Multimodal Neuromonitoring of ICP and $p_{bt}O_2$ in Severe Traumatic Brain Injury

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Conflict of Interest statement

Lecture honoraria and equipment from:

- Integra Neuroscience, USA
- Raumedic AG, Germany
- Sophysa, France

Outline

- ICP – current Brain Trauma Foundation Guidelines
- Problems with fixed ICP thresholds
- Why do we need additional parameters besides ICP and CPP?
- $p_{bt}O_2$ monitoring in TBI
- Relationship of $p_{bt}O_2$ monitoring with outcome

>22 mmHg

Carney, Neurosurgery 2017

ICP and CPP – current guidelines

TABLE 3. Updated Recommendations: Thresholds[a,b]

Topic	Recommendations
Blood pressure thresholds	Level III
	• **Maintaining SBP at ≥100 mm Hg for patients 50 to 69 years old or at ≥110 mm Hg or above for patients 15 to 49 or >70 years old may be considered to decrease mortality and improve outcomes.**
Intracranial pressure thresholds	Level IIB
	• **Treating ICP >22 mm Hg is recommended because values above this level are associated with increased mortality.**
	Level III
	• A combination of ICP values and clinical and brain CT findings may be used to make management decisions.
	*The committee is aware that the results of the RESCUEicp trial[2] were released after the completion of these Guidelines. The results of this trial may affect these recommendations and may need to be considered by treating physicians and other users of these Guidelines. We intend to update these recommendations if needed. Updates will be available at https://braintrauma.org/coma/guidelines.
Cerebral perfusion pressure thresholds	Level IIB
	• **The recommended target CPP value for survival and favorable outcomes is between 60 and 70 mm Hg. Whether 60 or 70 mm Hg is the minimum optimal CPP threshold is unclear and may depend upon the autoregulatory status of the patient.**
	Level III
	• Avoiding aggressive attempts to maintain CPP >70 mm Hg with fluids and pressors may be considered because of the risk of adult respiratory failure.
Advanced cerebral monitoring thresholds	Level III
	• Jugular venous saturation of <50% may be a threshold to avoid in order to reduce mortality and improve outcomes.

[a]CPP, cerebral perfusion pressure; CT, computed tomography; ICP, intracranial pressure; RESCUEicp trial, Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of ICP; SBP, systolic blood pressure.
[b]Bold: New or revised recommendations.

Carney, Neurosurgery 2017

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Carney, Neurosurgery 2017

But *wait:* Isn‘t there Level I evidence?

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.

Is ICP monitoring useful at all?

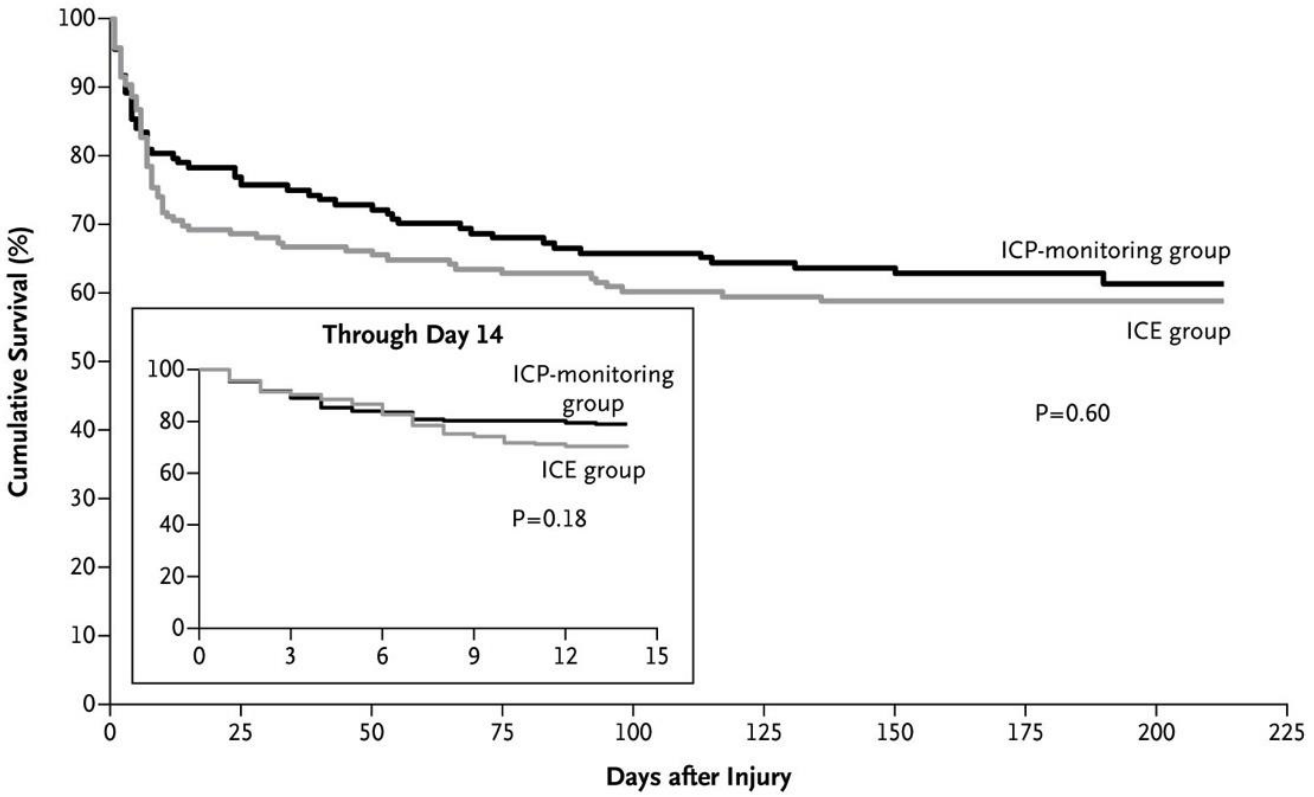

Figure 1. Cumulative Survival Rate According to Study Group.

A Kaplan–Meier survival plot based on the prespecified analysis shows the cumulative survival rate at 6 months among patients assigned to imaging and clinical examination (ICE) as compared with those assigned to intracranial-pressure (ICP) monitoring (hazard ratio for death, 1.10; 95% confidence interval [CI], 0.77 to 1.57). The inset shows the results of the post hoc analysis at 14 days (hazard ratio, 1.36; 95% CI, 0.87 to 2.11).

Chesnut et al., NEJM 2012

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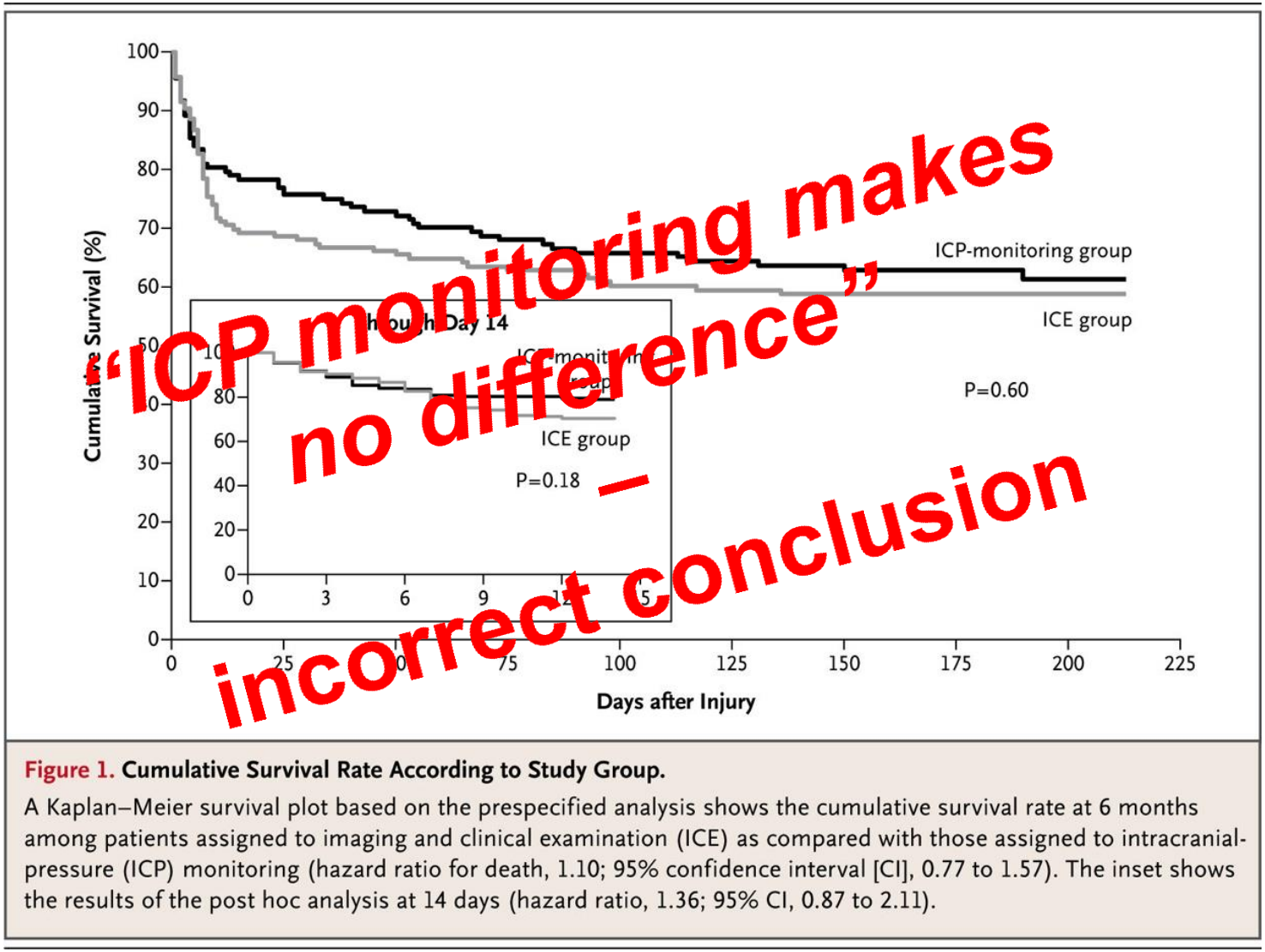

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Carney, Neurosurgery 2017

Where does the recommendation to treat ICP above 22 mmHg come from?

459 patients from the TBI database Cambridge, UK

mean values of whole monitoring time

stepwise χ^2-Test

...

	Alive	Dead	
PRx ≥ 0.10	46	90	$\chi^2 = 12.09$, $p = 0.005$
PRx < 0.10	45	204	

	Alive	Dead	
PRx ≥ 0.05	59	126	$\chi^2 = 13.45$, $p = 0.0002$
PRx < 0.05	32	168	

...

	Alive	Dead	
PRx≥0	70	169	$\chi^2 = 10.08$, $p = 0.0015$
PRx<0	22	124	

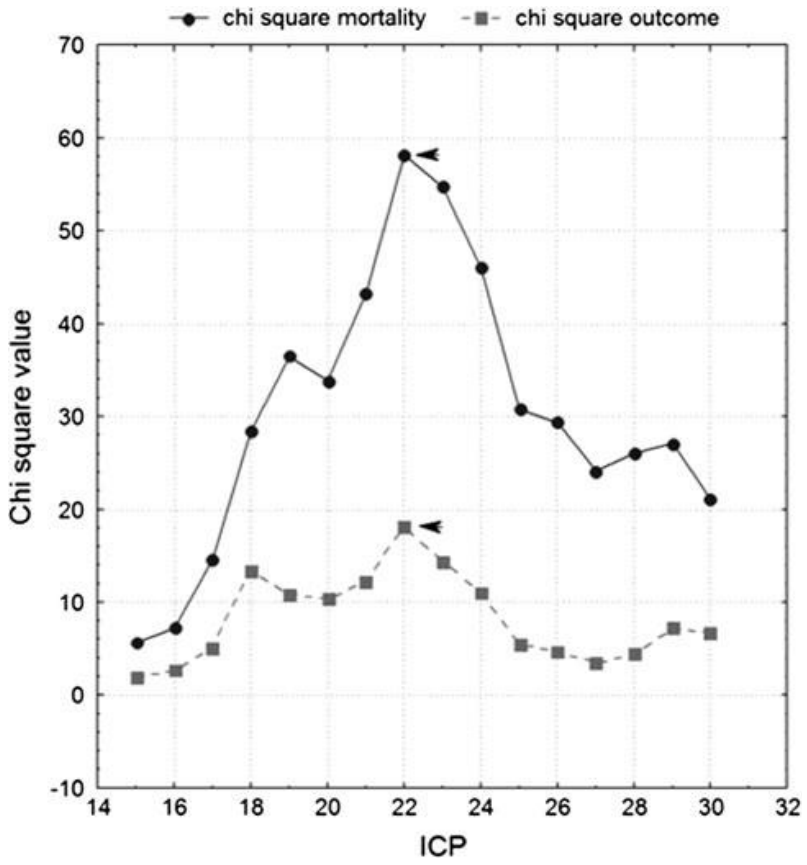


Fig. 4 Thresholds for ICP. *Arrows* indicate that 22 mmHg was the value returning the highest chi square scores for both mortality and outcome, and therefore the optimal threshold

Sorrentino, Neurocrit Care 2012, 16: 258-266

Where does the recommendation to treat ICP above 22 mmHg come from?

Table 1 Thresholds for ICP in mmHg

	n	Threshold for survival	Sensitivity (%) Specificity (%)	Threshold for favorable outcome	Sensitivity (%) Specificity (%)
All patients	459	22 (58.18, $P < 0.001$)	63 82	22 (18.15, $P < 0.001$)	81 48
>55 years	77	21 (5.60, $P = 0.018$)	75 62	18 (5.14, $P = 0.023$)	90 36
≤55 years	382	23 (58.56, $P < 0.001$)	66 85	22 (15.78, $P < 0.001$)	78 52
Females	102	23 (10.38, $P < 0.001$)	78 82	18 (8.23, $P = 0.004$)	80 51
Males	357	22 (44.97, $P < 0.001$)	62 82	22 (14.07, $P < 0.001$)	79 49
GCS ≤ 8	338	22 (43.76, $P < 0.001$)	66 80	22 (13.68, $P < 0.001$)	84 45
GCS ≥ 9	121	20 (11.46, $P < 0.001$)	40 89	NS	NS

Sorrentino, Neurocrit Care 2012, 16: 258-266

Intensity and duration of ICP raise vs outcome

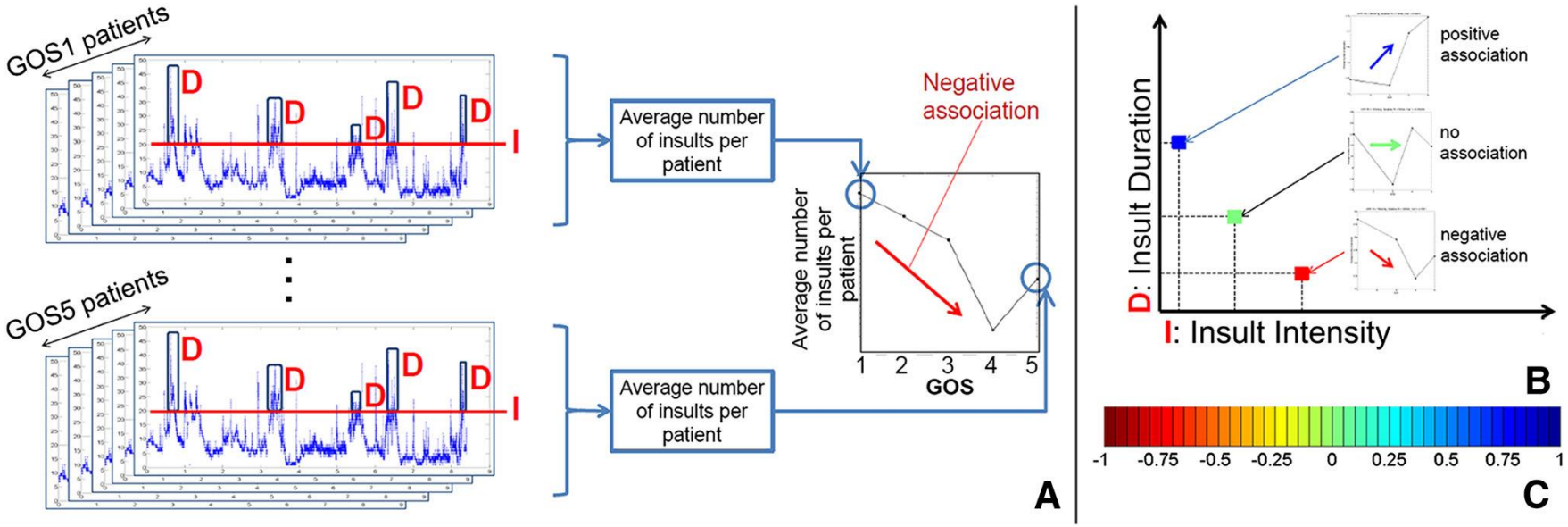
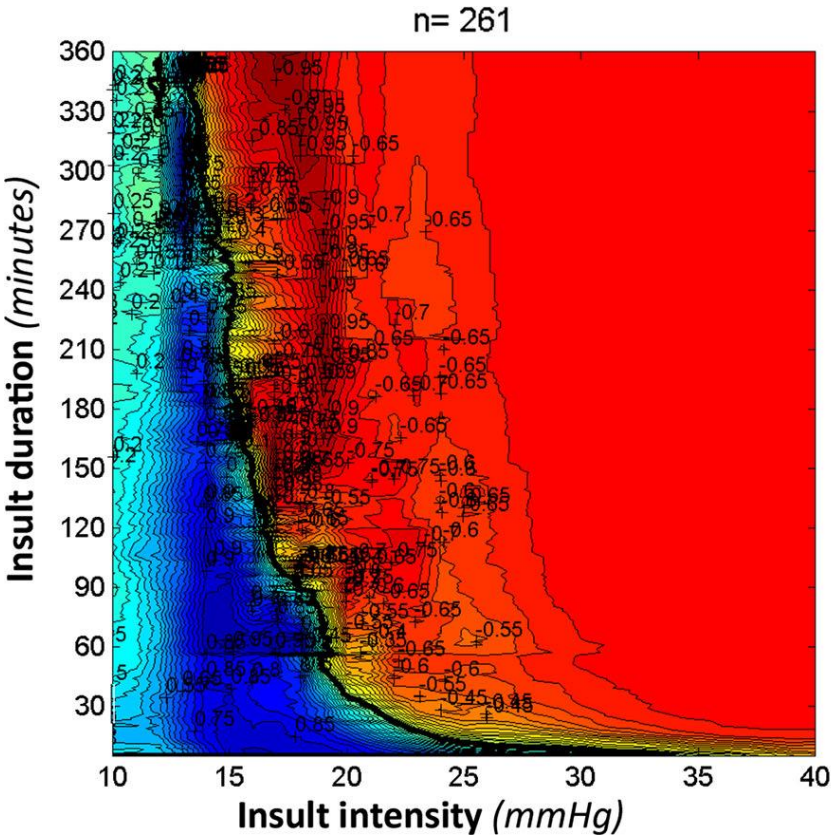


Fig. 1 Visualization methodology. The average number of insults of ICP above an intensity threshold *I* (in mmHg), lasting for at least a duration threshold *D* (in minutes) is computed for each GOS category and the Pearson correlation is computed (**a**). The correlation between GOS and the average number of insults per GOS category is computed for all *I* and *D* combinations (**b**) and given a colour according to a predefined colour map ranging from -1 in *dark red* to $+1$ in *dark blue* (**c**)

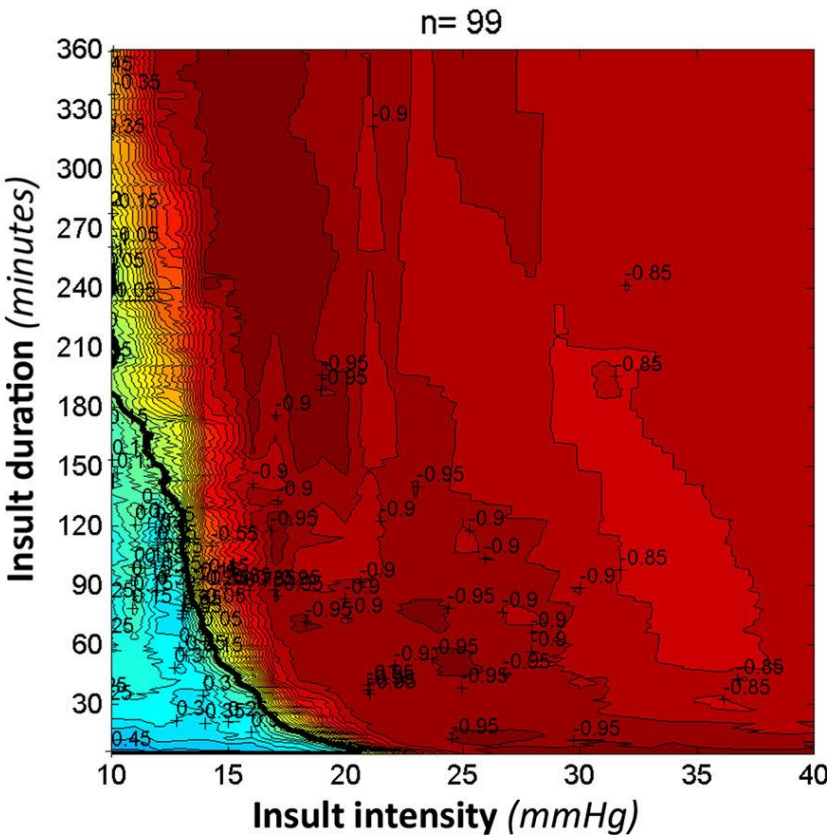
360 patients from the BRAIN-IT database

Güiza et al., ICM 2015

No equal threshold for all



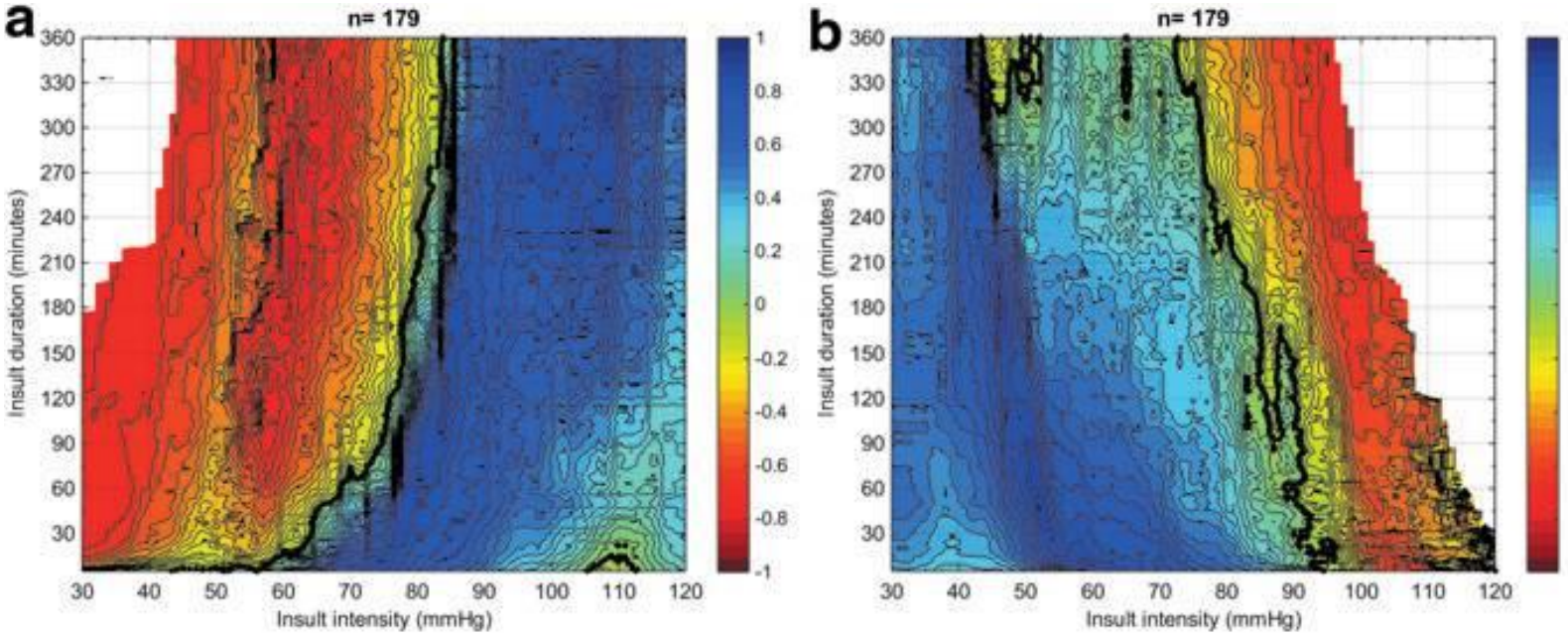
adults



children

Güiza et al., ICM 2015

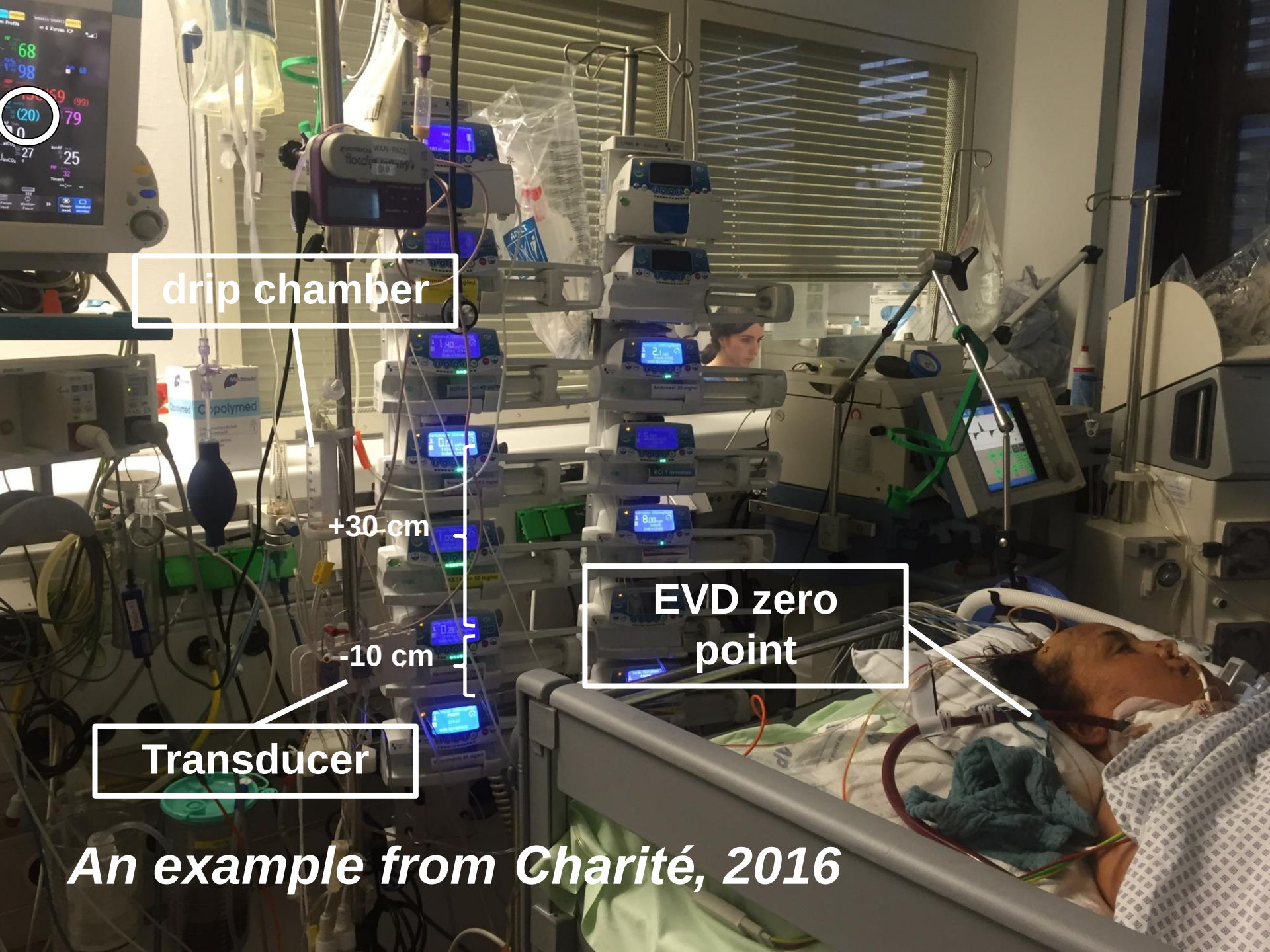
CPP: both too low and too high are bad



low CPP

high CPP

Güiza et al., J Neurotrauma 2017



An example from Charité, 2016

ICP and CPP – current guidelines

Major problems:

- **No reference of the zeroing level of APB and ICP**
- **Error dependent on probe type:**
  - **EVD:**
    level of ICP sensitive to zeroing error
    CPP correct (if ABP and ICP zeroed on the same level)
  - **parenchymal probe:**
    ICP correct
    CPP sensitive to zeroing errors of ABP

Carney, Neurosurgery 2017

RESCUEicp

408 patients from 10 to 65 years

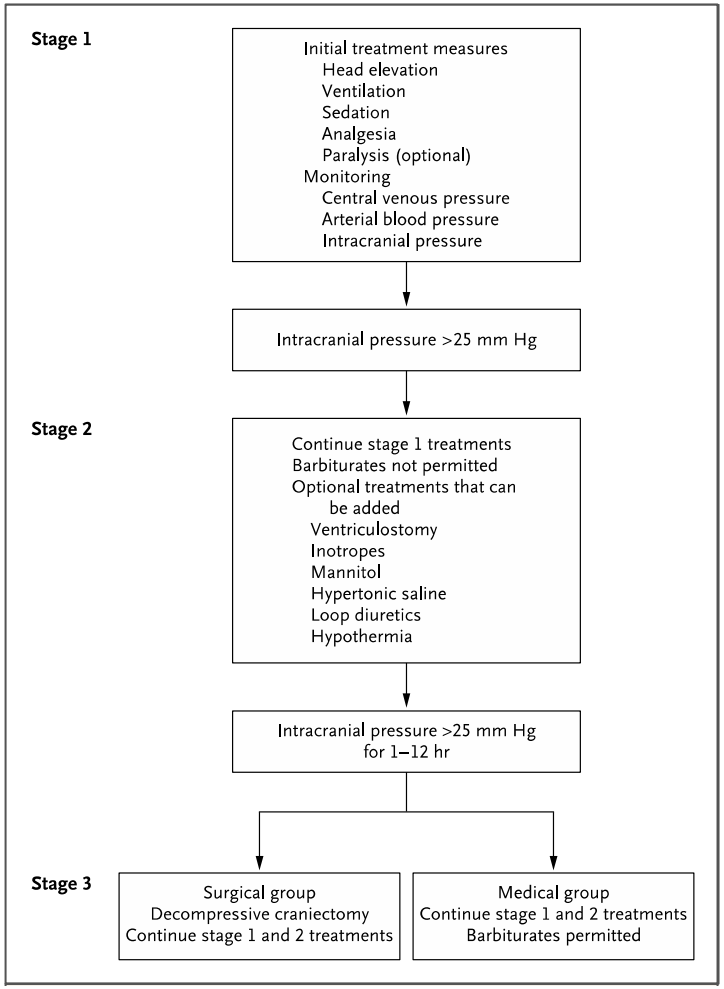
TBI with ICP > 25 mmHg for > 1 h

Multicenter trial, randomization 1:1

Decompressive craniectomy

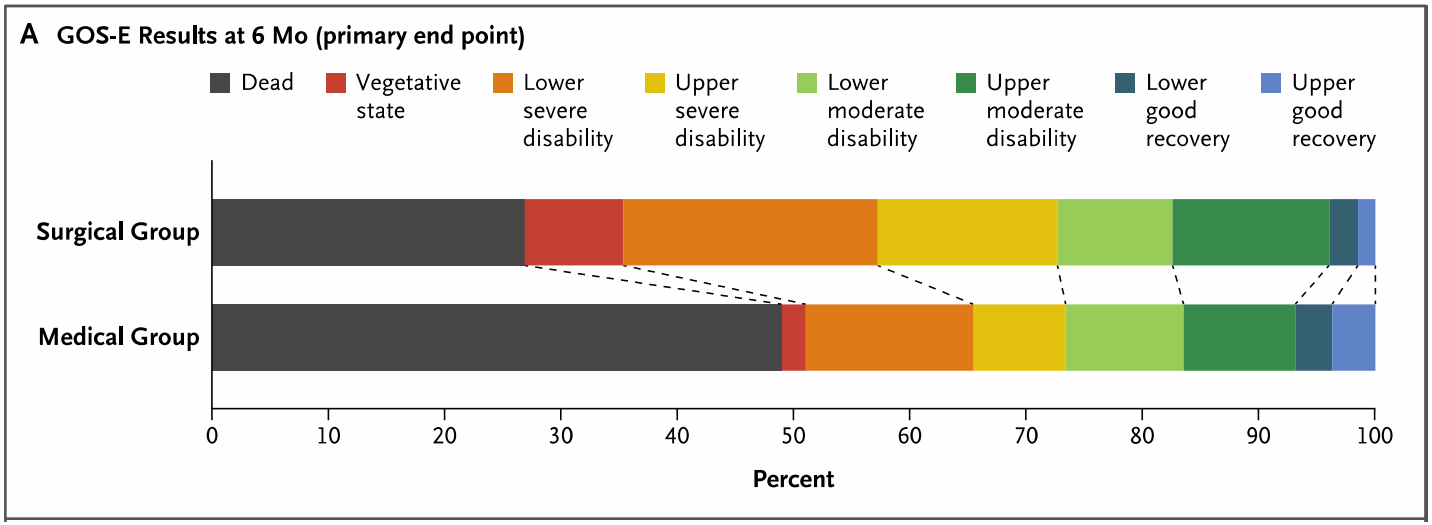
vs

conservative therapy



Hutchinson et al: NEJM 2016, 375: 1119-1130

RESCUEicp: results



difference between treatment groups: p < 0.001

Upper severe disability or better:

42,8% in surgical group

34,6% in conservative group

p= 0.12

Hutchinson et al: NEJM 2016, 375: 1119-1130

RESCUEicp: no equal benefit of surgery for all

·	Surgical Group	Medical Group	Absolute Difference (95% CI)
[illegible]	[illegible]	[illegible]	·
[illegible]	[illegible]	[illegible]	[illegible]

·

·	Surgical Group	Medical Group	Absolute Difference (95% CI)
[illegible]	[illegible]	[illegible]	·
[illegible]	[illegible]	[illegible]	[illegible]

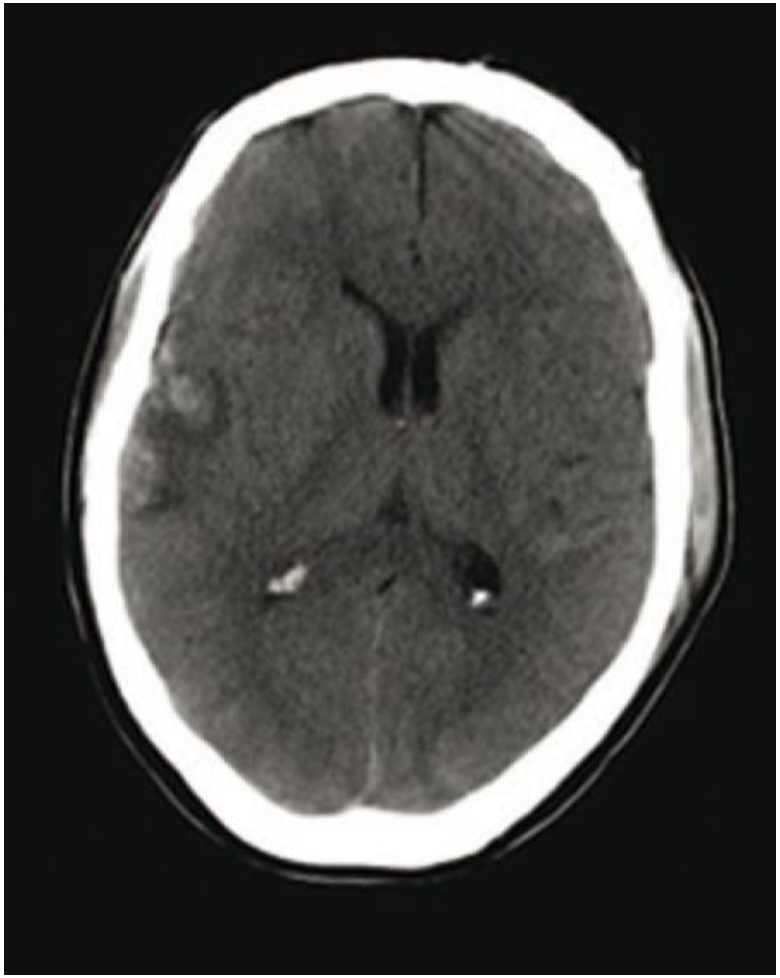
·

RESCUEicp: Class 1 evidence for ICP monitoring
(the same as the EUROTHERM 3235 or DECRA trials)

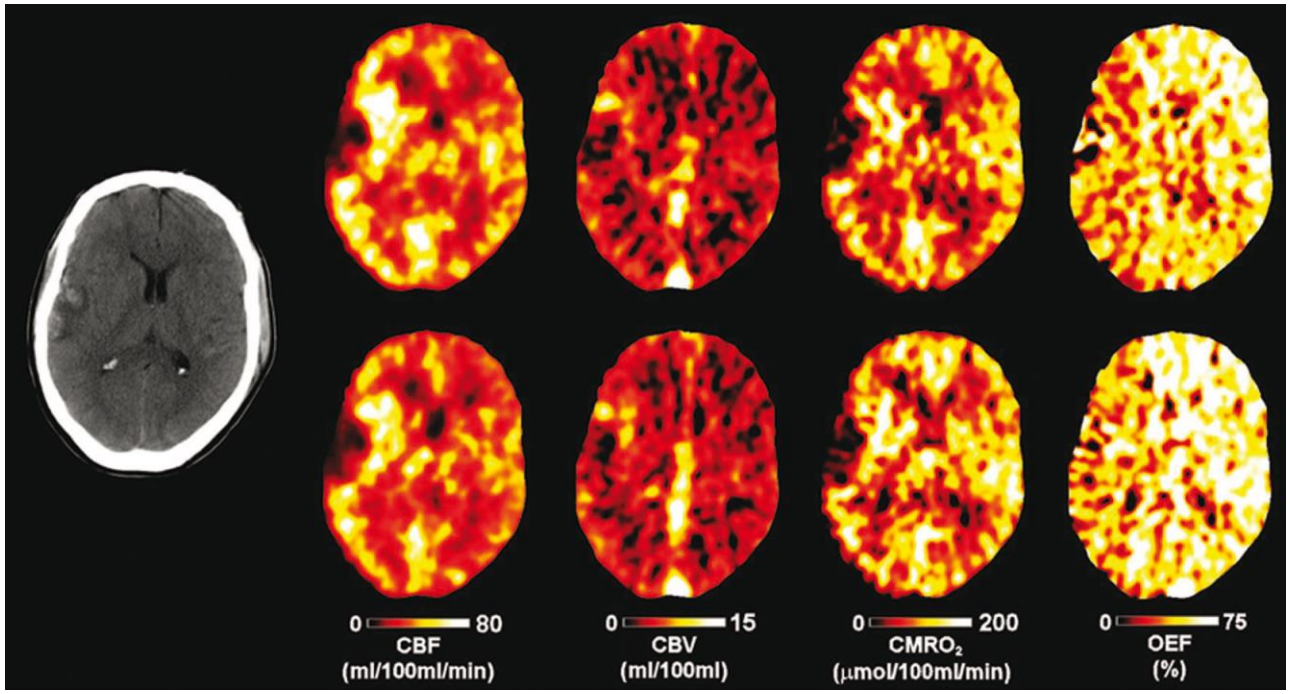
ICP monitoring is about correct decision making –
whom to treat and when with which method!

Hutchinson et al: NEJM 2016, 375: 1119-1130

Why it is not enough to measure just ICP



Hyperventilation and ischemia

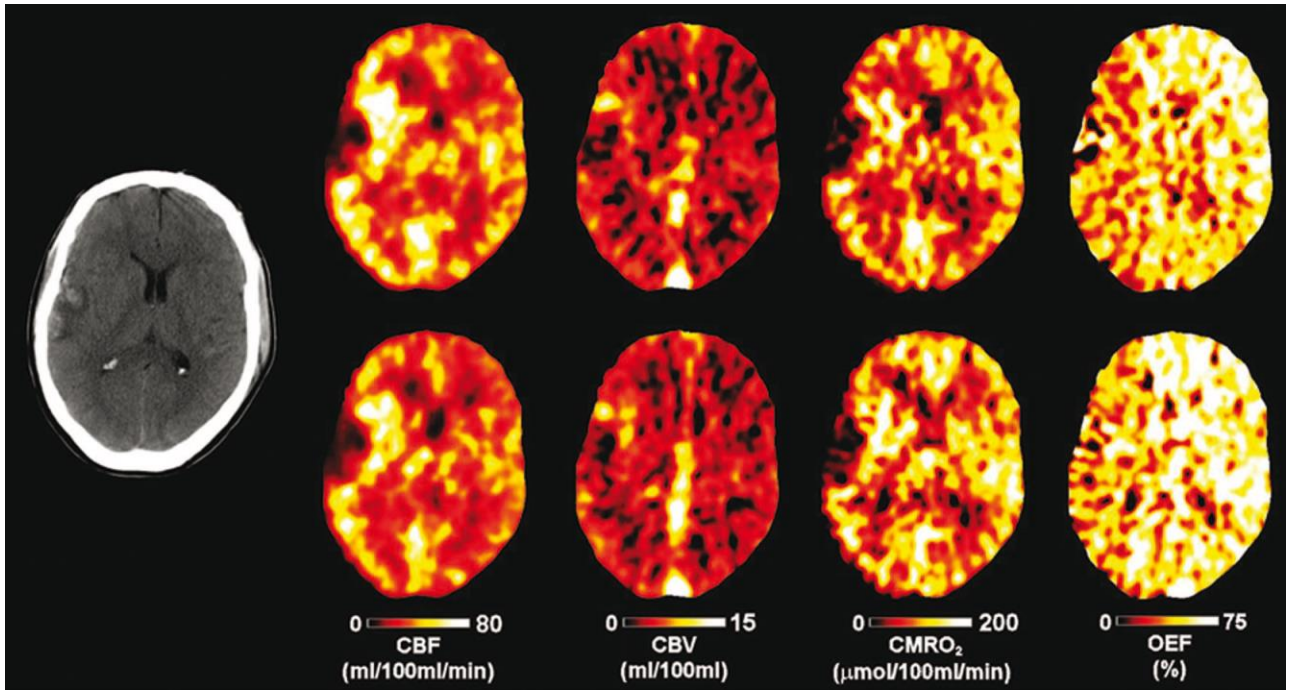


pCO2: 35 mmHg
ICP: 22 mmHg

pCO2: 29 mmHg
ICP: 17 mmHg

Coles, CCM 2007

Hyperventilation and ischemia



pCO2: 35 mmHg
ICP: 22 mmHg

pCO2: 29 mmHg
ICP: 17 mmHg

Ischemic brain volume: 44 ml vs 135 ml

Coles, CCM 2007

Advanced cerebral monitoring – current guidelines

TABLE 2. Updated Monitoring Recommendations[a,b]

Topic	Recommendations
Intracranial pressure monitoring	Level IIB
	• **Management of severe TBI patients using information from ICP monitoring is recommended to reduce in-hospital and 2-week post-injury mortality.**
	Recommendations from the prior (Third) Edition not supported by evidence meeting current standards.
	ICP should be monitored in all salvageable patients with a TBI (GCS 3-8 after resuscitation) and an abnormal CT scan. An abnormal CT scan of the head is one that reveals hematomas, contusions, swelling, herniation, or compressed basal cisterns.
	ICP monitoring is indicated in patients with severe TBI with a normal CT scan if ≥2 of the following features are noted at admission: age >40 years, unilateral or bilateral motor posturing, or SBP <90 mm Hg.
Cerebral perfusion pressure monitoring	Level IIB
	• **Management of severe TBI patients using guidelines-based recommendations for CPP monitoring is recommended to decrease 2-wk mortality.**
Advanced cerebral monitoring	Level III
	• Jugular bulb monitoring of $AVDO_2$, as a source of information for management decisions, may be considered to reduce mortality and improve outcomes at 3 and 6 mo post-injury.

[a] $AVDO_2$, arteriovenous oxygen content difference; CPP, cerebral perfusion pressure; CT, computed tomography; GCS, Glasgow Coma Scale; ICP, intracranial pressure; SBP, systolic blood pressure; TBI, traumatic brain injury.
[b] Bold: New or revised recommendations.

Carney, Neurosurgery 2017

Jugular bulb oximetry?

Advanced cerebral monitoring thresholds	Level III
	• Jugular venous saturation of <50% may be a threshold to avoid in order to reduce mortality and improve outcomes.

[a]CPP, cerebral perfusion pressure; CT, computed tomography; ICP, intracranial pressure; RESCUEicp trial, Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of ICP; SBP, systolic blood pressure.
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based on:

Jugular Bulb Monitoring of Arteriovenous Oxygen Content Difference			
Cruz, 1998[10]	Prospective, controlled but non-randomized and non-blinded study of 353 TBI patients undergoing continuous jugular bulb saturation and cerebral extraction of oxygen ($AVDO_2$) monitoring, in which GOS at 6 months was compared between patients who underwent monitoring and those who did not.	Class 3	Outcome at 6 months by GOS improved in patients who underwent SjO_2 and $AVDO_2$ monitoring. Monitoring SjO_2 may improve outcome in severe TBI. However, caution must be utilized in interpreting the results of this study as the non-randomized, non-blinded nature of the study may introduce treatment bias.
Le Roux 1997[11]	Prospective, observational study of 32 TBI patients with GCS ≤8 who underwent jugular bulb oxygen and $AVDO_2$ monitoring, in which the incidence of delayed cerebral infarction and GOS at 6 months post-injury was assessed.	Class 3	A limited improvement in elevated $AVDO_2$ after treatment (craniotomy or mannitol administration) was significantly associated with delayed cerebral infarction and unfavorable outcome. Lack of response of SjO_2 to treatment measures may be associated with poor outcome in severe TBI.
Robertson 1993[12]	Prospective, observational study of SjO_2 monitoring in 116 TBI patients (100 with closed head injury and 16 with penetrating head injury) in which desaturation episodes (SjO_2 <50%) were monitored and correlated to GOS at 3 months post-injury.	Class 3	The number of episodes of desaturation were found to be associated with mortality as follows: no desaturation episodes: mortality 18% one desaturation episode: mortality 46% multiple desaturation episodes: mortality 71%. Episodes of desaturation are related to mortality and GOS at 3 months.

Carney, Neurosurgery 2017

The work of Dr. Cruz?

Crit Care Med. 1998 Feb;26(2):344-51.

The first decade of continuous monitoring of jugular bulb oxyhemoglobinsaturation: management strategies and clinical outcome.

Cruz J[1].

Author information

Abstract

OBJECTIVE: To comparatively assess outcome of patients undergoing monitoring and management of cerebral extraction of oxygen along with cerebral perfusion pressure vs. outcome of patients undergoing monitoring and management of cerebral perfusion pressure alone in severe acute brain trauma.

DESIGN: Prospective, interventional study.

SETTING: Intensive care unit of a university hospital.

PATIENTS: Adults (n = 353) with severe acute brain trauma. A group of 178 patients underwent continuous monitoring and management of cerebral extraction of oxygen and cerebral perfusion pressure, while a control group of 175 patients underwent monitoring and management of cerebral perfusion pressure only.

INTERVENTIONS: Routine neuroemergency procedures.

MEASUREMENTS AND MAIN RESULTS: The two groups of patients were matched with regard to age, postresuscitation Glasgow Coma Scale scores, rates of acute surgical intracranial hematomas and brain swelling, pupillary abnormalities, early hypotensive events (before intensive care monitoring), as well as initial levels of intracranial pressure and cerebral perfusion pressure. Outcome at 6 months post injury was significantly better ($p < .00005$) in the 178 patients undergoing monitoring and management of cerebral extraction of oxygen along with cerebral perfusion pressure, than in the control group of 175 patients undergoing monitoring and management of cerebral perfusion pressure alone.

CONCLUSION: In patients with severe acute brain trauma and intracranial hypertension associated with compromised cerebrospinal fluid spaces, monitoring and managing cerebral extraction of oxygen in conjunction with cerebral perfusion pressure result in better outcome than when cerebral perfusion pressure is managed alone.

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Which allocation strate…

where?

	CEO_2 Group (n = 178)	CPP Group (n = 175)
Age (yr)[a]	30 ± 9	29 ± 8
GCS score[a]	5.5 ± 1	5.6 ± 1.2
ICP (mm Hg)[a]	33 ± 6	31 ± 5
CPP (mm Hg)[a]	56 ± 6	59 ± 7
EAH (%)[b]	14	11
PA (%)	29	32
SLV (%)	100	100
CBC (%)	64	62
AICH (%)	33	35

CEO_2, cerebral extraction of oxygen; CPP, initial cerebral perfusion pressure; GCS, postresuscitation Glasgow Coma Scale scores; ICP, initial intracranial pressure; EAH, early arterial hypotension; PA, pupillary abnormalities (excluding direct ocular trauma); SLV, small lateral ventricles; CBC, compromised basilar cisterns; AICH, acute intracranial hematomas on computed tomography scans of the head.

[a]Mean ± SD; [b]EAH values before monitoring ICP and CPP.

No statistically significant differences were found.

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CEO_2, cerebral extraction of oxygen; CPP, initial cerebral perfusion pressure; GCS, postresuscitation Glasgow Coma Scale …

	G-M	S	V-D	Total
CEO_2 Group (%)	132 (74)	25 (14)	21 (12)	178 (100)
CPP Group (%)	98 (56)	21 (12)	56 (32)	175 (100)

Distribution of patients in the "cerebral extraction of oxygen (CEO_2) group" and the "cerebral perfusion pressure (CPP) group," according to three major outcome categories of the Glasgow Outcome Scale: G-M, good recovery or moderate disability; S, severe disability; V-D, vegetative state or death. A significant difference was found ($p < .00005$).

Table 1. Six-month outcome in two groups of patients

The work of Dr. Cruz?

The Comprehensive International Center for Neuroemergencies, Cx. Postal 57011, Sao Paulo, Brazil

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CBC (%)	64	62
AICH (%)	33	35

CEO_2, cerebral extraction of oxygen; CPP, initial cerebral perfusion pressure; GCS, postresuscitation Glasgow Coma Scale …

	G-M	S	V-D	Total
CEO_2 Group (%)	132 (74)	25 (14)	21 (12)	178 (100)
CPP Group (%)	98 (56)	21 (12)	56 (32)	175 (100)

Distribution of patients in the "cerebral extraction of oxygen (CEO_2) group" and the "cerebral perfusion pressure (CPP) group," according to three major outcome categories of the Glasgow Outcome Scale: G-M, good recovery or moderate disability; S, severe disability; V-D, vegetative state or death. A significant difference was found ($p < .00005$).

Table 1. Six-month outcome in two groups of patients

The work of Dr. Cruz?

RESEARCH ETHICS

Doubts over head injury studies

Patients are receiving treatment that may be unsound as investigations by **Ian Roberts, Richard Smith, and Stephen Evans** raise questions about whether influential trials of high dose mannitol ever took place

Roberts, BMJ 2007

The work of Dr. Cruz?

" We are left with serious doubt about important studies but with no way of determining with confidence whether the results are fabricated or real.

The main author is dead. There is no institution to investigate. The implications for patients are serious.

They are being treated on the basis of potentially unreliable evidence. "

Roberts, BMJ 2007

The work of Dr. Cruz?

The first decade of continuous monitoring of jugular bulb oxy-hemoglobin saturation: Management strategies and clinical outcome

Cruz, Julio MD, PhD

Critical Care Medicine . 26(2):344-351, February 1998.

Author Information

From the Department of Neurosurgery, Allegheny University of the Health Sciences, Philadelphia, PA, and The Comprehensive International Center for Neuroemergencies, Sao Paulo, Brazil.

Address requests for reprints to: Dr. Julio Cruz, CICNEM, Cx. Postal 57011, Sao Paulo, SP 04093,

The work of Dr. Cruz?

The first decade of continuous monitoring of jugular bulb oxyhemoglobin saturation: Management strategies and clinical outcome

most likely fabricated

Cruz, Julio MD, PhD

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What was omitted from the Guidelines – evidence against $S_{jv}O_2$

J Neurosurg 85:751–757, 1996

Monitoring of cerebral oxygenation in patients with severe head injuries: brain tissue PO_2 versus jugular vein oxygen saturation

KARL L. KIENING, M.D., ANDREAS W. UNTERBERG, M.D., PH.D., TILLMAN F. BARDT, B.S., GERD-HELGE SCHNEIDER, M.D., AND WOLFGANG R. LANKSCH, M.D., PH.D.

Department of Neurosurgery, Virchow Medical Center, Humboldt-University of Berlin, Berlin, Germany

Monitoring of cerebral oxygenation is considered to be of great importance in minimizing secondary hypoxic and ischemic brain damage following severe head injury. Although the threshold for cerebral hypoxia in jugular bulb oximetry (measurement of O_2 saturation in the jugular vein ($SjvO_2$)) is generally accepted to be 50% oxygen saturation, a comparable value in brain tissue PO_2 ($PtiO_2$) monitoring, a new method for direct assessment of PO_2 in the cerebral white matter, has not yet been established. Hence, the purpose of this study was to compare brain $PtiO_2$ with $SjvO_2$ in severely head injured patients during phases of reduced cerebral perfusion pressure (CPP) to define a threshold in brain $PtiO_2$ monitoring. In addition, the safety and data quality of both $SjvO_2$ and brain $PtiO_2$ monitoring were studied.

In 15 patients with severe head injuries, $SjvO_2$ and brain $PtiO_2$ were monitored simultaneously. For brain $PtiO_2$ monitoring a polarographic microcatheter was inserted in the frontal cerebral white matter, whereas for $SjvO_2$ measurements were obtained by using a fiberoptic catheter placed in the jugular bulb. Intracranial pressure was monitored by means of an intraparenchymal catheter. Mean arterial blood pressure, CPP, end-tidal CO_2, and arterial oxygen saturation (pulse oximetry) were continuously recorded. All data were simultaneously stored and analyzed using a multimodal computer system. For specific analysis, phases of marked deterioration in systemic blood pressure and consecutive reductions in CPP were investigated.

There were no complications that could be attributed to the $PtiO_2$ catheters, that is, no intracranial bleeding or infection. The "time of good data quality" was 95% in brain $PtiO_2$ compared to 43% in $SjvO_2$; $PtiO_2$ monitoring could be performed twice as long as $SjvO_2$ monitoring. During marked decreases in CPP, $SjvO_2$ and brain $PtiO_2$ correlated closely. A significant second-order regression curve of $SjvO_2$ versus brain $PtiO_2$ ($p < 0.01$) was plotted. At a threshold of 50% in $SjvO_2$, brain $PtiO_2$ was found to be within the range of 3 to 12 mm Hg, with a regression curve "best fit" value of 8.5 mm Hg. There was a close correlation between CPP and oxygenation parameters ($PtiO_2$ and $SjvO_2$) when CPP fell below a breakpoint of 60 mm Hg, suggesting intact cerebral autoregulation in most patients.

This study demonstrates that monitoring brain $PtiO_2$ is a safe, reliable, and sensitive diagnostic method to follow cerebral oxygenation. In comparison to $SjvO_2$, $PtiO_2$ is more suitable for long-term monitoring. It can be used to minimize episodes of secondary cerebral maloxygenation after severe head injury and may, hopefully, improve the outcome in severely head injured patients.

What was omitted from the Guidelines – evidence against $S_{jv}O_2$

J Neurosurg 85:751–757, 1996

Monitoring of cerebral oxygenation in patients with severe head injuries: brain tissue PO_2 ve saturation

"*Time of good data quality*":
$S_{jv}O_2$: 43%
$P_{ti}O_2$: 95%

KARL L. KIENING, M.D., ANDREAS W. UNTERBER[illegible] GERD-HELGE SCHNEIDER, M.D., AND WOLFGANG R. LANKSCH, M.D., PH.D.

Department of Neurosurgery, Virchow Medical Center, Humboldt-University of Berlin, Berlin, Germany

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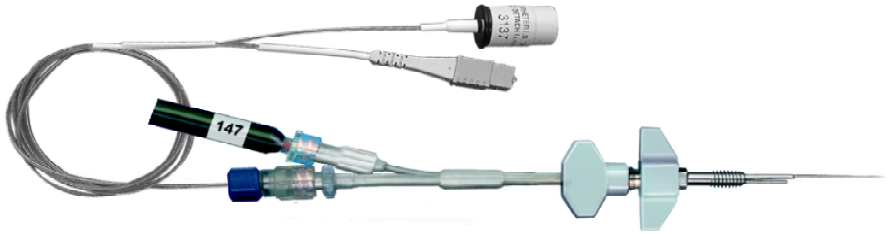
Brain tissue oxygen monitoring – available systems

established Standard:
Licox – System, since 1995
electrochemic system with Clark electrode,
14 mm^2 surface

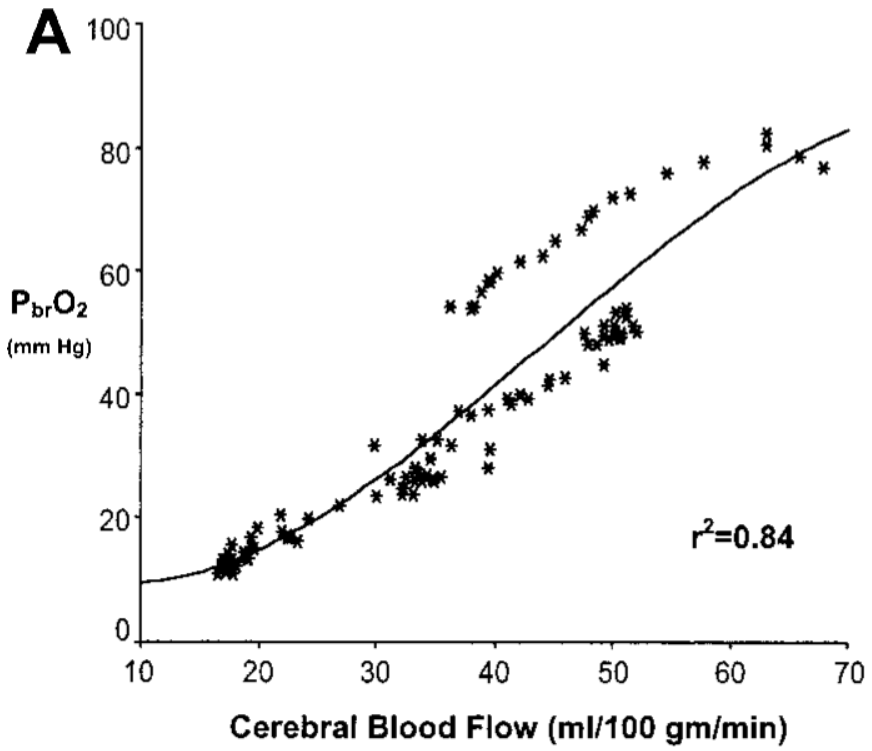


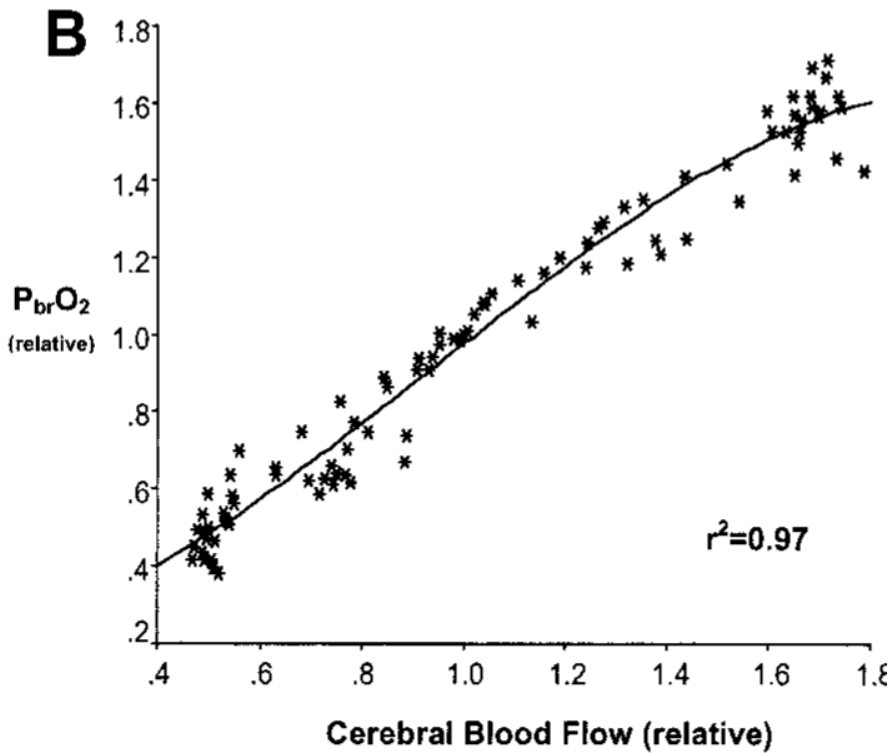
modified in 2005, since then temperature monitoring included in probe

New: Raumedic PTO probes,
available since 2006
Optical method, uses luminescence quenching by O_2
22 mm^2 surface

Advantage: $p_{bt}O_2$, ICP and temperature combined in one probe

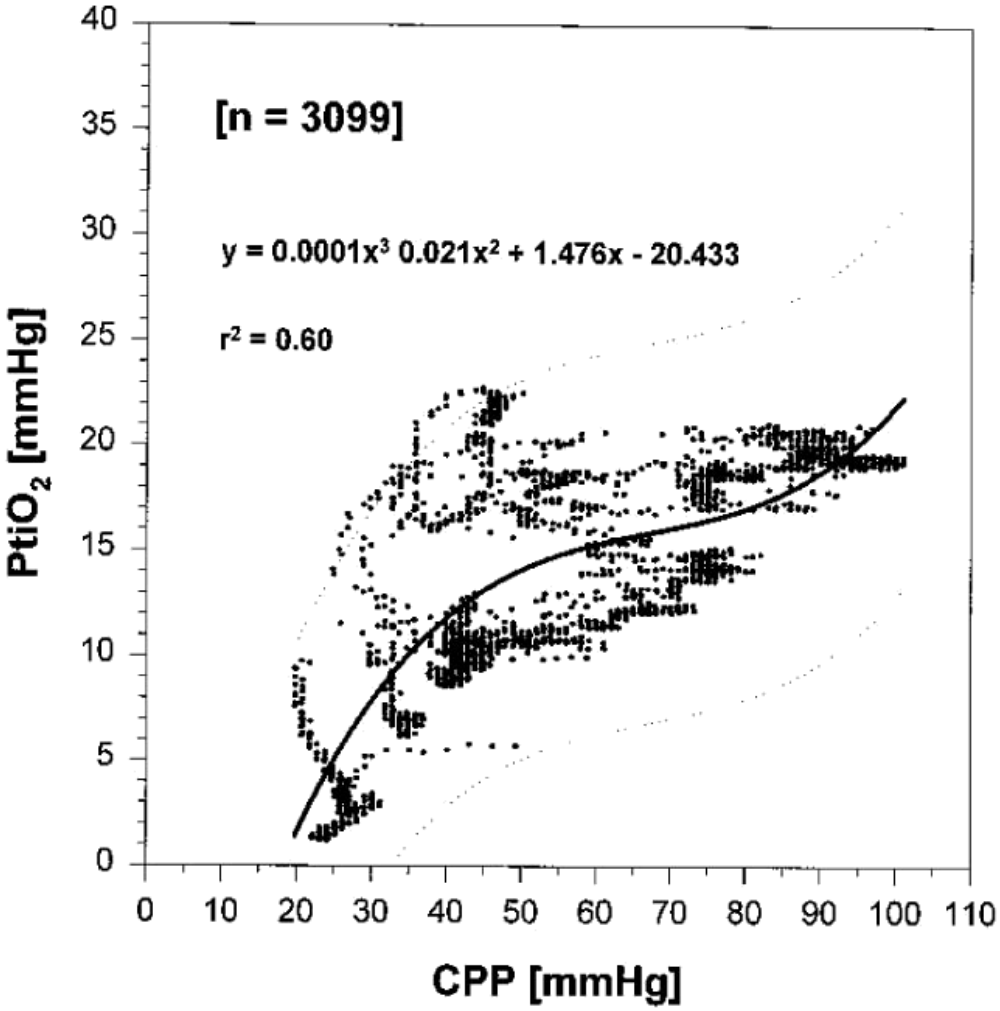
Correlation of $p_{br}O_2$ – rCBF in the healthy brain – a swine model





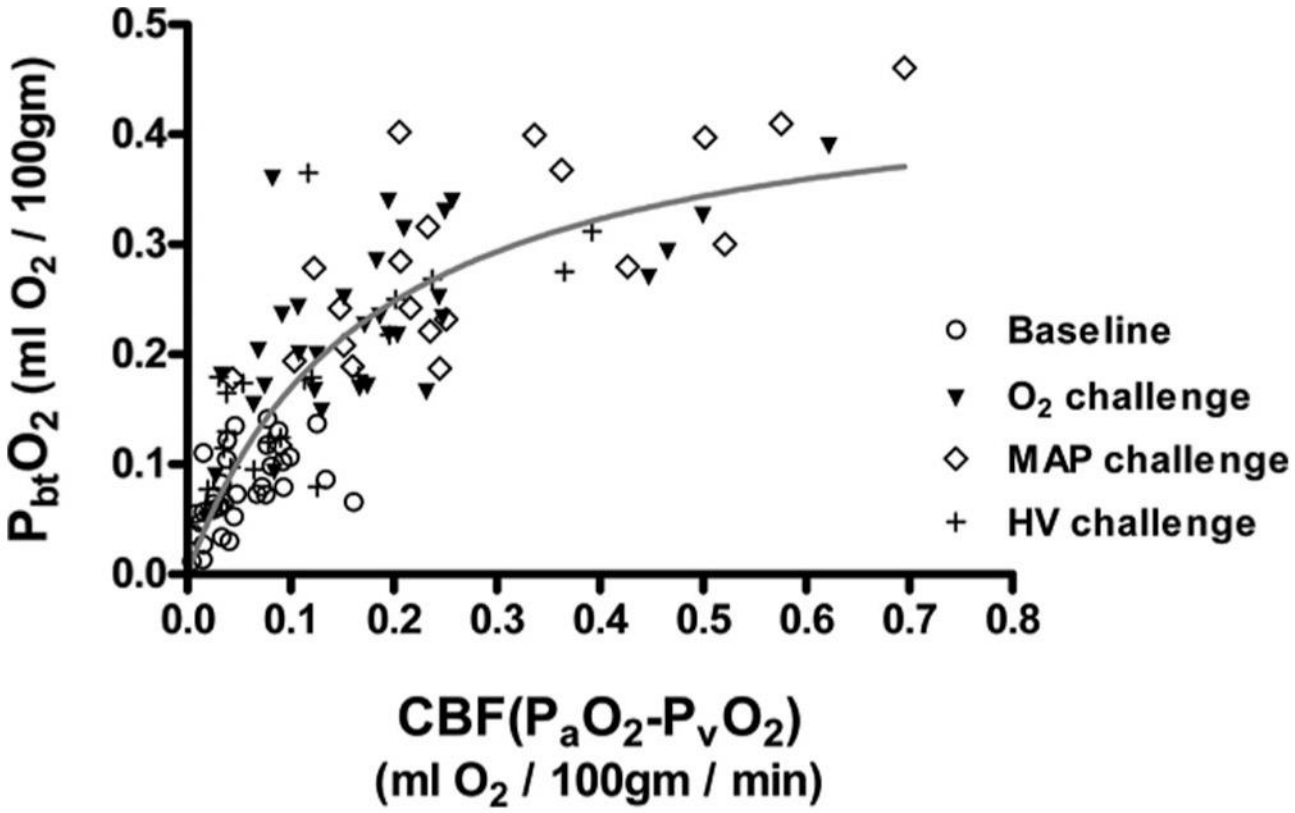
Hemphill, Neurosurgery 2001

Comparison of cerebral perfusion pressure CPP with $p_{bt}O_2$



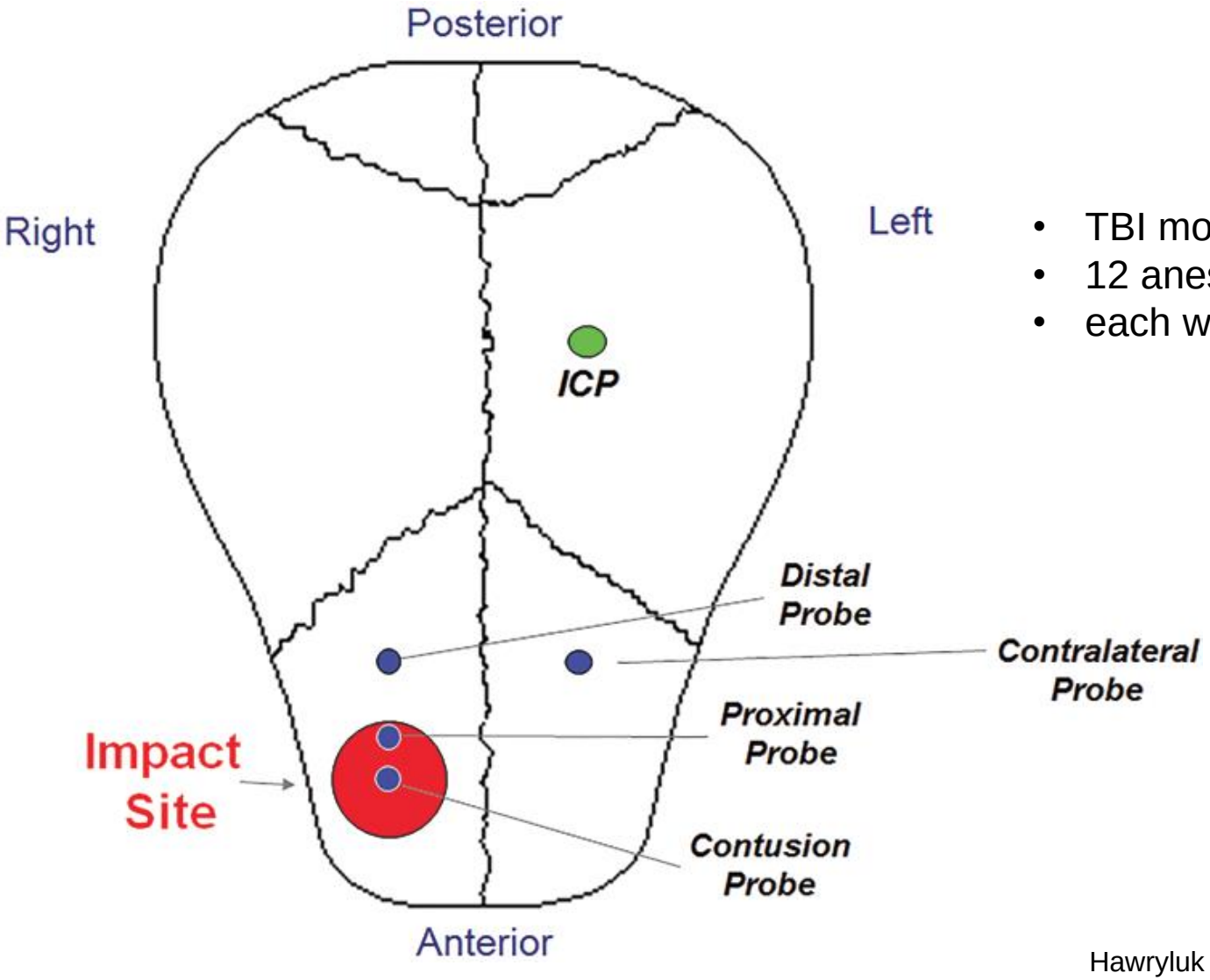
Kiening, JNS 1996

What is the physiologic meaning of the $p_{br}O_2$



Rosenthal, JNS 2008

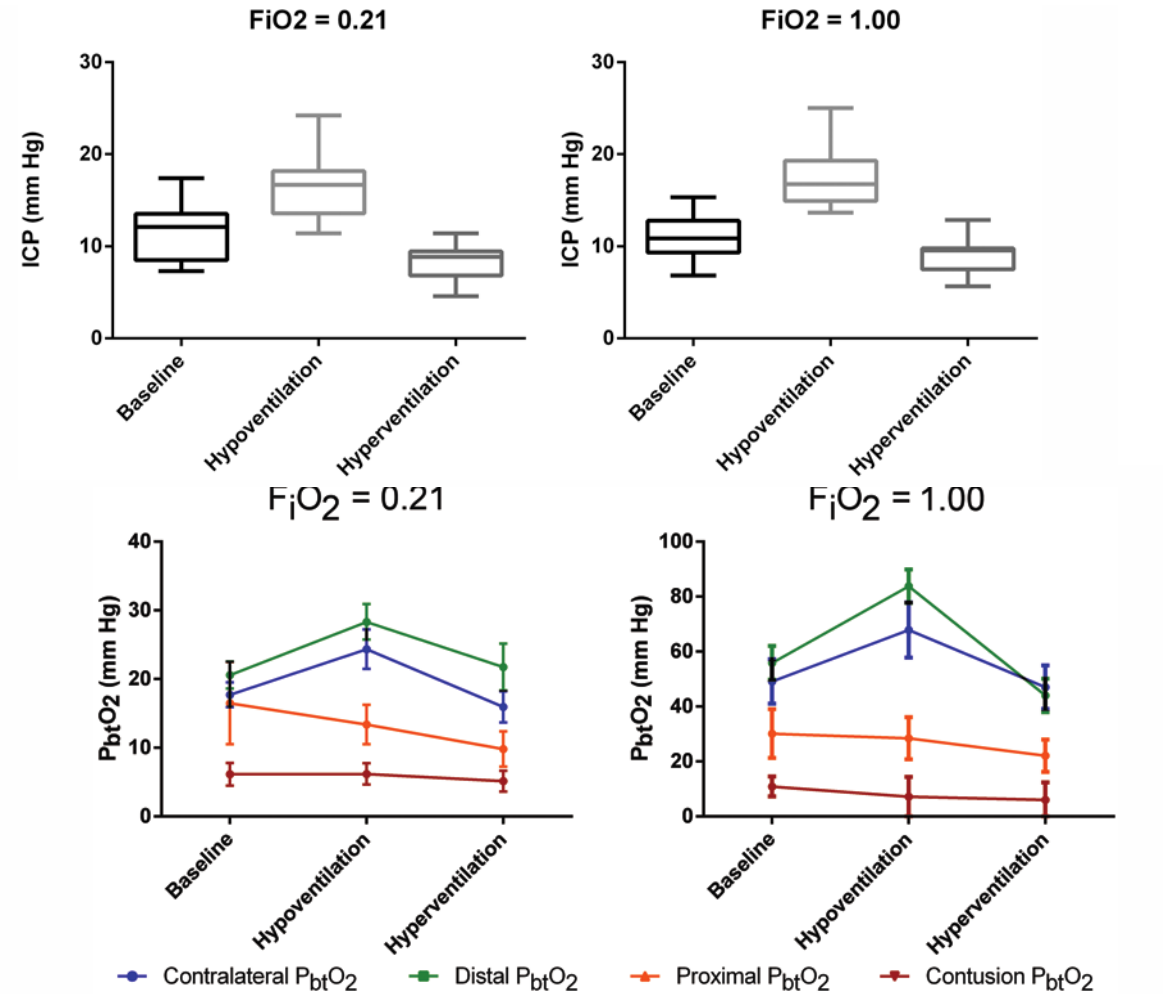
Normal values of $p_{br}O_2$ – but which tissue?



- TBI model
- 12 anesthesized swine
- each with 4 probes

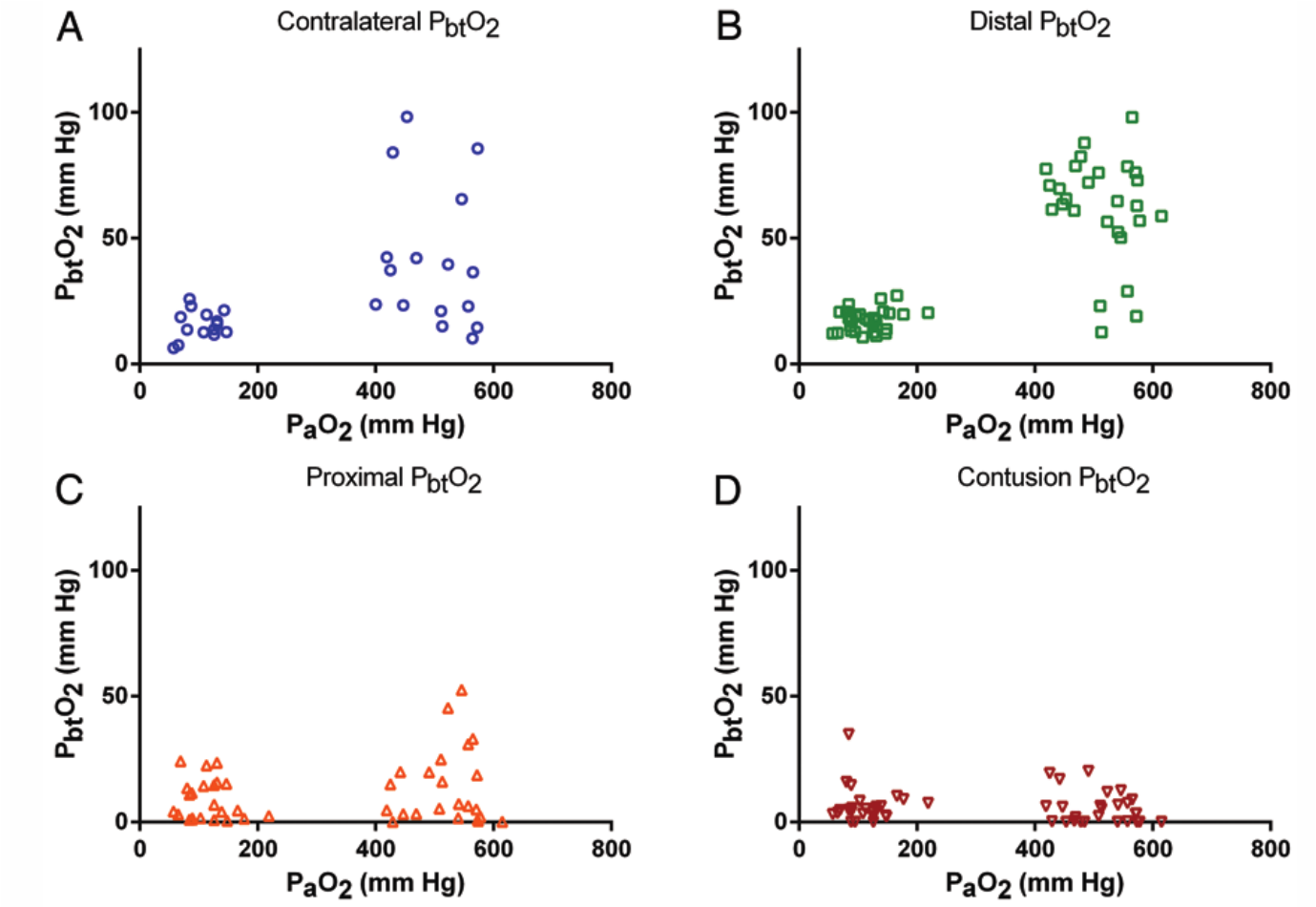
Hawryluk et al, JNS 2016

Normal values of $p_{br}O_2$ – but which tissue?



Hawryluk et al, JNS 2016

Normal values of $p_{br}O_2$ – but which tissue?



Hawryluk et al, JNS 2016

In humans: where to place the probe?

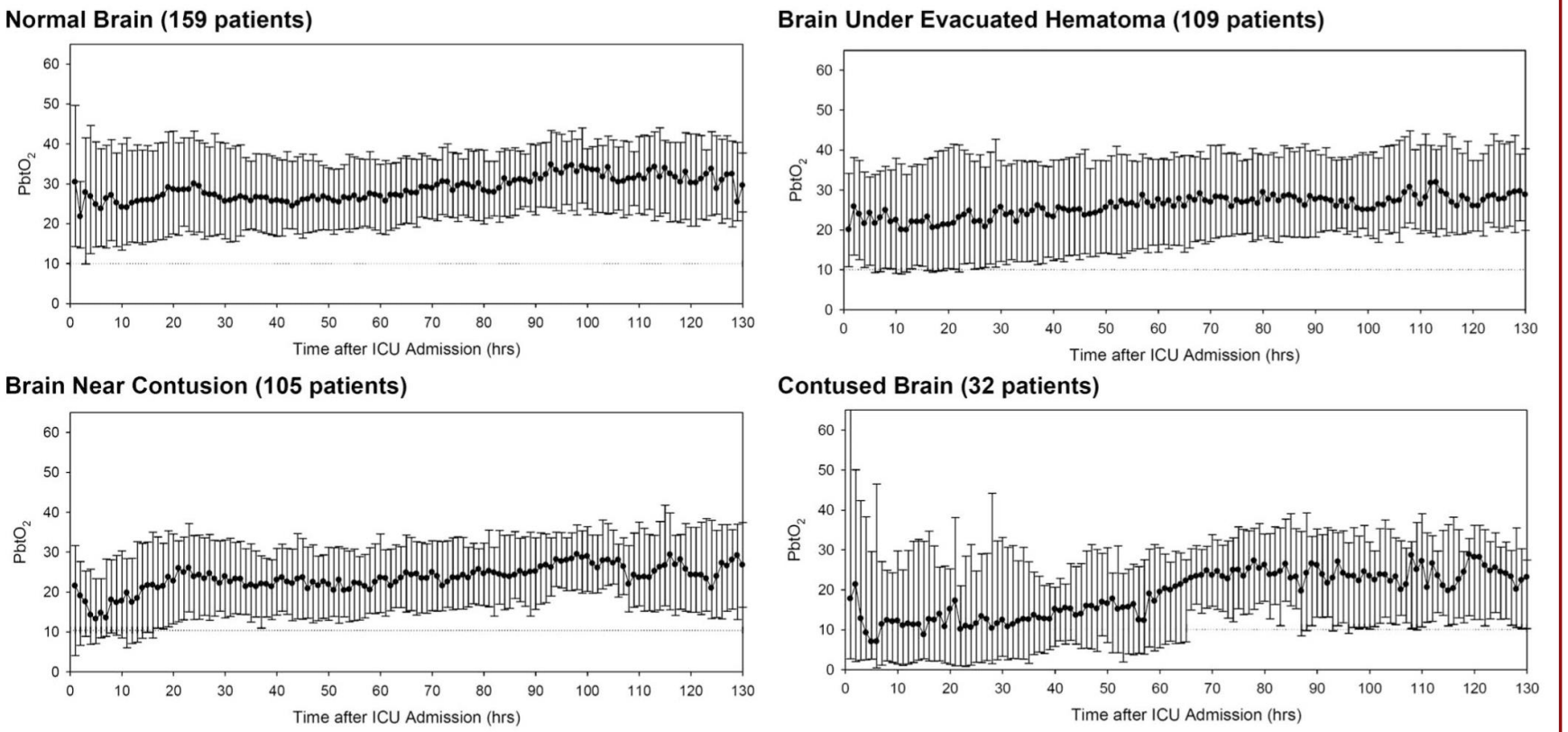


FIGURE 4. *Trend graphs of brain tissue P_{O_2} (Pbt_{O_2}) over time (median ± interquartile range) for the different catheter positions. ICU, intensive care unit.*

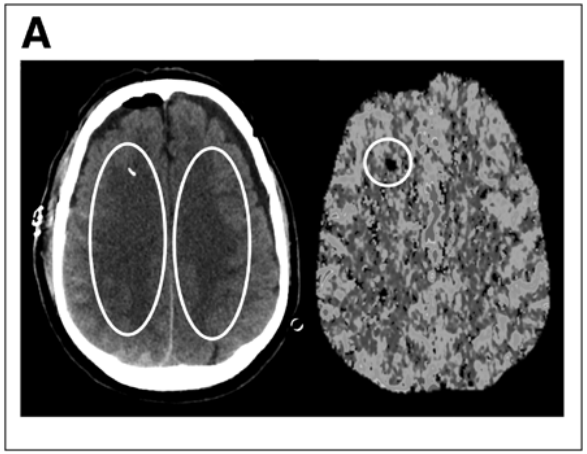
Ponce, Neurosurgery 2012

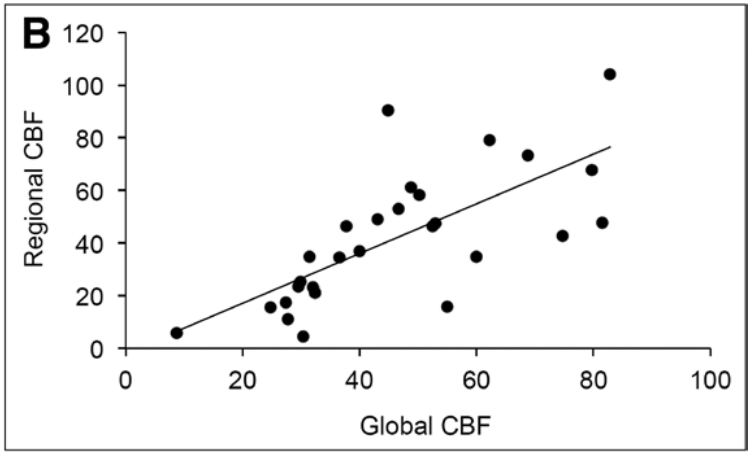
$p_{bt}O_2$ – probe position and outcome after TBI

Variable	Favorable Outcome, Mean ± SD, Median (Interquartile Range), or n (%)	Unfavorable Outcome, Mean ± SD, Median (Interquartile Range), or n (%)	Univariate Analysis *P*
Patients, n	129	276	
Demographic and injury severity variables			
Age	29.4 ± 12.6	37.4 ± 14.7	<.001
$Pbto_2$ catheter position			.03
Normal brain	61 (47.3)	98 (35.5)	
Abnormal brain	68 (52.7)	178 (64.5)	
$Pbto_2$ Variables			
Average $Pbto_2$, mm Hg	32.2 ± 16.3	25.1 ± 13.5	<.001
Average $Pbto_2$ × catheter position			
Normal brain	33.8 ± 19.4	31.4 ± 13.1	
Abnormal brain	28.8 ± 12.0	19.5 ± 13.7	
Time $Pbto_2$ < 10 mm Hg, h	0 (0-6.25)	6 (0-25.5)	<.001
Time $Pbto_2$ < 15 mm Hg, h	3 (0-19.25)	16 (3-42)	<.001
Time $Pbto_2$ < 20 mm Hg, h	11 (1.75-39.25)	31 (9.0-56.75)	<.001
$Pbto_2$ trend pattern			<.001
Never < 10 mm Hg	85 (65.9)	129 (46.7)	
Transiently < 10 mm Hg at start	39 (30.2)	90 (32.6)	
Persistently < 10 mm Hg or decreasing	5 (3.9)	57 (20.7)	

Ponce, Neurosurgery 2012

What is the accuracy of multimodal monitoring to detect hypoperfusion?



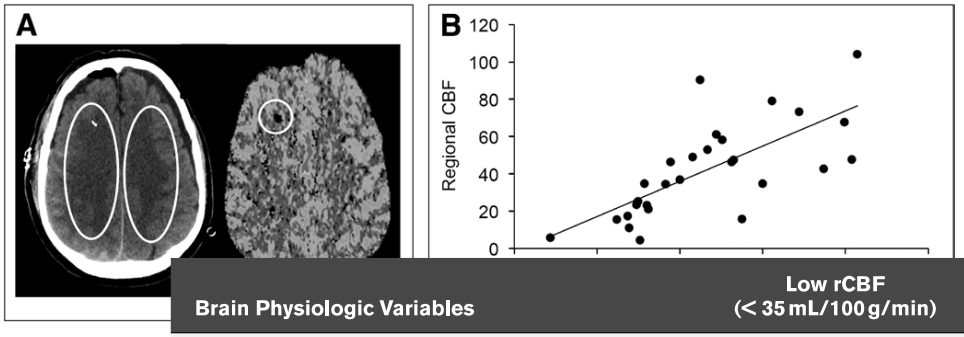


27 TBI patients

probe placement right frontal, regardless of injury

Bouzat et al, Crit Care Med 2015

What is the accuracy of multimodal monitoring to detect hypoperfusion?

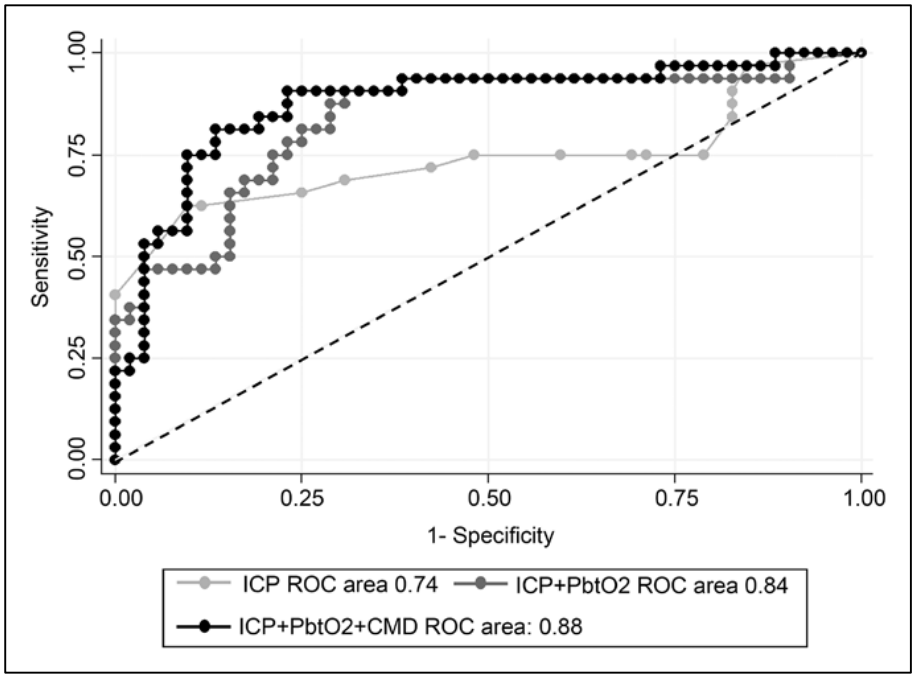


27 TBI patients

Brain Physiologic Variables	Low rCBF (< 35 mL/100 g/min)	Normal rCBF (≥ 35 mL/100 g/min)	*p*
CMD glucose (mmol/L)	0.95 (0.41–2.42)	1.38 (0.64–2.18)	**< 0.01**
CMD glucose < 1 mmol/ (% episodes)	57	22	**< 0.01**
CMD lactate (mmol/L)	3.15 (1.7–5.0)	3.26 (2.1–5.0)	0.22
CMD pyruvate (µmol/L)	106 (62–182)	118 (75–189)	0.15
CMD glutamate (µmol/L)	6.9 (1.1–37.2)	7.0 (2.4–26.4)	0.39
CMD LPR	30 (11–44)	28 (14–35)	0.62
CMD LPR > 40 (% episodes)	14	4	**0.03**
CMD LPR > 25 (% episodes)	70	61	0.24
$Pbto_2$ (mm Hg)[a]	21 (6–33)	27 (14–39)	**< 0.01**
$Pbto_2$ < 20 mm Hg (% episodes)	20	9	**0.04**
$Pbto_2$ < 15 mm Hg (% episodes)	16	5	**0.01**
$Pbto_2$ < 10 mm Hg (% episodes)	7	0	**0.01**
ICP (mm Hg)	15 (3–24)	12 (0–18)	0.11
ICP > 20 mm Hg (% episodes)	30	13	**< 0.01**
CPP (mm Hg)	70 (63–83)	72 (63–83)	0.39
CPP < 60 mm Hg (% episodes)	12	18	0.26

Bouzat et al, Crit Care Med 2015

What is the accuracy of multimodal monitoring to detect hypoperfusion?

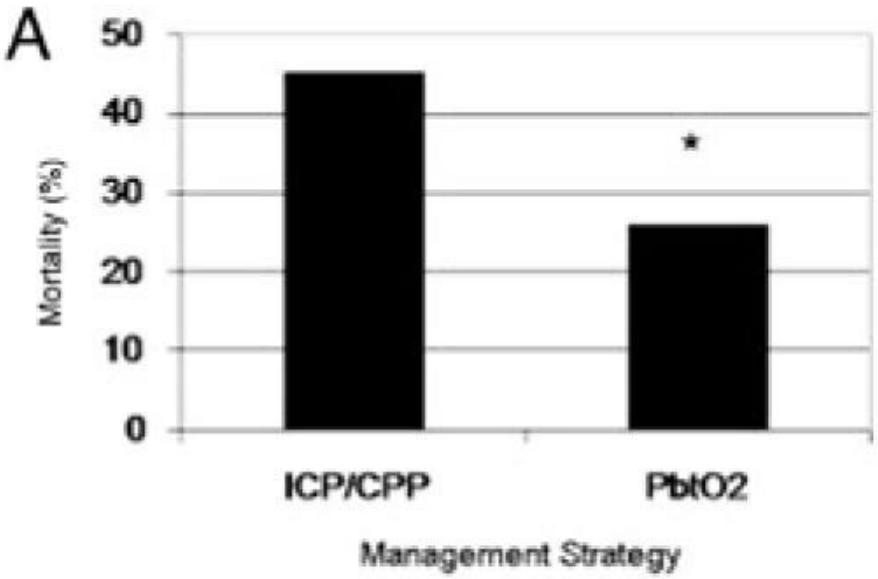


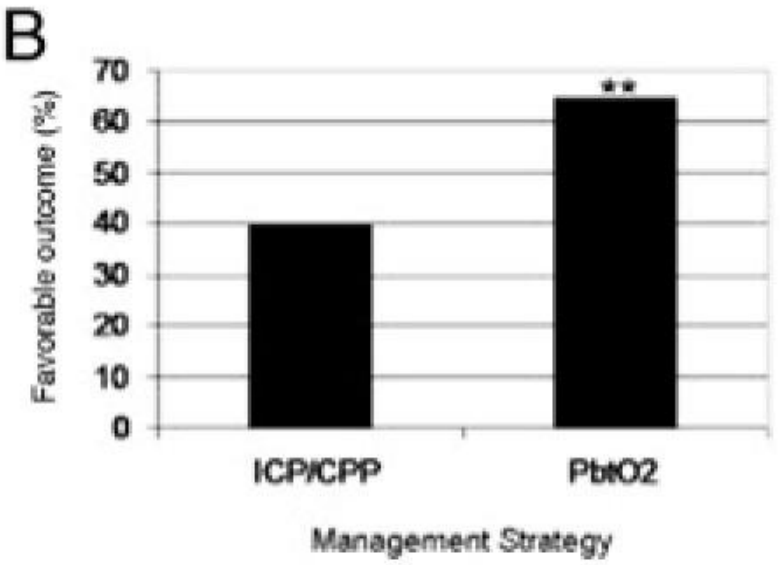
27 TBI patients

Variable	Area Under the ROC Curve	95% CI
ROC curve for ICP monitoring alone	0.74	0.61–0.87
ROC curve for ICP and CMD monitoring	0.79	0.69–0.90
ROC curve for ICP and $Pbto_2$ monitoring	0.84	0.74–0.93
ROC curve for ICP, $Pbto_2$, and CMD monitoring	0.88	0.79–0.96

Bouzat et al, Crit Care Med 2015

Outcome after TBI before and after introduction of $p_{br}O_2$ monitoring





Spiotta, JNS 2010

$p_{br}O_2$ – A metaanalysis in TBI patients

Table 3 Summary outcome from pooled analysis [21–24]

Study first author	Number of patients (evaluated)	ICP and $PbtO_2$-based care		ICP/CPP-based care		Odds ratio (95% CI)	Common odds ratio (95% CI)
		Unfavorable outcome (# patients)	Favorable outcome (# patients)	Unfavorable outcome (# patients)	Favorable outcome (# patients)		
McCarthy et al. [21]	145 (111)	34	29	32	16	1.7	
Meixenberger et al. [22]	93 (91)	18	34	18	21	1.6	
Narotam et al. [23]	180 (166)	44	83	22	17	2.4	
Spiotta et al. [24]	123 (123)	25	45	32	21	2.7	2.1 (1.4–3.1)

Outcome in these studies was reported using the Glasgow outcome score. *ICP* intracranial pressure, *CPP* cerebral perfusion pressure, *$PbtO_2$* brain tissue oxygen monitor, *CI* confidence interval. Patients in the $PbtO_2$ group received both ICP/CPP and $PbtO_2$ guided therapy whereas patients in the ICP/CPP group received only ICP-based care

Nangunoori, Neurocrit Care 2011

BOOST 2: prospective evaluation of a $p_{bt}O_2$- guided therapy after TBI

TBI with GCS 3-8 and requirement of ICP monitoring
10 centers in North America
Both groups received ICP- and Licox- $p_{bt}O_2$- probes

Intervention group:

therapy according to ICP and $p_{br}O_2$ values (ICP < 20 mmHg, $p_{bt}O_2$ > 20 mmHg)

randomized vs.

Control group:

therapy only according to ICP values (ICP < 20 mmHg)

Primary outcome: time of $p_{br}O_2$ < 20 mmHg

Okonkwo et al, CCM 2017

BOOST 2: prospective evaluation of a $p_{bt}O_2$- guided therapy after TBI

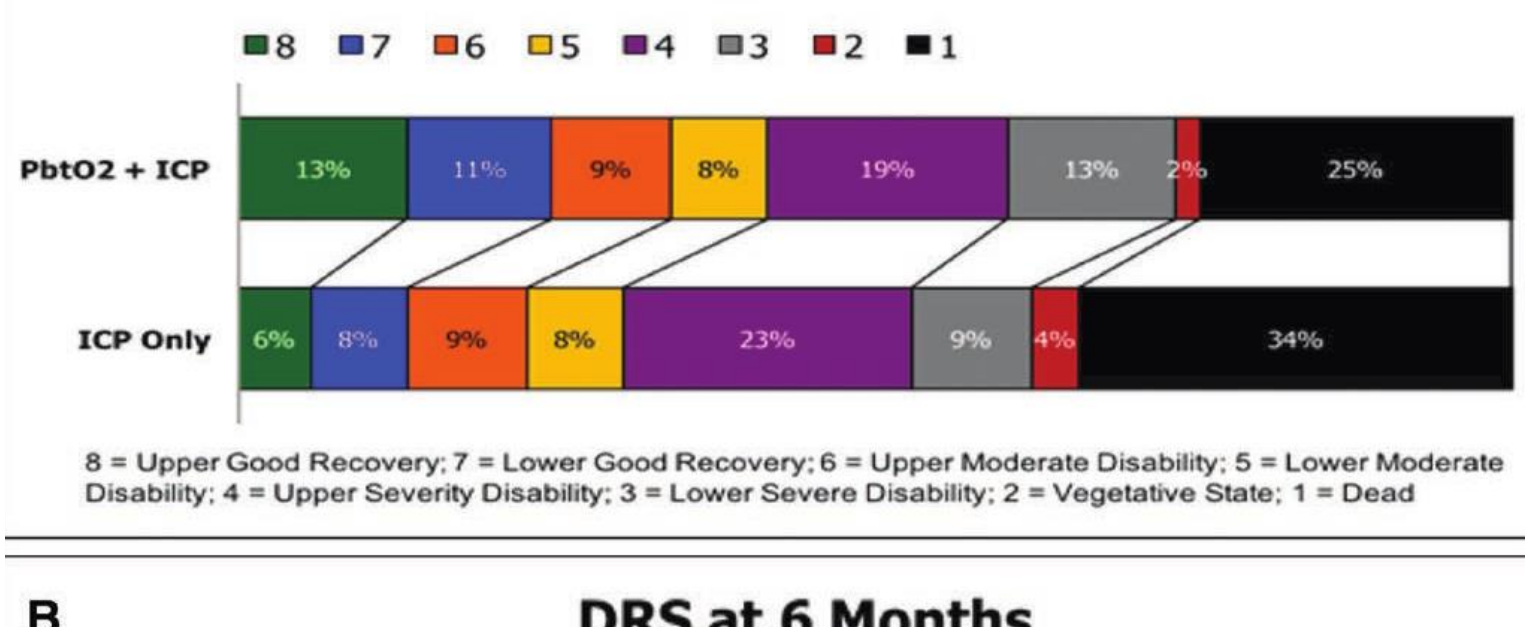
TABLE 2. Brain Tissue Oxygenation and Intracranial Pressure Parameters by Study Group

$PbtO_2$ 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
Intracranial Pressure Metric	**ICP Only, ($n = 57$), Mean ± SD; Median**	**$PbtO_2$ + ICP, ($n = 55$), Mean ± SD; Median**	***p***
Proportion of time above 20 mm Hg	0.15 (0.19); 0.10	0.12 (0.19); 0.04	0.115
Average depth (mm Hg)	1.6 (6.9)[a]; 0.4	0.7 (1.3)[a]; 0.3	0.194
Average depth (mm Hg) (excluding the two extreme outliers)	0.7 (0.9); 0.4	0.6 (0.9); 0.2	0.195
Area under the curve (mm Hg × hr)[b]	103 (408)[a]; 36	50 (88)[a]; 17	0.113
Area under the curve (mm Hg × hr)[b] (excluding the two extreme outliers)	50 (56); 34	41 (59); 15	0.115

Time of compromized $p_{bt}O2$ and ICP lower in the ICP+$p_{br}O_2$ group

Okonkwo et al, CCM 2017

BOOST 2: prospective evaluation of a $p_{bt}O_2$- guided therapy after TBI



Mortality and worse outcome (GOSe) lower in the ICP+$p_{bt}O_2$ group (p = ns)

Okonkwo et al, CCM 2017

Summary

- ICP and $p_{bt}O_2$ are outcome-relevant after TBI
- Weak evidence behind current Brain Trauma Foundation guidelines
- $p_{bt}O_2$ offers the opportunity of an individualized treatment
- More robust data than for other monitoring tools (NIRS, rCBF, $S_{jv}O_2$...)

- Goals: ICP < 20 mmHg, $p_{bt}O_2$ > 20 mmHg

Practical tips:

- Whom to monitor: severely affected, but salvagable patients
- Not every patient is salvable – and not every low $p_{bt}O_2$ leads to worse outcome
- Outcome effects are difficult to see and most likely lower than anticipated

just in case: stefan.wolf@charite.de