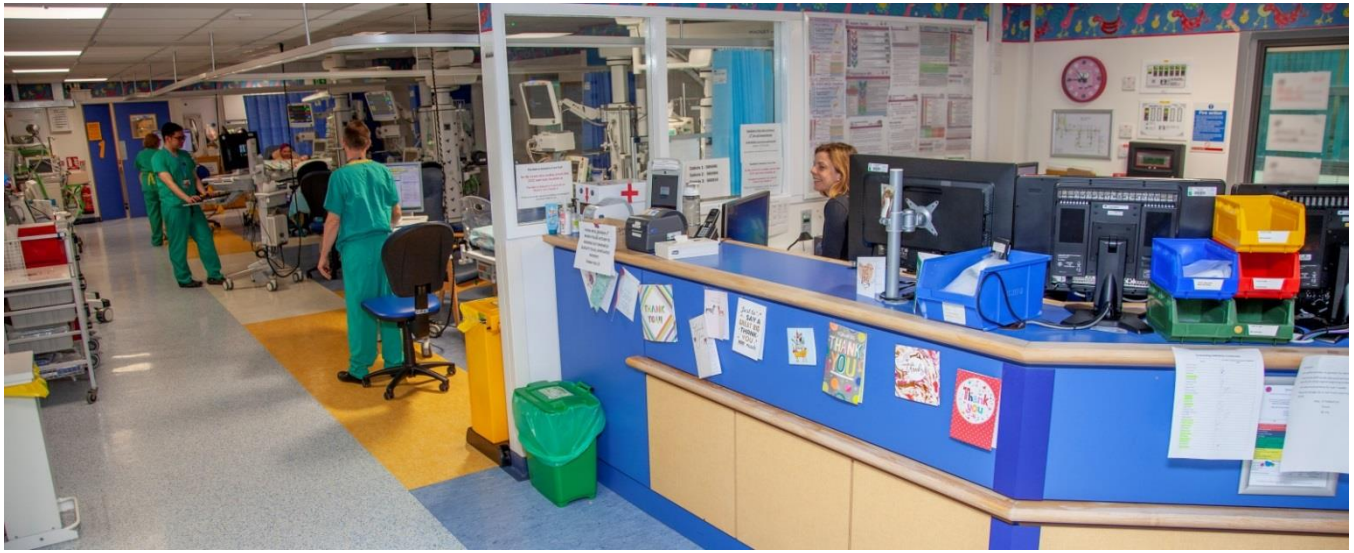
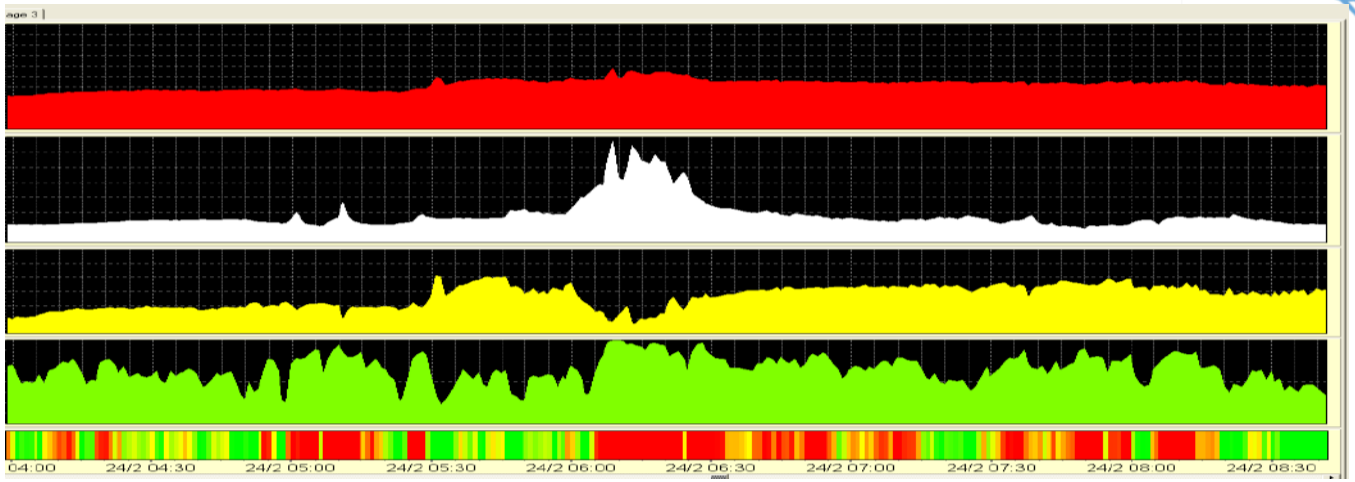


PICU monitoring with



UNIVERSITY OF CAMBRIDGE

Cambridge University Hospitals NHS
NHS Foundation Trust

Scale of Problem

- Brain injury kills five times more children than cancer
- Nearly 25% PICU adm: risk of acute neurological injury
- High incidence of traumatic brain injury (TBI)
  - In US: 35,000 severe TBI and 7440 deaths/yr (CDC)
- Apprx 50% poor neurological outcomes at 6 mo
- Mean age ~ 9 yrs, productive life-years 1.3 million/yr

PCCM 2011;12:601-2
Neurotherapeutics 2012;9:3-16

Trauma

Infection/
inflammation

Neuro-
Oncology

Hypoxic-
ischemic insult

Trau

fection/
mation

Secondary Insult

Neuro-
Oncology

Hypoxic-
ischemic insult

Critical Illness induced acute neurological injury

Tra

ection/
mation

Secondary Insult

Neuro-
Oncology

Hypoxic-
ischemic insult

Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation Guidelines, Executive Summary

TABLE 1. Updated Recommendations: Monitoring

Topics	Recommendations
Intracranial pressure monitoring	**Level III** **To Improve Overall Outcomes** III.1. Use of ICP monitoring is suggested.
Advanced neuromonitoring	**Level III** **To Improve Overall Outcomes** III.1. If $Pbro_2$ monitoring is used, maintaining a level > 10 mm Hg is suggested. *Note 1: There was insufficient evidence to support a recommendation for the use of a monitor of Po_2 in brain interstitium ($Pbro_2$) to improve outcomes.* *Note 2: Use of advanced neuromonitoring (brain oxygenation) should only be for patients with no contraindications to invasive neuromonitoring, such as coagulopathy, and for patients who do not have a diagnosis of brain death.*
Neuroimaging	**Level III** **To Improve Overall Outcomes** *III.1. Excluding the possibility of elevated ICP on the basis of a normal initial (0–6 hr after injury) CT examination of the brain is not suggested in comatose pediatric patients.* III.2. Routinely obtaining a repeat CT scan > 24 hr after the admission, and initial follow-up is not suggested for decisions about neurosurgical intervention, unless there is either evidence of neurologic deterioration or increasing ICP.

Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation

TABLE 2. Updated Recommendations: Thresholds

Topics	Recommendations
Threshold for treatment of intracranial hypertension	**Level III** **To Improve Overall Outcomes** III.1. Treatment of intracranial pressure targeting a threshold of < 20 mm Hg is suggested.
Thresholds for cerebral perfusion pressure	**Level III** **To Improve Overall Outcomes** III.1. Treatment to maintain a CPP at a minimum of 40 mm Hg is suggested. III.2. A CPP target between 40 and 50 mm Hg is suggested to ensure that the minimum value of 40 mm Hg is not breached. There may be age-specific thresholds with infants at the lower end and adolescents at or above the upper end of this range.
	Note 2: Use of advanced neuromonitoring (brain oxygenation) should only be for patients with no contraindications to invasive neuromonitoring, such as coagulopathy, and for patients who do not have a diagnosis of brain death.
Neuroimaging	**Level III** **To Improve Overall Outcomes** *III.1. Excluding the possibility of elevated ICP on the basis of a normal initial (0–6 hr after injury) CT examination of the brain is not suggested in comatose pediatric patients.* III.2. Routinely obtaining a repeat CT scan > 24 hr after the admission, and initial follow-up is not suggested for decisions about neurosurgical intervention, unless there is either evidence of neurologic deterioration or increasing ICP.

J Neurosurg 83:949–962, 1995

Cerebral perfusion pressure: management protocol and clinical results

MICHAEL J. ROSNER, M.D., SHEILA D. ROSNER, R.N., M.S.N., AND ALICE H. JOHNSON, R.N., B.S.N.

Division of Neurological Surgery, Department of Surgery, University of Alabama at Birmingham, Birmingham, Alabama

Intensive Care Med (2006) 32:1475–1484
DOI 10.1007/s00134-006-0294-3

REVIEW

Per-Olof Grände

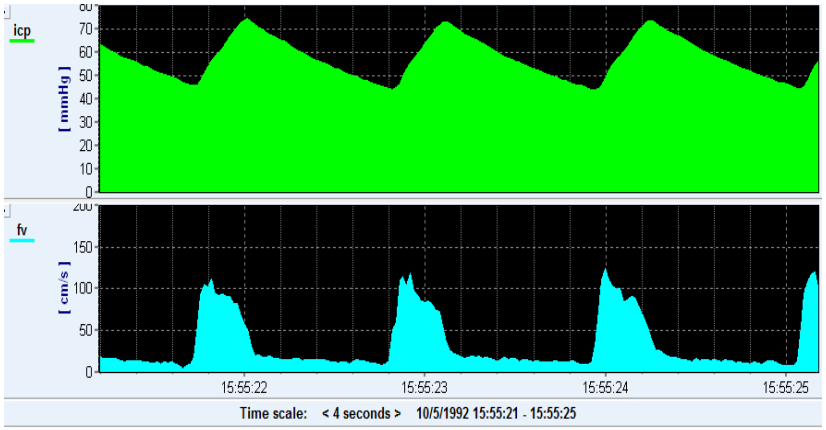
The "Lund Concept" for the treatment of severe head trauma – physiological principles and clinical application

CPP above : 70? ....65?...

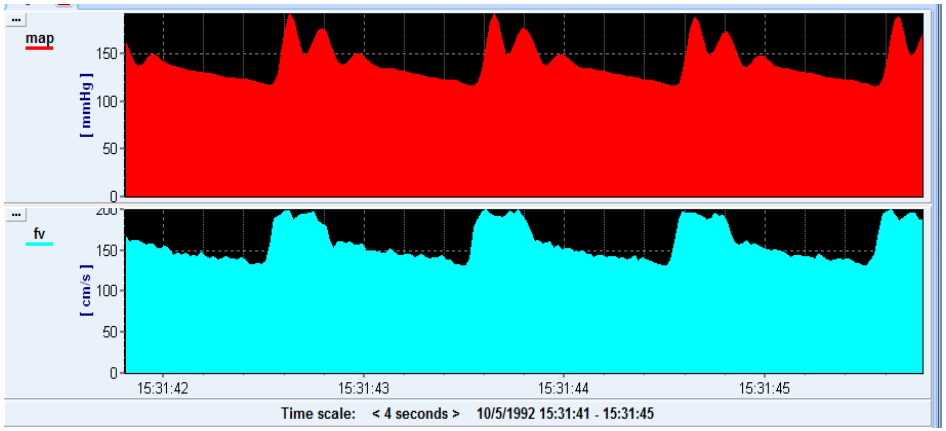
CPP may be low; ICP<15 mmHg

Set thresholds: Is it wise?

Too low CPP: ischaemia

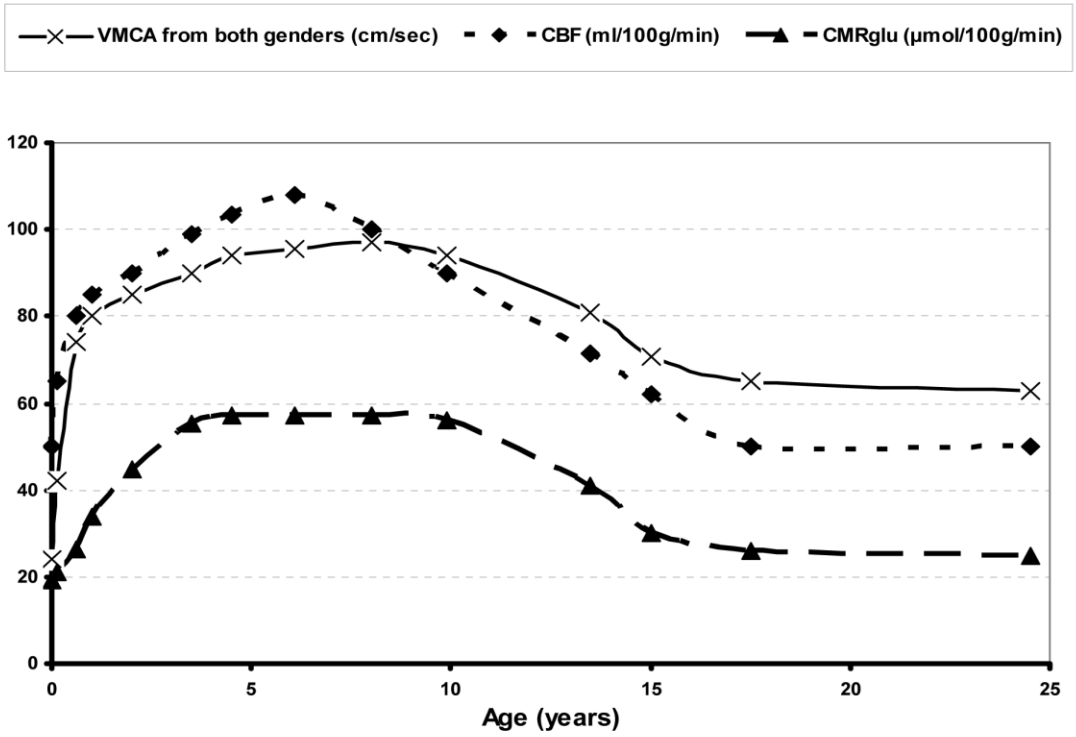


Too high CPP: hyperaemia



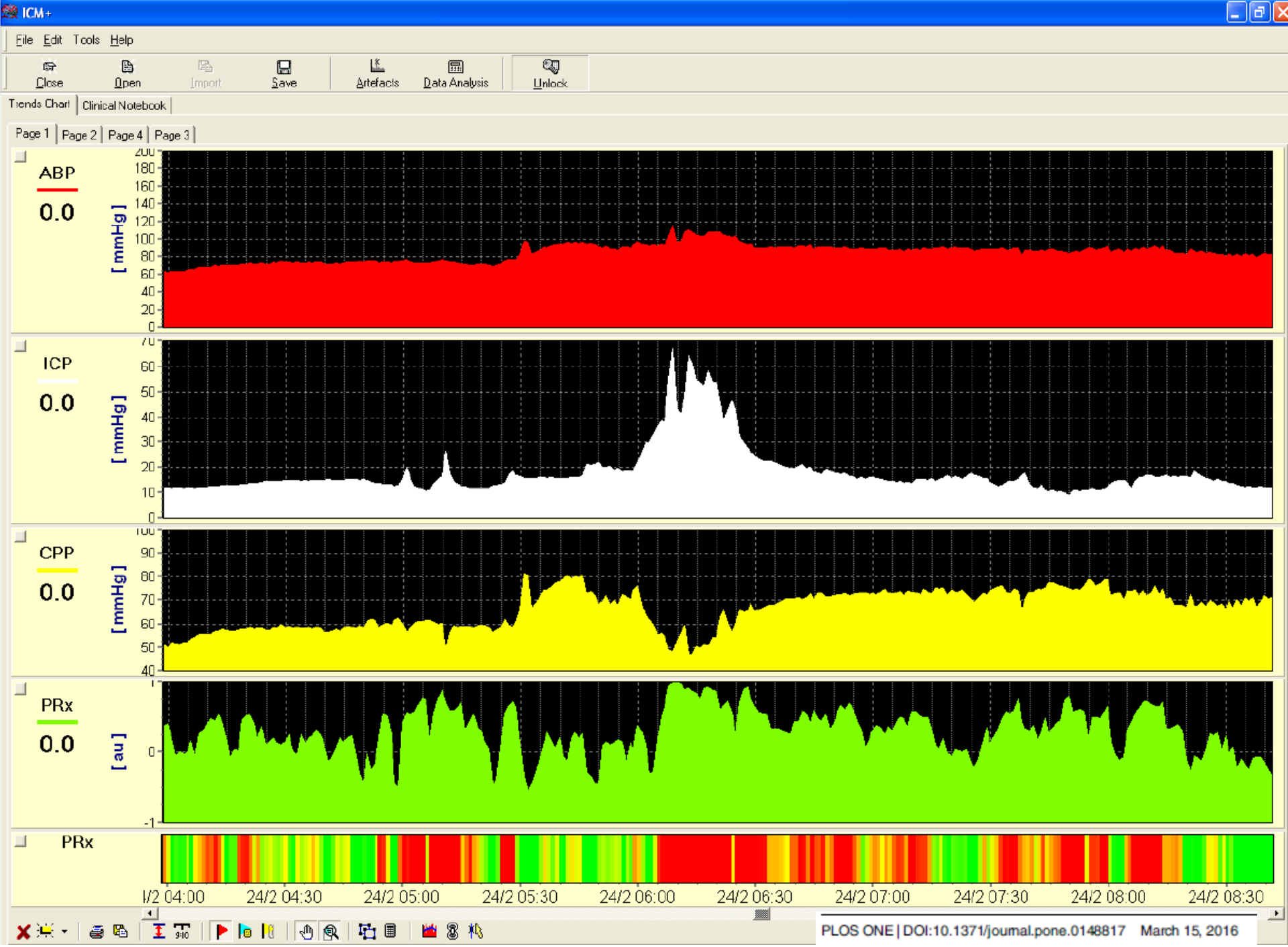
Cerebrovascular Dynamics in Children

- Age/gender related differences: ICP, CBF, CA
- LLA may not be lower in lower age groups
- Association of autoregulation with outcome
- Impaired CA in 29-63% paediatric TBI

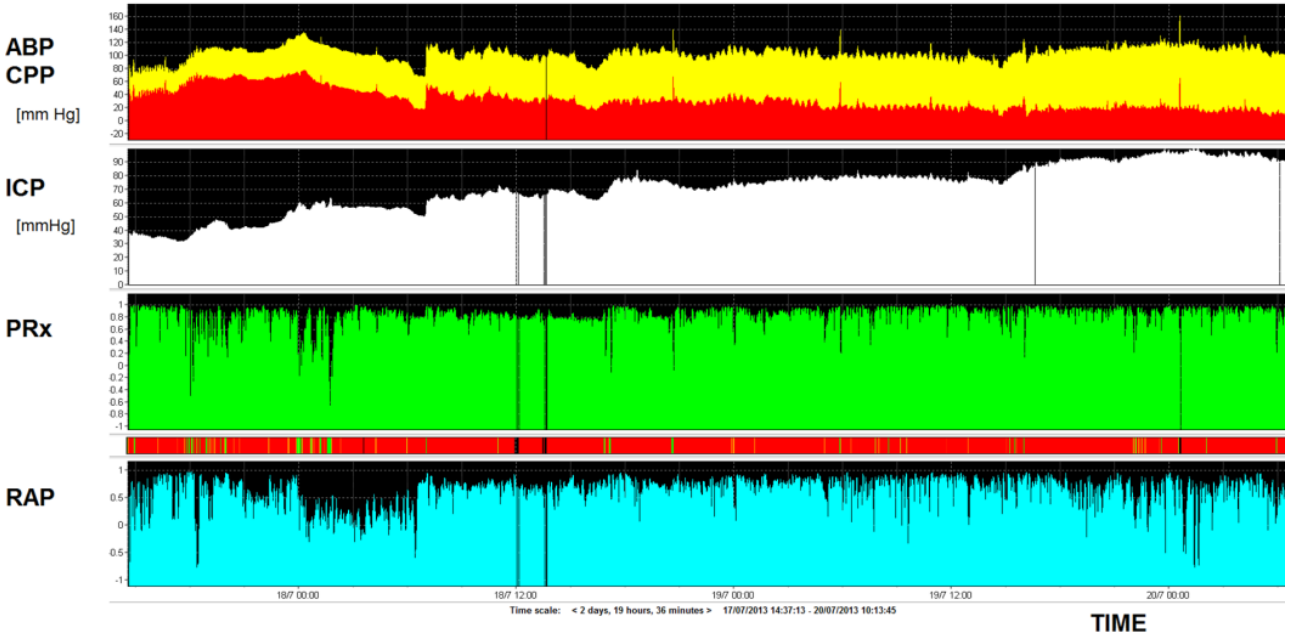


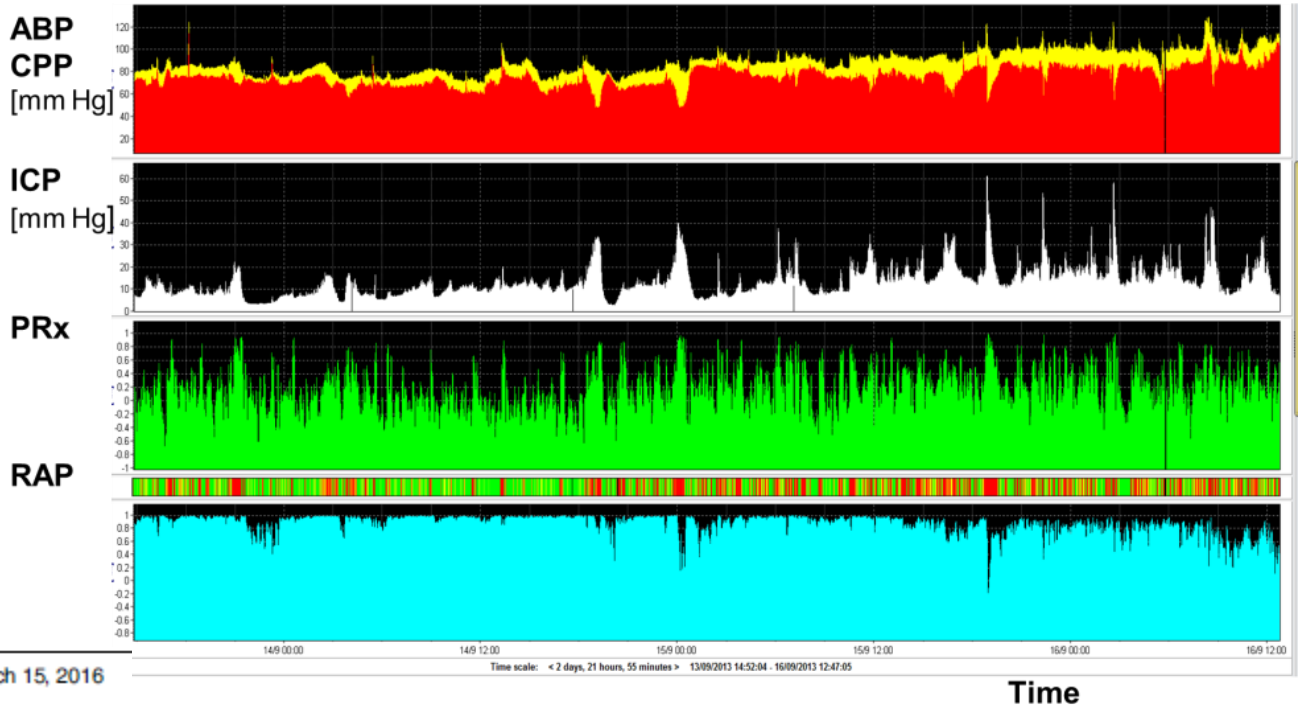
Age-related changes in mean flow velocity of middle cerebral artery (VMCA) in both genders, cerebral blood flow (CBF), cerebral metabolic rate of glucose (CMRglu) (Adult values: VMCA ~ 50 cm/sec, CBF 50 ml/100g/min, CMRglu 19-33 µmol/100g/min)

Pediatr Neurol 2008;38:225-34



PLOS ONE | DOI:10.1371/journal.pone.0148817 March 15, 2016


ABP
CPP
[mm Hg]
ICP
[mmHg]
PRx
RAP
18/7 00:00
18/7 12:00
19/7 00:00
19/7 12:00
20/7 00:00
Time scale: < 2 days, 19 hours, 36 minutes > 17/07/2013 14:37:13 - 20/07/2013 10:13:45
TIME


ABP
CPP
[mm Hg]
ICP
[mm Hg]
PRx
RAP
14/9 00:00
14/9 12:00
15/9 00:00
15/9 12:00
16/9 00:00
16/9 12:00
Time scale: < 2 days, 21 hours, 55 minutes > 13/09/2013 14:52:04 - 16/09/2013 12:47:05
Time

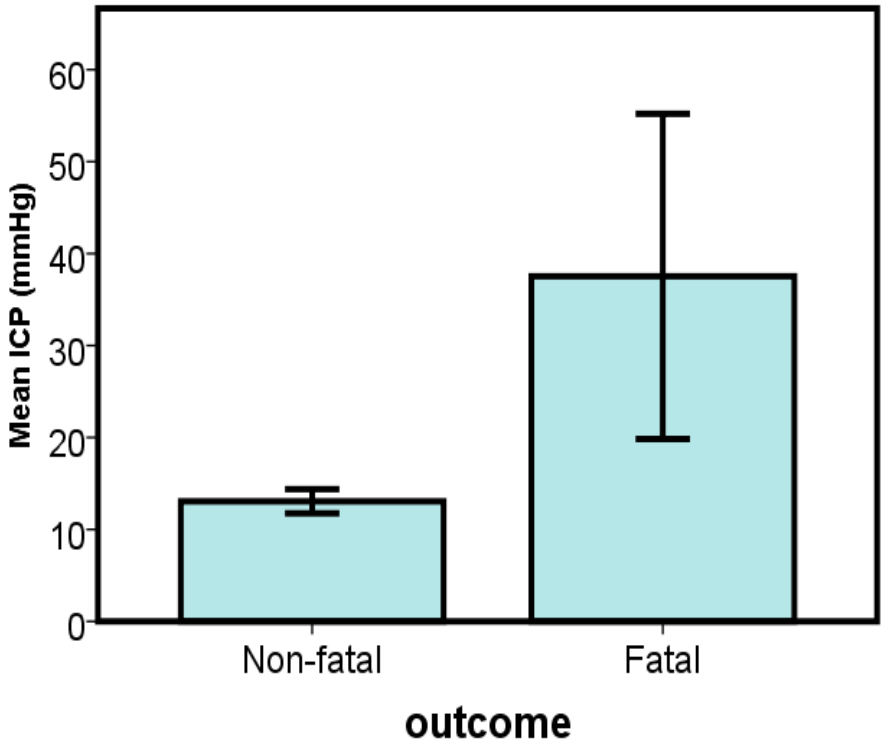
RESEARCH ARTICLE

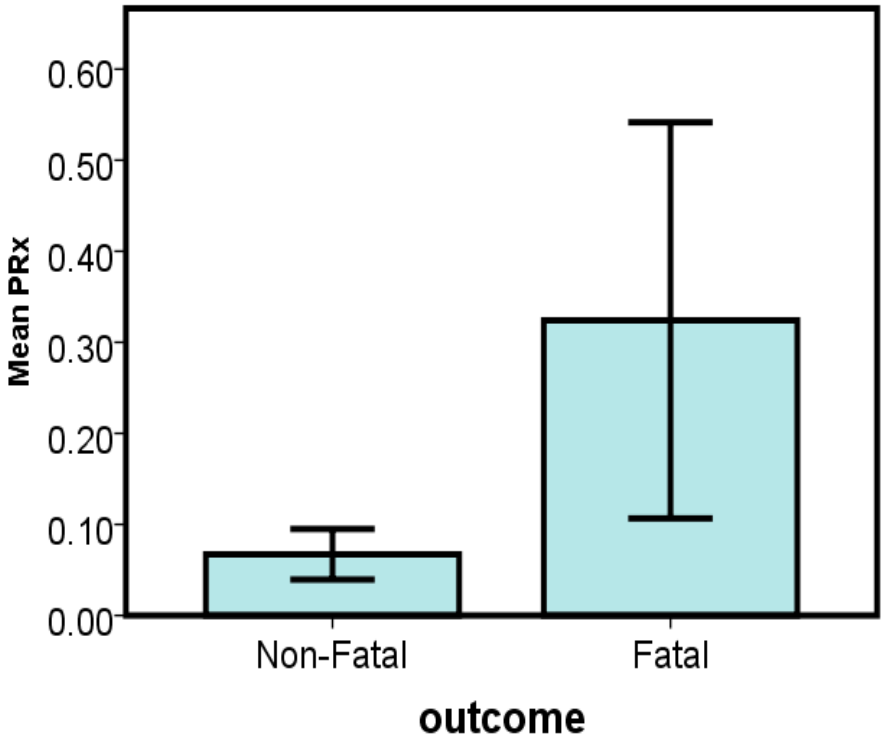
Continuous Multimodality Monitoring in Children after Traumatic Brain Injury—Preliminary Experience

Adam M. H. Young[1]*, Joseph Donnelly[1], Marek Czosnyka[1,3], Ibrahim Jalloh[1], Xiuyun Liu[1], Marcel J. Aries[1,4], Helen M. Fernandes[1], Matthew R. Garnett[1], Peter Smielewski[1], Peter J. Hutchinson[1], Shruti Agrawal[2]

- N=12 (8 survivors)

	Survivors (n = 7)		Non-survivors (n = 5)		P-value
	Median	IQR	Median	IQR	Mann-Whitney
ICP (mm Hg)	13.07	3.23	21.64	42.90	0.003
%time ICP > 20 mm Hg	9.73	9.84	60.47	67.40	0.003
MAP (mm Hg)	77.07	17.69	93.00	24.23	0.11
CPP (mm Hg)	63.42	8.10	61.11	38.62	0.91
CPPopt (mm Hg)	63.68	8.94	66.45	18.70	0.48
PRx (a.u.)	0.02	0.19	0.39	0.62	0.02
RAP (a.u.)	0.64	0.27	0.46	0.43	0.11
%time CPPopt available	55.96	13.84	43.48	28.32	0.02
Duration (hours)	75.3	22.3	82.3	61.8	0.87
%time CPPopt available	55.96	13.84	43.48	28.32	0.02
%time CPP-CPPopt < -10 mm Hg	4.70	5.68	15.17	30.74	0.04
%time CPP-CPPopt -10 to 10 mm Hg	90.68	12.64	70.61	21.78	0.02
%time CPP-CPPopt > 10 mm Hg	5.09	10.03	11.62	16.9	0.76





PLOS ONE | DOI:10.1371/journal.pone.0148817 March 15, 2016

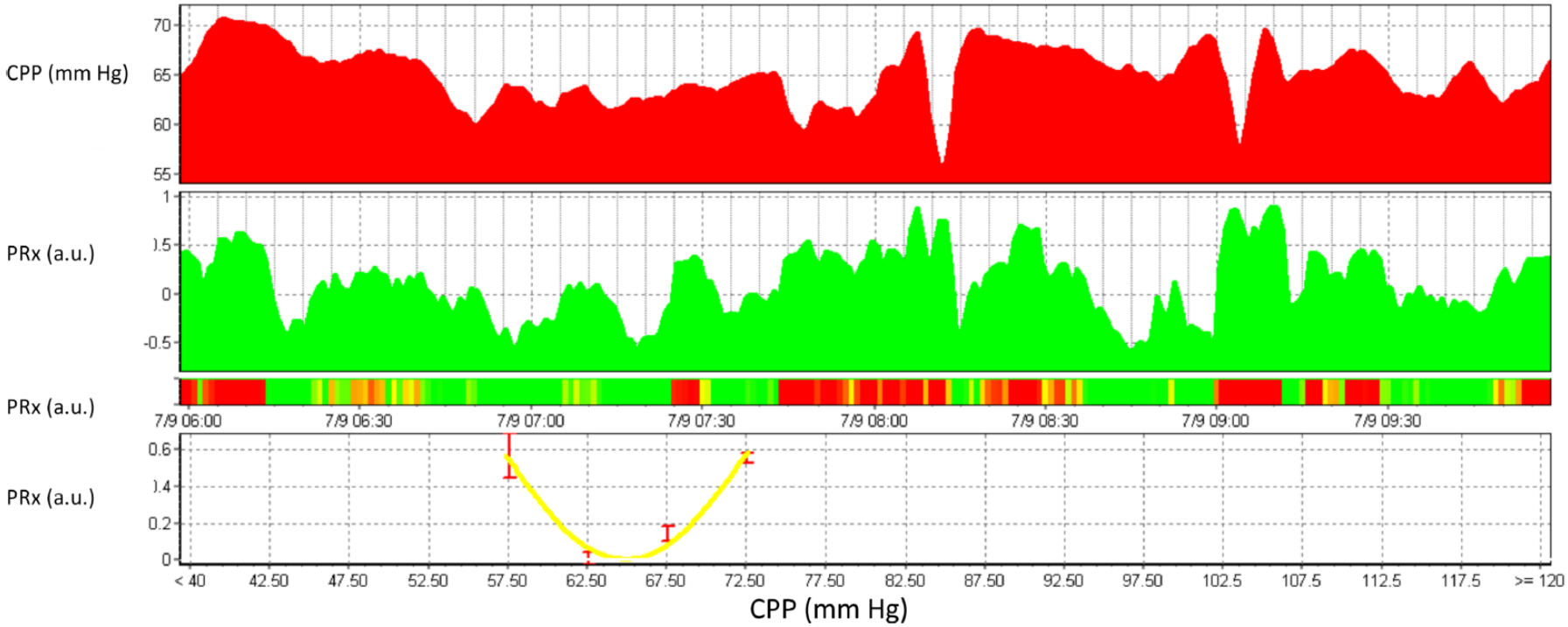


Fig 2. Example of a 4 hour epoch of multimodality monitoring signals in pediatric TBI. In this screenshot, CPP is shown in the top panel and the pressure reactivity index in the second panel over a 4 hour period from 06:00 to 10:00. In the third panel is a risk chart whereby a negative PRx (good autoregulation) is denoted by a grey colour, and a disturbed PRx (>0.3) is denoted in black. In two instances, CPP drops below 60 mm Hg. During these drops in CPP, PRx is deranged (black on the risk chart). On the bottom panel, CPP is plotted against PRx and a polynomial curve is fitted. The minimum of this curve is around 65 mm Hg, which would therefore indicate the optimal CPP at time point 10:00.

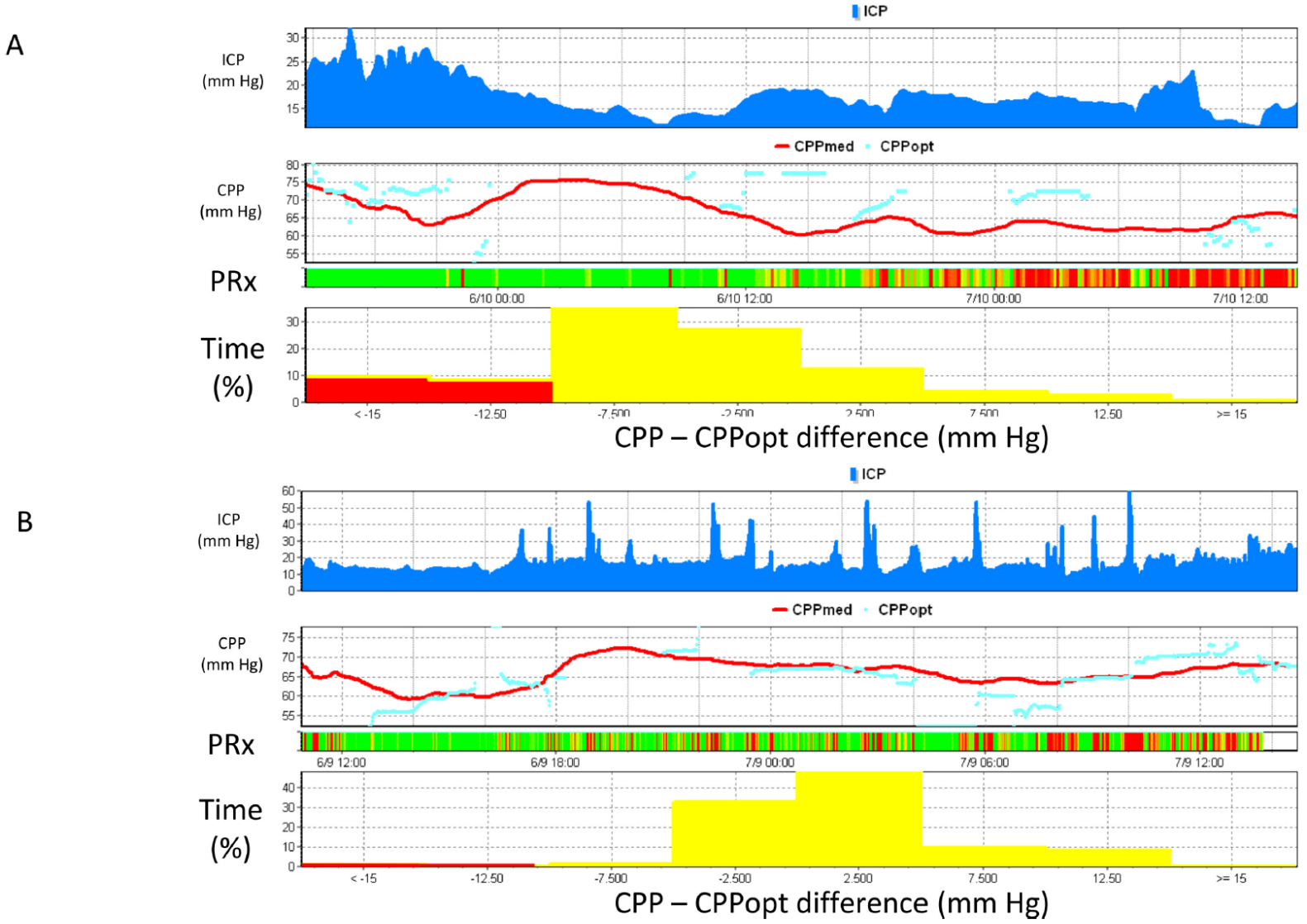
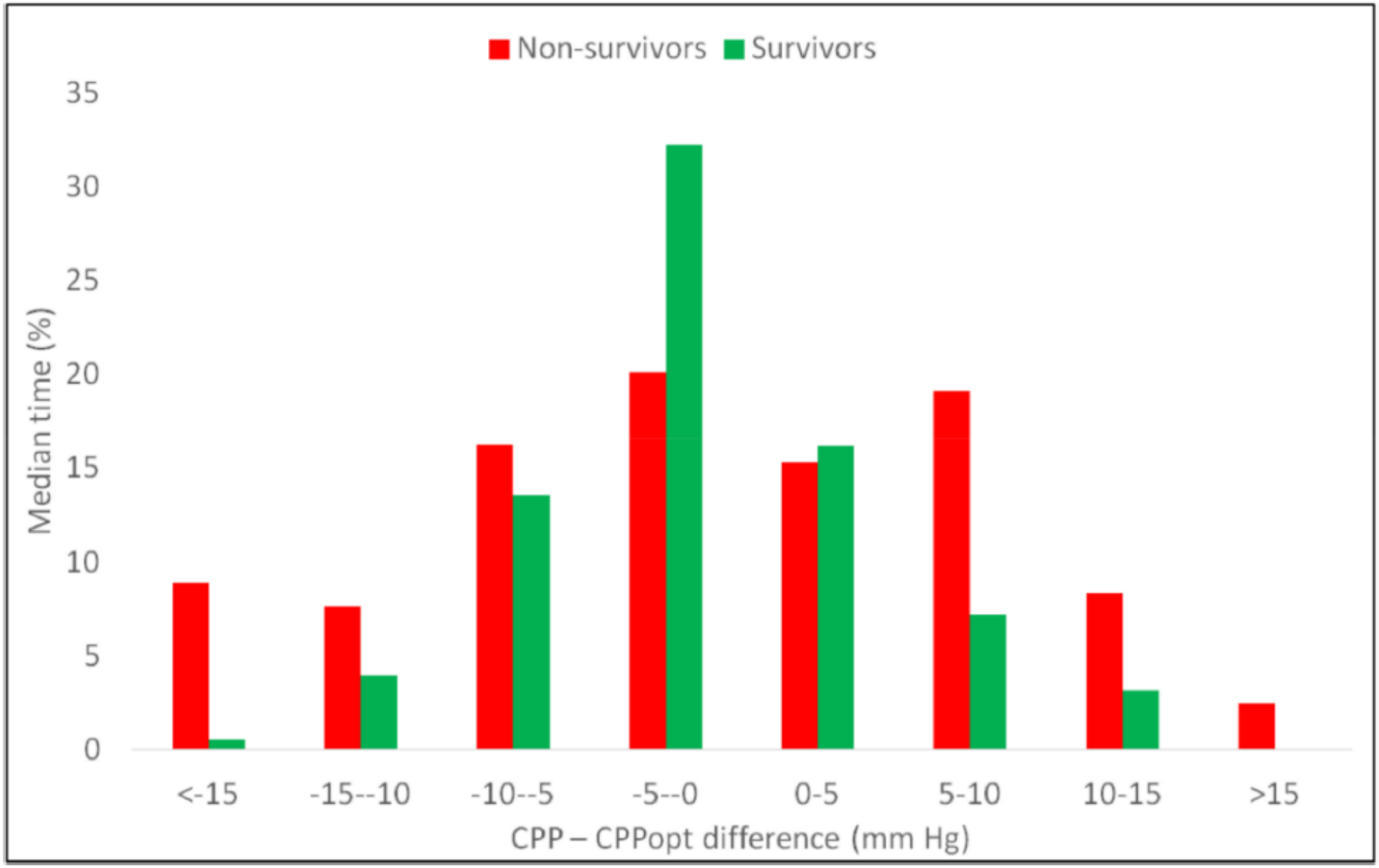


Fig 3. Real-time calculation of CPPoptimal in-vivo. Fig 3A is an example of a pediatric TBI patient. ICP is displayed in the top panel, followed by CPP (both the absolute CPP (line) and the calculated CPPopt (circles)), a risk chart of PRx and finally a histogram indicating the time spent at various distances from the calculated optimal CPP. Although this patients CPP was above 60 mm Hg for the whole of this recording, CPP was consistently below the calculated optimal CPP. This is depicted in the histogram which indicates that over this 2 day period, the patient spent almost 20% of time (expressed as a percentage of the total time CPPopt available) > 10 mm Hg below the instantaneous CPPopt. In the second day of this recording we see persistently disturbed PRx. This patient died three days after admission. Fig 3B shows an analogous example in another pediatric TBI patient. This patient demonstrated multiple plateau waves of ICP and a CPP between 60 and 70 mm Hg. Autoregulation as indicated by the PRx risk chart was mainly good. CPP was mainly close to the calculated optimal CPP as seen in both in the time series view (panel 2) and in the CPP-CPPopt time-histogram (bottom panel). This patient survived.


Non-survivors
Survivors
35
30
25
20
15
10
5
0
Median time (%)
<-15
-15--10
-10--5
-5--0
0-5
5-10
10-15
>15
CPP – CPPopt difference (mm Hg)

Sample Size calculation

- Based on our paediatric TBI experience
- Mean (± SD) PRx of 0.03 ± 0.13 for favourable outcome and mean (± SD) PRx of 0.10 ± 0.17 (SD) for unfavourable outcome
- One sided analysis, favourable: unfavourable ratio of 0.77 (80% power and alpha error of 5% & allowance for losses (protocol violations, withdrawal of consent, or loss of FU)
- Total: 135 patients.

action medical research for children

act Addenbrooke's Charitable Trust

STARSHIP

Studying Trends of AutoRegulation in Severe Head Injury in Paediatrics

STARSHIP

- Multicentre UK study: 10 sites
  - 135 patients over 3 years with one year follow-up
  - Objectives:
    - Primary: Optimal PRx with 12 mo outcome (GOSE peds)
    - Secondary: Optimal CPP
    - Research Database

STARSHIP

- 16 years or younger admitted to PICU
- TBI confirmed on CT or MRI
- Clinical requirement for monitoring ICP &ABP
- No exclusion criteria
- Consent for Follow-up before hospital discharge

STARSHIP: Sites

Cambridge University Hospitals (Sponsor)	Dr Shruti Agrawal (CI)
Birmingham Children's Hospital	Dr Hari Krishnan
Great Ormond Street Hospitals	Dr Harish Bangalore
Leeds Children's Hospital	Dr Santosh Sundarajan
Manchester Children's Hospital	Dr Gayathri Subramaniam
Nottingham Children's Hospital	Dr Dusan Raffaj
Oxford University Hospitals	Dr Avishay Sarfatti
Royal London Hospital	Dr Simona Lampariello
Sheffield Children's Hospital	Dr Anton Mayer
Southampton Children's Hospital	Dr Oliver Ross

STARSHIP

Progress (8th September 2019)

- Software licensing fee for ICM+ waivered for study
- Hardware supplies by Academic Neurosciences, Cambridge
- Study live from 1st July 2018, 10/10 sites set-up and recruiting
- 53 patients recruited, 2 refused consent, 2 technical problems
- Collaboration with KidsBrainIT.

Plateau waves in children

- 42 TBI patients 16 years old and younger
- Plateau waves:
  - ↑ICP > 40 for at least 5 minutes
  - Mean ICP < 25, 30 min prior to plateau wave
  - ↓ CPP > 15 from before to during plateau
  - ↓ ICP < 25, in 30 min following the plateau wave.

	Before plateau	During plateau	p-value
ICP (mm Hg)	17.50 (0.55)	45.15 (0.85)	<0.001
MAP (mm Hg)	88.34 (1.81)	92.61(2.41)	<0.001
CPP (mm Hg)	70.67 (1.91)	48.61 (2.24)	<0.001
PRx (a.u.)	-0.07 (0.03)	0.50 (0.06)	<0.001
$ETCO_2$ (mm Hg)	32.02 (0.61)	33.21 (0.71)	<0.001
HR (BPM)	89.68 (3.02)	88.65 (2.96)	0.9
HFrPow (a.u.)	0.97 (0.18)	1.03 (0.11)	0.74
LFHF (a.u.)	1.18 (0.20)	1.21 (0.14)	0.89
BRS (ms/mm Hg)	8.91 (1.31)	14.33 (4.38)	0.22

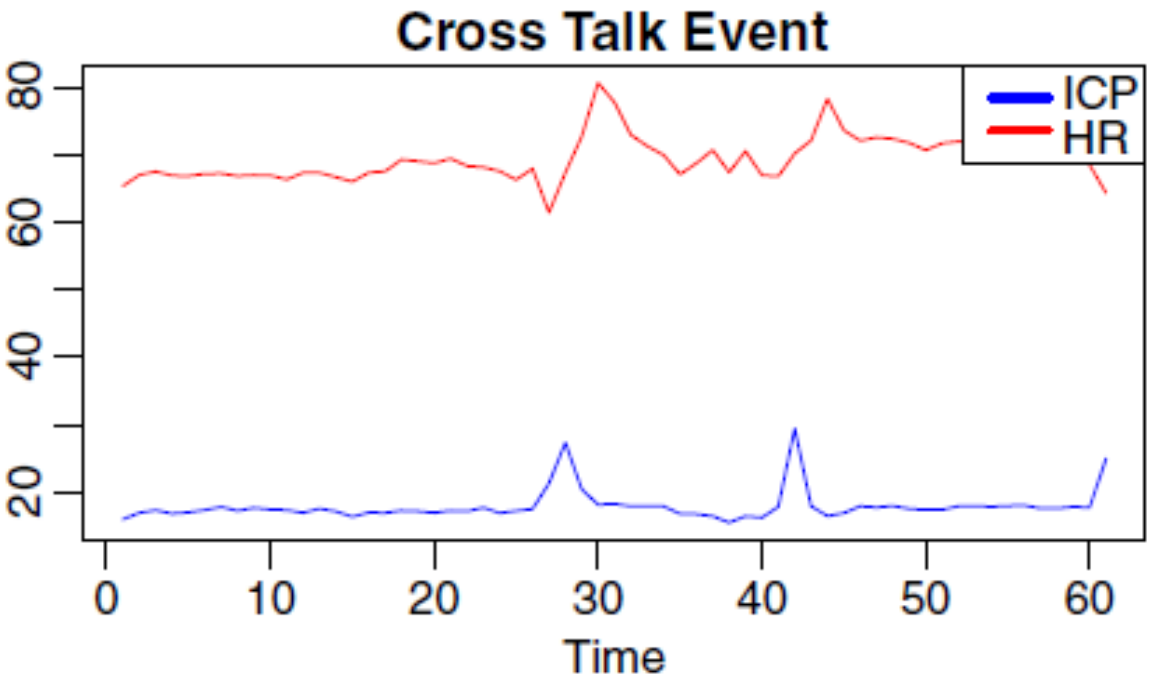
Plateau waves as frequent as in adult TBI.

Associated with ↑ $ETCO_2$ or ↑/↓ MAP.

Short-lived plateau did not affect prognosis

A multiplex network approach for the analysis of intracranial pressure and heart rate data in traumatic brain injured patients

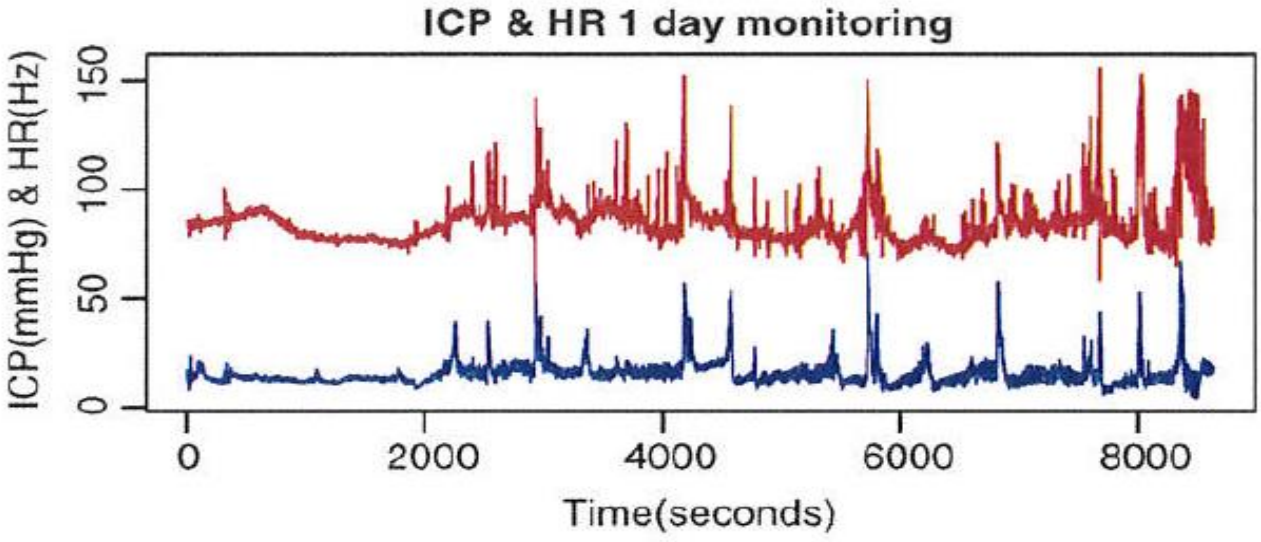
Giovanna Maria Dimitri*, Shruti Agrawal, Adam Young, Joseph Donnelly, Xiuyun Liu, Peter Smielewski, Peter Hutchinson, Marek Czosnyka, Pietro Lió and Christina Haubrich



Simultaneous Transients of Intracranial Pressure and Heart Rate in Traumatic Brain Injury: Methods of Analysis.

Dimitri GM[1], Agrawal S[2], Young A[3], Donnelly J[4], Liu X[4], Smielewski P[4], Hutchinson P[3], Czosnyka M[4], Lio P[1], Haubrich C[5,6].

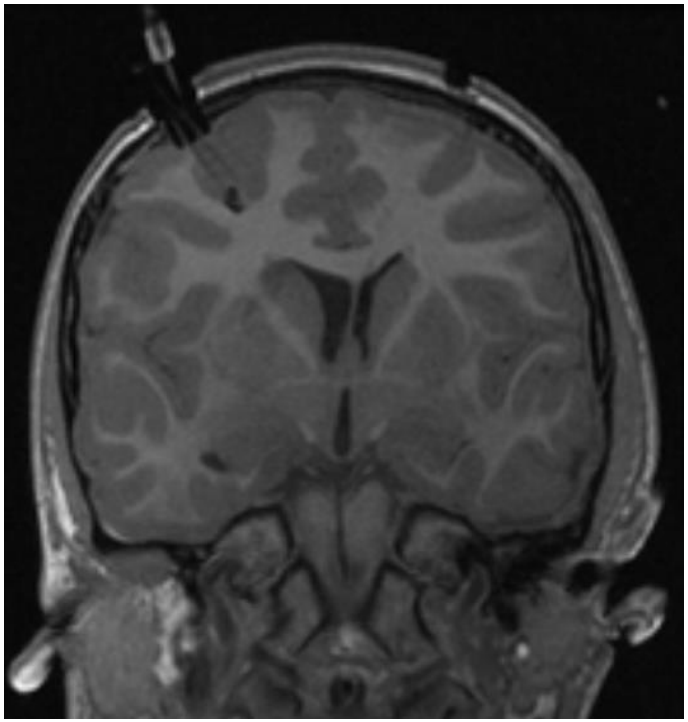
P1	P2	P3	P4	P5	P6	P7	P8	P9
17	32	65	20	1	23	22	43	55
P10	P11	P12	P13	P14	P15	P16	P17	P18
67	20	142	27	29	7	35	2	0
P19	P20	P21	P22	P23	P24	P25	P26	P27
1	19	188	55	2	15	0	14	17



Acta Neurochir Suppl. 2018;126:147-151. doi: 10.1007/978-3-319-65798-1_31.

Advanced Neuromonitoring in PTBI

- 10 patients > 3 years old with severe TBI
- Triple bolt: ICP, $PBtO_2$ and microdialysis catheter
- Glucose, lactate, pyruvate, glutamate and glycerol



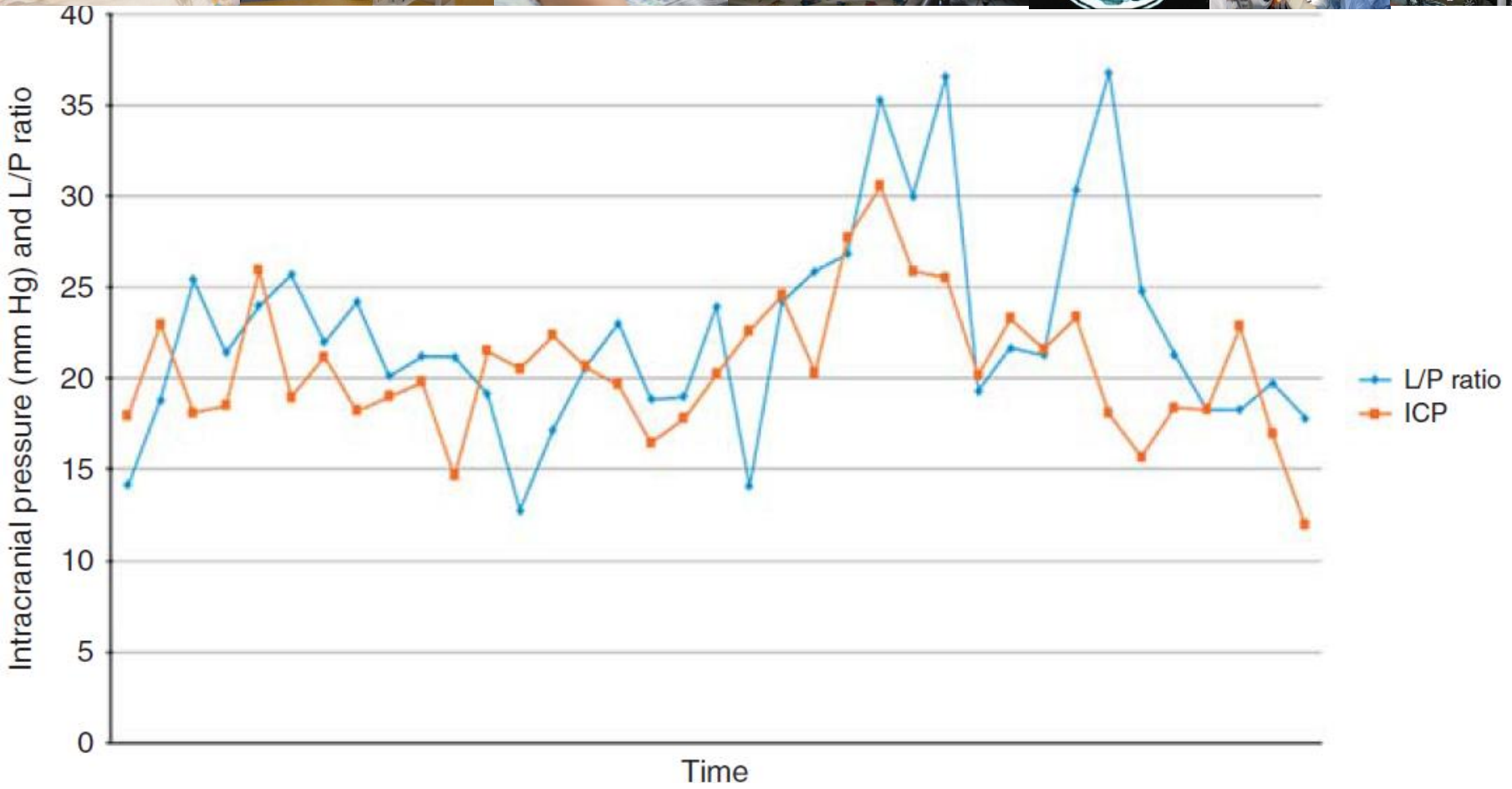
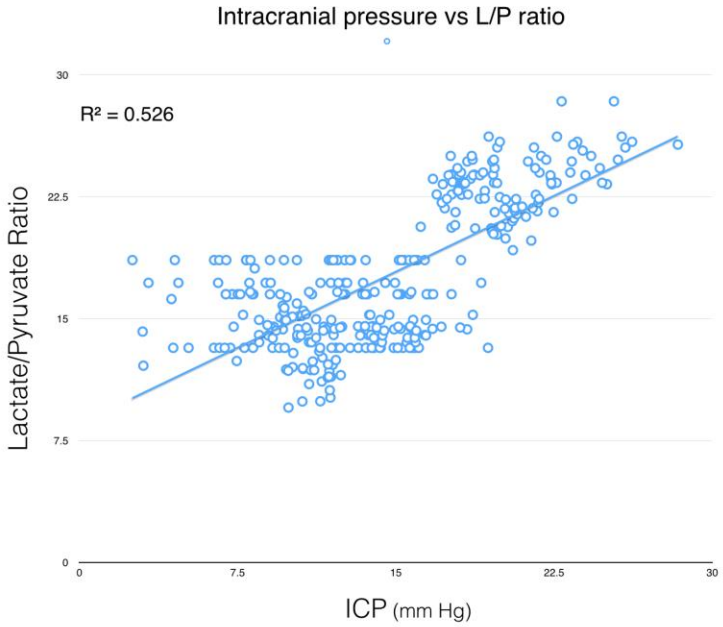


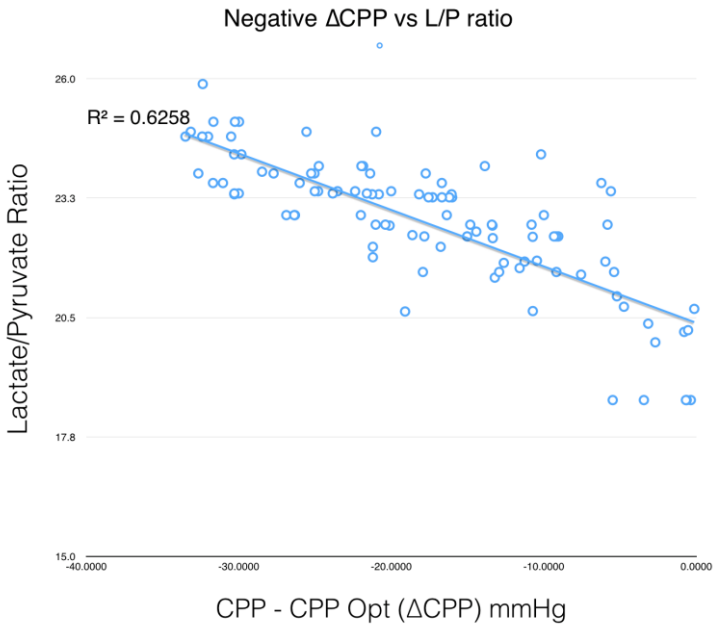
Figure 4. Time line of intracranial pressure (ICP) and microdialysis trace. This is a 7-year-old girl sustained severe traumatic brain injury (TBI) with moderate diffuse axonal injury (Marshall grade 3) on initial computed tomography (CT) scan. The timeline points represent 2-h sampling averages. A clear lag of one sampling point can be observed between the measured ICP and the lacate/pyruvate ratio.

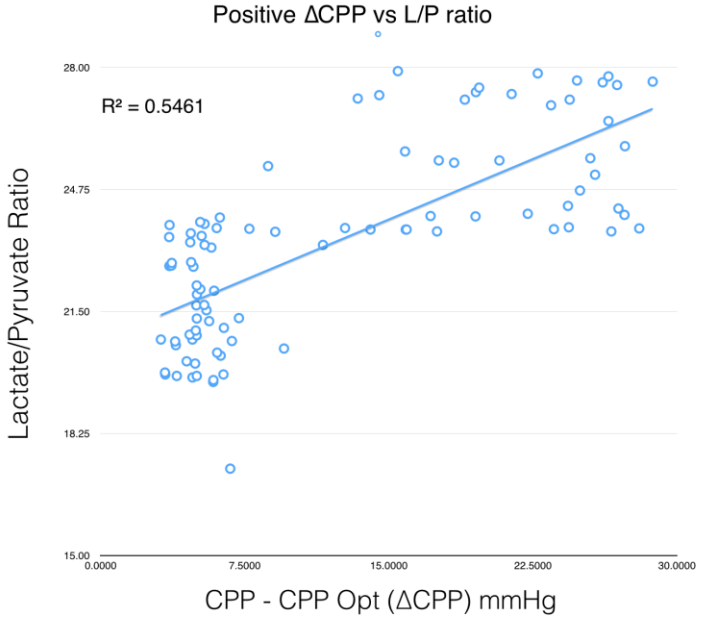
Multimodality neuromonitoring in severe pediatric traumatic brain injury

Adam M.H. Young[1], Mathew R. Guilfoyle[1], Joseph Donnelly[1], Peter Smielewski[1], Shruti Agarwal[2], Marek Czosnyka[1] and Peter J. Hutchinson[1]

Volume 83 | Number 1 | January 2018 Pediatric RESEARCH


Intracranial pressure vs L/P ratio
R² = 0.526
Lactate/Pyruvate Ratio
ICP (mm Hg)
30
22.5
15
7.5
0
0
7.5
15
22.5
30


Negative ΔCPP vs L/P ratio
R² = 0.6258
Lactate/Pyruvate Ratio
CPP - CPP Opt (ΔCPP) mmHg
26.0
23.3
20.5
17.8
15.0
-40.0000
-30.0000
-20.0000
-10.0000
0.0000


Positive ΔCPP vs L/P ratio
R² = 0.5461
Lactate/Pyruvate Ratio
CPP - CPP Opt (ΔCPP) mmHg
28.00
24.75
21.50
18.25
15.00
0.0000
7.5000
15.0000
22.5000
30.0000

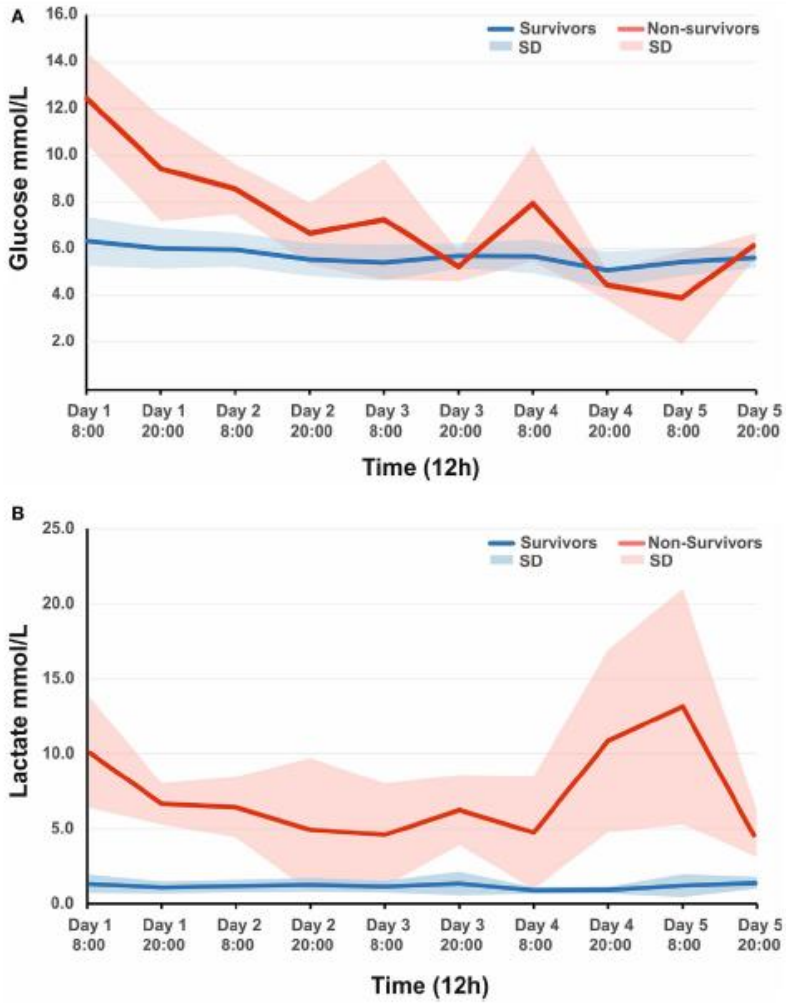


FIGURE 1 | **(A)** Observed mean arterial glucose (SD) in pediatric traumatic brain injury (TBI) patients during the first 5 days since ictus, stratified by fatal outcome. **(B)** Observed mean arterial lactate (SD) in pediatric TBI patients during the first 5 days since ictus, stratified by fatal outcome.

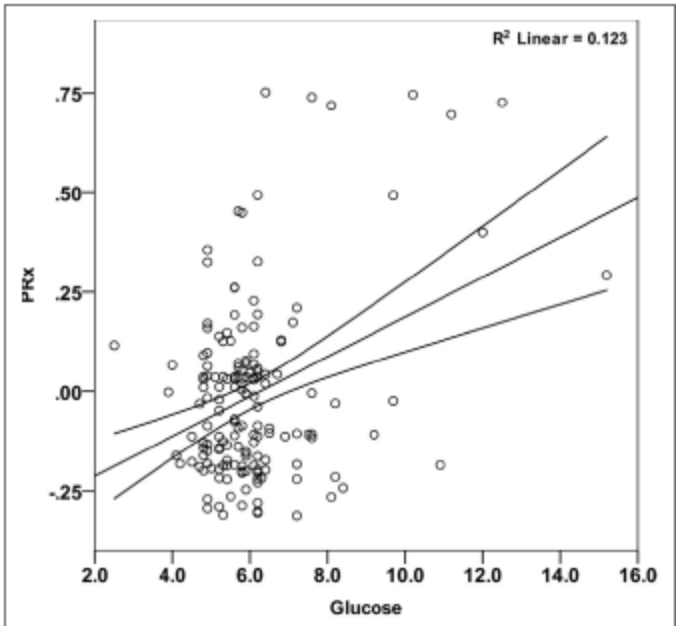


FIGURE 2 | Correlation between mean arterial glucose and PRx in pediatric traumatic brain injury patients during the first 5 days since ictus. There was a significant positive relationship between blood glucose and PRx (Pearson correlation = 0.351; $p < 0.001$). Each data point represents the mean of the available arterial glucose concentration and PRx measurements during the first 5 days since ictus.

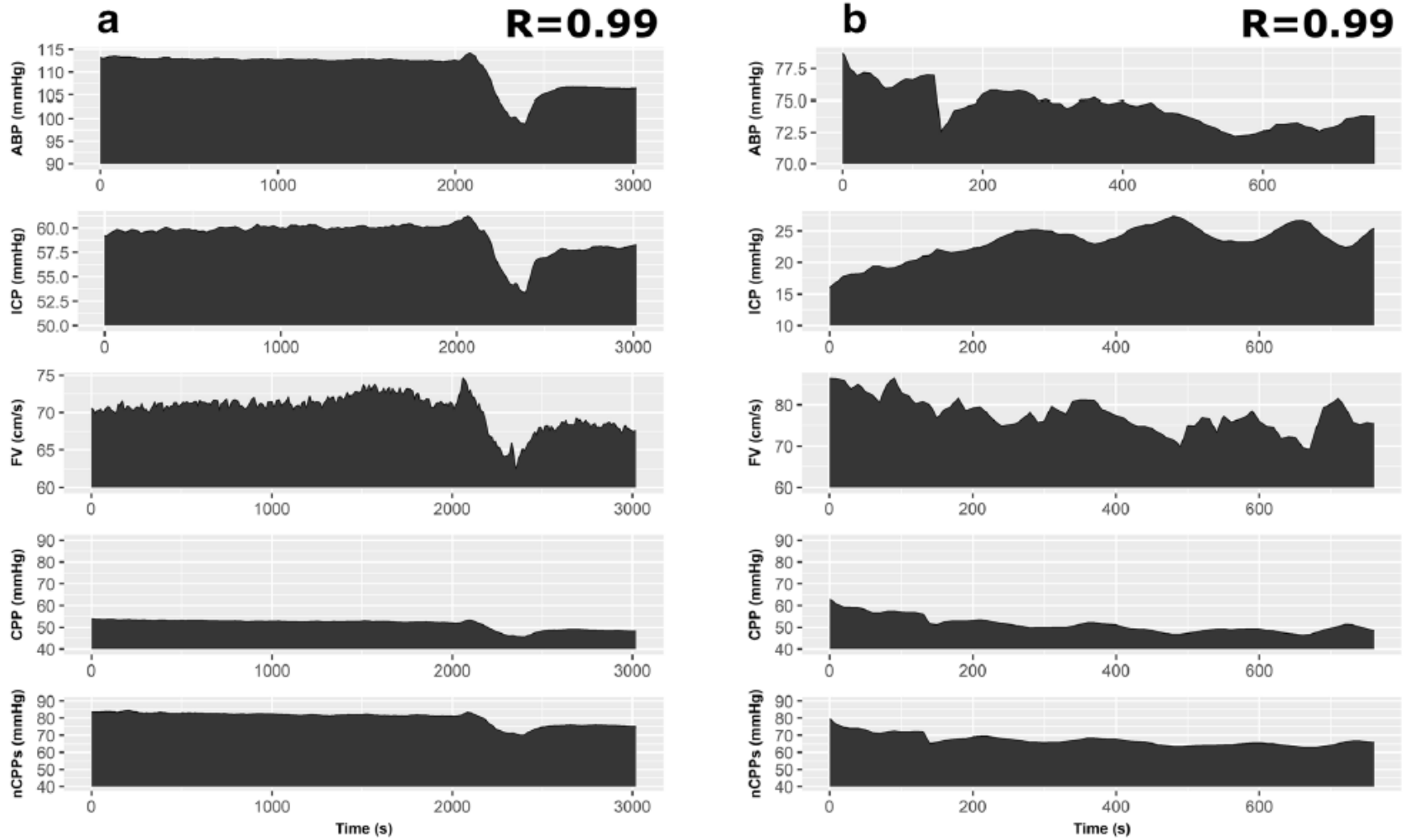
Transcranial Doppler

- Non-invasive
- Used in paeds TBI for autoregulation and blood flow measurement
- Figaji et al: 52 patients severe TBI
  - Autoregulatory index (ARI) after increasing ABP by 20%
  - Found correlation with ICP, $PbtO_2$
- Vavilala et al: 36 patients with severe TBI
  - ARI and MCA flow velocity measured
  - Good correlation of loss of autoregulation & outcome

J Neurosurg Pediatrics 2009;4:420-8
J Neurotrauma 2009. 10.1089/neu.2008.0770

Transcranial Doppler as a non-invasive method to estimate cerebral perfusion pressure in children with severe traumatic brain injury

Francisco Abecasis[1] · Danilo Cardim[2] · Marek Czosnyka[3,4] · Chiara Robba[5] · Shruti Agrawal[6]



Child's Nervous System
https://doi.org/10.1007/s00381-019-04273-2

NIRS measurements

FV [cm/s]

MAP [mmHg]

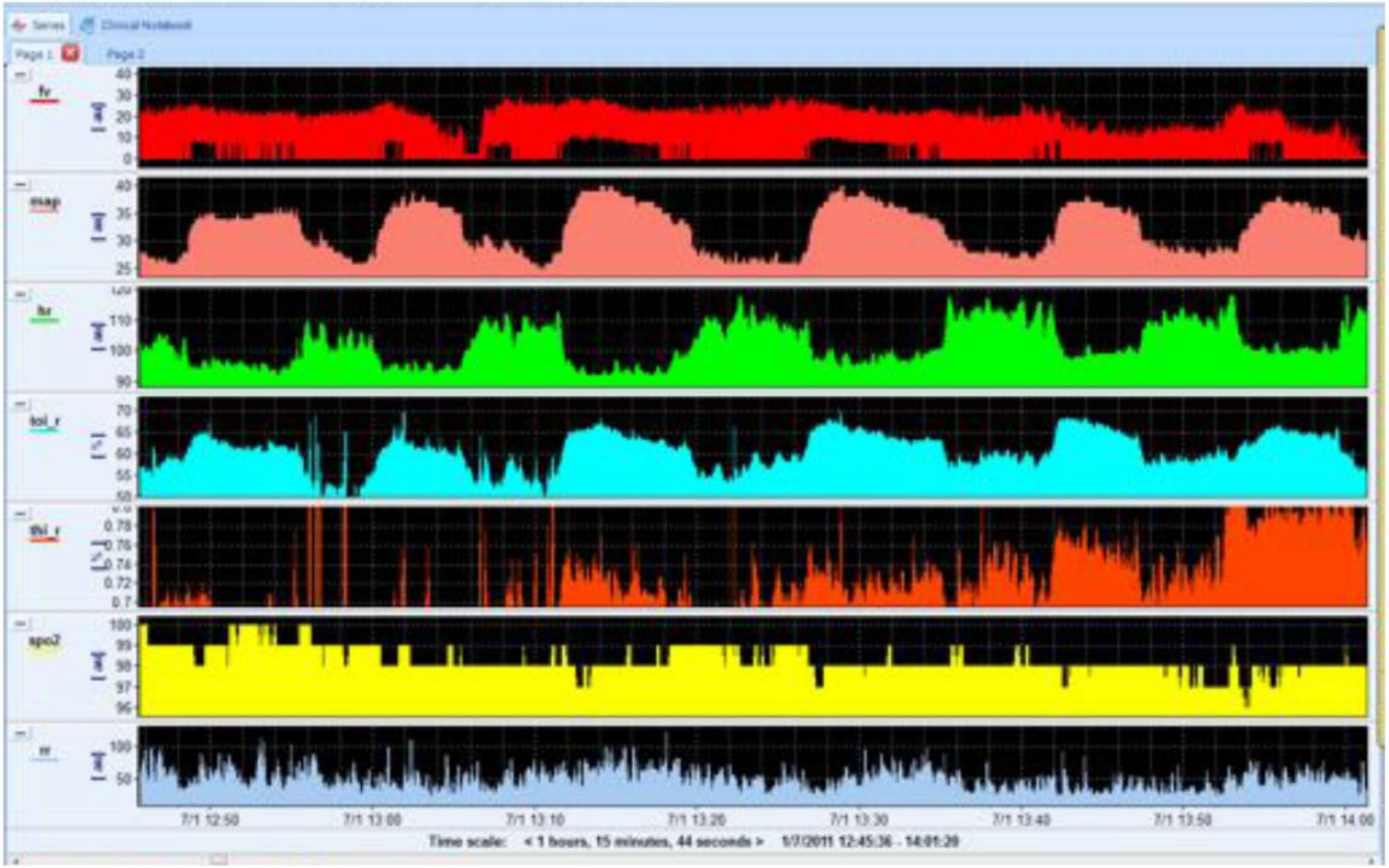
HR [c/min]

TOI [%]

THI [au]

SpO_2 [%]

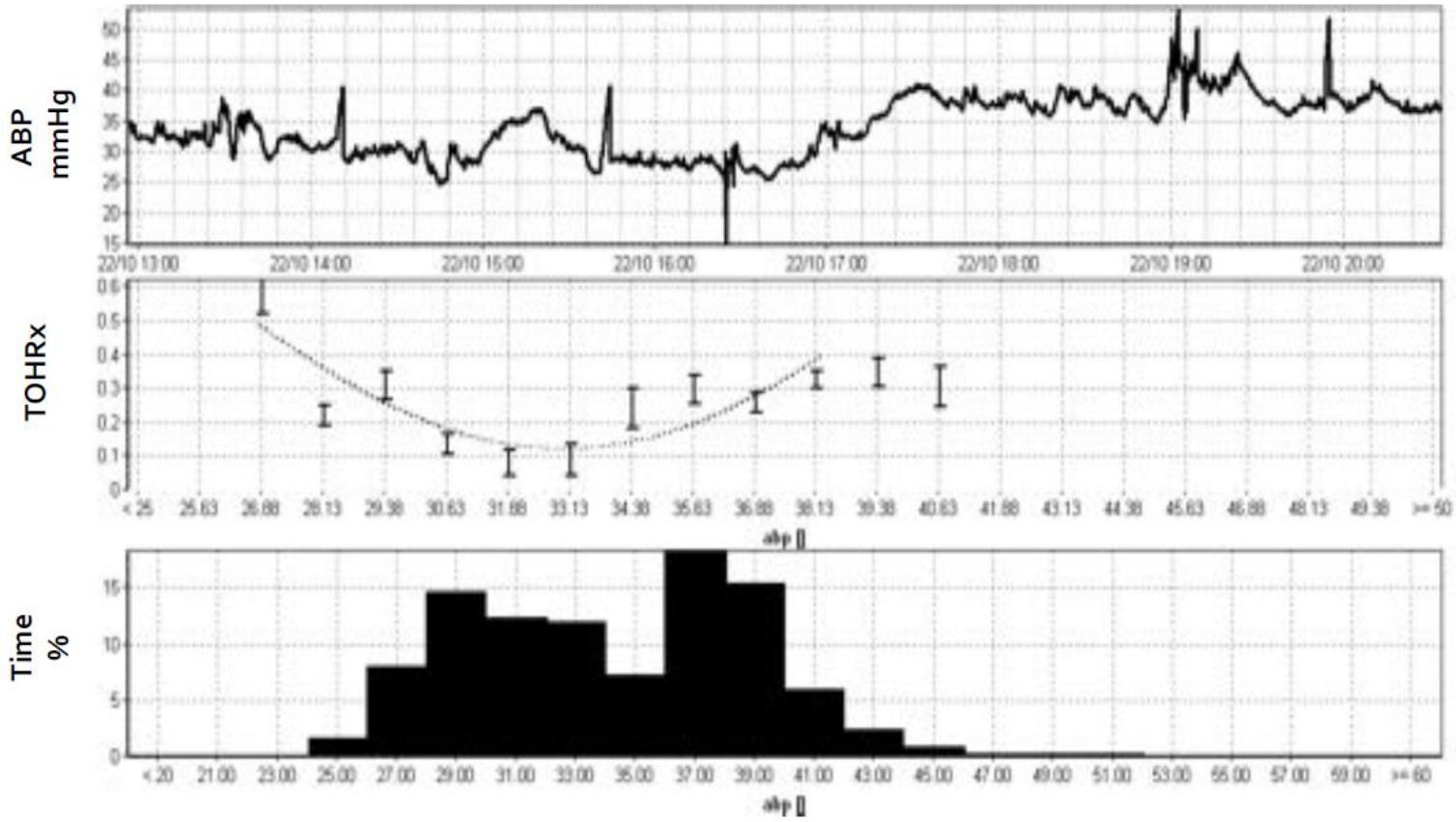
RR [c/min]



ICM+®

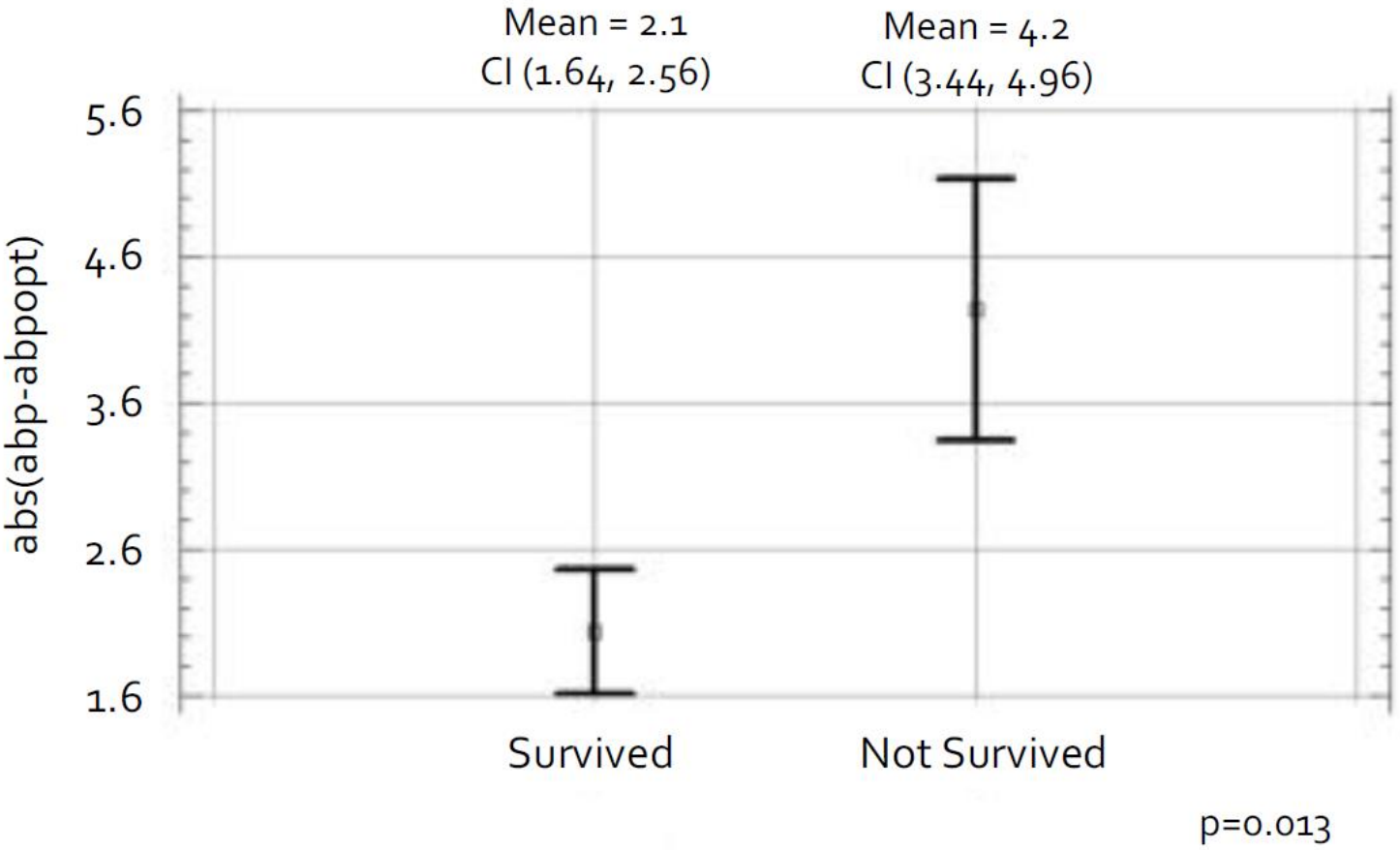
neoLAB
infant functional brain imaging
UCL | Cambridge

Determination of Optimal MABP in Preterm Infants



da Costa CS *J Pediatr* 2015;**167**:86-91

Optimal MABP vs Mortality



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Aspirations

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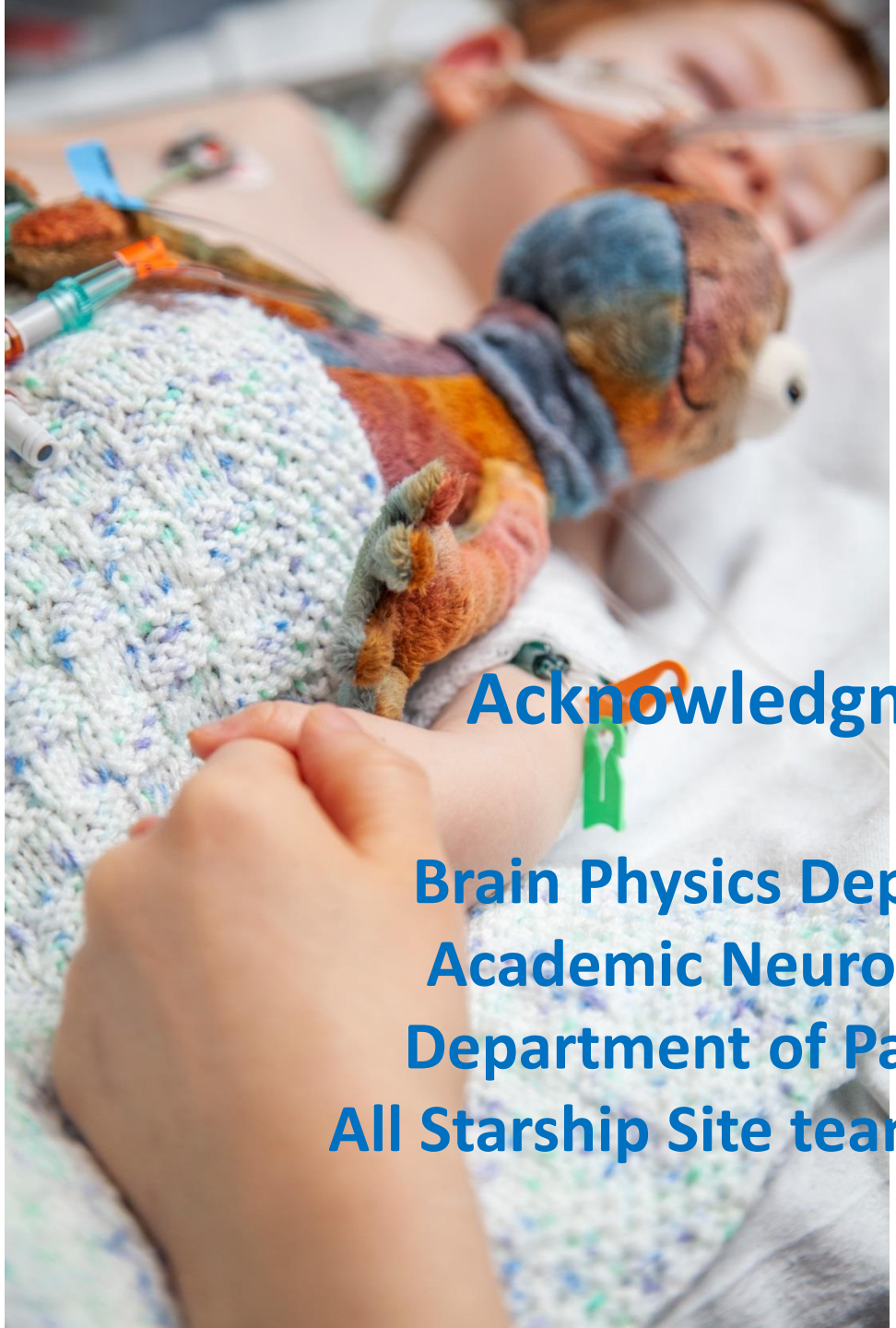
- Apply CA in non-TBI critically ill children

Aspirations

- Expand STARSHIP database
- Intro
- Non- nction
- Appl n



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