

The Role of MRI in Pediatric Cardiac Surgery

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Learning Objectives

- Discuss how MRI can help us understand short and longer term neurological injury and outcome
- Discuss insights from prenatal brain MRI in CHD
- Understand how brain immaturity in CHD can predispose patients to MRI injury
- Understand how quantitative MRI can provide important insights into brain growth and development
- Understand the relationship of perioperative MRI changes to longer term neurodevelopmental outcomes

Short Term Neurological Deficits After CHD Surgery

- Incidence 0-2% to 25%
- Austin *JTCVS* 1997;114:707 (6-25%, n=250)
 - Hemiparesis
 - Seizures
 - Prolonged coma
 - Choreoathetosis
- Menache *Ann Thorac Surg* 2002;73:1752 (2.3%, n=600)
 - Clinical seizures (1.3%)
 - Coma
 - Choreoathetosis
 - Encephalopathy
- Kussman *Anesth Analg* 2009;108:1122 (0%-n=104)

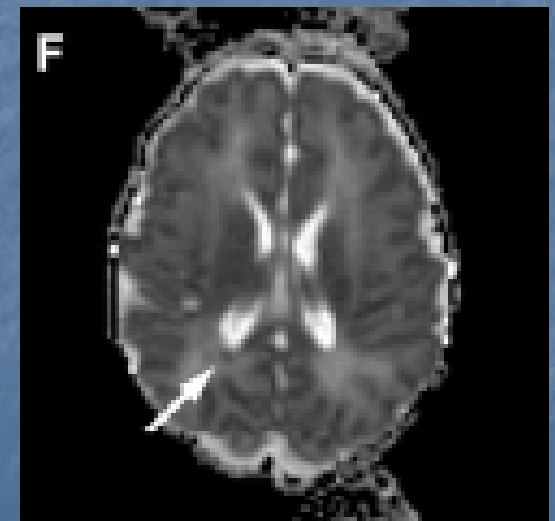
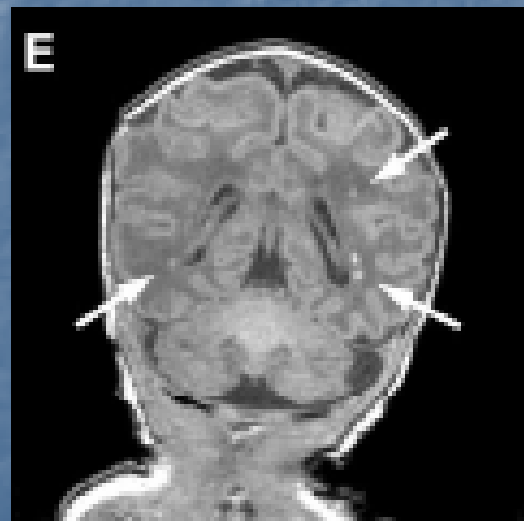
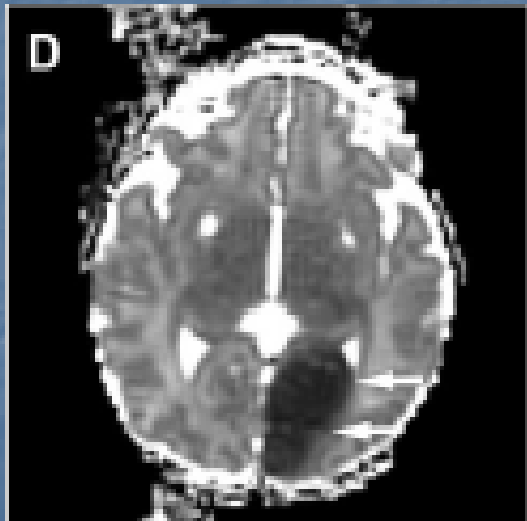
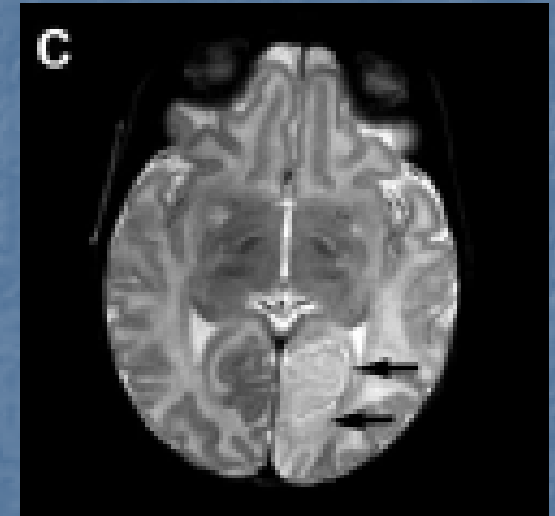
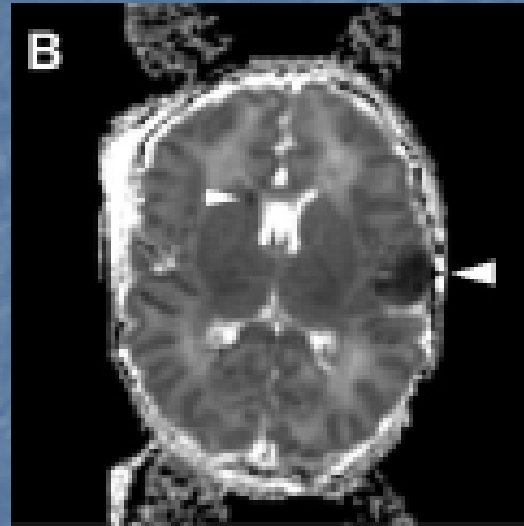
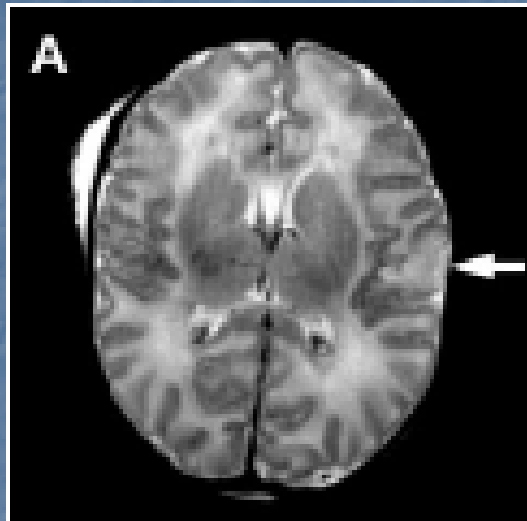
Adverse Long Term Neurodevelopmental Outcomes After CHD Surgery

- Up to 50% of neonates have long term deficits at age 5 years
- Creighton *Pediatrics* 2007;120:e478;
Majnemer *J Pediatr* 2006;148:72
 - Mild developmental delay
 - Fine motor and tone abnormalities
 - Attention-deficit hyperactivity disorder
 - Reading/language problems
- Similar to many VLBW infants

Etiology of Neonatal Brain Injury in CHD

- Preoperative brain injury
 - Diminished in utero blood flow and brain growth
 - J Thorac Cardiovasc Surg 2004;128:841
 - Brain immaturity in CHD:
 - Delayed structural maturation
 - J Thorac Cardiovasc Surg 2009;137:529
 - Delayed myelination and intracellular maturation
 - N Eng J Med 2007;357:1928
 - Delays in surgery in very cyanotic neonates
 - Not BAS
 - Circulation 2009;119:709
 - J Am Coll Cardiol 2009;53:1807
- Intra- and Postoperative Brain Injury
 - Prolonged low brain regional oxygen saturation
 - Prolonged DHCA, low flow ACP
 - Stroke 2007;38:736; J Thorac Cardiovasc Surg 2006;131:190

Brain Injury in Neonatal CHD



Fetal Brain MRI and CHD

Brain Volume and Metabolism in Fetuses With Congenital Heart Disease

Evaluation With Quantitative Magnetic Resonance Imaging and Spectroscopy

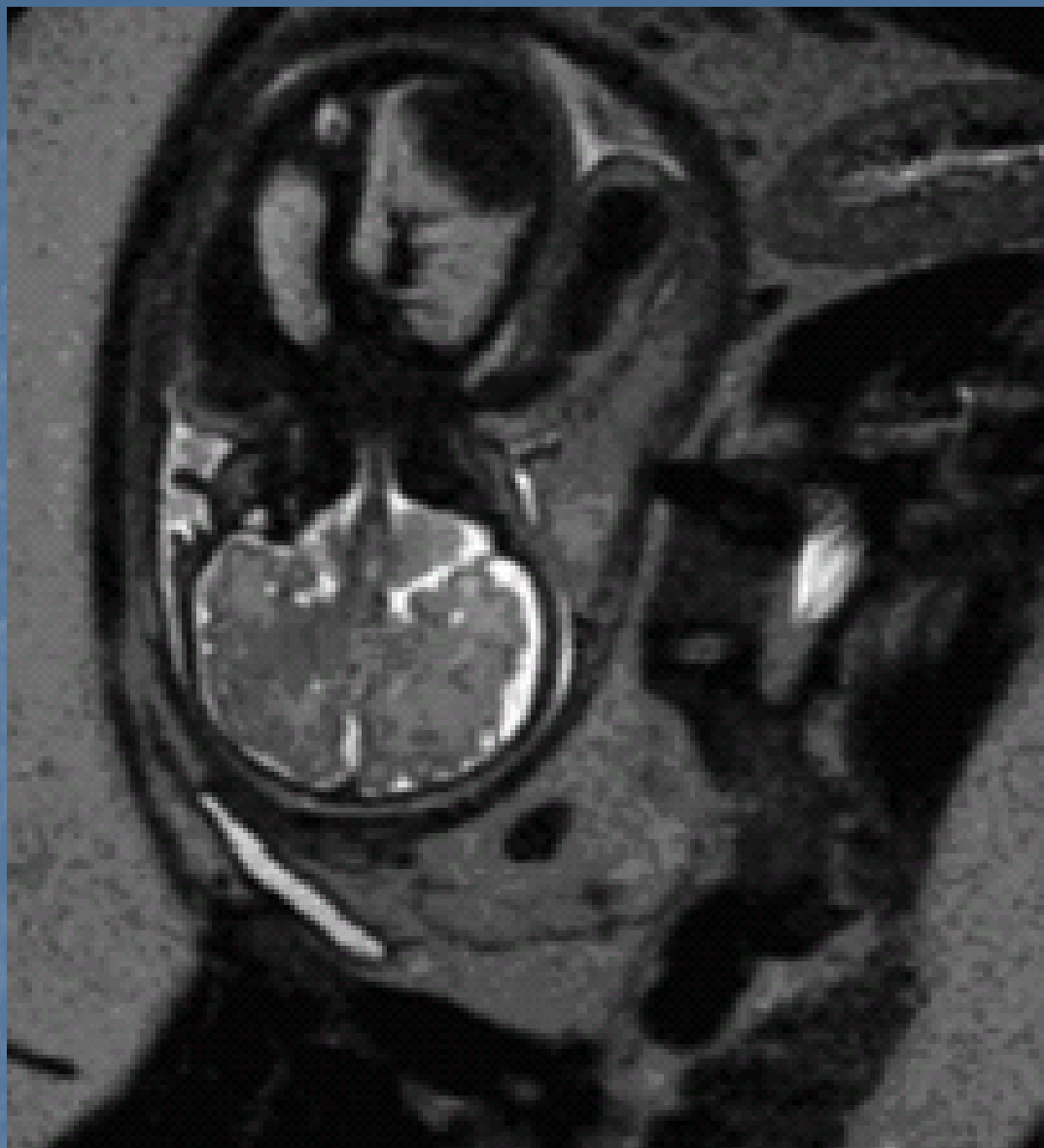
Catherine Limperopoulos, PhD; Wayne Tworetzky, MD; Doff B. McElhinney, MD;
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Circulation 2010;121:26-33

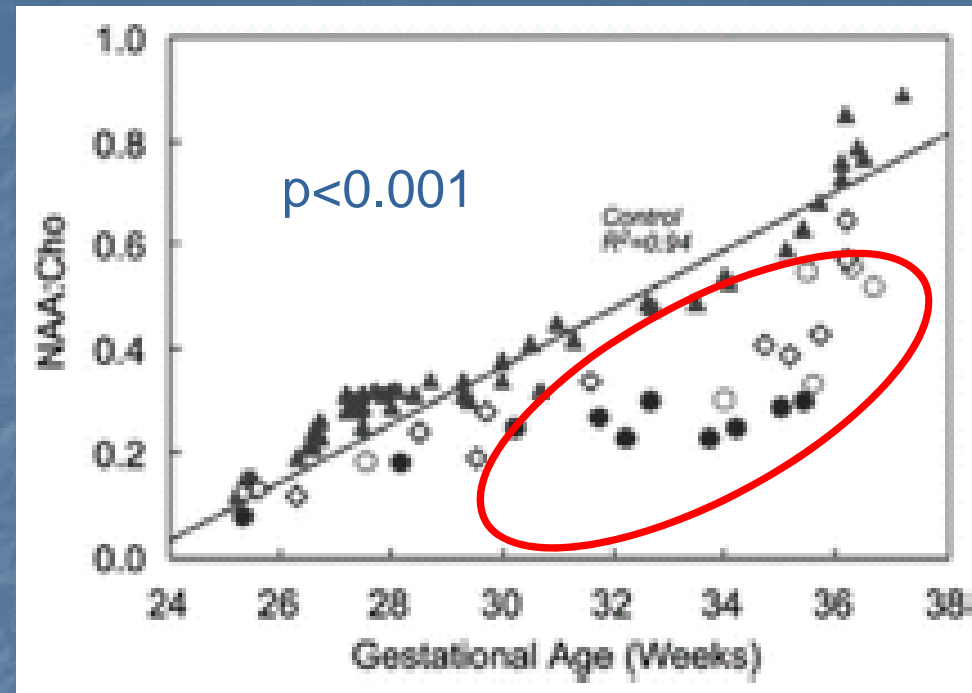
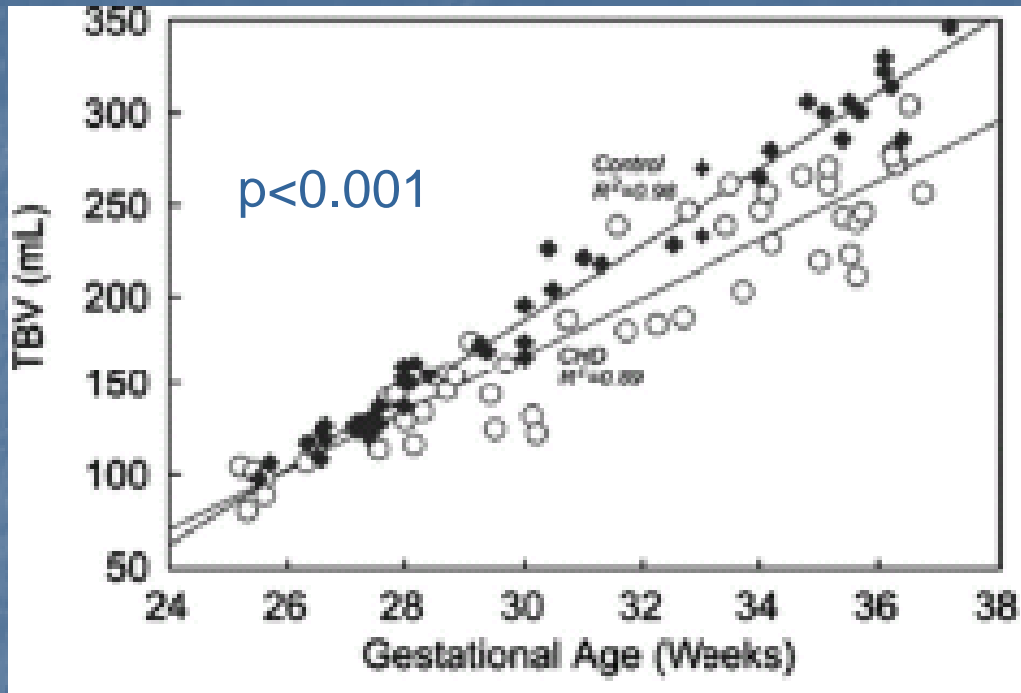
Fetal Brain MRI and CHD

- Fetal brain MRI at 25-37 weeks
- Fetal intracranial volume, CSF volume, total brain volume
- MR spectroscopy for NAA:choline, and lactate
- 55 CHD and 50 control fetuses

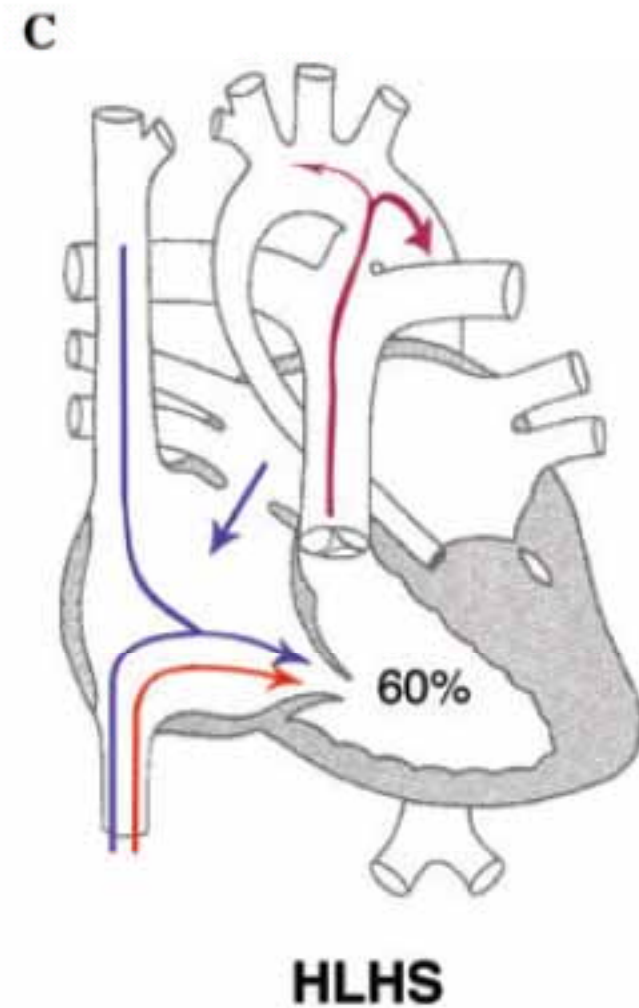
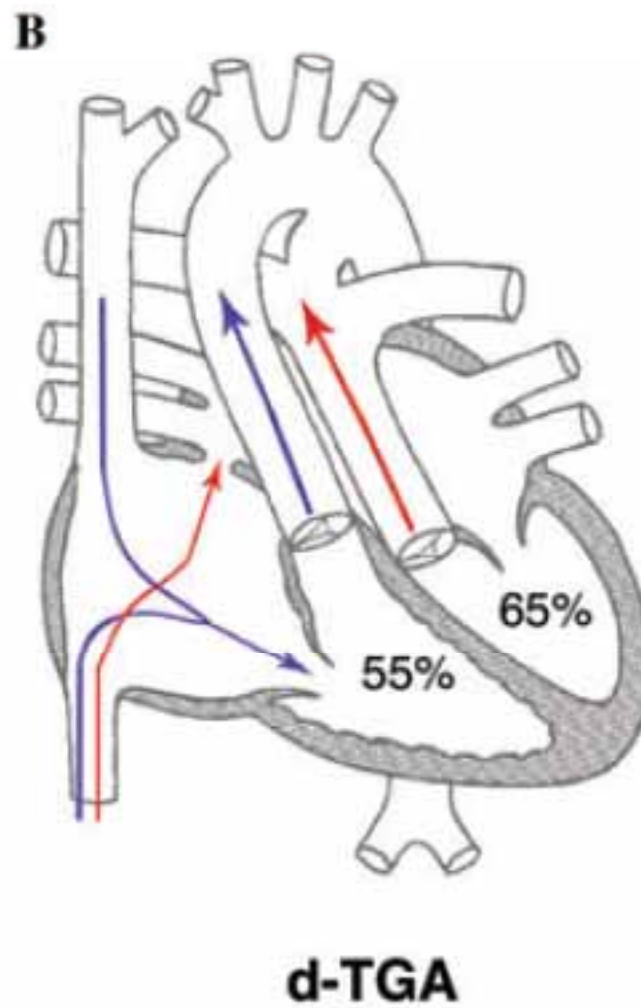
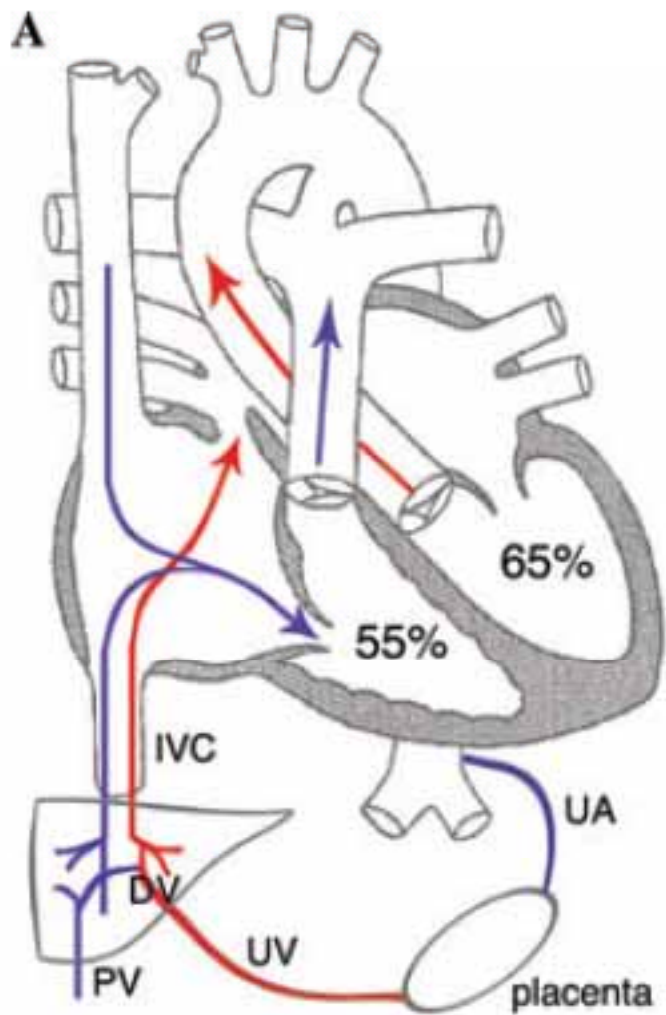
Circulation 2010;121:26-33



Circulation 2010;121:26-33



- In third trimester, TBV and ICV progressively smaller in CHD ($p < 0.001$)
 - Lower combined ventricular output from aorta independently associated with smaller TBV ($p < 0.001$)
 - NAA:choline significantly and progressively lower with advancing GA ($p < 0.001$)
- Cerebral lactate detected in 7 of 36 fetuses with HLHS or TGA



McQuillen PS, Miller SP. Ann NY Acad Sci 2010;1184:68-86

Brain immaturity is associated with brain injury before and after neonatal cardiac surgery with high-flow bypass and cerebral oxygenation monitoring

J Thorac Cardiovasc Surg 2010;139:543-56

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Stephen A. Stayer, MD,^{a,b,f} Ann R. Stark, MD,^{b,j} E. Dean McKenzie, MD,^{d,g} Jeffrey S. Heinle, MD,^{d,g}
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- Premise: the brains of neonates with complex CHD are structurally and biochemically immature
 - JTCVS 2009;137:529; NEJM 2007;357:1928
- Hypothesis: Brain immaturity is associated with pre- and postoperative brain injury

Study Purpose

- Determine the incidence of new hypoxic-ischemic brain lesions with high flow CPB and maximized oxygen delivery strategy in neonates after congenital heart surgery
- Determine whether standard and quantitative MRI changes are associated with adverse neurodevelopmental outcomes at 1 year
- Establish a baseline for future neuroprotection studies
- Determine patient and procedural factors associated with brain injury
 - Especially brain maturity

Methods

- IRB approval and parental consent
- Neonates (<30 days) undergoing surgery with hypothermic CPB (<30° C) for >60 minutes
- Single ventricle (SV) and two-ventricle (2V) repairs
- Exclusion criteria:
 - Gestational age <35 weeks
 - Weight <2.0 kg
 - CPR >3 minutes
 - Recognizable dysmorphic syndrome

Methods

- Anesthetic protocol
 - Fentanyl 100-400 mcg/kg
 - Midazolam 0.25-3 mg/kg
 - Isoflurane up to 1% end-tidal
 - No ketamine or barbiturates
- Perfusion protocol
 - pH stat management
 - Hematocrit 30-35%
 - 150 ml/kg/min flows at all times
 - Minimize DHCA
 - High flow ACP guided by NIRS and TCD

Methods

- Brain monitoring protocol:
 - NIRS to measure rSO₂ 12-24 hours pre-, intra-, and 72 hours postoperatively
 - Treatment protocol for rSO₂ <50%
 - Increase FiO₂
 - Increase PaCO₂
 - Increase hemoglobin
 - Increase cardiac output/O₂ delivery
 - Increase sedation/anesthesia
 - Decrease temperature
 - Increase flow or MAP on CPB
 - Did not track interventions/responses

Methods

- MRI protocol
 - 1.5 T scanner
 - T1 and T2-weighted images
 - Diffusion weighted and susceptibility weighted images
 - MR spectroscopy
 - MRI immediately preoperatively (GA), and 7-10d postoperatively (IV pentobarbital sedation)
- 3rd MRI at 3-6 months

Methods

- MRI Scoring
 - Single neuroradiologist unaware of diagnosis
 - MRI Injury Scale: WMI, hemorrhage, infarction, punctate lesions, lactate, SDH, DVST, IVH, congenital anomalies
 - Stroke 2007;38:736
 - Childs Total Maturation Score: rates myelination, cortical infolding, involution germinal matrix, bands of migrating glial cells
 - Am J Neuroradiol. 2001;22:1577-82

Methods

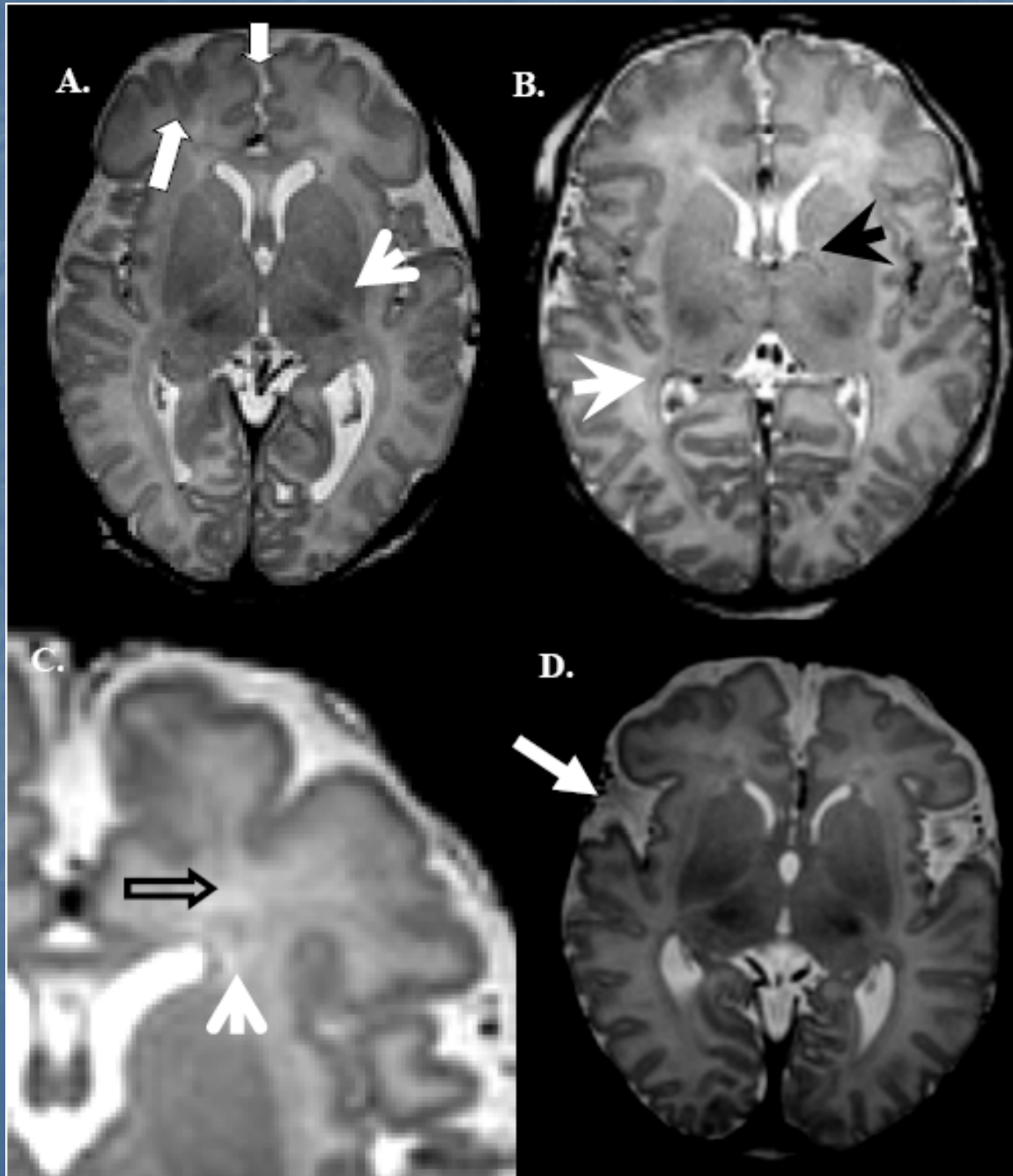
- T test, Mann-Whitney U test, chi-square, or Fisher exact tests used as appropriate
- Bivariate Spearman correlation used to associate pre- and intra/postoperative variables with brain injury
- Multivariable logistic regression analysis used for bivariate variables with $R > 0.2$
- 1° outcome: incidence of new WMI, hemorrhage, infarction
- Sample size analysis: 57 patients needed to detect a 40% incidence of new postoperative lesions with a power of 0.90 and α -level of 0.05

Appendix 3. Magnetic Resonance Imaging Brain Development/Maturity Scoring System

Category*	Designation/score	Definition
<u>Myelination (M)</u>	M1	Myelination evident in the brain stem, cerebellar peduncle, inferior colliculus, cerebellar vermis
	M2	M1 + subthalamic nucleus, globus pallidus, ventrolateral thalamus
	M3	M2 + caudal portion of the PLIC
	M4	M3 + complete PLIC
	M5	M4 + optic radiation
	M6	M5 + corona radiata
	M7	M6 + anterior limb of internal capsule
<u>Cortical infolding (C)</u>	C1	Frontal and occipital cortex completely smooth, insula wide open; thin bright cortical rim on T1, generally low-intensity WM on T1
	C2	Frontal cortex still very smooth, some sulci evident in occipital cortex; insula still wide with almost smooth internal surface; WM low intensity on T1
	C3	Frontal and occipital cortex similar number of convolutions; frontal sulci still quite shallow; internal surface of insula more convoluted; WM still somewhat low intensity on T1
	C4	Frontal and occipital cortex folded and rich in sulci; frontal sulci obvious along interhemispheric fissure; occipital WM separated into strands by deeper sulci; insula completely infolded; WM still distinguishable from gray matter on T1
	C5	Frontal and occipital WM separated into strands by deeper sulci; insula completely infolded; WM still distinguishable from gray matter on T1
	C6	As above but WM now isointense with gray matter on T1
<u>Germinal matrix (GM)</u>	GM1	Matrix seen in posterior horn, CTN, and anterior horns of the lateral ventricles
	GM2	Matrix seen at CTN and anterior horns of the lateral ventricles
	GM3	Matrix seen in the anterior horns only
	GM4	No germinal matrix evident
<u>Bands of migrating glial cells (B)</u>	B1	Broad band with additional narrower bands evident
	B2	Broad band alone
	B3	Narrow band alone
	B4	No bands seen

CTN, Caudothalamic notch; PLIC, posterior limb of the internal capsule; WM, white matter *From Childs.²¹

Childs Total Maturation Score Images



Licht et al JTCVS
2009;137:529

Preoperative MRI



Intubated GA immediately before transfer to OR

Postoperative Research Monitoring



Results

- 68 patients studied: 36 SV, 32 2V
- 97.1% 30 day in hospital survival
- 7 late deaths between 19 days and 6 months postop
 - 6 Norwood stage I palliation before second stage; sudden cardiac arrest at home or in hospital
 - 1 DILV patient after bidirectional Glenn of P. aeruginosa septic shock

Patient Surgical Data

<u>Parameter</u>	<u>Single Ventricle,</u> <u>n=36</u>	<u>Two Ventricle,</u> <u>n=32</u>
Age (days)	7 (5-10.5)	8 (5.5-13.5)
Weight (kg)	3.02 ± 0.36	<u>3.30 ± 0.52*</u>
Operation: Norwood Stage I	35	
ASO, AAA,PAB	1	
ASO	0	21
Truncus arteriosus repair	0	5
AAA, VSD repair	0	6
CPB time (min)	216 ± 58	220 ± 68
AoXcl time (min)	103 ± 36	<u>128 ± 44*</u>
DHCA time (min)	13 ± 8 (30 pts)	11 ± 5 (4 pts)
ACP time (min)	76 ± 20 (36 pts)	<u>27 ± 17 (7 pts)*</u>
ACP flow rates (ml/kg/min)	56 ± 10 (36 pts)	63 ± 13 (7 pts)
Intraoperative rSO ₂ minutes <45%	45 ± 49	<u>15 ± 31*</u>
Postoperative rSO ₂ minutes <45%	287 ± 408	<u>1 ± 3*</u>

Results: Primary Outcome

- **NEW** postoperative WMI, hemorrhage, infarction: 36%
 - 45% SV vs. 25% 2V (p=0.13)
- **NEW** postoperative WMI: 15%
 - 23% SV vs. 6% 2V (p=0.09)

Results: Secondary Outcomes

- ***PREOPERATIVE*** WMI, hemorrhage, infarction: 28%
 - 28% in both SV and 2V
- ***PREOPERATIVE*** WMI: 16%
 - 13% SV vs. 19% 2V (p=0.83)
- Late Death in 7/35 SV vs. 0/32 2V (p=0.01)

MRI Results

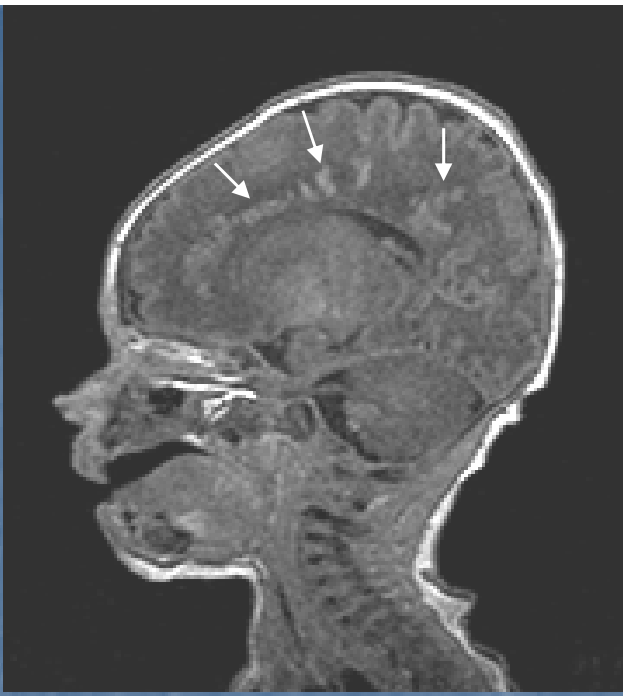
<u>Parameter</u>	<u>Single Ventricle,</u> <u>n=36</u>	<u>Two Ventricle, n=32</u>
MRI postoperative day	7 (7-9)	7 (7-9)
Preoperative WMI, no., (%)	5(13)	6 (19)
7-day postoperative WMI, no., (%)	<u>13(37)†</u>	<u>2 (6)*</u>
Preoperative infarct, no., (%)	5 (14)	7 (22)
7-day postoperative infarct, no., (%)	11 (31)	11 (34)
Preoperative IP hemorrhage, no., (%)	0	0
7-day postoperative IP hemorrhage, no., (%)	3 (9)	2 (6)

*p≤0.05 between groups; †p ≤0.05 within groups

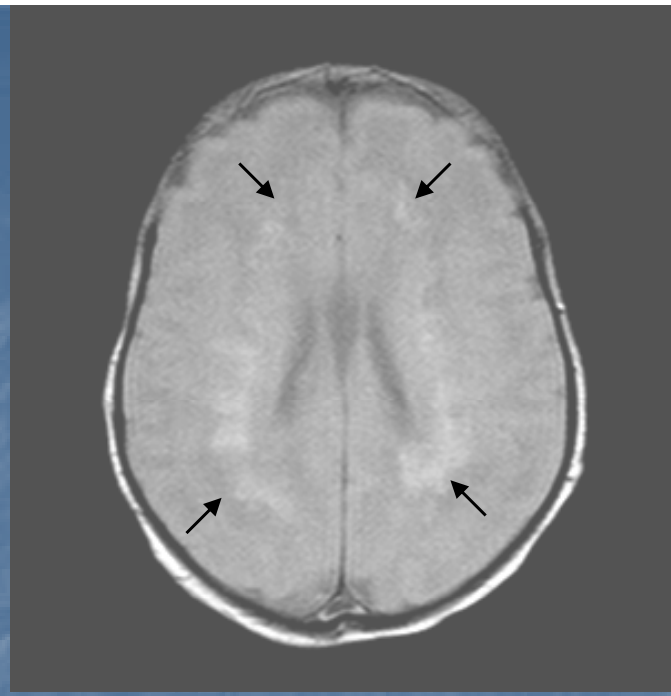
MRI Results

<u>Parameter</u>	<u>Single Ventricle,</u> <u>n=36</u>	<u>Two Ventricle,</u> <u>n=32</u>
New 7-day postoperative WMI, no., (%)	8 (23)	2 (6)
New 7-day postoperative WMI, infarct, or IP hemorrhage, no., (%)	16 (45)	8 (25)
Preoperative total MRI abnormality score	1.8 ± 2.6	2.3 ± 2.8
7-day postoperative total MRI abnormality score	<u>3.8 ± 4.2†</u>	3.2 ± 3.7

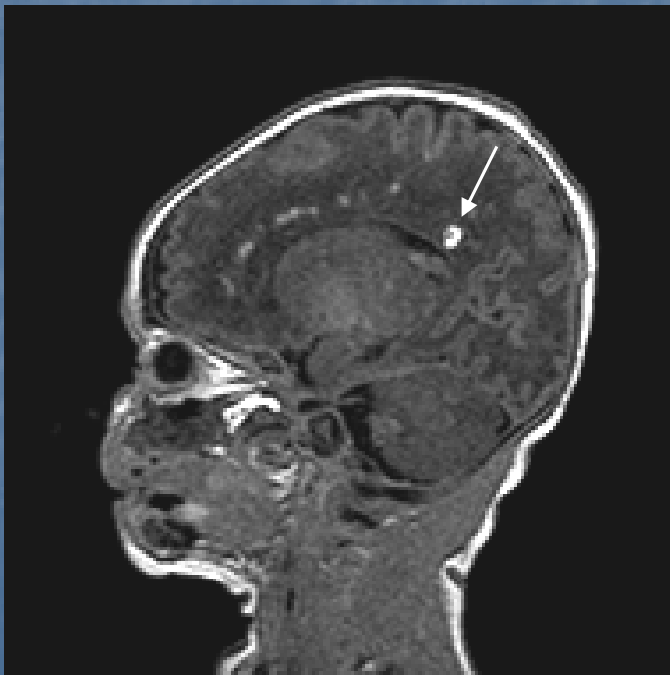
†p ≤0.05 within groups



Preop T1 HLHS



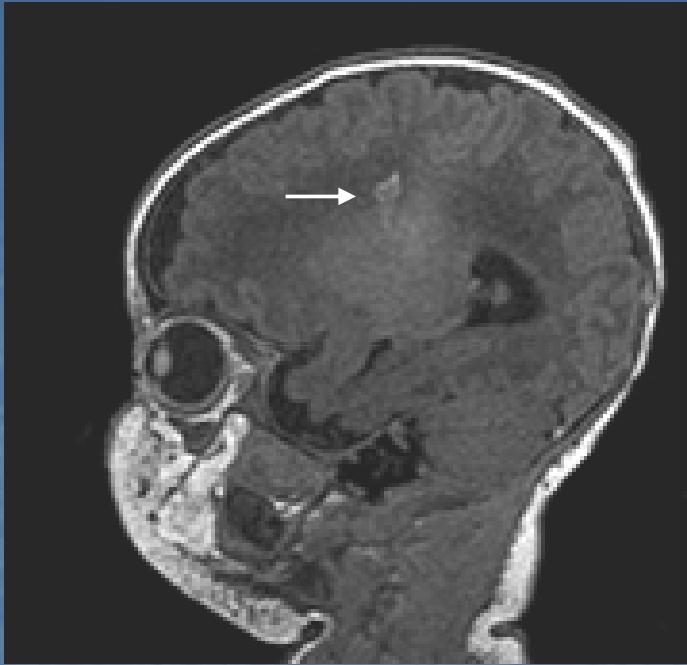
Preop T2 HLHS



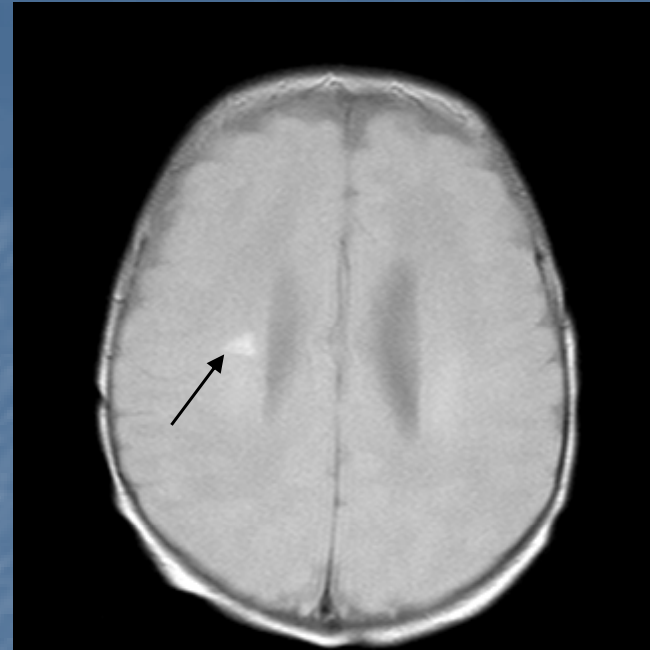
Postop T1 HLHS



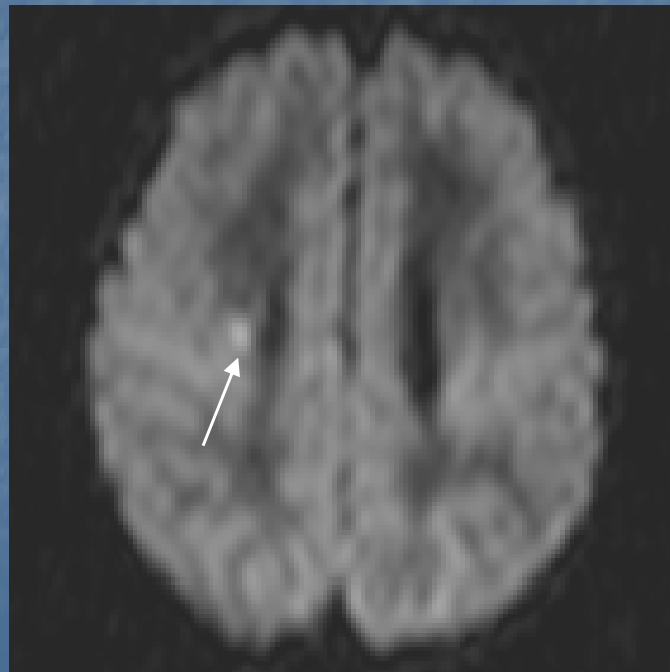
Postop T2 HLHS



Postop T1 HLHS



Postop T2 HLHS



Postop DWI HLHS

Brain Maturity Scores

- GA SV 38.3 ± 1.2 wks vs. 2V 38.8 ± 1.3 wks ($p=0.1$)
- Mean TMS SV 11.8 ± 1.5 and 2V groups 11.8 ± 1.0
 - GA 38 weeks
- 14 of 68 patients (21%) TMS < 10 (35 weeks GA), but only 4/68 with GA 35 weeks ($p=0.02$)

Important Associations With MRI Brain Injury—Multivariate Analysis

- Preoperative low TMS score (increasing brain immaturity) associated with:
 - Presence of preoperative WMI ($p=0.002$)
 - Severity of postoperative brain injury ($p=0.01$)
 - Postoperative late death ($p=0.008$)

Brain Immaturity and Brain Injury

- Immature TMS associated with pre and postoperative brain injury:
 - 7 of 13 patients with TMS <10 (35 wks) had new moderate postop brain injury
 - Only 10 of 54 with TMS >10 had moderate postop injury (p=0.01)
 - Preoperative WMI more likely with TMS<10 (5/13 vs. 6/55, p=0.03)
 - Postoperative WMI also more likely with TMS<10 (6/13 vs. 9/54, p=0.05)

Important Associations With MRI Brain Injury—Multivariate Analysis

- Single ventricle diagnosis associated with:
 - Presence of postoperative WMI ($p=0.02$)
 - Late death ($p=0.004$)
- Sustained low diastolic BP associated with:
 - NEW postoperative WMI/infarction/hemorrhage ($p=0.039$)

Lack of Association With MRI Brain Injury-Multivariate Analysis

- Gestational age
- Performance of balloon atrial septostomy
- CPB time, aortic crossclamp time, ACP time
- Use of ACP vs. full flow CPB
- $rSO_2 < 45\%$ for > 240 minutes in perioperative period (univariate $p=0.057$)
- Mean rSO_2 on Postoperative day #1, #2, #3
- Lowest sustained postoperative SBP, SaO_2

Discussion Points

- Brain injury also found among prematures, especially WMI
 - Immature oligodendrocyte WM precursors
- Etiologies: hypoxemia, inflammation, neurotoxic drugs
- MRI injury associated with adverse long term neurodevelopmental outcomes in prematures and FT with asphyxia

Vulnerable Periods of White Matter Development

D. Licht, CHOP, AATS 2009

Conception

23 Wk

32 Wk

Term Birth

Back et al 2001

Neurulation

Migration



3-4 Wk

20 Wk

WM precursors vulnerability

Myelination

Chen-Yu et al
*Am J
Neuroradiol*
1995; 16:1677



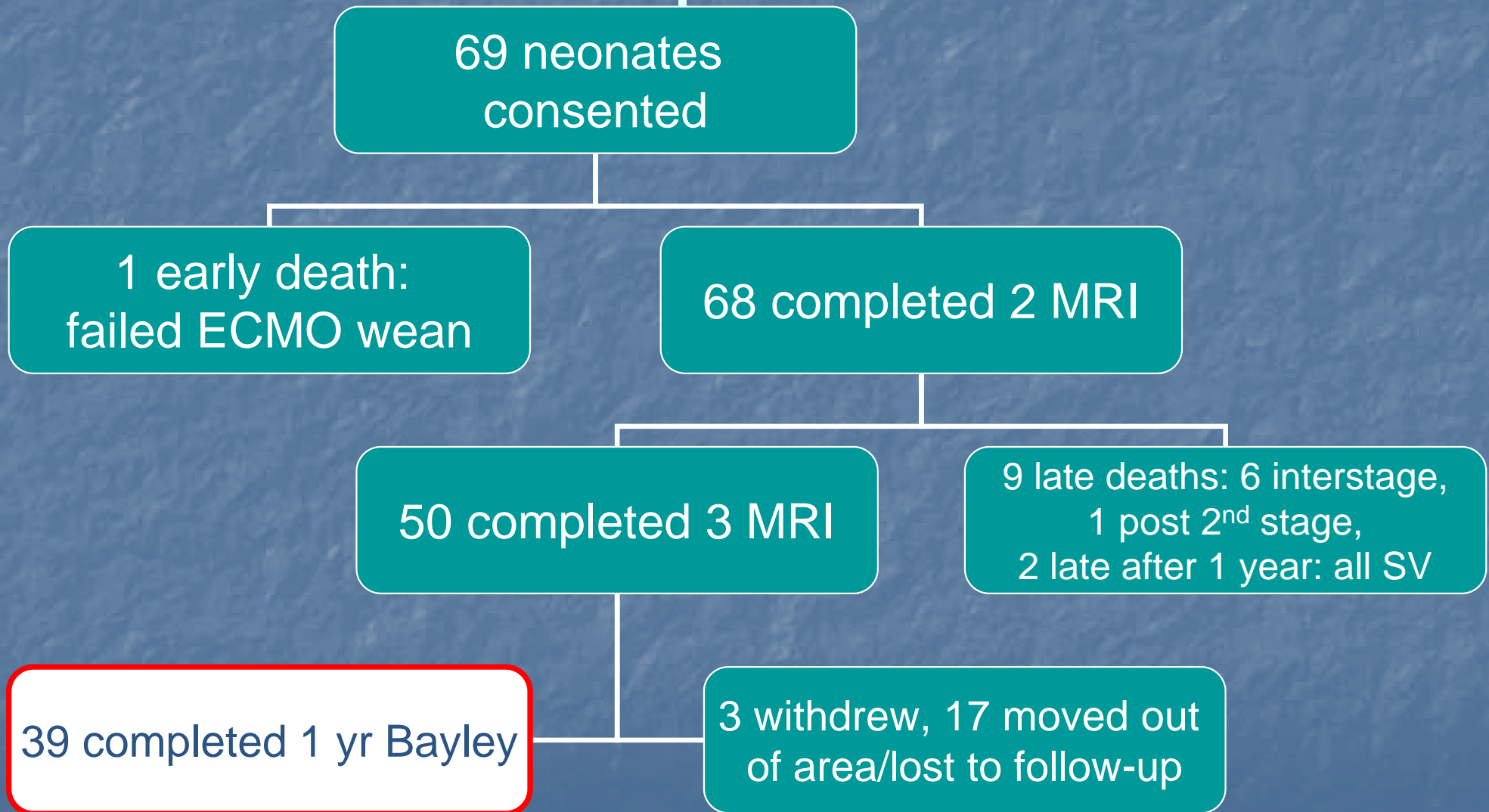
MRI Study Conclusions

- The association with brain immaturity and brain injury in neonatal CHD surgery is an important new finding
- Should timing of delivery be altered?
 - Postpone/delay any elective delivery as late as possible?
- Should surgical/CPB strategy be altered?
 - Delay CPB until brain more mature (BT shunt off CPB, hybrid Norwood)?

3rd MRI 3-6 months

- 50 patients
- New findings 27%--all minor
- Complete resolution of MRI2 findings—38%
- Partial resolution of findings—20%
- Evidence for neuroplasticity?

1-Year Bayley Scales of Infant Development III



Overall Group Outcomes

All patients, n=39	<u>MDI</u>	<u>PDI</u>
Mean \pm SD	100.0 \pm 14.7	87.9 \pm 15.9
Median (25-75th%)	100 (90-110)	91 (77-99)
Range (min-max)	65-130	52-121
# pts <70	1	6
# pts <85	4	11
# pts >115	4	1

Univariate Analysis

- Dependent variables: MDI and PDI
- Independent variables tested:
 - SV/2V, GA, **brain TMS, MRI brain injury**, CPB time, minutes $rSO_2 < 45\%$, # operations, ECMO, ICU LOS, chromosome abnormality, maternal IQ, dose benzodiazepines, dose isoflurane
- $P < 0.1$ for multivariable model:
 - MDI: maternal IQ, abnormal chromosomes, ICU LOS, ECMO, >1 CPB surgery
 - PDI: maternal IQ, abnormal chromosomes, ICU LOS
 - **NOT** standard MRI findings

Stepwise Multivariable Analysis

- MDI: maternal IQ ($p=0.005$), abnormal chromosomes ($p<0.001$), >1 CPB surgery ($p=0.019$)
 - 55% of variability
 - Abnormal chromosome = 25 point decrease MDI
- PDI: maternal IQ ($p=0.002$), abnormal chromosomes ($p=0.015$), CPB time ($p=0.016$)
 - 49% of variability
 - Abnormal chromosome = 15 point decrease PDI

Limitations

- Small patient numbers
 - Focus on complete follow-up
- 1 yr Bayley may not predict school performance
 - “Catch up” development after critical illness
 - 3 yr Bayley, 5 yr ND testing

Subtle hemorrhagic brain injury is associated with neurodevelopmental impairment in infants with repaired congenital heart disease

JTCVS 2009;138:374

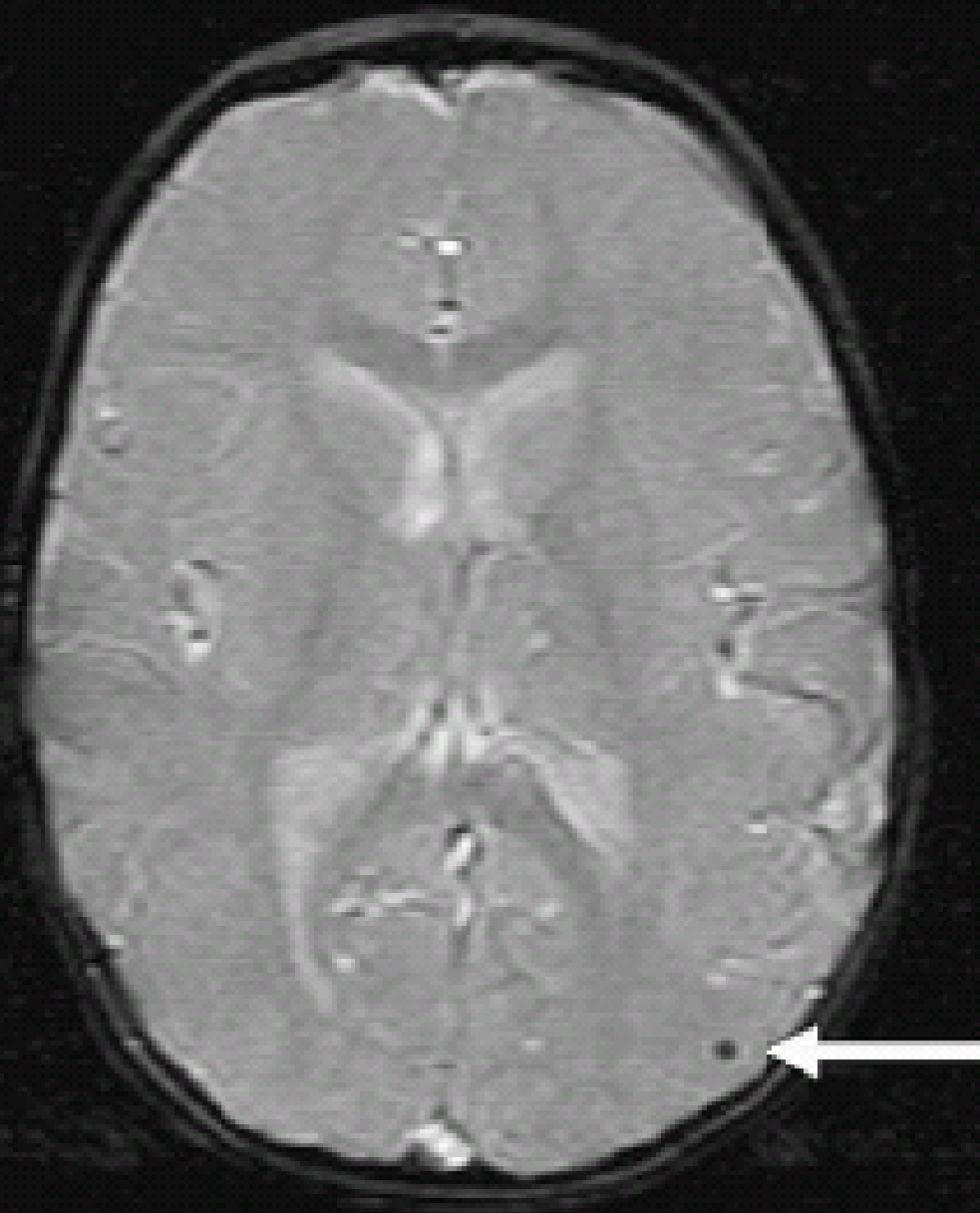
Janet S. Soul, MD, CM,^{a,f} Richard L. Robertson, MD,^{b,g} David Wypij, PhD,^{c,h,k} David C. Bellinger, PhD, MSc,^{a,f} Karen J. Visconti, PhD,^e Adré J. du Plessis, MBChB, MPH,^{a,f} Barry D. Kussman, MBBCh,^{d,i} Lisa A. Scoppettuolo, MS,^{c,k} Frank Pigula, MD,^{e,j} Richard A. Jonas, MD,^{e,j} and Jane W. Newburger, MD, MPH^{c,h}

- 48 two ventricle patients in hematocrit trial
- Less than 9 months of age
- D-TGA, TOF, VSD
- Brain MRI at 1.2 ± 0.2 years
- Correlation with Bayley Scales of Infant Development II

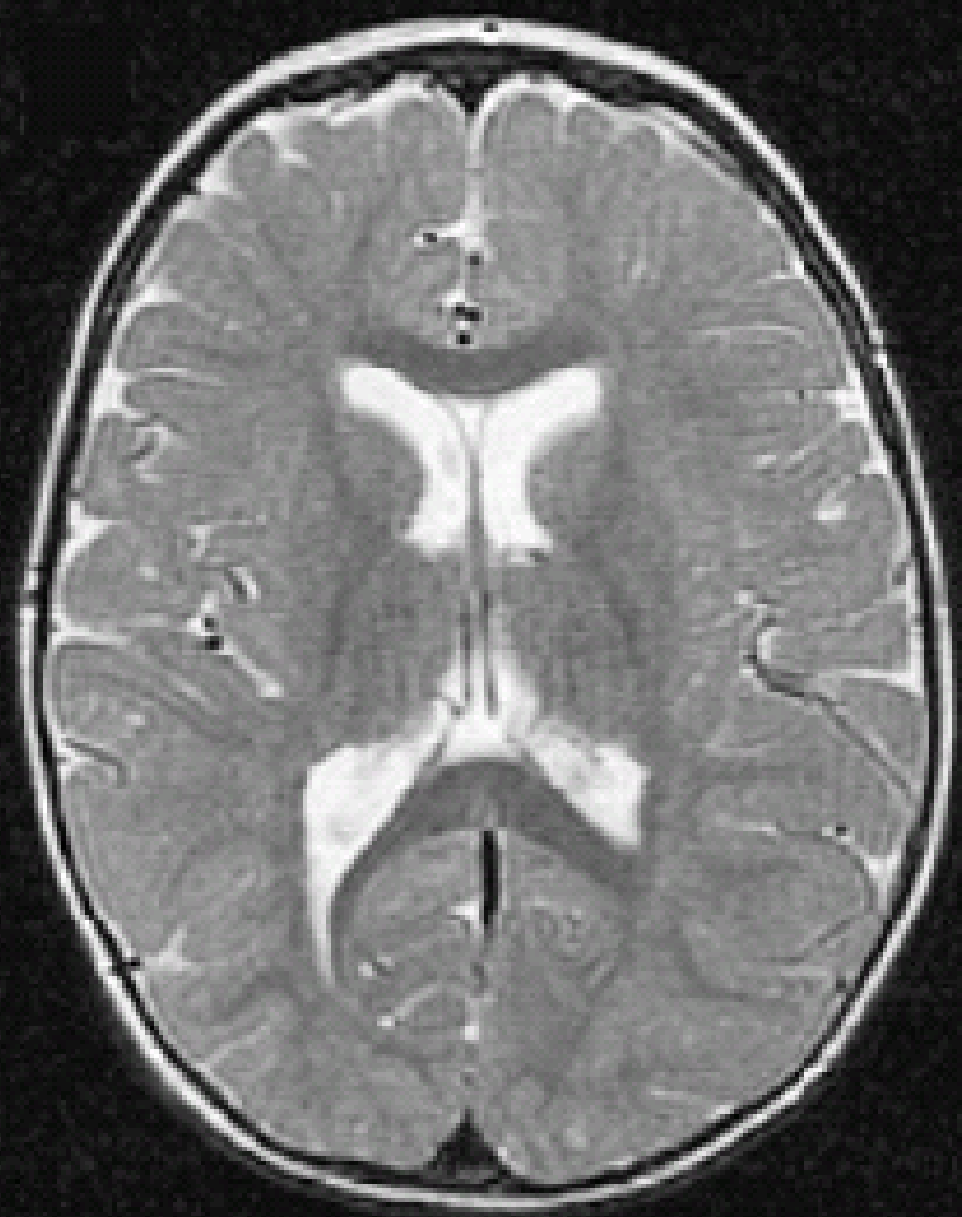
TABLE 2. Qualitative evaluation of magnetic resonance imaging outcomes according to diagnosis group

Variable	ALL (N = 48)	TGA (N = 19)	TOF (N = 20)	VSD (N = 9)	P value*
Age at MRI, mean ± SD (y)	1.2 ± 0.2	1.1 ± 0.1	1.2 ± 0.2	1.3 ± 0.3	.10
	No. with abnormality (%)				
Any acquired or developmental abnormalities	23 (48)	5 (26)	11 (55)	7 (78)	.03
Focal or multifocal abnormalities	19 (40)	4 (21)	9 (45)	6 (67)	.06
Focal infarction or atrophy	1 (2)	1 (5)	0	0	.58
Brain mineralization/hemosiderin	18 (38)	3 (16)	9 (45)	6 (67)	.03
Diffuse abnormalities	3 (6)	1 (5)	1 (5)	1 (11)	.79
Delayed myelination	1 (2)	0	0	1 (11)	.19
Ventriculomegaly	1 (2)	1 (5)	0	0	.58
T2 hyperintensities/gliosis/periventricular leukomalacia	2 (4)	0	1 (5)	1 (11)	.49
Developmental abnormalities	4 (8)	0	3 (15)	1 (11)	.23
Major malformation	0	0	0	0	1.0
Minor malformation	4 (8)	0	3 (15)	1 (11)	.23

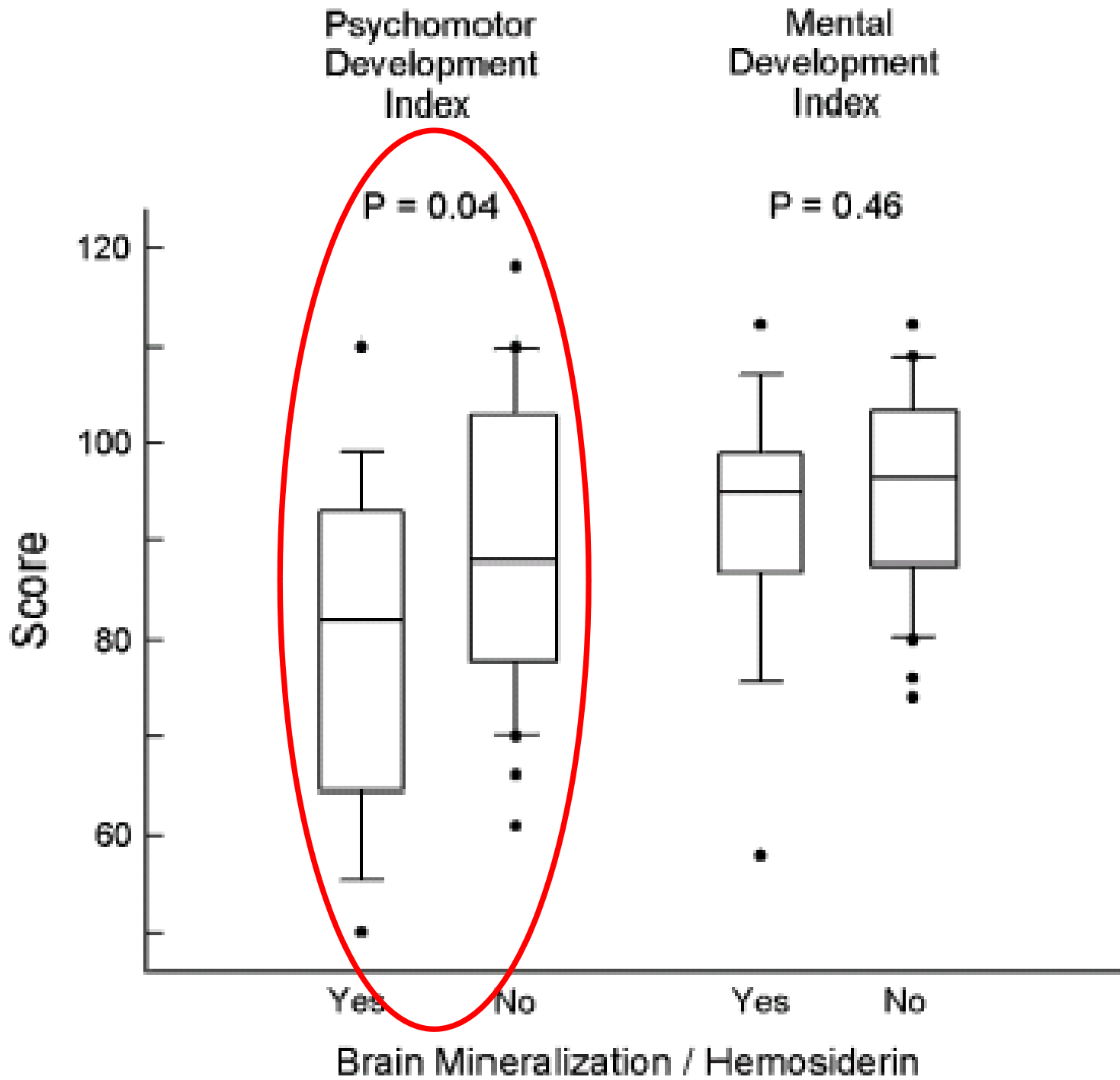
- 18 patients (38%) had brain mineralization/hemosiderin on susceptibility weighted images
- This was associated with lower PDI (80 ± 17 vs. 90 ± 15 , $p=0.04$)
- Very low incidence of focal or diffuse abnormalities on T1 or T2 weighted images



A

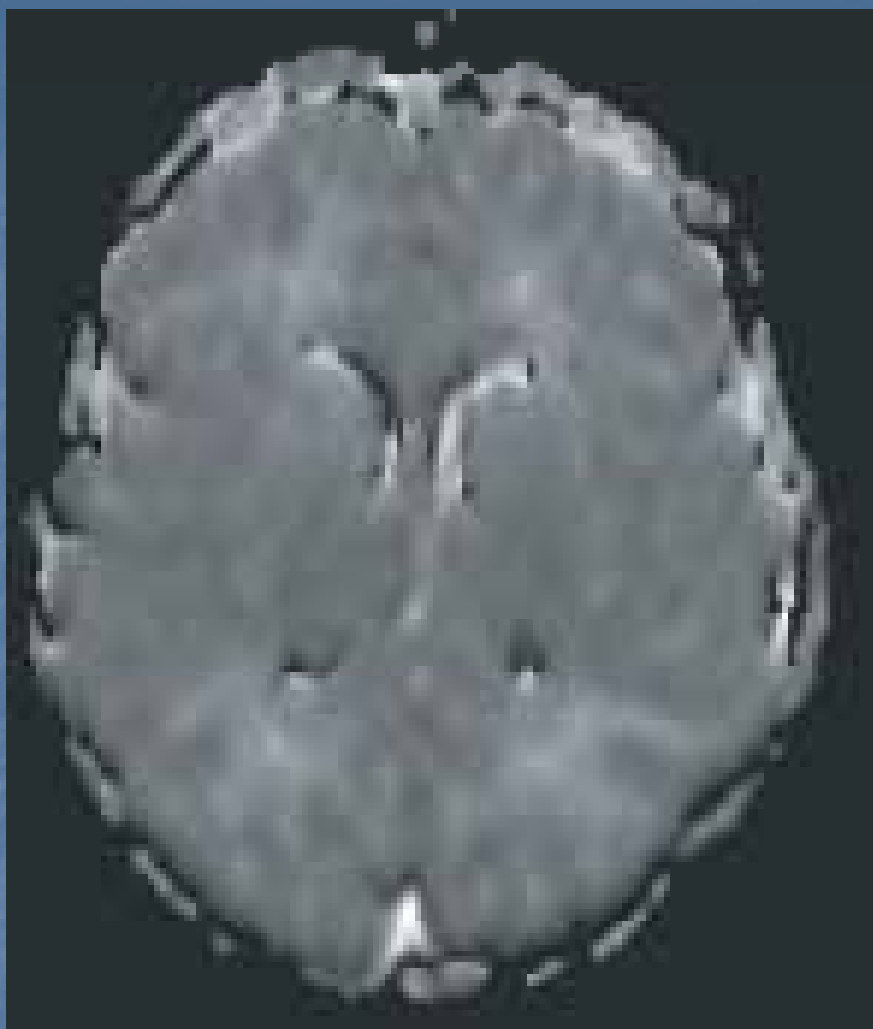


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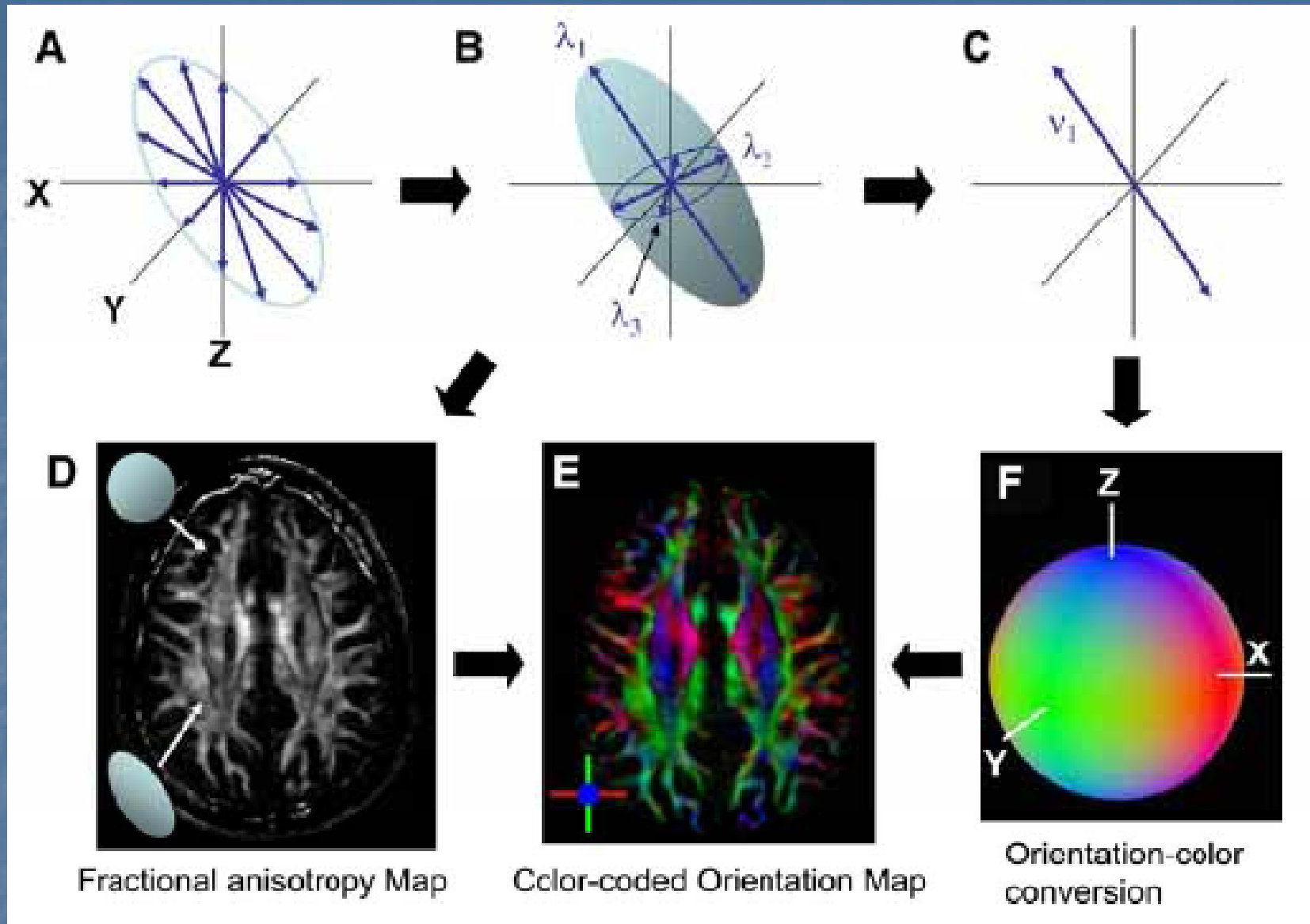


Quantitative MRI

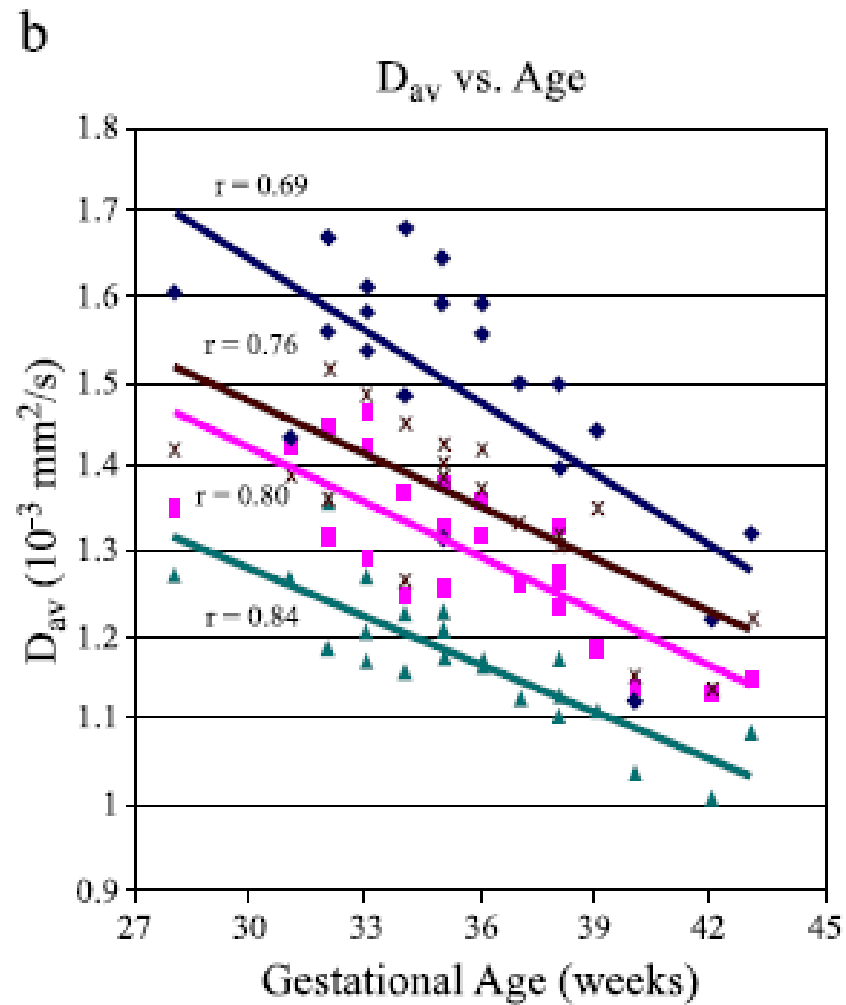
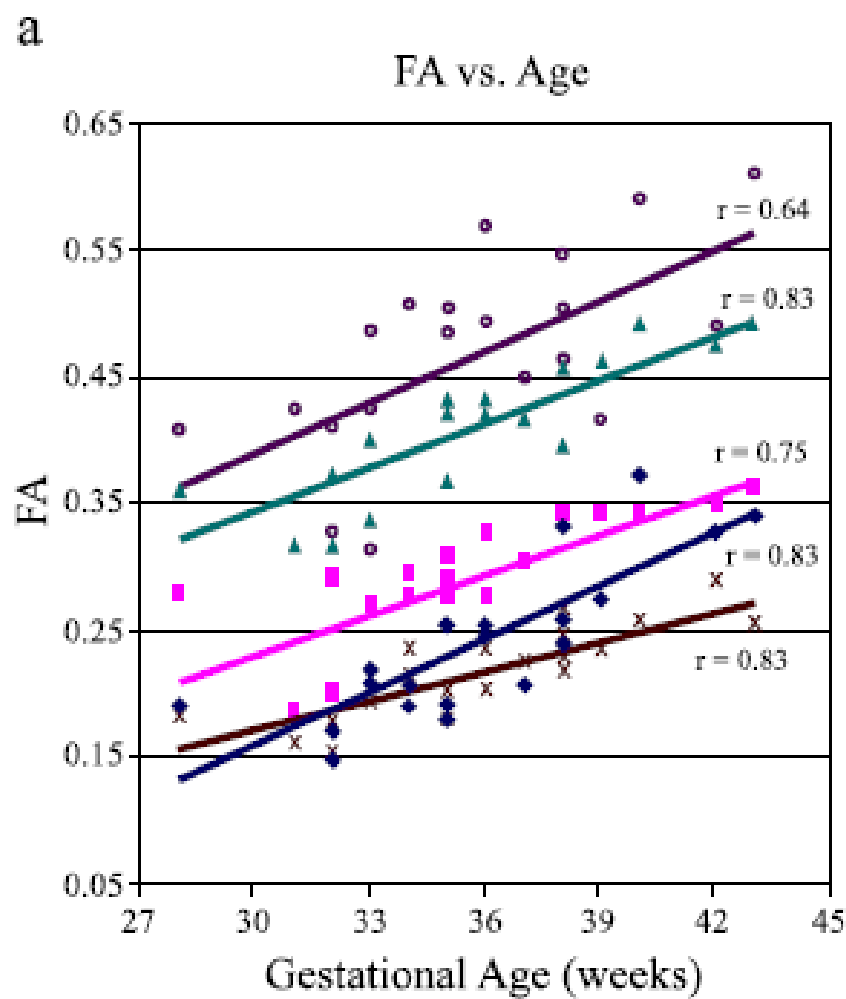
- Search for explanations as to why PDI lags behind MDI
 - Injured vs. non-injured brain
 - Effects of anesthetics, cyanosis, repeat surgery
- Diffusion weighted imaging
 - Fractional anisotropy
 - Average diffusion coefficient
 - Known changes with myelination
- MR spectroscopy
 - N-acetylaspartate to choline ratio increases with neuronal development, myelination
- Volumetrics
 - Growth of white/gray matter, total brain volume
 - ?White matter volumes lower with injured white matter, leading to lower PDI?
- Diffusion Tensor Tractography
 - Track development of fiber tracts



Dav map: average diffusion distance of water molecules in magnetic field per pixel



FA: fractional anisotropy or shape of water diffusion ellipsoid in magnetic field. From Mori
Neuron 2006;51:527



■ Anterior Limb IC
 ▲ Posterior Limb IC
 ◆ Centrum Semiovale
 × External Capsule
 ○ Splenium

FA increases and D_{av} decreases with brain maturation. Partridge Neuroimage 2004;22:1302

Pyramidal Tract Maturation after Brain Injury in Newborns with Heart Disease

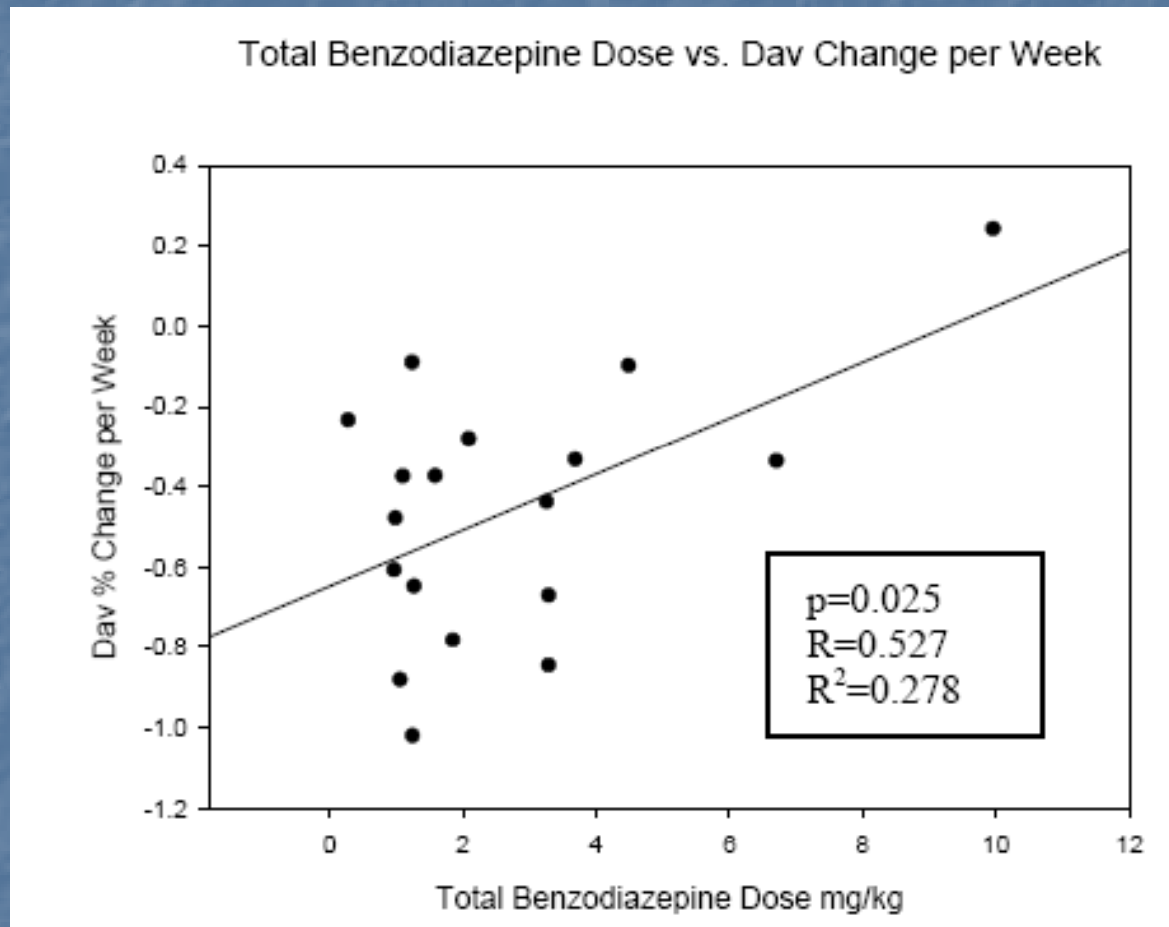
Savannah C. Partridge, PhD,^{1,2} Daniel B. Vigneron, PhD,¹ Natalie N. Charlton,¹ Jeffrey I. Berman, PhD,¹ Roland G. Henry, PhD,¹ Pratik Mukherjee, MD, PhD,¹ Patrick S. McQuillen, MD,³ Tom R. Karl, MD,^{3,4} A. James Barkovich, MD,^{1,3,5} and Steven P. Miller, MD^{3,5,6}

Table 3. Maturation Changes (%) in Diffusion Tensor Imaging Values for the Pyramidal Tracts Measured by the Diffusion Tensor Tractography and Manual Region of Interest Methods

DTI Parameter	Measurement Technique	No Injury	Postoperative Injury	Preoperative Injury	<i>p</i>
FA	DTT: whole tract, median (min, max)	4.43 (-0.35,16.9)	2.44 (-2.2, 8.2)	0.90 (-2.4, 3.7)	0.02 ^a
	Manual ROI: centrum semiovale, median (min, max)	-0.94 (-19.4,52.1)	6.33 (-14.2,30.2)	3.97 (-15.9,16.2)	0.8
	Manual ROI: PLIC, median (min, max)	4.27 (-4.5,27.6)	1.28 (-1.1,12.4)	-0.81 (-2.8,7.3)	0.1
D _{av}	DTT: whole tract	-1.99 (-13.4,0.9)	-2.94 (-6.6, -0.4)	-1.00 (-5.3,1.0)	0.2
	Manual ROI: centrum semiovale, median (min, max)	-4.00 (-12.6,4.0)	-6.42 (-13.2,-2.8)	-0.12 (-4.4, 8.7)	0.2
	Manual ROI: PLIC, median (min, max)	-1.61 (-5.6,-0.5)	-2.50 (-9.0,0.1)	-0.16 (-2.8,3.0)	0.1

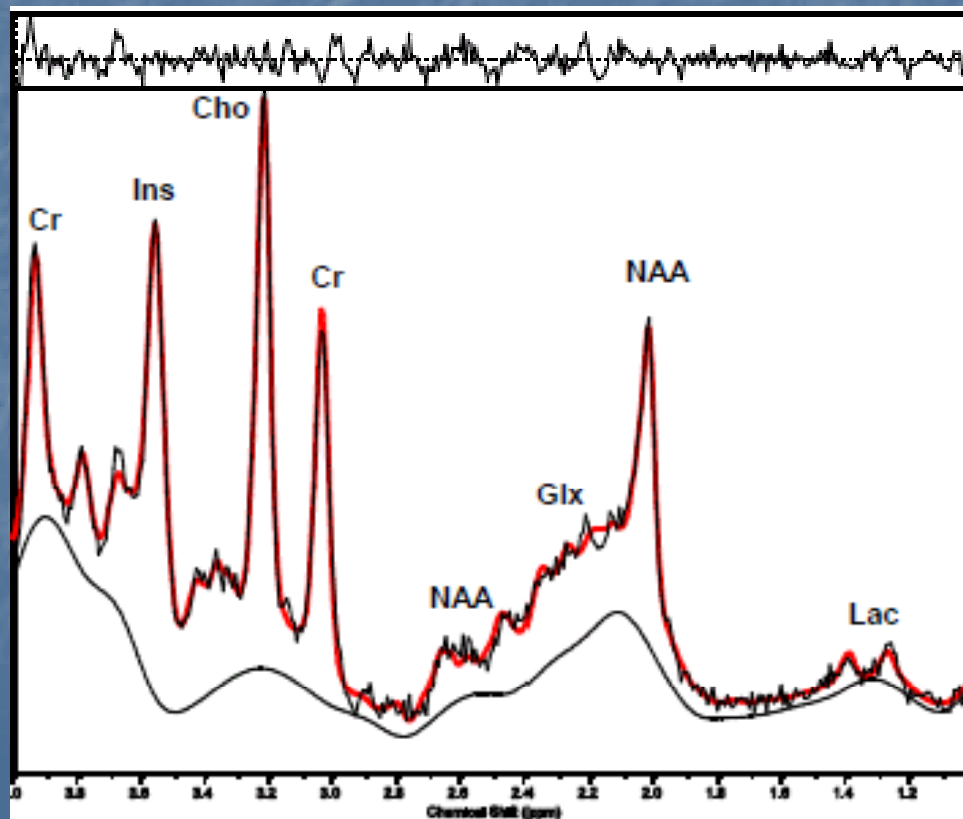
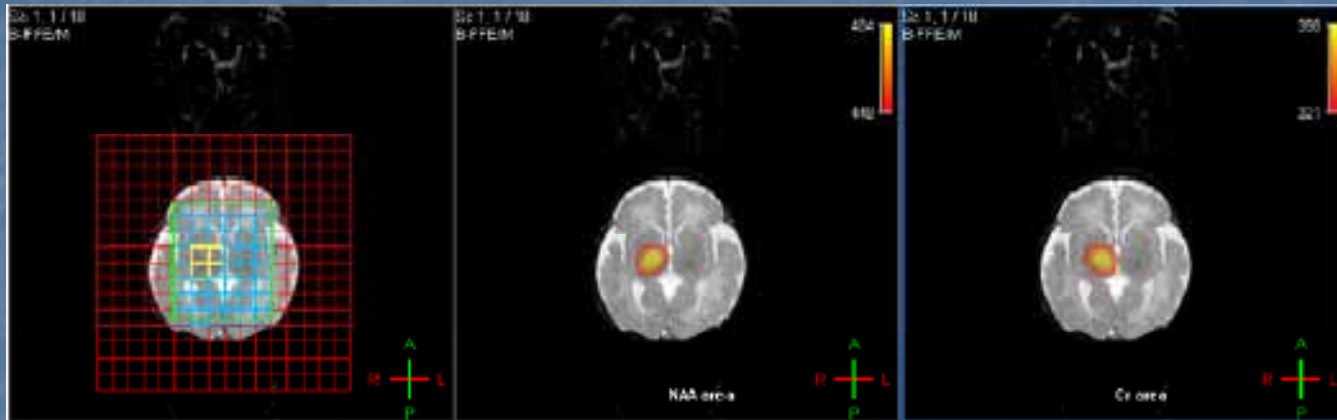
Conclusion: Brain maturation is impaired in injured areas after neonatal CHD surgery.

Anesthetics and Brain Maturation: Average Diffusion Coefficient

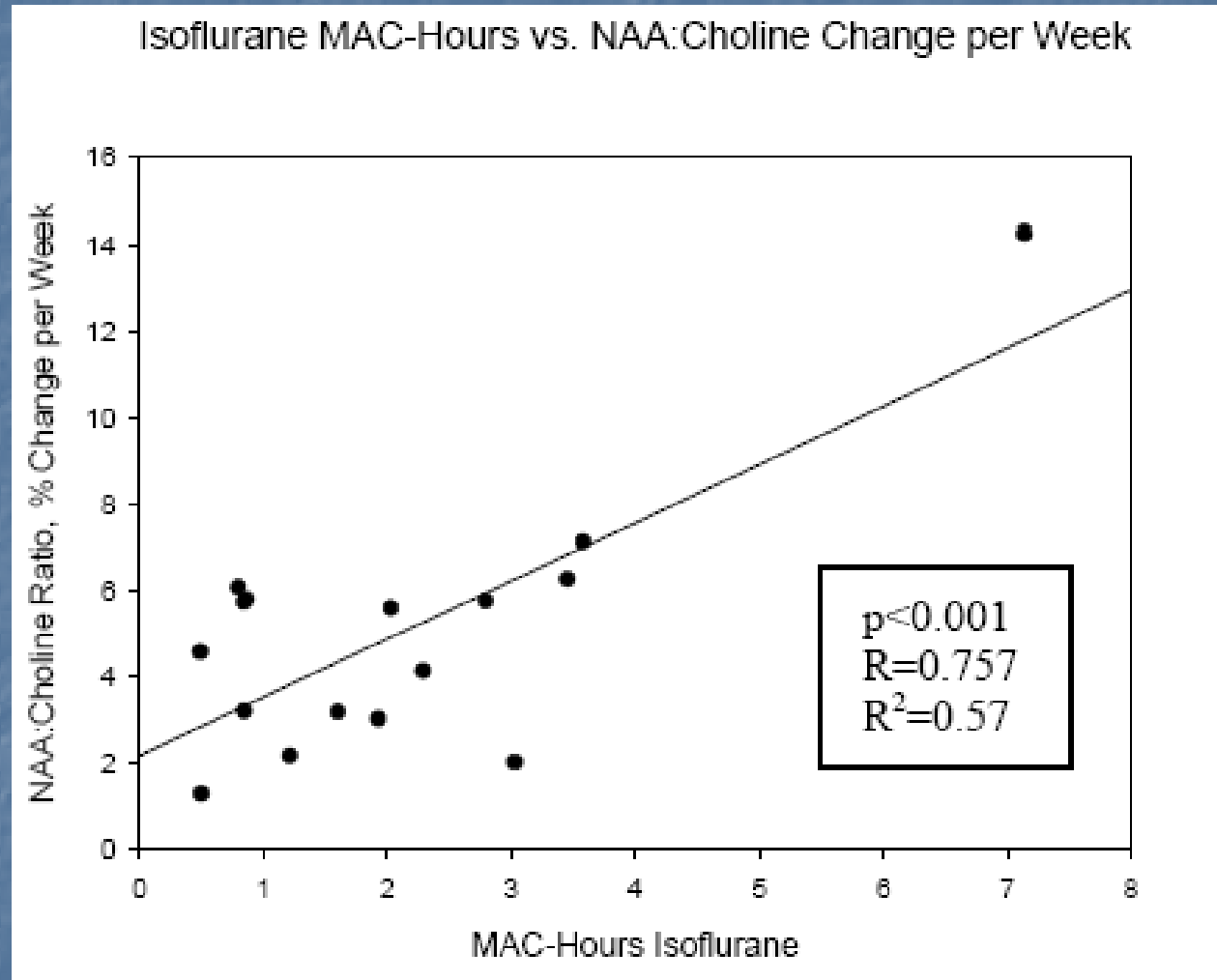


18 2-ventricle patients with normal SpO_2 , rSO_2 , cardiac output.
IARS Abstract ISS2, March 2010

Magnetic Resonance Spectroscopy



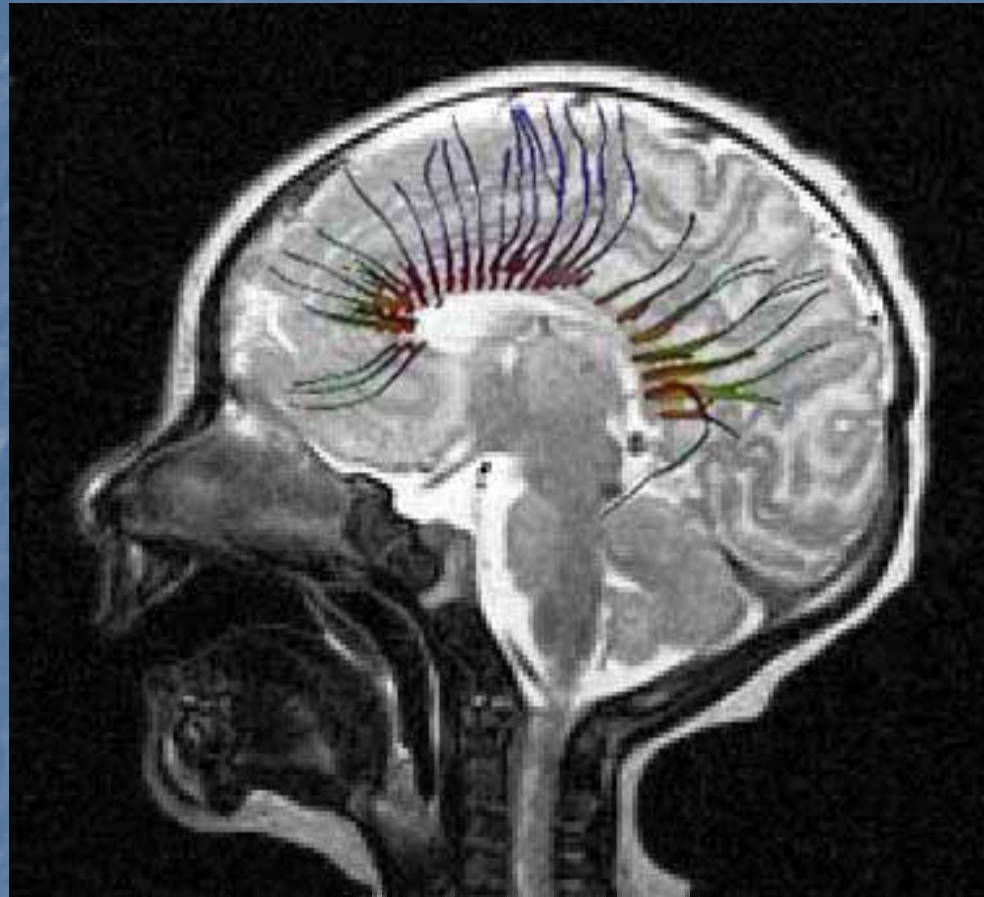
Anesthetics and Brain Maturation: MR Spectroscopy



18 2-ventricle patients with normal SpO₂, rSO₂, cardiac output

IARS Abstract ISS2, March 2010

Diffusion Tensor Tractography



Preop TGA: Corpus callosum, green = AP fibers, blue superior-inferior, red right to left

Volumetric Measurements



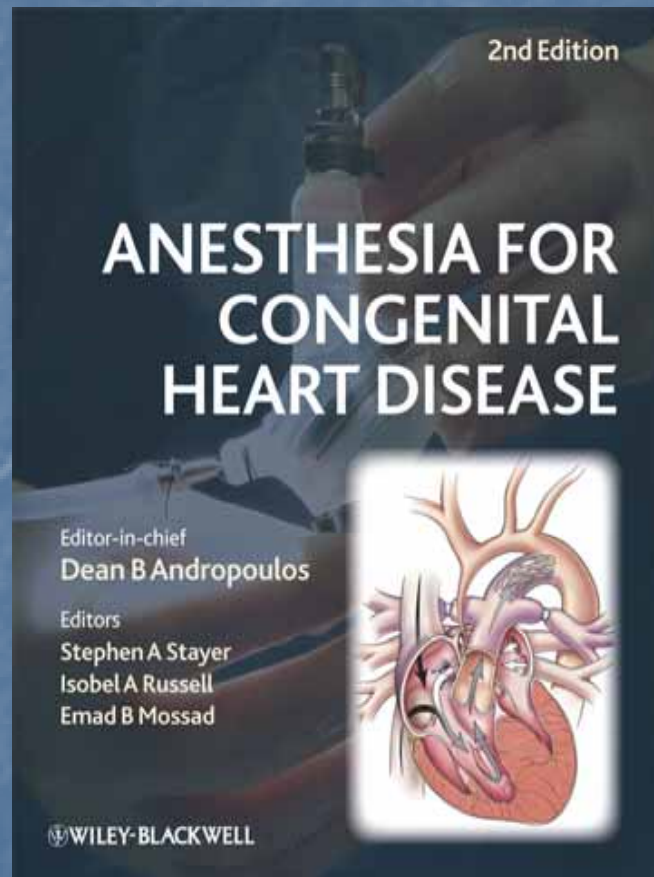
Measuring, either manually or with automated techniques, the volumes of gray/white matter, CSF, total brain volume, and other structures: correlate with later neurodevelopmental outcomes.

Nishida et al. *NeuroImage* 2006:32:1041

Conclusions

- MRI studies demonstrate structural and biochemical immaturity of the neonatal brain in CHD
 - Brain immaturity correlates with brain injury
- Standard MRI changes after surgery are mild and more data is needed to correlate with 1 yr and later outcomes
 - Hemosiderin deposits from remote small hemorrhage/ischemic areas affect PDI
- Quantitative MRI an important tool
 - Brain growth, myelination, function
 - Will assess correlation with later outcomes
 - Particularly in search for etiology of PDI < MDI

Anesthesia for Congenital Heart Disease 2nd Edition



Editor-in-Chief Dean B. Andropoulos

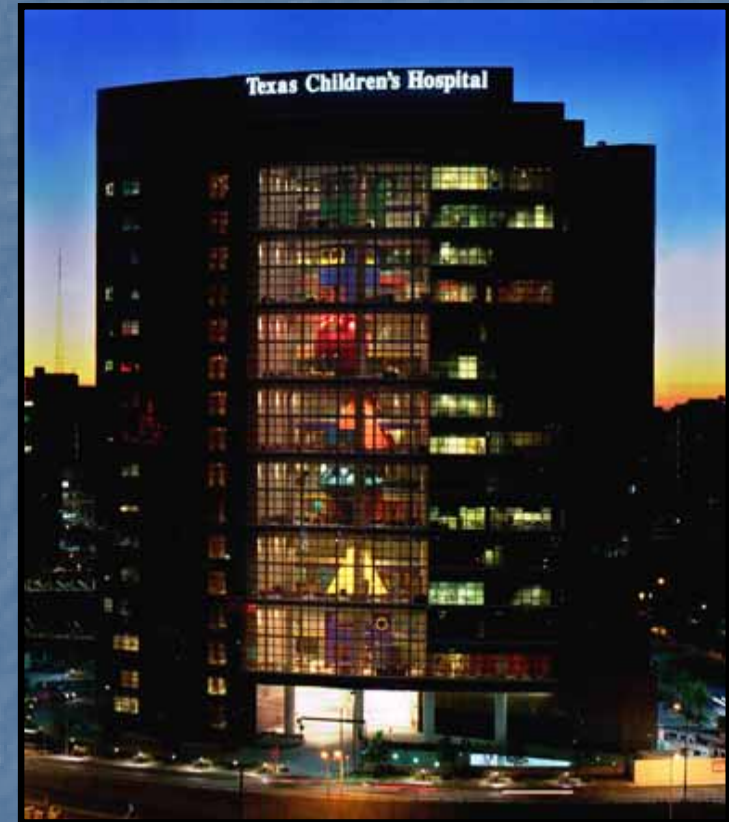
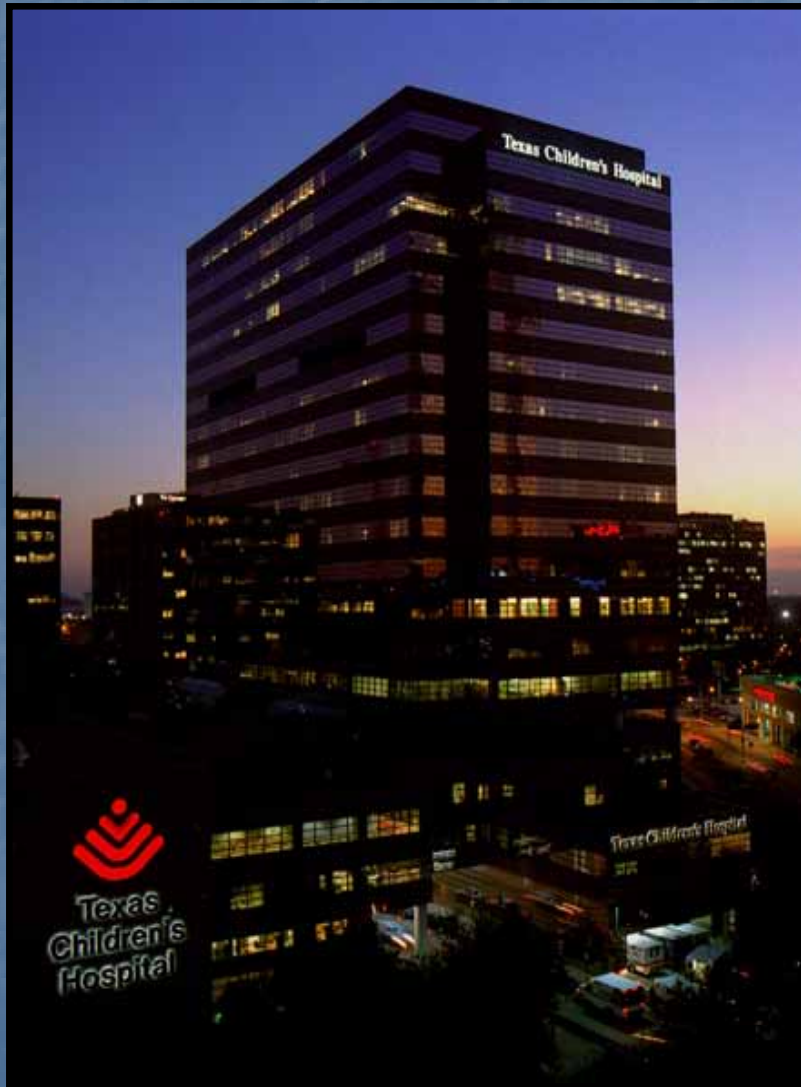
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and Emad B. Mossad

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