Network Neonatale Italiano

1° Meeting del Network Neonatale Italiano

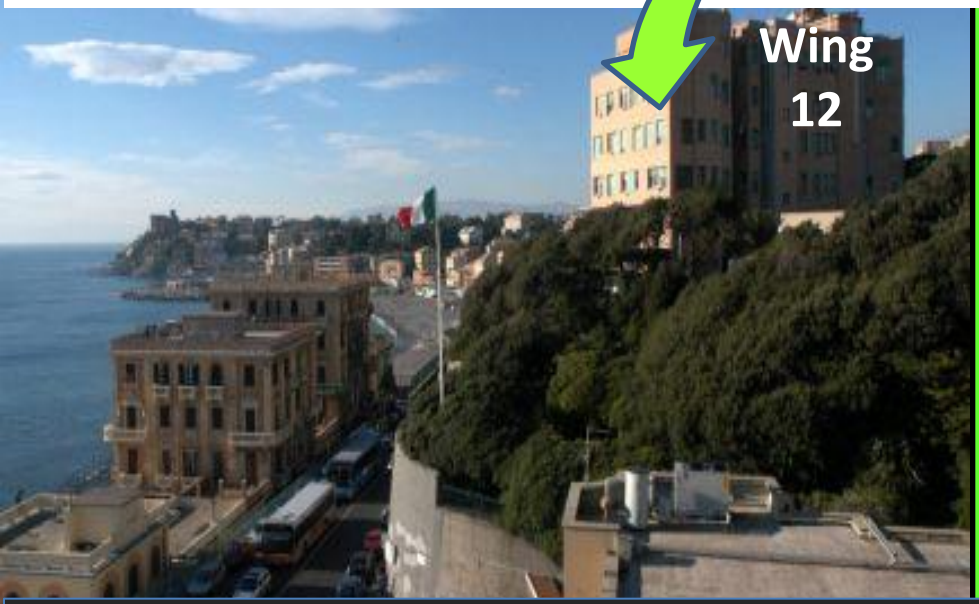
Il Network per il governo clinico, la ricerca e la formazione

Aula Magna dell'Università degli Studi di Milano

Via Festa del Perdono 7 - Milano

12 novembre 2014

Reparto Immaturi 1938

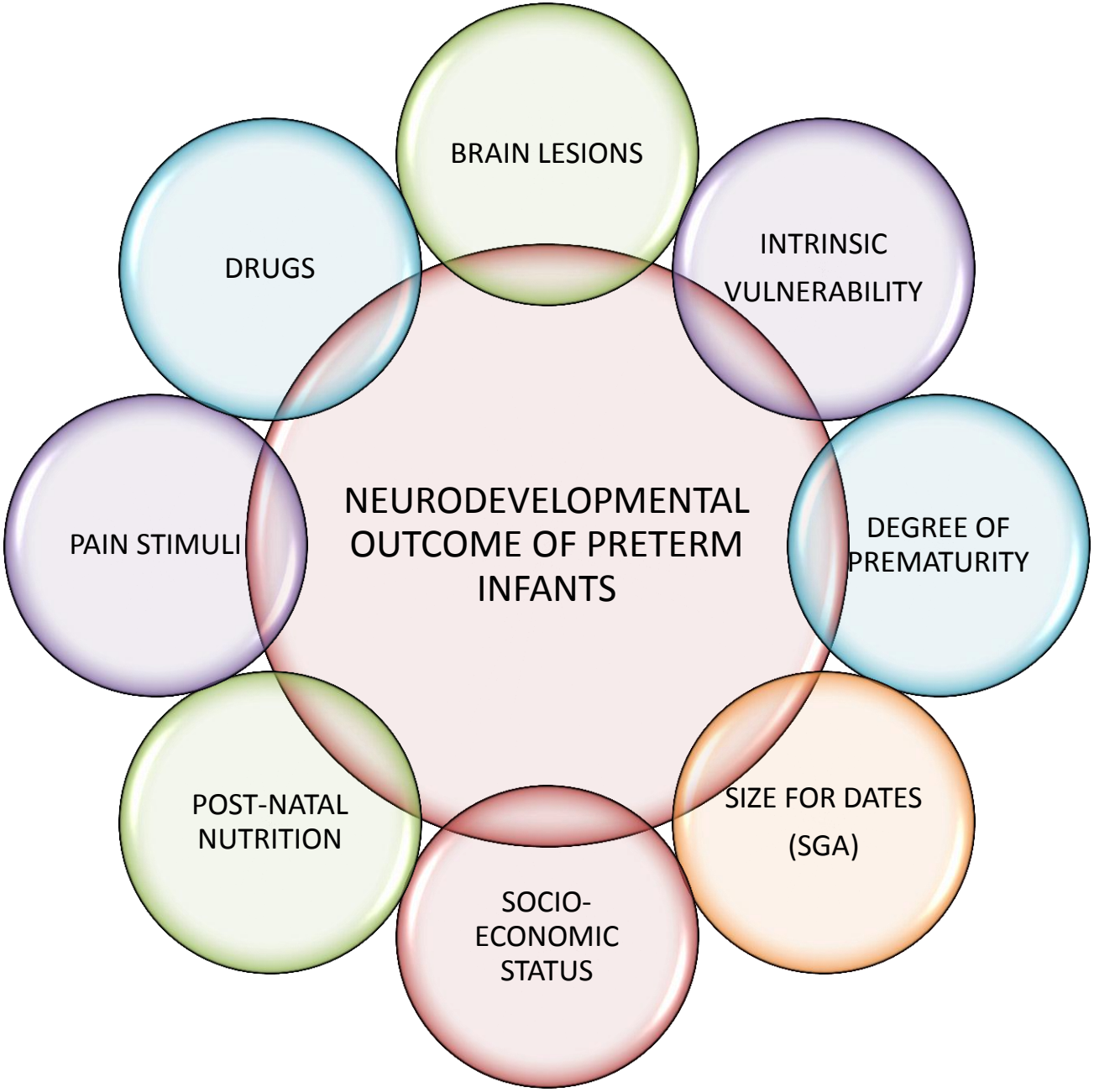


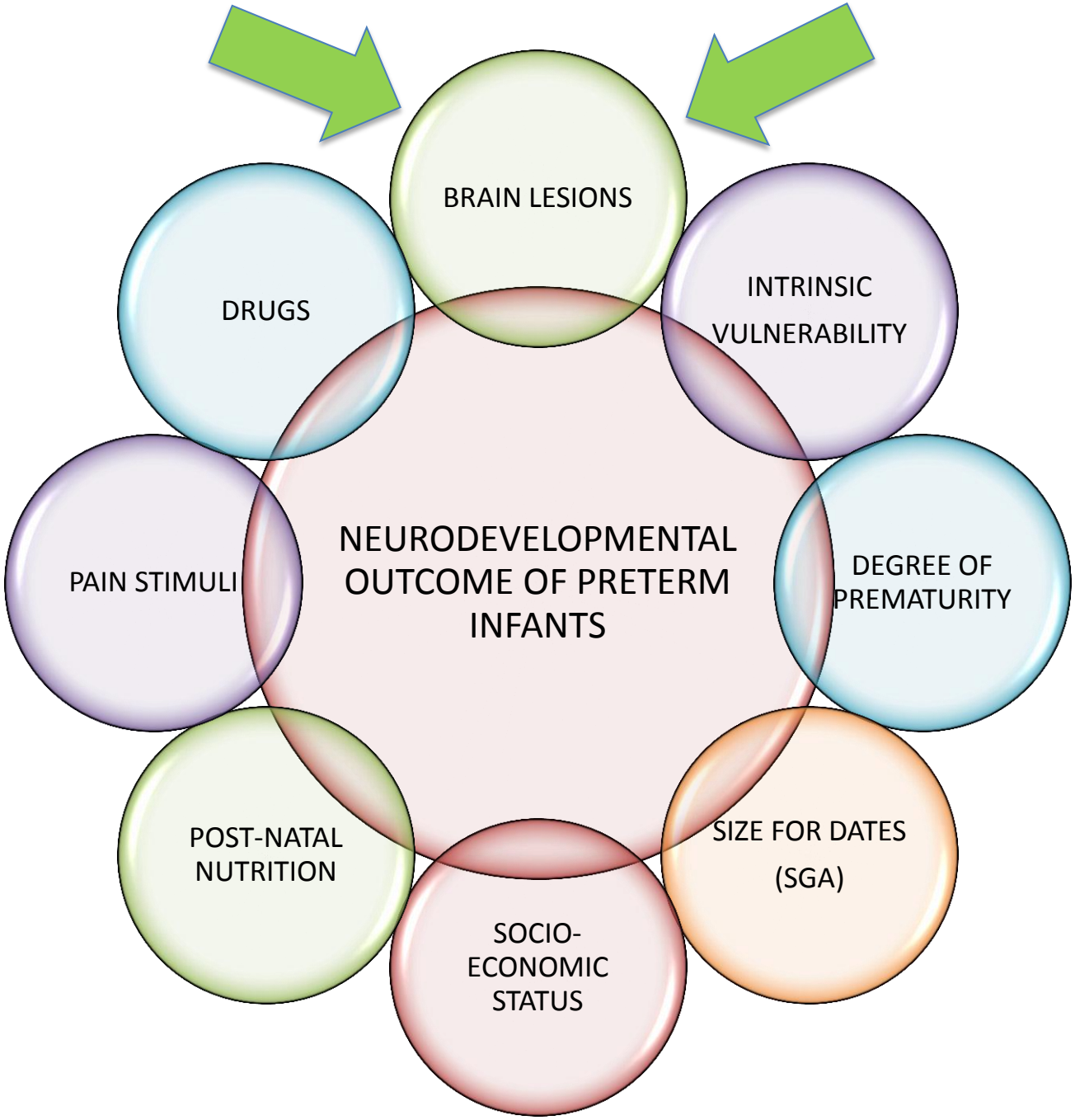
Wing 12

Proposta di studio: emorragia cerebellare

Neonatal Intensive Care Unit "G.Gaslini" Children's Hospital IRCCS Genoa

Luca A. Ramenghi MD PhD


BRAIN LESIONS
INTRINSIC VULNERABILITY
DEGREE OF PREMATURITY
SIZE FOR DATES (SGA)
SOCIO-ECONOMIC STATUS
POST-NATAL NUTRITION
PAIN STIMULI
DRUGS
NEURODEVELOPMENTAL OUTCOME OF PRETERM INFANTS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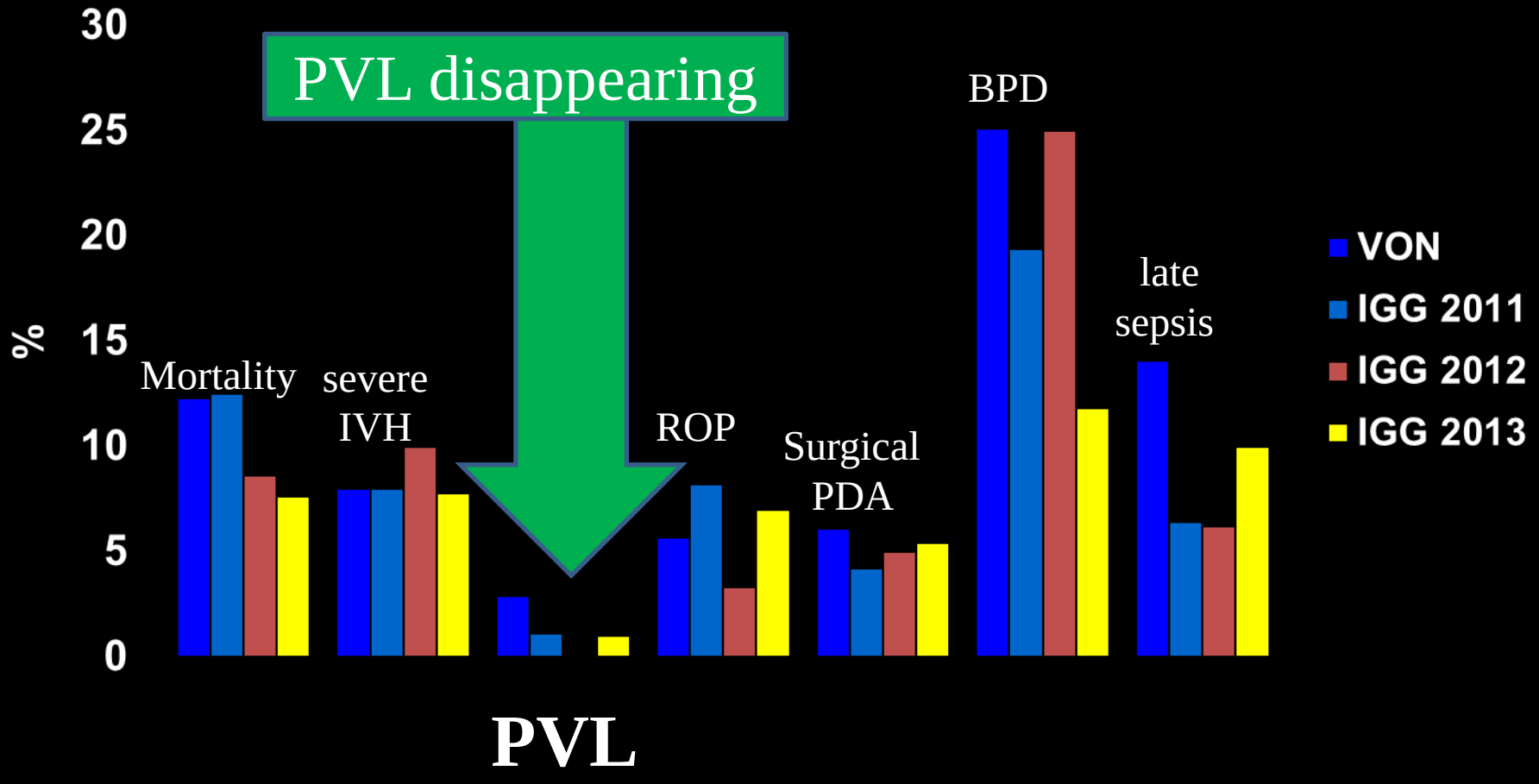
La natura e l’incidenza delle lesioni cerebrali dei VLBW si è modificata ?

Major outcomes in VLBW



VON = **V**ermont **O**xford **N**etwork (> 6000 neonati)

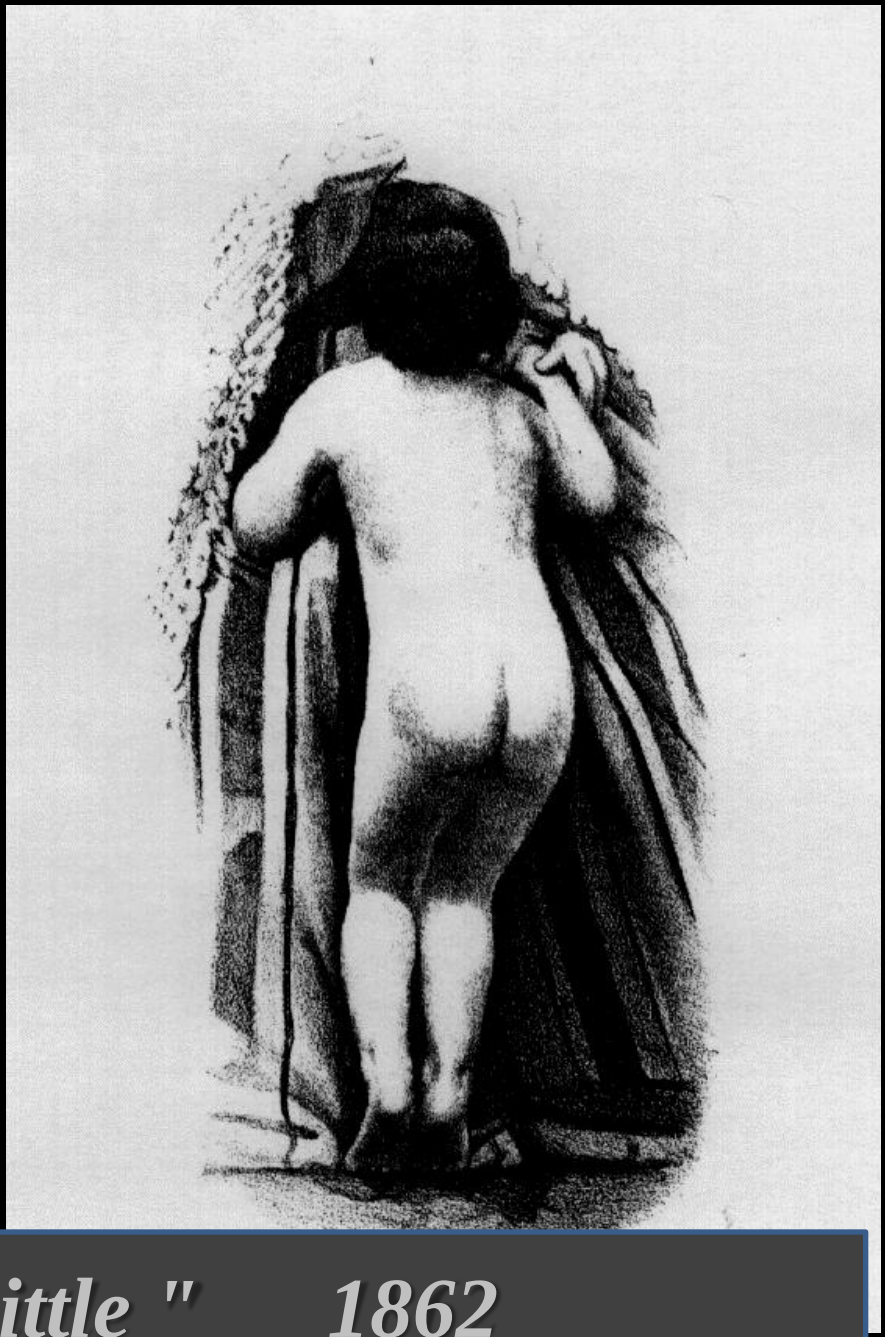
IGG 2011 = 102 VLBW

IGG 2012 = 112 VLBW

IGG 2013 = 98 VLBW

IGG = Istituto Giannina Gaslini IRCCS Genoa

Figure 66 William John Little (1810–1894)



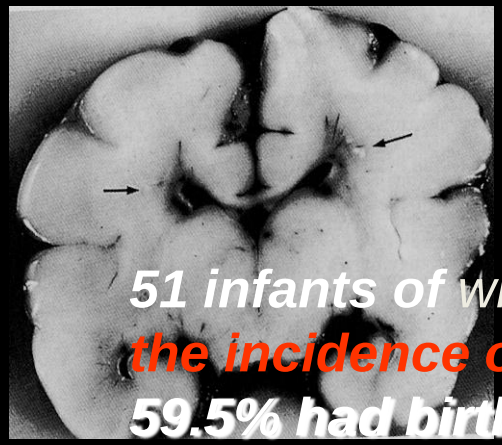
" Morbo di Little " 1862

- W.J.Little "*On the influence of abnormal parturition, difficult labours, premature birth, and asphyxia neonatorum, on the mental and physical condition of the child, especially in relation to deformities*"

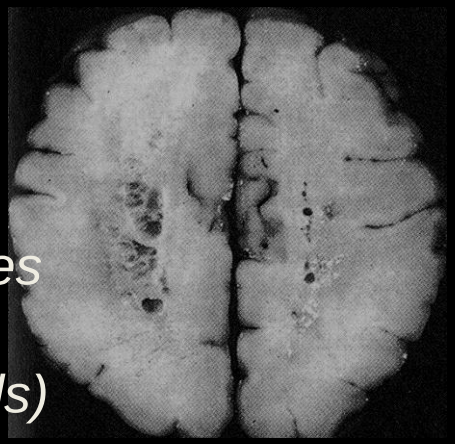
Transaction of the Obstetrical Society of London (1862)

•Betty Banker
Jeanne Claude Larroche

to draw attention to a unique diseas of cerebral white matter wich has been encountered with great frequency among infants who died at the Children's Hospital Medical Center, Boston…periventricular leukomalacia

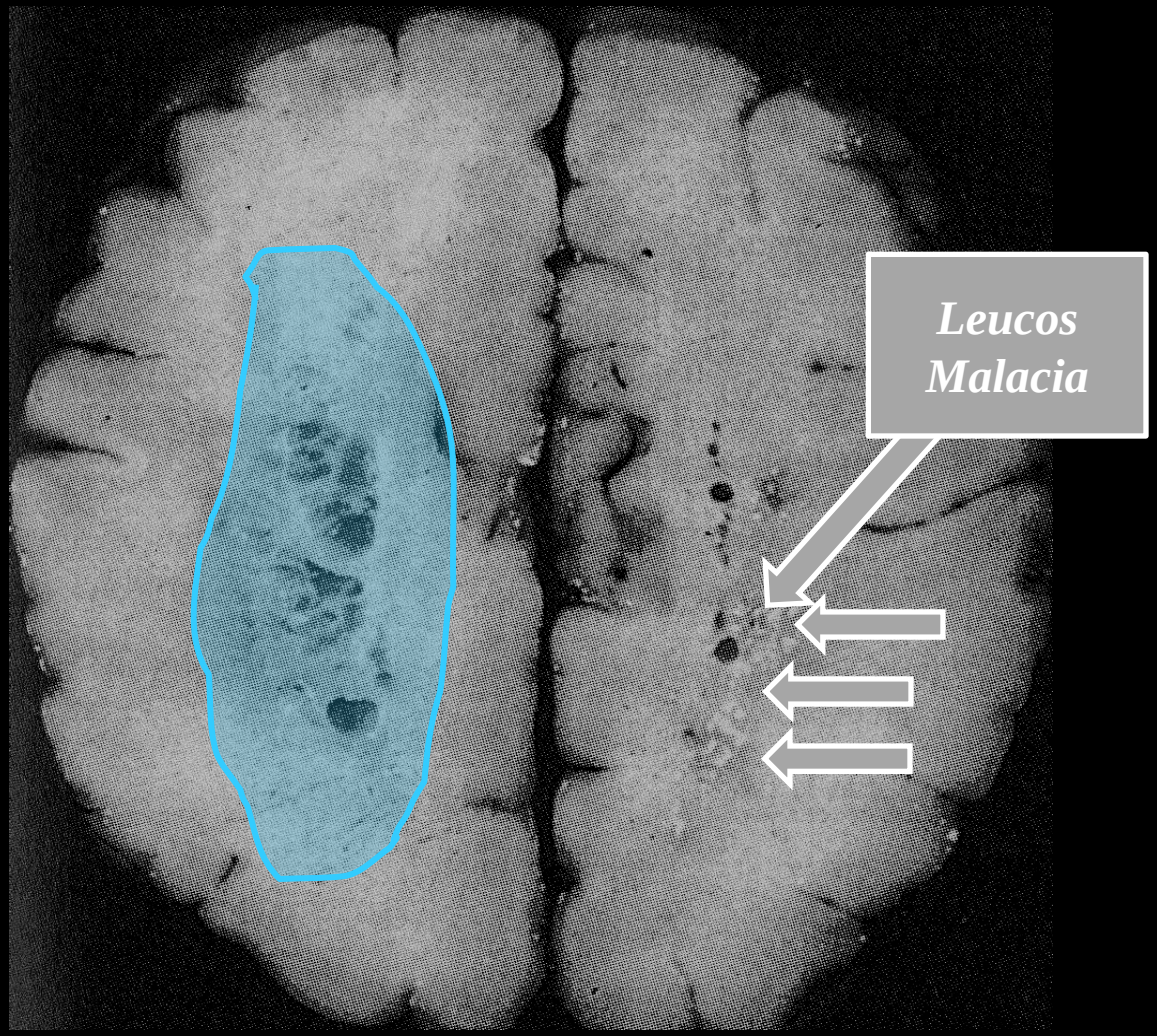


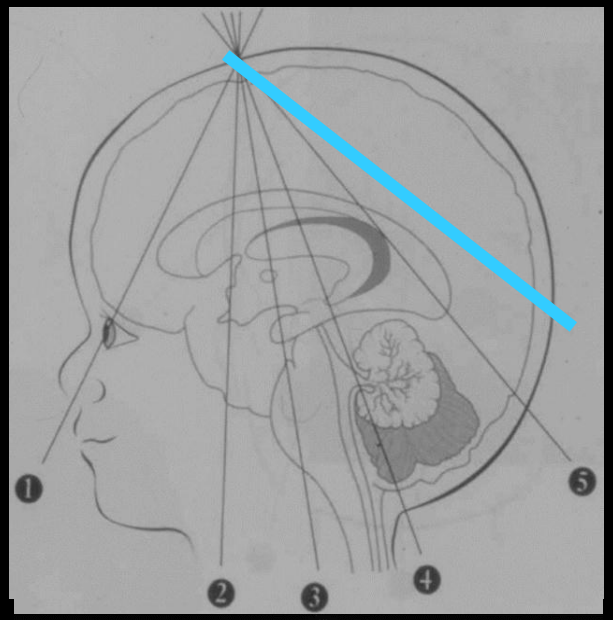
Annals of Neurology (1962)

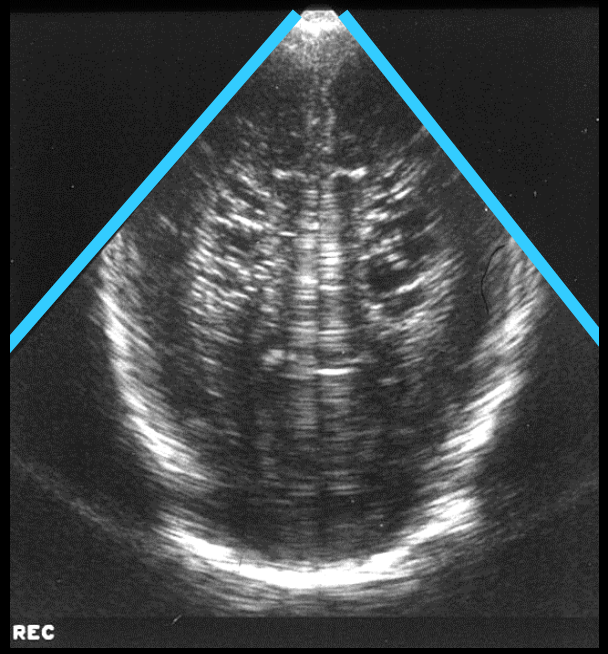


***51 infants of** which 26 were males and 25 were females*
the incidence of prematurity was 74.4%
***59.5% had birth** weight below 2500 grams (5 ½ pounds)*
Anoxia ..this was present in every infant in this series….
The anoxic episode was always severe in degree and did not merely constitute a terminal event…
The majority of infants had a period of apnea or cardiac arrest requiring resuscitation
*20/51 had apnea at birth (**what we would call today asphyxia !!!!!***

"In vivo" Ultrasound diagnosis of PVL





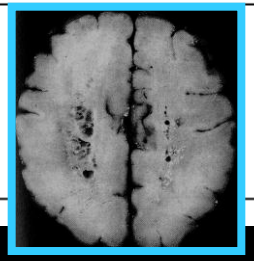


Banker-Larroche *Ann Neurol 1962*

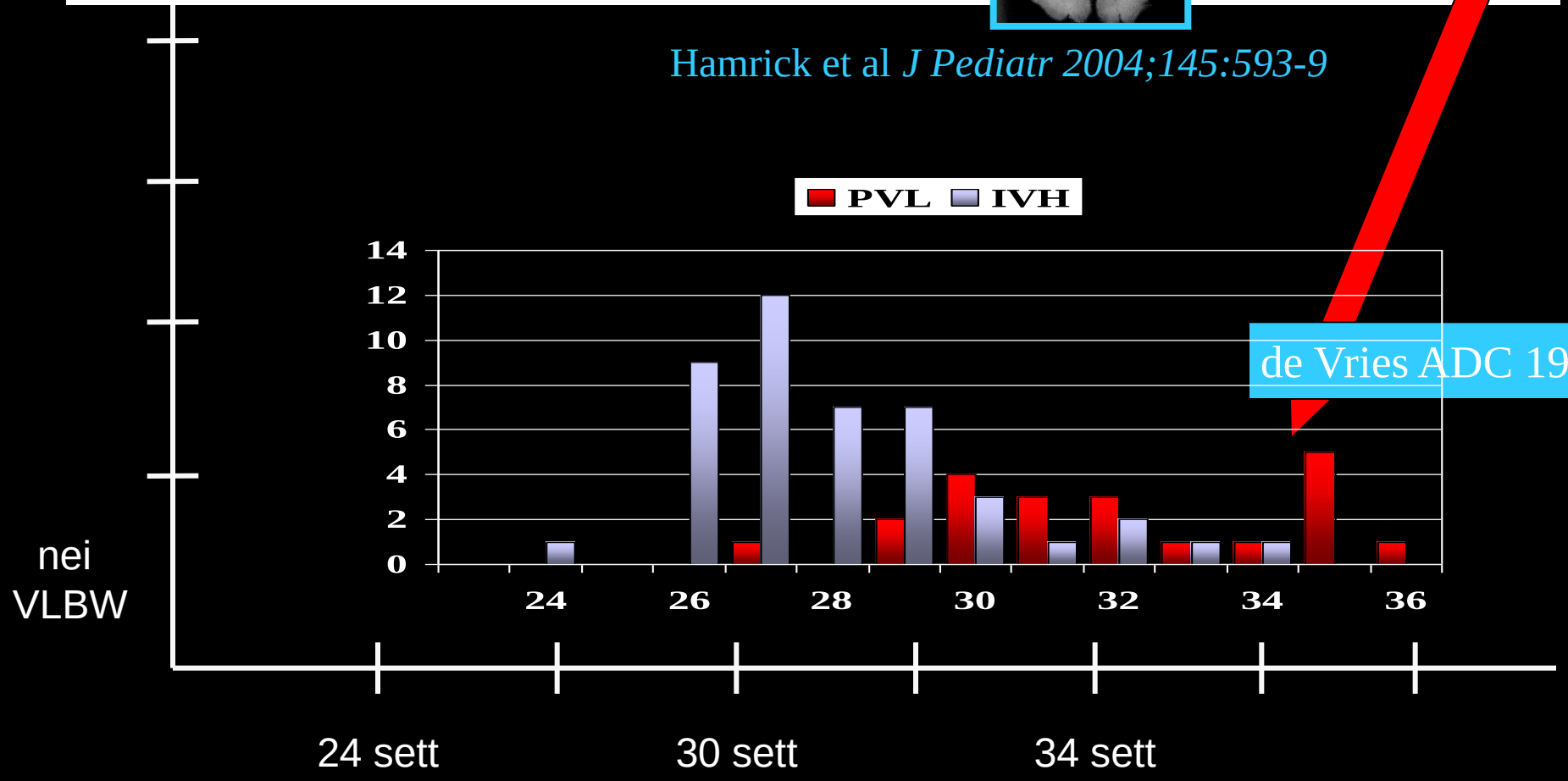
Pape et al *Lancet 1979*

Table III. Cystic PVL by birth year period in newborn infants age 24 to 27 weeks and 28 to 35 weeks at birth

Year	Total at risk age 24–27 wk	Cystic PVL	Total at risk Age 28–35 wk	Cystic PVL
1992–1993	113	6 (5.3%)		4 (0.9%)
1994–1996	183	5 (2.7%)		5 (0.7%)
1997–1999	189	2 (1.1%)		3 (0.4%)
2000–2002	185	0		2 (0.3%)



Hamrick et al *J Pediatr 2004;145:593-9*



de Vries ADC 1986

www.jpeds.com • THE JOURNAL OF PEDIATRICS

Decreasing Incidence and Severity of Cerebral Palsy in Prematurely Born Children

Ingrid C. van Haastert, MA, Floris Groenendaal, MD, PhD, Cuno S. P. M. Uiterwaal, MD, PhD, Jacqueline U. M. Termote, MD, PhD, Marja van der Heide-Jalving, MD, Maria J. C. Eijsermans, PPT, Jan Willem Gorter, MD, PhD, Paul J. M. Helders, MSc, PhD, Marian J. Jongmans, MSc, PhD, and Linda S. de Vries, MD, PhD

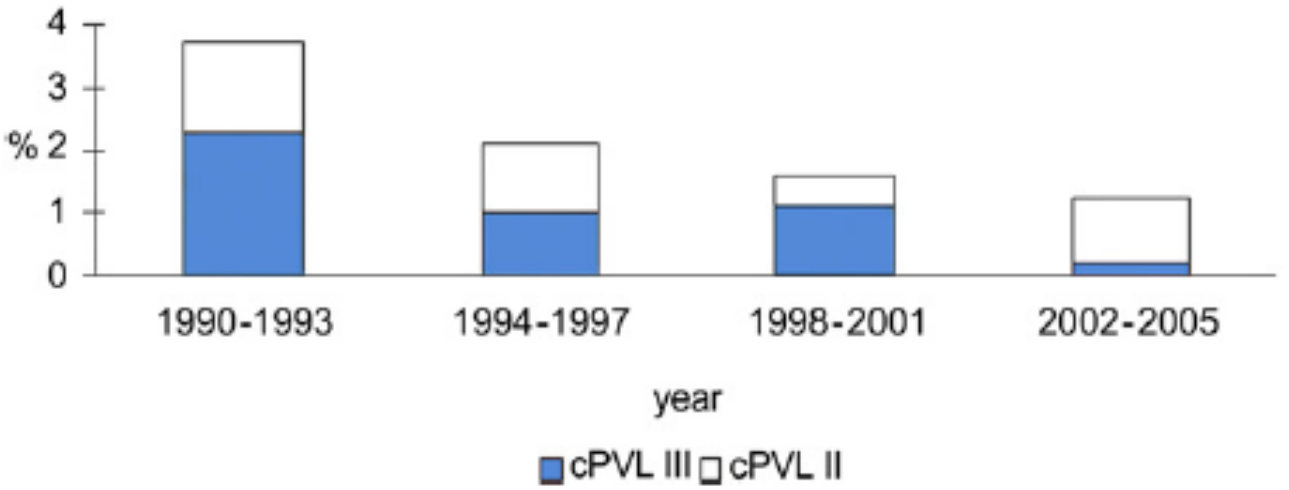
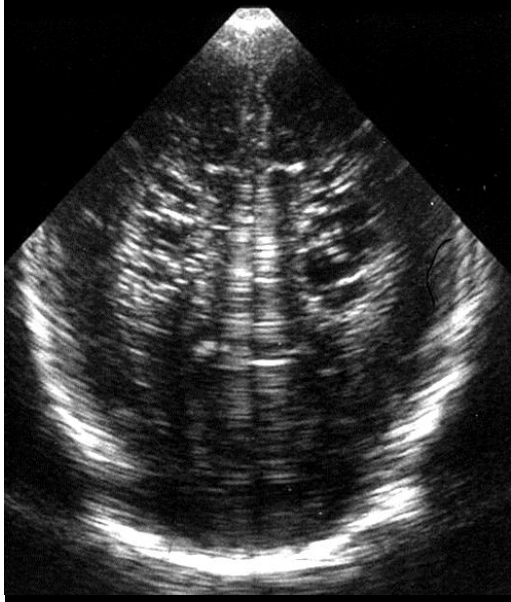


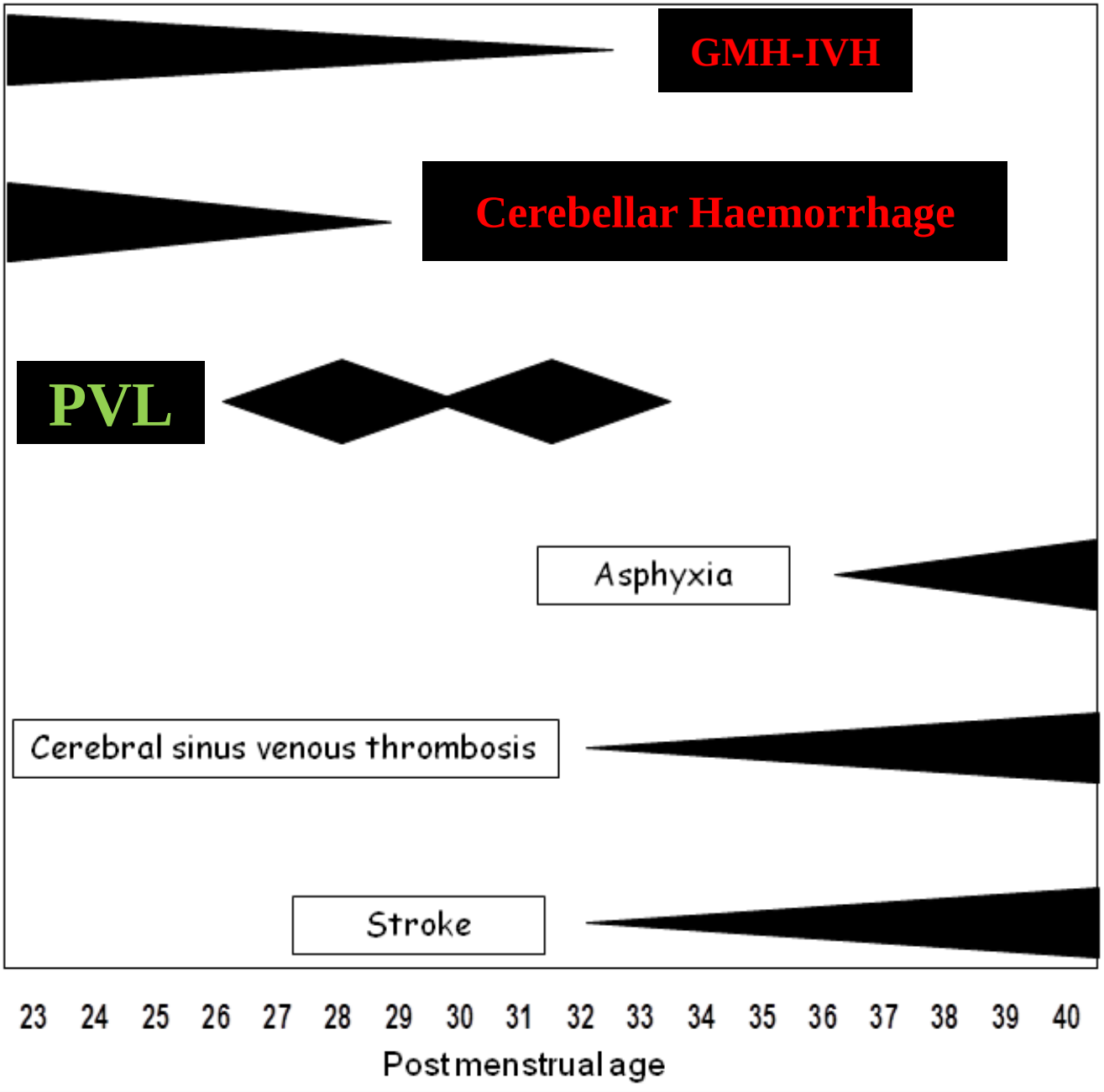
Figure 4. C-PVL grade II and III within total cohort.

(J Pediatr 2011;159:86-91)



PVL like lesions With obvious spasticity

Very prem with less overt brain lesions and cognitive problems



Sannia et al. (2012) Different gestational ages and changing vulnerability of the premature brain

Quanto accurati siamo nella diagnosi di queste lesioni ?

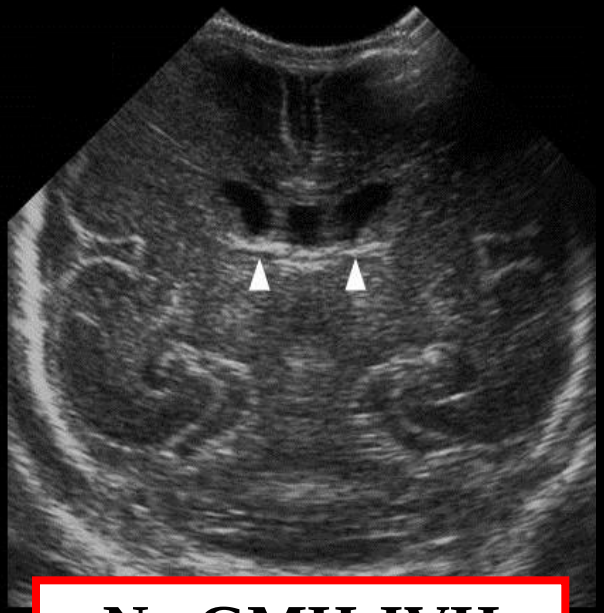
Accuracy in diagnosing Brain Lesions

Susceptibility-Weighted Imaging (SWI)

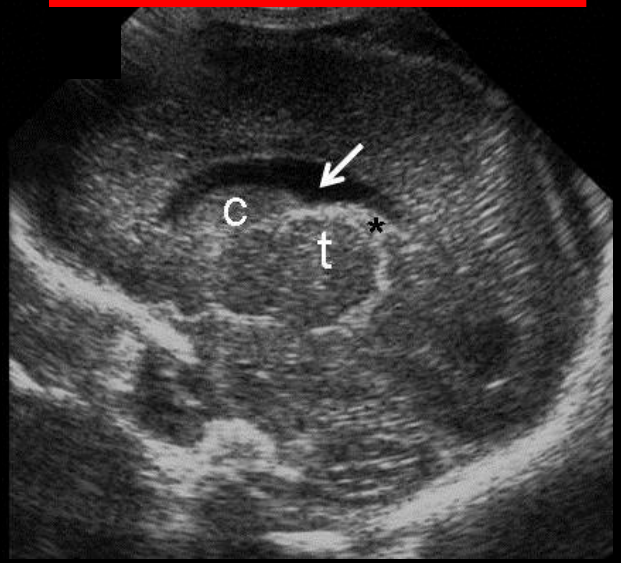
Susceptibility Weighted Imaging

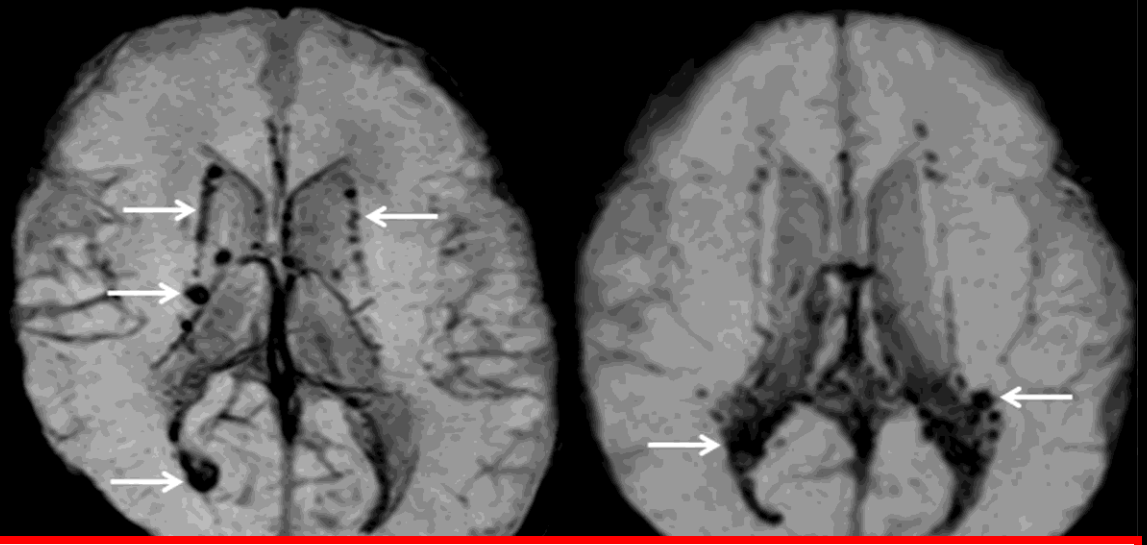
- SWI: it is a new MR technique, highly capable to identify iron, calcification (calcium), air ….
- Even in the premature baby is able to identify the venous system and small venous vessels
- Superior to gradient-echo standard to diagnose minor haemorrhages (Nandigam RN, AJNR 2009)

Ultrasound SWI

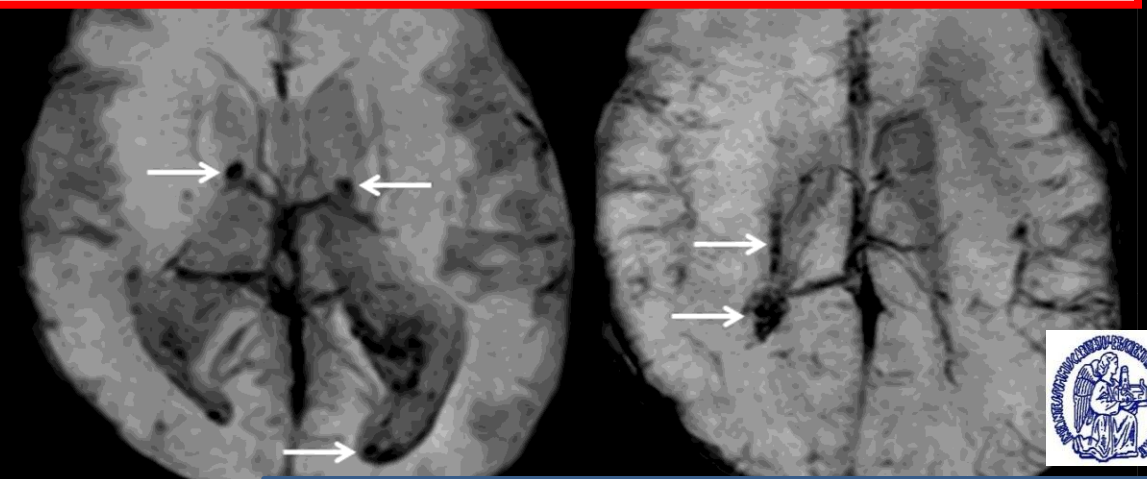


No GMH-IVH





GMH-IVH of low degree at term corrected age

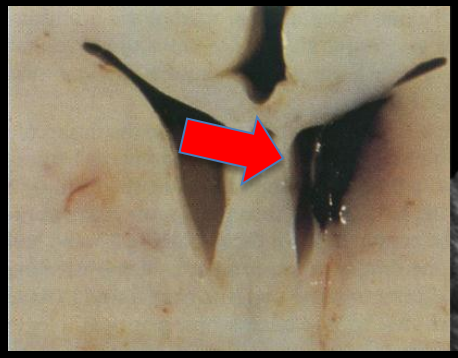


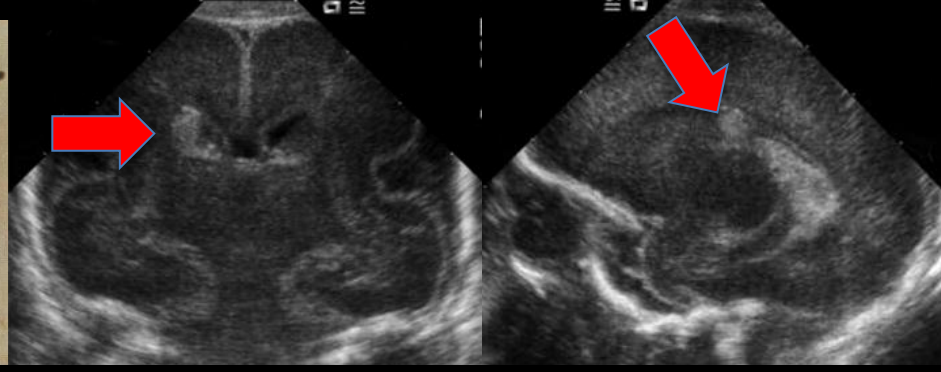
"Gaslini Children's Hosp" - Genoa 2013

Table 1. Number (percentage) of low-grade GMH-IVH detected by cranial ultrasound (CUS) and by magnetic resonance SWI.

	CUS ($n = 60$)	SWI ($n = 60$)
Grade I GMH-IVH	7/60 (11.7%)	–
Grade II GMH-IVH	8/60 (13.3%)	–
Low-grade GMH-IVH (grade I–II)	15/60 (25.0%)	25/60 (41.7%)
No GMH-IVH	38/60 (63.3%)	28/60 (46.7%)

Low Grade **GMH-IVH**: is ultrasound good enough ? Parodi et al 2013





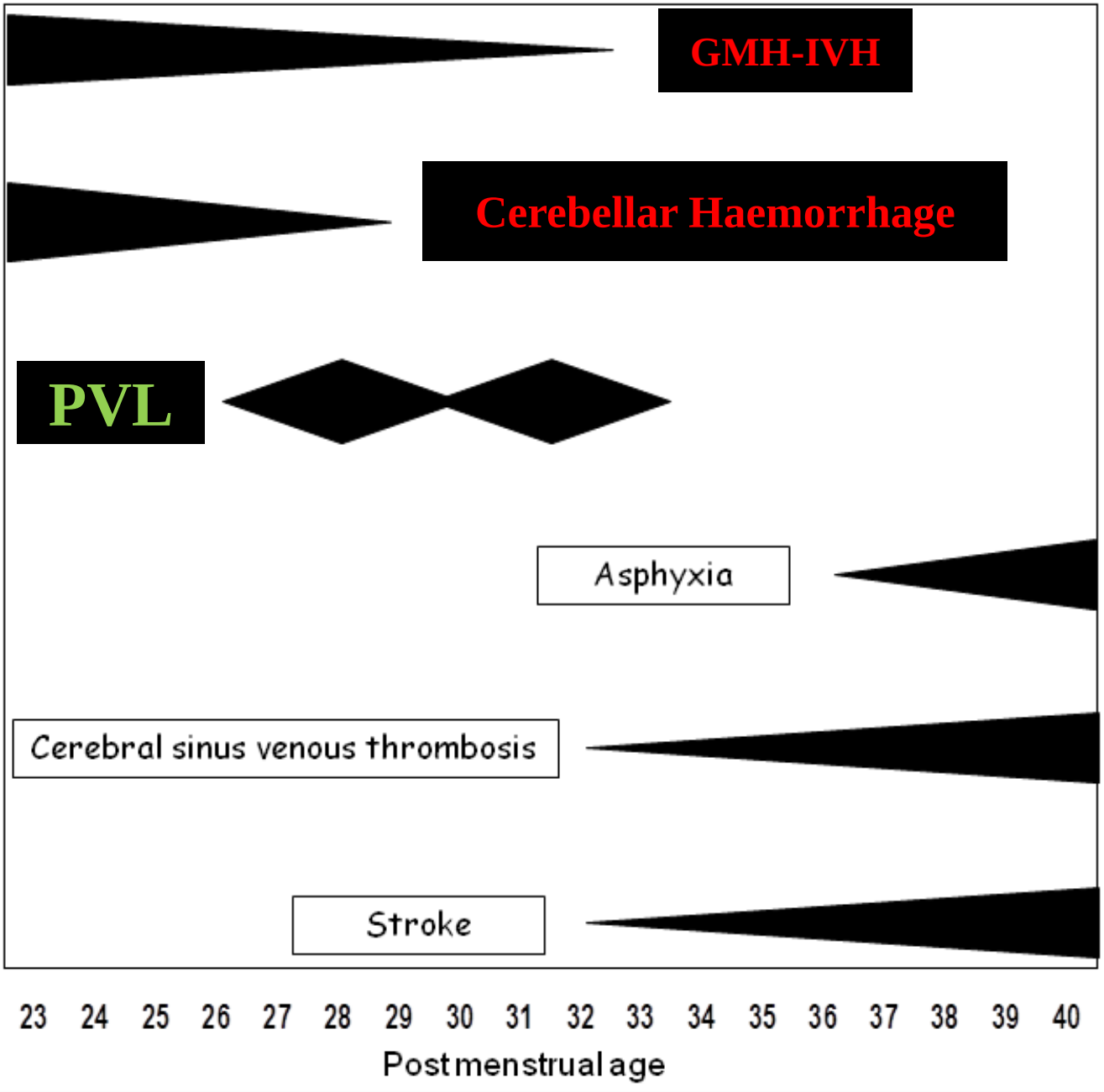
GMH Germinal-Matrix Haemorrhage **IVH Intraventricular Haemorrhage**

- Ultrasound has low sensibility although good specificity in diagnosisng GMH-IVH

- GMH-IVH is underdiagnosed ?

- Studies on low grade GMH-IVH at US and outcome how accurate they are ?

Parodi et al. 2013



Sannia et al. (2012) Different gestational ages and changing vulnerability of the premature brain

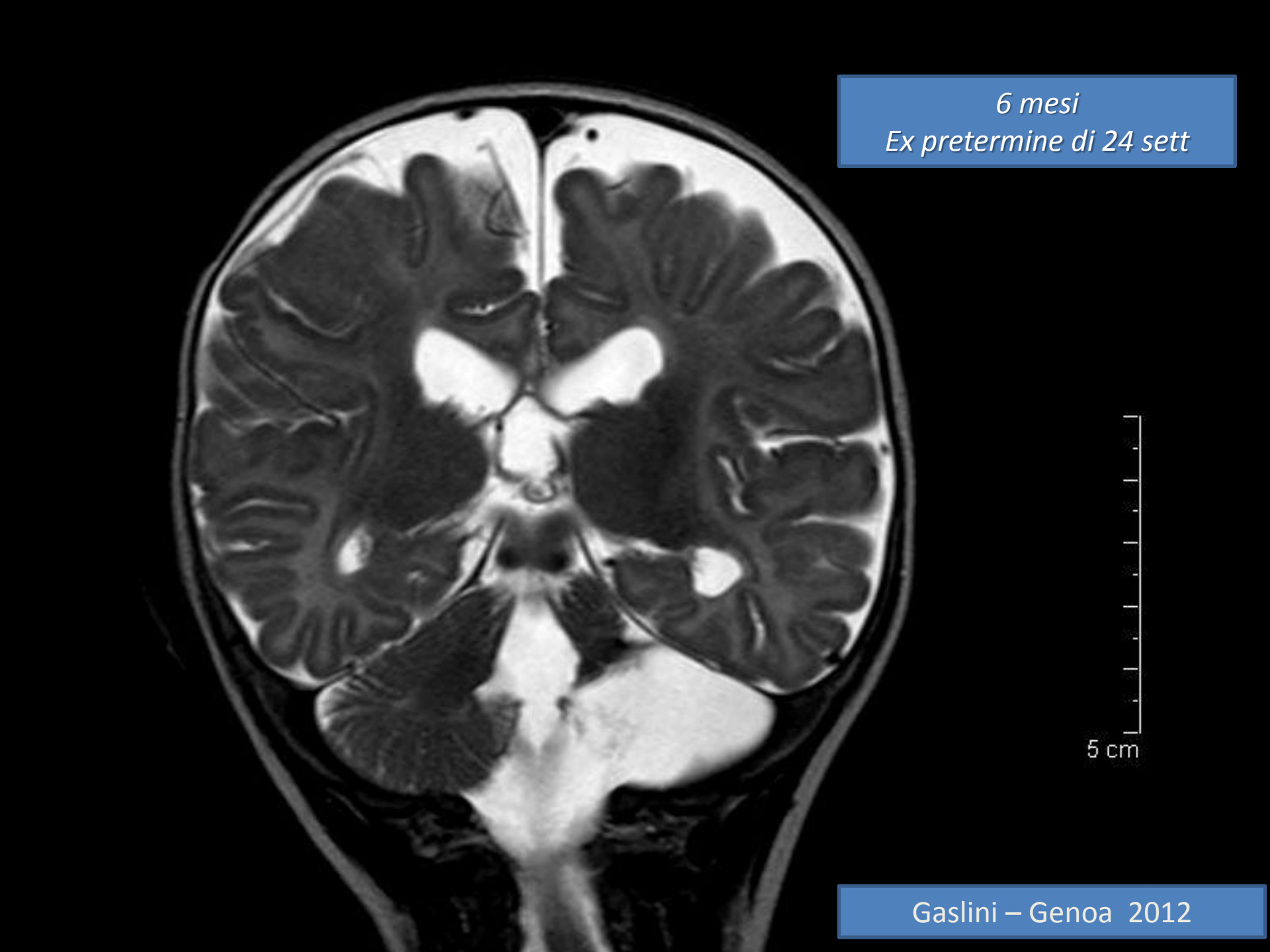
Il cervelletto del pretermine e le emorragie cerebellari

Cosa sapevamo ?

FREQUENCY OF PRIMARY CEREBELLAR HEMORRHAGE IN AUTOPSY SERIES BEFORE 1994

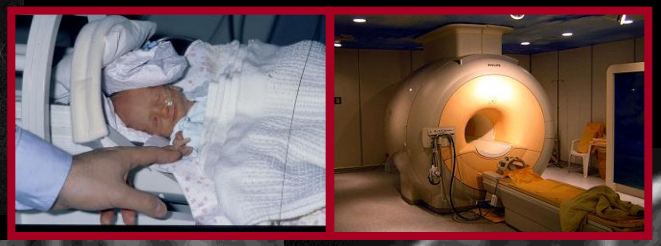
Study	Infant characteristics	Proportion
Grunnet and Shields	20-32 wks gest., no anomaly	12/88 (14%)
Martin et al	All infants admitted to NICU	33/157 (21%)
Pape et al	< 1501 g	20/106 (19%)
Shuman & Oliver	≤ 32 wks gestation	9/47 (19%)
Donat et al	All neonatal deaths	10/71 (14%)
Panet et al	≤ 2000 g	23/82 (28%)
	Average of all series	107/551 (19%)

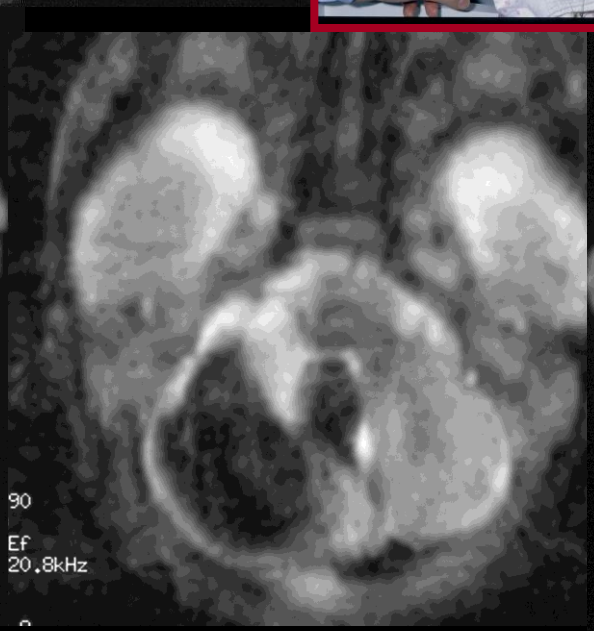
Cosa capitava ?
(o forse capita ?)


6 mesi
Ex pretermine di 24 sett
5 cm
Gaslini – Genoa 2012

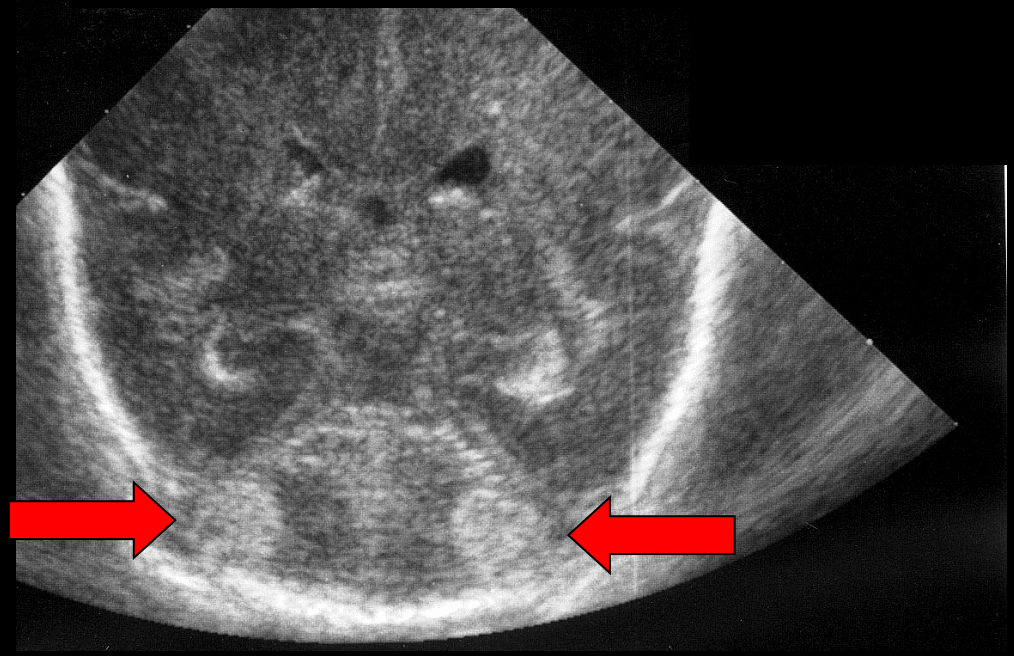
Cosa sappiamo oggi ?

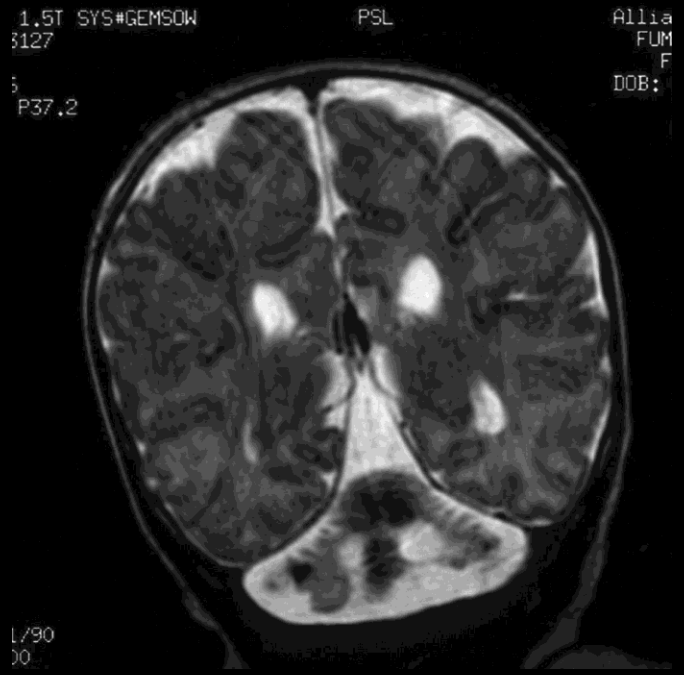
Ecografia coronale posteriore

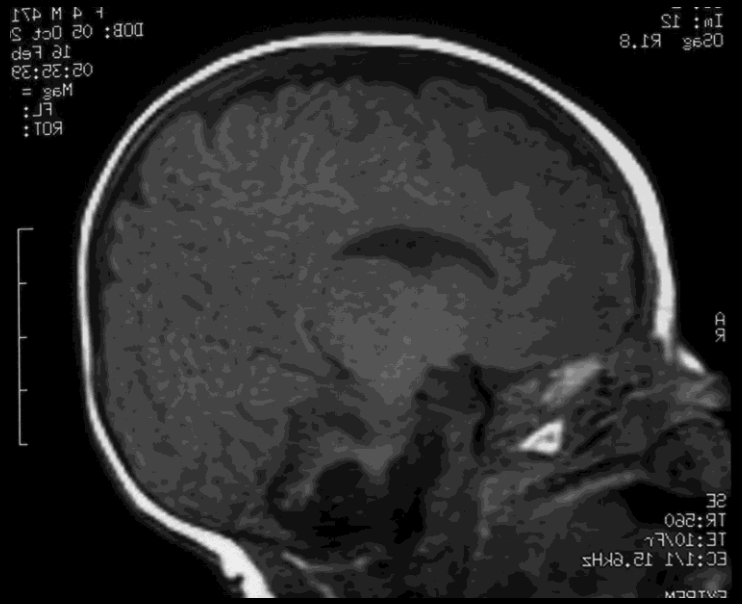


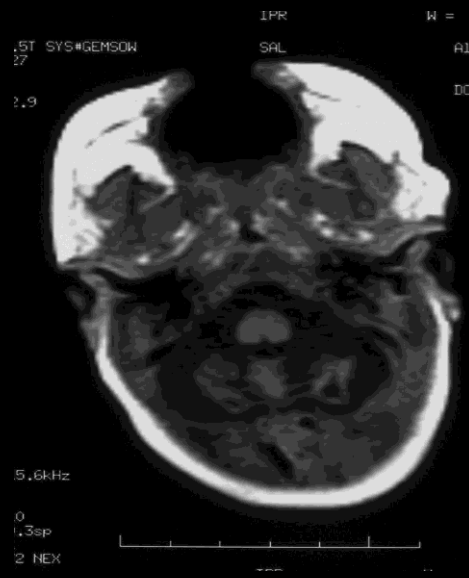


Mangiagalli - Milano 2003

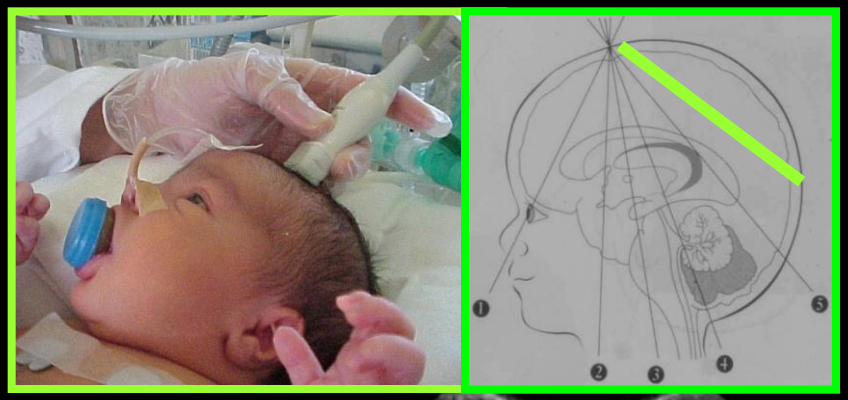






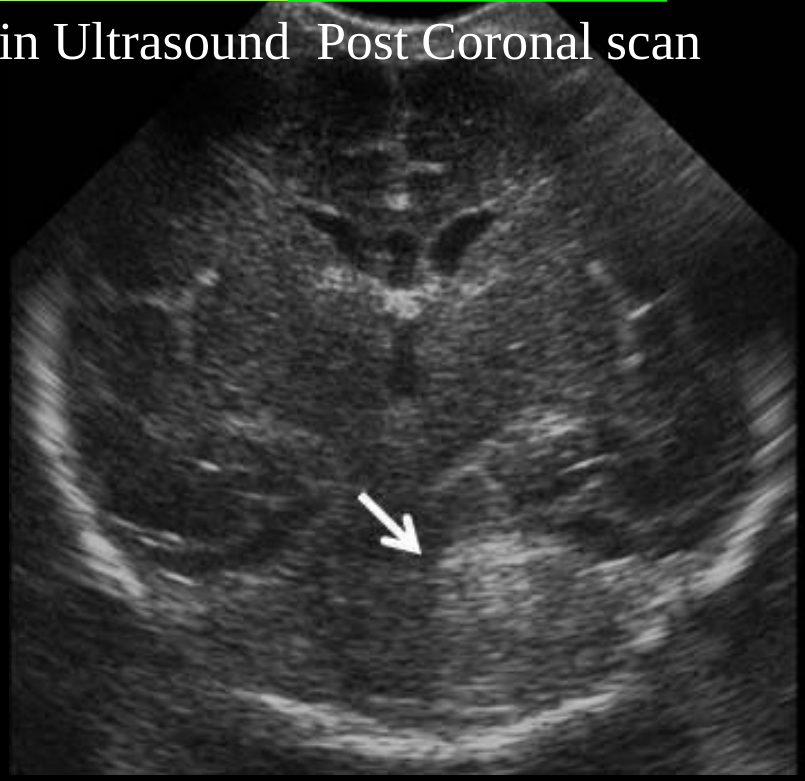


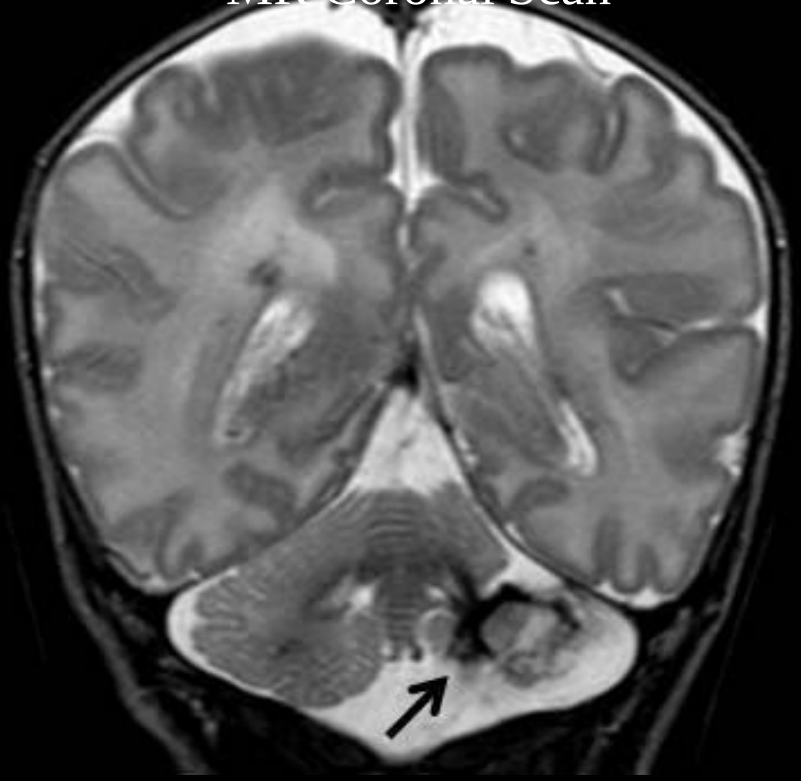
Mangiagalli - Milano 2003



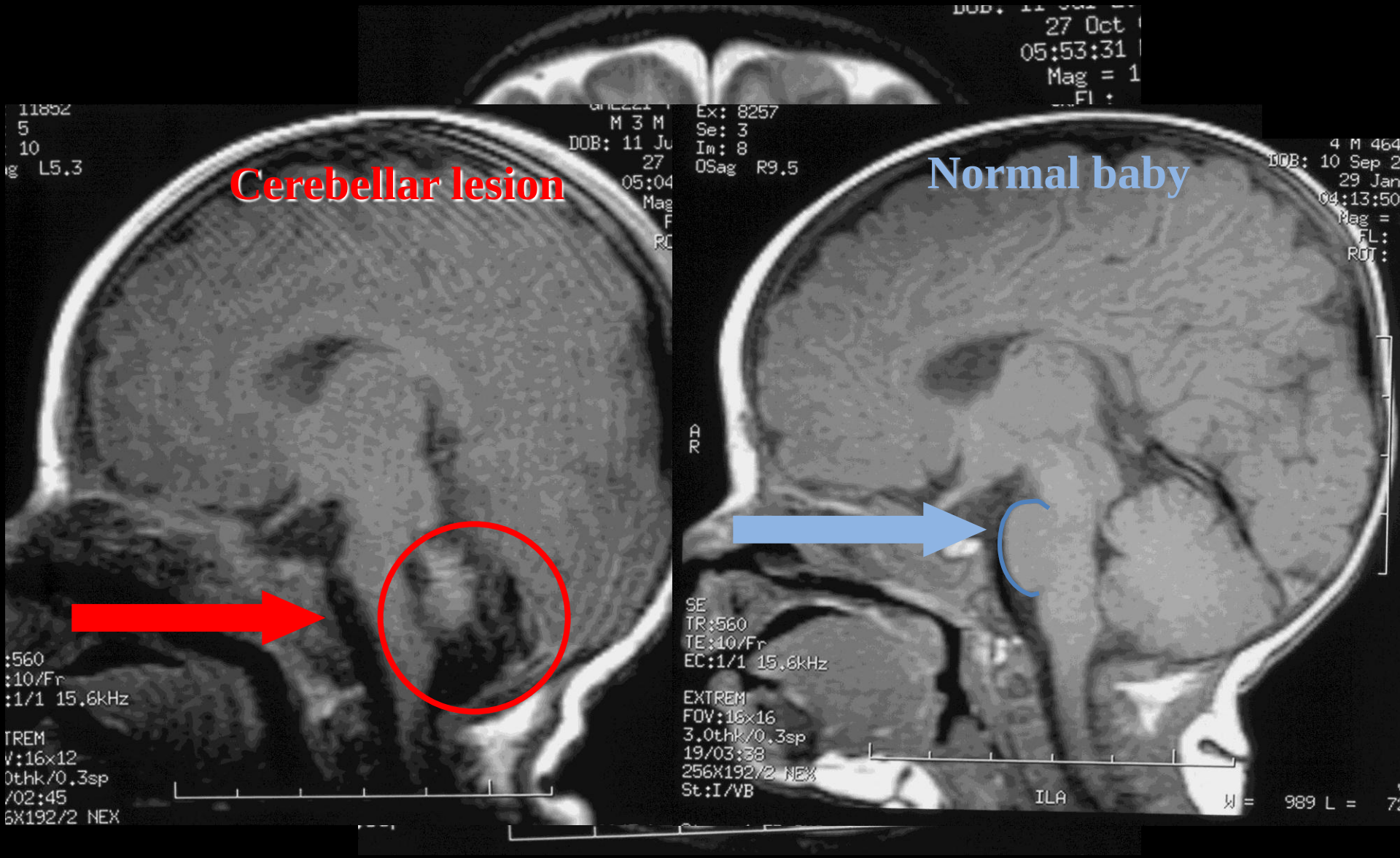
Brain Ultrasound Post Coronal scan

MR Coronal Scan





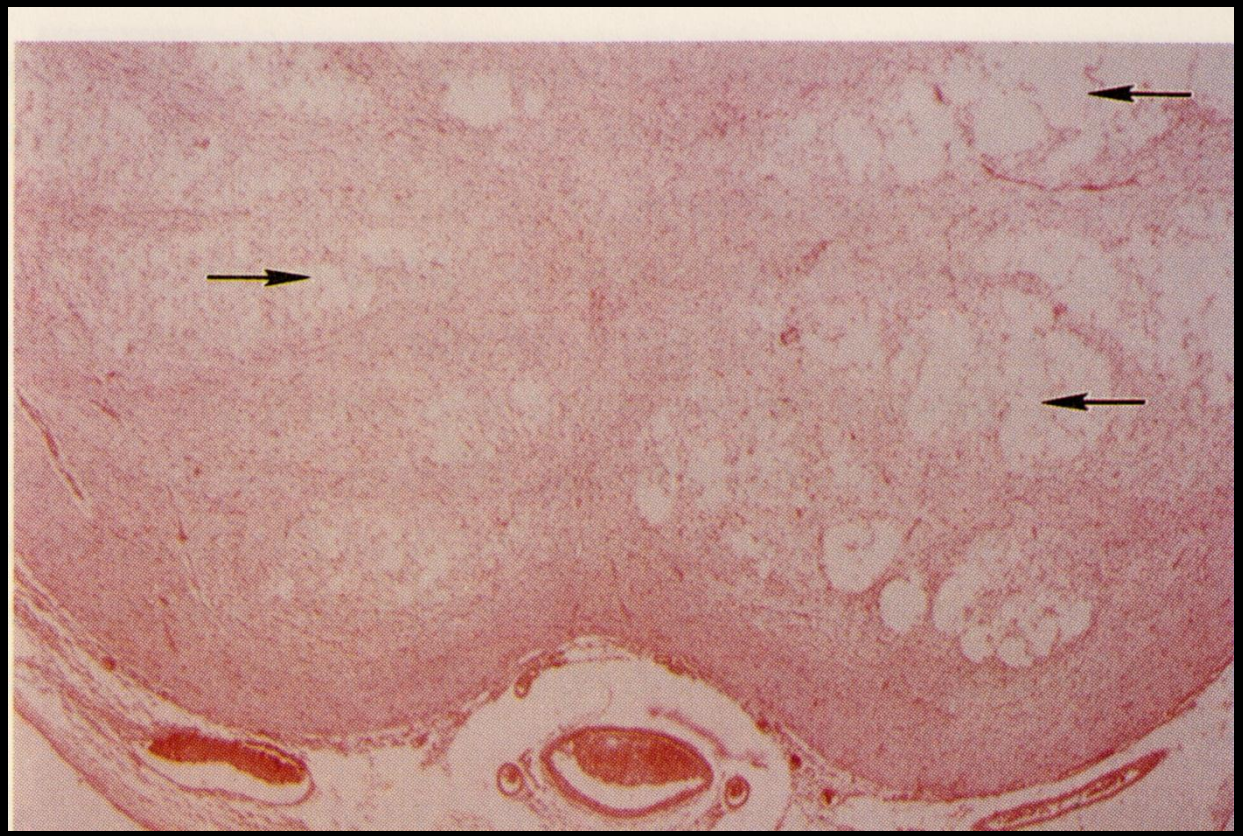
Massive cerebellar haemorrhage



MR at 38 wks of corrected age
of a preterm baby of 23 wks + 5 days (680gr weight)
born after spontaneous delivery with severe acidosis at birth

MR at 39 wks of corrected age
of a normal preterm baby (born at 27 wks)

Pontosubicular neuronal necrosis

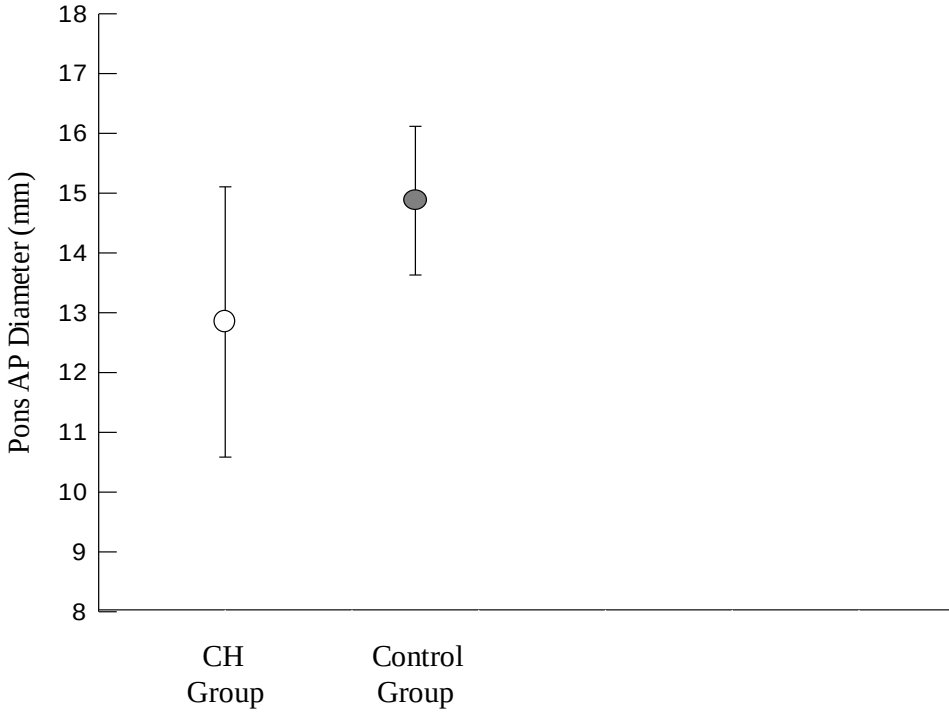


Ponto-subicolar lesions in perinatal anoxia Friede Arch Pathol 1972

59% of prem autopsy !… *Skullerud & Westre Acta Neuropathologica1986*

~ 15% of prem autopsy…..Grunnnet 1979 Torvik 1992

Effects Of Cerebellar haemorrhage On Pons Development in ELBW Infants



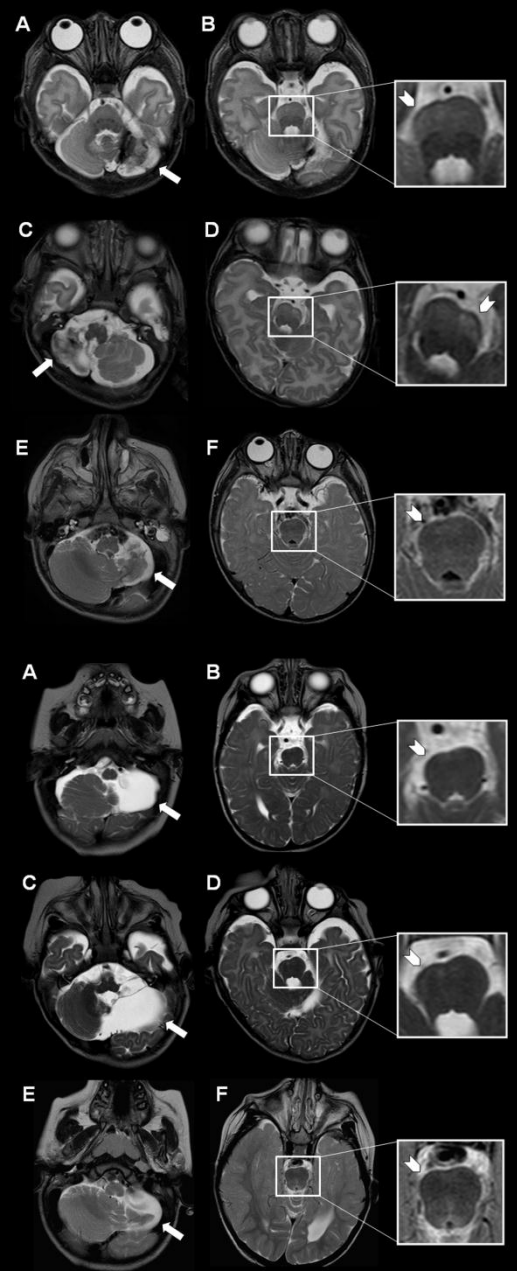
Fumagalli et al FBS 2009

Remote effects of cerebellar haemorrhage: impaired pons development

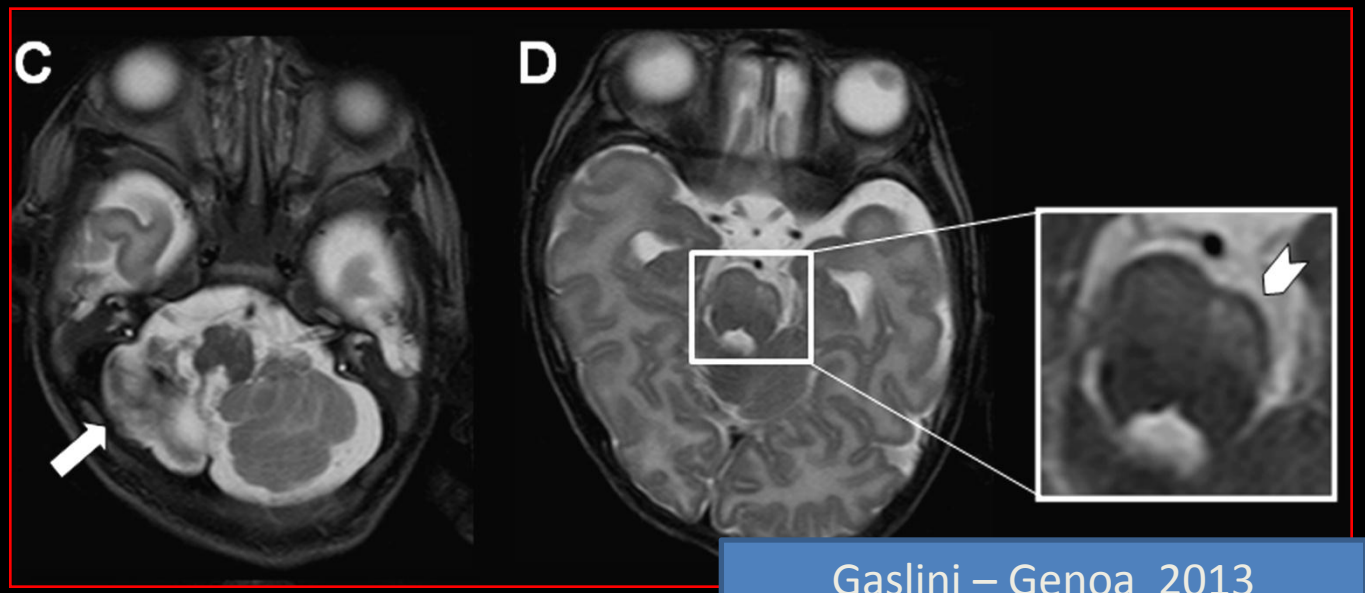
Normal preterm baby at term

Fumagalli M et al , .Front Biosci 2009

Submitted to "Cerebellum " – Genoa 2014

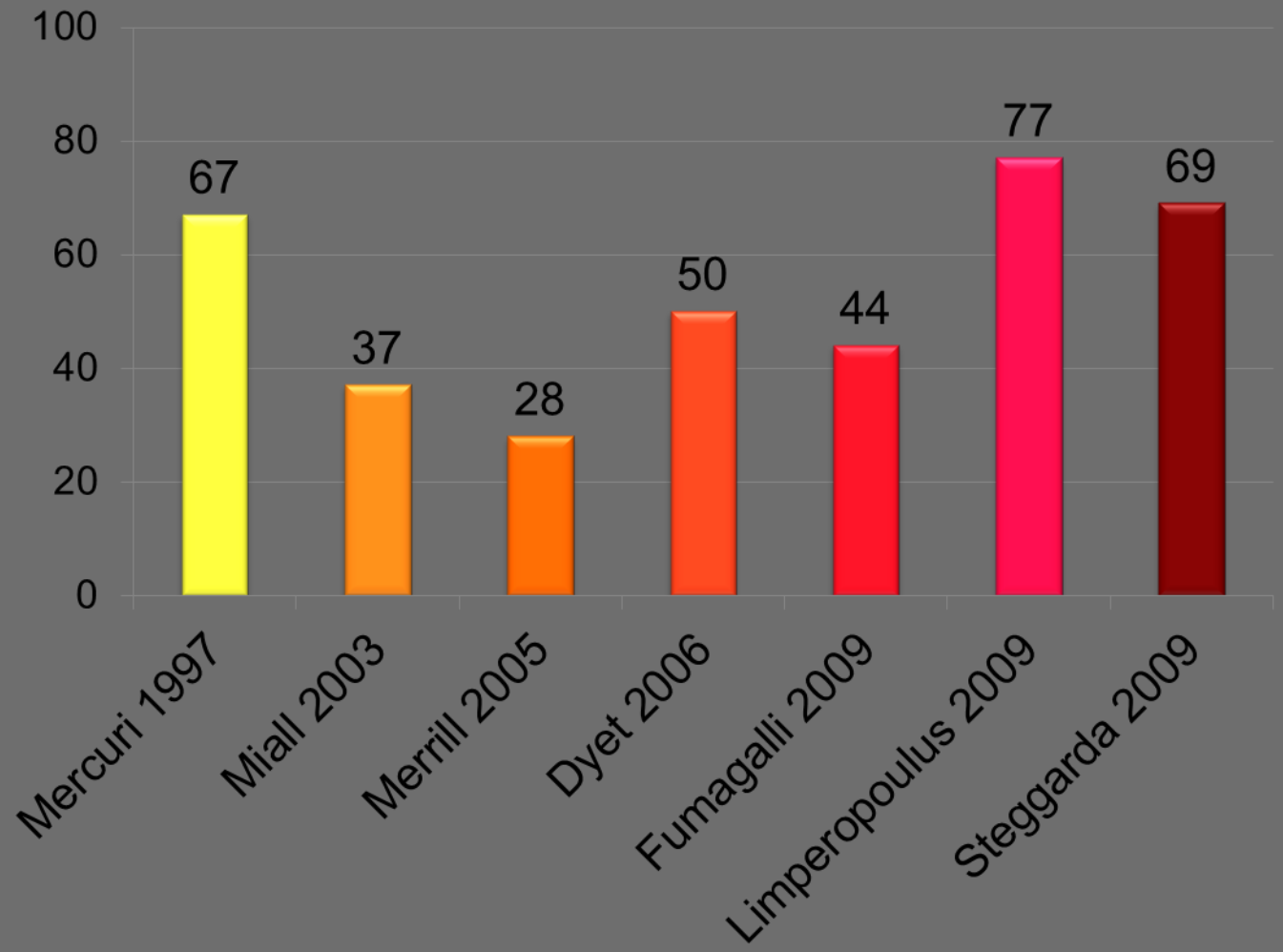


Crossed pontine hemiatrophy associated with unilateral cerebellar hemorrhage in premature infants



Gaslini – Genoa 2013

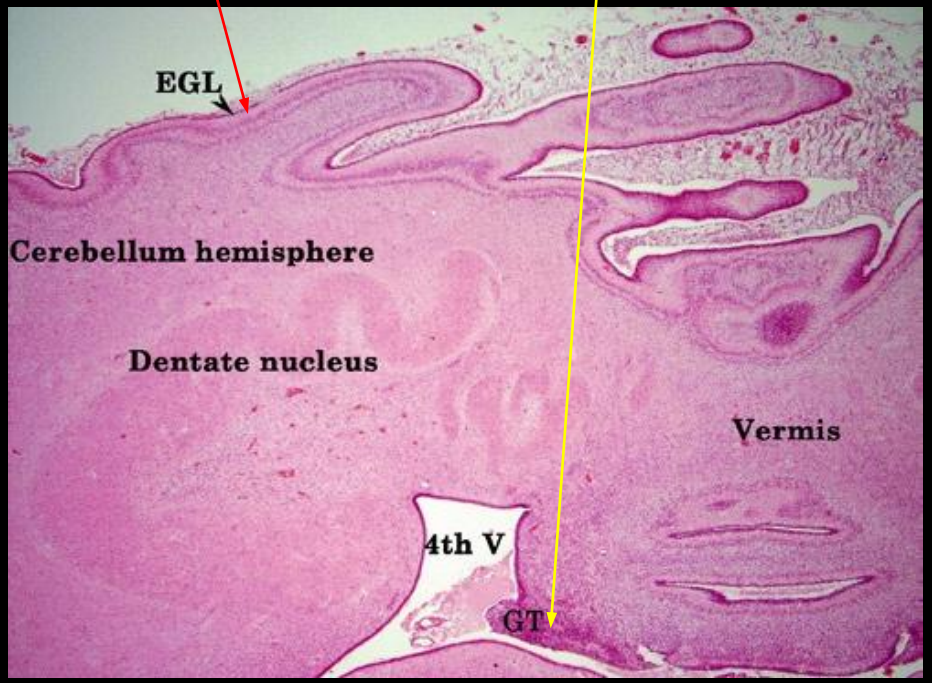
How frequent is the association between cerebellar haemorrhage and GMH-IVH ?



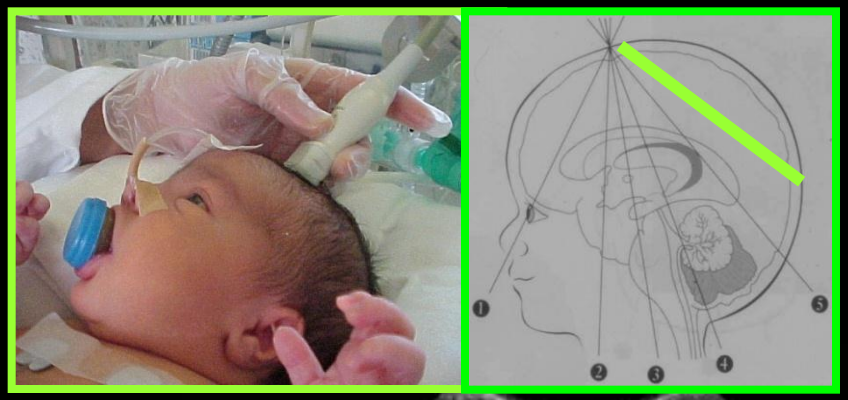
GMH-IVH and cerebellar hemorrhage: a common pathogenesis?

Cerebellar hemorrhage may originate:

- From subependymal germinal matrix (IV ventricle roof)
- From external granular layer of cerebellar cortex

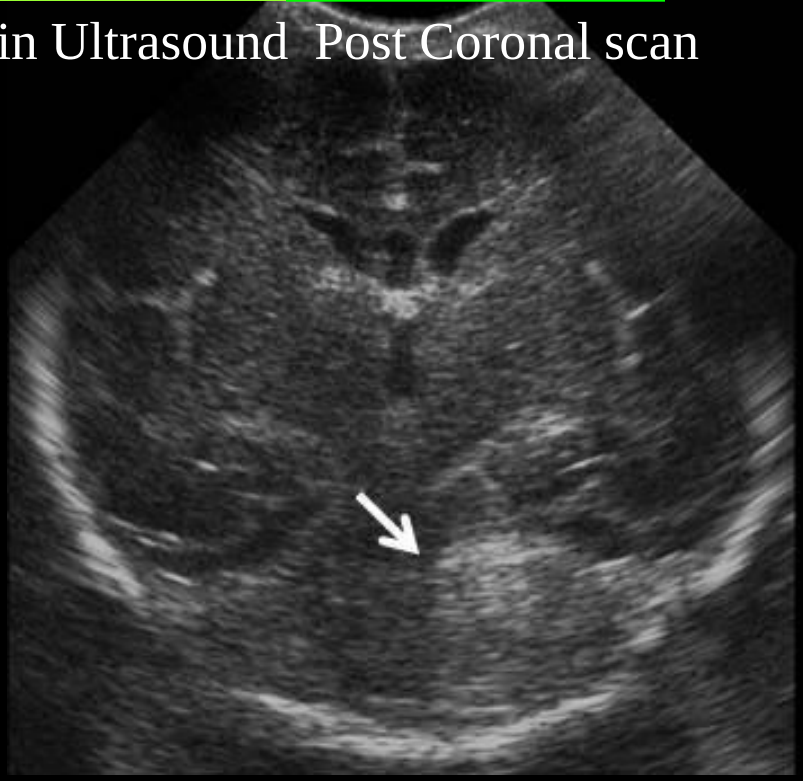


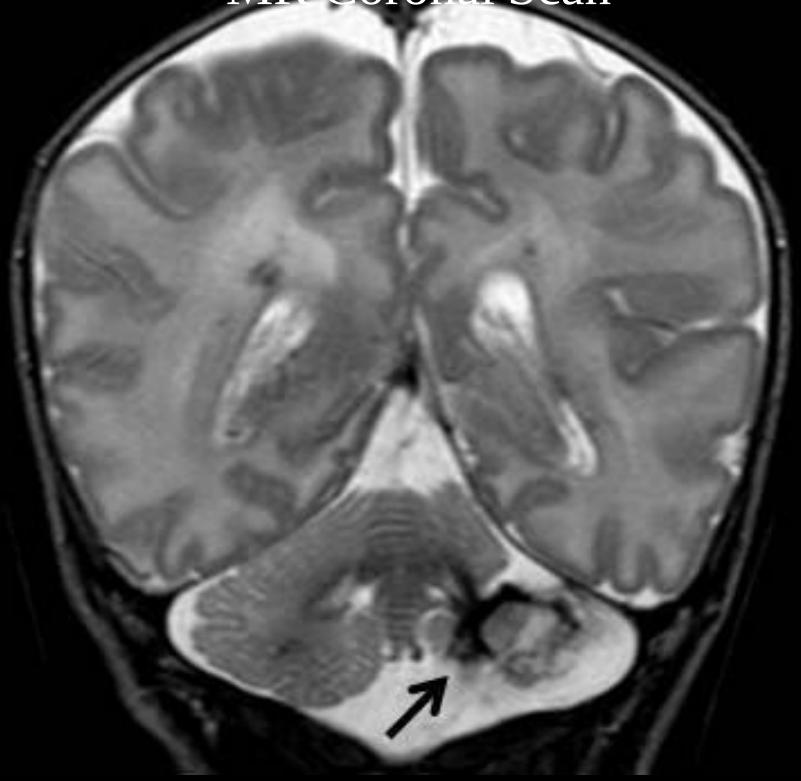
From Germinal Matrix to Cerebellar Haemorrhage: Fumagalli ….Ramenghi JMFNM 2013



Brain Ultrasound Post Coronal scan

MR Coronal Scan





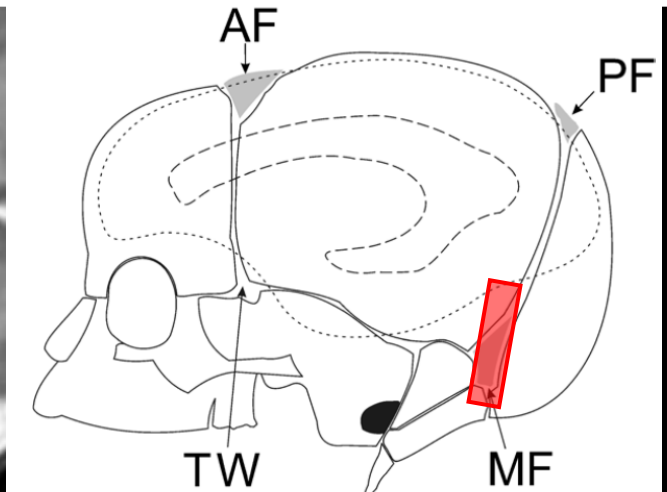
Massive cerebellar haemorrhage

"Gaslini Children's Hosp" - Genoa 2013

Mastoid window: pseudo-coronal scan

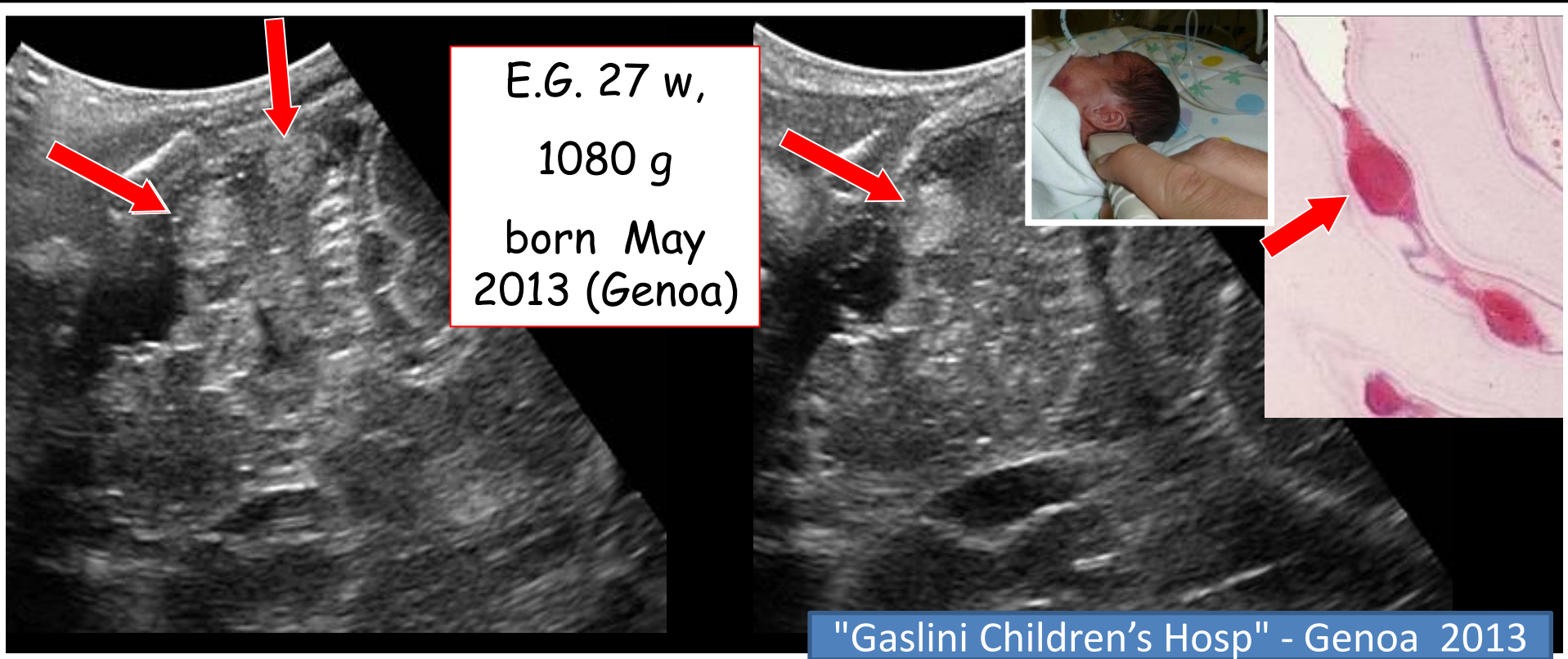
Coronal T2 MRI

Pseudo-coronal US



Cerebellar hemorrhage originating from external granular layer of cerebellar cortex

Limperopoulos C, Pediatrics 2005 & 2007

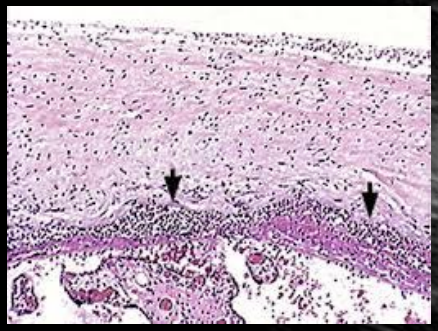


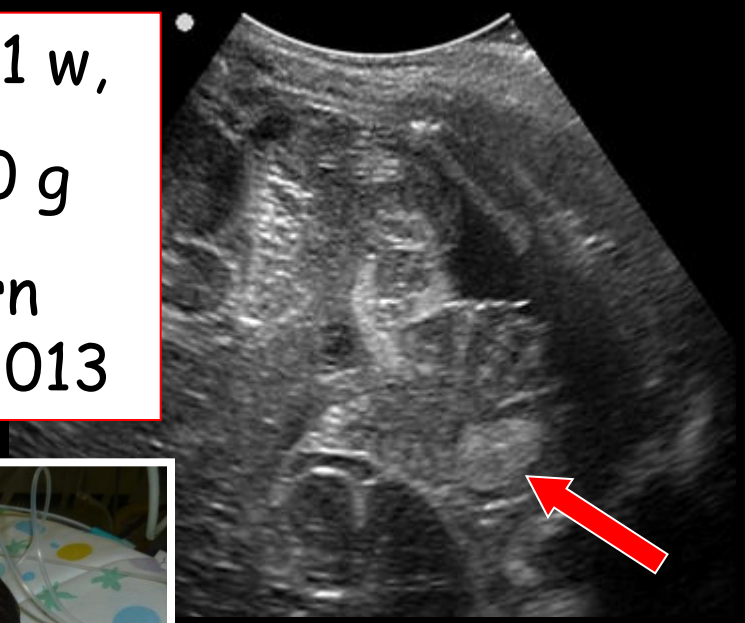
Small : mastoid window vs MR

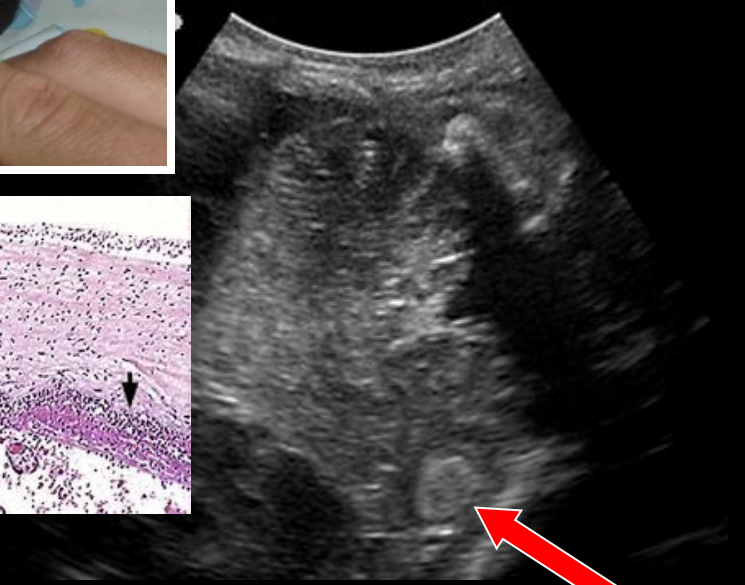
GA. 31 w,

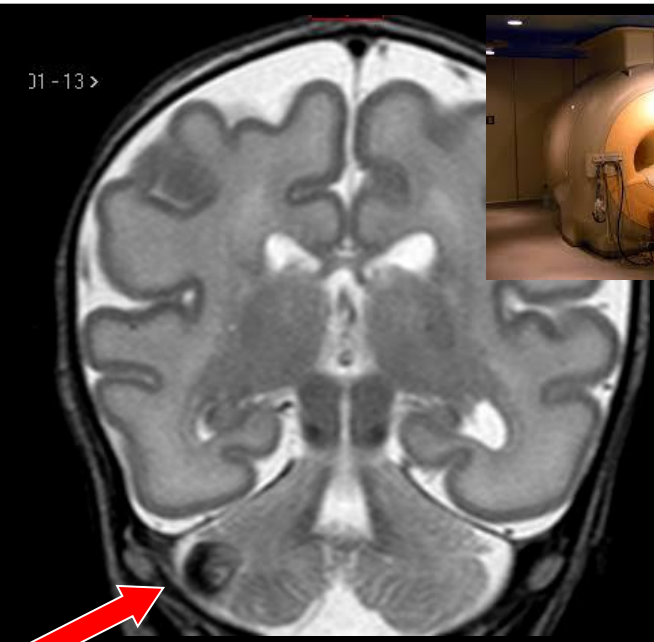
1570 g

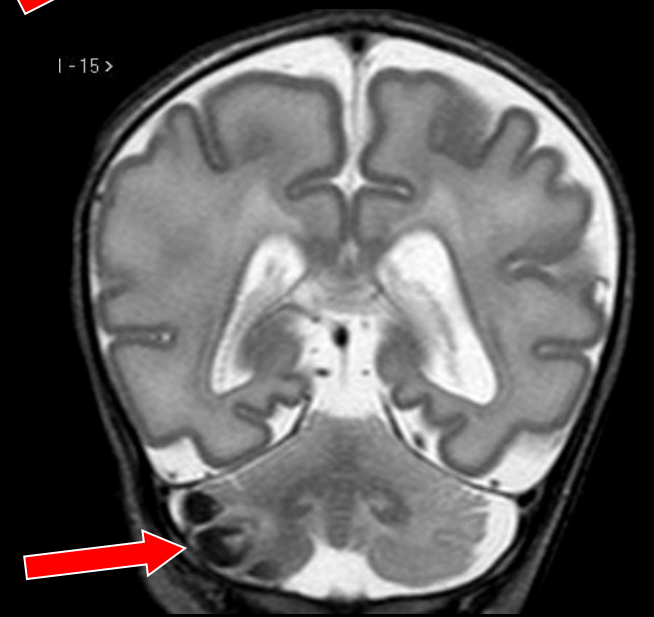
born
Aug 2013







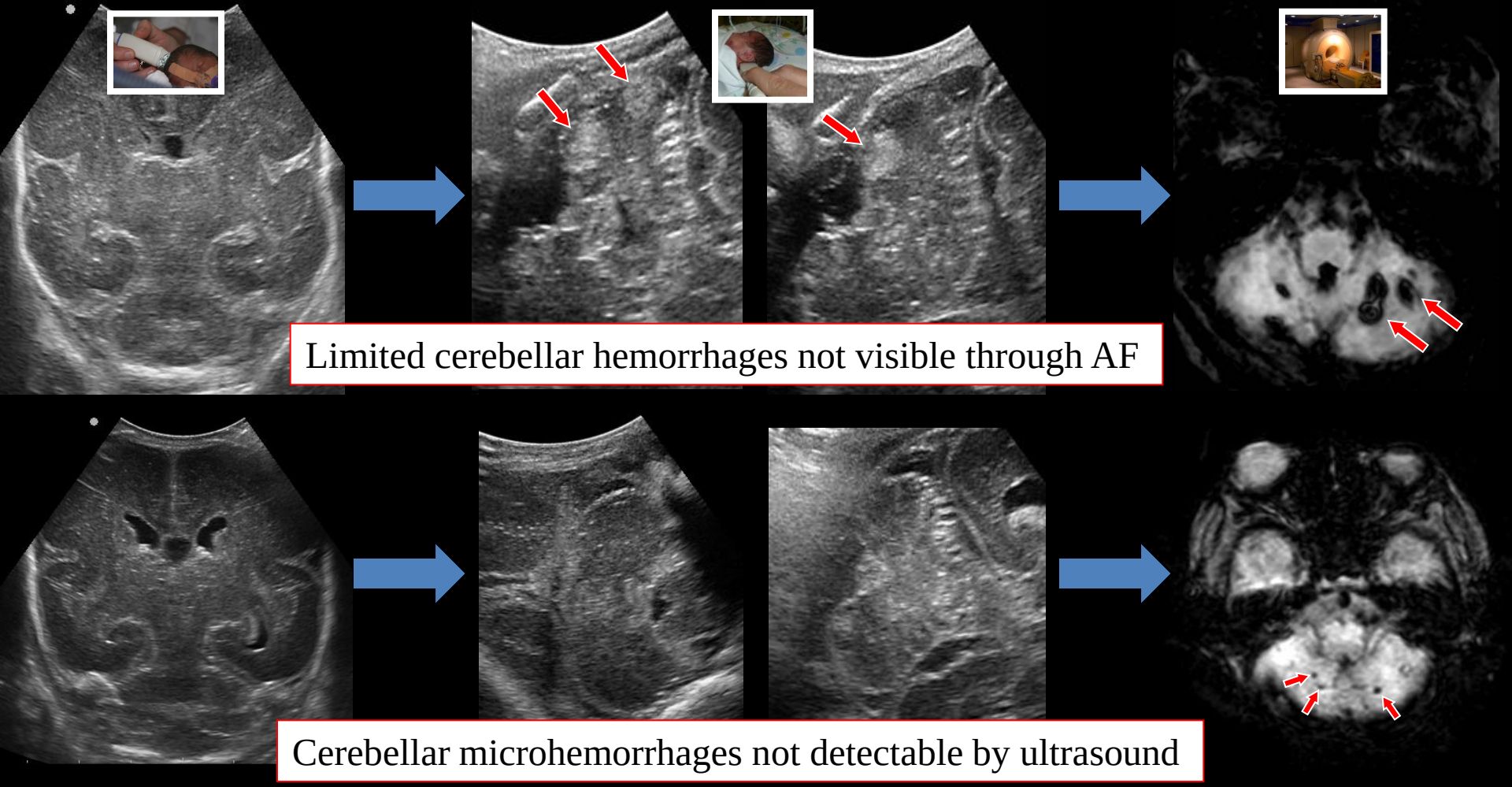




PLF = MF
Postero-lateral = mastoid
AF = anterior fontanelle

Cerebellar haemorrage size	AF	PLF	SWI
Massive cerebellar hemorrhages (>1/3 of cerebellum)	2/128 (1,6%)	2/128 (1,6%)	**2/128 (1,6%)**
Limited cerebellar hemorrhages (size ≥5 mm and <1/3 of cerebellum)	2/128 (1,6%)	5/128 (3,9%)	**5/128 (3,9%)**
Cerebellar microhaemorrhages (microCBH) (size <5 mm)	0/128 (0%)	0/128 (0%)	**20/128 (15,6%)**
All cerebellar haemorrhages	**4/128 (3,1%)**	**6/128 (4,7%)**	**26/128 (20,3%)**

Parodi et al. Arch Dis Child (under revision)

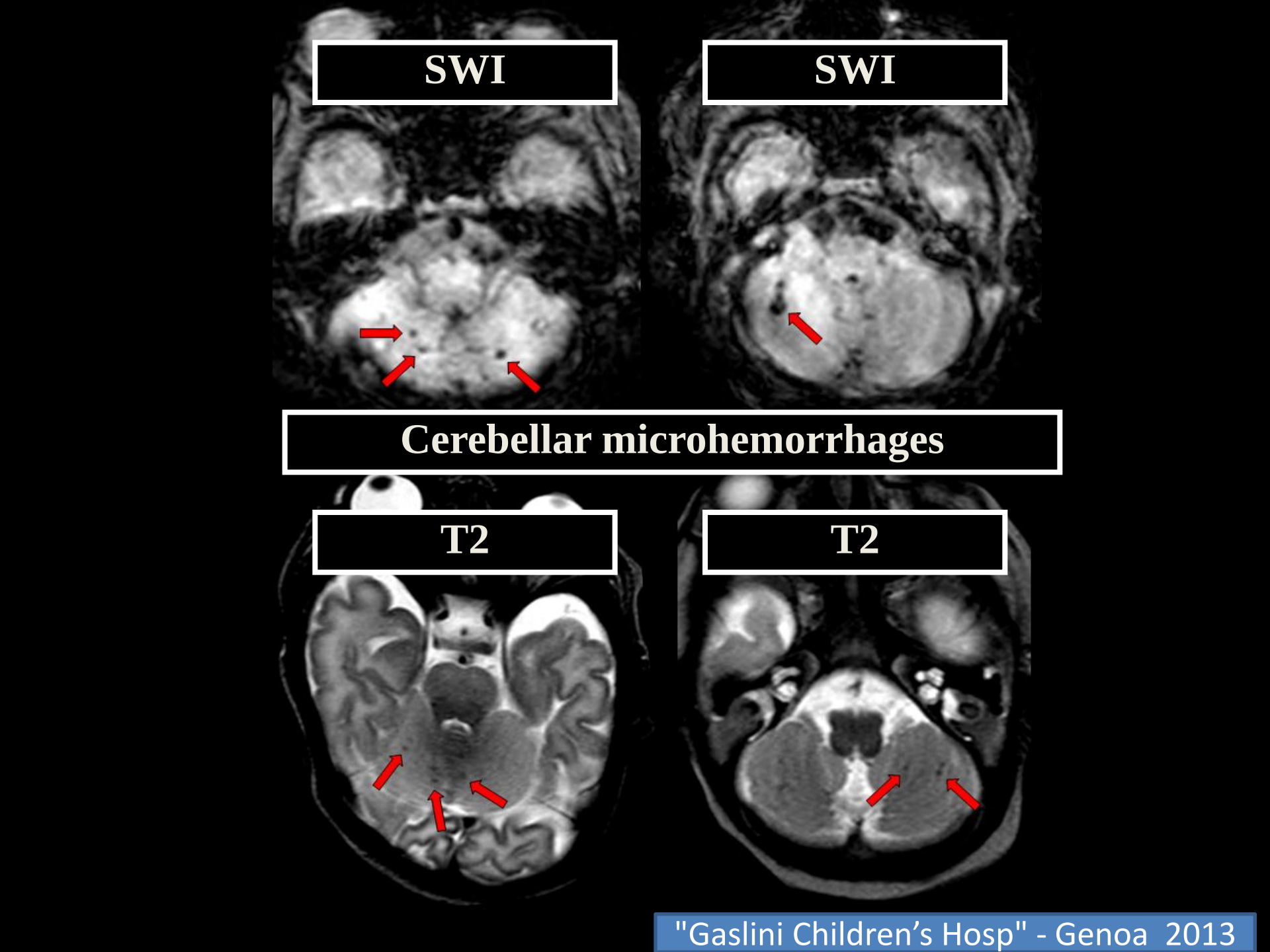


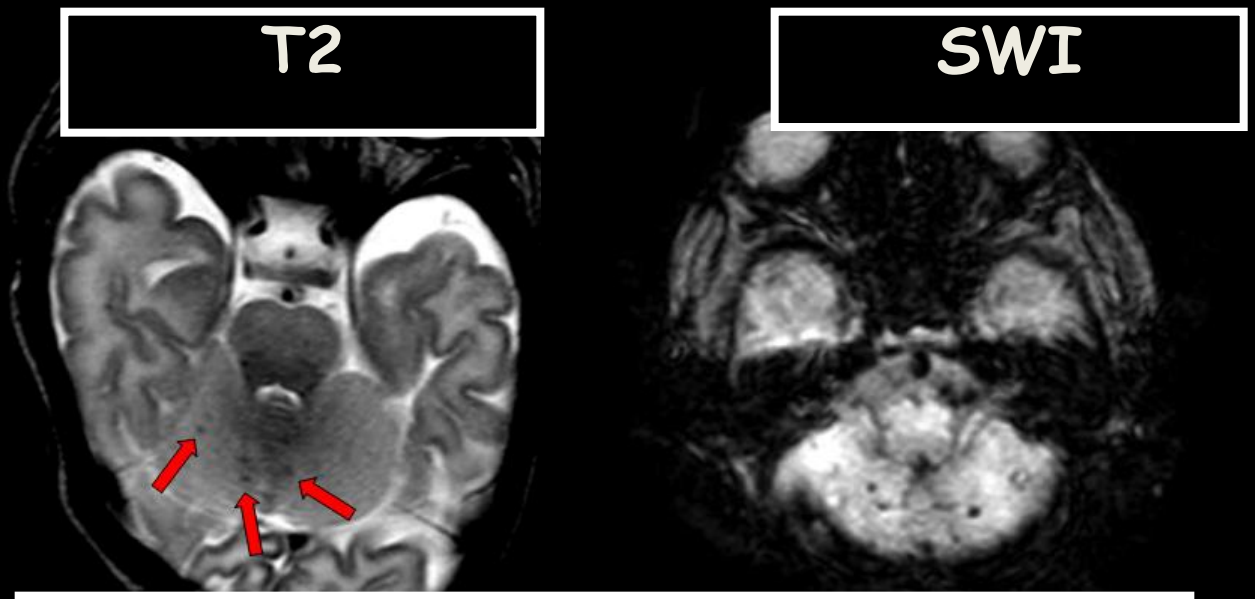
Conclusions

1)Overall ultrasound sensitivity seems surprisingly low when microhemorrhages are included

2) Microhemorrhages proved to be undetectable by ultrasound

3) The routine use of MF allows a better detection of limited hemorrhages when compared to AF


SWI
SWI
Cerebellar microhemorrhages
T2
T2
"Gaslini Children's Hosp" - Genoa 2013

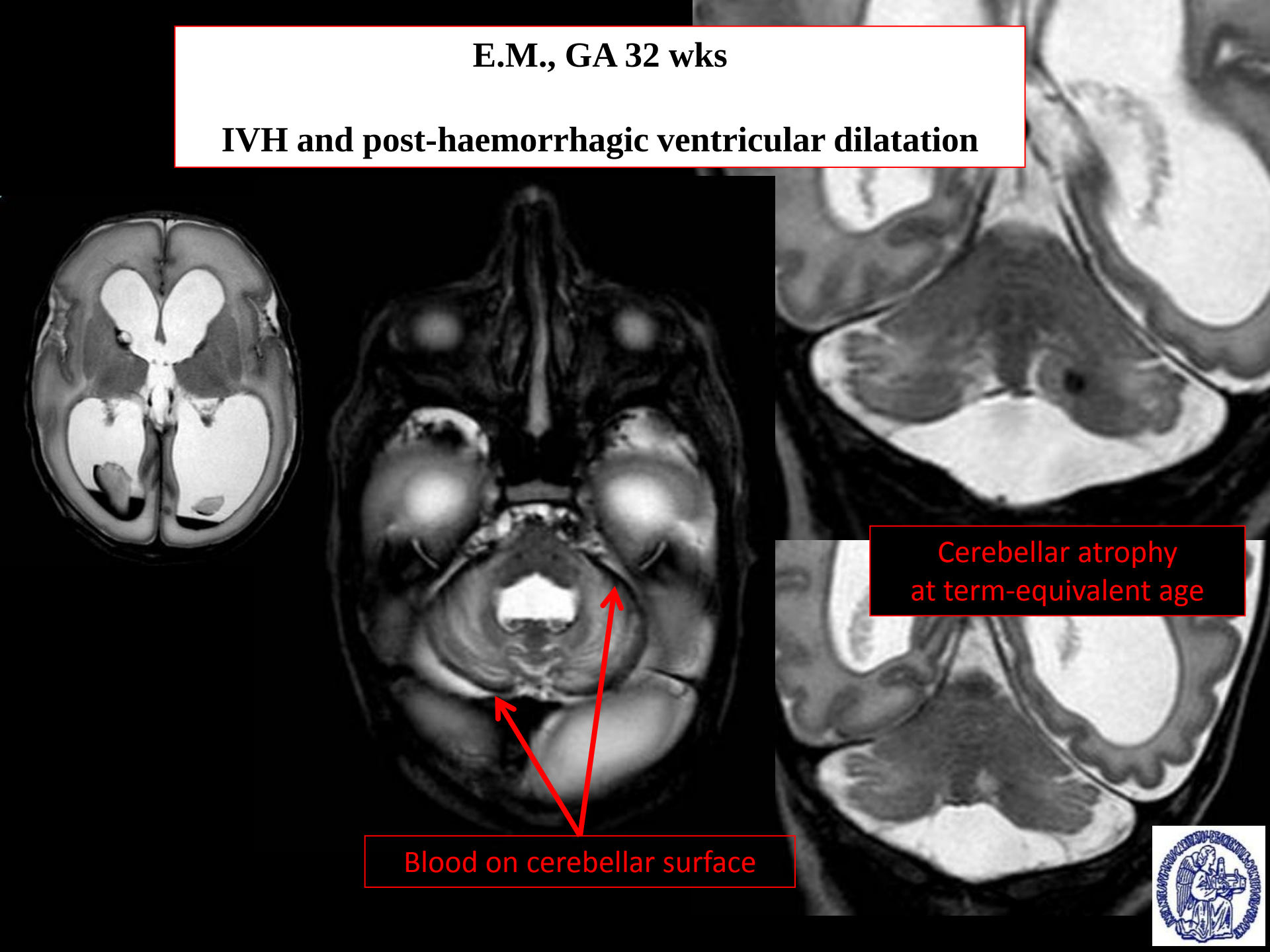


Cerebellar microhemorrhages

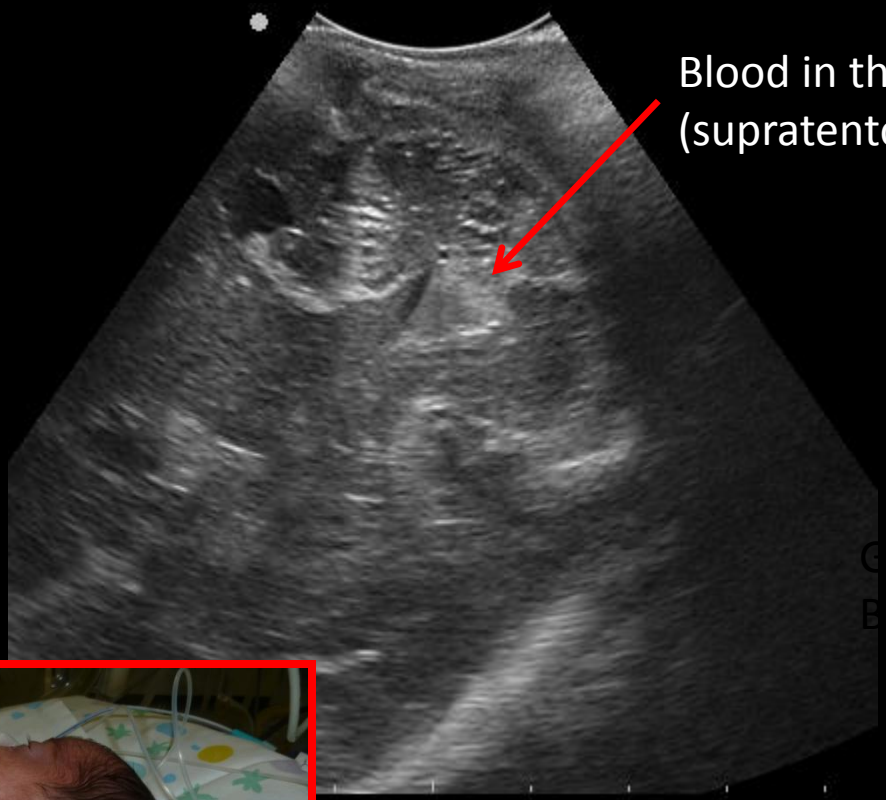
Micro-Cerebellar Haemorrhages: Can we ignore them !

E.M., GA 32 wks

IVH and post-haemorrhagic ventricular dilatation

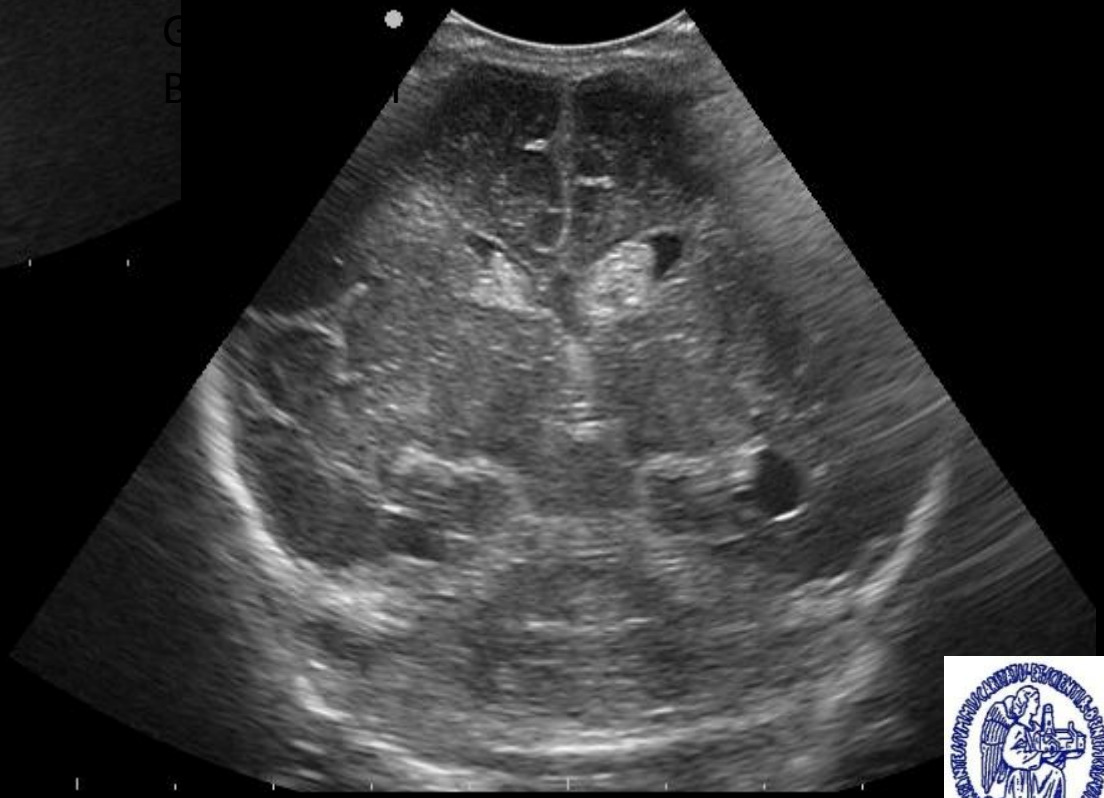


Blood in the fourth ventricle
(supratentorial origin)



Blood in the fourth ventricle
(supratentorial origin)

Should we be worried ?



Proposta

Proposta …… per diventare Giganti

Proposta, conosciuto anche con il titolo alternativo di *Mettete dei fiori nei vostri cannoni*, fu scritta dai Giganti ……-La canzone fu presentata dai Giganti, al Festival di Sanremo 1967 e si classificò al terzo posto

L'embrione dei **Giganti** prende vita nel 1959 al Santa Tecla di Milano, dove la formazione spesso si esibì accompagnando Ghigo Agosti sostituendo la precedente formazione degli "Arrabbiati" con Gaber

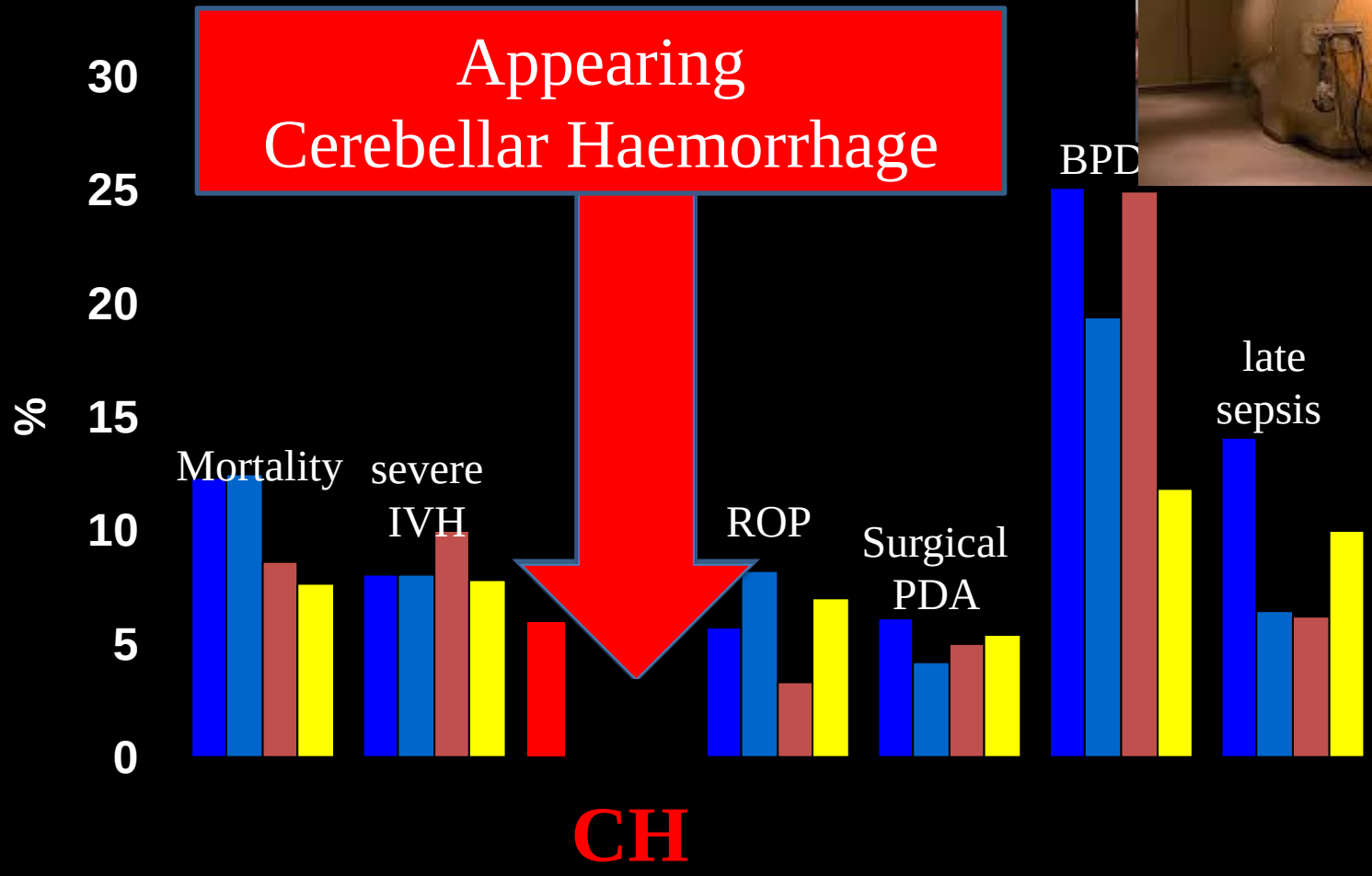
Proposta …… per diventare Giganti

- ("core dello studio")
  Diagnosi di emorragia cerebellare con US (utilizzando le diverse finestre acustiche)

- Diagnosi confermata con RM alla TCA

- Epidemiologia lesioni VLBW e Follow-up

Major outcomes in VLBW



CH

VON = **V**ermont **O**xford **N**etwork (> 6000 neonati)

IGG 2011 = 102 VLBW

IGG 2012 = 112 VLBW

IGG 2013 = 98 VLBW

IGG 2014 = 103 VLBW (ad oggi)

IGG
Istituto Giannina Gaslini

Proposta …… per diventare Giganti

- NICU Gaslini, NICU Lecco, NICU Mangiagalli, NICU Buzzi , NICU Modena e ??
- Inizio 1° Gennaio

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