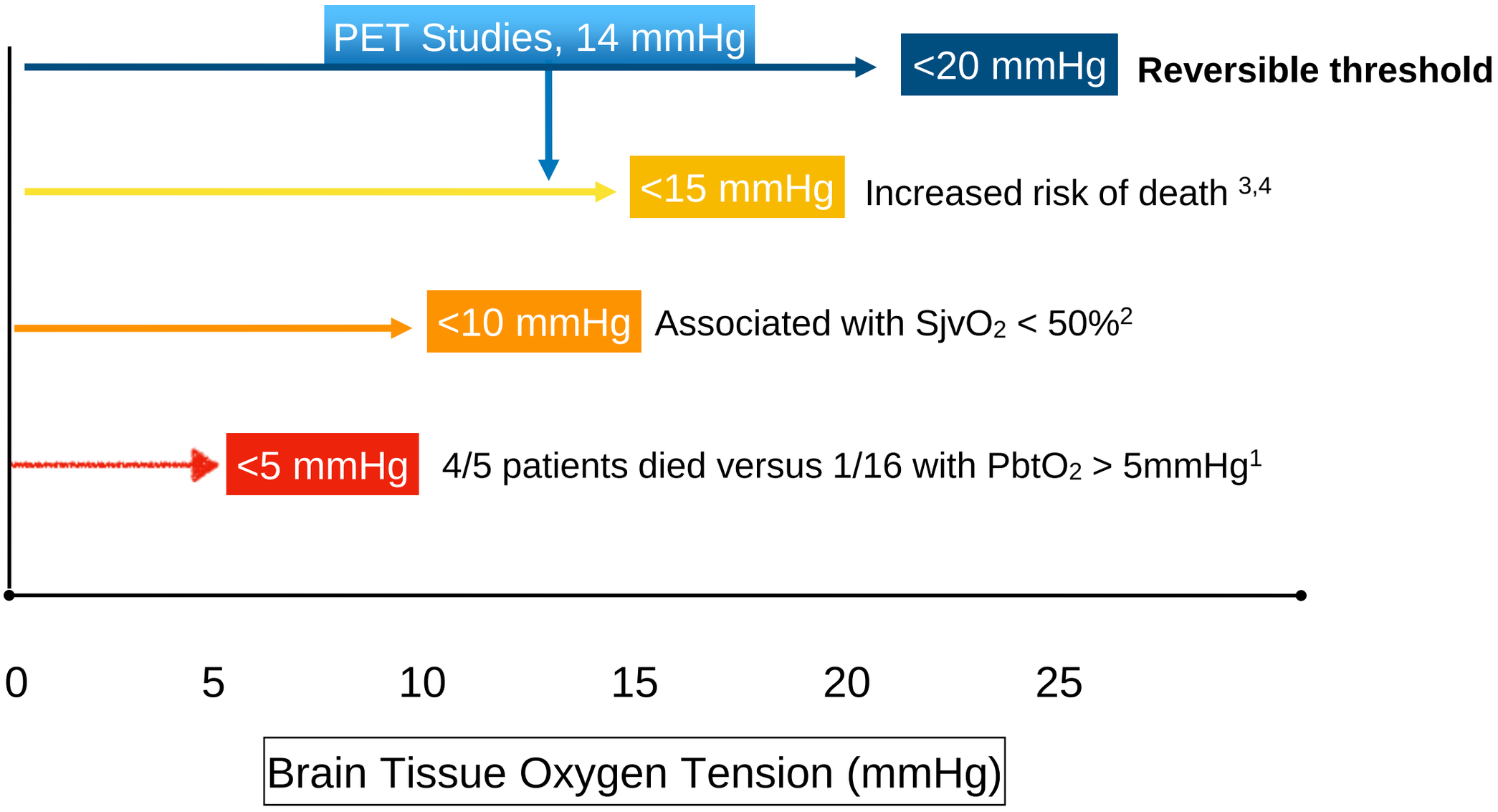
What is the ischaemic threshold?

There is *insufficient* evidence to support a Level I or Level II recommendation for Advanced Cerebral Monitoring **thresholds**

Brain Trauma Foundation, 2016

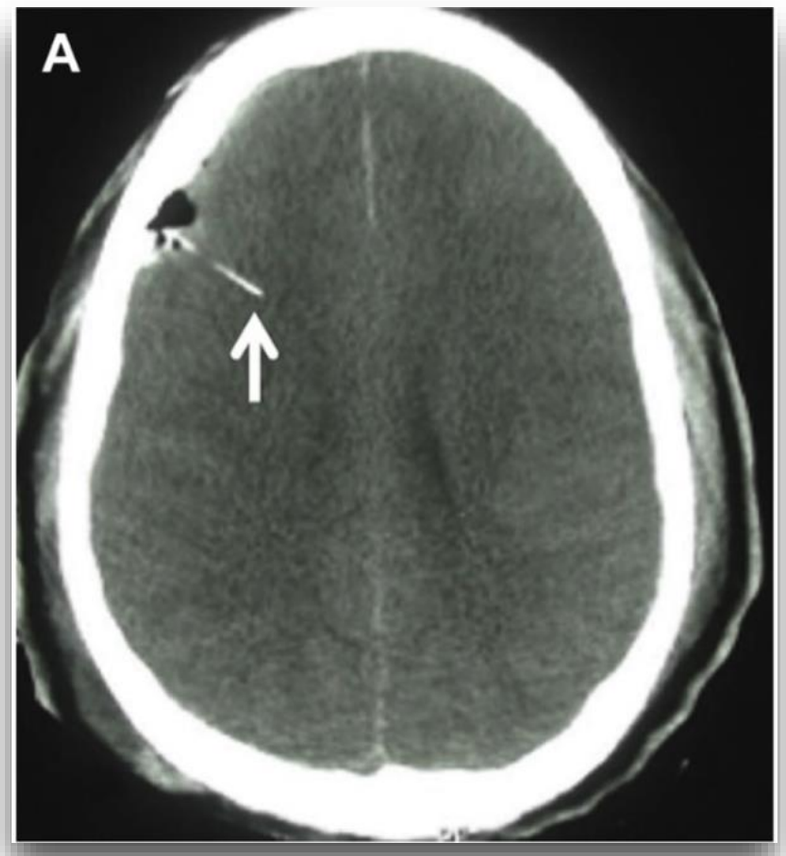
Brain Trauma FOUNDATION

What is the ischaemic threshold?



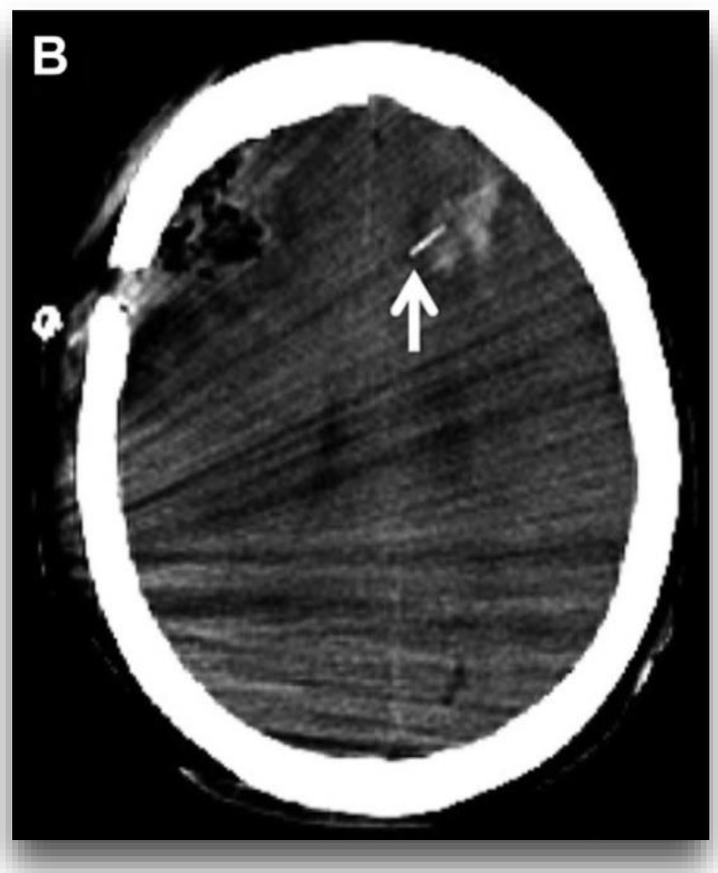
[1]Van Santbrink et al. Continuous monitoring of partial pressure of brain tissue oxygen in patients with severe head injury. Neurosurgery 1996; 38: 21-31
[2]Kiening et al. Monitoring of cerebral oxygenation in patients with severe head injuries: PbtO2 versus SvO2. J Neurosurg 1996; 8:751-757
[3]Van den Brink et al. Brain Oxygen Tension in Severe Head Injury. Neurosurgery 2000 46(4):868-878
[4]Valadka et al. Relationship of brain tissue PO2 to outcome after severe head injury. CCM 1998; 26(9): 1576-1581

Where should the probe be placed?



Normal appearing white matter

Adjacent to penumbral area



Within a contusion

*CT scan confirmation of probe position essential for interpretation of results

Who should insert the probe?

Neurosurgeon

Intensivist

How should the number be used?

- Static Index
  - Baseline $PbtO_2$
- Dynamic Index
  - $PbtO_2$ Reactivity
  - $PbtO_2$ Autoregulation

Current Situation

There is *<u>insufficient</u>* evidence to support a Level I or Level II or Level III recommendation for **Advanced Cerebral Monitoring**

Brain Trauma Foundation, 2016

Brain Trauma FOUNDATION

Brain Trauma Foundation

Reference	Study Design	PbtO2 Threshold	Outcome
Martini 2009	Retrospective cohort n=629	20 mmHg	Increased mortality & worse outcomes
Green 2013	Retrospective cohort n=74	20 mmHg	No difference in mortality or outcome
Lee 2010	Randomised trial n=45	20 mmHg	No difference in mortality Favourable neurology
McCarthy 2009	Prospective cohort n=145	20 mmHg	No difference in mortality or outcome
Meixensberger 2003	Prospective cohort n=93	10 mmHg	Non significant trend to improved outcomes
Narotam 2009	Prospective cohort n=139	20 mmHg	Improved outcomes & mortality
Spiotta 2010	Prospective cohort n=123	20 mmHg	Improved outcomes & mortality

Brain Trauma Foundation

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How should the number be used?

BOOST-II

Brain Oxygen Optimization in Severe Traumatic Brain Injury Phase-II: A Phase II Randomized Trial*

David O. Okonkwo, MD, PhD[1]; Lori A. Shutter, MD[1]; Carol Moore, MA[2]; Nancy R. Temkin, PhD[3]; Ava M. Puccio, RN, PhD[1]; Christopher J. Madden, MD[4]; Norberto Andaluz, MD[5]; Randall M. Chesnut, MD[3]; M. Ross Bullock, MD, PhD[6]; Gerald A. Grant, MD, FACS[7]; John McGregor, MD[8]; Michael Weaver, PhD[9]; Jack Jallo, MD, PhD[10]; Peter D. LeRoux, MD, FACS[11]; Dick Moberg, MSE[12]; Jason Barber, MS[3]; Christos Lazaridis, MD[13]; Ramon R. Diaz-Arrastia, MD, PhD[14]

Critical Care Medicine
2017 45(11):1907-1914

How should the number be used?

- Two-arm, single-blind, prospective, multicentre RCT
  - Phase II trial
  - Ten ICU's in USA
  - 119 adults with severe TBI

- *Hypothesis*: A management protocol informed by $PbtO_2$ & ICP values would reduce the total burden of brain hypoxia

- Randomised to ICP alone or ICP + $PbtO_2$ (> 20 mmHg)
  - Least trauma affected frontal lobe
  - Control group also had $PbtO_2$ probes

BOOST-II

How should the number be used?

The $PbtO_2$ Treatment Protocol

	ICP < 20	ICP ≥ 20
$pBtO_2 \geq 20$	**Type A** No interventions directed at $pBtO_2$ or ICP needed	**Type B** Interventions directed at lowering ICP
$pBtO_2 < 20$	**Type C** Interventions directed at increasing $pBtO_2$	**Type D** Interventions directed at lowering ICP and increasing $pBtO_2$

Tiered Physiological Interventions

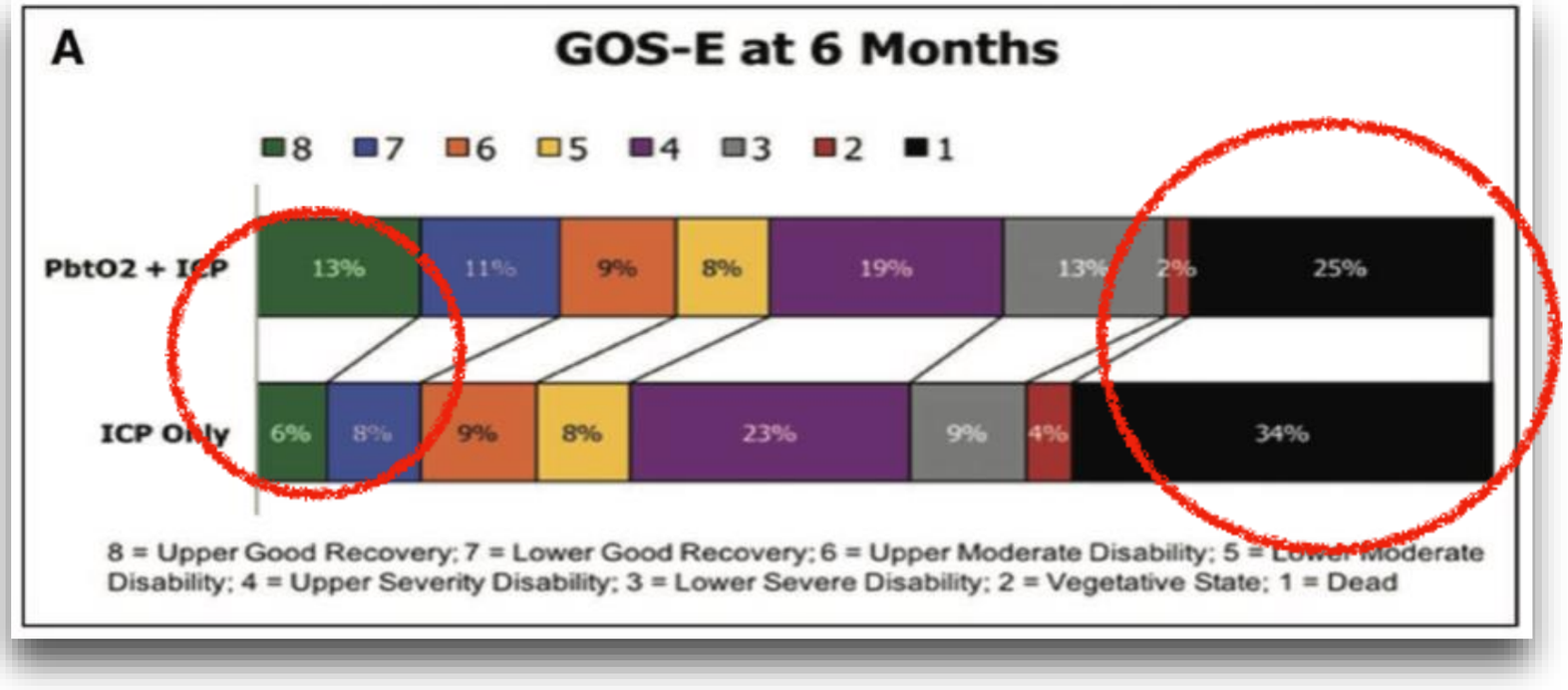
- Isolated ICH (B)
- Isolated brain hypoxia (C)
- Both ICH and brain hypoxia (D)

Type C (ICP <20mmHg and $Pbt0_2$ <20mmHg)
TIER 1 (1). Adjust head of bed to improve brain oxygen level. (2). Ensure Temperature < 38°C. (3). Increase CPP to 70 mm Hg with fluid bolus. (4). Optimize hemodynamics. (5). Increase PaO_2 by increasing FiO2 to 60%. (6) Increase PaO_2 by adjusting PEEP. (7) Add EEG monitoring . (8) Consider adding AED's, either Dilantin or Keppra, for 1 week only.
TIER 2 (1). Adjust ventilator parameters to increase PaO_2 by increasing FiO_2 to 100%. (2). Increase PaO_2 by adjusting PEEP. (3). Increase CPP up to a maximum of 70 mmHg with vasopressors. (4). Adjust ventilatory rate to increase $PaCO_2$ to 45 – 50 mm Hg. (5). Transfuse PRBCs to goal Hgb >10g/dL. (6). Decrease ICP to <10 mm Hg. 6a. CSF drainage. 6b. Increased sedation.

How should the number be used?

TABLE 2. Brain Tissue Oxygenation and Intracranial Pressure Parameters by Study Group

$PbtO_2$ Metric	ICP Only, ($n = 58$), Mean ± SD; Median	$PbtO_2$ + ICP, ($n = 55$), Mean ± SD; Median	p
Proportion of time below 20 mm Hg	0.44 (0.31); 0.45	0.15 (0.21); 0.07	0.0000147
Average depth (mm Hg)	3.6 (3.9); 2.3	1.0 (2.0); 0.2	0.0000005
Area (over) the curve (mm Hg × hr)[b]	255 (291); 187	58 (97); 14	0.0000002



BOOST-II

How should the number be used?

- Brain Tissue Oxygen Reactivity
  - Prediction tool in first 24 hours after injury

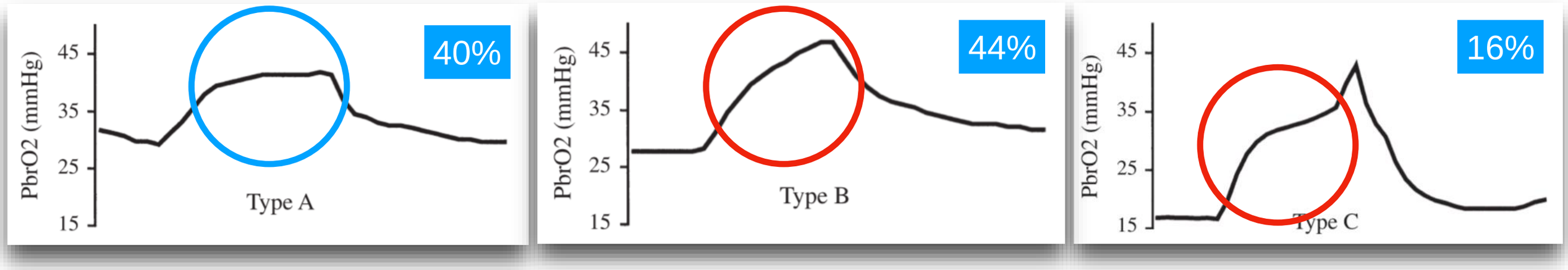
- Oxygen regulatory mechanisms in healthy brains
  - i.e. any rise in PaO_2 results in no change or a minimal rise in $PbtO_2$

- Severe TBI leads to a loss of oxygen regulation
  - Any rise in PaO_2 leads to a rise in $PbtO_2$

van Santbrink et al. Brain tissue oxygen response in severe TBI. Acta Neurochir 2003; 145:429-38.

How should the number be used?

- Increase FiO_2 1.0 for 15 mins daily for 5 days



- Predicts outcomes
  - Curve type A predictive of a favourable outcome (i.e. a less variable response)

van Santbrink et al. Brain tissue oxygen response in severe TBI. Acta Neurochir 2003; 145:429-38
Figaji et al. The effect of increased inspired fraction of oxygen on $PbtO_2$ in children with severe TBI. 2010 Neurocritical Care 12;430-437

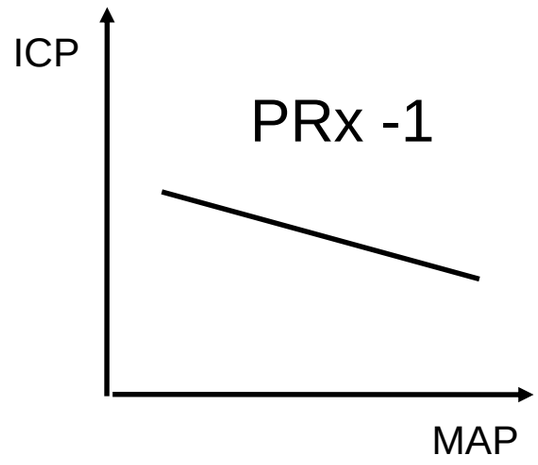
How should the number be used?

- Brain Tissue Autoregulation
  - Oxygen reactivity index (ORx)
  - Ability of brain to maintain $PbtO_2$ despite △CPP
  - Identify individual CPP targets

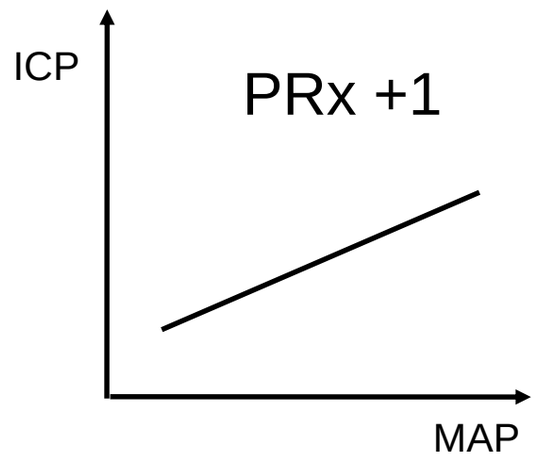
- Pressure reactivity index (PRx)
  - Moving Pearson's correlation coefficient
  - Between MAP & ICP
  - Values -1 to +1

How should the number be used?

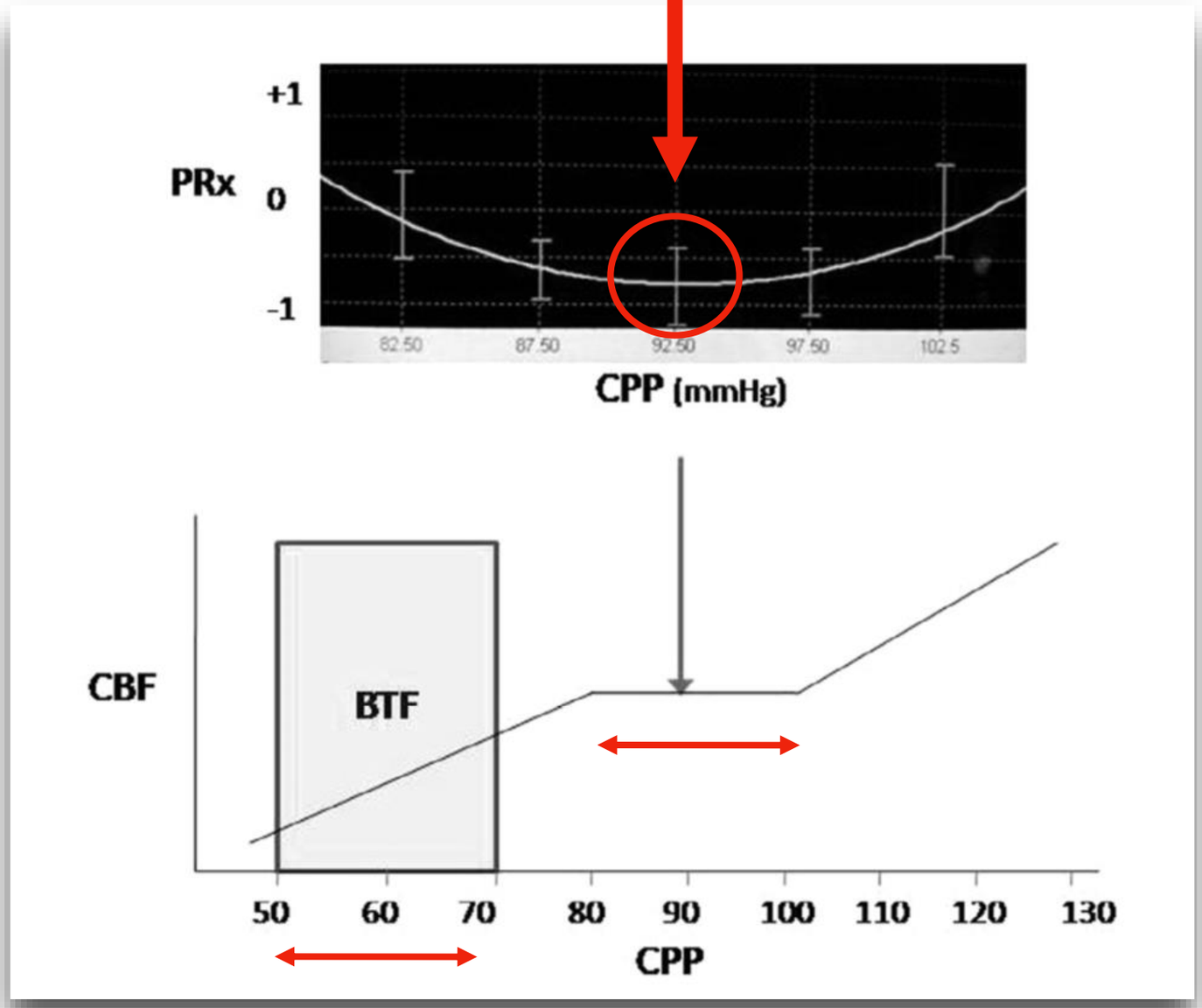
- Intact cerebral autoregulation
  - ↑ in MAP = ↓ in CBF and ↓ ICP
  - Negative correlation: MAP & ICP
  - PRx -1



- Impaired cerebral autoregulation
  - ↑ in MAP = ↑ in CBF and ↑ ICP
  - Positive correlation: MAP & ICP
  - PRx +1

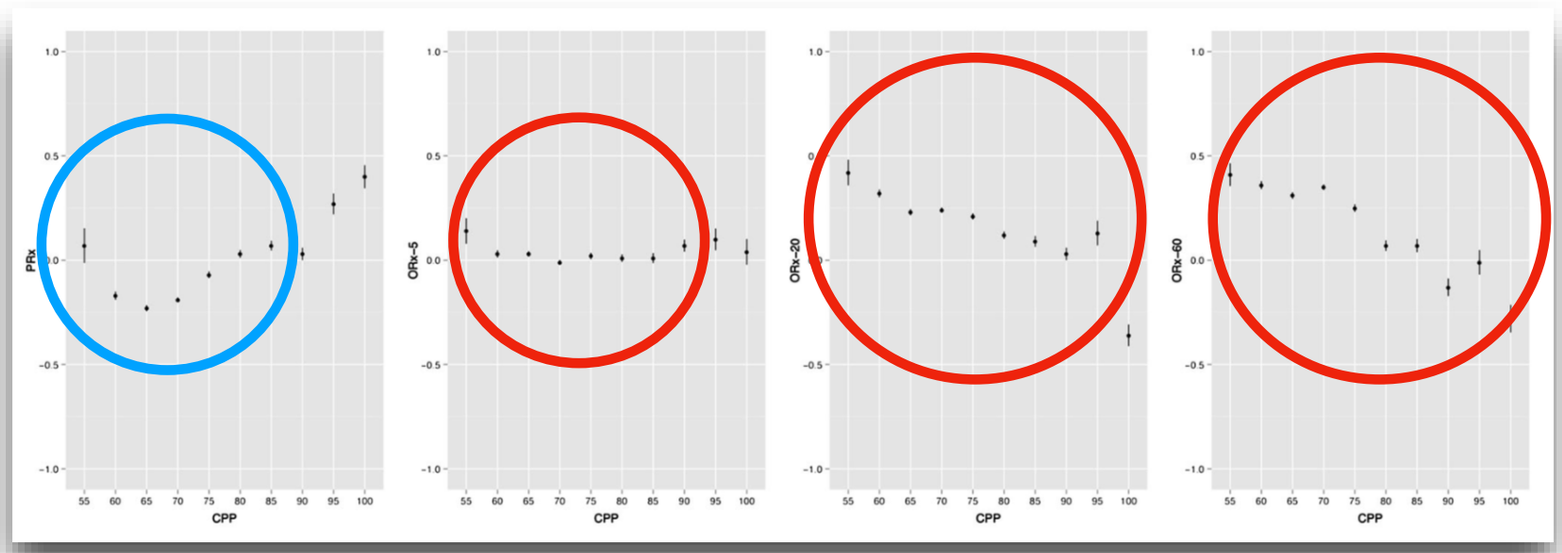


Deriving CPP_{OPT}



How should the number be used?

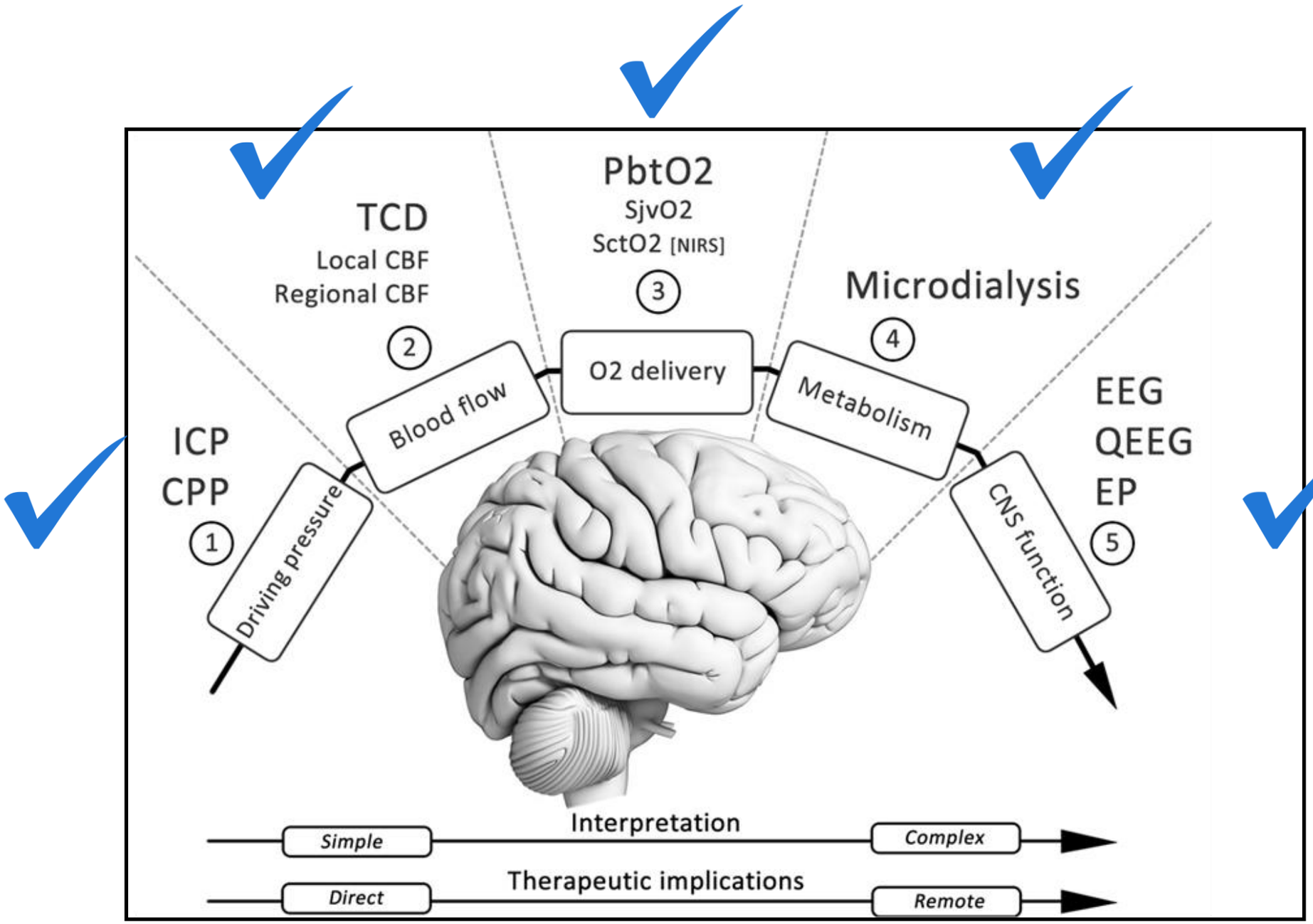
- ORx
  - ORx was not correlated with PRx
  - ORx could not predict patient outcome
  - ORx could not be used to calculate an individual optimised CPP (CPP_{OPT})



Andresen et al. Further Controversies About $PbtO_2$ Pressure-Reactivity After TBI. Neurocrit Care 2017; epub ahead of print

BOOST-III BONANZA

Multimodality Monitoring



Thank you