

Il programma di Follow-up e l'Outcome del neonato con asfissia perinatale



Bambino Gesù
OSPEDALE PEDIATRICO

Hypoxic-Ischaemic Encephalopathy (HIE)

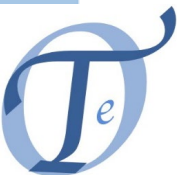
- 1-6/1000 live full-term births
- 10-60% mortality in the moderate-severe encephalopathy
- 25% permanent neurological sequelae:
 - Cerebral palsy
 - Cognitive deficits
 - Epilepsy
 - Central visual deficits
 - Hearing neuropathy
 - Neuropsychological pathology



Cooling for newborns with hypoxic ischaemic encephalopathy
(Review)

Jacobs SE, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG **2007**

Department of Medical and Surgical Neonatology



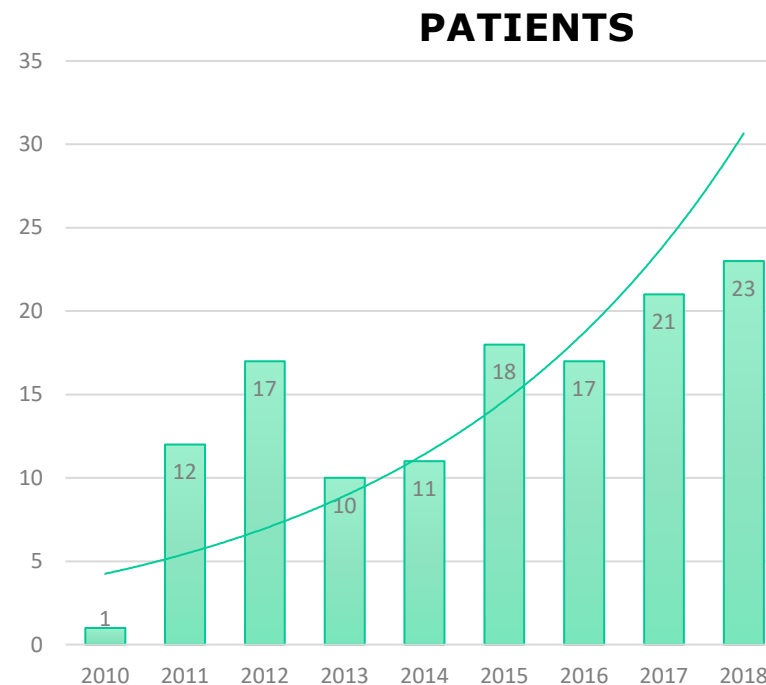
immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

HIE newborns treated with hypothermia: DNMC-OPBG 2010-2018

YEARS	PATIENTS
2010	1
2011	12
2012	17
2013	10
2014	11
2015	18
2016	17
2017	21
2018	23



TOT 130

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

HIE newborns treated with hypothermia: DNMC-OPBG 2010-2018

- Mortality Rate: 4.6% (6/130)
- 4 early exit (pulmonary hypertension or intractable discoagulopathy)
- Follow-Up (FU) program since 2013

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

Who needs FU?

- Preterm infants
- Small for gestational age (SGA)
- Congenital brain or heart malformations, genetic syndromes or inborn errors of metabolism
- Infants requiring major surgery
- Neonatal infections
- **Hypoxic-Ischaemic Encephalopathy (HIE)**

Long term follow up of high risk children: who, why and how?

Doyle et al. *BMC Pediatrics* 2014, 14:279

Department of Medical and Surgical Neonatology

Why do they need follow-up?

Goals of FU program:

- To detect early neurodevelopmental delay in order to promote/apply appropriate interventions
- To provide ongoing support to vulnerable children and their families after discharge
- To **warrant and improve long-term outcome of high-risk infants**

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

Which outcome to follow?

Auxological

Neuromotor

Nephrological

Neurodevelopmental

Cardiological

Neurophysiological

Respiratory

Neuroimaging

Behavioral development

Quality of life



Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net

Long-term outcome after neonatal hypoxic-ischaemic encephalopathy

Linda S de Vries,¹ Marian J Jongmans²

Arch Dis Child Fetal Neonatal Ed 2010;**95**:

Long-term follow-up shows that cognitive and memory difficulties may follow even in children without motor deficits. It is therefore recommended to perform follow-up assessment into childhood in children with and without adverse neurological outcome in early infancy.

Original article

Long-term motor and behavioral outcome after perinatal hypoxic-ischemic encephalopathy

Petra E.M. van Schie ^{a,b,*}, Josephine Schijns ^{e,f}, Jules G. Becher ^a,
Frederik Barkhof ^c, Mirjam M. van Weissenbruch ^d, R. Jeroen Vermeulen ^{e,g}

Conclusions: Half of the children without CP had impaired motor ability at school age. A normal outcome after HIE at young age does not necessarily imply a good outcome at school age, even when neonatal MRI does not show any abnormalities. More research is needed on the behavioral and cognitive consequences of HIE at school age and on the consequences for quality of life for children with and without CP.

FU PROGRAM

Department of Medical and Surgical Neonatology



Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

77
newborns

FU DNMC OPBG 2013 - 2017

➤ Mortality Rate: 3,9% (3/77)

➤ 16,2 % (12/74) patients lost during FU

62
infants

* 1° year of age -→ Neonatal FU

* From the 2° year of age:

- **Adverse outcome** -→ Neurology Departement + Neonatology FU
- **Normal outcome** -→ Neonatology FU + Clinical Psychology Unit

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

TIMEPOINT

OUTCOME	3 months	6 months	9 months	12 months
Auxological	+	+	+	+
Laboratory test on blood and urine	+		+	
Neuromotor + FKT		+		+
Neurodevelopmental*		+		+
Cerebral US	+			
EEG	(+)			
MRI		(+)		+
Renal US	+		+	
Nephrological	+		+	
Oculistic				+
Cardiac			+	

*Bayley scales III

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

Auxological Outcome in HIE infants treated with hypothermia at 1 year

- Weight and Length in normal range
- Head Circumference $<2SD$ in 7/62 (11,3%)



Neurological and Neurodevelopmental Outcome

Neurological outcome	N (%)
Normal	48/62 (77,4%)
Mild delay	7/62 (11,3%)
Cerebral Palsy (PC)	6/62 (9,6%)
Hearing impairment	2/62 (3,2%)
Visual impairment	2/62 (3,2%)
Congenital myopathy	1/62 (1,6%)

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

Bayley-Scales of Infant and Toddler Development III



Bayley

Scales of Infant and
Toddler Development™

THIRD EDITION



Neurodevelopmental Outcomes in Neonates with Mild Hypoxic Ischemic Encephalopathy Treated with Therapeutic Hypothermia

Am J perinatol 2018

Rakesh Rao, MD¹ Shamik Trivedi, MD² Amy Distler, RN¹ Steve Liao, MD¹ Zachary Vesoulis, MD¹

Conclusion Developmental outcomes of neonates with mild HIE/TH were similar to healthv. term-born neonates.

Journal of Perinatology (2014) 34, 629–633

© 2014 Nature America, Inc. All rights reserved 0743-8346/14

www.nature.com/jp

ORIGINAL ARTICLE

Neurodevelopmental outcomes after hypothermia therapy in the era of Bayley-III

LF Chalak¹, TL DuPont¹, PJ Sánchez¹, A Lucke¹, RJ Heyne¹, MC Morriss² and NK Rollins²

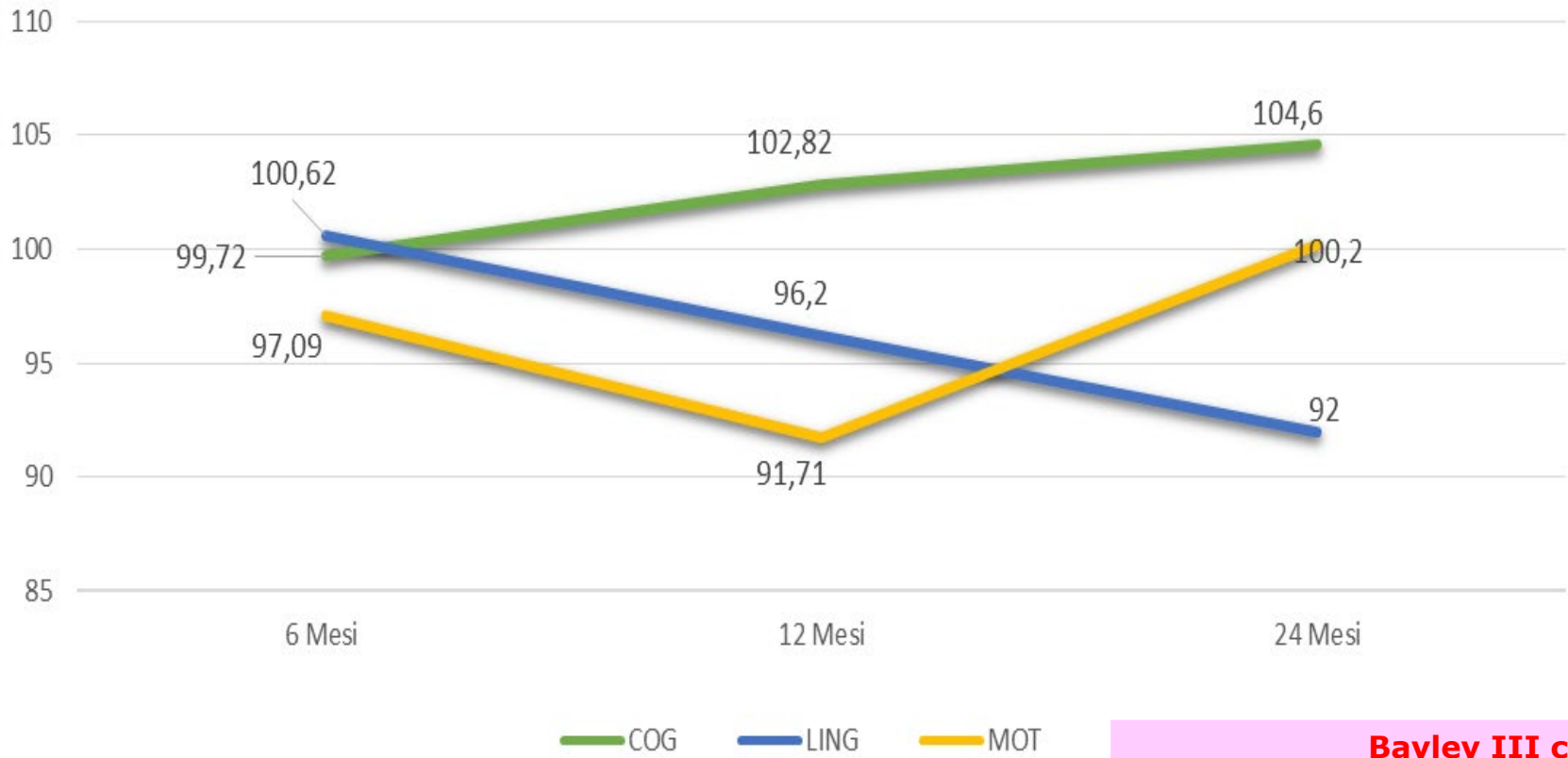
Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

BAYLEY III ASSESSMENT (mean)



— COG — LING — MOT
DEVELOPMENTAL DOMAINS

Bayley III composite scores

100 ± 15	Mean
<85 (>1 SD below the mean)	Mild to moderate delay
<70 (>2 SD below the mean)	Significant delay

* M.F. Coletti – Clinical Psychology Unit-
Departement of Neurosciences and
Neurorehabilitation (DNN)

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Prediction of Neuromotor Outcome in Perinatal Asphyxia: Evaluation of MR Scoring Systems

A. James Barkovich, Beatrice Latal Hajnal, Daniel Vigneron, Augusto Sola, J. Colin Partridge, Faith Allen, and Donna M. Ferriero

AJNR Am J Neuroradiol 19:143–149, January 1998

Barkovich MRI score

- 0** no abnormalities in the basal ganglia or cortex
- 1** an abnormal signal in the basal ganglia or thalamus
- 2** an abnormal signal in the cortex
- 3** an abnormal signal in the cortex and basal nuclei (basal ganglia or thalami)
- 4** an abnormal signal in the entire cortex and basal nuclei

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

Outcome and neonatal MRI

within 10 days of age:

- All CP (6/6) have a pathological MRI
- 4/7 infants with mild delay have a pathological MRI
- 3/7 infants with mild delay have a normal MRI
- 2/48 infants with normal outcome have a pathological MRI

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

Outcome and MRI at FU

PATIENTS N° 24	NEONATAL MRI	12 MONTHS MRI
14	NORMAL	NORMAL
1	NORMAL	Cerebellar neoformation
4	PATHOLOGICAL	NORMAL
5*	PATHOLOGICAL	PATHOLOGICAL

TOT 24

***4 CP, 1 NEUROFIBROMATOSIS TYPE 1**

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net

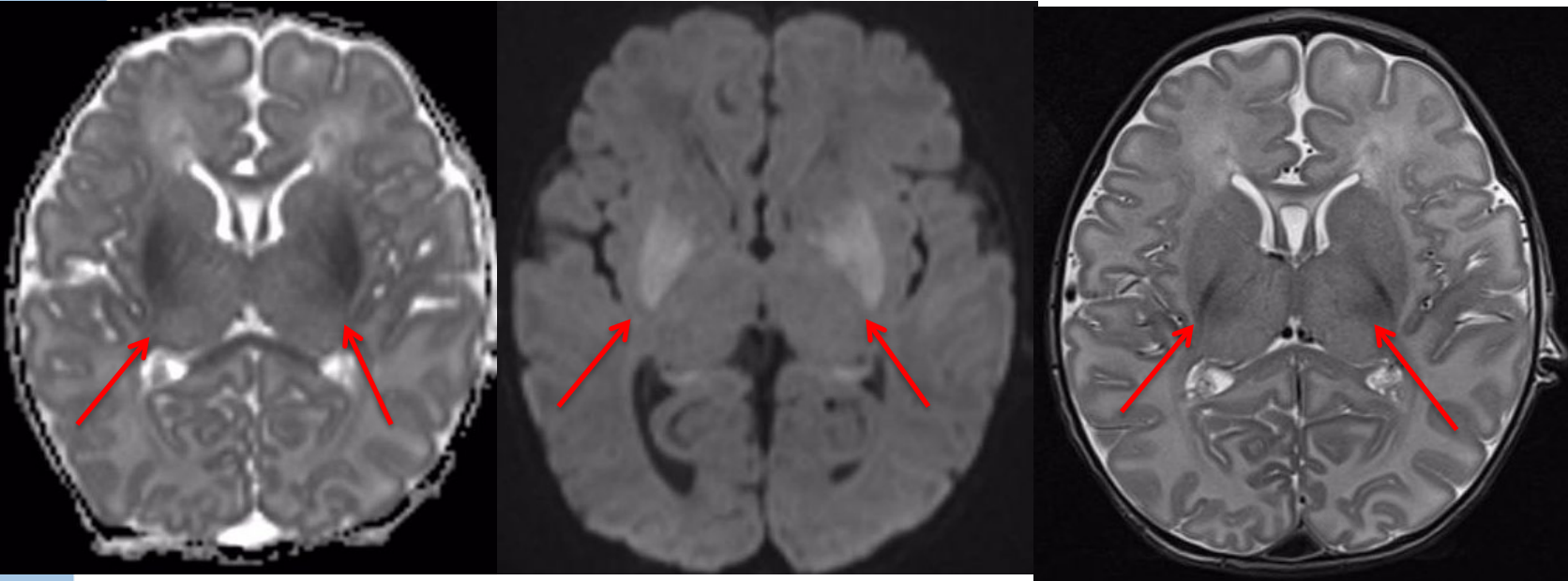


Bambino Gesù
OSPEDALE PEDIATRICO

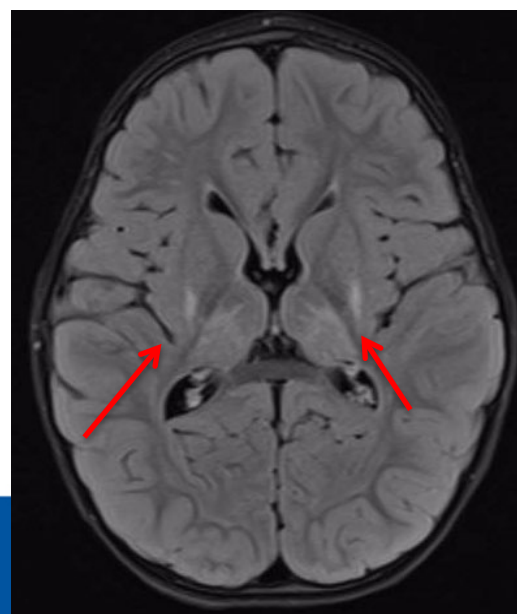
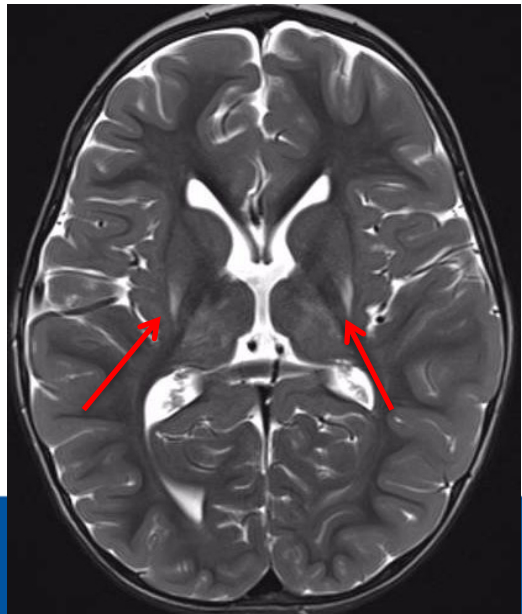
ADC

DWI

T2

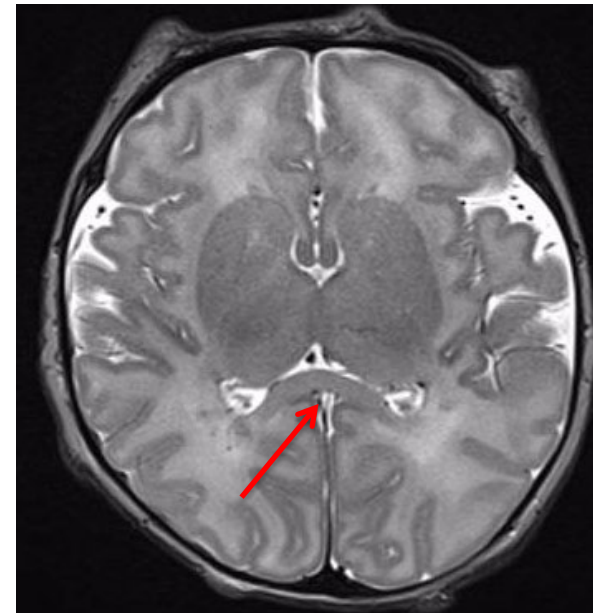
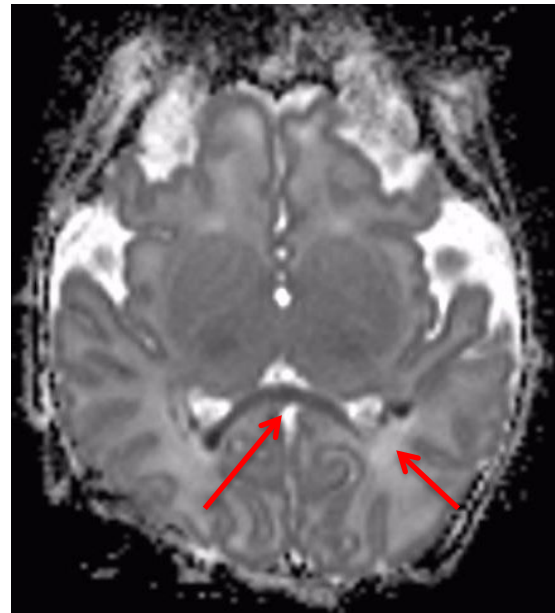
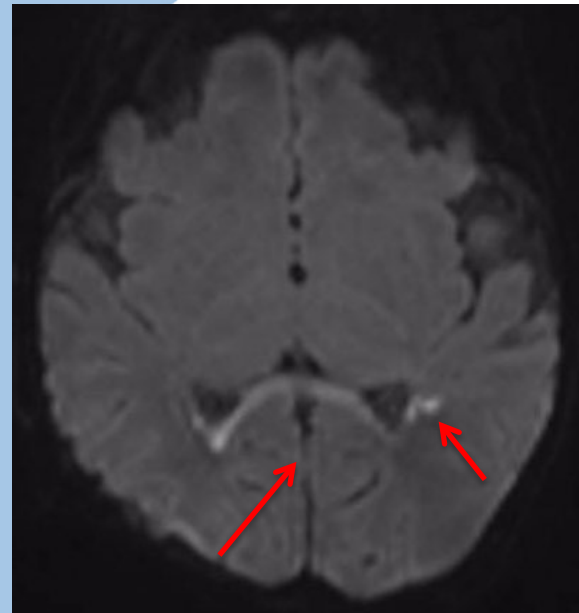


NEONATAL MRI
GLOBUS PALLIDUS AND CORPUS CALLOSUM ALTERATIONS



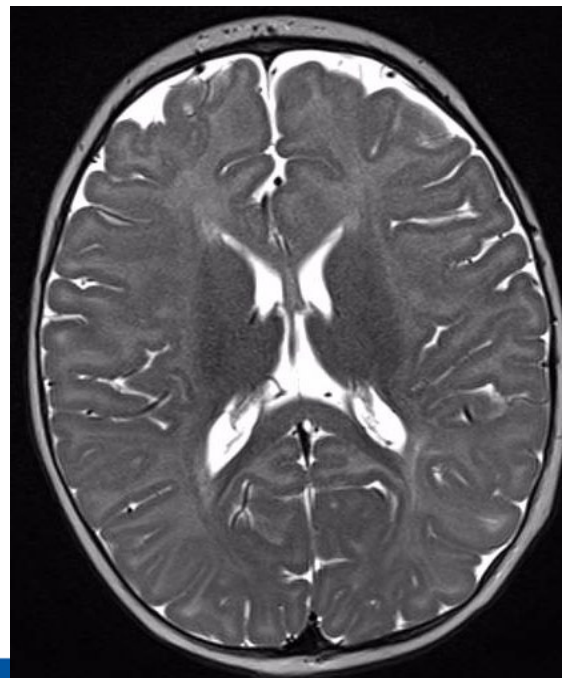
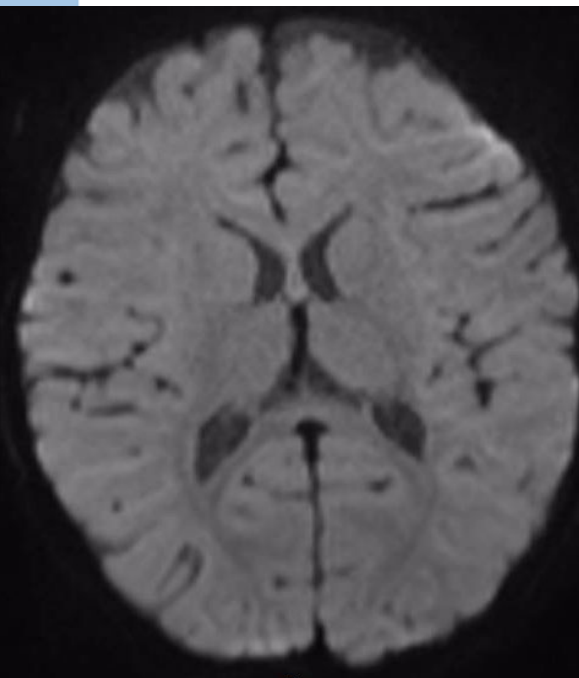
AT 1 YEAR
GLIOTIC SEQUELAE IN PUTAMEN AND THALAMUS

* **D.Longo – Neuroradiology Unit**



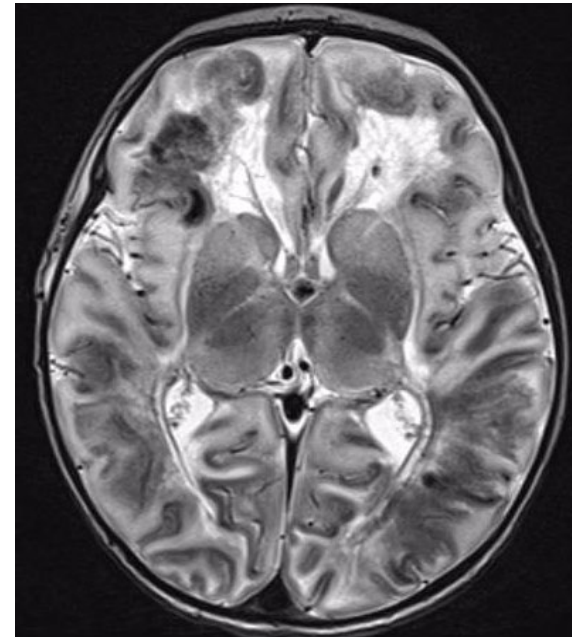
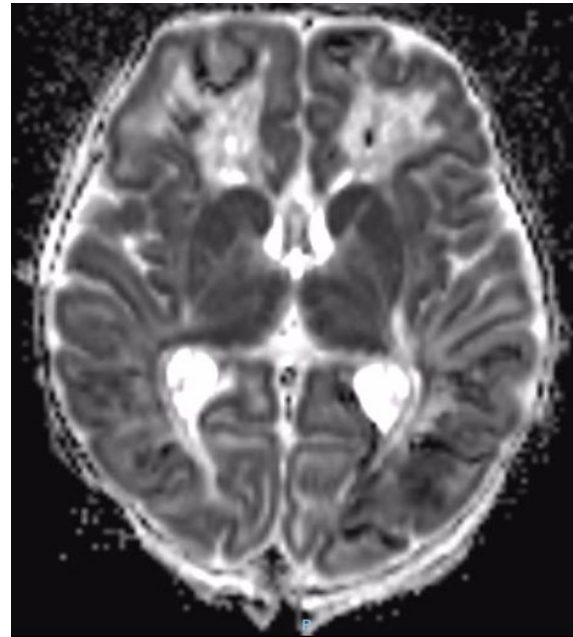
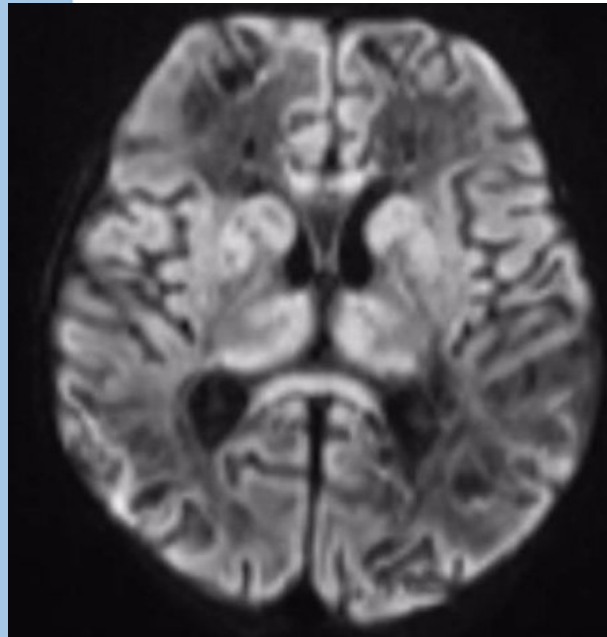
NEONATAL MRI

SPLENIAL OF THE
CORPUS
CALLOSUM
LESIONS



AT 6 MONTHS
NORMAL MRI

* **D.Longo – Neuroradiology Unit**

DWI**ADC****T2**

**SEVERE
ASPHYXIA**

**EXTENSIVE
INVOLVEMENT
OF CORTEX,
THALAMI AND
BASAL
GANGLIA**

THE JOURNAL OF
**MATERNAL-FETAL
& NEONATAL
MEDICINE**

<http://informahealthcare.com/jmf>
ISSN: 1476-7058 (print), 1476-4954 (electronic)

J Matern Fetal Neonatal Med, Early Online: 1–4
© 2015 Taylor & Francis. DOI: 10.3109/14767058.2015.1070138



ORIGINAL ARTICLE

Mild hypothermia and hemorrhagic lesions in neonates with hypoxic-ischemic encephalopathy: experience in an outborn center

Immacolata Savarese¹, Martina Balestri², Fiammetta Piersigilli¹, Paola Giliberti¹, Francesca Campi¹, Jole Rechichi¹, Vito Mondì¹, Francesco Gesualdo³, Daniela Longo⁴, Maria Roberta Cilio², and Andrea Dotta¹

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net

Hemorrhagic lesions at DNMC

- 33,8% (25/74) newborn with hemorrhagic lesions
- 36% (9/25) patients born from distocian delivery (vacuum-assisted birth)
- 80% (20/25) no brain injury at neonatal MRI
- 12% (3/25) patients lost at FU
- 68,2% (15/22) normal outcome at 12 months
- 1 CP

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

Hemorrhagic lesions at DNMC

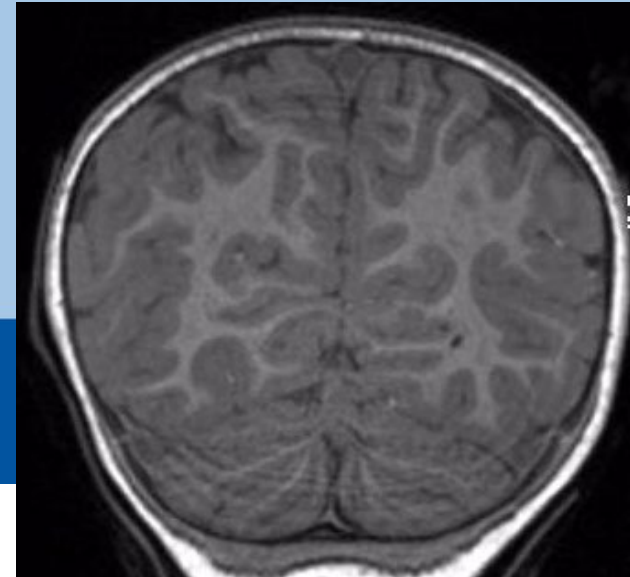
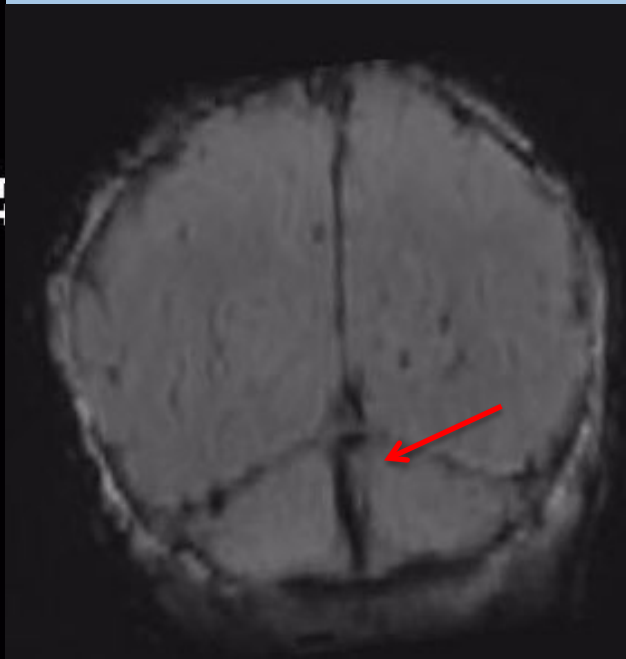
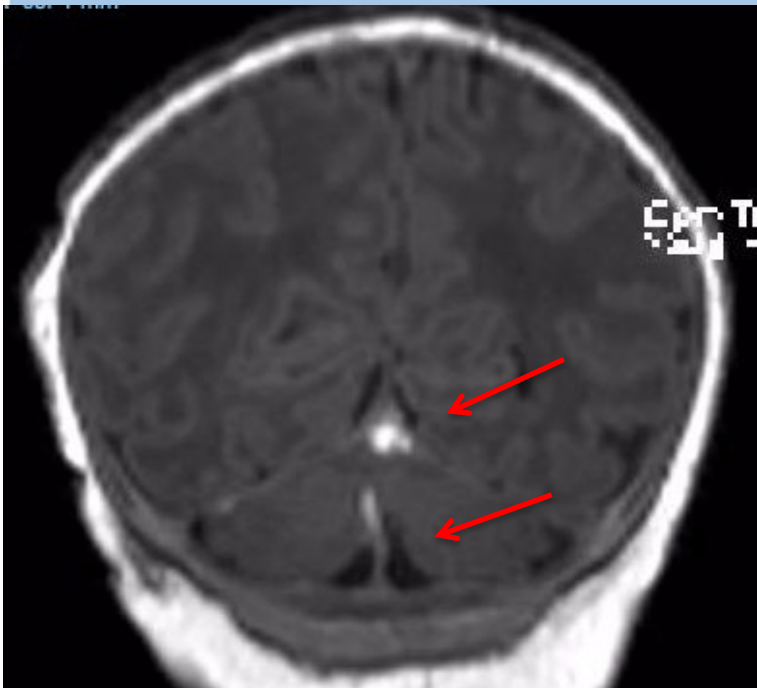
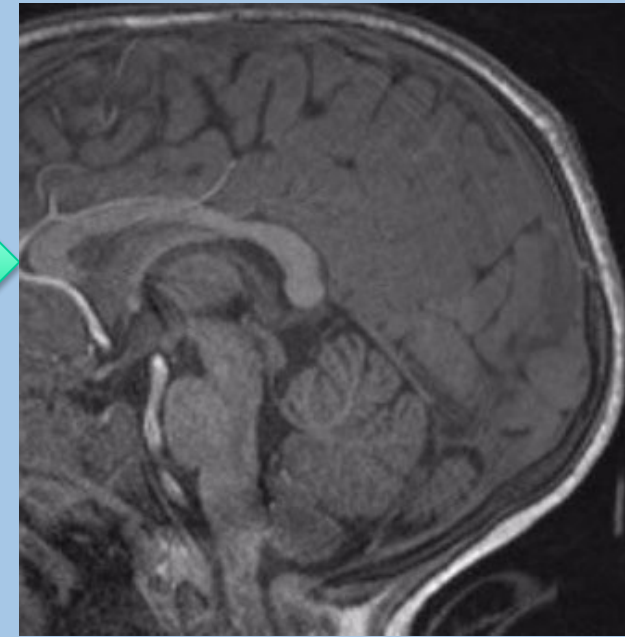
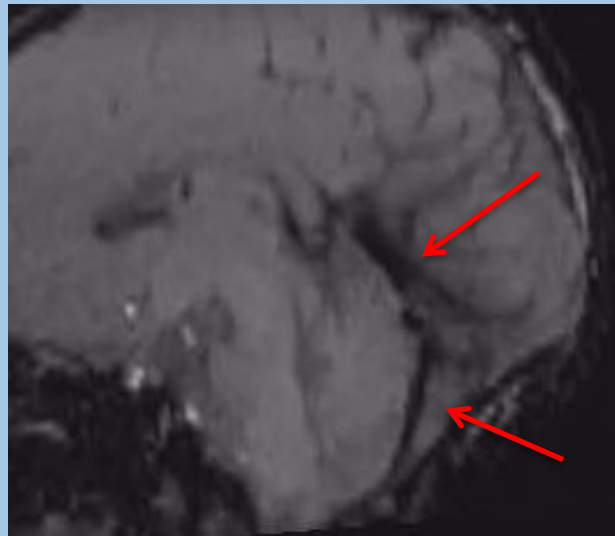
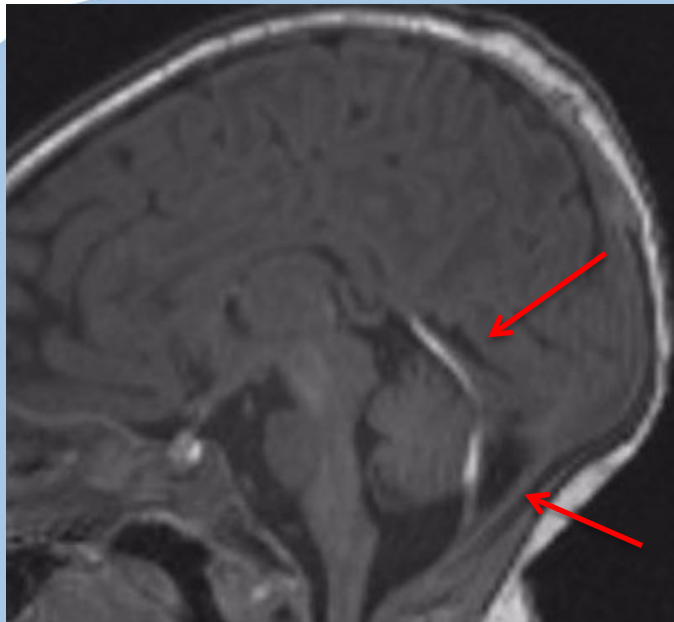
- Infants are followed by serial ultrasound controls, agree with neurosurgeons

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net

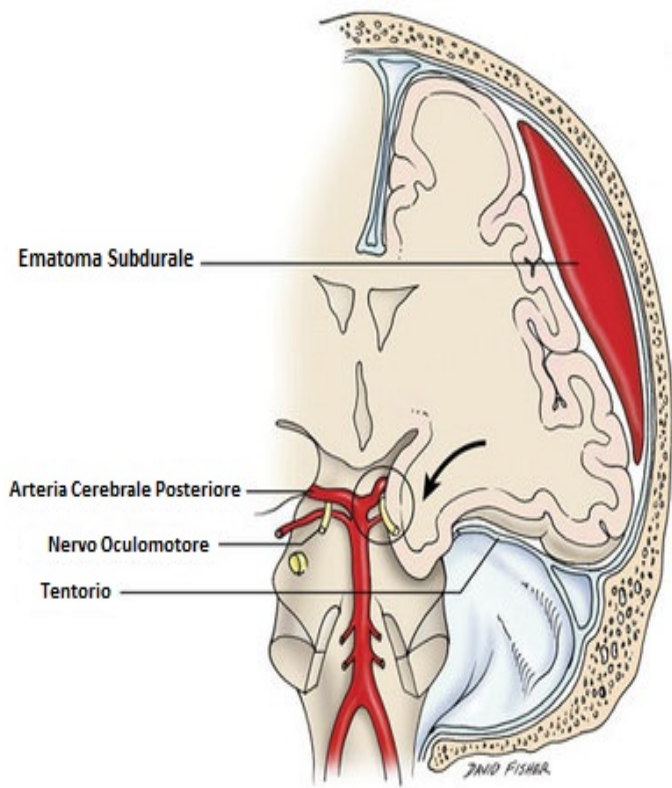


Bambino Gesù
OSPEDALE PEDIATRICO

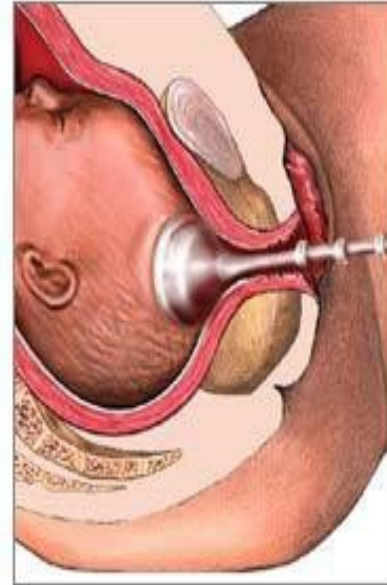


Neonatal MRI

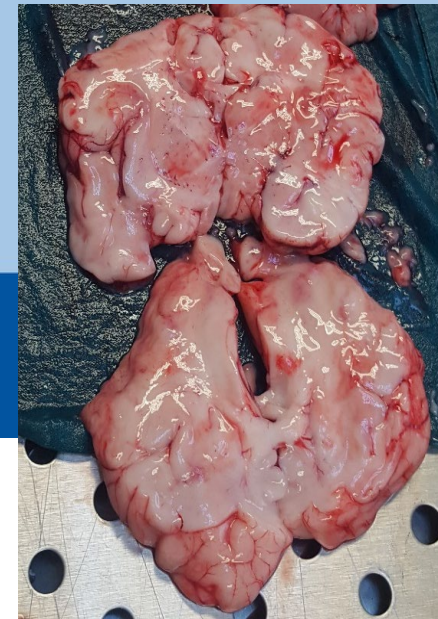
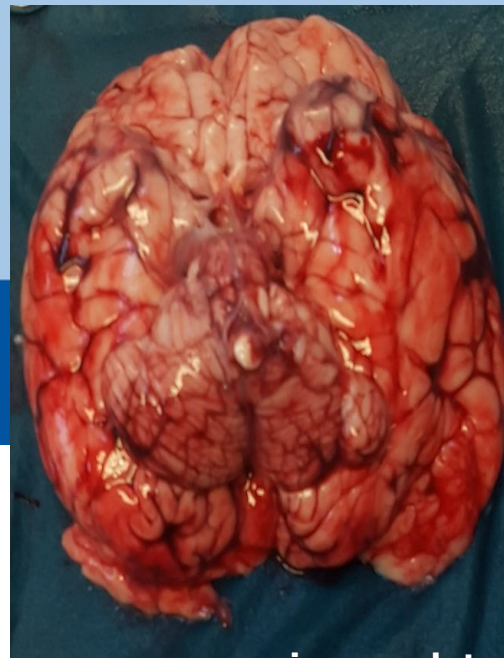
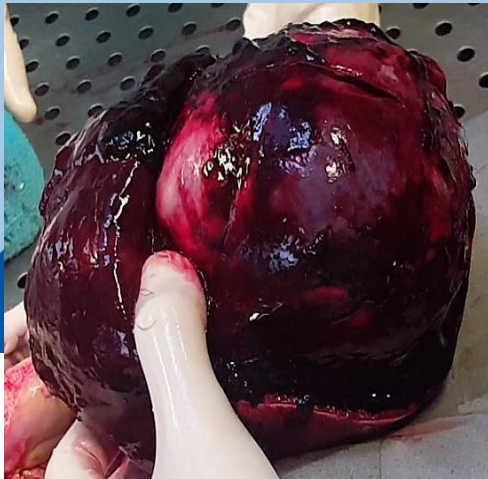
At 1 year



Vacuum-assisted birth



Forceps-assisted birth



Seizures and outcome

Electrographic seizures are associated with brain injury in newborns undergoing therapeutic hypothermia

Divyen K Shah,^{1,2} Courtney J Wusthoff,³ Paul Clarke,⁴ John S Wyatt,⁵ Sridhar M Ramaiah,⁴ Ryan J Dias,¹ Julie-Clare Becher,⁶ Olga Kapellou,⁷ James P Boardman^{6,8}

Shah DK, et al. *Arch Dis Child Fetal Neonatal Ed* 2014;**99**:F219–F224. doi:10.1136/archdischild-2013-305206

Determinants of Outcome After Head Cooling for Neonatal Encephalopathy

John M. Keogh

Pediatrics 2007;120;171

DOI: 10.1542/peds.2007-0602

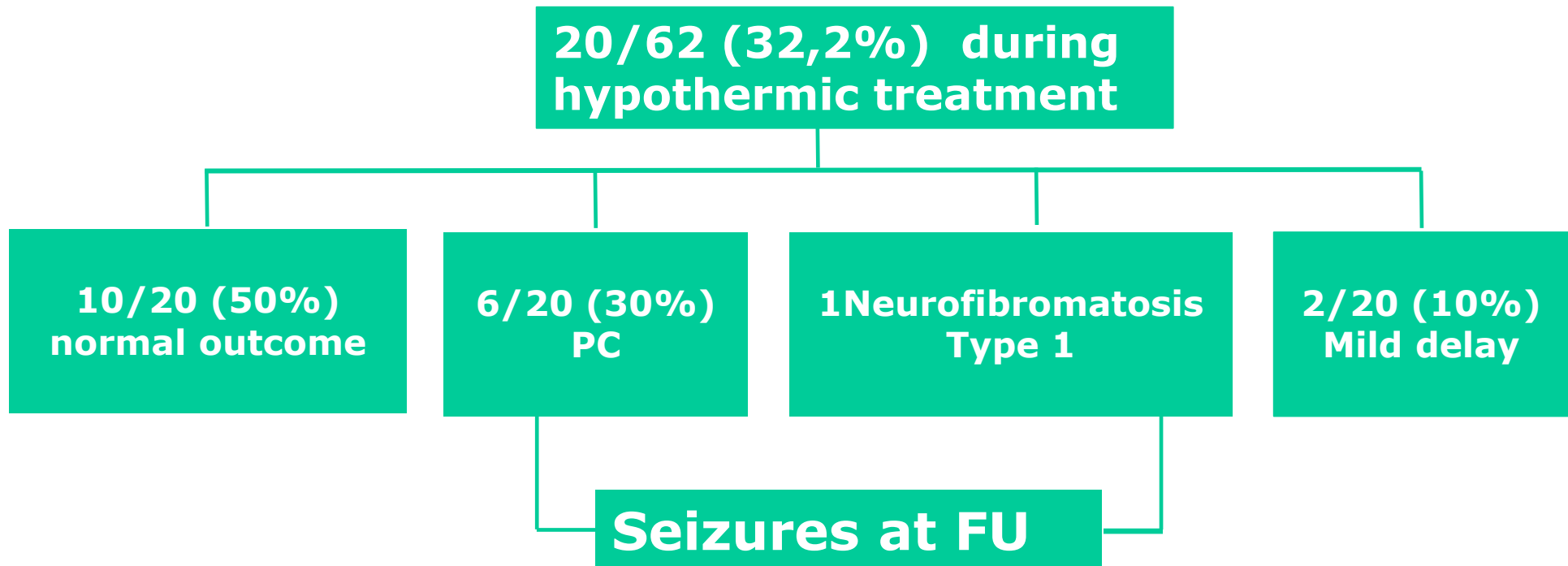
Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

Seizures and outcome



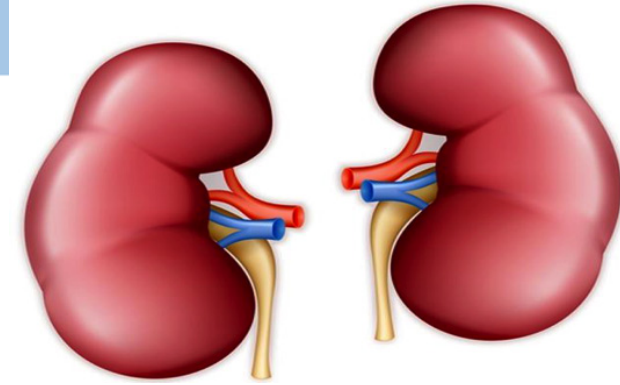
Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



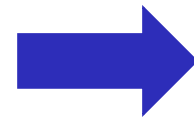
Bambino Gesù
OSPEDALE PEDIATRICO

Nephrological FU



At 3th and 9th month:

- Nephrological evaluation
- Blood pressure measurement
- Monitoring of renal function on blood and urine
- Assessment of renal dimension, by renal US



**Hypertension,
Chronic renal failure**



Renal hypoplasia

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

CONCLUSIONI

FU del bambino a Rischio di Sviluppo

Neonatologi

- Auriti Cinzia
- Braguglia Annabella
- Calzolari Flaminia
- Campi Francesca
- De Marchis Chiara
- Monaco Francesca
- Piersigilli Fiammetta
- Rechichi Jole
- Savarese Imma
- Savignoni Ferdinando

Chirurghi Neonatali

- Conforti Andrea
- Fusaro Fabio
- Iacobelli Barbara Daniela
- Iacusso Chiara
- Morini Francesco
- Totonelli Giorgia
- Valfrè Laura

- Pediatria
- Malattie rare

- Aite Lucia
- Bevilacqua Francesca
- Bucci Silvia
- Coletti Maria Franca

Psicologhe

- Santi Roberta
- Stabile Tina
- Nicastro Marina
- Fierro Stefania
- D'Astore Michela

Infermiere

- Calzolari Flaminia
- Columbo Claudia
- Landolfo Francesca
- Savignoni Ferdinando

Spirometria



DNMC

OPBG

Department of Medical and Surgical Neonatology

immacolata.savarese@opbg.net



Bambino Gesù
OSPEDALE PEDIATRICO

Take Home Messages

- **Therapeutic Hypothermia improves Outcome** of infants with perinatal asphyxia
- **Clinical Recommendations:**
 - ✓ **Early** physiotherapeutic **evaluation** and **intervention**
 - ✓ **Multidisciplinary** and **Long-term FU**
 - ✓ **Nefrological FU** to detect hypertension and chronic renal failure
- **Multicentre Collaborations** with clinical trials and disease registries
- **More Researchs are needed on the long-term effects** of Hypothermia

Department of Medical and Surgical Neonatology

"The shared long-term goal for families and professionals is to work toward ensuring that high risk children maximize their potential and become productive and valued members of society"



Thank you!

