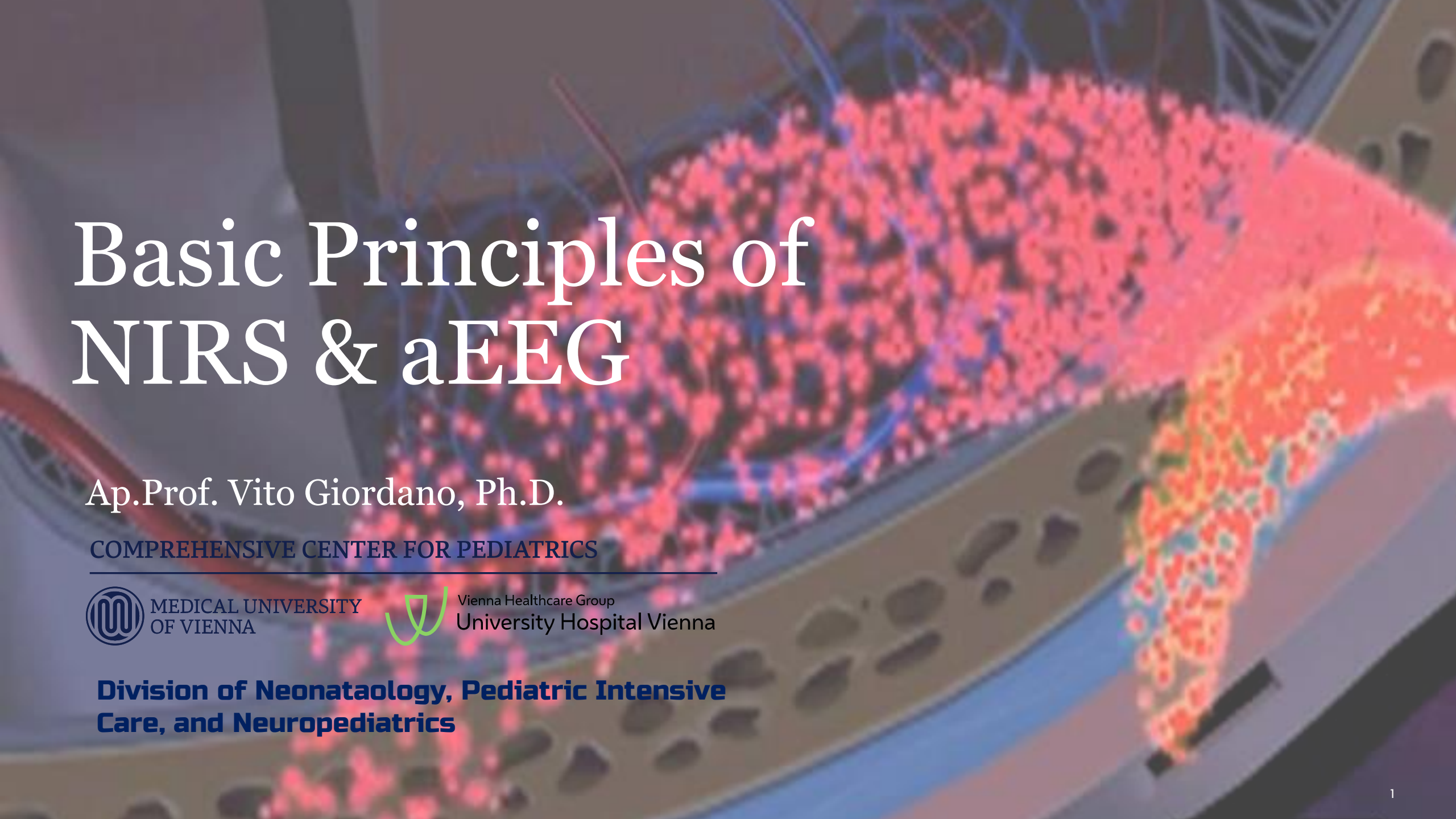

Basic Principles of NIRS & aEEG

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COMPREHENSIVE CENTER FOR PEDIATRICS

MEDICAL UNIVERSITY OF VIENNA

Vienna Healthcare Group
University Hospital Vienna

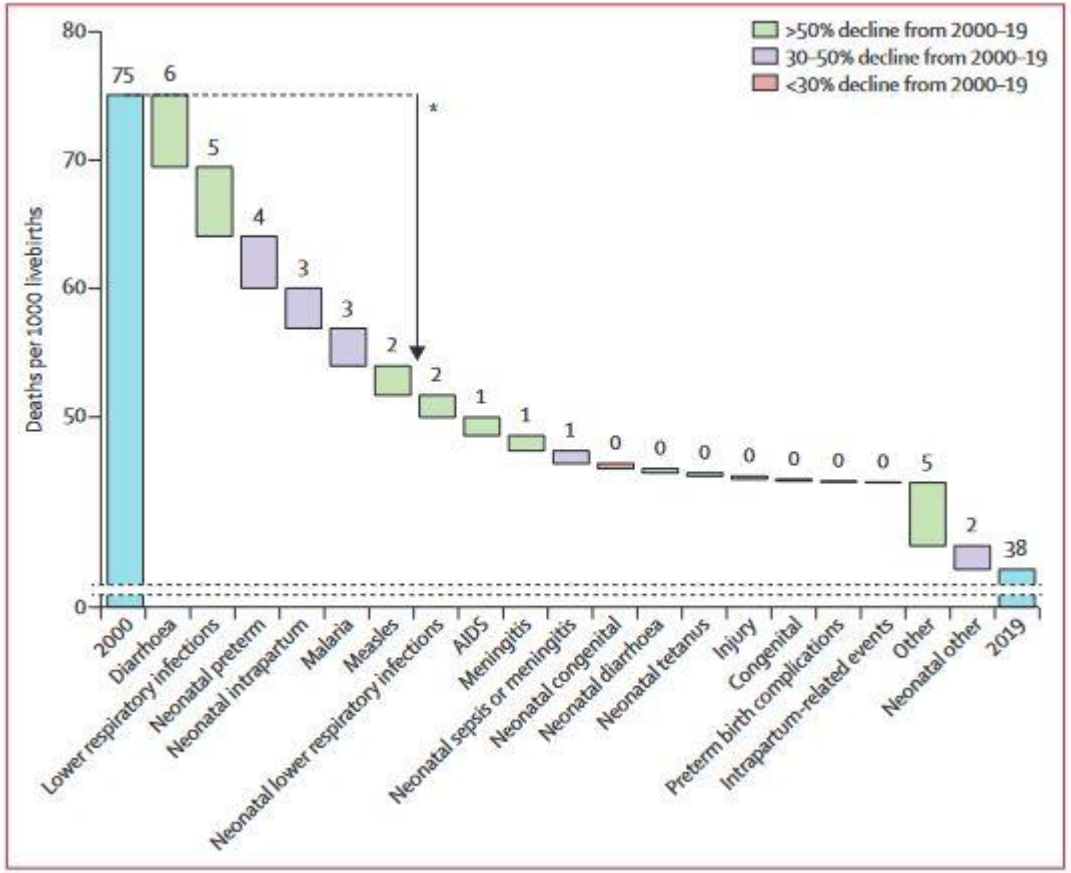
Division of Neonataology, Pediatric Intensive Care, and Neuropediatrics

Neonatal Causes of Mortality (Perin ., et al 2022. *The Lancet*)

	Estimated number in millions (95% UR*)	Cause-specific mortality rate per 1000 live births (95% UR)
Children aged 0–59 months		
Preterm birth complications	0·94 (0·86–1·06)	6·72 (6·15–7·60)
Lower respiratory infections†	0·74 (0·62–0·84)	5·30 (4·44–6·01)
Intrapartum-related events	0·62 (0·57–0·70)	4·41 (4·10–4·98)
Diarrhoea	0·48 (0·40–0·55)	3·47 (2·88–3·94)
Congenital abnormalities	0·40 (0·38–0·45)	2·89 (2·69–3·25)
Sepsis or meningitis	0·27 (0·24–0·31)	1·93 (1·71–2·19)
Other conditions	1·85 (1·74–2·11)	13·23 (12·47–15·12)
Neonates aged 0–27 days		
Preterm birth complications	0·88 (0·81–1·00)	6·31 (5·77–7·17)
Intrapartum-related events	0·58 (0·53–0·65)	4·18 (3·81–4·68)
Congenital abnormalities	0·24 (0·21–0·28)	1·70 (1·49–2·01)
Lower respiratory infections†	0·20 (0·17–0·26)	1·46 (1·23–1·83)
Sepsis or meningitis	0·20 (0·17–0·23)	1·41 (1·23–1·67)
Diarrhoea	0·03 (0·03–0·04)	0·24 (0·20–0·30)
Tetanus	0·01 (0·01–0·01)	0·06 (0·04–0·07)
Other conditions	0·30 (0·25–0·36)	2·13 (1·78–2·60)
Children aged 1–59 months		
Lower respiratory infections†	0·54 (0·43–0·61)	3·84 (3·05–4·40)
Diarrhoea	0·45 (0·37–0·51)	3·23 (2·65–3·68)
Malaria	0·42 (0·34–0·50)	2·98 (2·40–3·56)
Injuries	0·25 (0·23–0·29)	1·79 (1·61–2·05)
Measles	0·18 (0·12–0·46)	1·31 (0·83–3·32)
Congenital abnormalities	0·17 (0·15–0·19)	1·20 (1·10–1·37)
Meningitis	0·07 (0·06–0·08)	0·53 (0·43–0·59)
Preterm birth complications	0·06 (0·05–0·06)	0·41 (0·33–0·43)
AIDS	0·06 (0·04–0·08)	0·40 (0·29–0·58)
Intrapartum-related events	0·03 (0·04–0·05)	0·23 (0·25–0·33)
Other conditions	0·64 (0·55–0·71)	4·57 (3·91–5·07)

Other conditions among children aged 1–59 months included causes originated during the perinatal period, cancer, severe malnutrition, and other specified causes. UR=uncertainty range. *UR is defined as the 2·5–97·5 centile. †Lower respiratory infections were formerly referred to as pneumonia.

Table 2: **Estimated number of deaths by cause and cause-specific mortality rate in 2019**



***63% of the reduction is due to lower respiratory infections, neonatal preterm birth complications, neonatal intrapartum-related events**

Role of Neuromonitoring

1. Is the brain working normally?
2. Has the infant suffered brain injury?
3. Which is the severity level of the injury and how is the brain adapting
4. Is further evaluation needed?

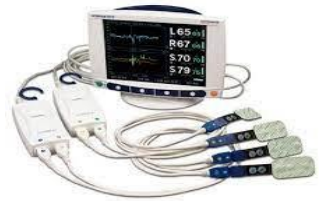
Neuromonitoring in a Neonatal Intensive Care Unit (NICU)

Neuromonitoring	Clinic	CUS	aEEG/EEG/EP	NIRS	MRT
Seizures	±	+	++	-	++
Asphyxie/HIE	++	+	++	+	++
IVH/PHH	±	++	++	+	+
Congenital heart deases	±	+	+	++	+
Preterm < 28 GW	±	++	++	±	+
Stroke	±	+	+	-	++
Enzephalitis/Meningitis	+	±	++	-	+
Malformation	+	+	+	-	++
metabolic disorders	+	±	+	-	+

Klebermass-Schrehof K., Internal Guidlines

NIRS - Basics

What is NIRS?



NIRS is a **trend** monitor system

NIRS is a ***non-invasive*** monitoring technique for cerebral & somatic oxygenation.

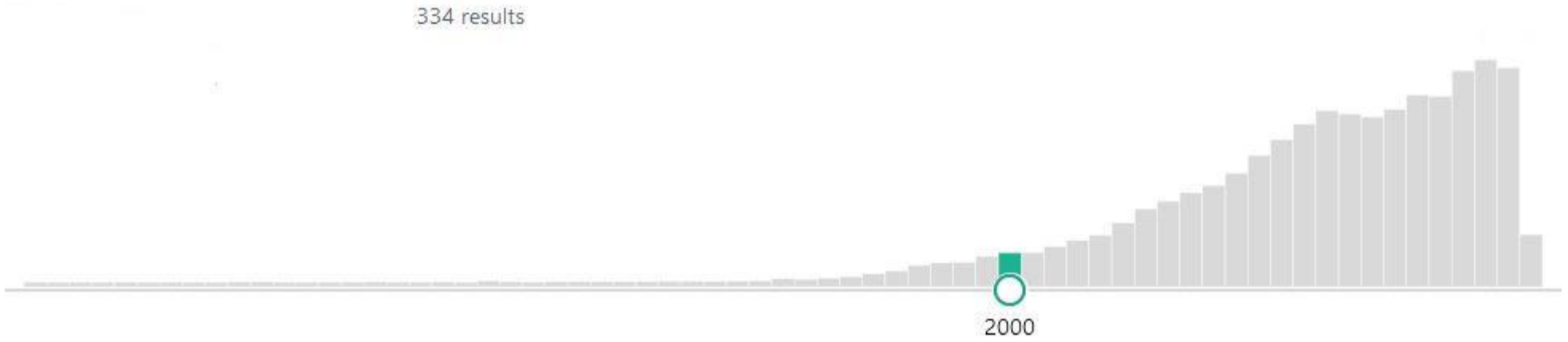
NIRS is an indirect indicator of perfusion adequacy. Therefore, it allows ***continuous*** information on oxygen supply-versus-demand balance.

NIRS is a ***real time*** measurements based on two principles. First, light in the near-infrared zone can pass through the thin skin, bone, and other tissues. Second, the appropriate choice of near-infrared wave-lengths allows interpretation of changes in light absorption that reflect oxygenation.

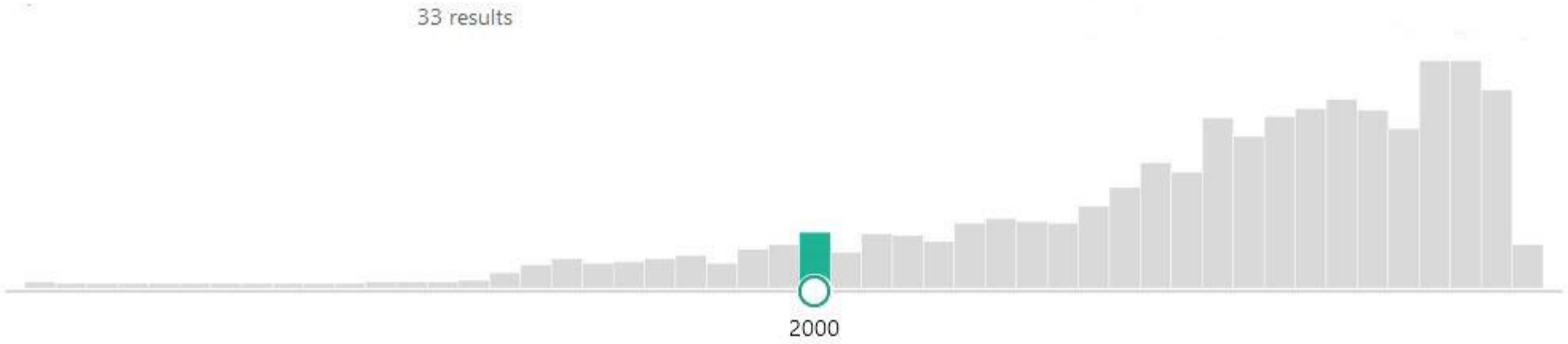
G.S. Umamaheswara Rao, S. Bansal, in Essential of NeuroanesthesiaEssentias, 2017
André Y. Denault, Tanya Mailhot, in Neuromonitoring techniques Neuromonitoring, 2018
Lilly Bogičević, et al., in Handbook of Developmental Neurotoxicology, 2018

Publication History

Adults



Neonates



Historical Facts

Science
Volume 198, Issue 4323
Dec 1977

In 1977, Frans Jöbsis, who is considered the father of in vivo nearinfrared spectroscopy (NIRS), demonstrated for the first time that ight in the red to near-infrared range can travel through the scalp, skull and cerebrospinal fluid into the brain and return to be measured at the surface

VOLUME 75 • FEBRUARY 1985 • NUMBER 2

Pediatrics

Noninvasive Monitoring of Cerebral Oxygenation in Preterm Infants: Preliminary Observations

Jane E. Brazy, MD, Darrell V. Lewis, MD, Michael H. Mitnick, PhD, and Frans F. Jöbsis vander Vliet, PhD

From the Departments of Pediatrics and Physiology Duke University Medical Center Durham, North Carolina

Seminars in Fetal & Neonatal Medicine (2006) 11, 498–502

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ScienceDirect

journal homepage: www.elsevier.com/locate/siny

Seminars in FETAL & NEONATAL MEDICINE

Is near-infrared spectroscopy living up to its promises?

Gorm Greisen*

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ACTA PÆDIATRICA
NURTURING THE CHILD

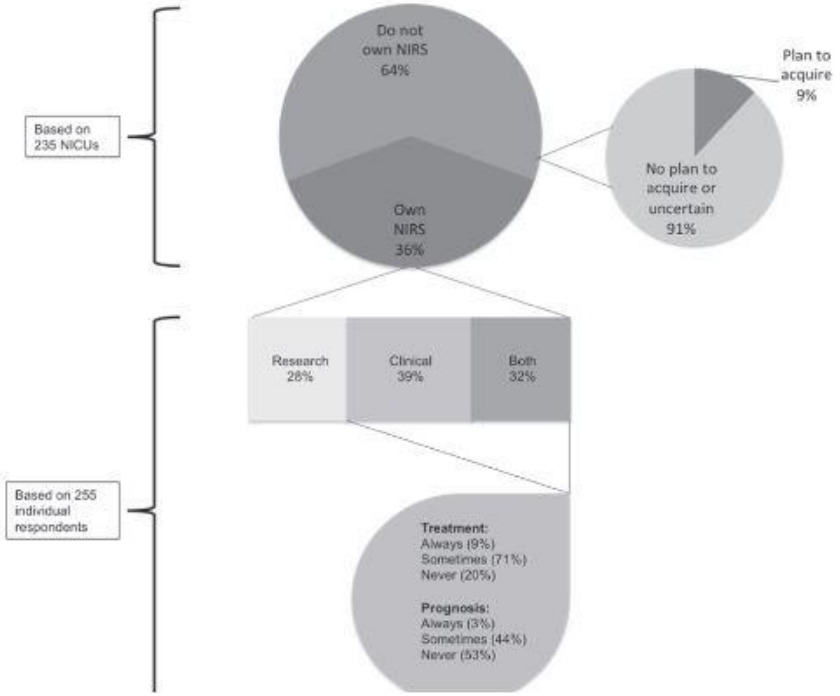
Acta Paediatrica ISSN 0803-5253

REGULAR ARTICLE

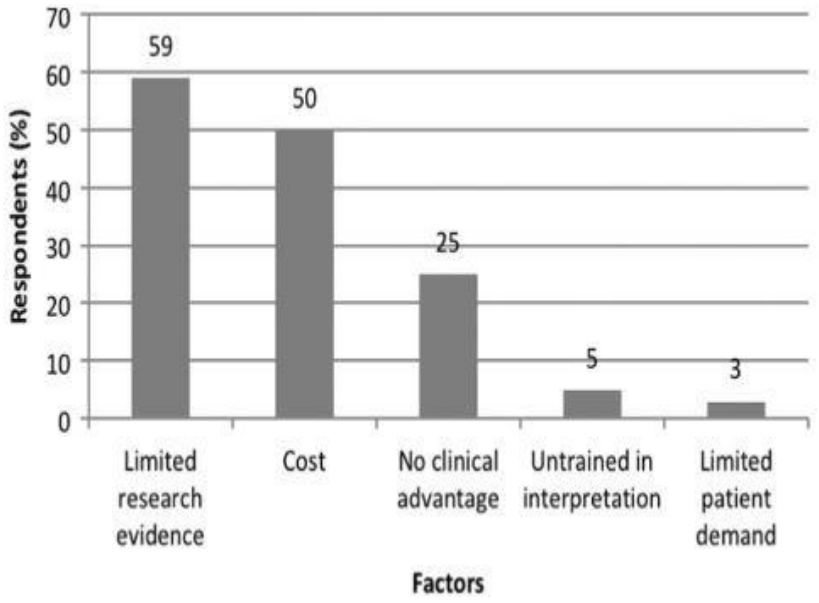
Patterns of use of near-infrared spectroscopy in neonatal intensive care units: international usage survey

Carol Lu Hunter[1,2], Ju Lee Oei[1,2], Keiji Suzuki[3], Kei Lui[1,2], Timothy Schindler (tschindl@med.usyd.edu.au)[1,2]

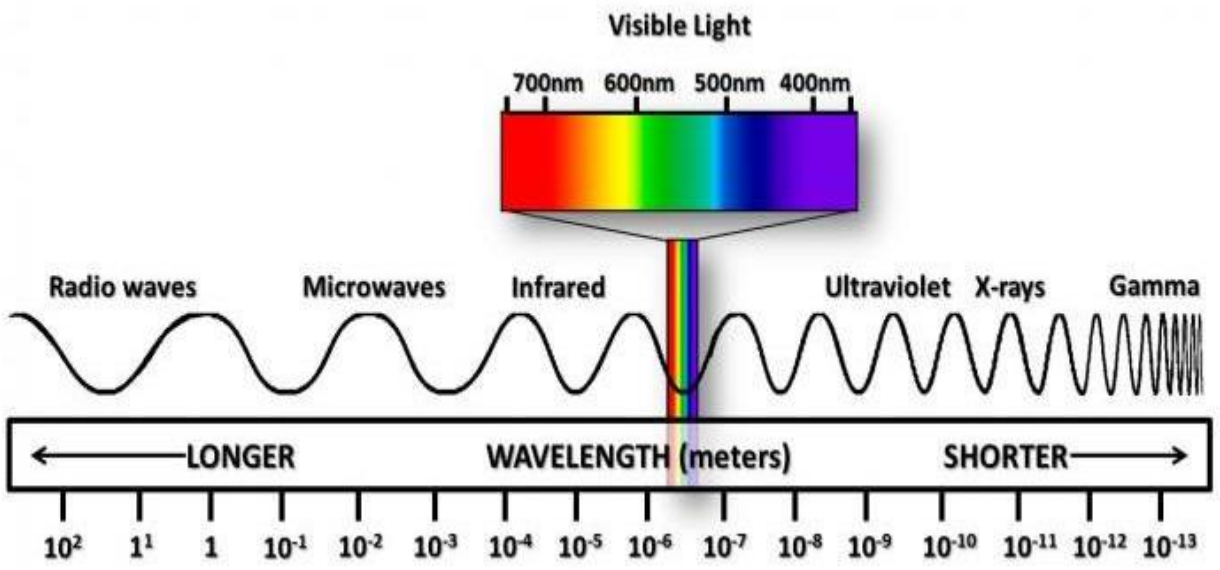
1.Department of Newborn Care, Royal Hospital for Women, Randwick, NSW, Australia
2.Faculty of Medicine, University of New South Wales, Kensington, NSW, Australia
3.Department of Paediatrics, Tokai University School of Medicine, Isehara, Japan

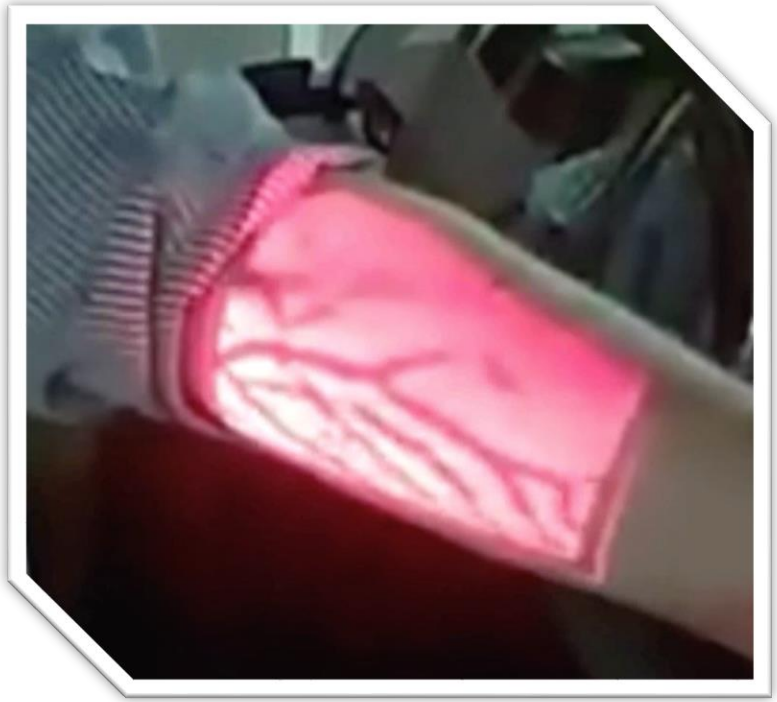


International Survey:
- 235 NICU
- 36% have a NIRS monitor
- Only 9% use NIRS to guide clinical managment
- 3% use NIRS to assess prognosis



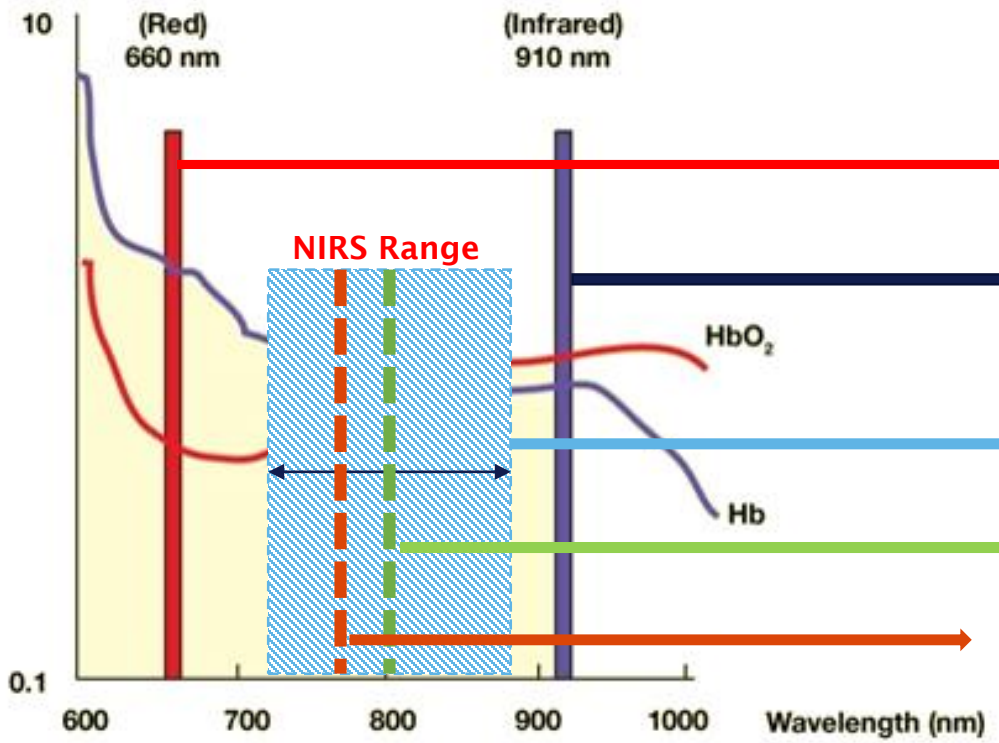
Electromagnetic spectrum





- Biological Tissues such as scalp and skull are relatively transparent to red & infrared light
- Oxy and deoxy hemoglobin instead selectively absorb red and infrared light

Principles of light absorption



Deoxygenated hemoglobin absorb more **red** light (600-750 wavelength)

Oxygenated hemoglobin absorb more **infrared** light (850-1000 nm wavelength)

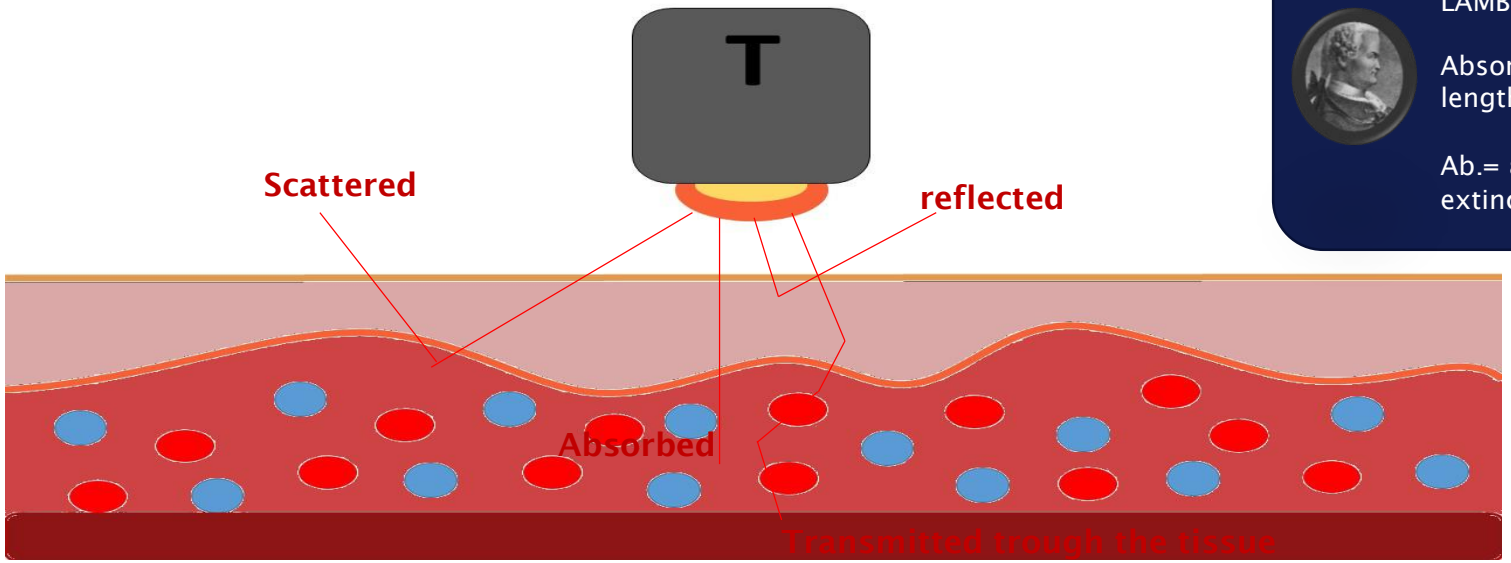
NIRS measures approximately between 730 – 880 nm

Both oxygenated hemoglobin and deoxygenated hemoglobin absorb light at 800 nm

At 760 nm absorption is primarily deoxygenated

Vesoulis ZA et al., Journ Perinat 2021

Principles of light absorption



LAMBERT:

Absorbance depends on lengths.

Ab.= ε (molecular extinction equation) * L

BEER:

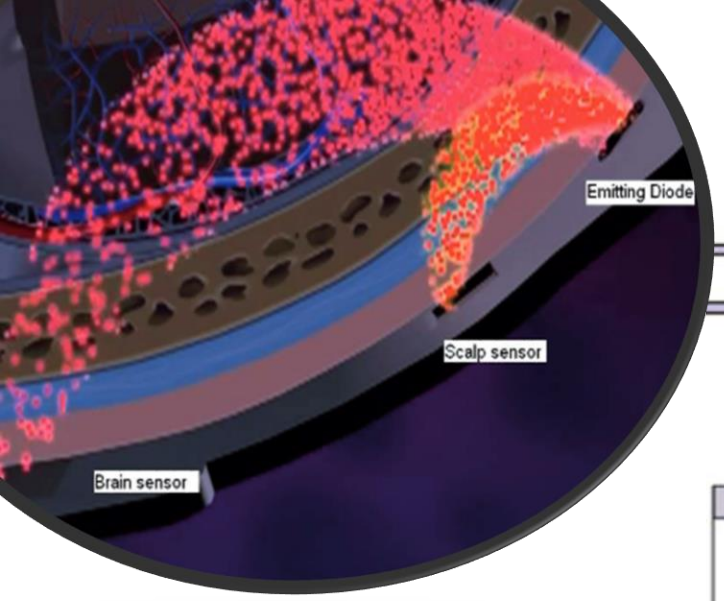
Absorbance depends on concentration.

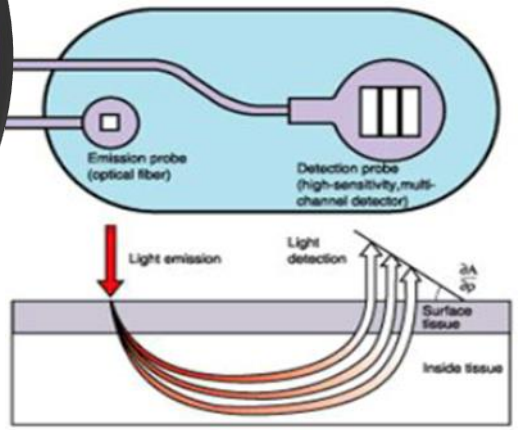
Ab.= ε (molecular extinction equation) * C

Lambert-Beer:
$\log_{10}$ In-light/out-light= ε * L * C

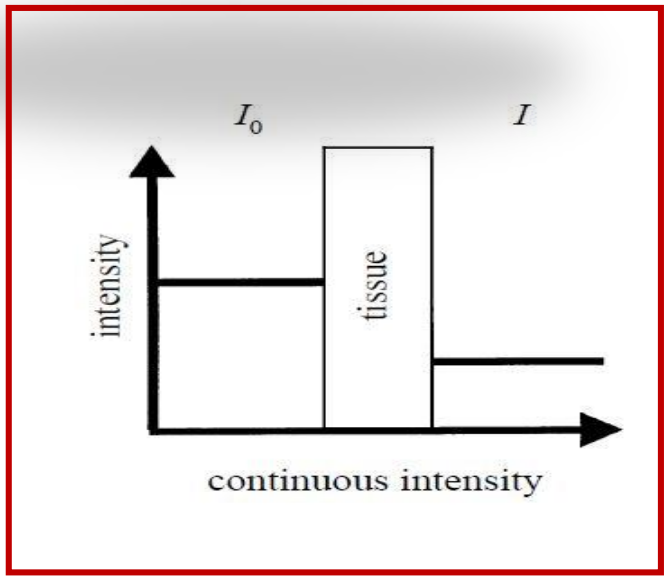
Mod. Lambert-Beer:
$\log_{10}$ In-light/out-light= ε * L * ΔC *DPF
(Differential Pathlength Factor)

Principles of light absorption





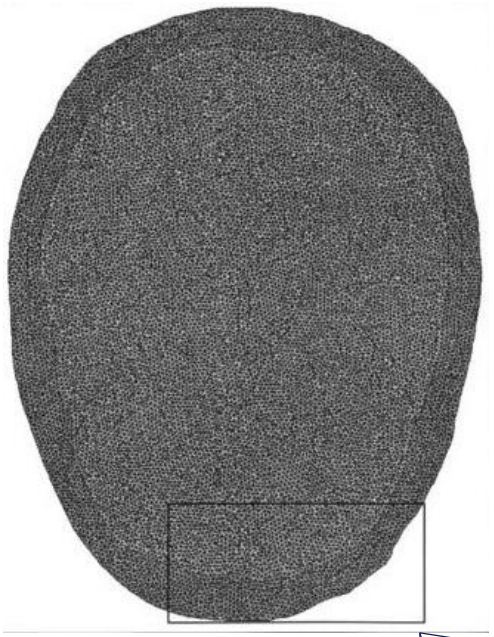
Two depth of light are used to subtract out data from the skin and the skull, resulting in brain oxygenation values.



The instrument emits light at a constant intensity, and detects this light whose intensity is attenuated after passing a tissue.

Fischer GW et al., HSR 2010
Delpy et al, Phil Trans R Soc Lond B 1997, 352:649

Cerebral NIRS:



Regional Tissue Oxygen Saturation (rScO2)

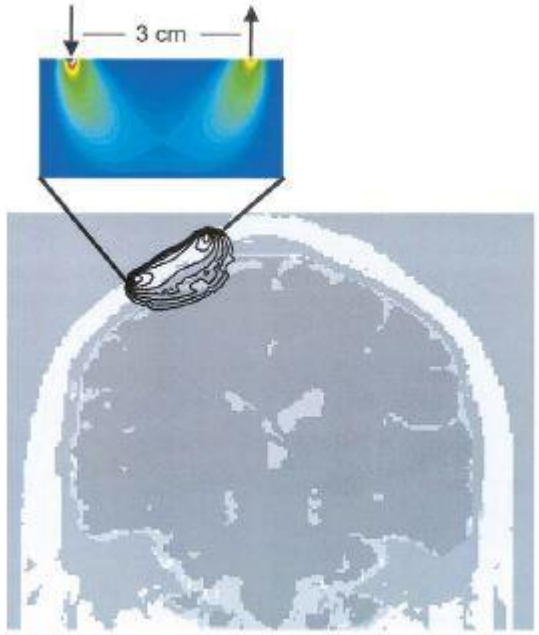
$$rScO2 = \frac{HbO2}{HbO2 + HHb}$$

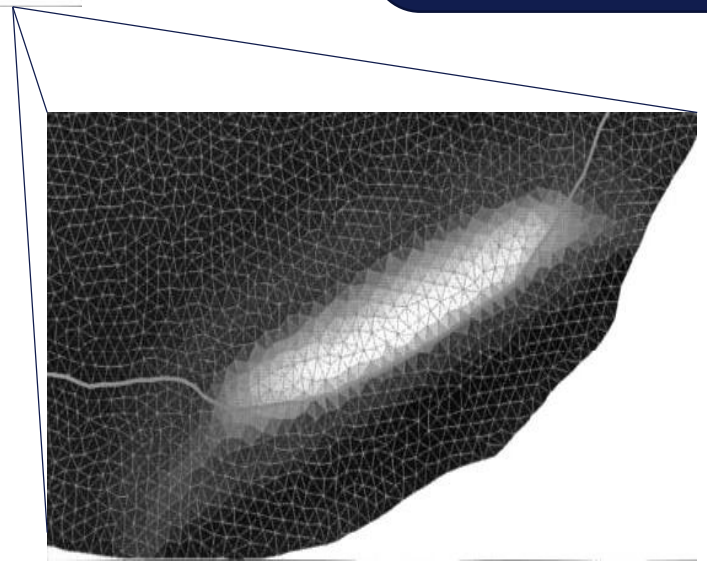
HHb: Deoxy hemoglobin
HbO2: Oxy hemoglobin

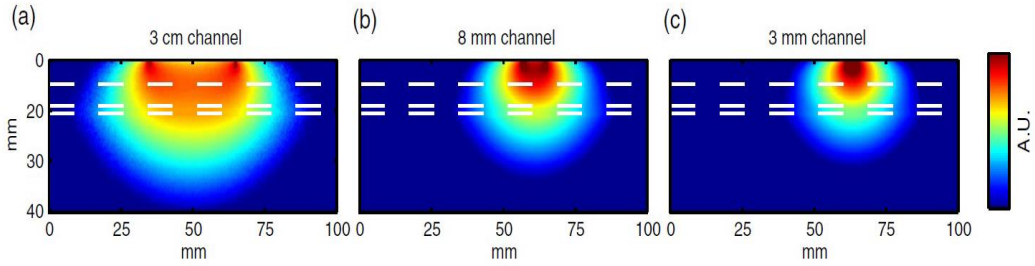
Fractional Tissue Oxygenation extraction (FTOE)

$$FTOE = \frac{SaO2 - rScO2}{SaO2}$$

SaO2: Arterial oxygen saturation







Strangman G et al., Biol Psychiatry, 2002
Delpy et al, Phil Trans R Soc Lond B 1997

Basic Interpretation of rScO2

rScO2 facts:

- Balance between regional oxygen delivery & consumption
- Can be interpreted as Absolut values (thresholds) or as dynamic changes in course of a diseases
- rStO2 is closer to SvO2 than SaO2; however, rStO2 does not represent/equate SvO2 since they do not always parallel each other

Contribution vessels:

All vessel under 0.1 mm in the following hypothetical percentage:

- Arterioral= 10%
- Capillary= 20%
- Venular= 70%

Arterial:venous proportion 25:75

rScO2 Vs TOI?

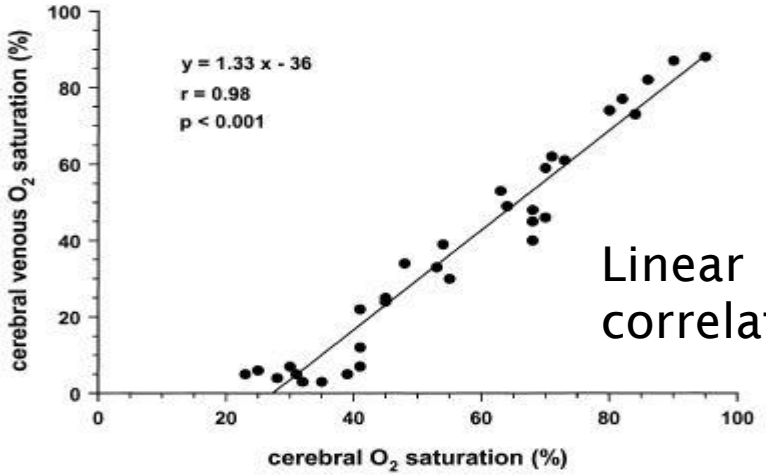
For calculation of TOI, the absorption is measured at three points very near to each, while calculation of

rScO 2 scattering is measured at the first optode and deducted from the measurements of the second optode.

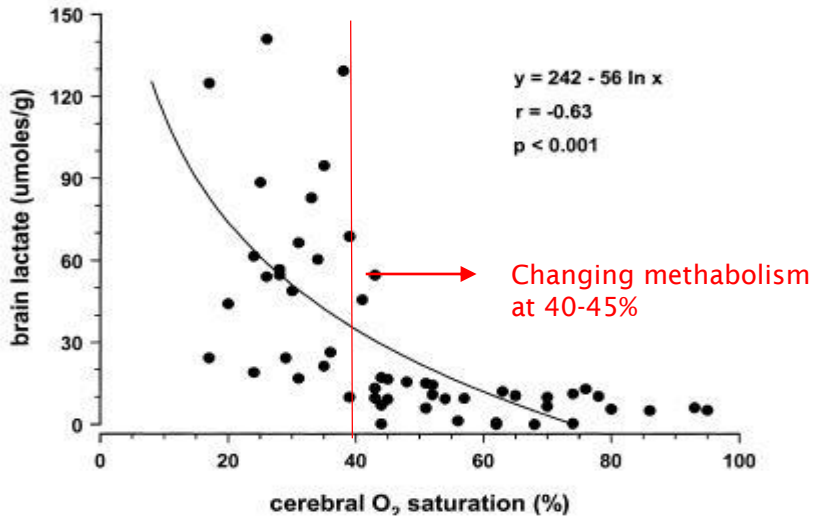
Both TOI and rScO 2 reflect the saturation of oxygen in veins (70–80%), and arteries (20–25%)

Watzman et al, Anesthesiology 2000
Weindling M et al, Early Hum Develop 2010
Ikeda et al., Anesth Analg 2014
Van bel et al., Neonatology 2008

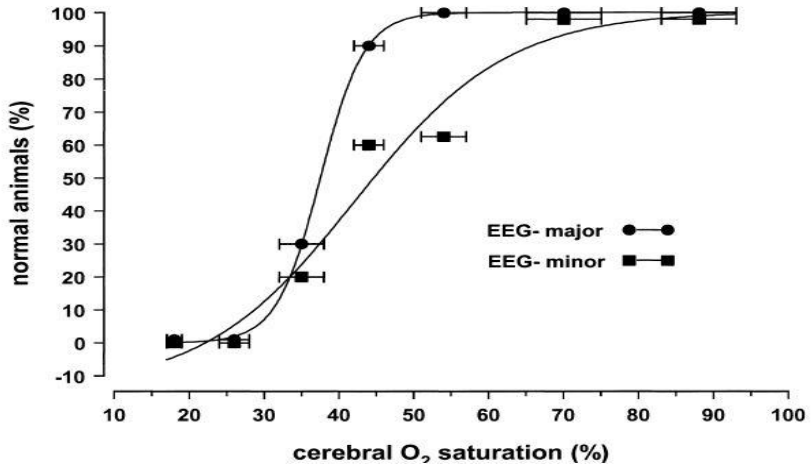
Basic Interpretation of rScO2

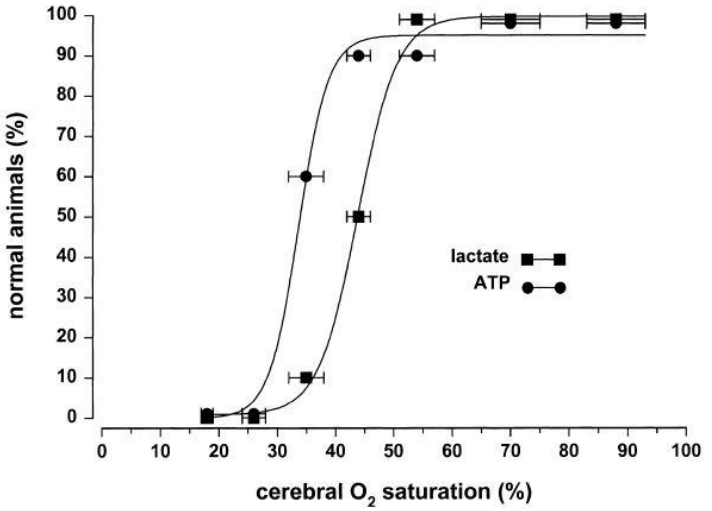


Linear correlation



Changing methabolism at 40-45%

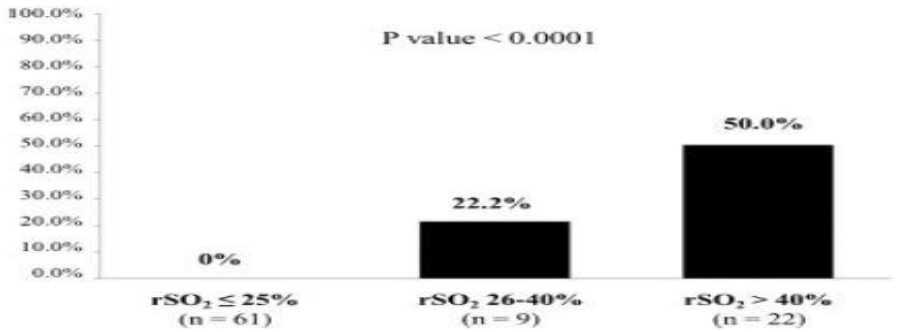




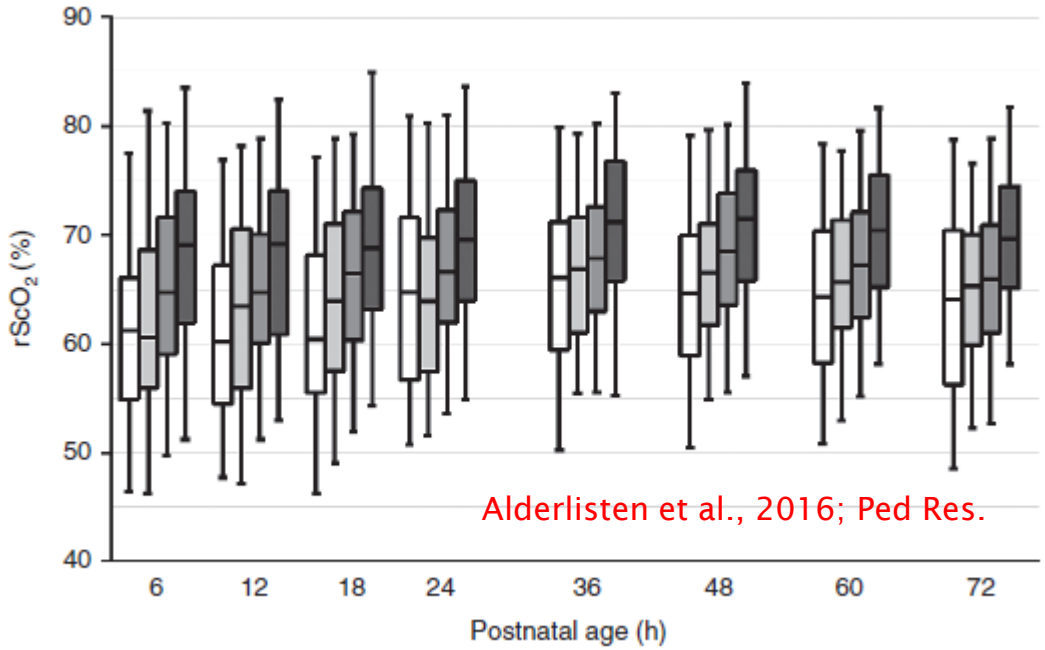
Kurth et al., J Cerb Blood Flow Metab 2002

Basic Interpretation of rScO2

Neurological outcomes in adults patients in relation to rCSO2 at admission (Ito N et al., Resuscitation 2012)



Regional cerebral oxygen saturation on hospital arrival is a potential novel predictor of neurological outcomes at hospital discharge in patients with out-of-hospital cardiac arrest



Alderlisten et al., 2016; Ped Res.

FACIT:
- Absolute normal values are between 55% and 85%.
- Normal values in preterm infants increase after birth, after 36 hours they decrease again.
- Normal values show, that the 10th and 90th percentile slightly increase with gestational age.
- In preterm infants with 24/25 wGA the percentile thresholds are 53-80% at 72h.
- In preterm infants with 30/31 wGA the percentile thresholds are 55-85% at 72h.

Basic Interpretation of NIRS signal (28 days of life)

Table 3 Estimated cerebral tissue oxygenation through repeated modeling in 7-day intervals over the first 28 days of life by gestational age.

Gestational age	Cerebral tissue oxygen satuartion by Day of life, mean (95% CI)				
	1st Day	7th Day	14th Day	21st Day	28th Day
23 0/7–23 6/7	76.8 (76.7, 76.9)	70.5 (70.4, 70.5)	64.1 (64.0, 64.2)	57.8 (57.6, 58.0)	51.5 (51.2, 51.7)
24 0/7–24 6/7	76.4 (76.3, 76.4)	70.5 (70.4, 70.5)	64.6 (64.5, 64.7)	58.7 (58.6, 58.9)	52.9 (52.7, 53.1)
25 0/7–25 6/7	75.9 (75.9, 76)	70.5 (70.5, 70.6)	65.1 (65.0, 65.2)	59.7 (59.6, 59.8)	54.3 (54.1, 54.4)
26 0/7–26 6/7	75.5 (75.4, 75.5)	70.5 (70.5, 70.6)	65.6 (65.5, 65.6)	60.6 (60.5, 60.7)	55.6 (55.5, 55.8)
27 0/7–27 6/7	75.1 (75.0, 75.1)	70.5 (70.5, 70.6)	66.0 (66.0, 66.1)	61.5 (61.5, 61.6)	57.0 (56.9, 57.1)
28 0/7–28 6/7	74.6 (74.6, 74.6)	70.6 (70.5, 70.6)	66.5 (66.5, 66.6)	62.5 (62.4, 62.5)	58.4 (58.4, 58.5)
29 0/7–29 6/7	74.2 (74.1, 74.2)	70.6 (70.6, 70.6)	67.0 (67.0, 67.0)	63.4 (63.3, 63.5)	59.8 (59.7, 59.9)
30 0/7–30 6/7	73.7 (73.7, 73.87)	70.6 (70.6, 70.6)	67.5 (67.4, 67.5)	64.3 (64.3, 64.4)	61.2 (61.1, 61.3)
31 0/7–31 6/7	73.3 (73.2, 73.4)	70.6 (70.6, 70.7)	67.9 (67.9, 68)	65.3 (65.2, 65.4)	62.6 (62.5, 62.7)
32 0/7–32 6/7	72.9 (72.8, 72.9)	70.6 (70.6, 70.7)	68.4 (68.3, 68.5)	66.2 (66.1, 66.3)	64.0 (63.8, 64.1)
33 0/7–33 6/7	72.4 (72.3, 72.5)	70.7 (70.6, 70.7)	68.9 (68.8, 69)	67.1 (67, 67.3)	65.4 (65.2, 65.6)
34 0/7–34 6/7	72.0 (71.9, 72.1)	70.7 (70.6, 70.7)	69.4 (69.3, 69.5)	68.1 (67.9, 68.2)	66.8 (66.5, 67.0)

The more mature the preterm infants the less the cerebral tissue oxygen saturation

but the higher the ability to extract Oxygen (FTO2).

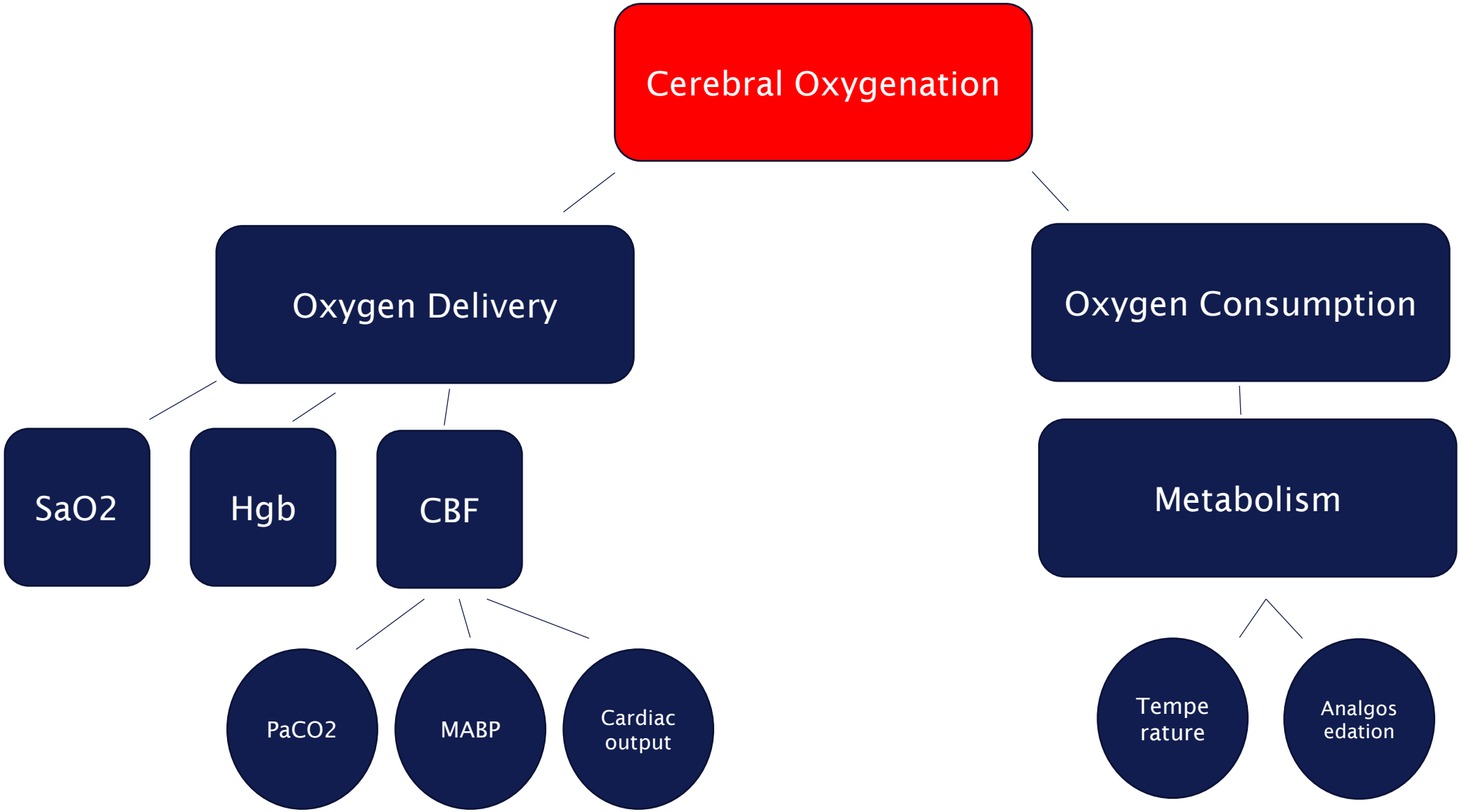
Mohamed M., et al., J Perinat 2021

Normal regional tissue oxygen saturation in neonates: a systematic qualitative review (Bruckner M., Ped Res 2021)

Author	Neonates (n)	Gestational Age (weeks)	Device	Body Site	Values	Age at Assessment
Xue et al.	230	>= 37	FORESIGHT (neonatal sensor)	Cerebral	Min 2: 49.0%, Min 5: 64.5%, Min 10: 74.0%, Min 30: 82.0%, Min 60: 81.0%	First hour after birth
Ozawa et al.	127	>= 37	Toccare KN-15	Cerebral	Min 1: ~45%, Min 5: ~52%, Min 10: ~56%	First 10 min after birth
Kato et al.	88	34 - 42	Toccare KN-15	Cerebral	Min 1: ~42%, Min 5: ~52%, Min 10: ~56%	First 10 min after birth
Montaldo et al.	61	>= 37	EQUANOX 7600	Cerebral, Renal, Abdominal	Cerebral, Renal, Abdominal data available see ref	First 9 hours after birth
Baik et al.	140	>= 37	NIRO 200NX	Cerebral	Min 1: N/A, Min 5: 66%, Min 10: 75%	First 15 min after birth
Pichler et al.	354	>= 37	INVOS 5100c	Cerebral	Min 1: N/A, Min 5: 65%, Min 10: 70%	First 15 min after birth
Fauchère et al.	20	>= 37	NIRO 300	Cerebral	Min 1: N/A, Min 5: N/A, Min 10: N/A	First 36 hours after birth
Roerdink et al.	159	34 - 42	INVOS 4100c, NIRO 200NX	Cerebral, Muscle	INVOS: 84 (6)%, NIRO: 70 (7)%; ; 92% INV; 78%NIRO	First 15 min after birth
Bailey et al.	38	>= 37	INVOS 5100c	Cerebral, Renal, Abdominal	Day 1c: 78.2 (7.9)%, Day 2c: 78.3 (6.1)%; Day 1r: 92%; Day 2r: 88%; Day 1a: 69; Day 2a: 75%	First 2 postnatal days
Bernal et al.	26	>= 37	INVOS 5100b	Cerebral, Renal	Day 1: 76.8 (8.5)%, Day 2: 86.8 (8.1)%	First 2 postnatal days

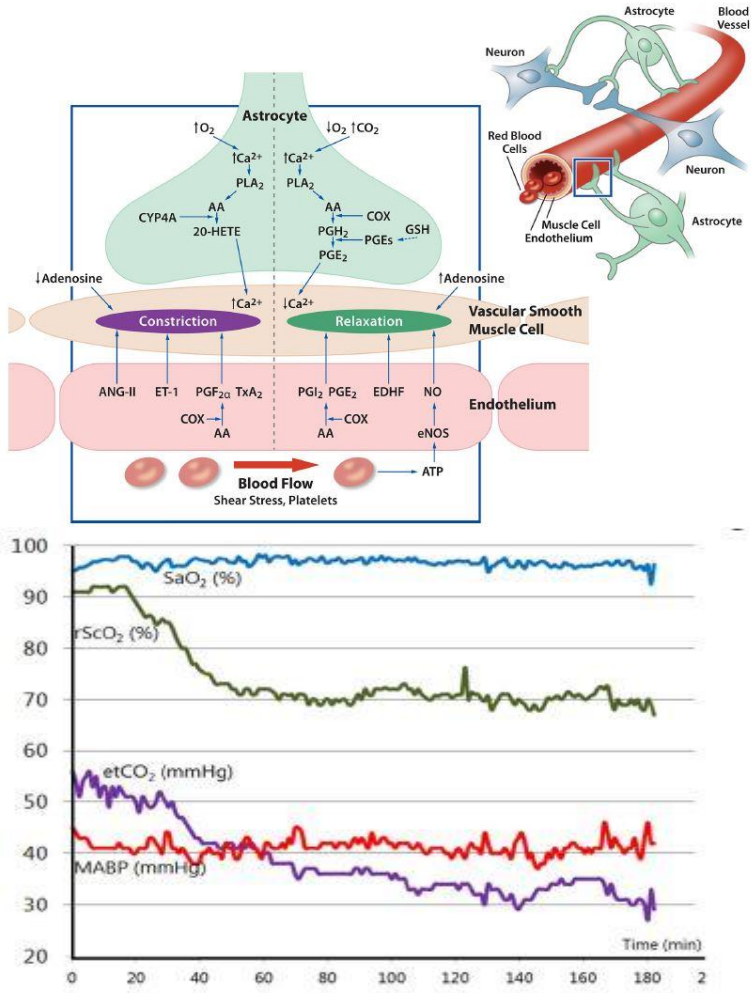
Normal regional tissue oxygen saturation in neonates: a systematic qualitative review (Bruckner M., Ped Res 2021)

Pichler et al.	27	< 37	INVOS 5100c (neonatal sensor)	Cerebral	Min 1: N/A, Min 5: N/A, Min 10: N/A	First 15 min after birth
Fuchs et al.	51	< 37	FORESIGHT	Cerebral	Min 1: 37%, Min 5: ~72%, Min 10: ~79%	First 10 min after birth
Wolfsberger et al.	100	< 37	NIRO 200	Muscle	0-6 hrs: 70%, 7-12 hrs: 72%, 13-18 hrs: 73%	First 24 hours after birth
Hoeller et al.	87	< 37	NIRO 200 NX	Cerebral, Muscle	Hour 4: 71.0 (10.5)%, Hour 14: 68.6 (11.7)%, Hour 24: 70.1 (10.3)%	First 30 hours after birth
Alderliesten et al.	999	< 32	INVOS 4100, INVOS 5100c	Cerebral	INVOS: 84 (6)%, NIRO: 70 (7)%	First 72 hours after birth
Naulaers et al.	15	< 32	NIRO 300	Cerebral	Day 1: 57.0 (54.0–65.7)%, Day 2: 66.1 (61.9–82.2)%, Day 3: 76.1 (67.1–80.1)%	First 3 postnatal days
Harer et al.	32	< 32	INVOS 5100c (neonatal sensor)	Renal	Day 2: 62.5 (57–65.7)%, Day 4: 59.1 (57–59.9)%, Day 7: 60.3 (57.8–66.9)%	Day 2 to Day 7
Van der Heide et al.	220	< 32	INVOS 5100c (neonatal sensor)	Abdominal	Day 1: 48.2 (16.6)%, Day 4: 38.7 (16.6)%	First week after birth
Patel et al.	78	< 32	InSpectra 650	Abdominal	Day 1: 73.8 (1.8)%, Day 3: 80.0 (1.4)%, Week 1: 77.3 (14.4)%	First week after birth
Howarth et al.	43	< 30	NIRO 300	Cerebral, Abdominal	Week 1: 65.4%, Week 4: 60.1%, Week 8: 56.8%	First 8 weeks after birth


Cerebral Oxygenation
Oxygen Delivery
Oxygen Consumption
SaO2
Hgb
CBF
Metabolism
PaCO2
MABP
Cardiac output
Tempe rature
Analgos edation

Respiration

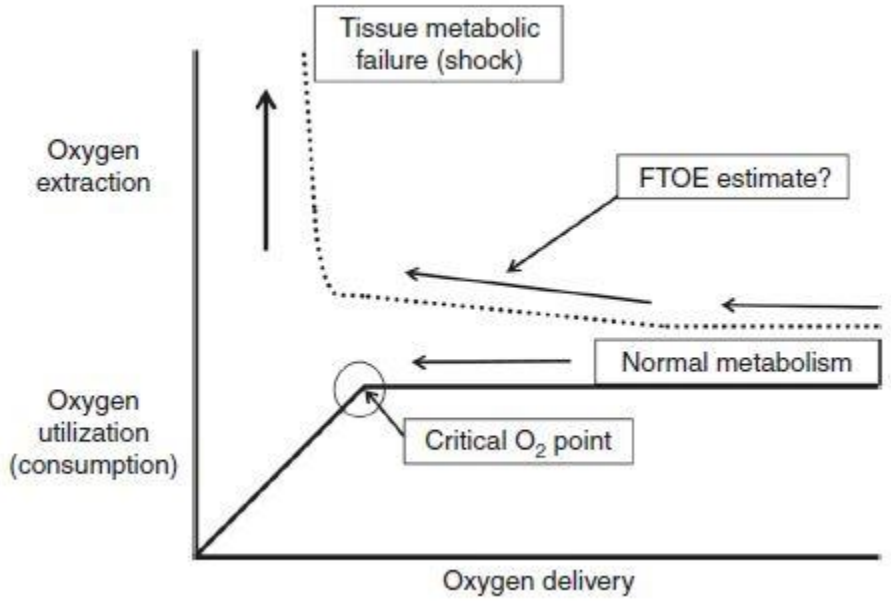
- Ventilation can impact cerbral circulation
- Cerebral oxygenation can also be affected by the type of ventilation support during surgery
- Ventilation is the main regulatory mechanism of arterial carbon dioxide pressure (pCO2)
- pCO2 can affect blood circulation and perfusion by altering arterial vessel
- Hypercapnia=Vasodilatation
- Hypocapnia=Vasocostriction



Dix et al., Front Ped 2017
Beaudin AE et al., J Appl Physiol 2017

Fractional Tissue Oxygen extraction:

…More information on dynamic changes (oxygen delivery vs consumption)
…Combine changes in SpO2 & rStO2)



tissue oxygen utilization remains relatively constant across a range of oxygen delivery with oxygen extraction stable to meet tissue metabolic requirements.

Initially, decreases in oxygen delivery produce subtle increases in oxygen extraction to maintain tissue homeostasis.

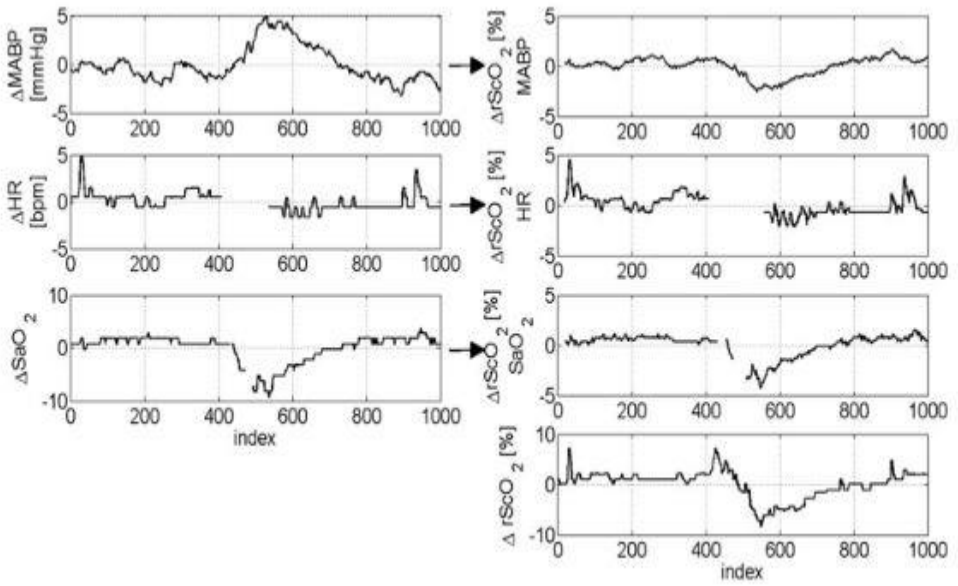
However, with further oxygen deprivation, a threshold is crossed ("the critical O2 point") beyond which ongoing tissue oxygen utilization becomes oxygen delivery-dependent.

Below the critical O2 point, dramatic increases in oxygen extraction are theorized as necessary to maintain tissue metabolic needs.

Mintzer and Moore, Ped Res. 2019

Autoregulation & Hypotension

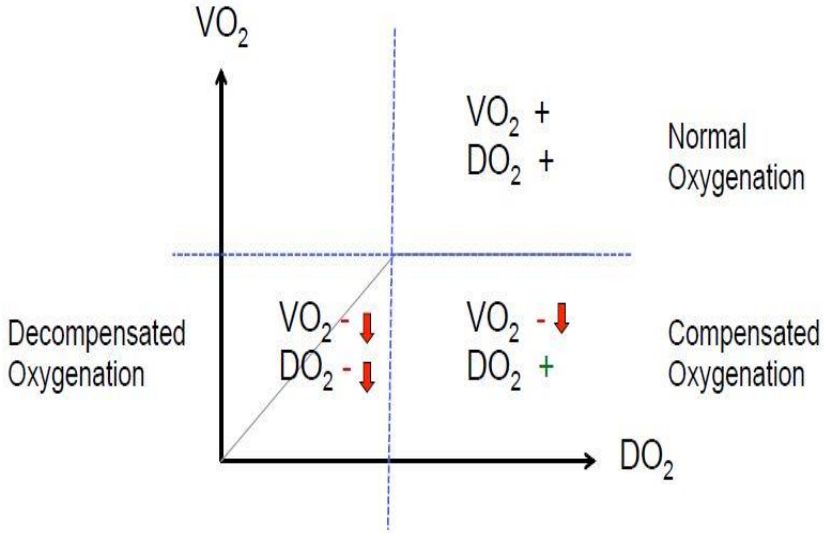
- Cerebral autoregulation is the ability to maintain stable cerebral perfusion and oxygenation during fluctuations in blood pressure
- Hypotension can cause a severe reduction in cerebral perfusion and impairment of cerebral autoregulation, leading to inadequate perfusion
- CHR monitor should include measurements of MABP, partial pressure of CO 2 (PaCO 2) and a surrogate marker for neurogenic activity (HR). In addition, measurements of SaO 2 should also be included in order to decouple its dynamics from NIRS measurements.



Dix et al., Front Ped 2017
Caicedo et al., Springer 2016

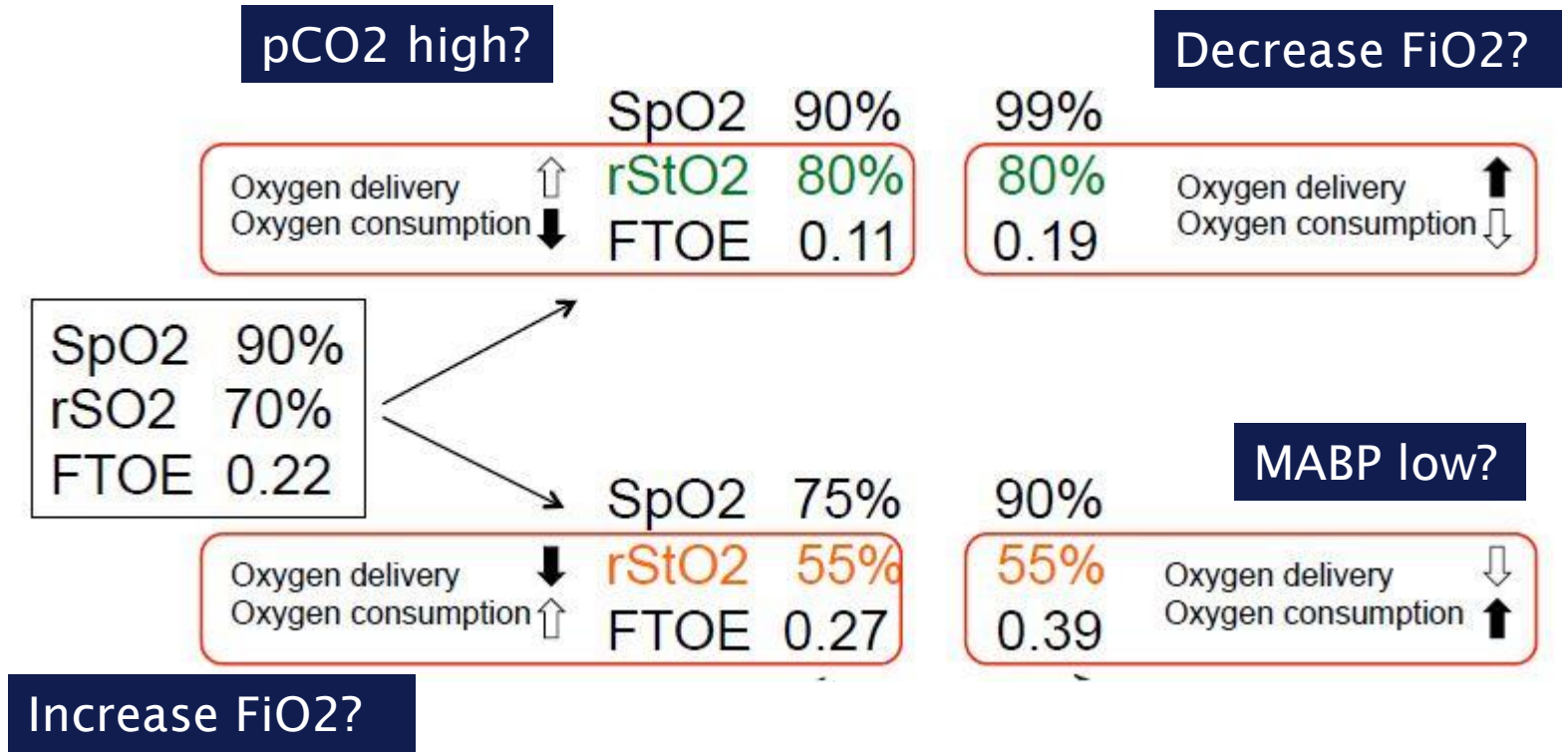
Fractional Tissue Oxygen extraction:

…More information on dynamic changes (oxygen delivery vs consumption)
…Combine changes in SpO2 & rStO2)



$$FTOE=(SaO2-rScO2)/SaO2$$

NORMAL FTOE is 20-30% (0.2-0.3)



Uni.Prof. B. Urlesberger, Medical University of Graz

Neuroprotective Approach

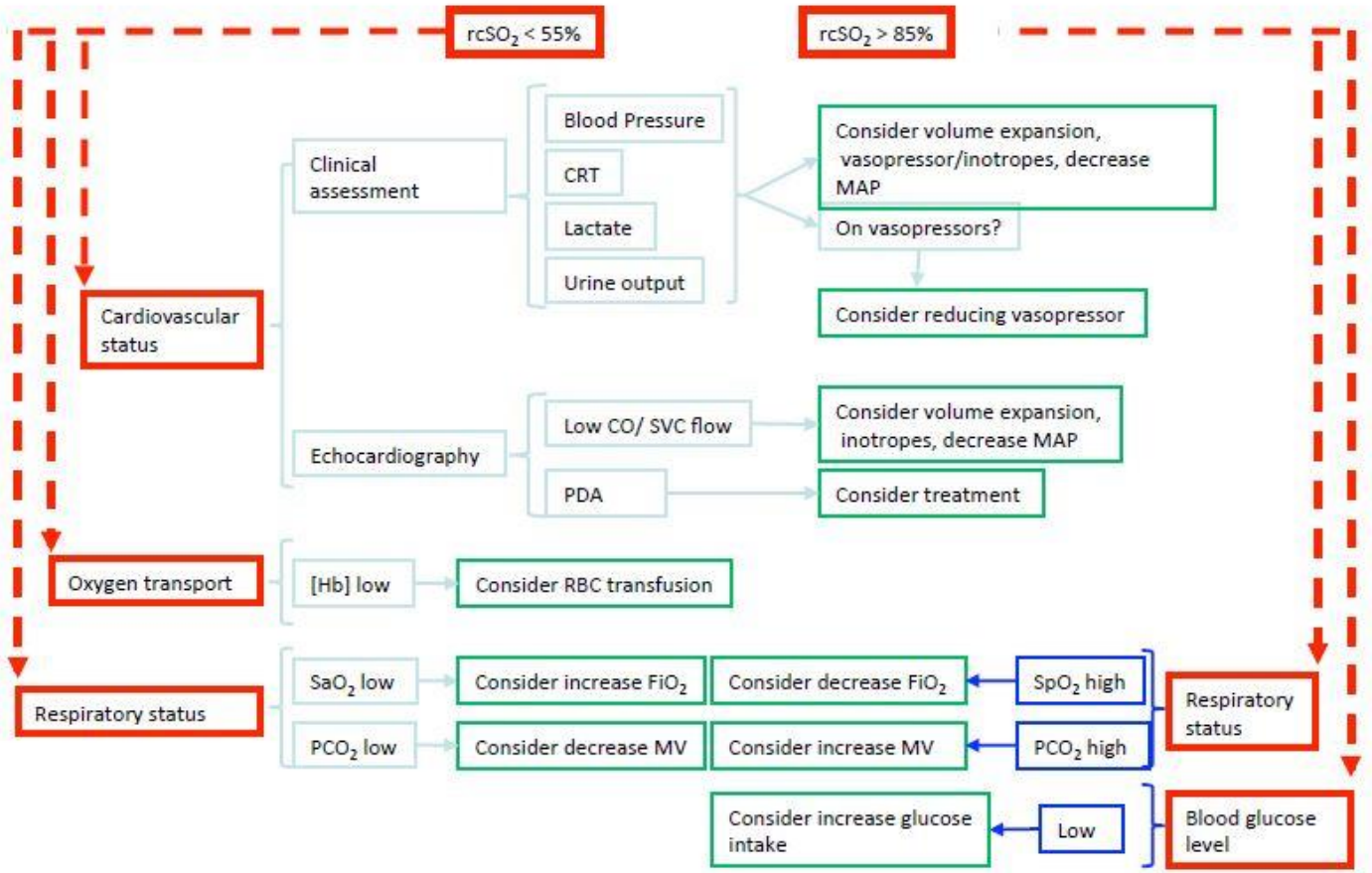
Neonatology
Research Briefings

The SafeBoosC Phase II Randomised Clinical Trial: A Treatment Guideline for Targeted Near-Infrared-Derived Cerebral Tissue Oxygenation versus Standard Treatment in Extremely Preterm Infants

Adelina Pellicer* Gorm Greisen* Manon Benders* Olivier Claris* Eugene Dempsey* Monica Fumagalli* Christian Gluud* Cornelia Hagmann* Lena Hellström-Westas* Simon Hyttel-Sorensen* Petra Lemmers* Gunnar Naulaers* Gerhard Pichler* Claudia Roll* Frank van Bel* Wim van Dewerwe* Maria Skoog* Martin Wolf* Topun Austin* and the SafeBoosC Trial Group

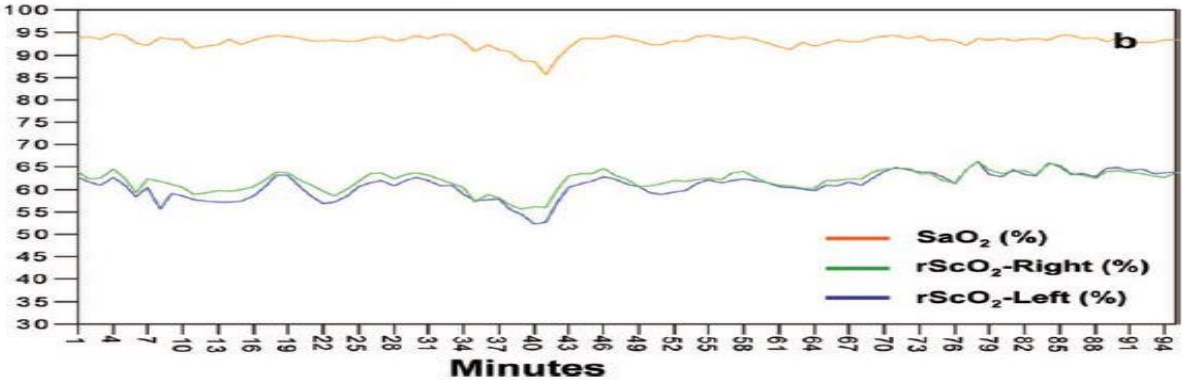
SafeBoosC

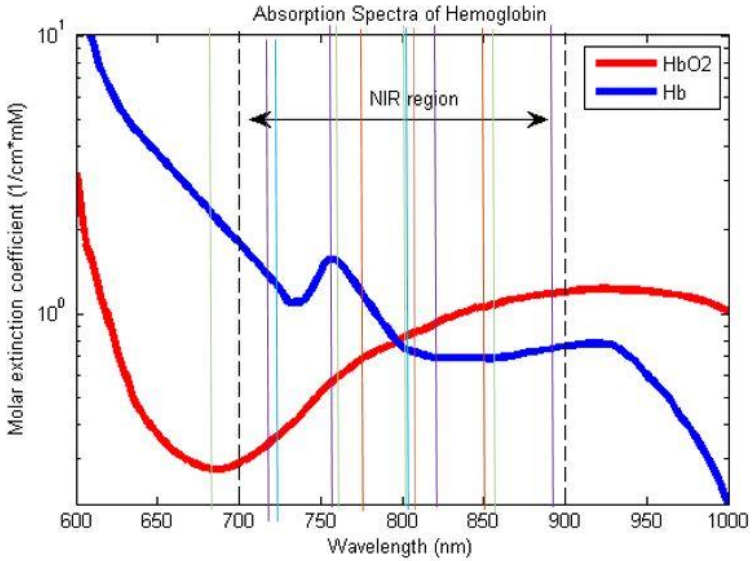
Treatment Protocol



What to know further…

$$rScO_{2\text{-neo}} = 0.8481 \times rScO_{2\text{-adult}} + 19.11$$





NIRO 200: 775, 810, 850 nm
INVOS: 730, 810 nm
Fore Sight: 690, 780, 805, 850 nm
Equanox: 730, 760, 810, 880

Vesoulis et al., J Perinat. 2021

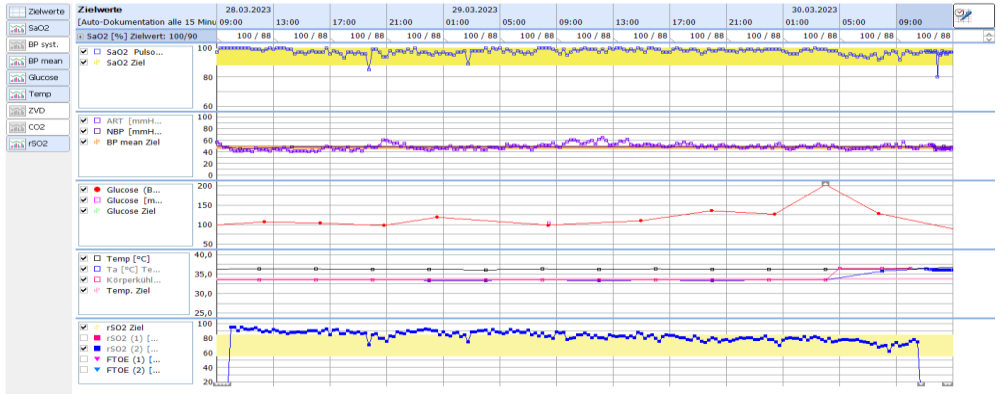
Device Name	Manufacturer	Regulatory approval[a]
BabyLux	BabyLux Project	Pre-market testing, investigational use only
EGOS-600	Tsinghua University	China
FORE-SIGHT Elite	Edwards	USA, EU, Japan
INVOS 5100c	Medtronic	USA, EU, Japan
MetaOx	ISS	Pre-market testing, investigational use only
NIRO 200NX	Hamamatsu Photonics	USA, EU, Japan
O3	Masimo	USA
OxyPrem 1.4	OxyPrem	EU
SenSmart X-100	Nonin	USA, EU, Japan

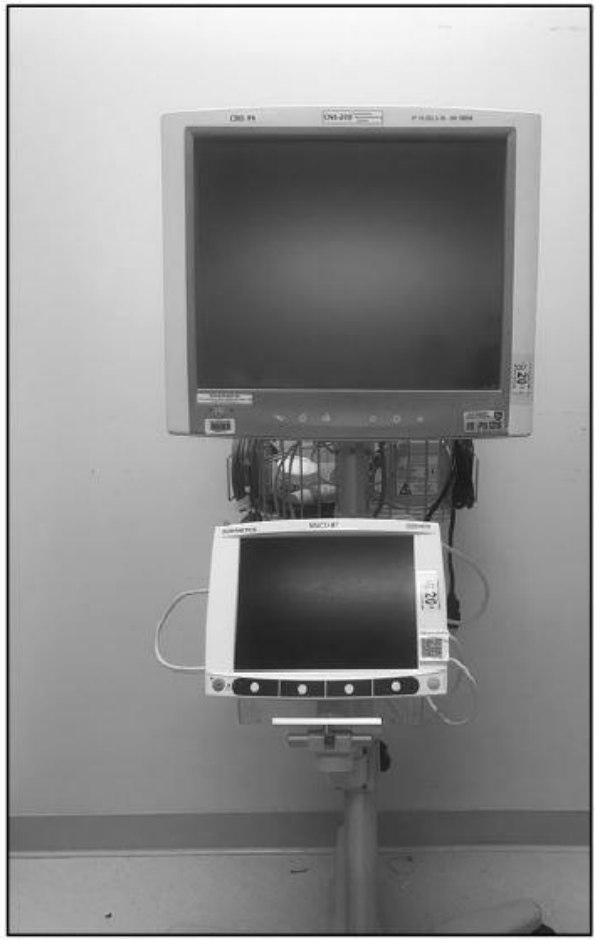
(Dix ML et al., 2013; Sood et al., 2015; Lemmers et al. 2009)

Commercially available data capture platform

Name	Manufacturer	Data export format	Type of data capture	Other features and notes
VitalSync	Medtronic	CSV	Hub	•Can also be used as a clinical tool and features some "early warning" algorithms •Works with INVOS monitors
FS DAQ	Edwards	CSV	Hub	•Works with ForeSight monitors
SenSmart Data Management	Nonin	CSV	NIRS only	•Works with Nonin X-100 monitors •No synchronization with other monitors
OxyPrem	Oxyprem	CSV, XLS	NIRS only	•Works with OxyPrem 1.4 monitor •Indirect capture via webpage interface, requires internet access •No synchronization with other monitors
ixTrend	ixitos	CSV	Hub or server	•Captures all data from the patient monitor, requires Philips patient monitor •Compatible with multiple brands of NIRS monitors (via IntelliBridge module) •NIRS monitor must be connected to patient monitors to be added to the data stream
BedMaster EX	Excel Medical	Proprietary[a]	Server	•Captures all data from the patient monitor, compatible with GE and Philips patient monitors •Compatible with multiple brands of NIRS monitors •NIRS monitor must be connected to the patient monitor or separately to BedMaster server to be included in the data stream
Data Warehouse Connect	Philips	HL7	Server	•Captures all data from the patient monitor, requires Philips monitor •Compatible with multiple brands of NIRS monitors (via IntelliBridge module) •NIRS monitor must be connected to patient monitors to be added to the data stream
ICM+	Cambridge Enterprise	HDF5, CSV	Hub	•Captures all data from the patient monitor, works with Philips and GE monitors •Compatible with many NIRS monitors •Can interface with other ICU monitors (intracranial pressure, EEG, etc.) •Has many built-in analytic tools, especially for autoregulation
SignalBase	University of Utrecht	Proprietary	Hub	•Integrated platform to capture patient data, amplitude-integrated EEG, and NIRS (INVOS) signals •Includes visualization and autoregulation analytic tools
CNS Monitor	Moberg ICU Solutions	Proprietary[a]	Hub	•Conventional EEG monitor •Built in compatibility with more than 30 different patient monitors include NIRS and patient monitors

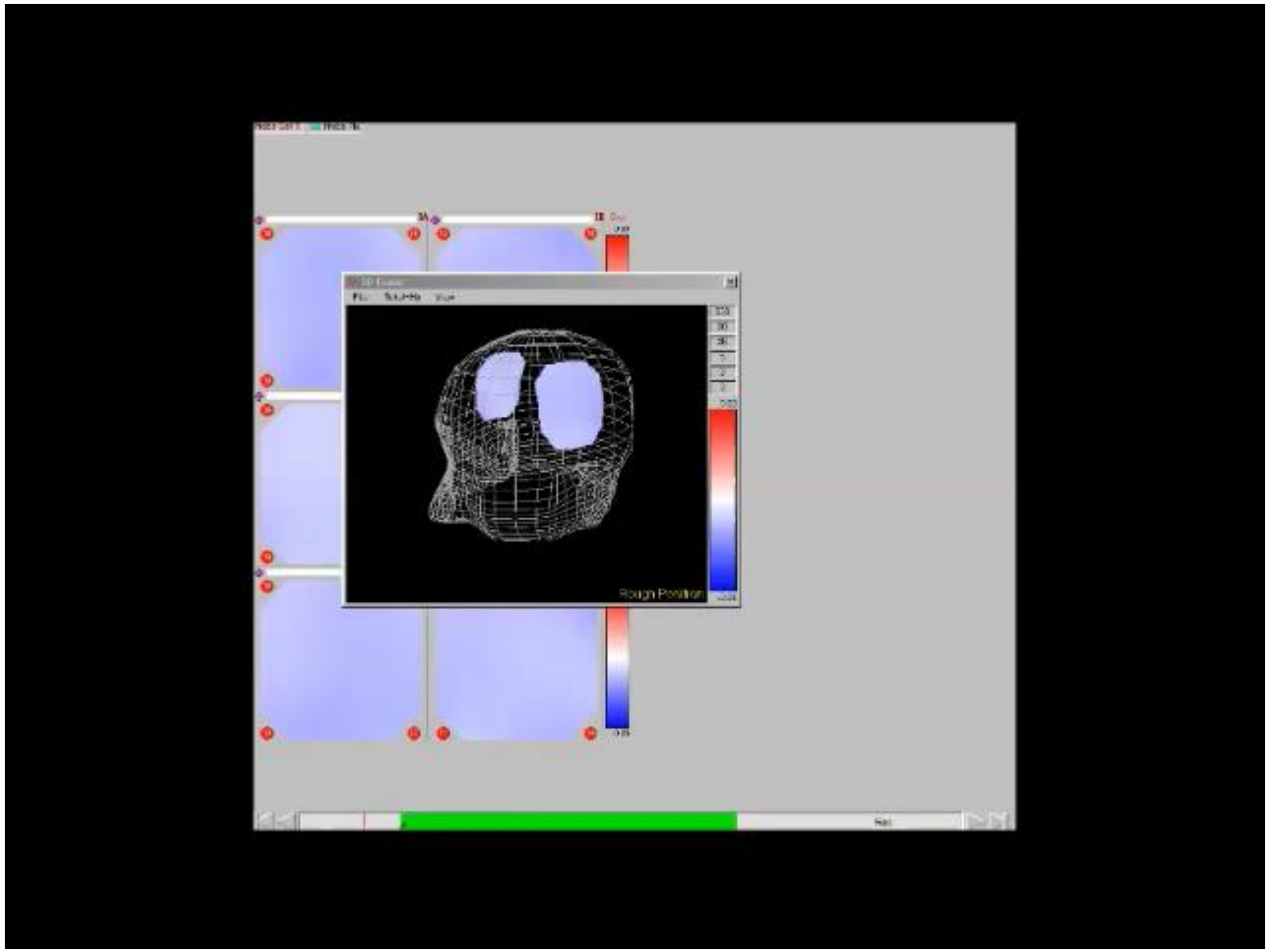
[a]Files can be converted to other formats via conversion tools available upon request from the manufacturer.

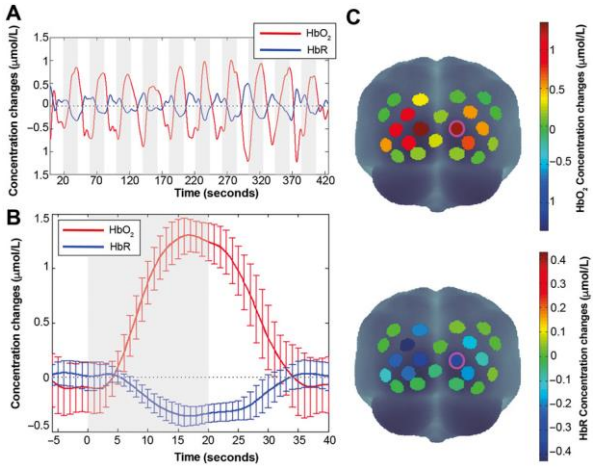




VESOULIS AV et al. J Perinat 2021

What to know further…fNIRS





Clinical application?

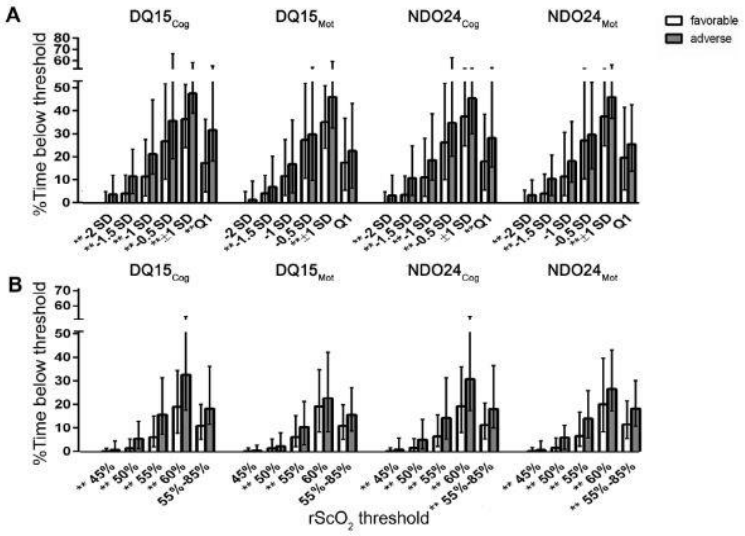
Patent Ductus Arteriosus
Respiration
Autoregulation
Hypotension
RBCT
HIE
Neurodevelopmental outcomes

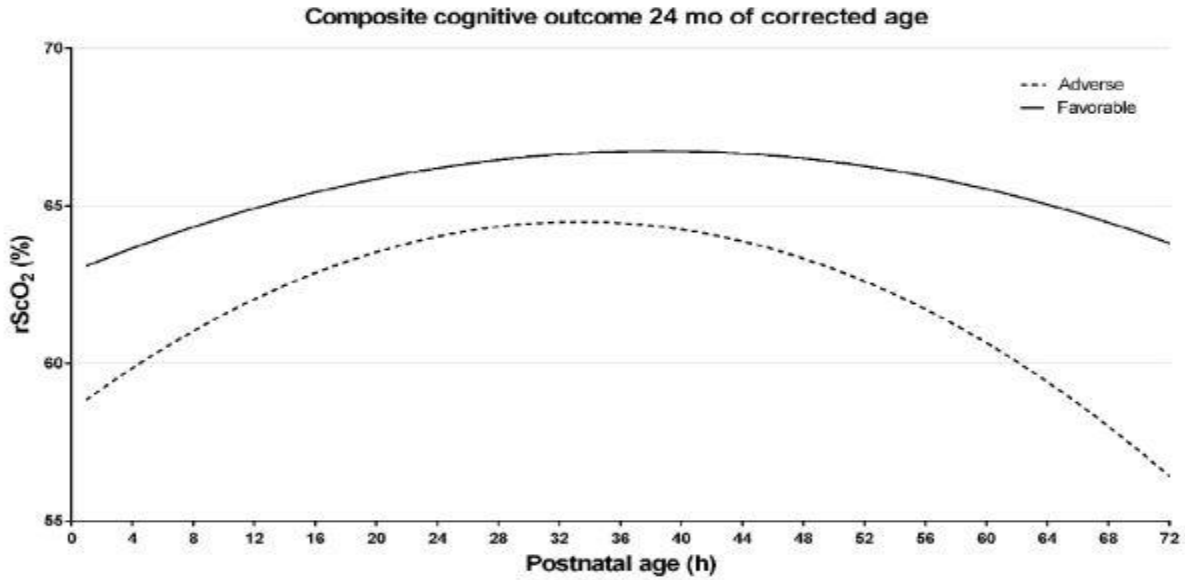
THE JOURNAL OF PEDIATRICS • www.jpeds.com

ORIGINAL ARTICLES

Low Cerebral Oxygenation in Preterm Infants Is Associated with Adverse Neurodevelopmental Outcome

Thomas Alderliesten, MD, PhD[1], Frank van Bel, MD, PhD[1], Niek E. van der Aa, MD, PhD[1], Paul Steendijk, MSc, PhD[2], Ingrid C. van Haastert, MA, PhD[1], Linda S. de Vries, MD, PhD[1], Floris Groenendaal, MD, PhD[1], and Petra Lemmers, MD, PhD[1]





Low, but not high, rScO2 was associated with an unfavorable cognitive outcome. This suggests the use of a threshold of rScO2 <55% for future clinical studies when using adult near-infrared sensors (rScO2 <65% for neonatal sensors, approximately).

ORIGINAL ARTICLE

FREE PREVIEW

Cerebral Oximetry Monitoring in Extremely Preterm Infants

Mathias L. Hansen, M.D., Ph.D., Adelina Pellicer, M.D., Ph.D., Simon Hyttel-Sørensen, M.D., Ph.D., Ebru Ergenekon, M.D., Ph.D., et al.

April 20, 2023

N Engl J Med 2023; 388:1501-1511

DOI: 10.1056/NEJMoa2207554

Cerebral Oximetry Monitoring in Extremely Preterm Infants

Hansen ML et al. DOI: 10.1056/NEJMoa2207554

CLINICAL PROBLEM

The use of cerebral oximetry monitoring to guide the treatment of extremely preterm infants is increasing, yet evidence for its effects on clinical outcomes is lacking.

CLINICAL TRIAL

Design: A phase 3, multinational, pragmatic, open-label, randomized, controlled trial examined whether treatment guided by cerebral oximetry for the first 72 hours after birth would result in a better outcome than usual care in extremely preterm infants.

Intervention: 1601 infants born before 28 weeks' gestation were assigned, within 6 hours after birth, to cerebral oximetry monitoring or usual care; 1579 of these infants (98.6%) were evaluated for the primary outcome. In the cerebral oximetry group, intervention was considered at the hypoxic threshold of 55%. The primary outcome was a composite of death or survival with severe brain injury at 36 weeks' postmenstrual age.

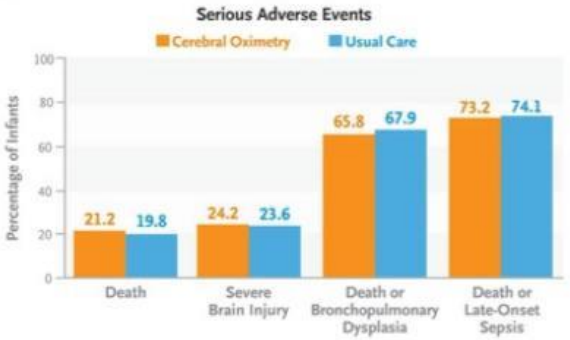
RESULTS

Efficacy and Safety: Among evaluable infants, the incidence of death or severe brain injury did not differ significantly between the cerebral oximetry group and the usual-care group. The incidences of other serious adverse events — including death alone, severe brain injury alone, death or bronchopulmonary dysplasia, and death or late-onset sepsis — also did not differ materially between the groups.

LIMITATIONS AND REMAINING QUESTIONS

- Diagnosis of severe brain injury was based on routine cerebral ultrasonography and imaging reports; magnetic resonance imaging was not used, and cerebral ultrasound images did not undergo central adjudication.
- Less than 80% of infants underwent cerebral ultrasonography both early and late in their clinical course.
- Only short-term outcomes were assessed; follow-up at a corrected age of 2 years is ongoing to assess neurodevelopmental and other outcomes.

Links: Full Article | NEJM Quick Take



CONCLUSIONS

In extremely preterm infants, treatment guided by cerebral oximetry monitoring for the first 72 hours after birth was not associated with a lower incidence of death or severe brain injury at 36 weeks' postmenstrual age than usual care.

NIRS - Summary

Pro

- Easy to use
- Trend Monitoring
- Performable at the Patient´s bedside
- Added Info in the clinical setting

- Range: 55-85
- FTOE for more dynamic interpretation

Contra

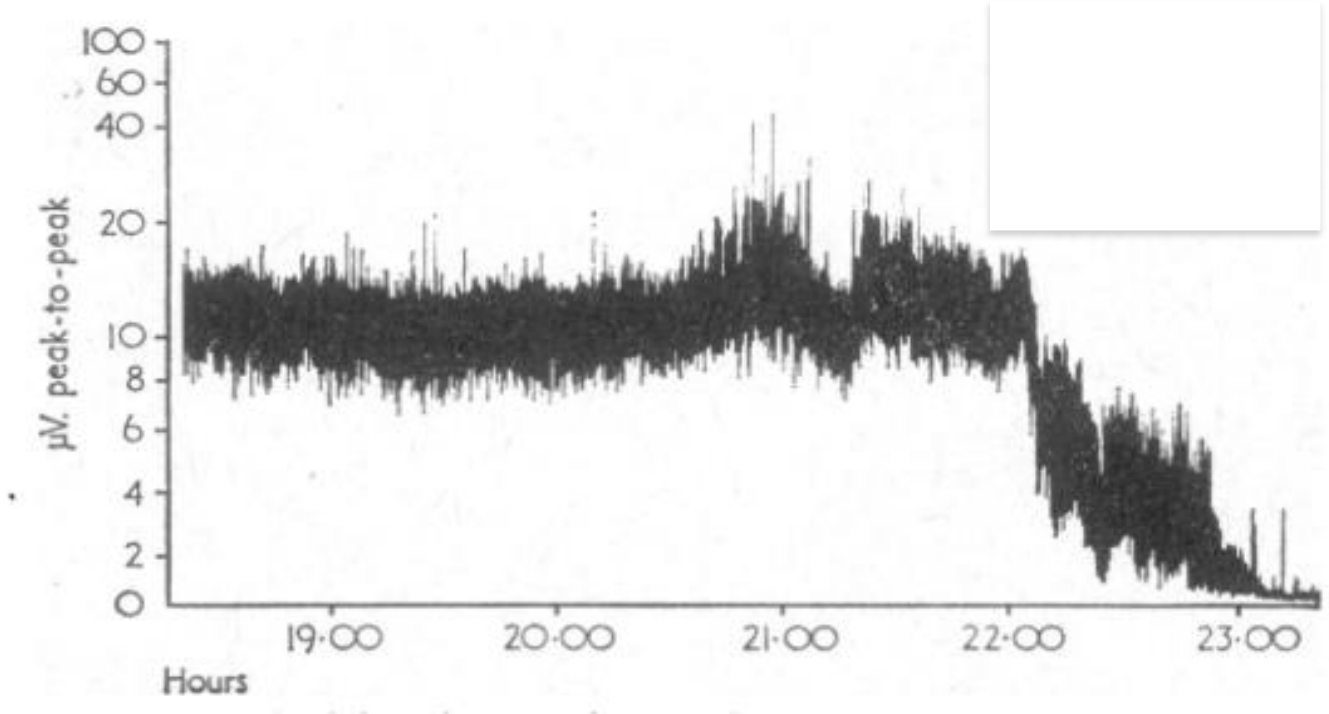
- Not stand alone monitoring
- Interpretation depend on several factors
- Extra cable for a patient in intensive setting
- Variability of device output
- Expensive

aEEG

Amplitude integrated EEG (aEEG)

Device for Continuous Monitoring of Cerebral Activity in Resuscitated Patients

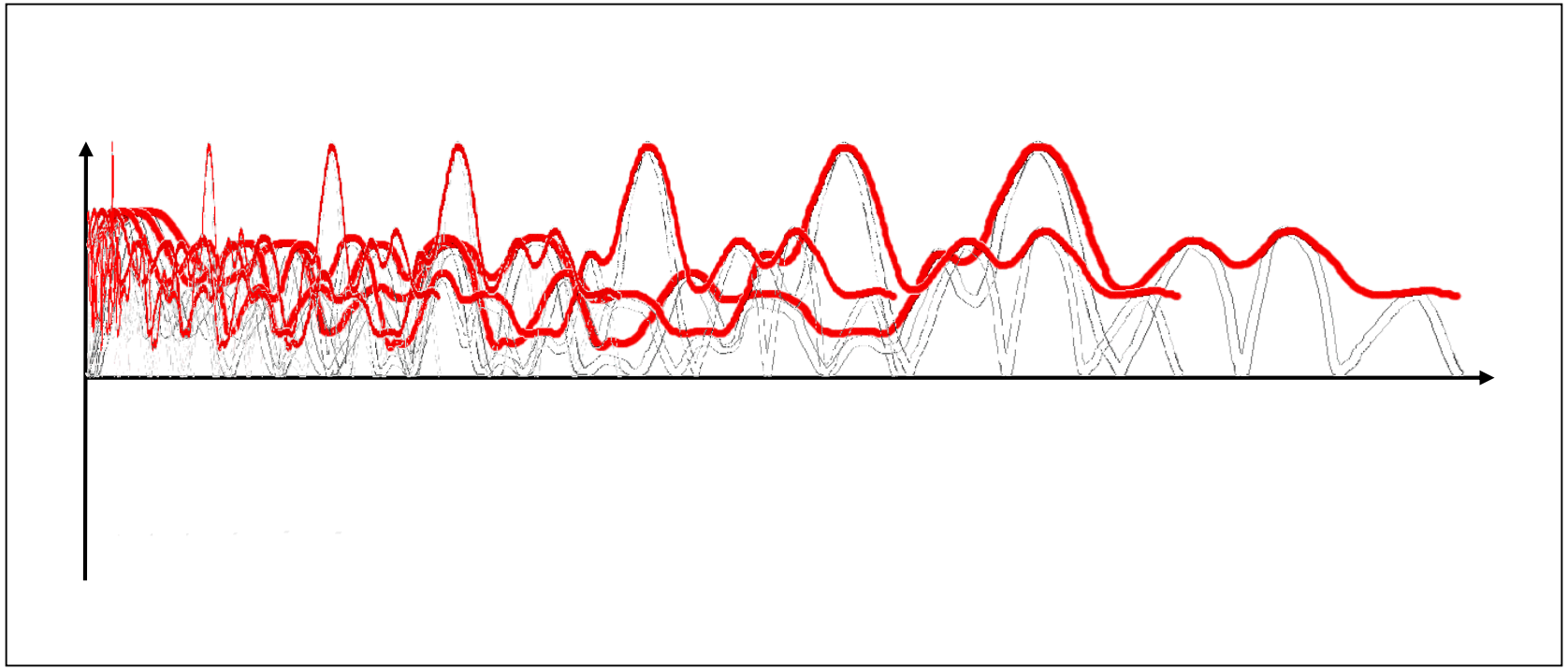
Mr. D. MAYNARD, Dr. PAMELA F. PRIOR



29 November 1969

BRITISH MEDICAL JOURNAL

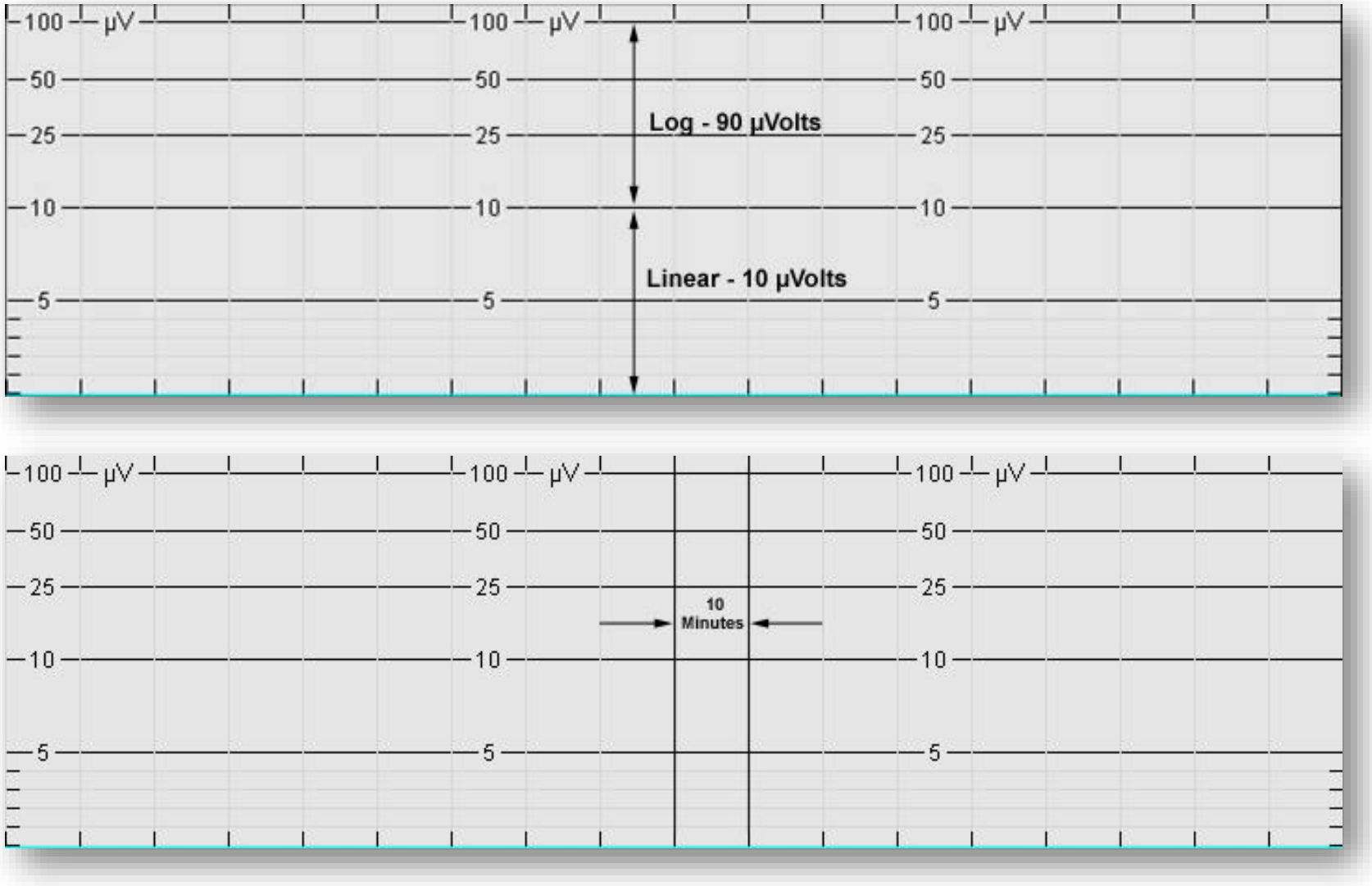
The amplitude-integrated EEG (aEEG)



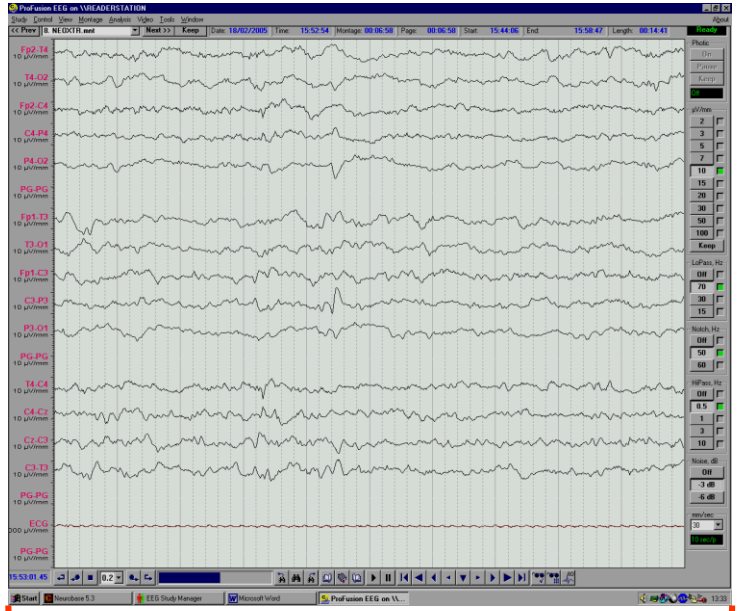
Time compressed → 6 cm/h

Copyright J.W.Richter

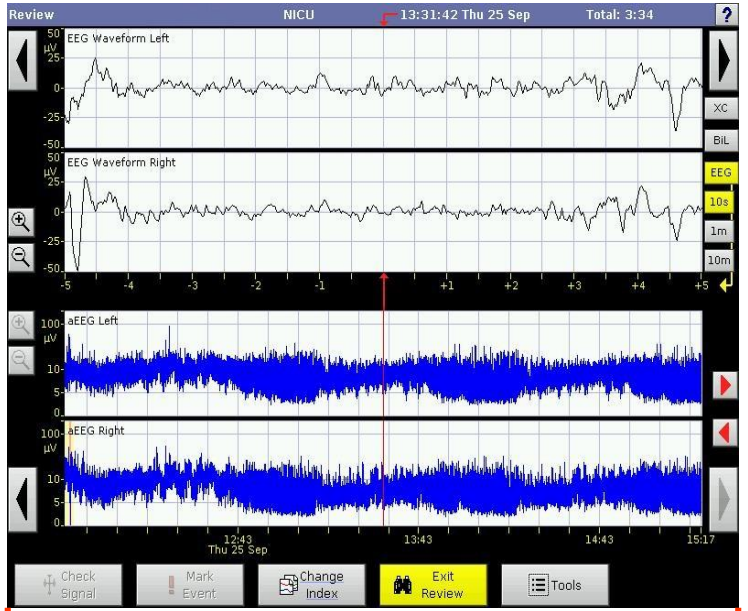
Data visualization



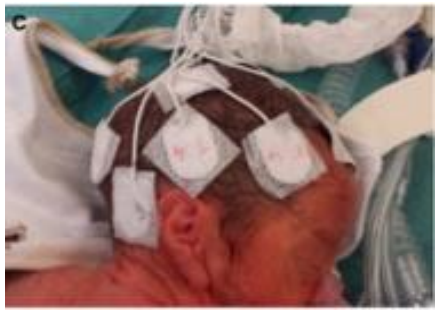
EEG Vs aEEG

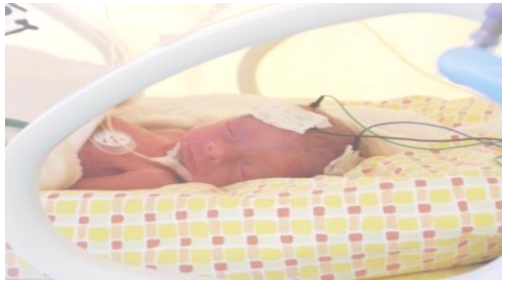


10 s conventional EEG

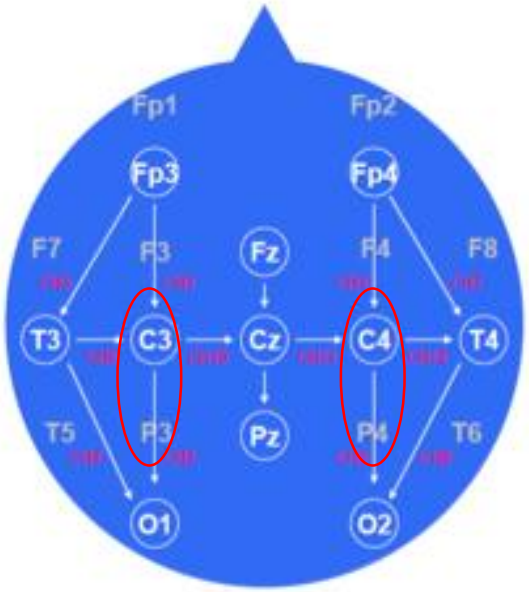


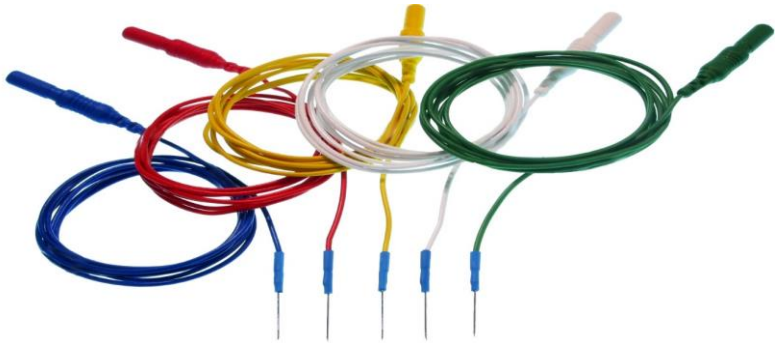
3.5 h aEEG

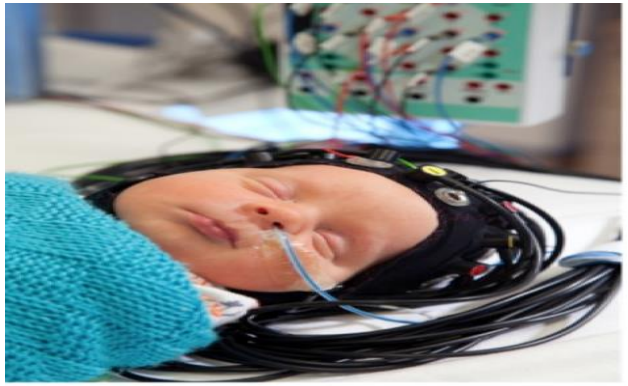




Electrodes Placement:







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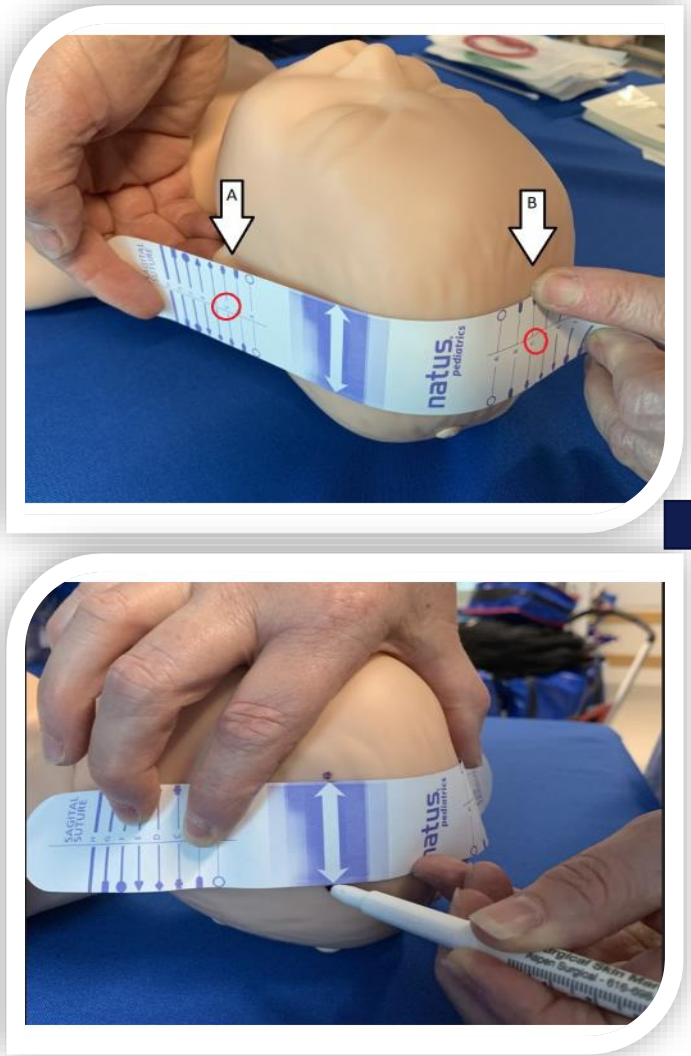
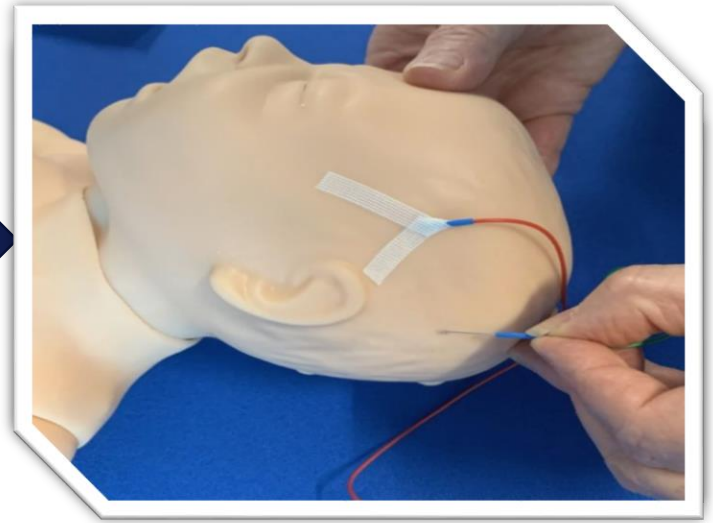
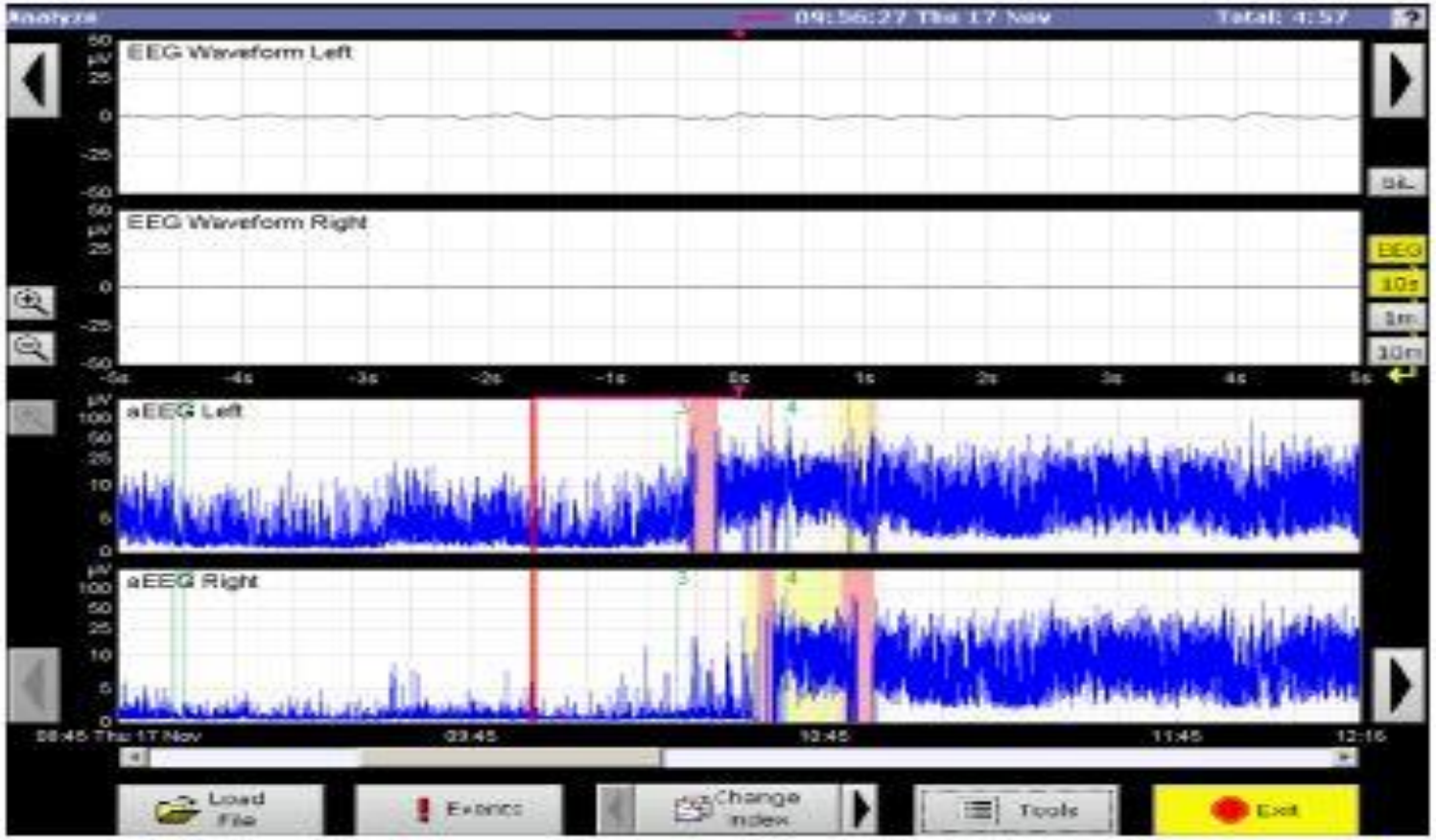


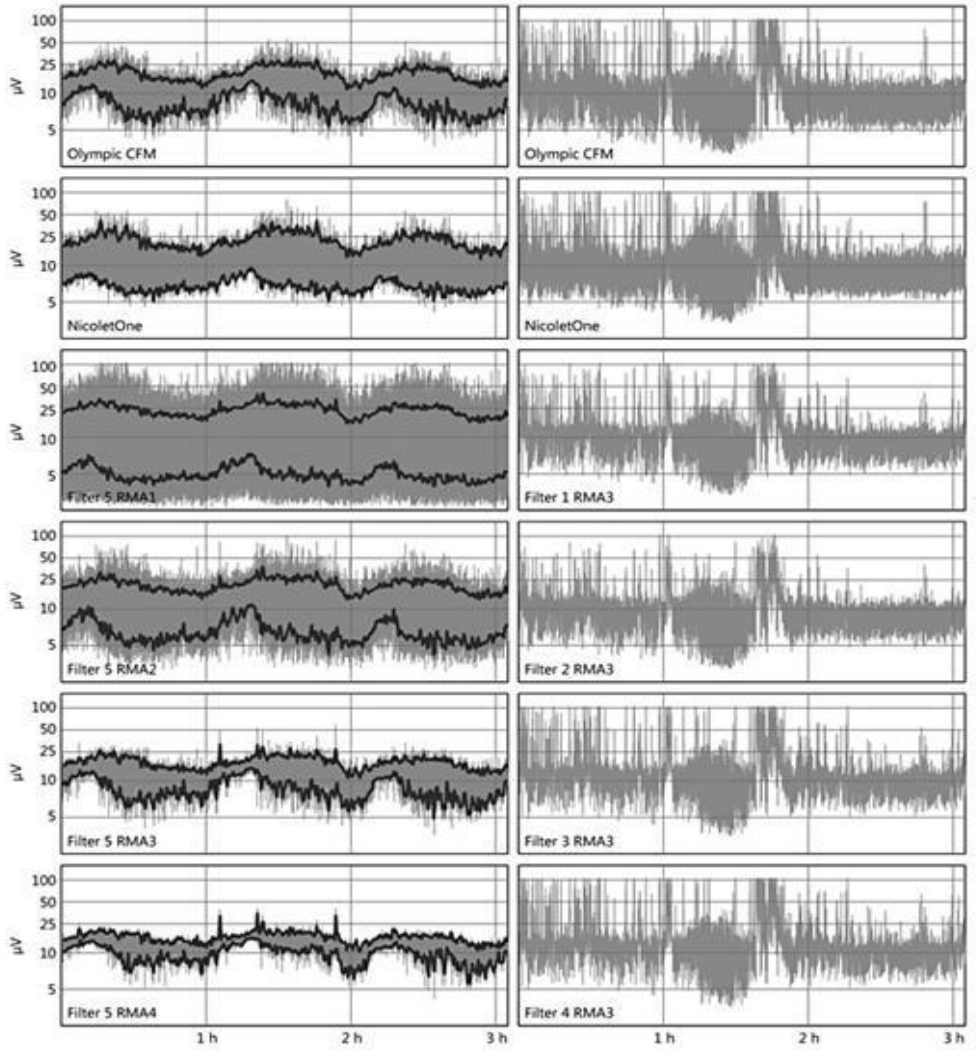


Willson et al., JoVE 2024

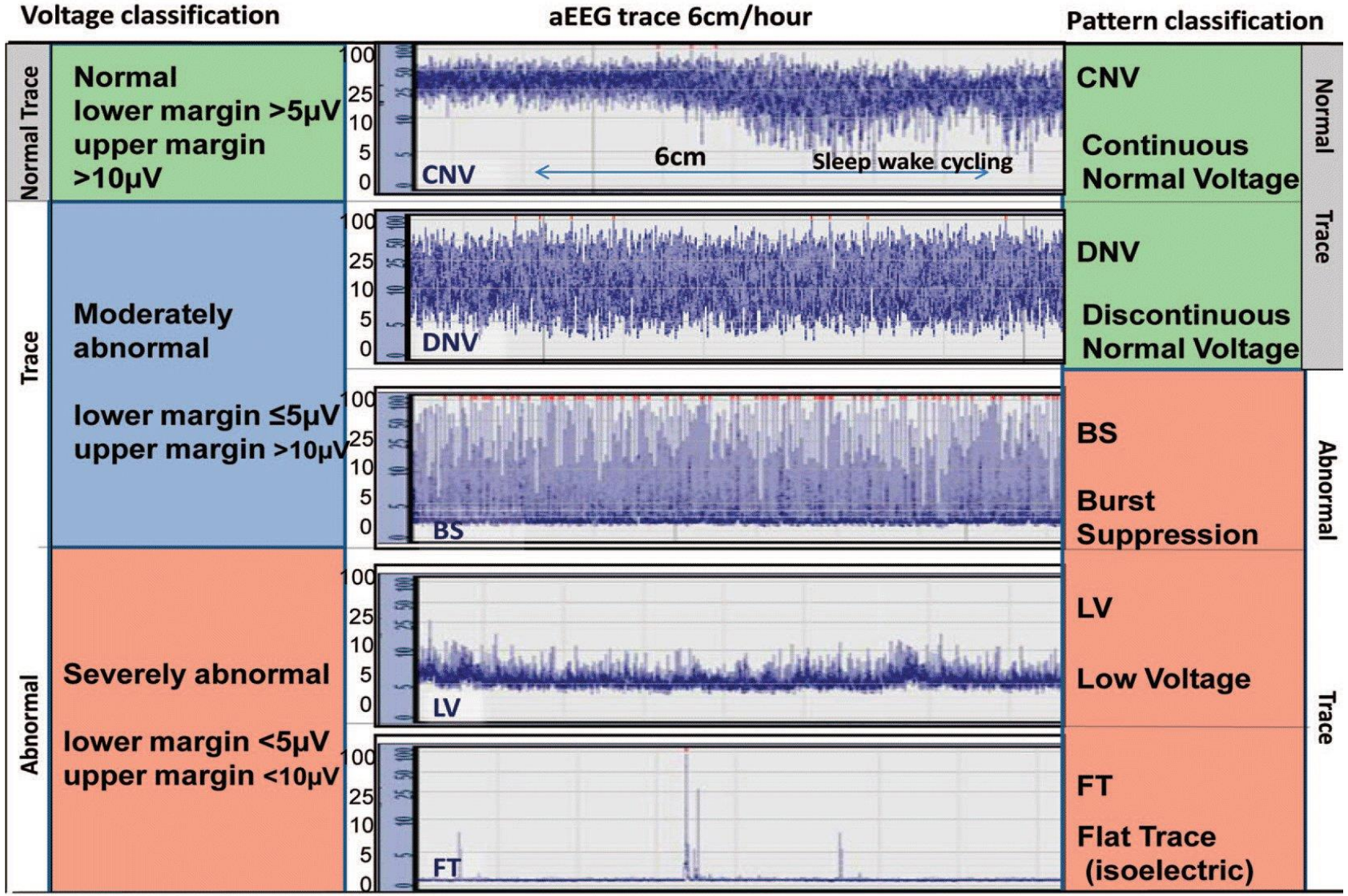
Elctrodes to close to each other – „Bridge“



Are all aEEG system equal?



Werther et al., Neonatology 2017



From Thoresen M, et al. Effect of hypothermia on amplitude-integrated electroencephalogram in infants with asphyxia. Pediatrics. 2010 Jul;126(1):e131-9. PMID:9563847 Reprinted with permission of The American Academy of Pediatrics

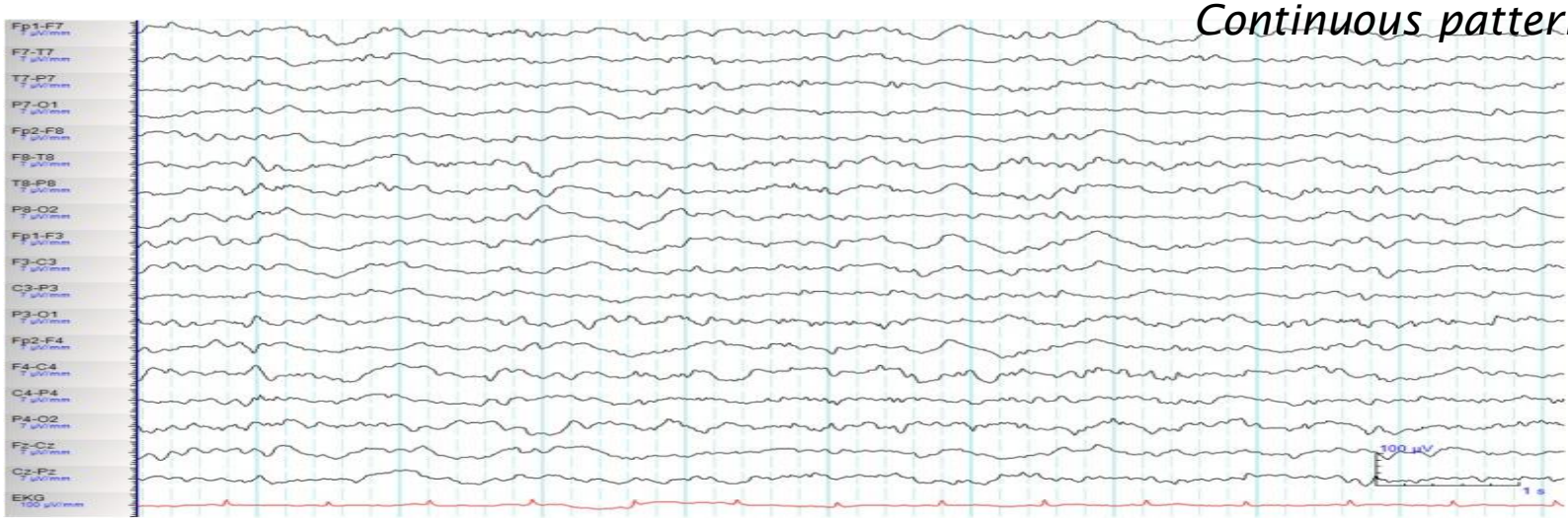
Background & SWC maturation

SSW	Dominating Backgroud	SWC	Min Ampl	Max Ampl
24-25	DC	Imminent Immature	2 to 5	25 to 50
26-27	DC	Imminent Immature	2 to 5	25 to 50
28-29	DC/C	Immature/developed	2 to 5	25 to 50
30-31	C/DS	Immature/developed	2 to 6	20 to 30
32-33	C/DS in Quiet sleep	developed	2 to 6	20 to 30
34-35	C/DS in Quiet sleep	developed	3 to 7	15 to 25
36-37	C/DS in Quiet sleep	developed	4 to 8	17 to 35
38+	C	developed	7 to 8	15 to 25

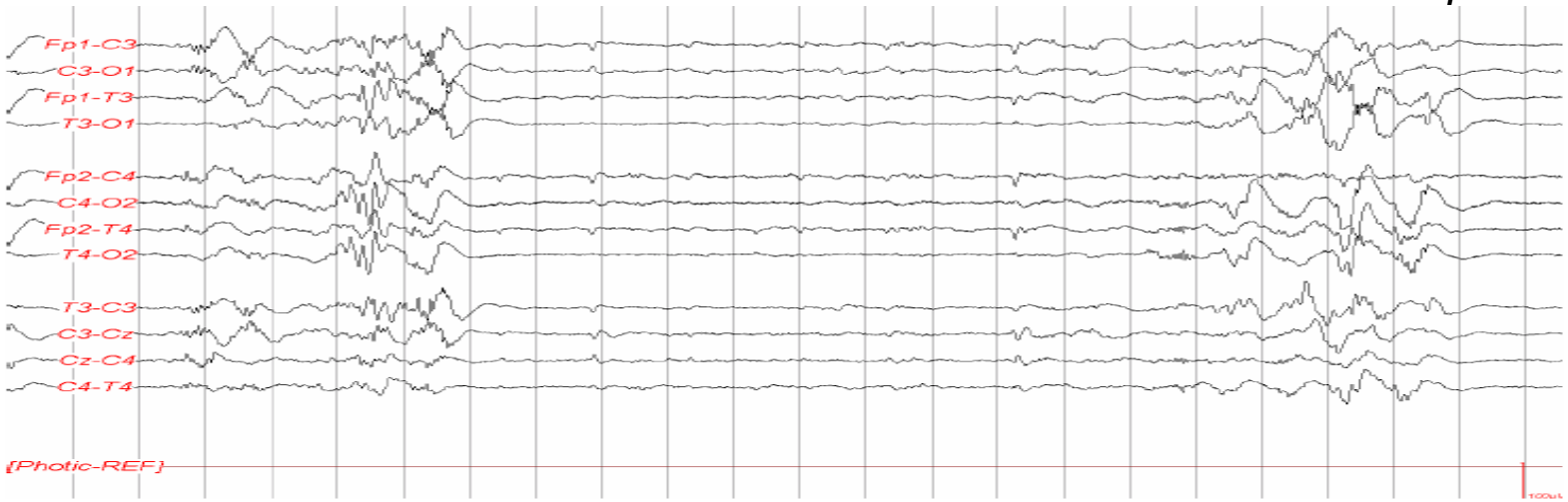
Hellström-Westas L et al, Neoreviews 2006;7:e76-87

Continuity Vs Discontuinity

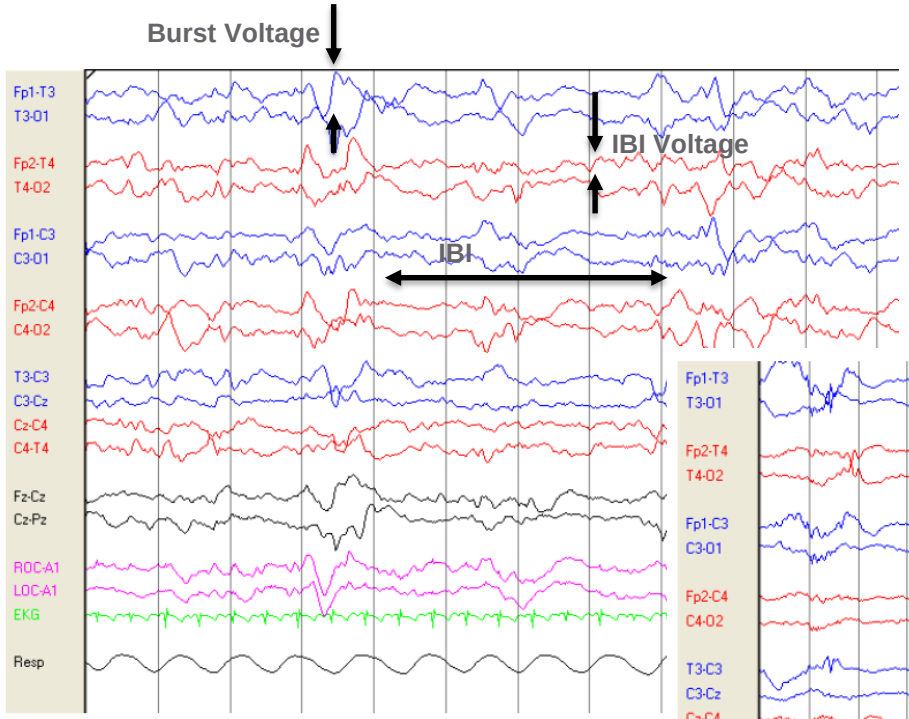
Continuous pattern



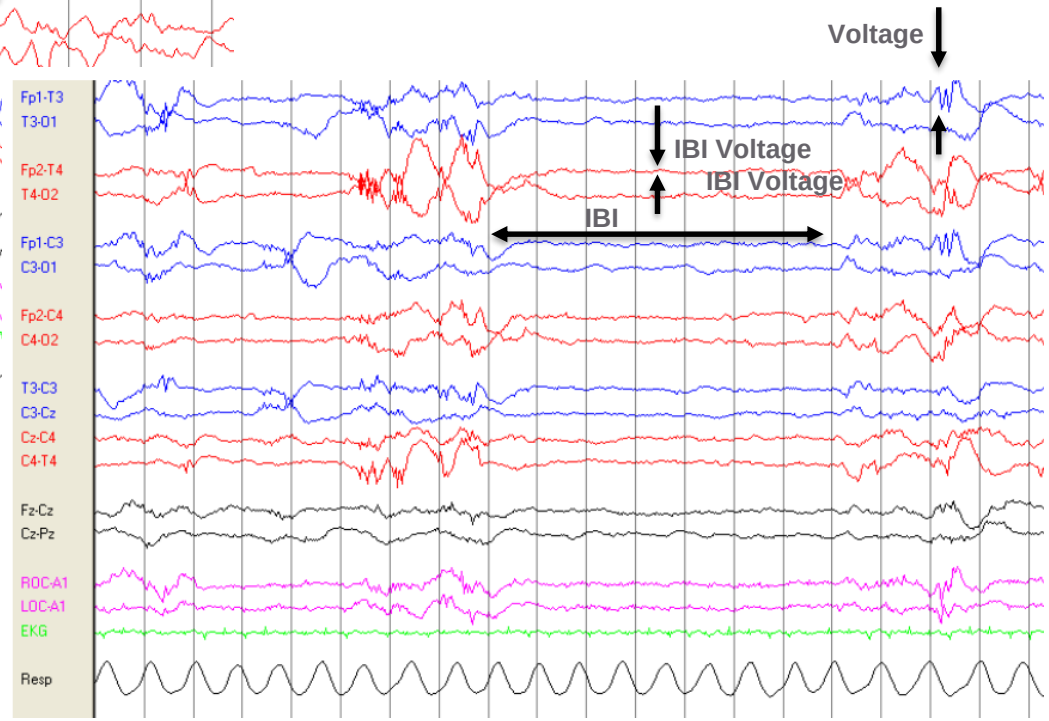
discontinuous pattern



Discontinuity:

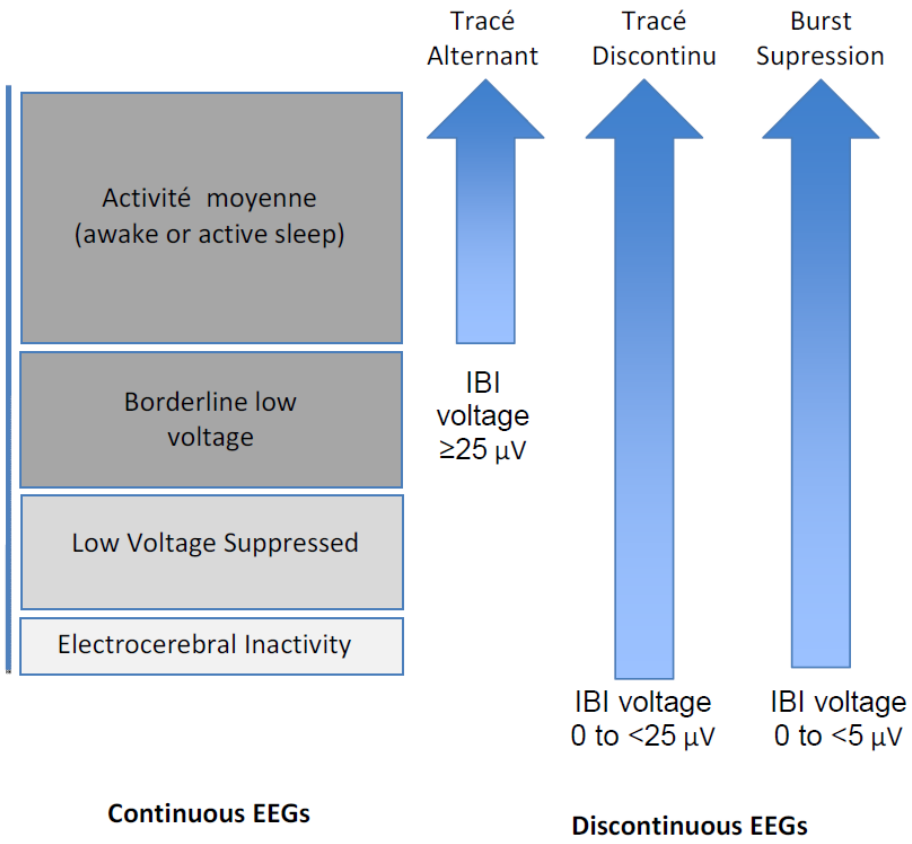


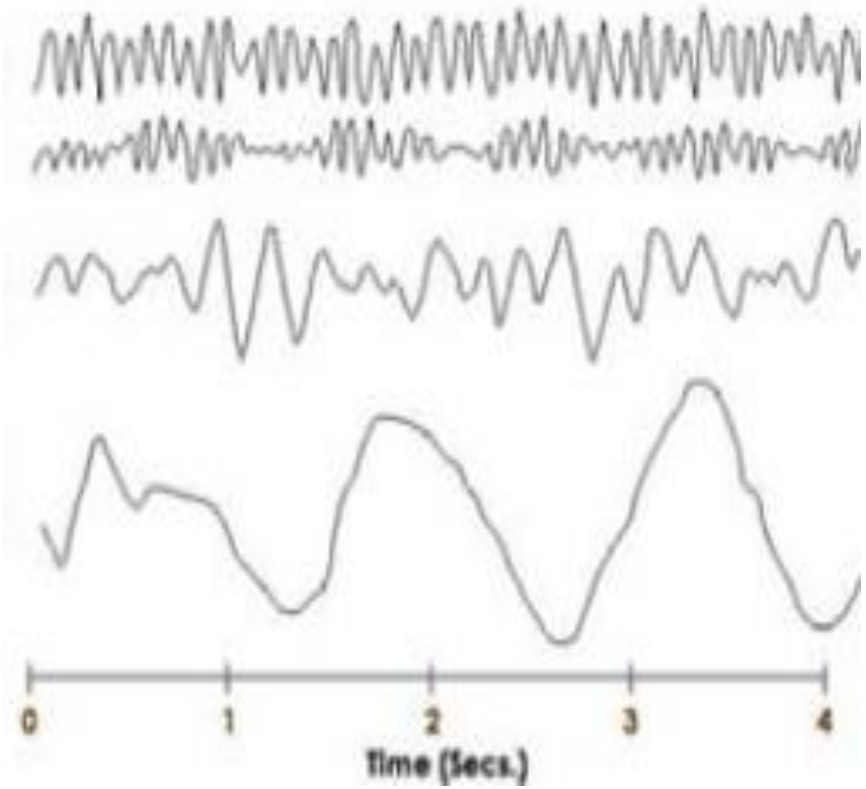
tracé alternant



tracé discontinu

Classification:

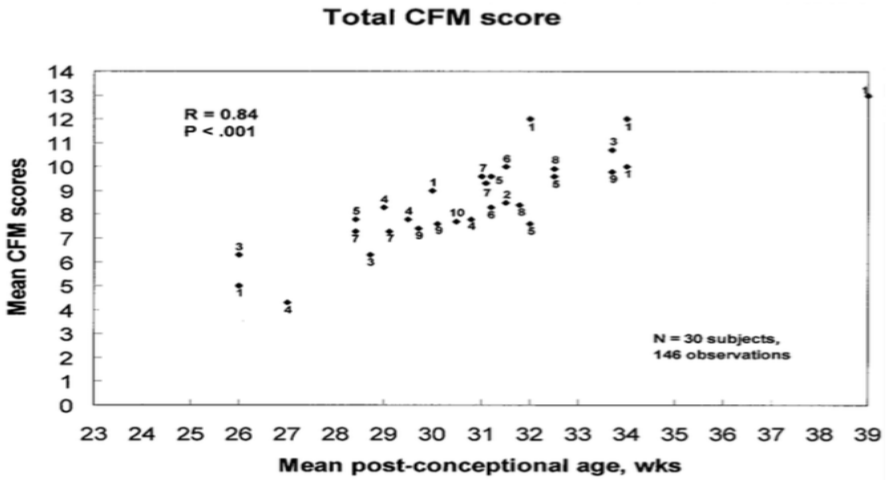


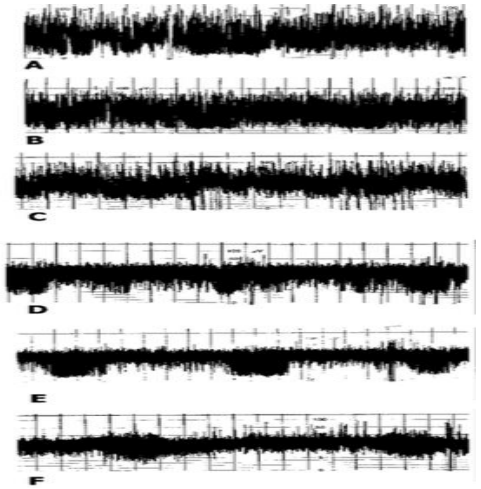


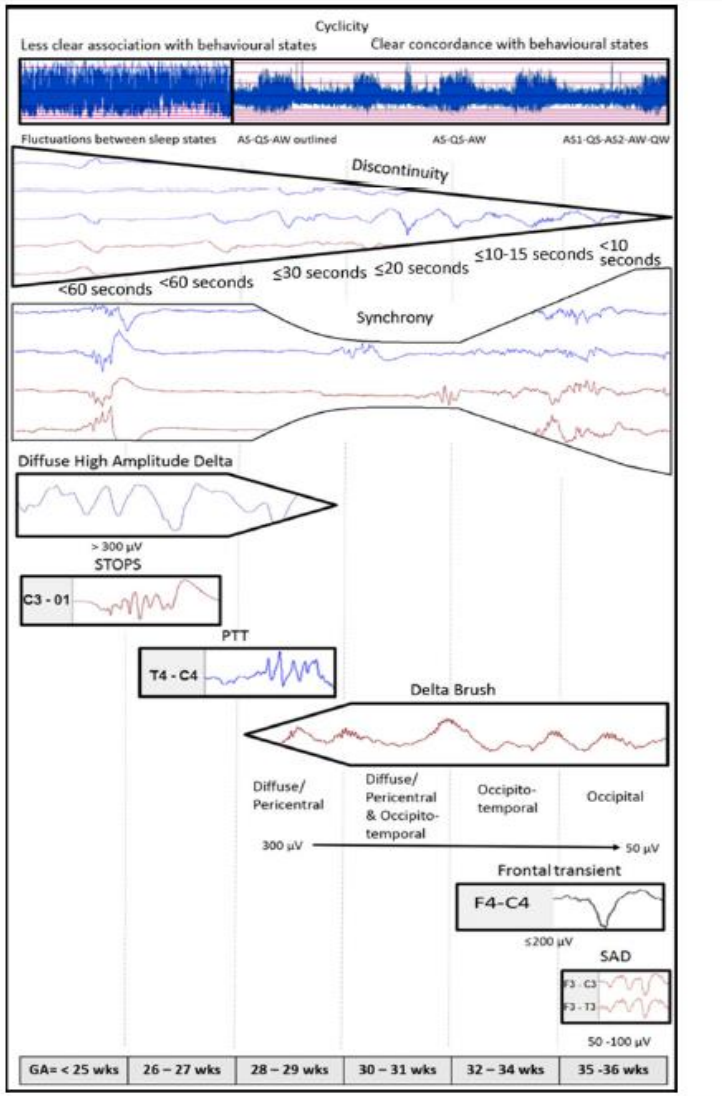
Source: Tsuchida et al., 2013. ACNS Standardized EEG Terminology and Categorization for the Description of Continuous EEG Monitoring in Neonates: Report of the American Clinical Neurophysiology Society Critical Care Monitoring Committee. Journal of Clinical Neurophysiology 30, 161–173. doi:10.1097/WNP.0b013e3182872b24

Burdjalov Score: (Burdjalov et al., 2003)

Score	Continuity	Cycling	Amplitude of Lower Border	Bandwidth Span and Amplitude of Lower Border
0	Discontinuous	None	Severely depressed (<3 μV)	Very depressed: low span (≤15 μV) and low voltage (5 μV)
1	Somewhat continuous	Waves first appear	Somewhat depressed (3–5 μV)	Very immature: high span (>20 μV) or moderate span (15–20 μV) and low voltage (5 μV)
2	Continuous	Not definite, somewhat cycling	Elevated (>5 μV)	Immature: high span (>20 μV) and high voltage (>5 μV)
3		Definite cycling, but interrupted		Maturing: moderate span (15–20 μV) and high voltage (>5 μV)
4		Definite cycling, noninterrupted		Mature: low span (<15 μV) and high voltage (>5 μV)
5		Regular and mature cycling		

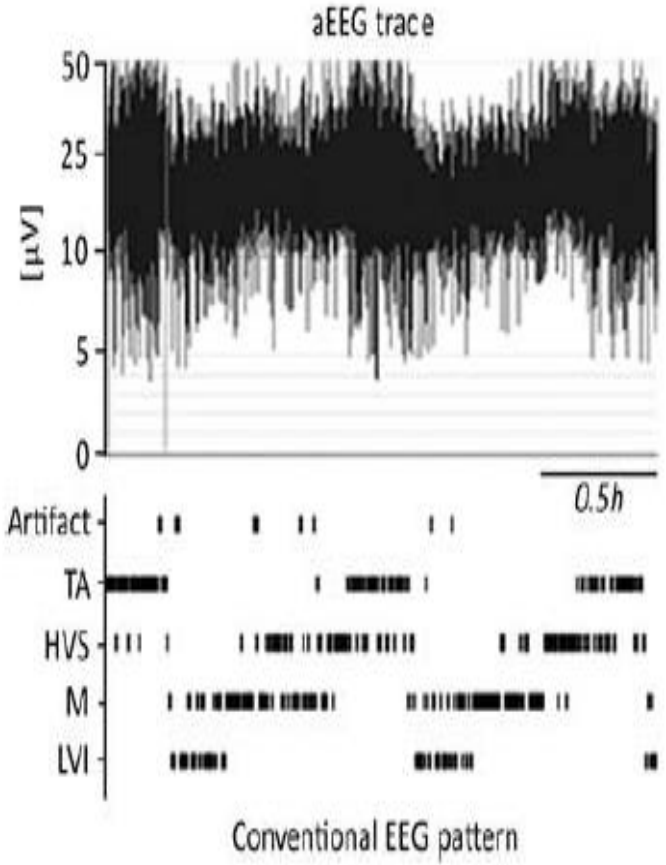


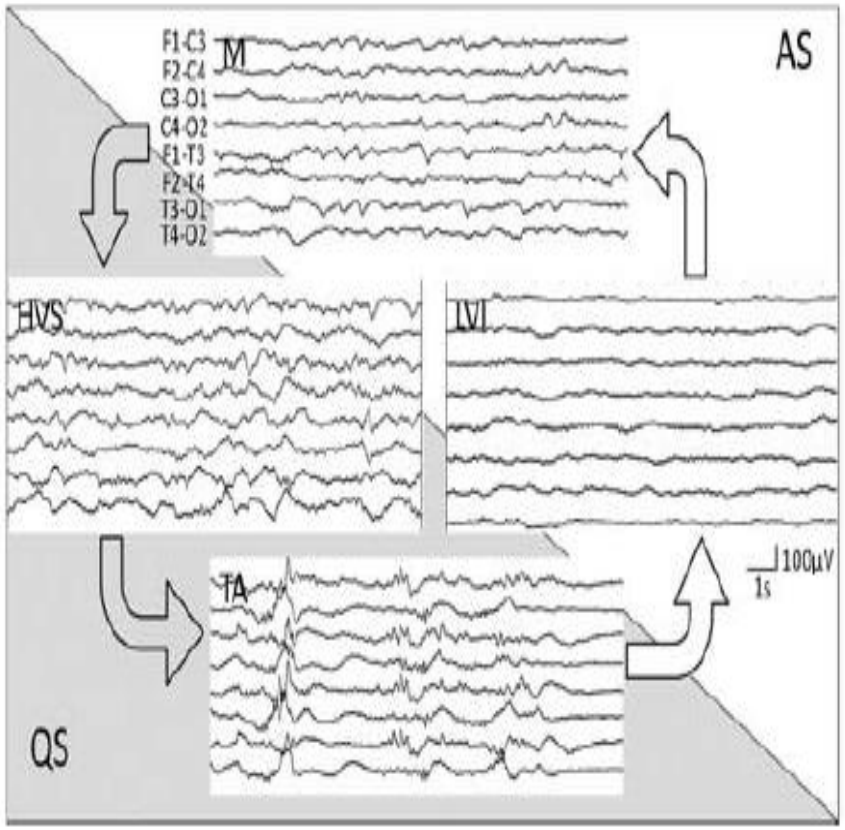




(Pavlidis et al., 2017)

New terminology: “Cyclicity”

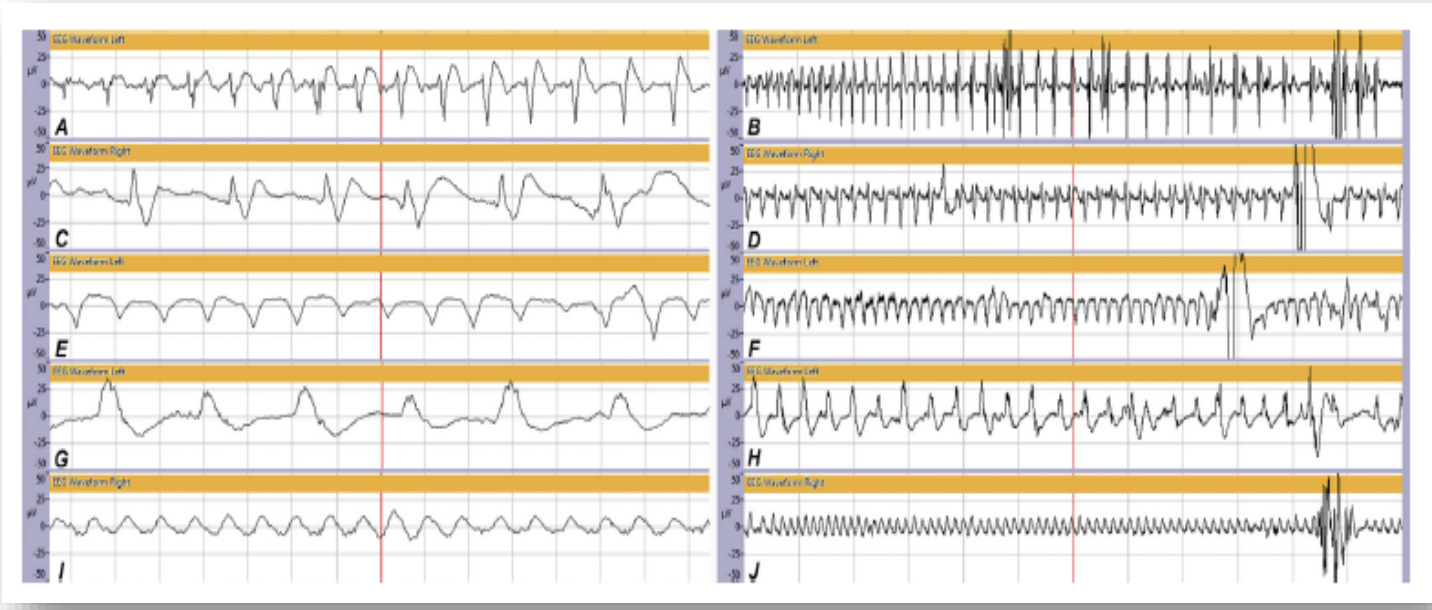




(Kidokoro et al., 2012)

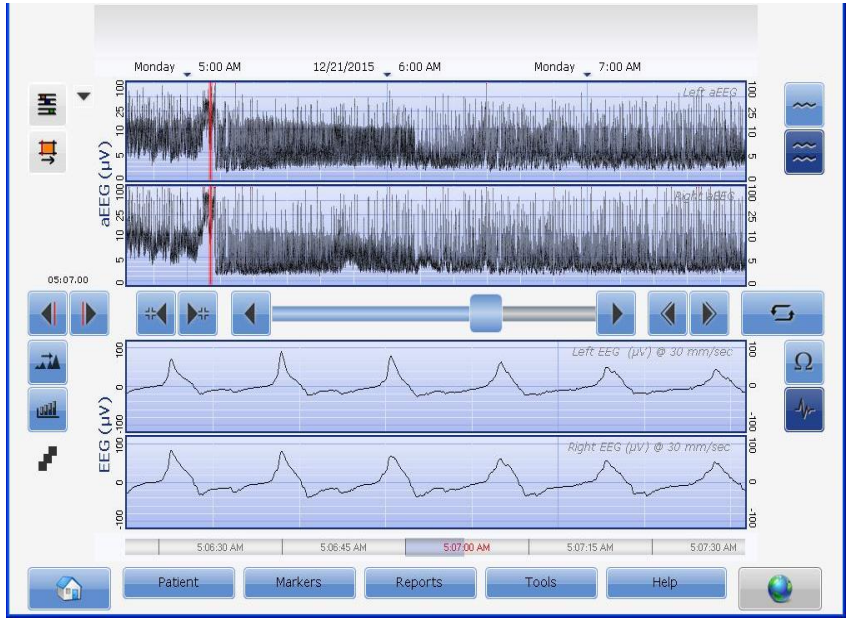
Seizures:

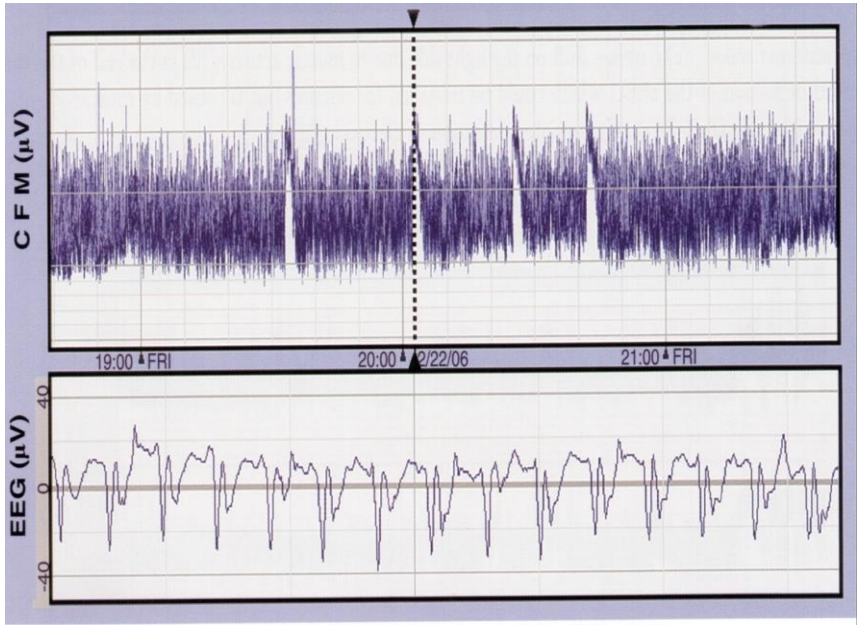
- Single Seizures: isolated seizures with at least a duration of 10 sec.
- Repetitive Seizures: single seizures appear frequently (30 min interval duration)
- Status epilepticus: continuous ongoing seizures for >30 minutes

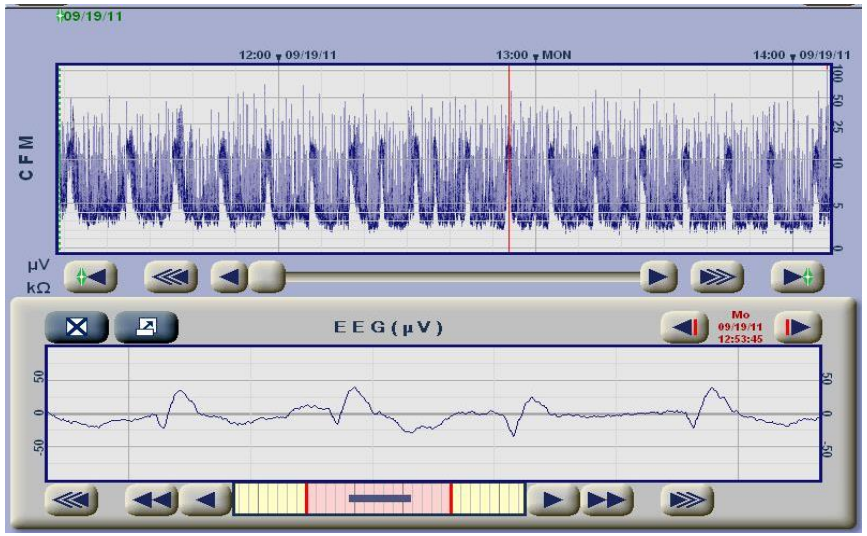


- **Ictal discharge (A,B):** rhythmic activity, spike waves, lasting at least **10s** with a clear begin, middle and end. Showing also evolution in frequency and amplitude.
- **Periodic epileptiform discharges (PED) (C,D):** sharp waves followed by a pronounced incision and a slow wave. These complex repeat every 0.5-4 sec and is associated usually with brain lesion and poor outcomes
- **PED-like waves**, Mono-rhythmic activity, synchronized delta slow activity (E,F)
- **Zeta Waves (G,H):** slow wave with a rapid negative first phase, followed by a relatively slower positive second phase of crossing the baseline. Generally occurs in trains of several seconds. Usually associated with IVH.
- **Sinusoidal waves (I,J):** low delta frequency usually frontal or occipital

Weeke et al., Clin Neurophysiology 2017


Monday 5:00 AM
12/21/2015 6:00 AM
Monday 7:00 AM
Left aEEG
Right aEEG
aEEG (µV)
05:07.00
Left EEG (µV) @ 30 mm/sec
Right EEG (µV) @ 30 mm/sec
EEG (µV)
5:06:30 AM
5:06:45 AM
5:07:00 AM
5:07:15 AM
5:07:30 AM
Patient
Markers
Reports
Tools
Help


C F M (µV)
19:00 FRI
20:00 2/22/06
21:00 FRI
EEG (µV)

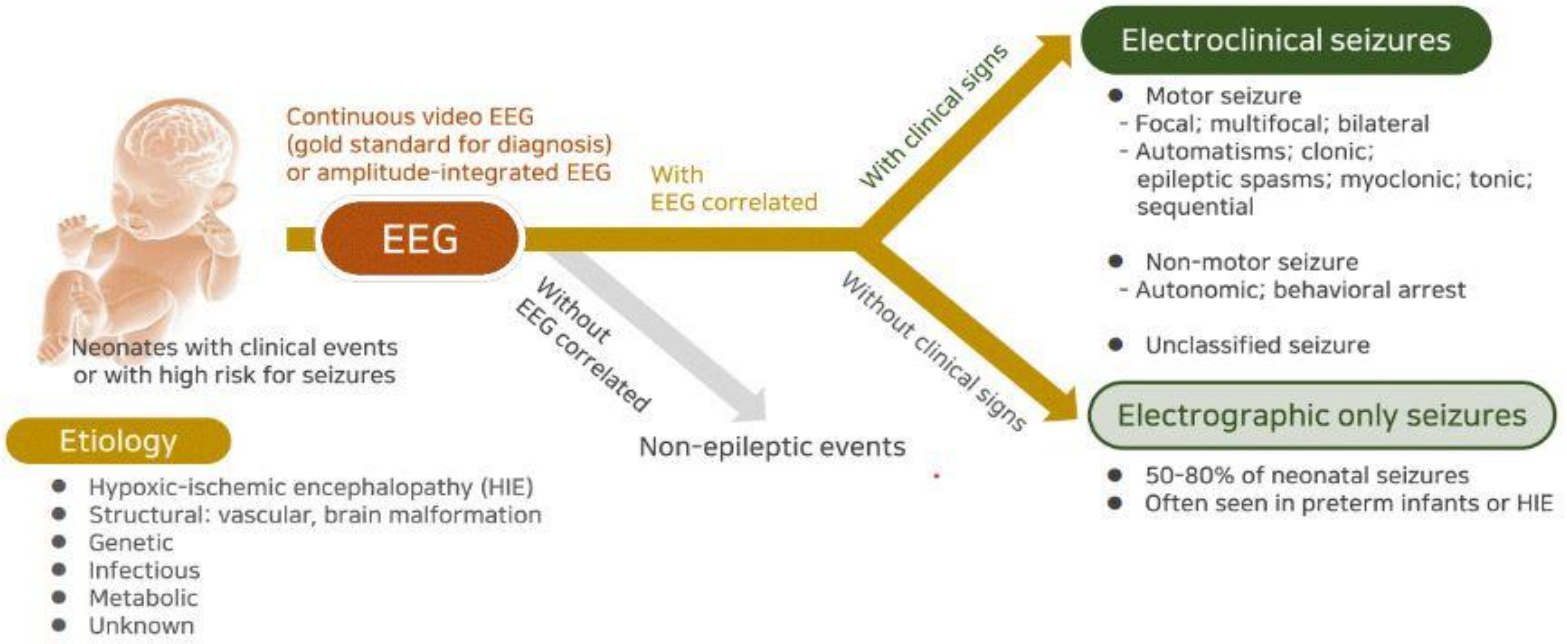

09/19/11
12:00 09/19/11
13:00 MON
14:00 09/19/11
C F M
µV
kΩ
EEG(µV)
Mo
09/19/11
12:53:45

SPECIAL REPORT

Epilepsia

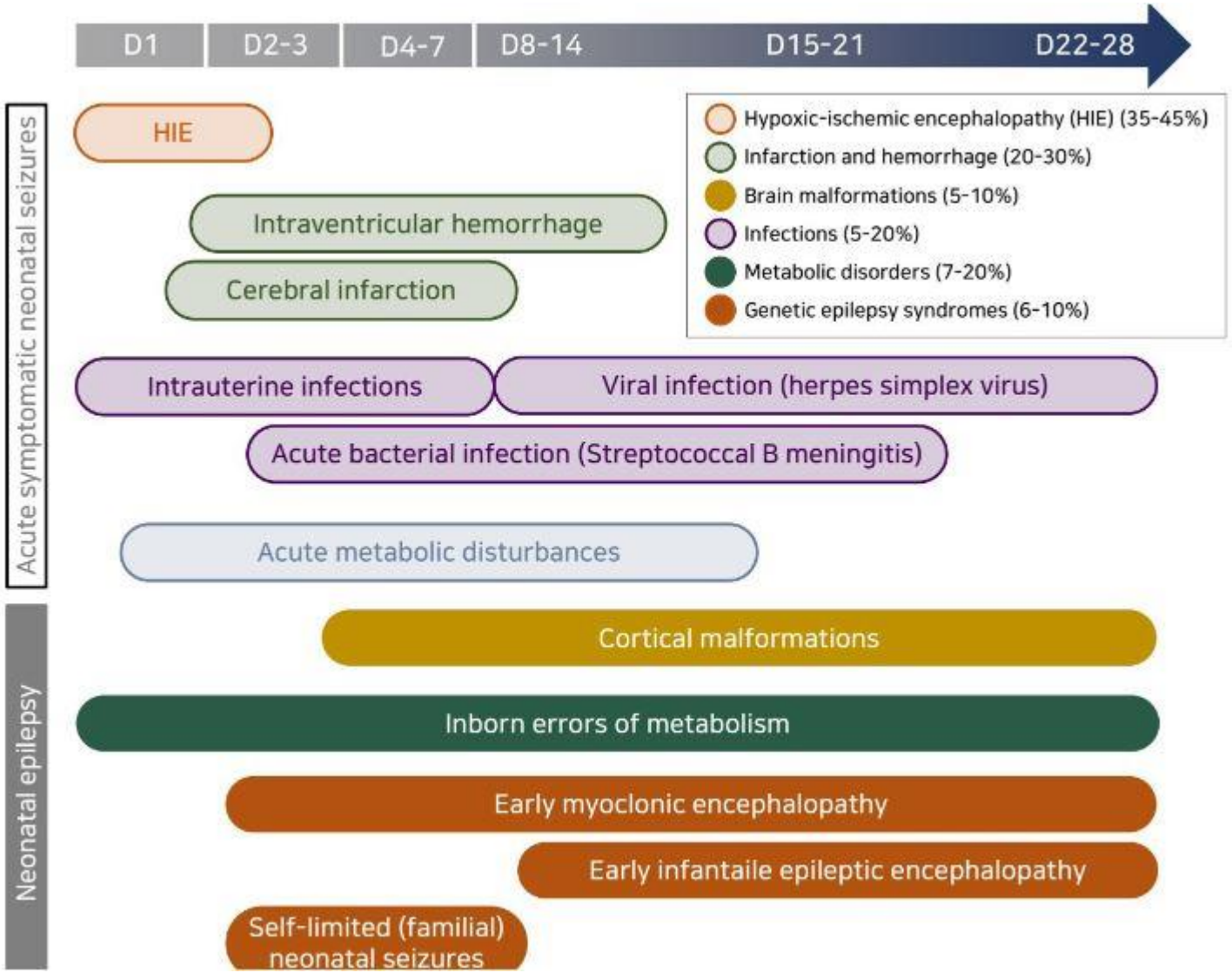
The ILAE classification of seizures and the epilepsies: Modification for seizures in the neonate. Position paper by the ILAE Task Force on Neonatal Seizures

Ronit M. Pressler[1,2] | Maria Roberta Cilio[3] | Eli M. Mizrahi[4] | Solomon L. Moshé[5,6] | Magda L. Nunes[7] | Perrine Plouin[8] | Sampsa Vanhatalo[9] | Elissa Yozawitz[5,6] | Linda S. de Vries[10] | Kollencheri Puthenveettil Vinayan[11] | Chahnez C. Triki[12] | Jo M. Wilmshurst[13] | Hitoshi Yamatomo[14] | Sameer M. Zuberi[15]



Kim et al., 2022

Etiologies of neonatal seizures according to seizure onset timing.



Kim et al., 2022

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Allan H. Ropper, M.D., *Editor*

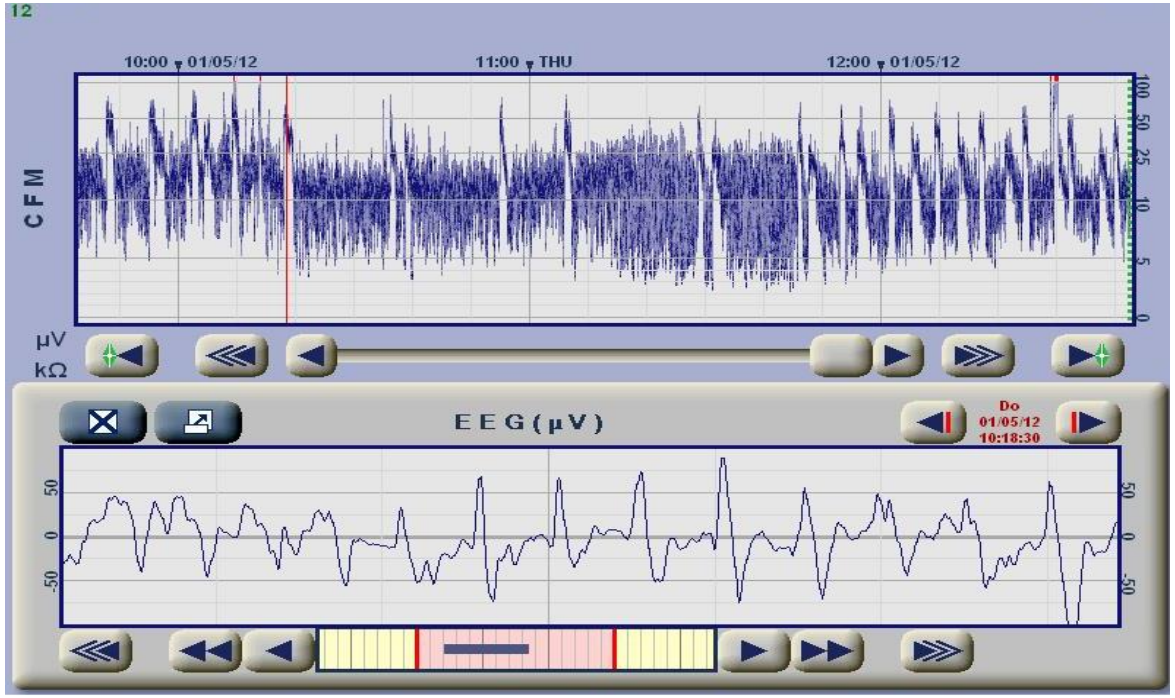
Neonatal Seizures

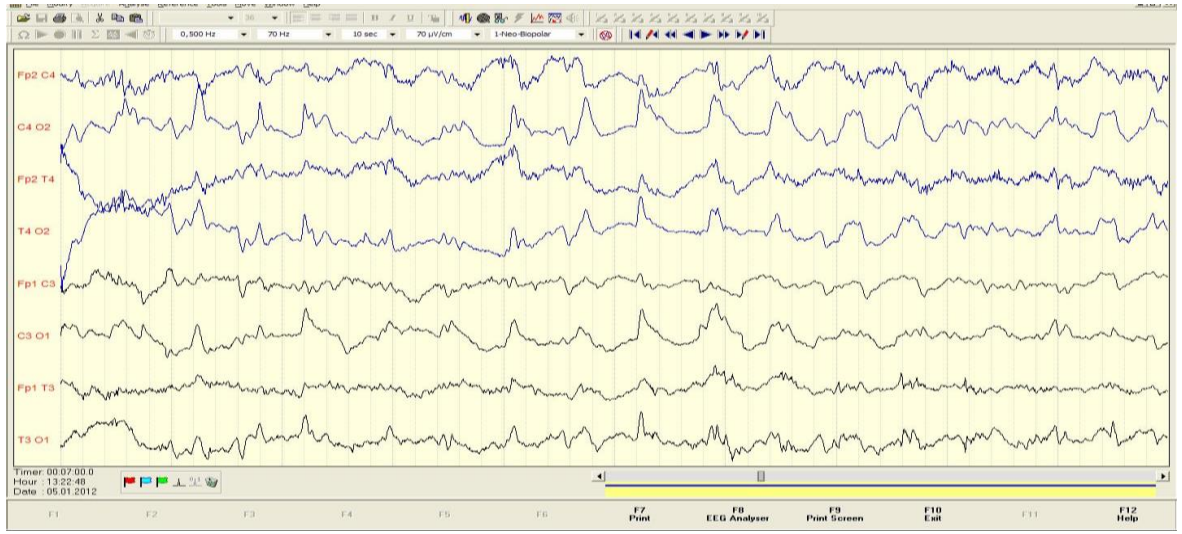
Elissa Yozawitz, M.D.

Table 3. Approximate Doses of the Main Antiseizure Medications for the Treatment of Neonatal Seizures.*

Medication	Loading Dose†	Maintenance Dose†	Comments
Phenobarbital	20 mg/kg of body weight; second loading dose, if required: 10–20 mg/kg, administered intravenously‡	5 mg/kg of body weight per day, administered intravenously or orally	FDA-approved; enhances GABAA inhibitory activity
Phenytoin	20 mg/kg of body weight, administered intravenously over 30-min period	5 mg/kg of body weight per day, administered intravenously in two divided doses, adjusted according to response and plasma concentration	Off-label use; voltage-gated sodium-channel blocker
Levetiracetam	40 mg/kg of body weight, administered intravenously; second loading dose, if required: 20 mg/kg	40–60 mg/kg of body weight per day, administered intravenously, or given orally in three divided doses	Off-label use; binds to SV2A and impedes synaptic vesicle trafficking
Midazolam	0.05–0.15 mg/kg of body weight	1 μg/kg of body weight per minute (60 μg/kg per hour), administered as a continuous infusion, increased in steps of 1 μg/kg per minute; maximum dose: 5 μg/kg per minute	Off-label use; GABAA agonist
Lidocaine	2 mg/kg of body weight, administered intravenously over 10-min period	7 mg/kg of body weight per hour, administered intravenously for 4 hr, then 3.5 mg/kg per hour for 12 hr, then 1.75 mg/kg per hour for 12 hr, and then stopped	Off-label use; voltage-gated sodium-channel blocker

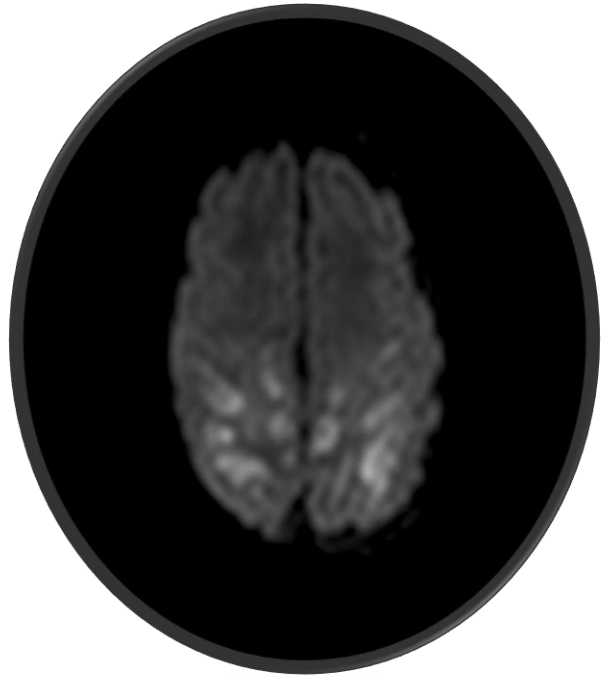
* Information on doses is from Dehkharghani,[12] Sharpe et al.,[13] Van Den Broek et al.,[15] Pisano et al.,[16] Castro Conde et al.,[17] Sands et al.,[18] Favié et al.,[19] and Pressler et al.[3] Other agents that may be used, depending on the clinical presentation, family history, laboratory tests, and EEG findings, include pyridoxine, pyridoxal-5-phosphate, and carbamazepine. FDA denotes Food and Drug Administration, GABAA γ-aminobutyric acid type A, and SV2A synaptic vesicle protein 2A.
† Opinions about dosing vary, and the doses shown should be taken as approximate values.
‡ Higher doses of phenobarbital may be given with careful cardiorespiratory monitoring.





Patient A.M.

- SSW: 24+3
- Kor.: 35+2
- IUGR: 603g
- IVH ll Re
- ROP 2



aEEG - Summary

- Quick Setup
- Lower Technical Demand
- Simple and User-Friendly
- Portable and Bedside Use
- **Cost-Effective**
- Continuous Monitoring
- Detects Neonatal Seizures
- Early Detection of Brain Dysfunction
- Assesses Brain Maturation
- Supports Therapeutic Decision Making

Katrin Klebermaß-Schrehof
Katharina Goeral
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Anastasia Dressler
Julia Buchmayer
Sophie Stummer
Philipp Steinbauer
Raphaela Jernej
Johannes Mader
Nadine Pointner
Simon Knoll
Naomi Adjoa Acquah

Thank you for your attention

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