



# Neuro-monitoring

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# Scope

- Importance of Neuro-monitoring esp HIE
- **Tools**
  - Neurological Examination
  - Conventional cEEG
  - Amplitude integrated EEG
  - Near Infra-red Spectroscopy
  - MRI brain
  - MR spectroscopy
  - Ultrasonography and Dopplers
  - Heart rate variability, Biomarkers and VEP/SEP

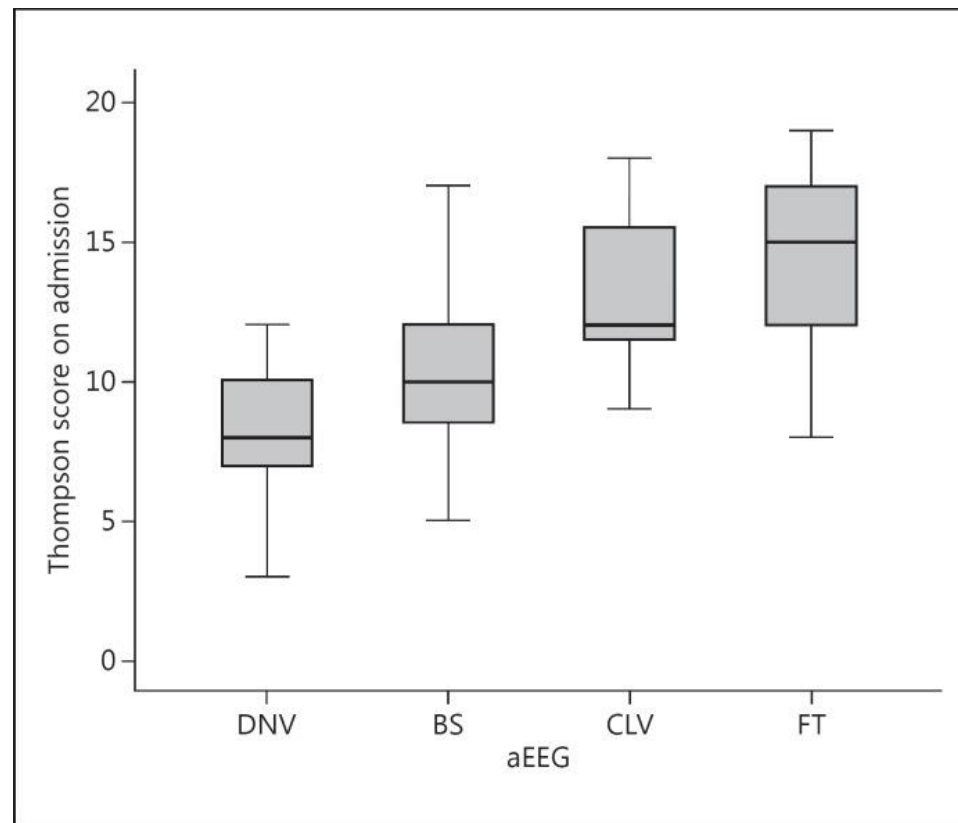


# Introduction

- Neuro-monitoring –Brain function
  - Functional activity/Structural /Oxygenation/Blood Flows/Metabolites
  - Continuous/Real time/Intermittent
- Provides critical diagnostic information
- Real time assessment of irreversible neuronal loss/injury
- Individualised Neuroprotective and Neuro-restorative therapy
- Prognostic Information

stage	Stage-1(mild)	Stage-2(moderate)	Stage-3(severe)
Level of consciousness	Hyperalert; irritable	Lethargic or obtunded	Stuporous, comatose
Muscle tone	Normal	Mild hypotonia	Flaccid
Autonomic function	Generalized sympathetic	Generalized parasympathetic	Both system depressed
Pupils	Mydriasis	Miosis	Midposition, often unequal; poor light reflex
Seizures	None	Common, focal or multifocal	Uncommon (excluding decerebration)
Duration of symptoms	<24 hours	2 to 14 days	Hours to weeks
Outcome	About 100% normal	80% normal, abnormal if symptoms more than 5 to 7 days	About 50% die, remainder with severe sequelae

Score Sign	0	1	2	3
Tone	Normal	Hyper	Hypo	Flaccid
LOC	Normal	Hyperalert, stare	Lethargic	Comatose
Fits	None	< 3/day	>2/day	
Posture	Normal	Fisting, cycling	Strong distal flexion	Decerebrate
Moro	Normal	Partial	Absent	
Grasp	Normal	Poor	Absent	
Suck	Normal	Poor	Absent ± bites	
Respiration	Normal	Hyperventilation	Brief apnea	IPPV (apnea)
Fontanelle	Normal	Full, not tense	Tense	



Peak score of 15 or more  
positive predictive value 92%  
negative predictive value of 82% for  
abnormal outcome

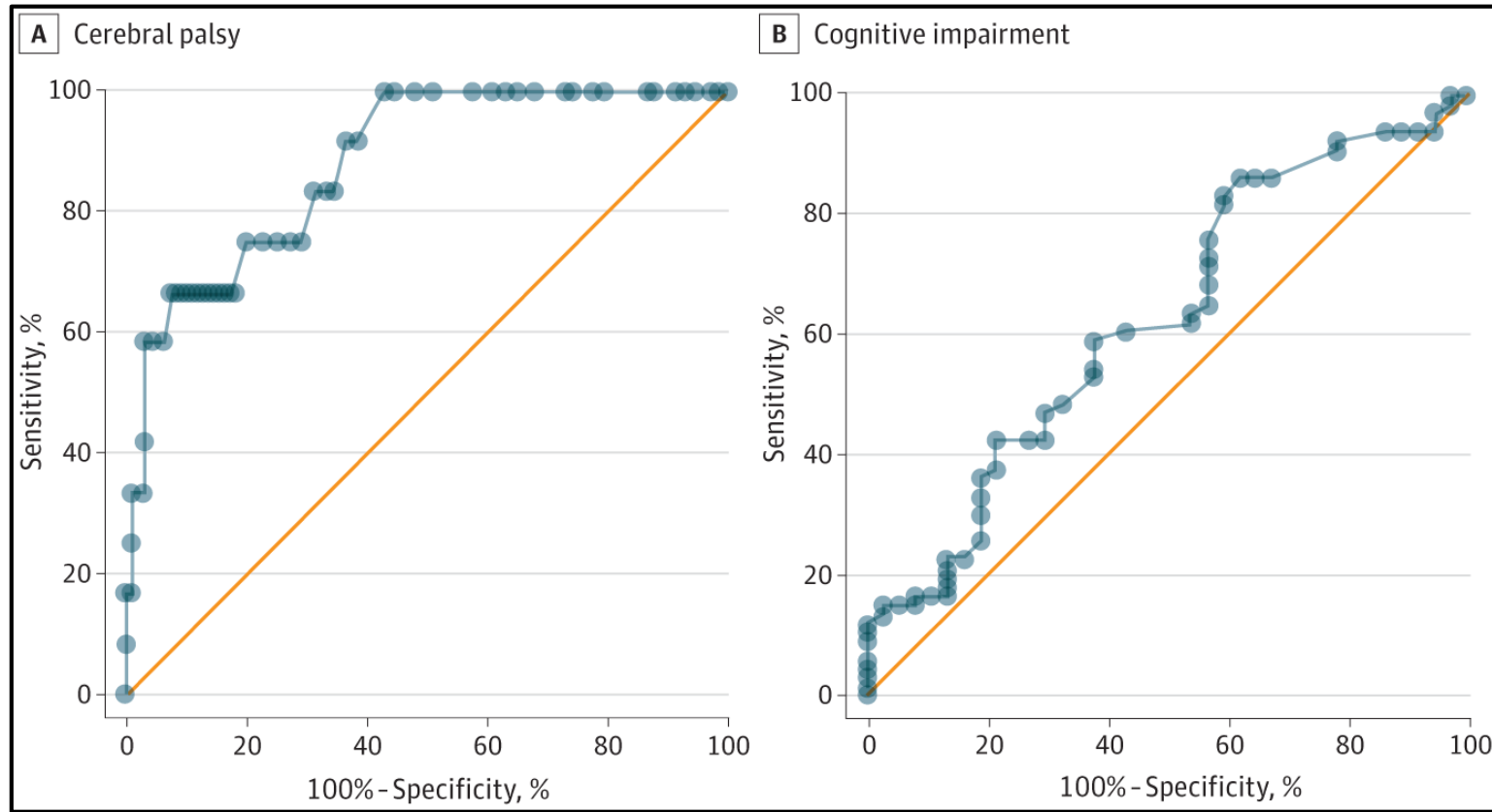
### ROC analysis of Thompson score and aEEG versus outcome

	Cut-off value	AUC (95% CI)	Sensitivity	Specificity
Thompson score	11	0.84 (0.75–0.91)	0.76	0.83
aEEG	CLV or worse	0.84 (0.76–0.91)	0.60	0.93



From: **Early Neurodevelopmental Assessments for Predicting Long-Term Outcomes in Infants at High Risk of Cerebral Palsy**

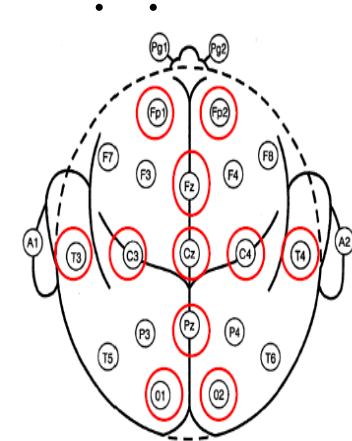
JAMA Netw Open. 2024;7(5):e2413550. doi:10.1001/jamanetworkopen.2024.13550



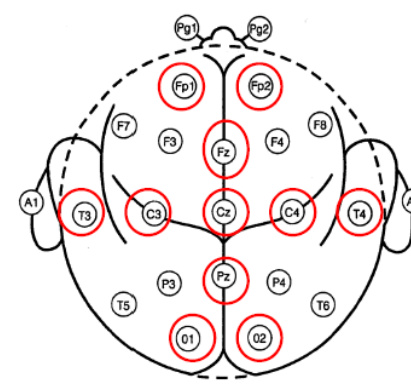
Receiver Operating Characteristic Curve for Hammersmith Infant Neurological Examination Scores in Predicting Cerebral Palsy and Cognitive Impairment. The area under the curve was 0.88 (95% CI, 0.79-0.97) for cerebral palsy (A) and 0.62 (95% CI, 0.51-0.73) for cognitive impairment (B).

# Conventional cEEG

- Spot EEG/ cEEG (24 h or more)/Video EEG
- **Gold standard for seizure detection**
- Electrographic Seizures
  - Sudden, repetitive, evolving & stereotyped episode of abnormal electrographic activity with amplitude of atleast 2uV & a duration of 10 secs
- **Prognostication based on background**



# Conventional cEEG



- **Electrographic Seizures**

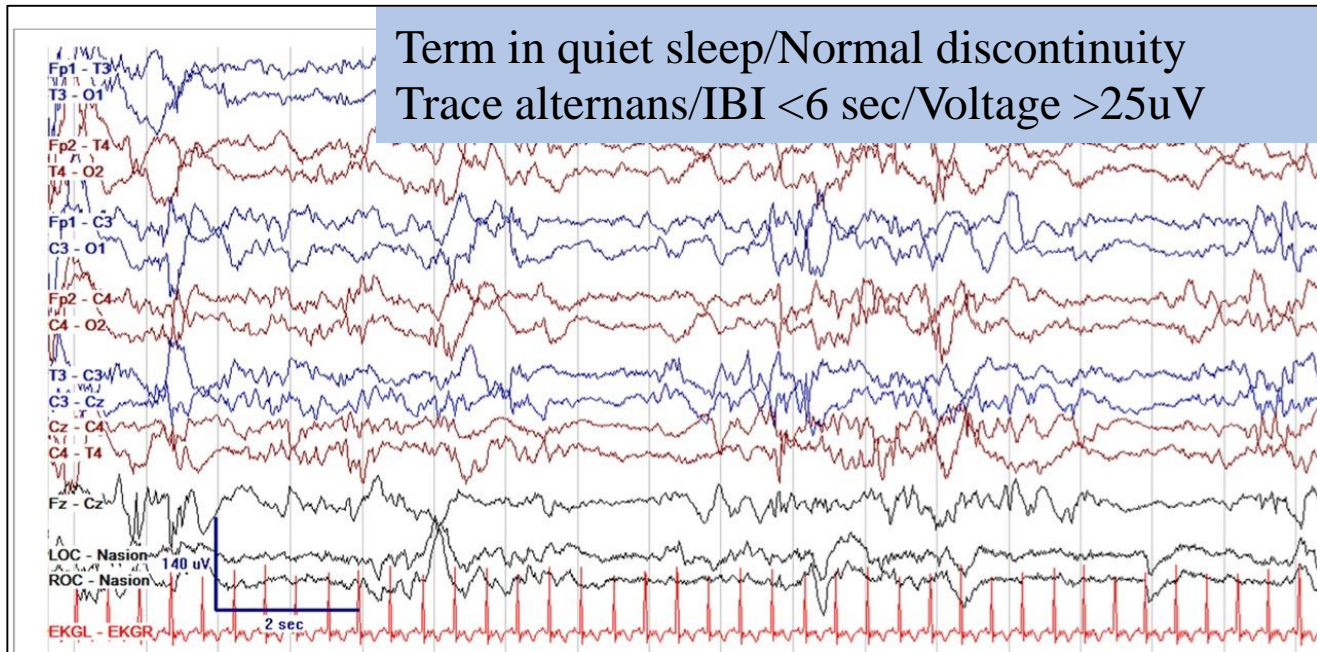
- Avoid over-treating non-epileptic movements or under-treating true seizures.
- Sub-clinical seizures
- Reduction of dose and duration of AEDs
- High Electrographic activity –risk factor for mortality/Poor NDO

- **Background**

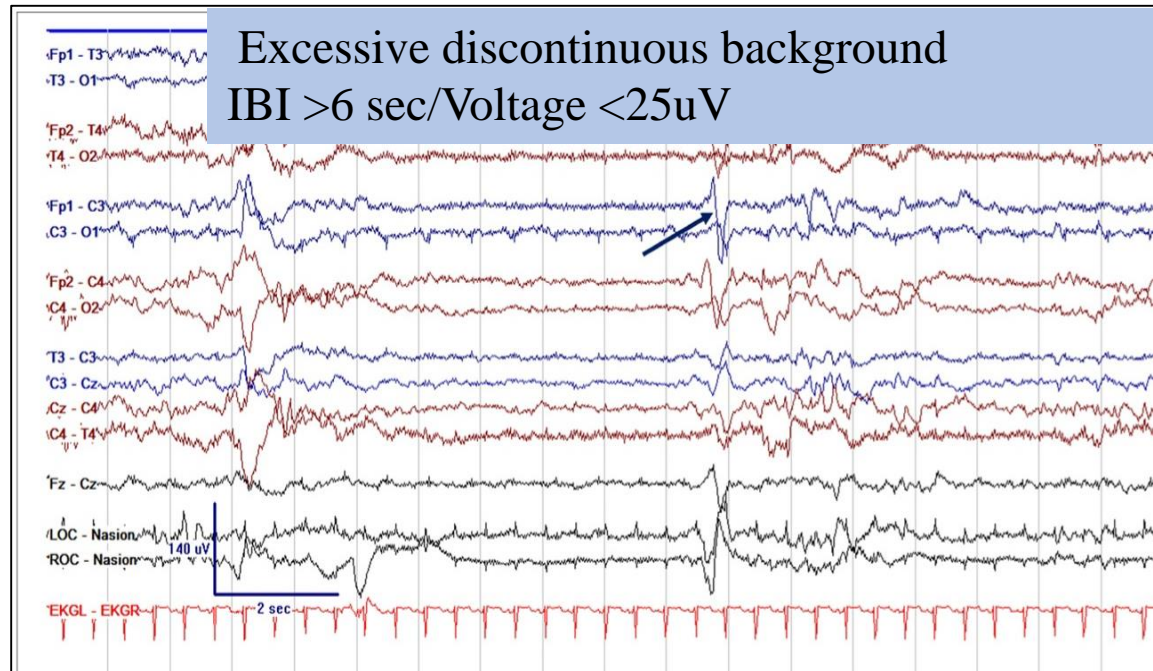
- Normal
- Excessive Discontinuity
- Low amplitude/Burst Suppression
- Asymmetry-lateralised brain injury



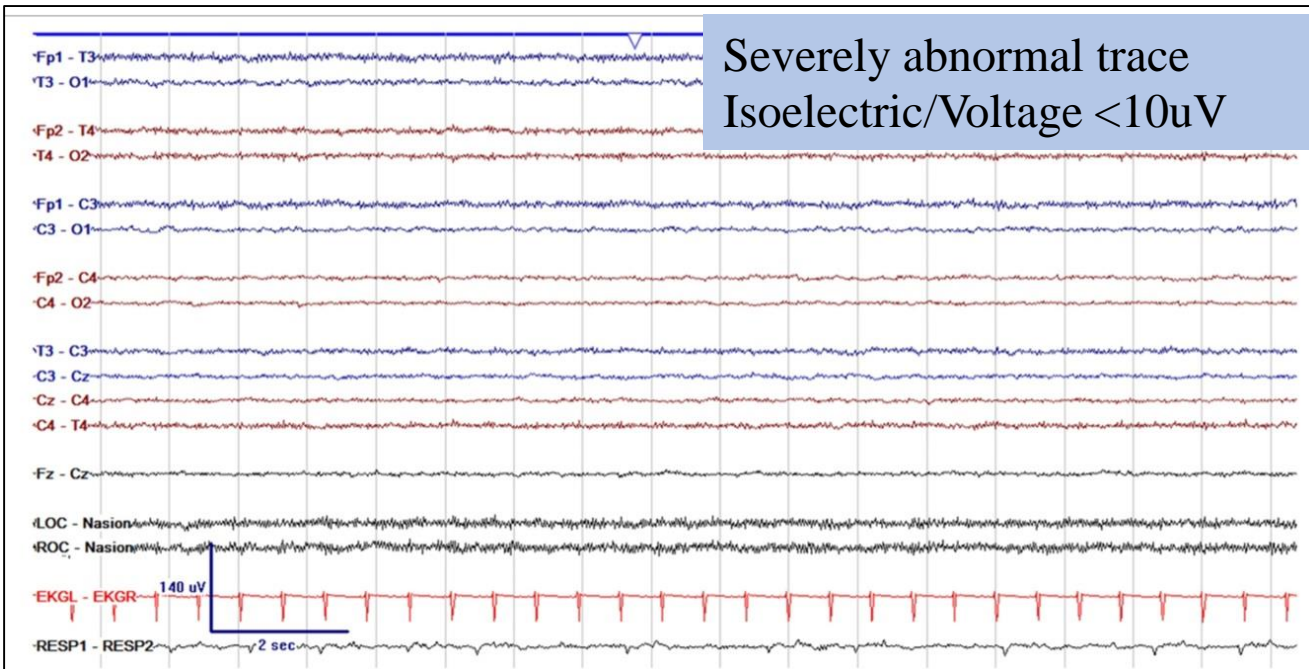
Term in quiet sleep/Normal discontinuity  
Trace alternans/IBI <6 sec/Voltage >25uV



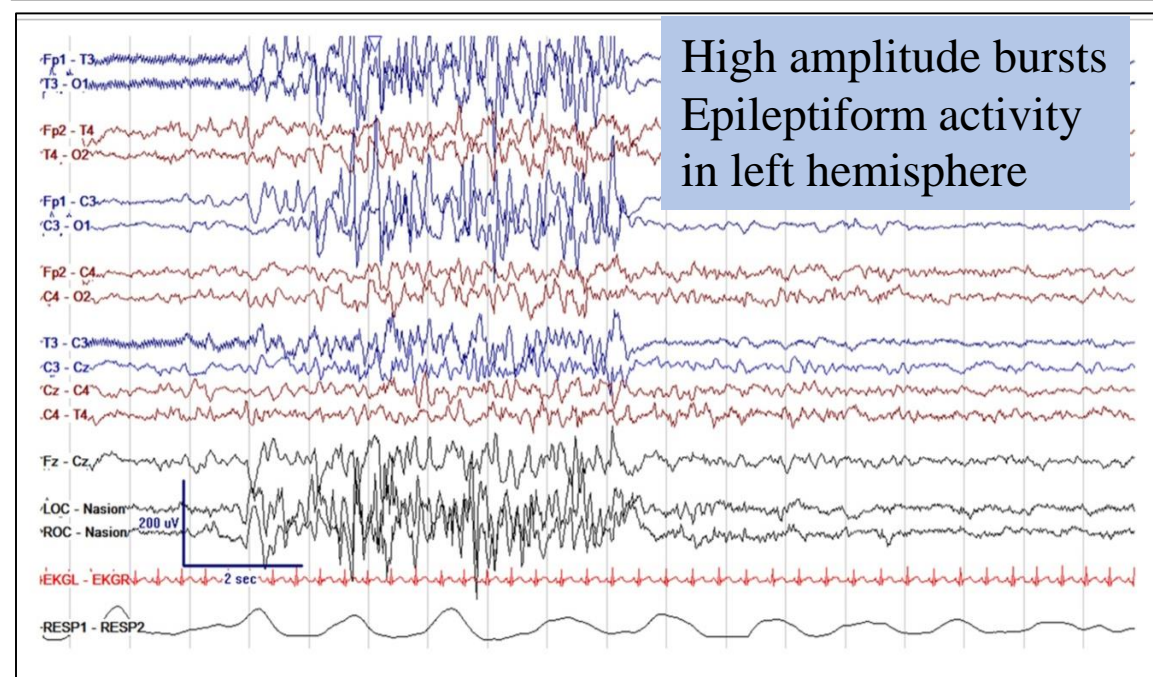
Excessive discontinuous background  
IBI >6 sec/Voltage <25uV



Severely abnormal trace  
Isoelectric/Voltage <10uV



High amplitude bursts  
Epileptiform activity  
in left hemisphere



# Prognostication

EEG Background	Neurological Sequelae
Normal	≤10%
Severe abnormalities <sup>†</sup>	≥90%
Moderate abnormalities <sup>‡</sup>	~50%

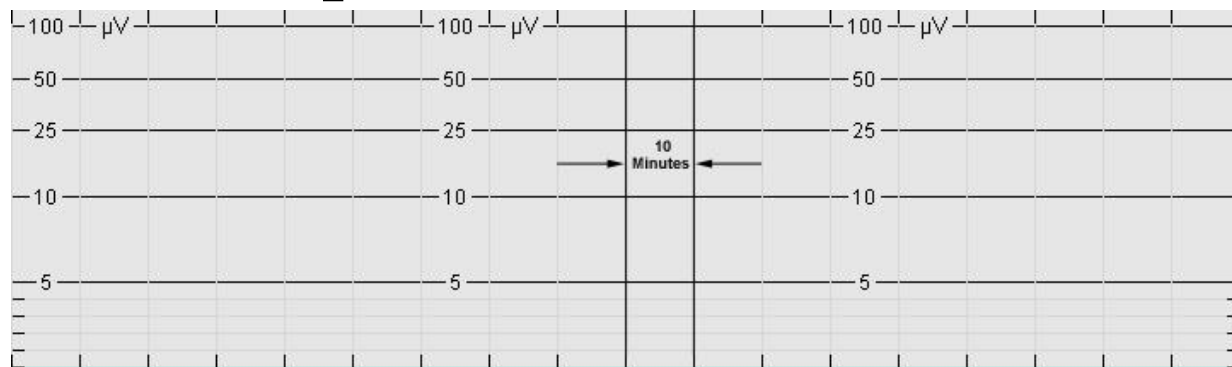
\*Based primarily on data reported in references 401, 402, and 404 and includes both full-term and premature infants.  
<sup>†</sup>Burst-suppression pattern, prolonged (>20-second) interburst interval, marked voltage suppression, and electrocerebral silence.  
<sup>‡</sup>Voltage asymmetries and "immaturity."

- Bad prognostic indicators-
  - Burst suppression pattern associated with unfavourable outcome.
  - Predominant interburst interval >20 sec is associated with poor outcome.
  - Abnormal EEG persisting at 48 hours is associated with poor outcome.
- Good prognosis indicators-
  - Early return of sleep wake cycling
  - Normalisation of background confers good prognosis.



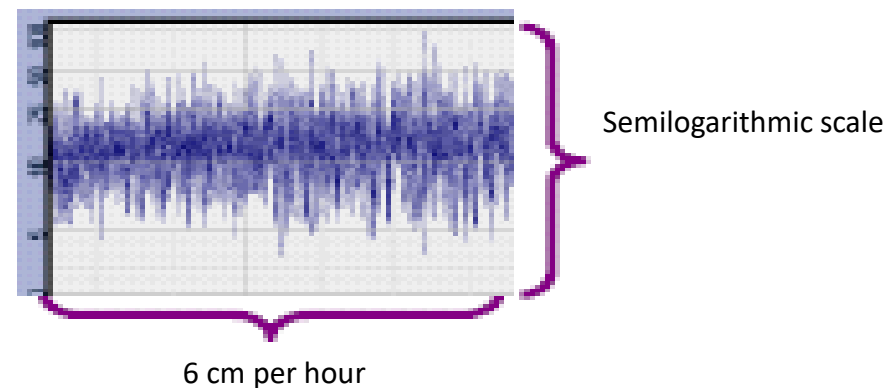
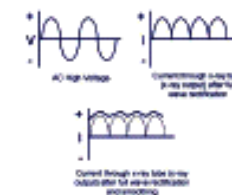
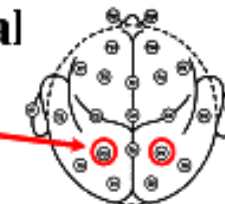
# Amplitude Integrated EEG (aEEG)

- Modification of raw EEG
- Special Wide band Filter- $<2\text{Hz}$  to  $>15\text{Hz}$
- **Semi-logarithmic amplitude compression**
  - Linear between 0 and 10 mcv
  - Logarithmic from 10 to 100 mcv
- **Peak-to-peak Rectification/Monophasic**
- **Time Compression**

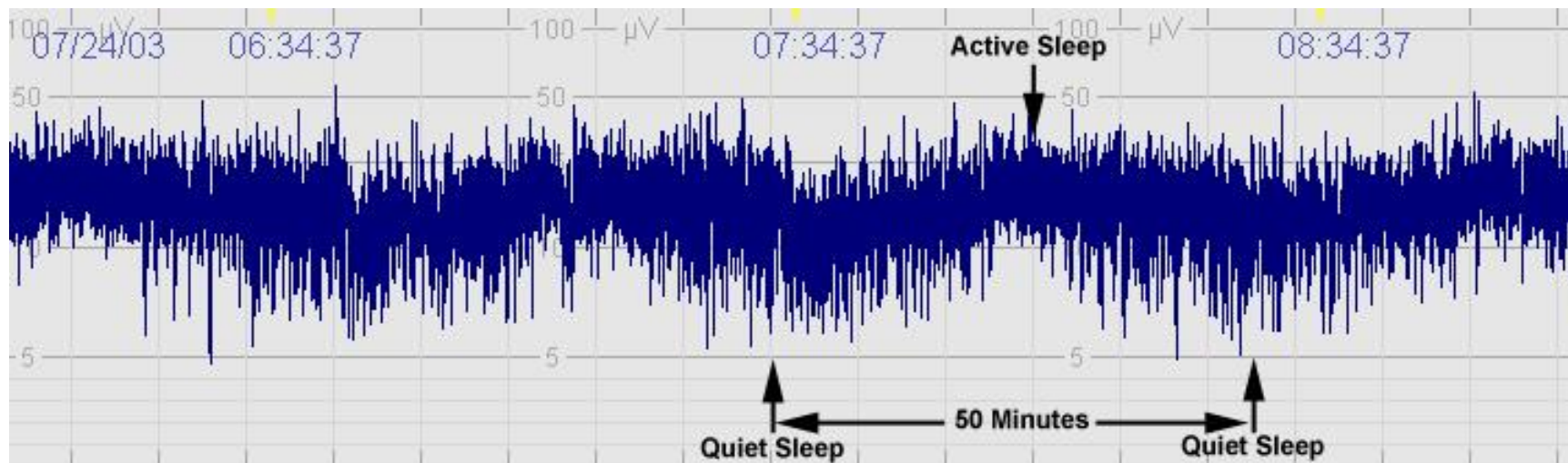
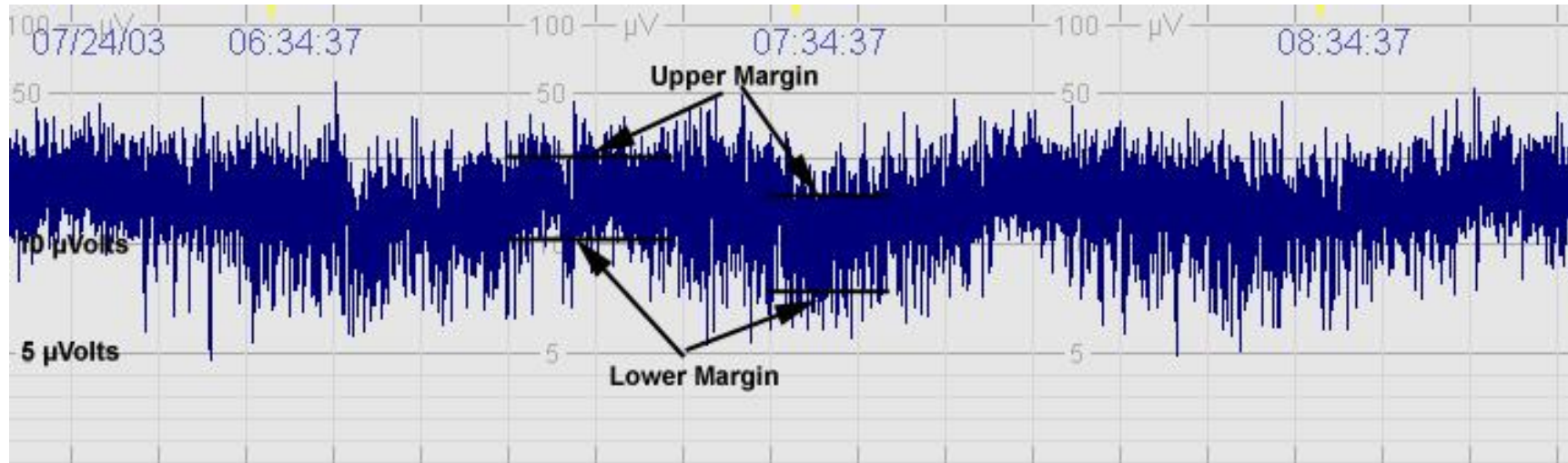


## aEEG Signal Processing

- **Amplification of EEG signal**
  - from P3/P4
- **Filtering:**
  - $<2\text{Hz}$ ,  $>15\text{Hz}$ : Sweating and muscle artifact
  - Asymmetric band pass filtering
    - Equal emphasis to different frequencies
- **Rectification and smoothing**
  - Of EEG wave

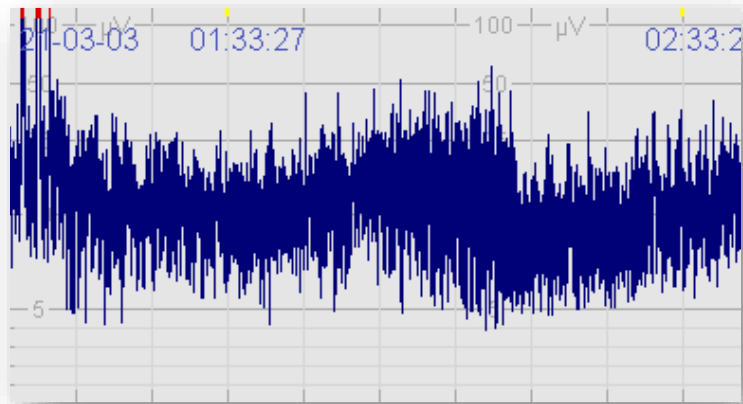


# Upper/Lower Margins

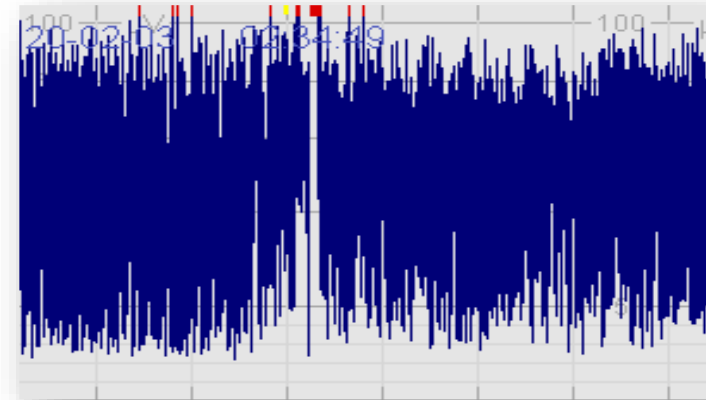


# Al Naqeeb (Pediatrics 1999)

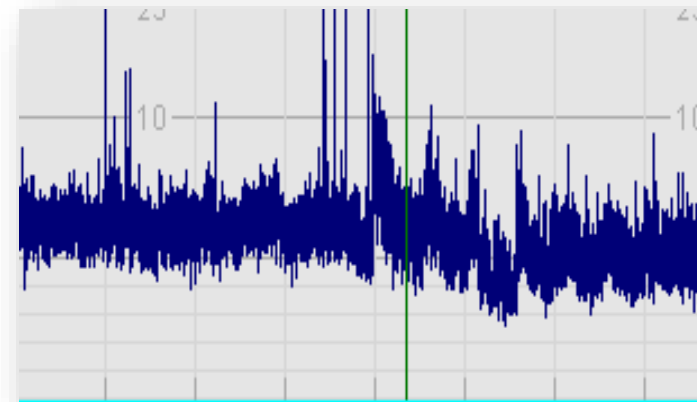
Normal (UM>10 $\mu$ v; LM>5 $\mu$ v)



Moderately abnormal (UM>10 $\mu$ v; LM $\leq$  5 $\mu$ v)



Severely abnormal (UM<10 $\mu$ v; LM $\leq$  5 $\mu$ v)



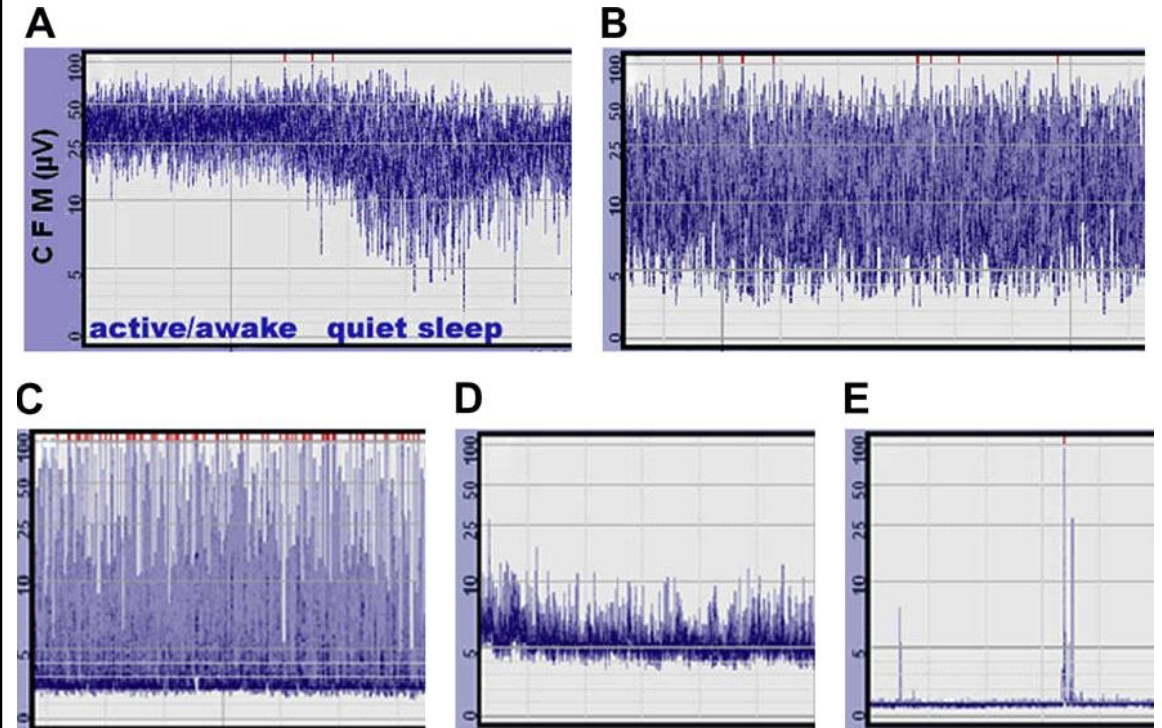
**Seizure activity was defined, but not SWC**





# Suggested Classification of aEEG Patterns in Preterm and Term Infants Background Pattern- Hellstorm and Westas 2006

- **Continuous (C):** continuous activity with lower (min. amp. (5)–7–10 mV max. Amp. 10–25(–50) mV.
- **Discontinuous (DC):** discontinuous background ,min. amp. variable, but below 5 mV, max. amp. above 10 mV.
- **Continuous low voltage (CLV):** continuous background pattern of low voltage (around or below 5 mV).
- **Burst suppression (BS):** discontinuous background with min. amp. without variability at 0–1(2) mV, and bursts with amp>25 mV.
  - **BS+** denotes burst density 100 or > bursts/h, and **BS-** means burst density < 100 bursts/h.
- **Inactive, flat (FT):** mainly inactive (isoelectric) background <5 mV



Included

- SWC
- Seizures



# Amplitude Integrated EEG (**aEEG**)

- Global Electrocortical Activity
- Limited number of electrodes
- Will not localize lesion/May not see focal seizures
- **Poor Outcome**
  - Severe background pattern within 6 h
  - Delayed onset of SWC after 36 hours after birth
- In infants with good outcome- background pattern normalises by 24-36 hours when treated with normothermia and by 48-72 hours when treated with hypothermia

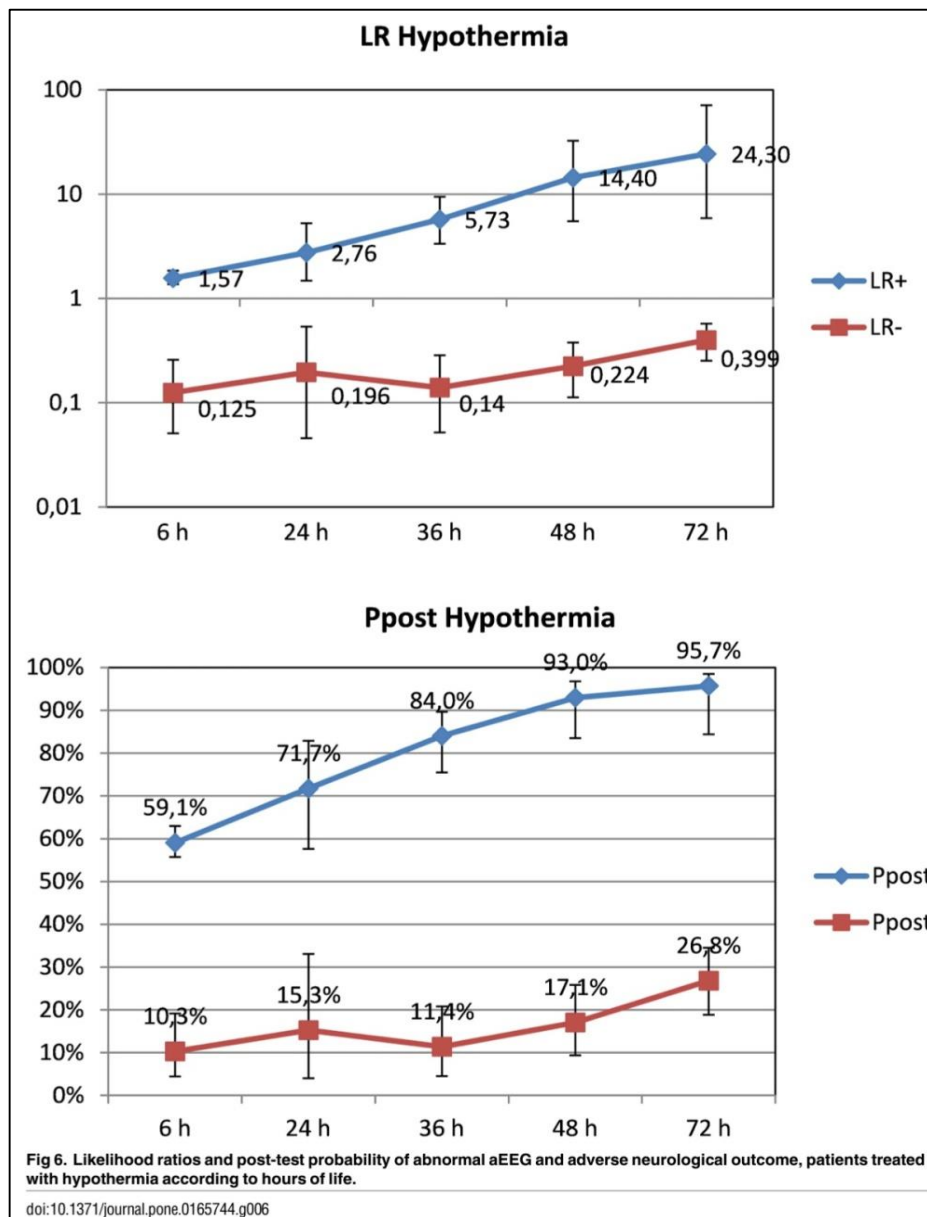
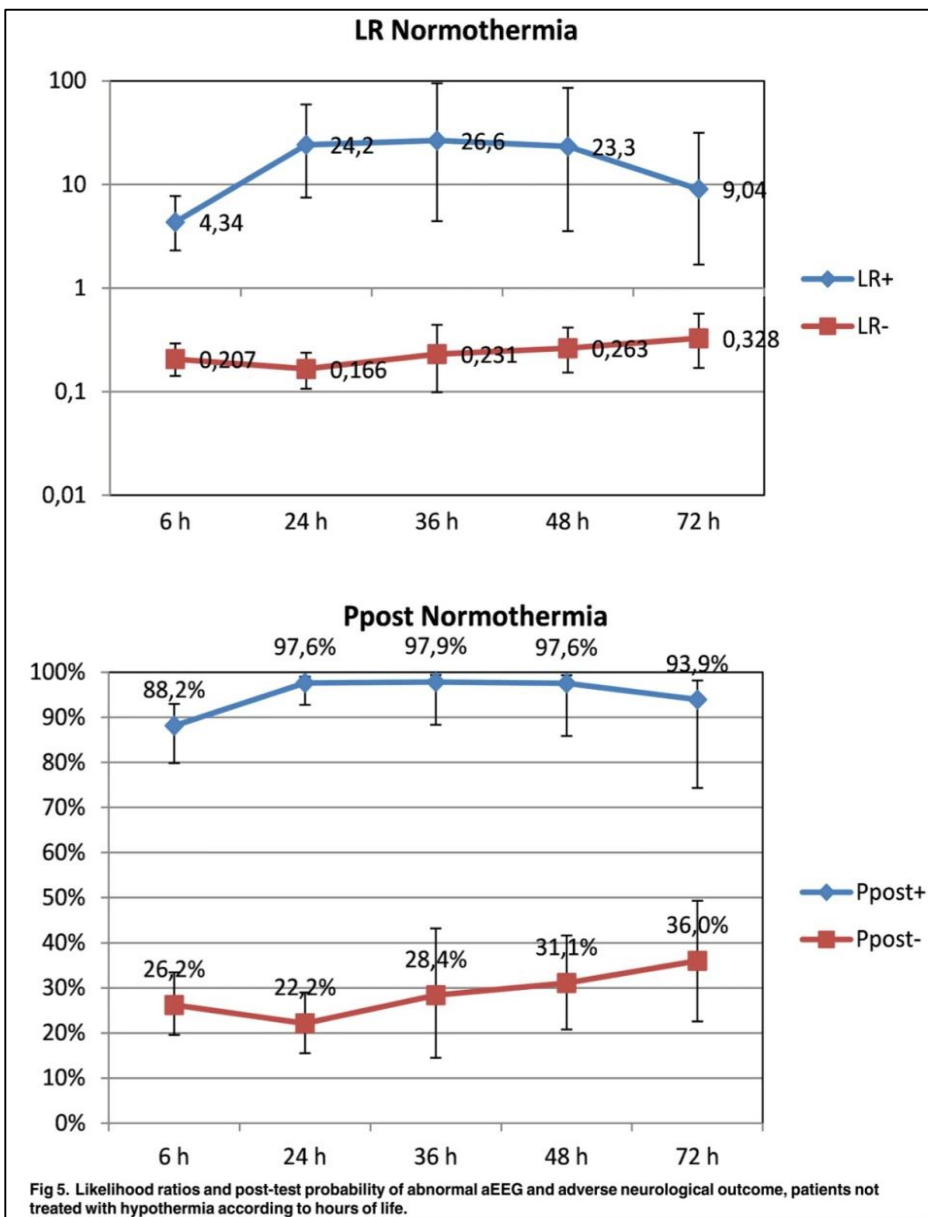
Neonatal Encephalopathy (NE) (n = 65)					
Moderate NE (n = 39)			Severe NE (n = 26)		
<i>a</i> EEG findings	Normal 14 (35.8)	Moderate 21 (53.8)	Severe 4 (10.2)	Moderate 05 (80.7)	Severe 21 (19.2)
<b>Composite Outcome</b>					
Abnormal	0	11 (52.3)	4 (100)	03 (60)	20 (95.2)
Normal	11 (78.5)	08 (38.0)	0	02 (40)	01 (4.7)
Lost to Follow up	03 (21.4)	02 (9.5)	0	0	0

**Figure 2.** *a*EEG abnormality in moderate and severe encephalopathy (Levene staging) and their composite outcome.

**Table 3.** Predictive ability of clinical staging, *a*EEG, EEG, and neuroimaging for adverse neurodevelopment.

	Sensitivity	Specificity	PPV	NPV
Sarnat Staging	63.1 (46-77)	86.4 (64.0-96.4)	88.9 (69.7-97.1)	57.6 (39.4-74.0)
Abnormal <i>a</i> EEG	100 (88.5-100)	54.2 (33.2-73.8)	77.5 (63.0-87.7)	100 (71.6-100)
Severely abnormal <i>a</i> EEG	100 (82.8-100)	92.8 (64.2-99.6)	96 (77.7-99.8)	100 (71.6-100)
Standard EEG	69.4 (51.7-83.1)	75 (52.9-89.4)	80.6 (61.9-91.9)	62.1 (42.4-78.7)
Neuroimaging	73.7 (56.6-86.0)	70.8 (48.7-86.5)	80 (62.5-90.1)	62.9 (42.5-79.9)

Singh A, Saluja S, Kler N, Garg P, Soni A, Thakur A. Amplitude integrated EEG: how much it helps in prognostication in neonatal encephalopathy? J Matern Fetal Neonatal Med. 2022 Dec;35(25)



TH era  
17 studies,  
N=360

- No TH-  
Max  
reliability 36  
hours.
- With TH-  
Max  
reliability at  
72 hours.

# Near Infra-red Spectroscopy

- Detector emits infrared light
- Absorbed differentially by hemoglobin
- Residual light reflected back-detectors
- Calculates regional oxygen saturation (rSO<sub>2</sub>)

$$rSO_2 = \frac{HbO_2}{(HbO_2 + HHb)}$$

- Normal Cerebral rSO<sub>2</sub> is around 60% to 75%
- Fractional tissue oxygen extraction (FTOE)
- Balance between O<sub>2</sub> Delivery and consumption
  - **FTOE=[(SaO<sub>2</sub>-rSO<sub>2</sub>)/SaO<sub>2</sub>]**

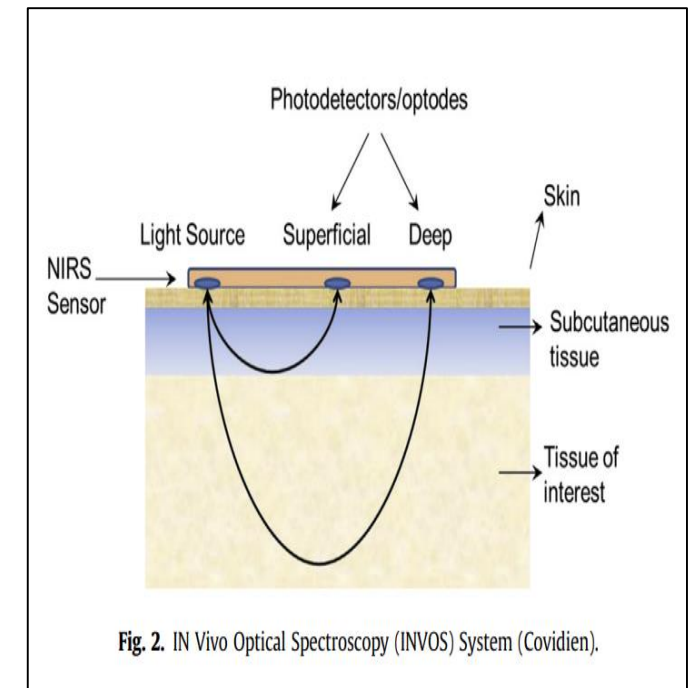
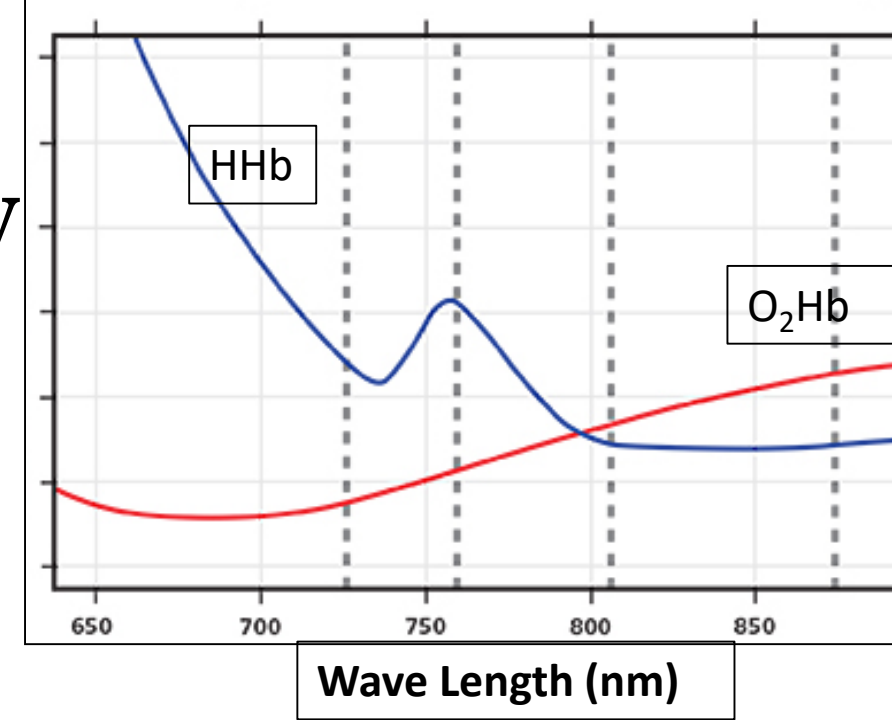
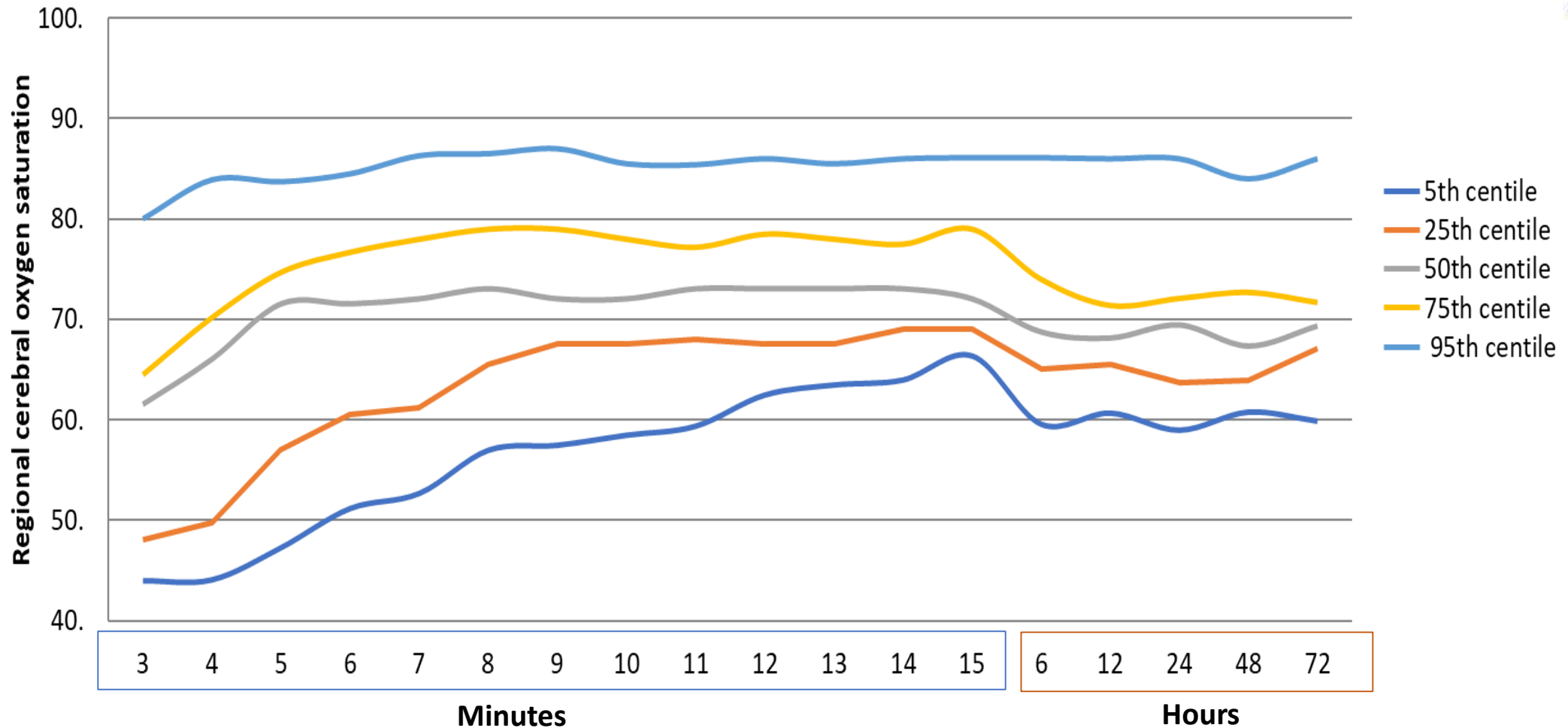
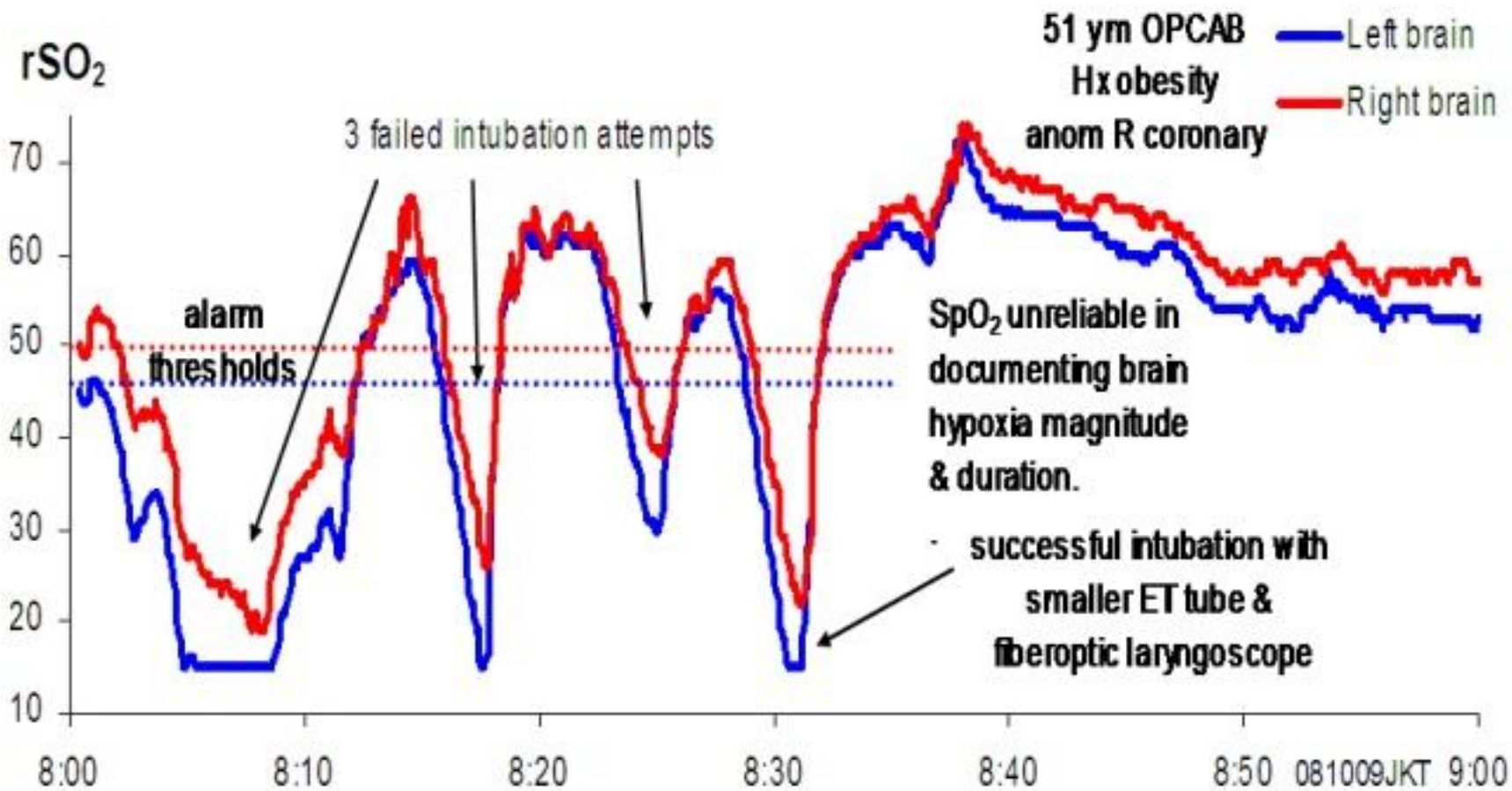


Fig. 2. IN Vivo Optical Spectroscopy (INVOS) System (Covidien).

# Regional Cerebral Oxygenation Saturation SGRH Data during transition

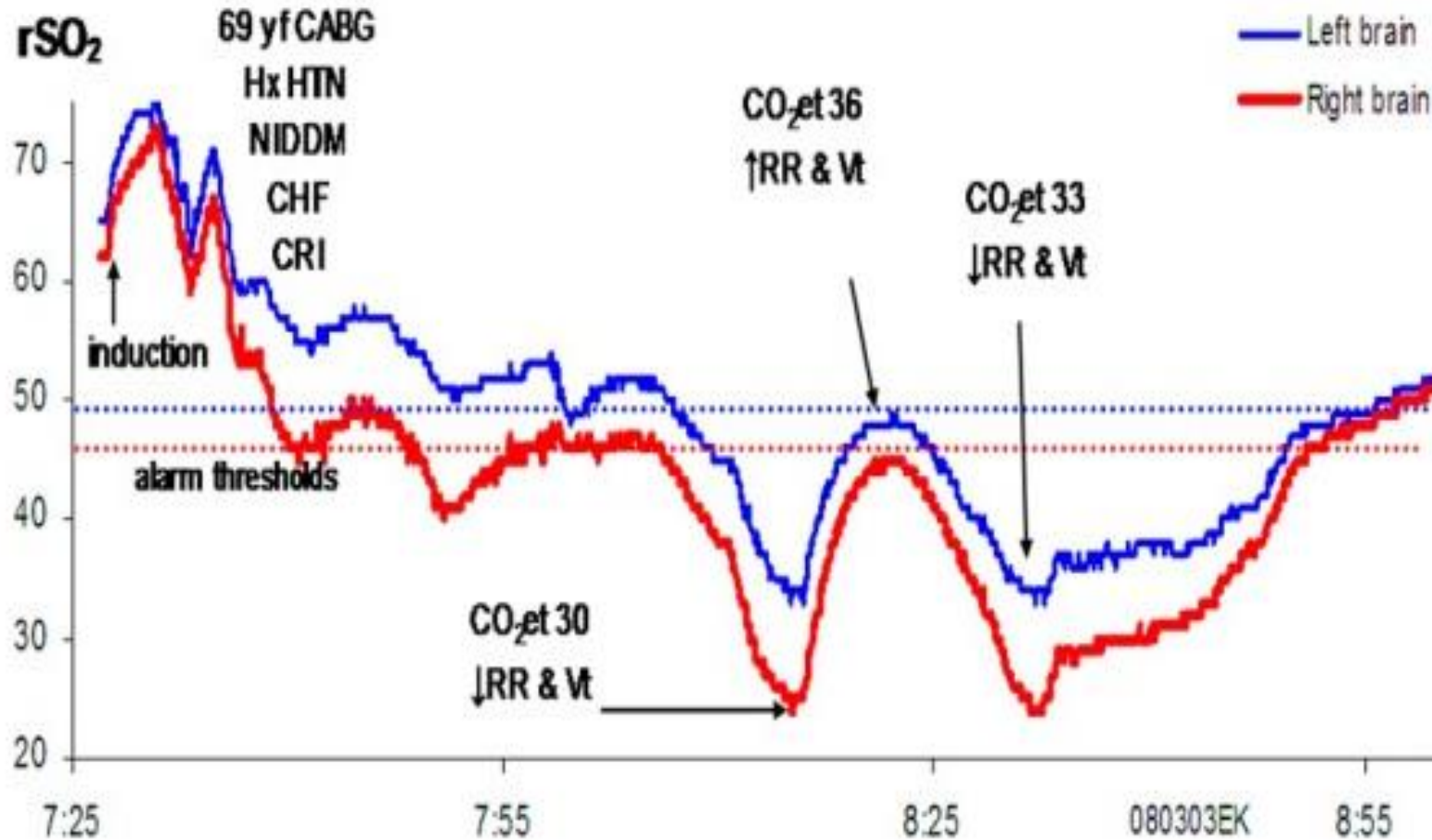


# rSO<sub>2</sub> & Brief Hypoxic Episodes

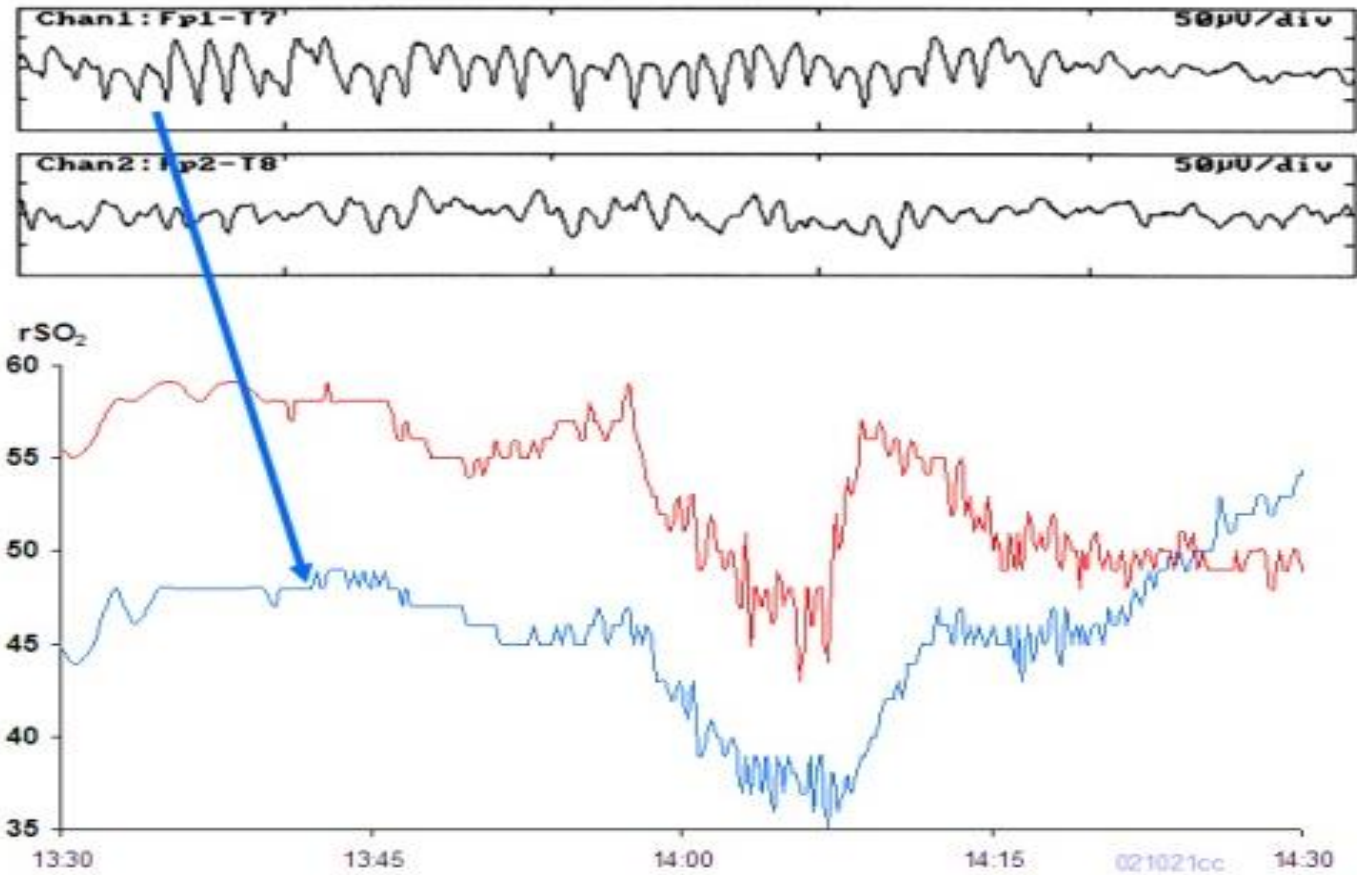




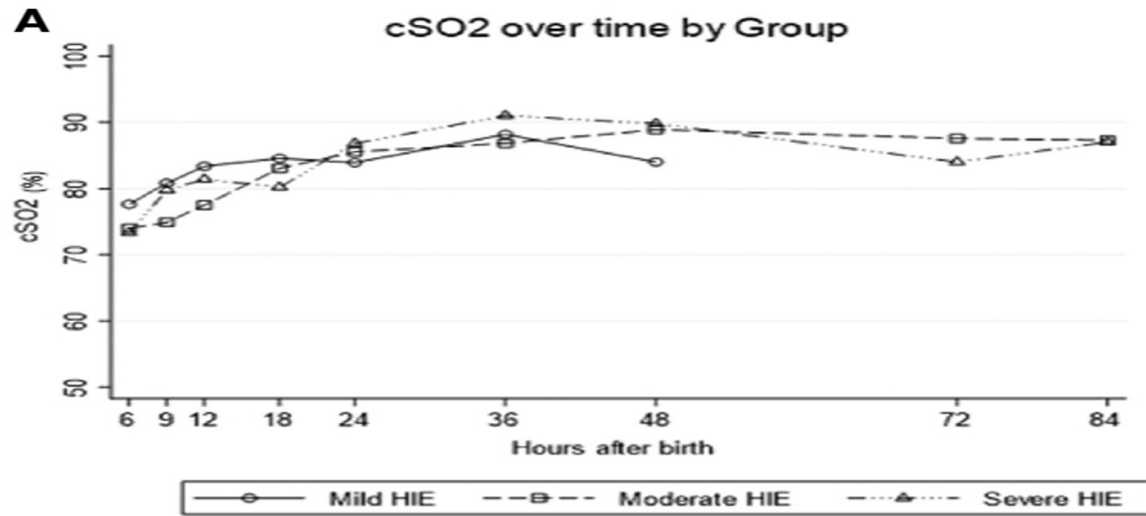
# rSO<sub>2</sub> & Hypo/Hypercarbia



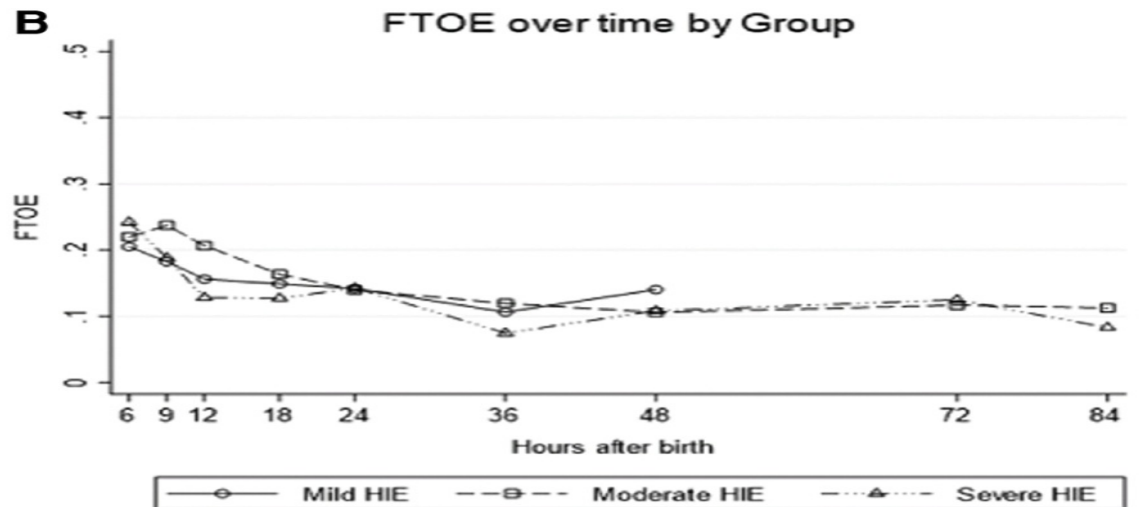
# rSO<sub>2</sub> & Seizure Activity



# NIRS changes in HIE



cSO<sub>2</sub> increases  
over 1<sup>st</sup> 24 hrs



cFTOE decreases  
over 1<sup>st</sup> 24 hrs

# rSO<sub>2</sub> & Cooling

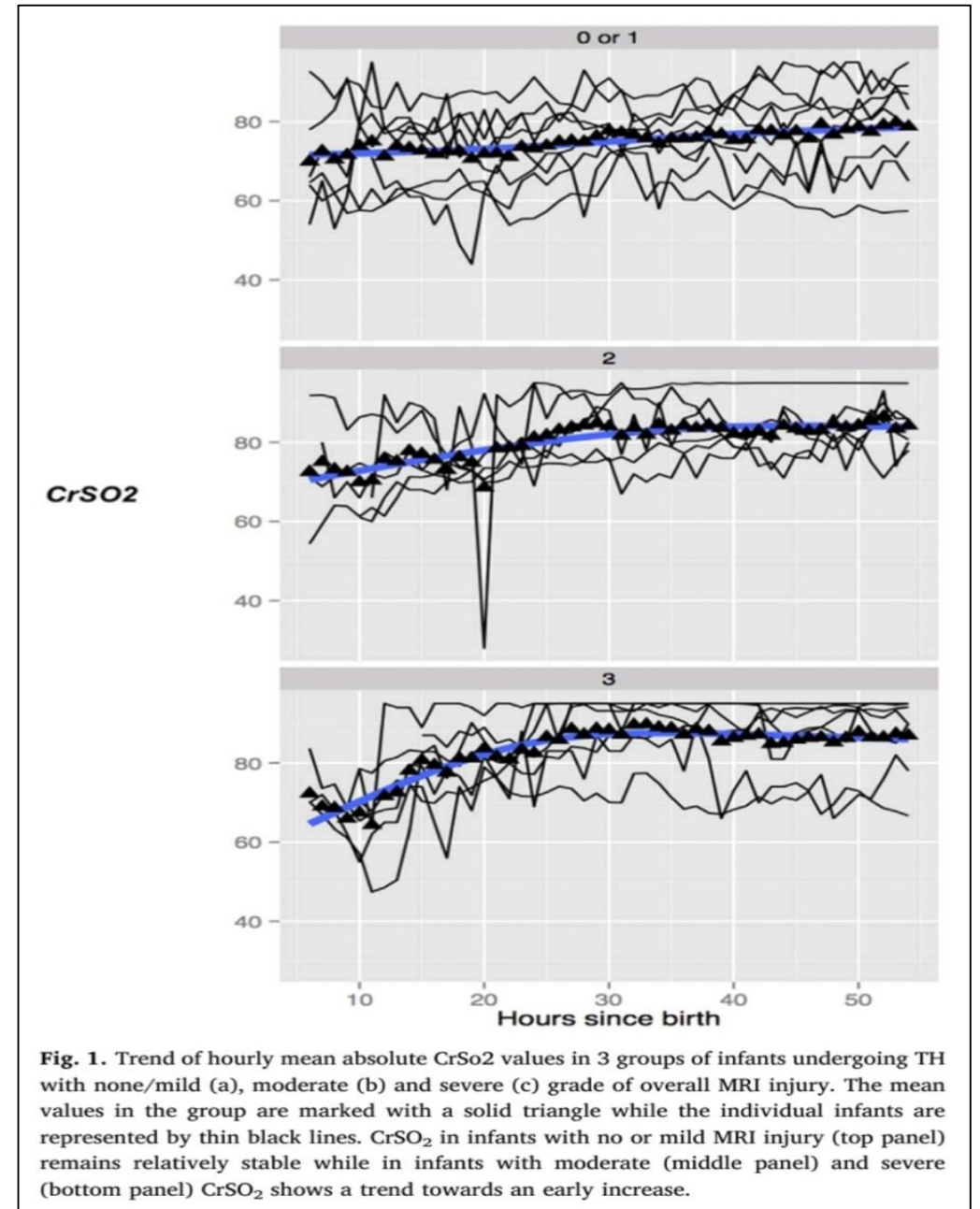
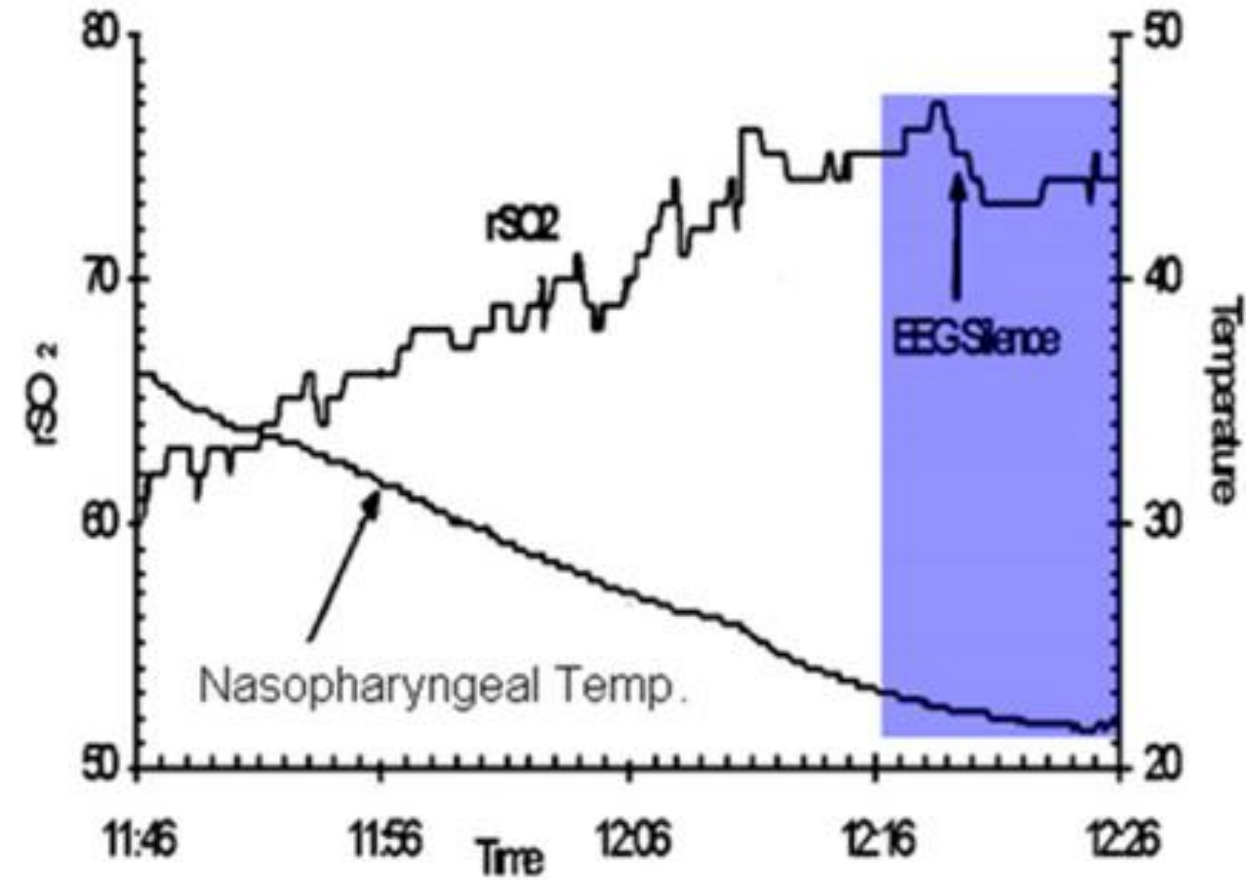


Fig. 1. Trend of hourly mean absolute CrSO<sub>2</sub> values in 3 groups of infants undergoing TH with none/mild (a), moderate (b) and severe (c) grade of overall MRI injury. The mean values in the group are marked with a solid triangle while the individual infants are represented by thin black lines. CrSO<sub>2</sub> in infants with no or mild MRI injury (top panel) remains relatively stable while in infants with moderate (middle panel) and severe (bottom panel) CrSO<sub>2</sub> shows a trend towards an early increase.

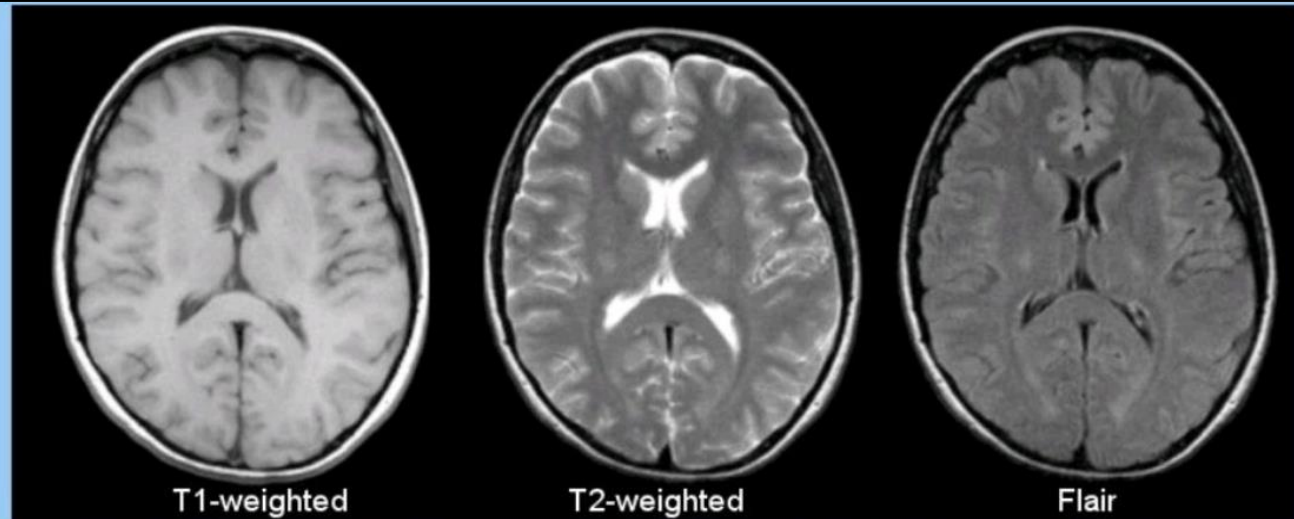
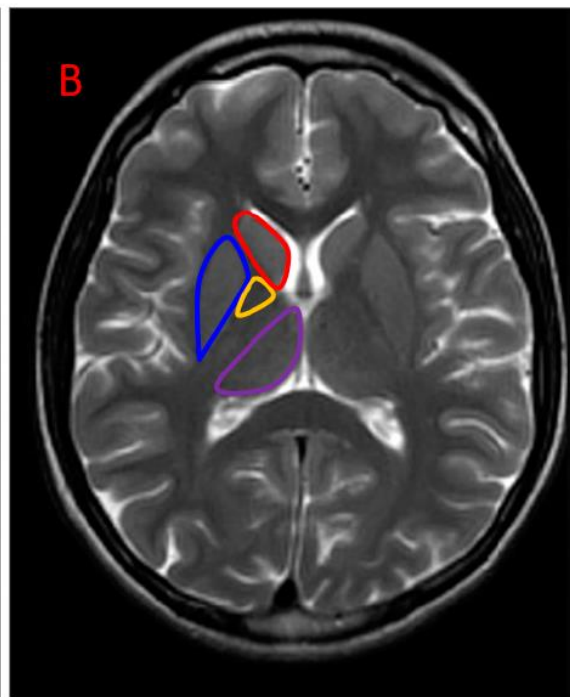
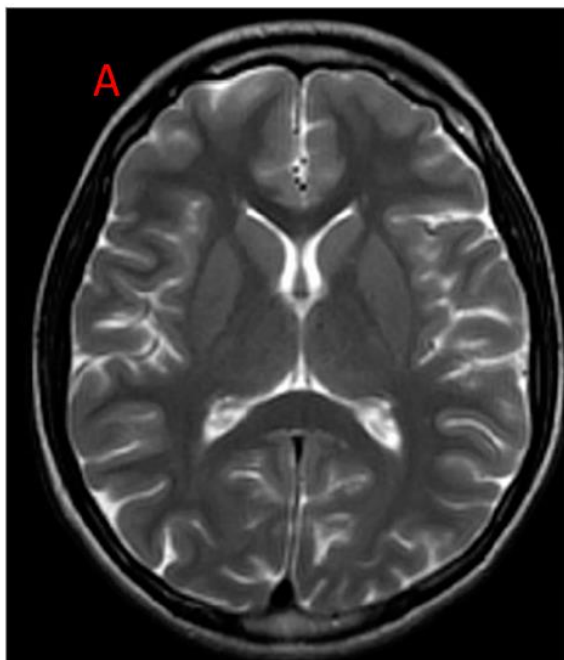
# Examples -Prognostic Value of NIRS for NDO



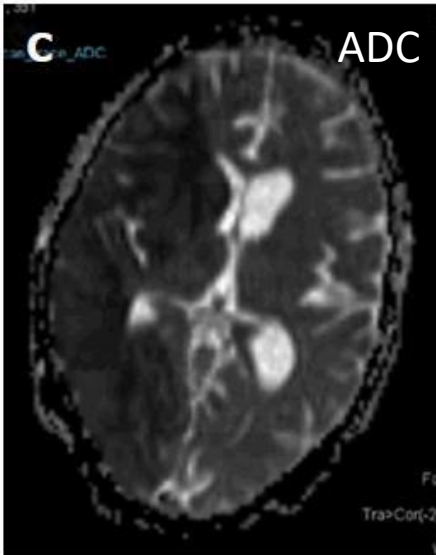
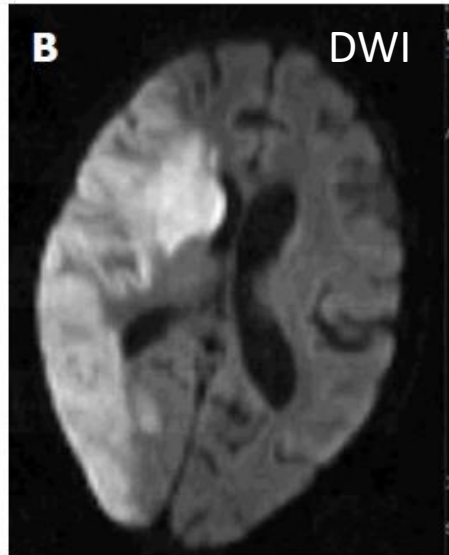
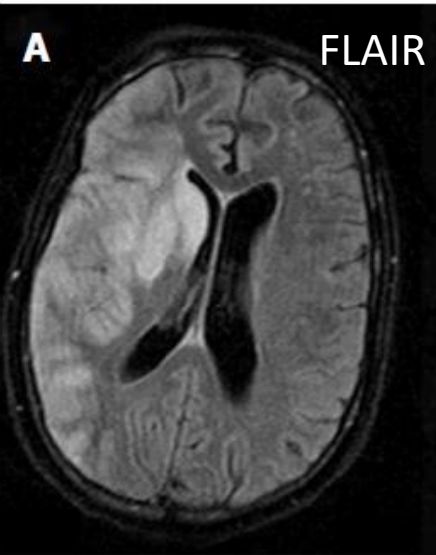
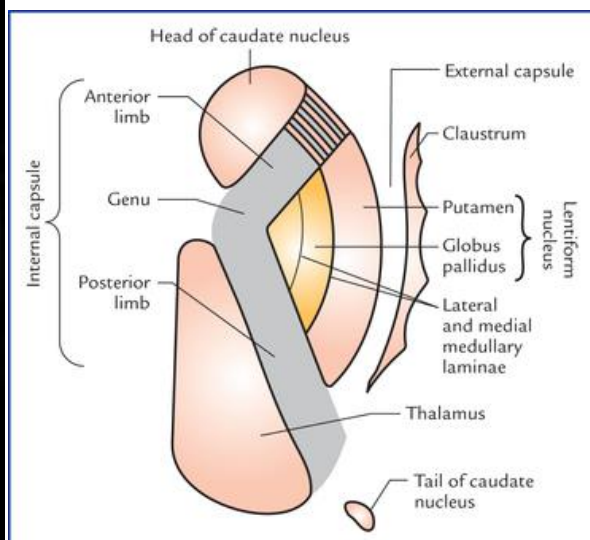
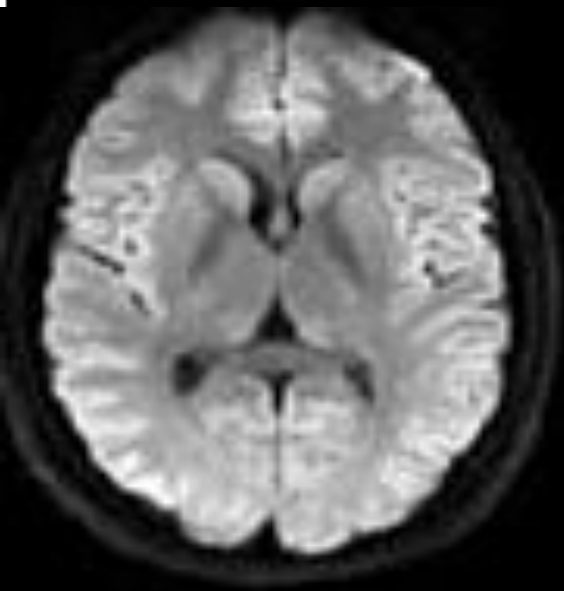
- Post cardiac surgery
- Cerebral oxygenation and hypoxic ischemic encephalopathy (HIE)
  - Between 24-36 hrs, higher CrSO<sub>2</sub> –increased odds of mod-severe abnormalities on brain MRI
  - Per 10% increase in Crso<sub>2</sub>, (OR 3.78 CI 1.23-11.6), Max at 30 hr
  - CrSO<sub>2</sub> increased more rapidly in infants with greater injury
  - Higher CrSO<sub>2</sub> beyond 24 hrs correlates with greater odds of worse BSID scores.
- Hypotension
  - cRSO<sub>2</sub> <50% -adverse neurodevelopmental outcomes



# MRI Brain

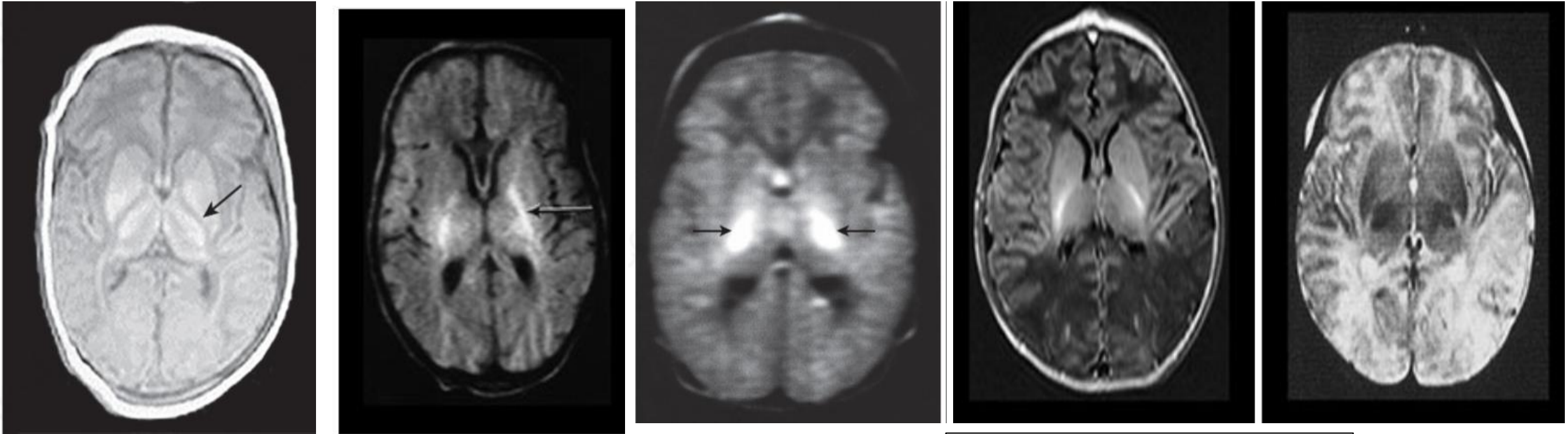


Tissue	T1-Weighted	T2-Weighted	Flair
CSF	Dark	Bright	Dark
White Matter	Light	Dark Gray	Dark Gray
Cortex	Gray	Light Gray	Light Gray
Fat (within bone marrow)	Bright	Light	Light
Inflammation (infection,)	Dark	Bright	Bright





# MRI Findings



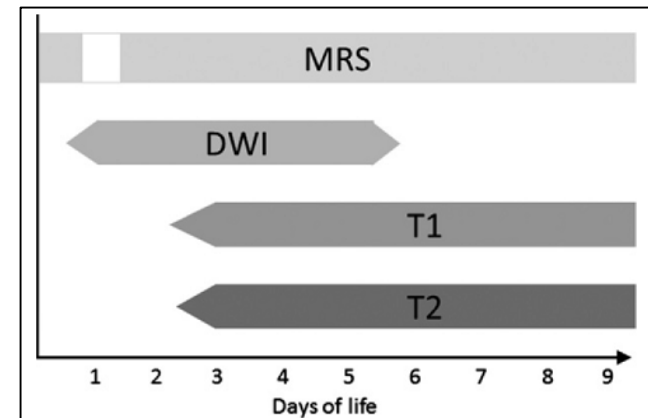
T1-PLIC Sign

DWI-DWI-Diffusion restriction in posterior limb of internal capsule

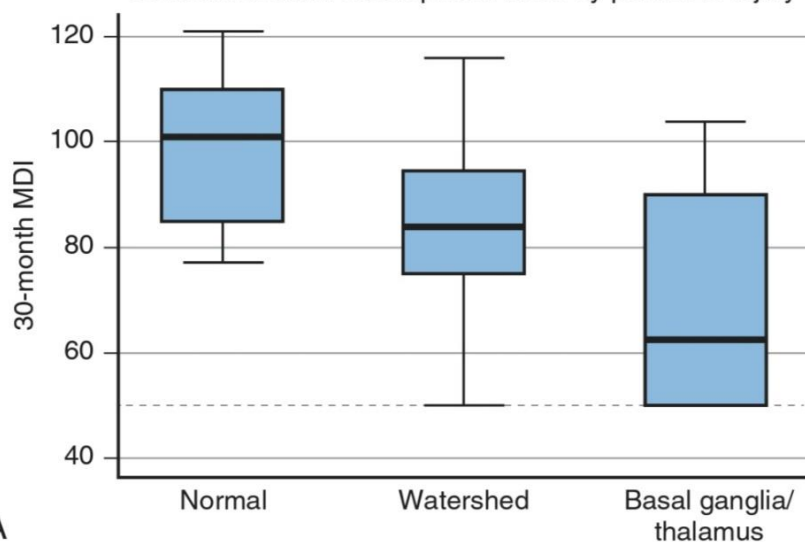
DW1-DWI-Diffusion restriction in Basal ganglia and thalamus (BGT)

T2- loss of differentiation in temporo-occipital lobe

DW1-restricted diffusion in temporo-occipital lobe

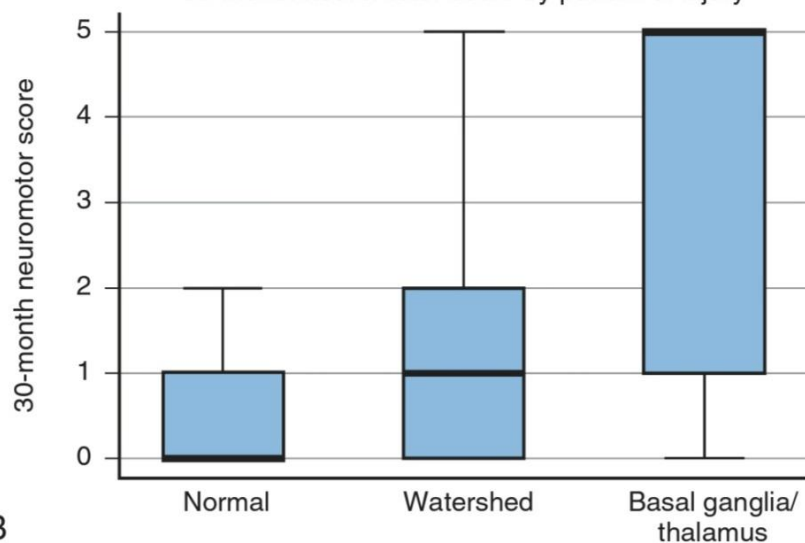


30-month mental development index by pattern of injury



A

30-month neuromotor score by pattern of injury



B

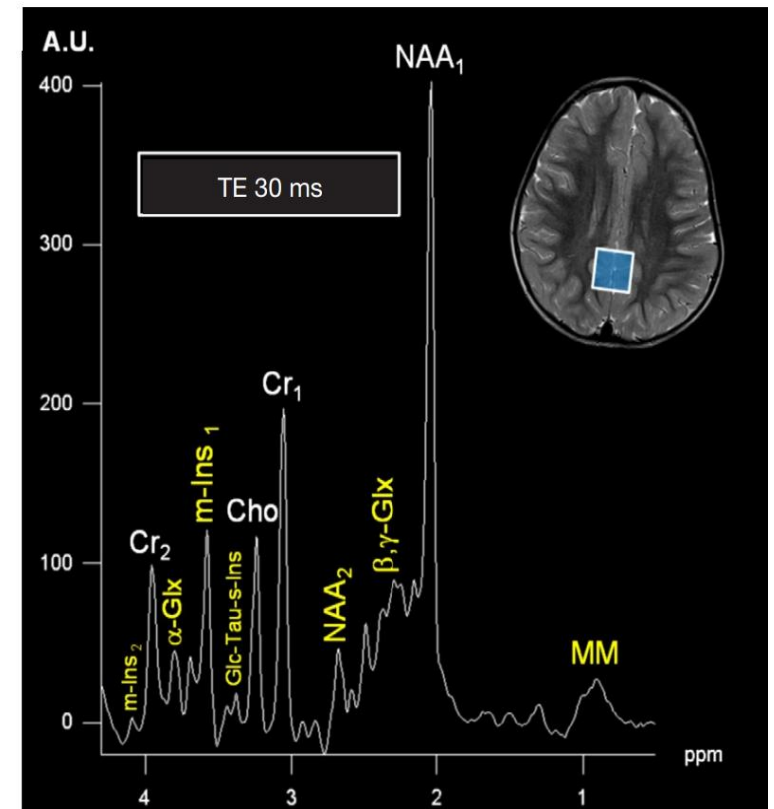
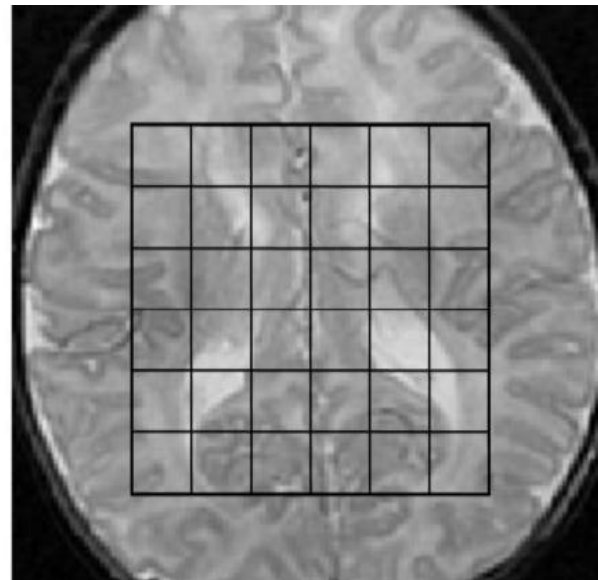
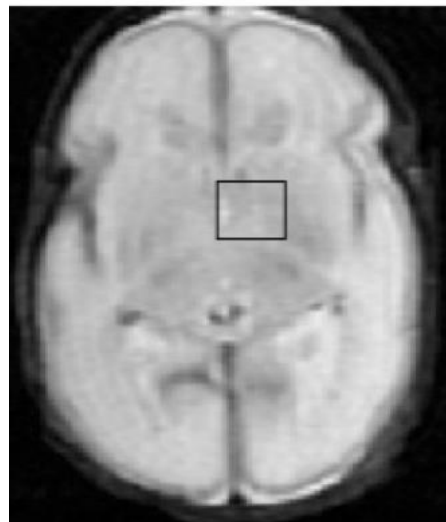
Patterns of brain injury in term neonatal encephalopathy. J Pediatr. 2005;146:453-460. Miller Sp et al.

	PPV	NPV
<b>T1 T2 abnormalities (n=122)</b>		
PLIC score	88	63
Mod/sev in BGT	88	68
Mod/Sev in white matter	84	54
Mod/sev in cortical gray matter	89	58
<b>Diffusion abnormalities (n=121)</b>		
PLIC score	87	60
Mod/sev in BGT	89	65
Mod/Sev in white matter	85	55
Mod/sev in cortical gray matter	89	59

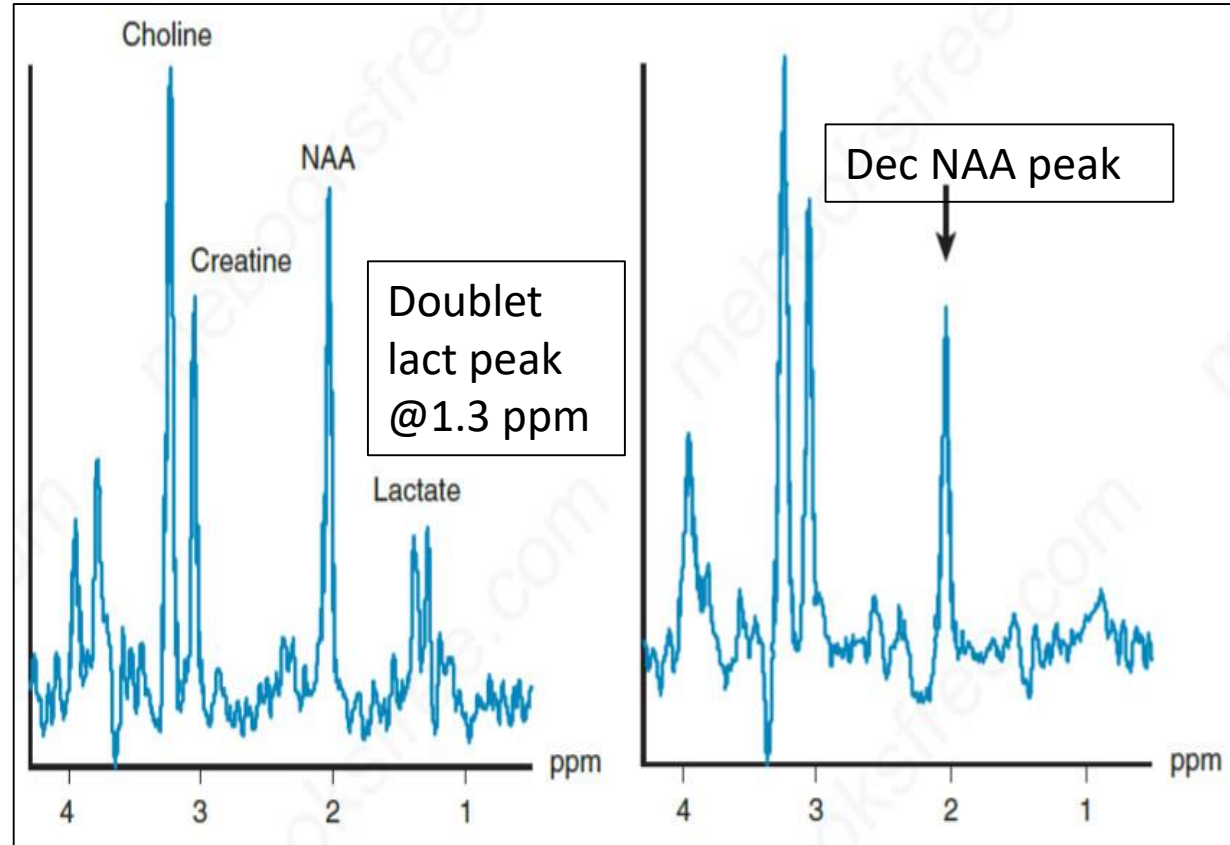
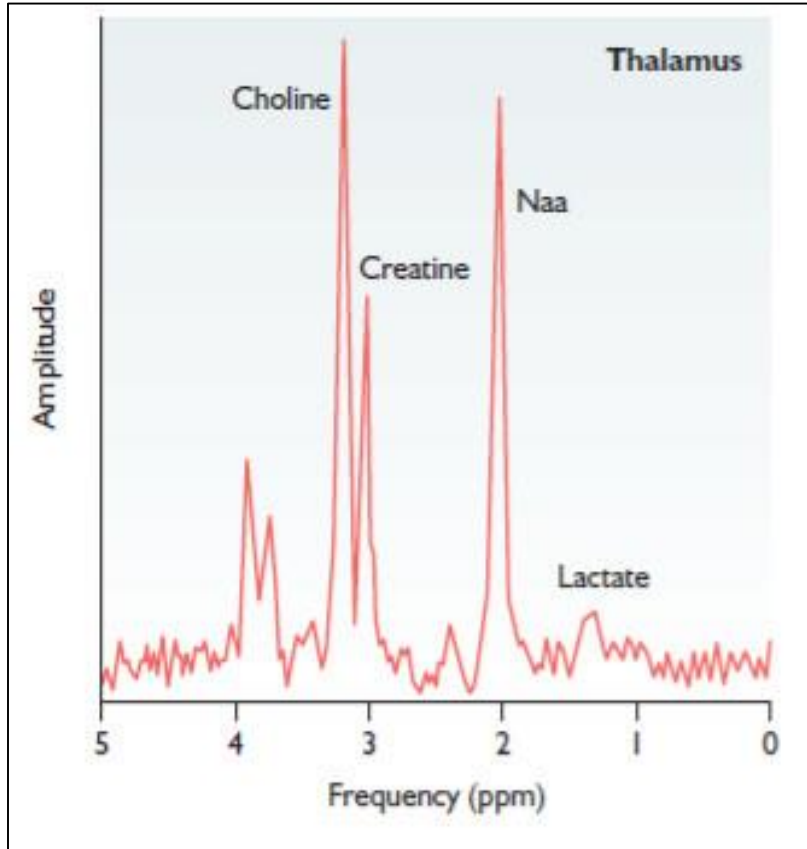
Cheong JL et al; Prognostic utility of MRI in neonatal HIE:substudy of a randomised trial. Arch Pediatr Adolesc Med. 2012 Jul 1;166(7):634-40

# MR Spectroscopy

- Metabolic status in the tissue-often precedes anatomical changes
- Different metabolites-characteristic resonant frequencies
- X axis- chemical shift axis
- Y-axis-signal intensity
- Voxels



# MR Spectroscopy



**High Lac/Cr, low NAA/Cr and low NAA/Cho ratios** within examined regions of the brain including deep grey matter nuclei as well as white matter are associated with an adverse outcome in infants with perinatal asphyxia

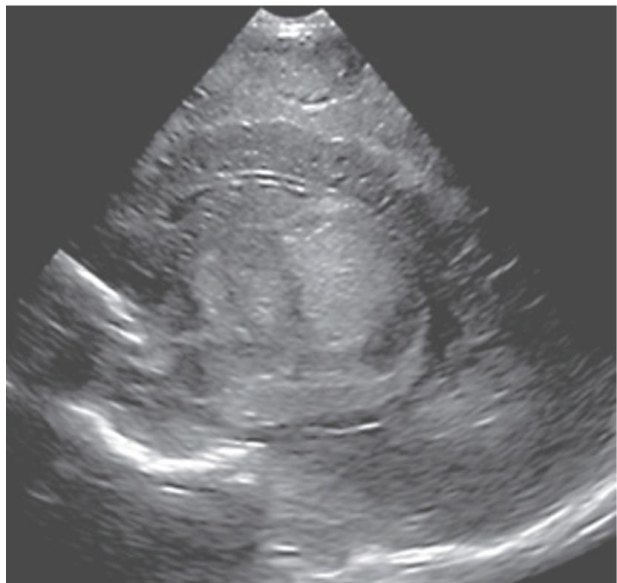
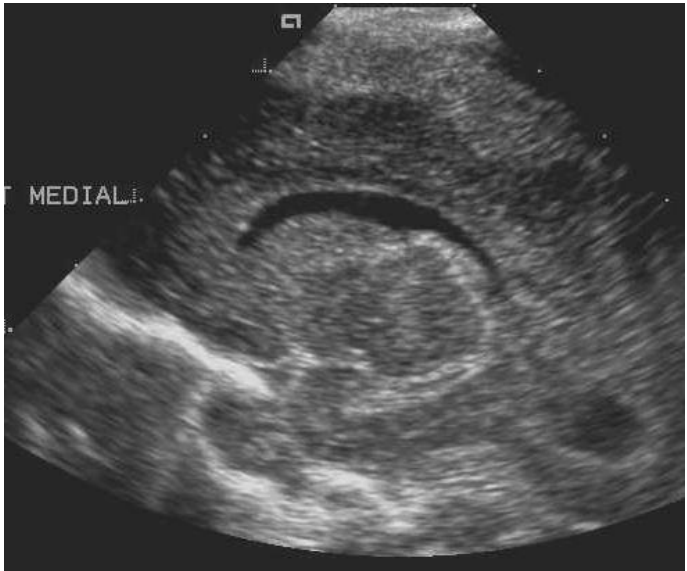
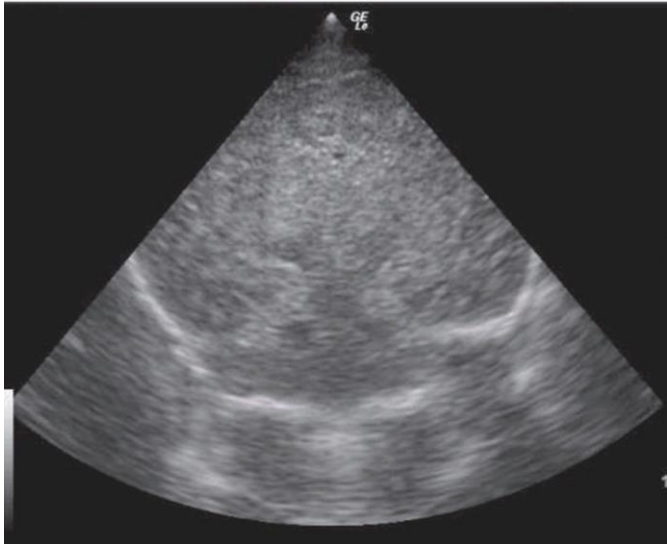
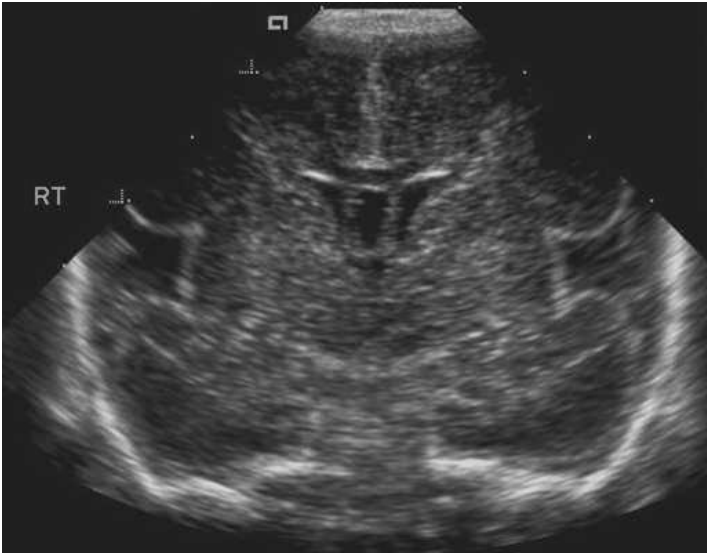
In first 2 weeks, severity of **decline of PCr/Pi** associated with worse outcome at 4 years



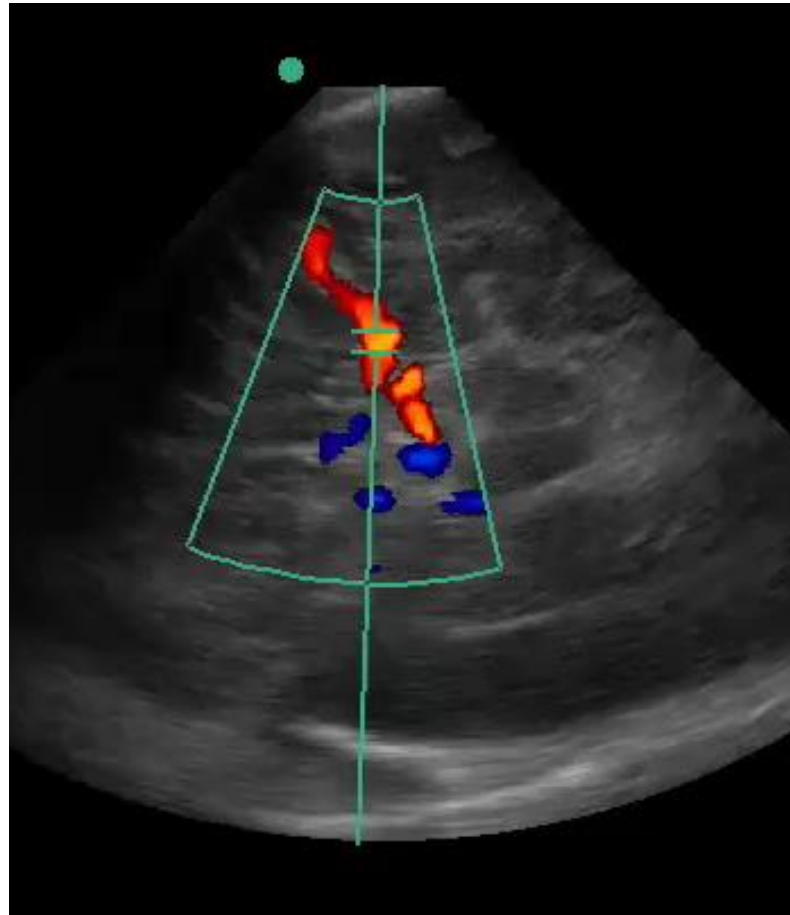
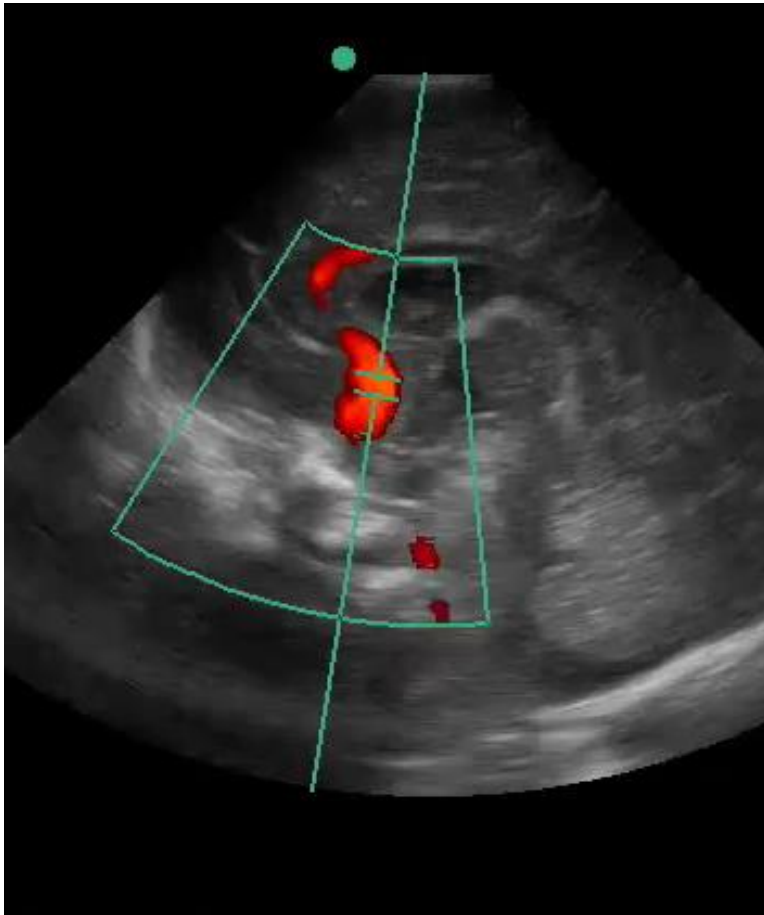
# Cranial Ultrasound & Doppler



Sir Ganga Ram Hospital



# Dopplers and Cerebral Blood Flow



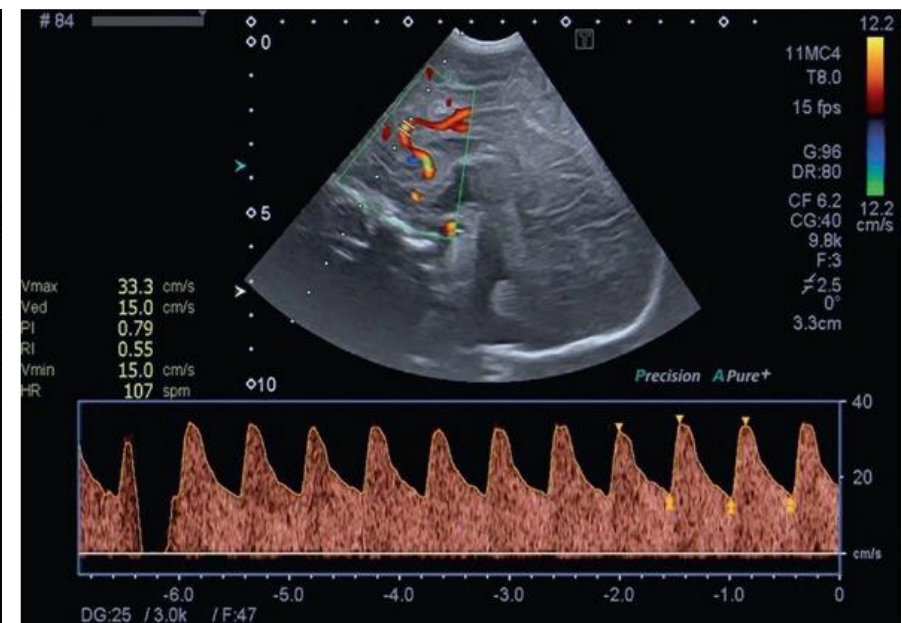
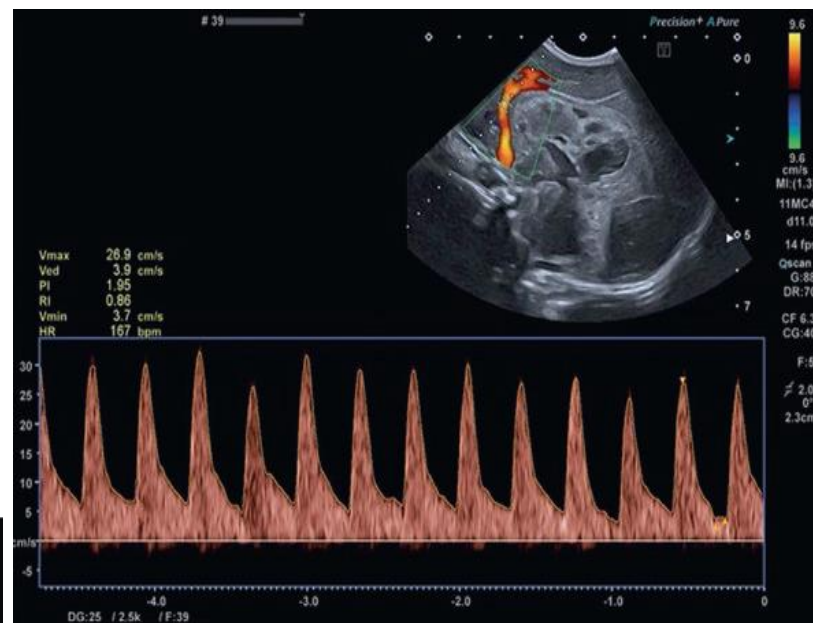
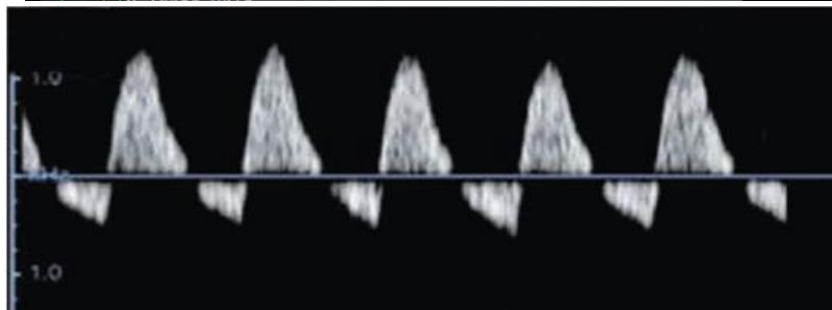
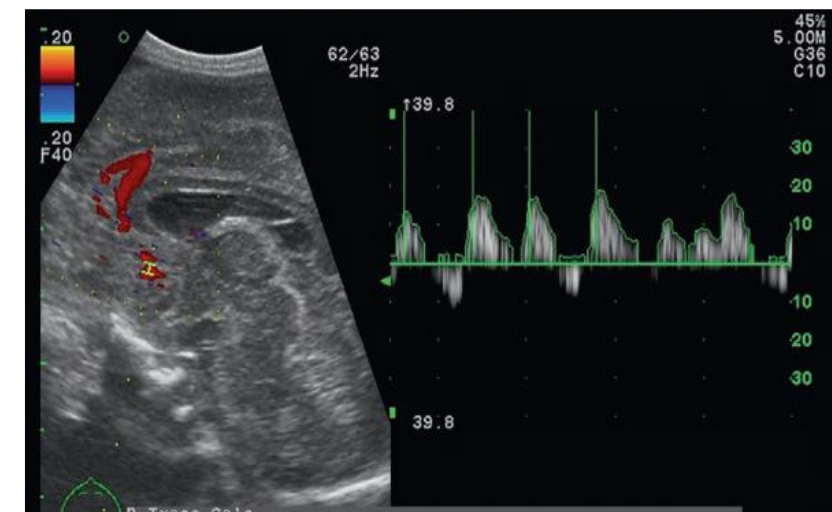
# Anterior Cerebral A

CBF	2-8 h (n=50)	24 h (n=75)	Day 3 (n=71)	Day 7 (n=72)	Day 14 (n=70)	Day 28 (n=55)	P value
PSV	26.53 (8.56)	29.96 (6.41)	31.8 (7.62)	36.29 (8.29)	41.69 (7.39)	51.35 (9.36)	<0.001 (5,6)
EDV	9.22 (2.91)	10.88 (2.85)	10.87 (2.8)	11.51 (3.47)	11.98 (3.23)	13.9 (3.24)	0.001 (6)
MV	17.75 (3.97)	17.8 (3.92)	18.34 (3.48)	20.48 (5.3)	21.69 (3.82)	25.84 (3.27)	0.001(6)
RI	0.64 (0.08)	0.64 (0.06)	0.65 (0.08)	0.68 (0.08)	0.71 (0.07)	0.72 (0.07)	0.09

Data are presented in Mean  $\pm$  SD. Repeated Measures ANOVA test used followed by multiple comparisons using Bonferroni corrections between baseline to other time points. 5=Day 14 and 6=Day 28. PSV-Peak systolic velocity. EDV-End diastolic velocity, MV-Mean velocity and RI-Resistive index.

Thakur A, Jain P, Modi M, Singh A, Kansal B, Kler N. Normative Values of Cerebral Blood Flow Velocities in Very Low Birth Weight Neonates During First 28 Days of Life. Indian Pediatr. 2024 Sep 15;61(9):835-838.





Abnormal RI associated with significantly higher risk of death/Abnormal neurodevelopment at 6-12 months.(75% vs 10%) RR- 7.5 (95% CI 2.0- 8.6)-Kumar et al Indian Pediatr 2016;53;1079-82

Condition	Physiology	Findings
Hypovolemia/Hypotension	Impaired autoregulation	Beat to beat variability/reversal may precede IVH
PHVD	Increased ICP	High PSV, low diastolic flow-Inc RI
HIE esp 6-24 hrs Stroke	Luxury perfusion, increased diastolic flow	Decreased RI, <0.55 (poor outcome) If persists after TH-poor outcome



# Miscellaneous

- Heart Rate Variability-Autonomic
  - LFn ( Normalised LF)- reflects sympathetic activity
  - HFn (Normalised HF)- reflects parasympathetic activity
- Evoked Potentials-VEP/SEP
- Biomarkers
  - Brain specific proteins eg neuron specific enolase,S 100,Glial acidic protein etc or signaling molecules cytokines/trophic factors
    - Blood
    - CSF

# Key Messages

- EEG- Seizures/Severe Background
- Amplitude EEG-Early severe persistence
- NIRS-rSO<sub>2</sub>
- MRI-Patterns of injury-High PPV
- MRS-Metabolites
- USG and Dopplers-Patterns
- Evoked Potentials
- HR Variability and Bio-Markers

# Thank you

