

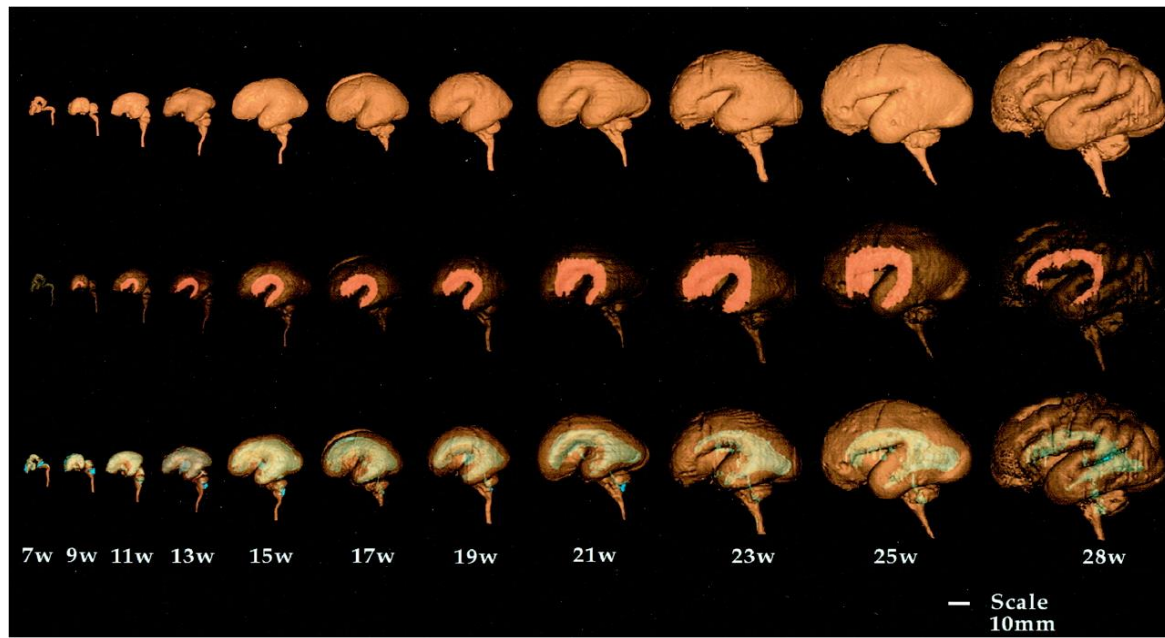


Corticale ontwikkeling bij foetus met aangeboren hartafwijkingen

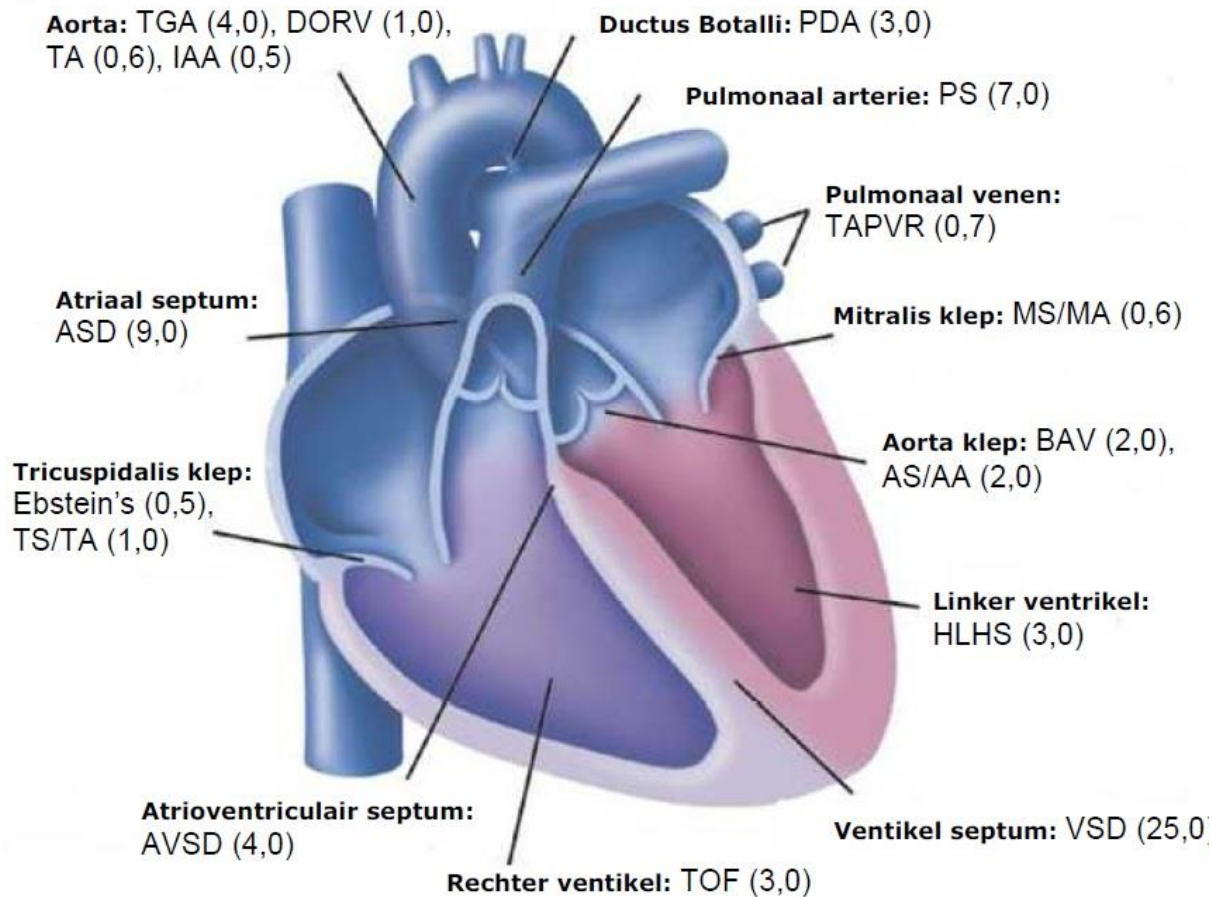
BEN symposium 2018

Sheila Everwijn

Arts prenatale diagnostiek/Promovendus



Incidentie CHD



Figuur 1: Prevalentie verschillende hartafwijkingen per 10.000 geboorten

Shift Hart → Brein

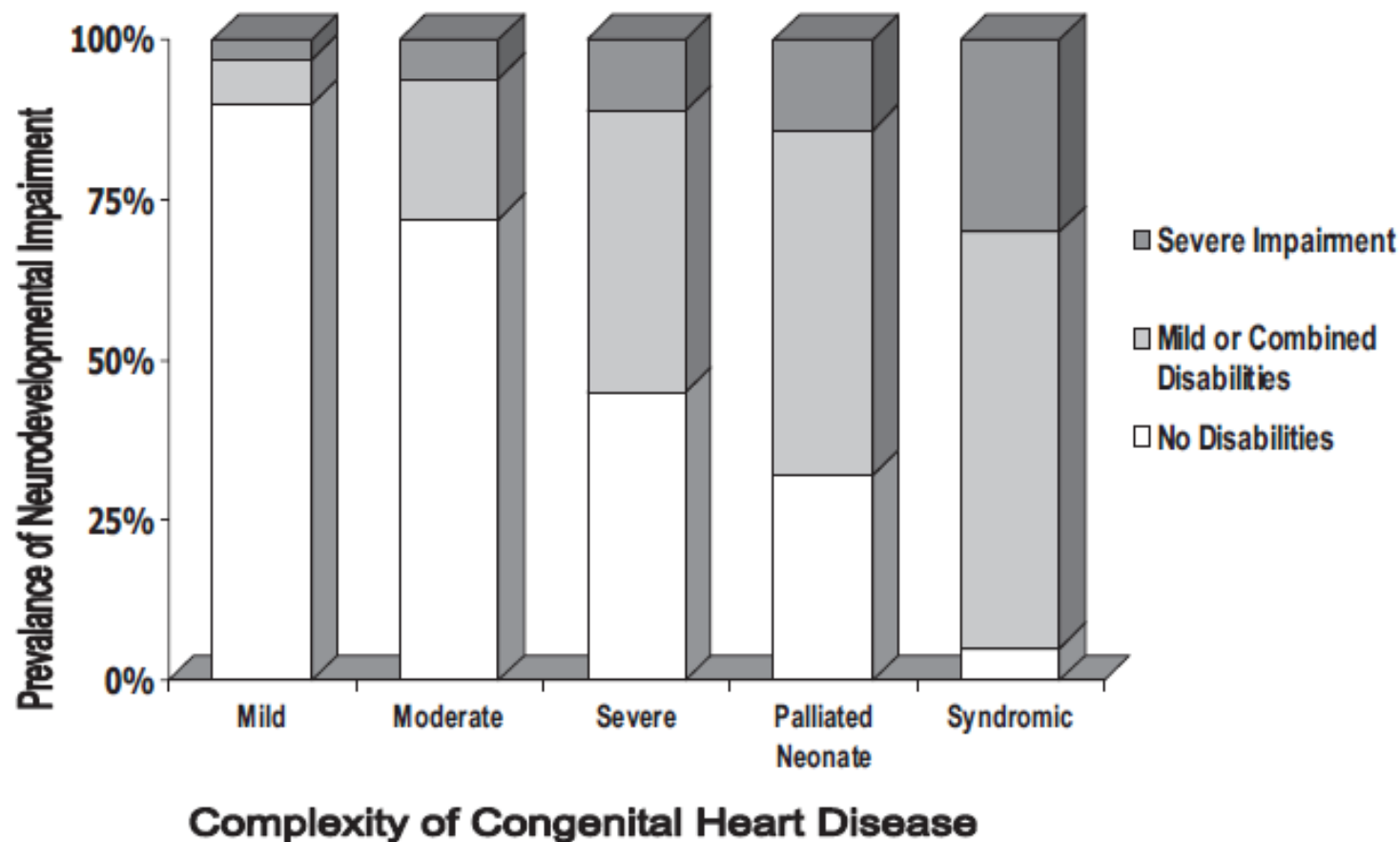
Marino – Neurodevelopmental outcomes in children with CHD: evaluation and management

Circulation 2012 – American Heart Association

At risk for developmental delay op gebied van:

1. Intelligentie
2. Academische prestaties
3. Taal(begrip, spraak)
4. Visueel
5. Executieve functies
6. Fijne en grove motoriek
7. Psychosociale aanpassing

Shift Hart -> Brein



Adolescents With d-Transposition of the Great Arteries Corrected With the Arterial Switch Procedure

Neuropsychological Assessment and Structural Brain Imaging

Inclusie:

- 139 TGA casus
- 55 controles

Methoden:

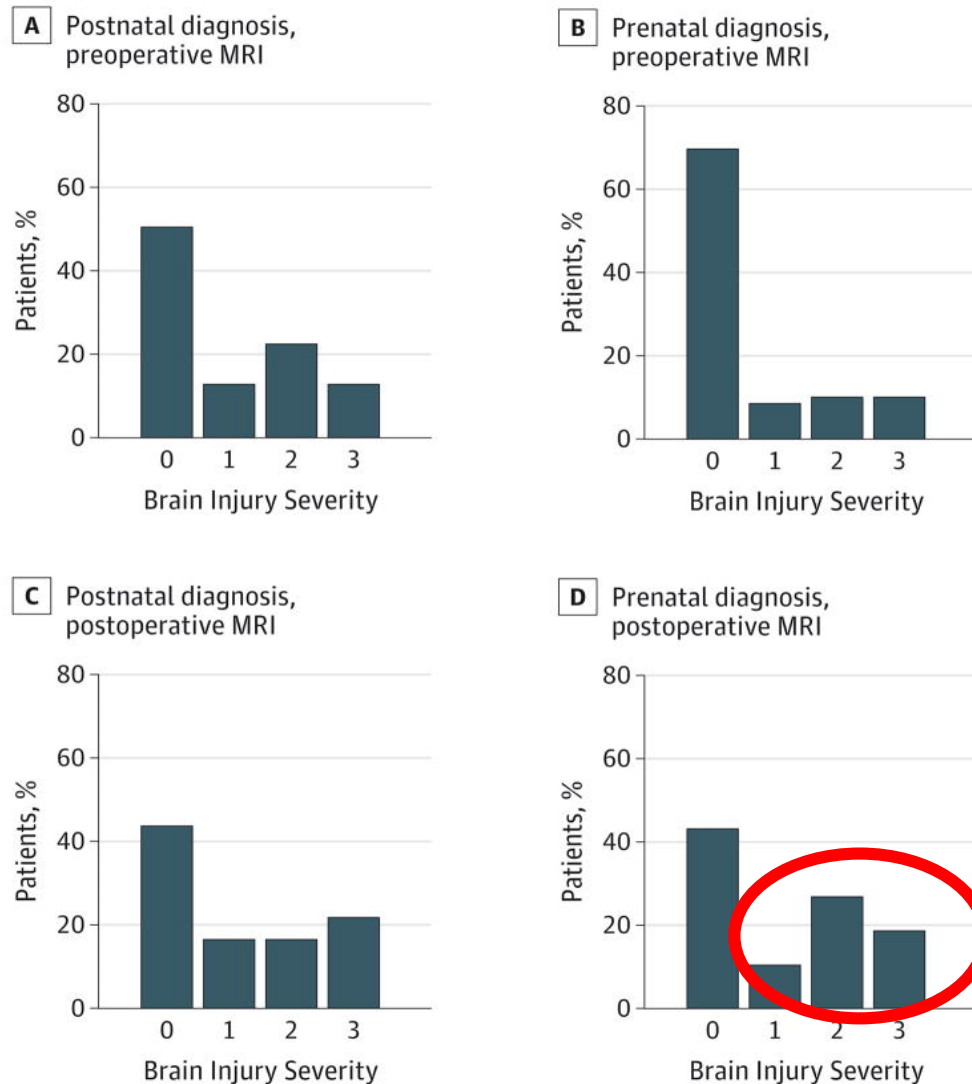
Neuropsychologische testen en MRI op leeftijd 16.1 jaar

Conclusie:

- Lagere scores op academische prestaties, geheugen, aandacht, planning&uitvoering en sociale vaardigheden.
- Meer dan 65% heeft professionele hulp nodig gehad op het gebied van school/werk.
- 12 kinderen(9%) nam medicatie voor ADHD.
- 1/3 van de onderzochte patienten liet structurele breinafwijkingen zien op MRI.

Association of Prenatal Diagnosis of Critical Congenital Heart Disease With Postnatal Brain Development and the Risk of Brain Injury

Figure 1



Peyvandi et al. JAMA Pediatrics. April 2016

Hypothese : oorzaken van breinschade bij CHD

Factoren die van invloed kunnen zijn (Majnemer 2009)

- Preoperatief
 - Type CHD / geboortegewicht/ haemodynamische instabiliteit
- Peroperatief
 - OK-tijd / thrombo-embolische complicaties / operatie techniek / leeftijd neonaat
- Postoperatief
 - Persisterende cyanose / hemodynamische instabiliteit / complicaties
- Prenataal??



PRENATAL DIAGNOSIS

[Explore this journal >](#)

Review

Fetal brain imaging in isolated congenital heart defects – a systematic review and meta-analysis

Fenna A. R. Jansen , Sheila M. P. Everwijn, Robert Scheepjens, Theo Stijnen, Cacha M. P. C. D. Peeters-Scholte, Jan M. M. van Lith, Monique C. Haak

First published: 19 June 2016 [Full publication history](#)

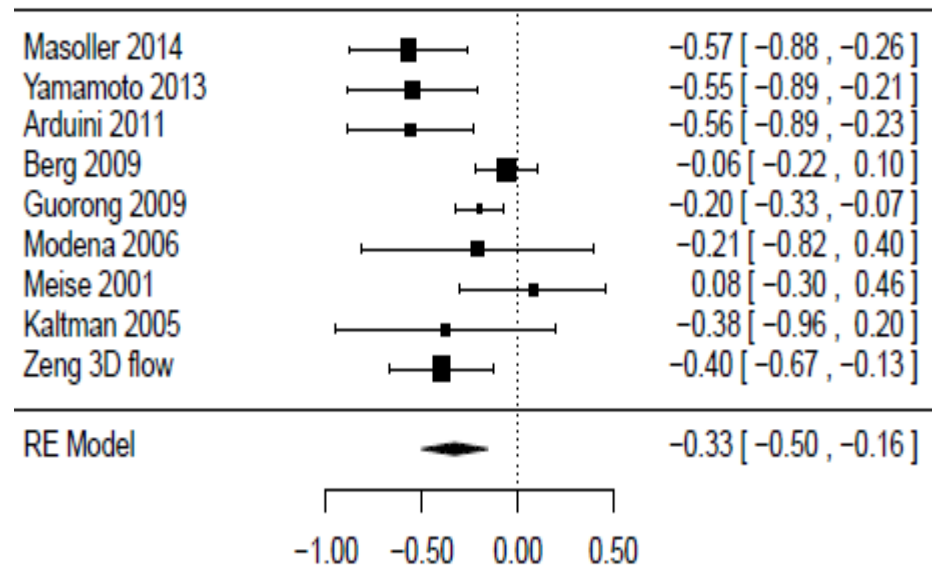
- Inclusion MRI or ultrasound data
- 34 artikelen geïnccludeerd
- Analyse van HC-groei, structurele breinafwijkingen, flows



-Gecombineerde CHD –
effect richting
Brainsparing

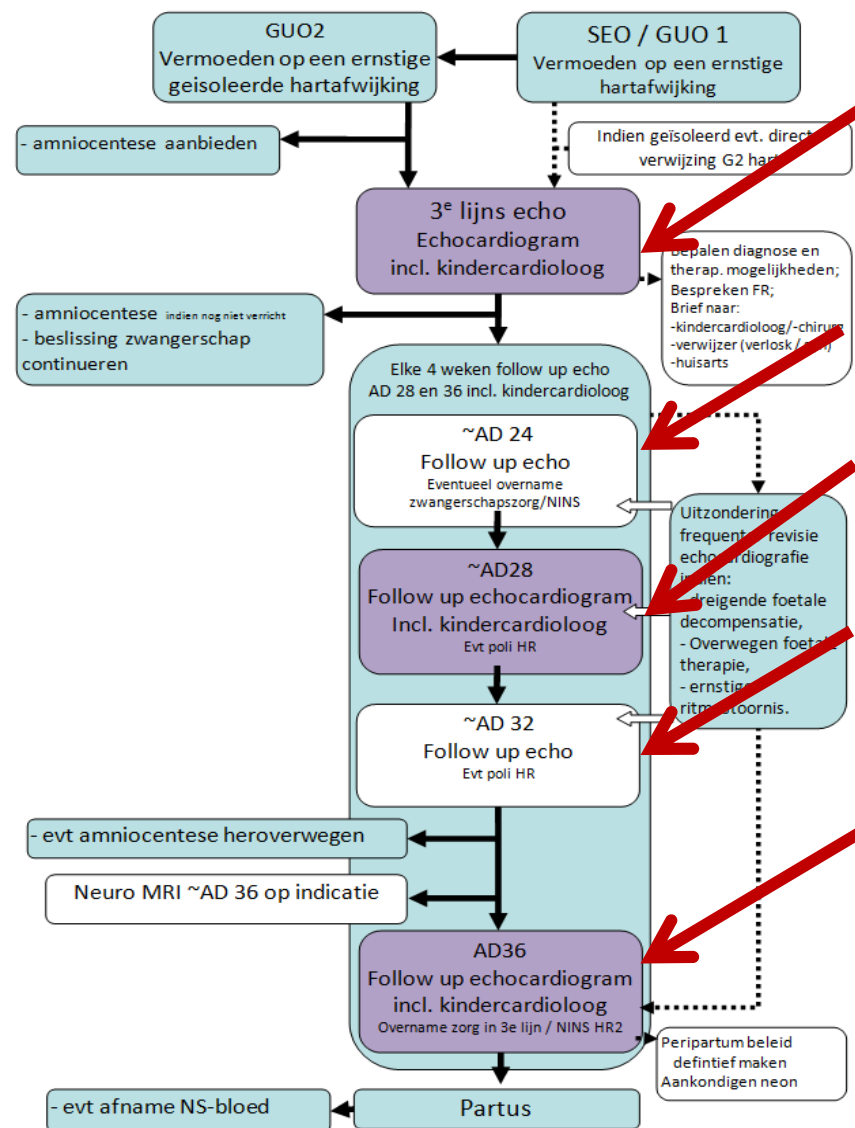
-Brainsparing bij IUGR =
beschermend effect

-Tekenen van brein
schade?



Bias in literatuur PRe natale hersenschade

- Niet opeenvolgende casus
- Selectiebias waarbij alleen ernstige casus worden geïncludeerd
- Niet meerdere metingen per zwangerschap



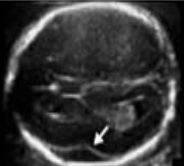
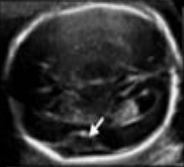
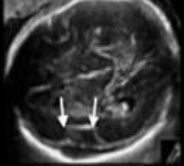
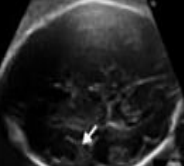
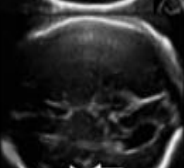
Grade	Definition & diagram	Example
1	Shallow indentation 	
2	Obtuse angular shape  	
3	Acute angles, < 50% operculization 	
4	≥ 50% operculization 	
5	Complete operculization 	

Figure 2 Cortical grading of the Sylvian fissure.

Ultrasound Obstet Gynecol 2010; 36: 700–708

Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.7705

Grade and symmetry of normal fetal cortical development: a longitudinal two- and three-dimensional ultrasound study

L. R. PISTORIUS*, P. STOUTENBEEK*, F. GROENENDAAL†, L. DE VRIES†, G. MANTEN*, E. MULDER* and G. VISSER*

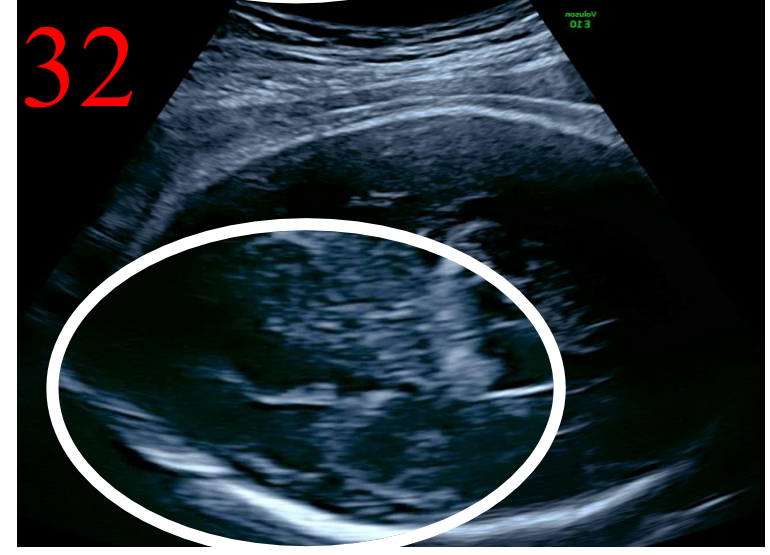
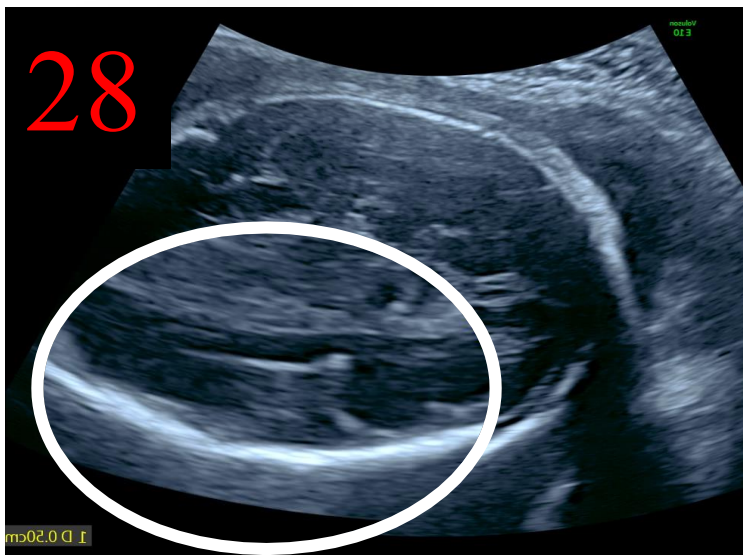
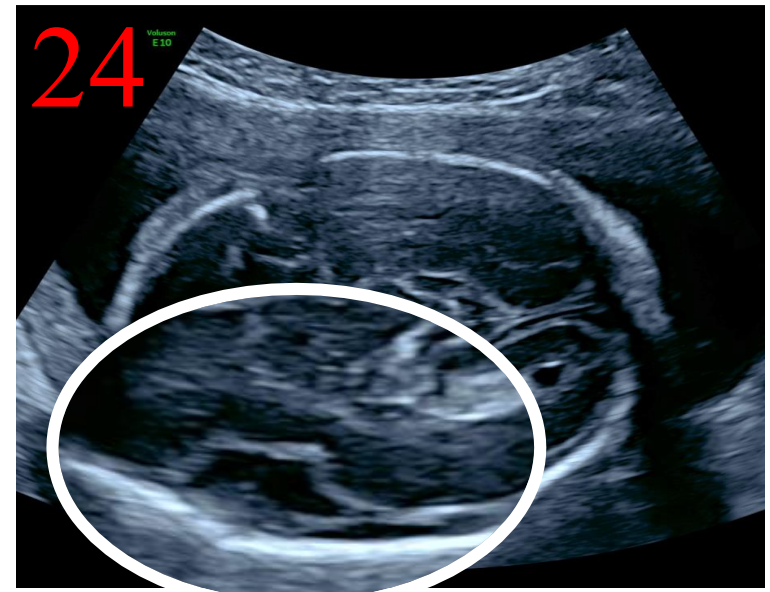
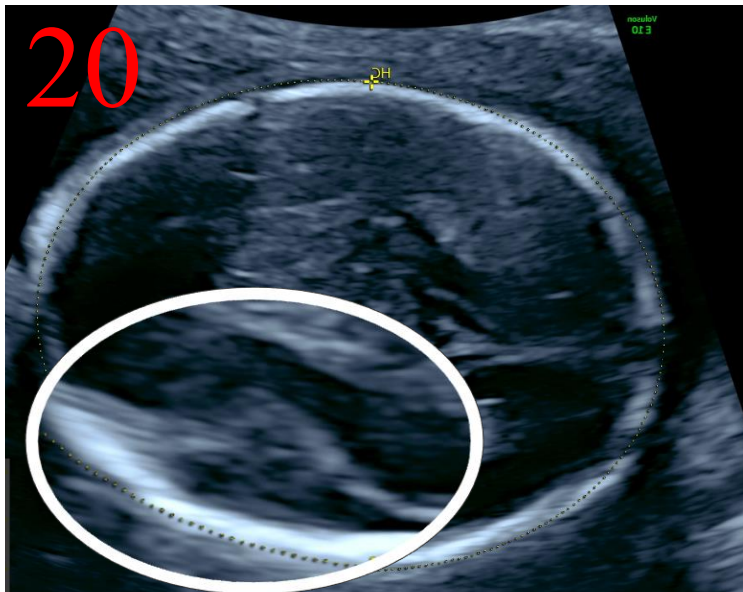
Departments of *Obstetrics and Gynaecology and †Neonatology, University Medical Centre Utrecht, Utrecht, The Netherlands

KEYWORDS: brain; cerebral cortex; fetus; longitudinal studies; prenatal; second trimester; third trimester; ultrasonography

Stadiëring fissuur van Sylvius

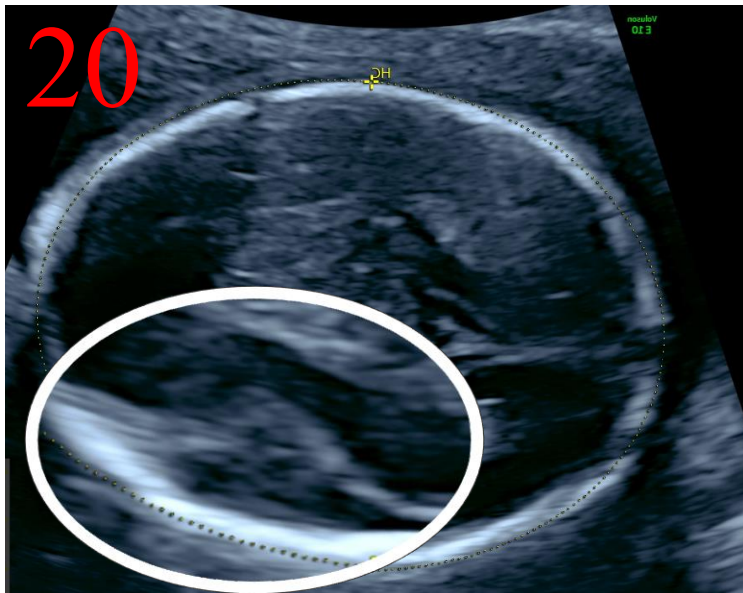
					
Geen	Ondiepe indentatie	Hoekige vorm	< 50% Opercularisatie	≥ 50% Opercularisatie	Compleet
0	1	2	3	4	5

Fissuur van Sylvius



Grade	Definition & diagram
1	Shallow indentation 
2	Obtuse angular shape 
3	Acute angles, < 50% operculization 
4	≥ 50% operculization 
5	Complete operculization 

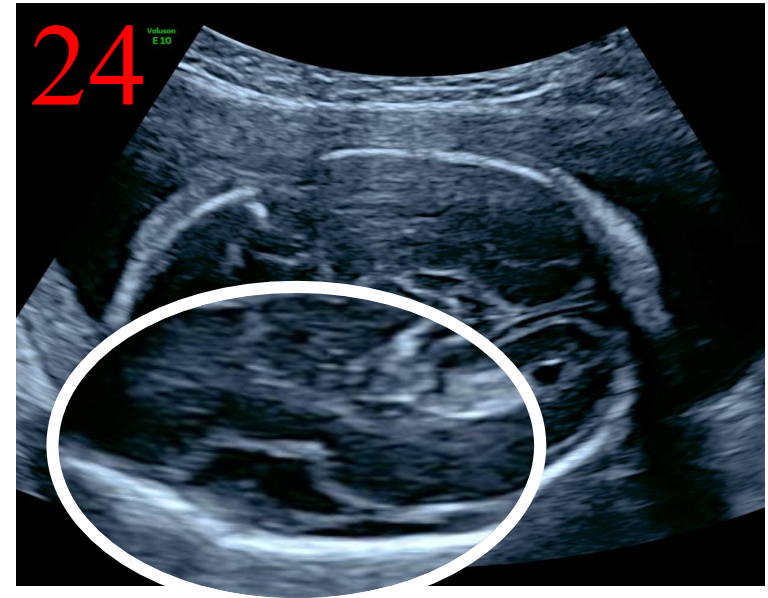
Fissuur van Sylvius



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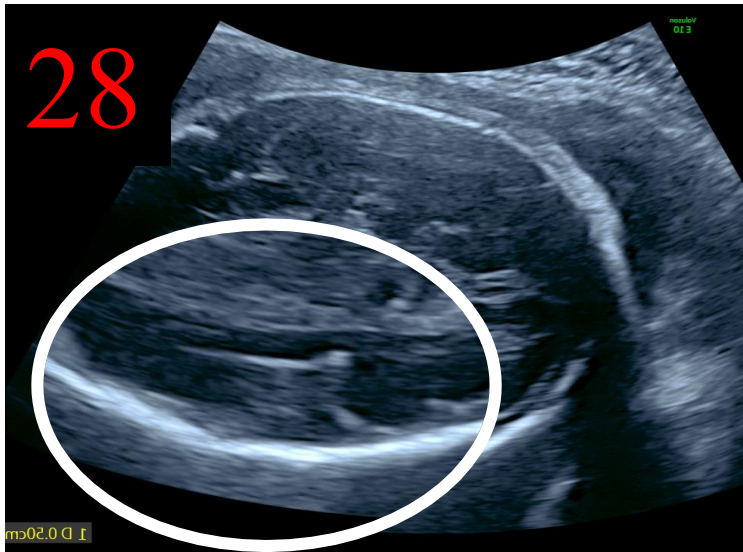
Fissuur van Sylvius

Grade	Definition & diagram
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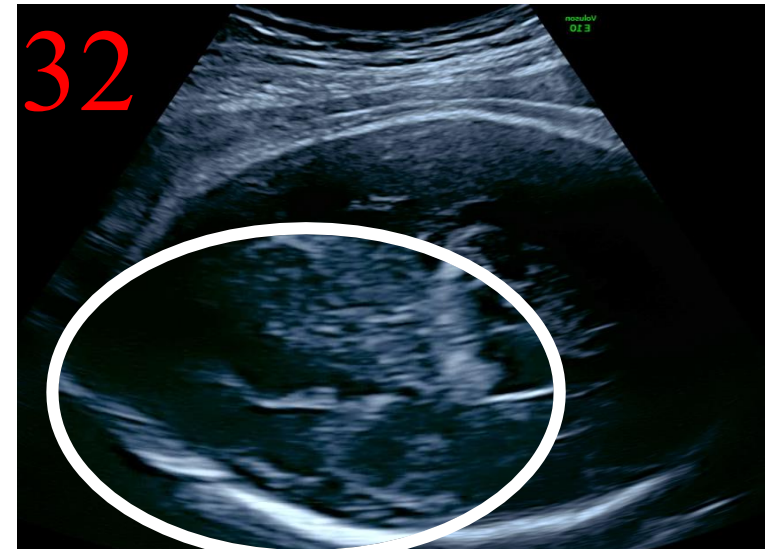
Fissuur van Sylvius

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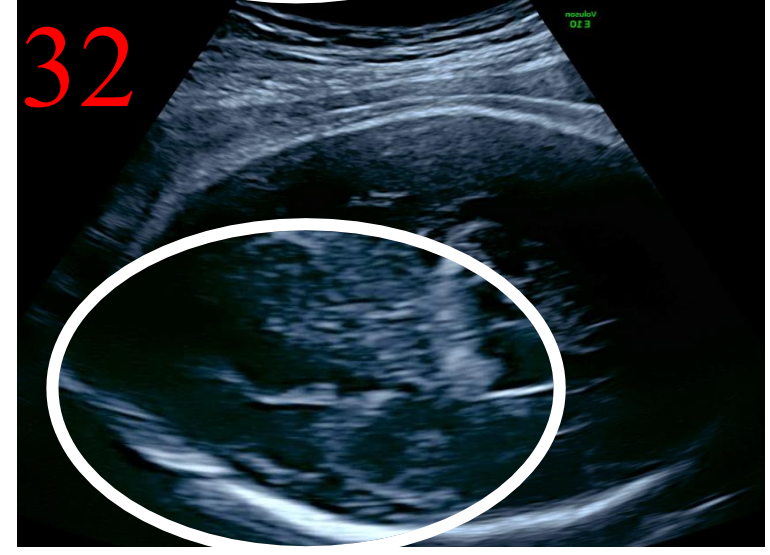
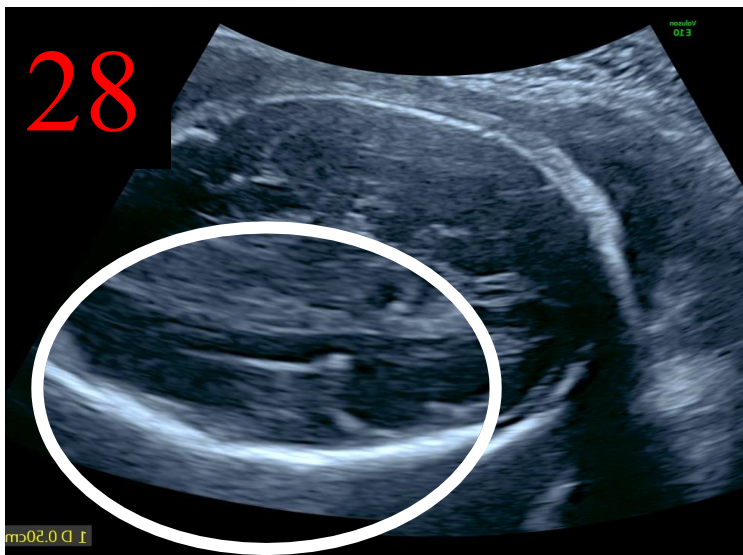
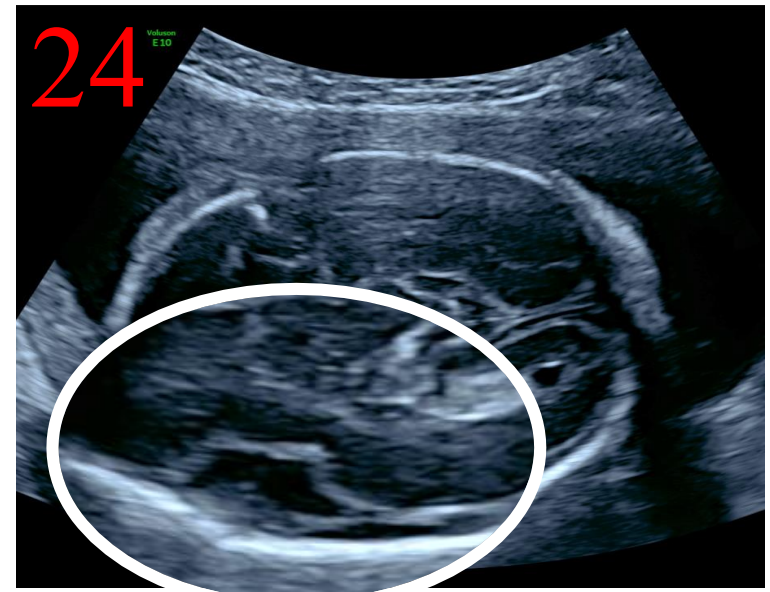
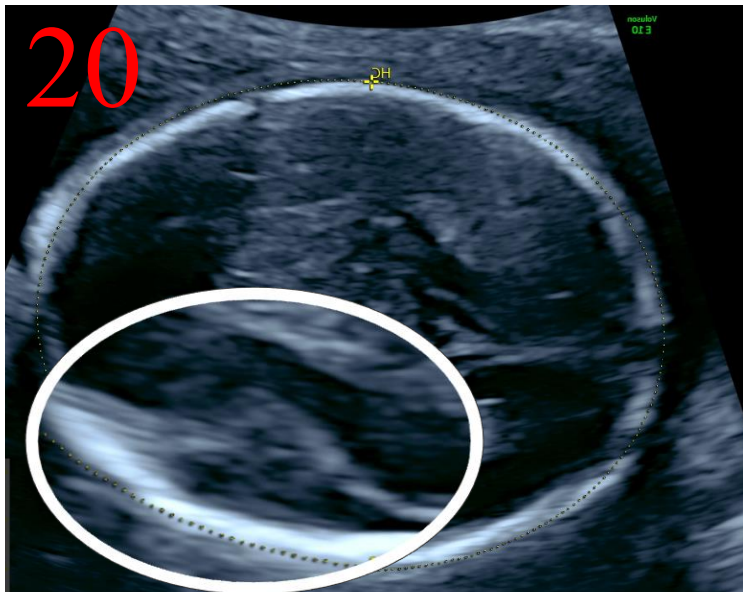


Fissuur van Sylvius

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Fissuur van Sylvius



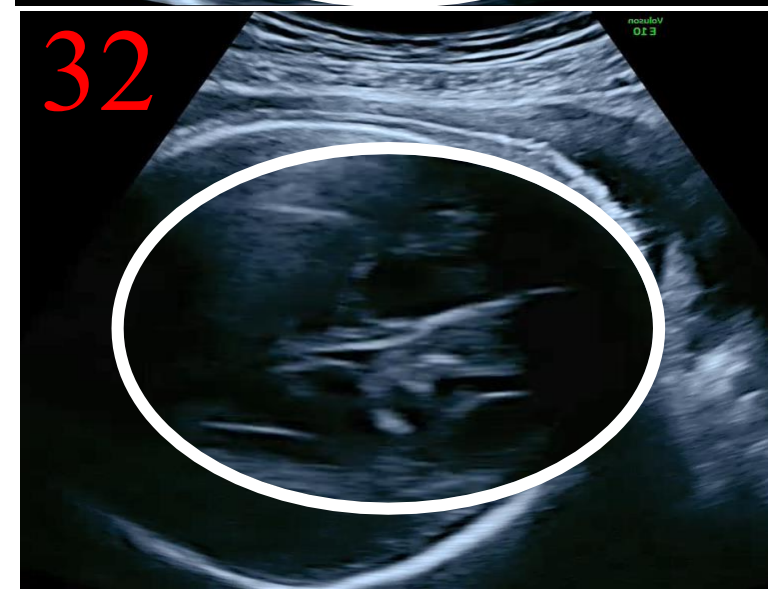
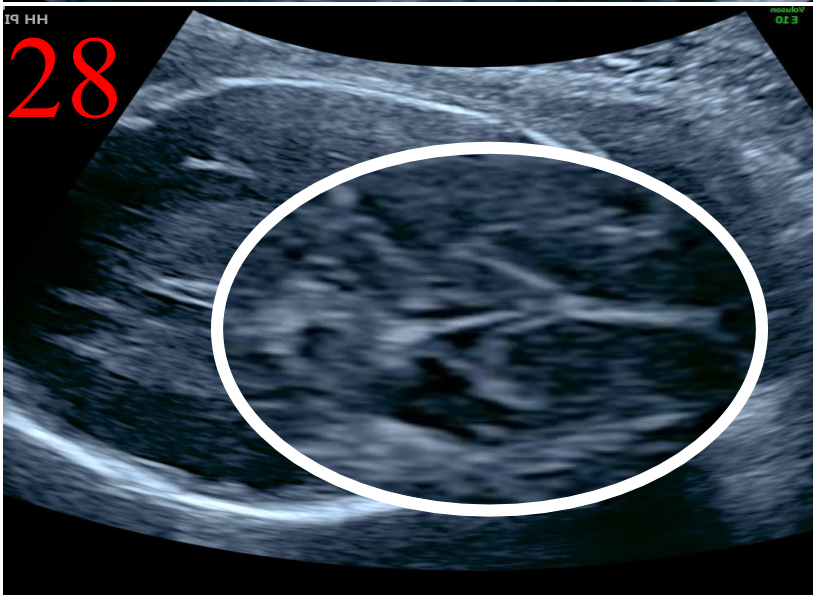
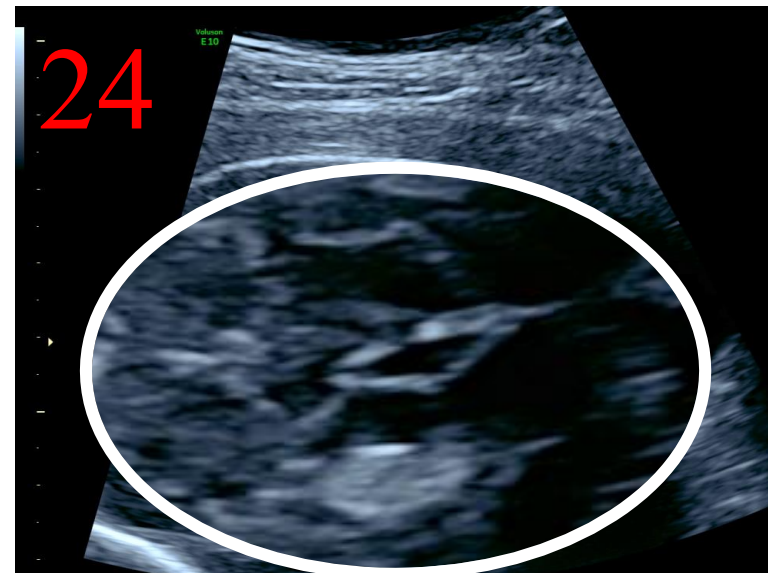
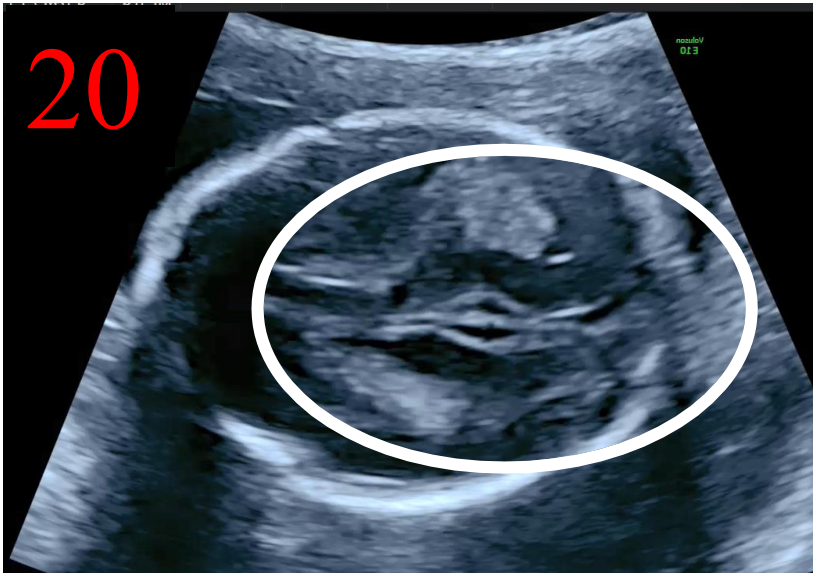
Grade	Definition & diagram
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4	≥ 50% operculization 
5	Complete operculization 

Stadiëring diverse sulci

					
Geen	Ondiepe indentatie of echogene spot	Hoek $>60^\circ$	Hoek $<60^\circ$	I- of J- vorm	Vertakt
0	1	2	3	4	5

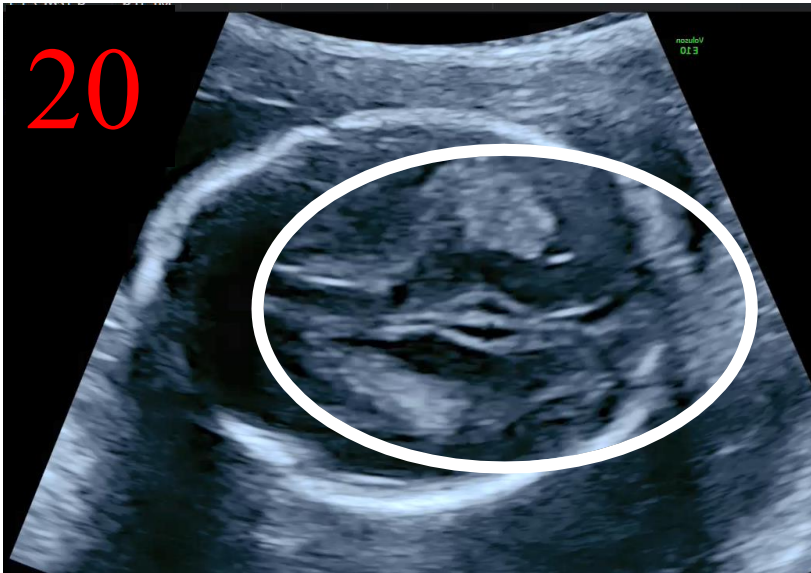
Parieto-occipitale fissuur

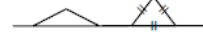
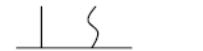
Grade	Definition & diagram
0	None visible 
1	Earliest changes (shallow indentation or echogenic dot) 
2	Broad V (width ≥ depth) 
3	Y or narrow V (depth > width) 
4	I- or J-shaped 
5	Branched 



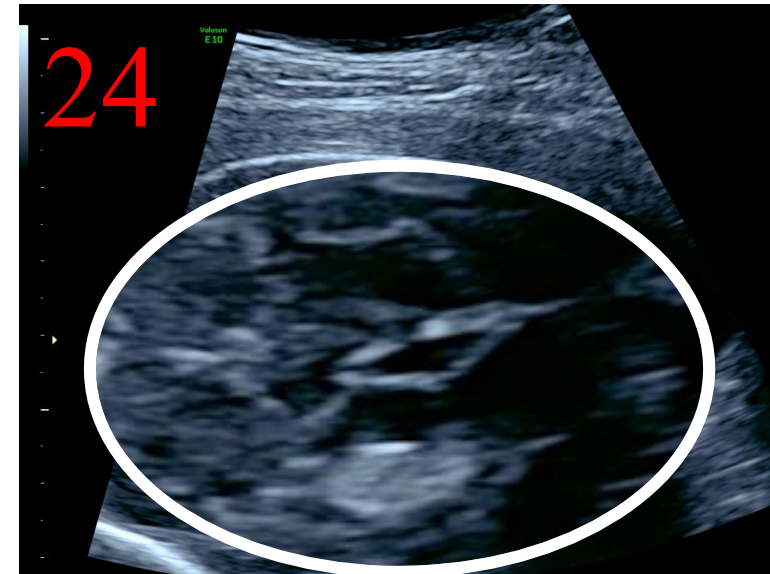
Parieto-occipitale fissuur

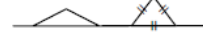
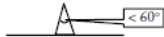
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Grade	Definition & diagram
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3	Y or narrow V (depth > width) 
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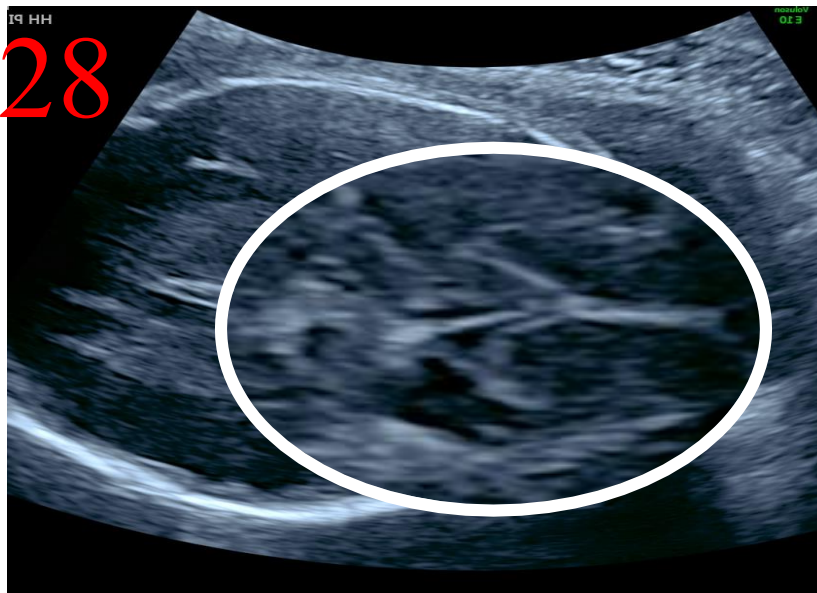
Parieto-occipitale fissuur



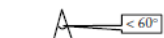
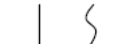
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Parieto-occipitale fissuur

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4	I- or J-shaped 
5	Branched 



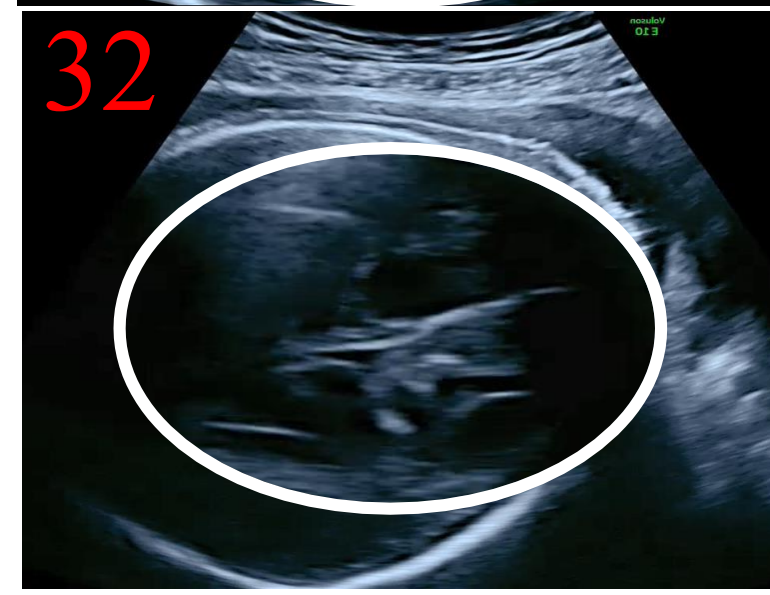
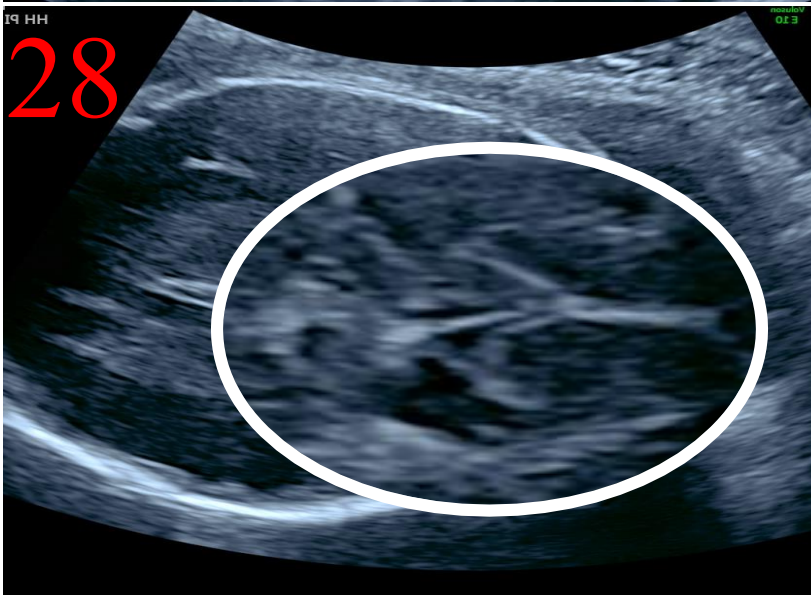
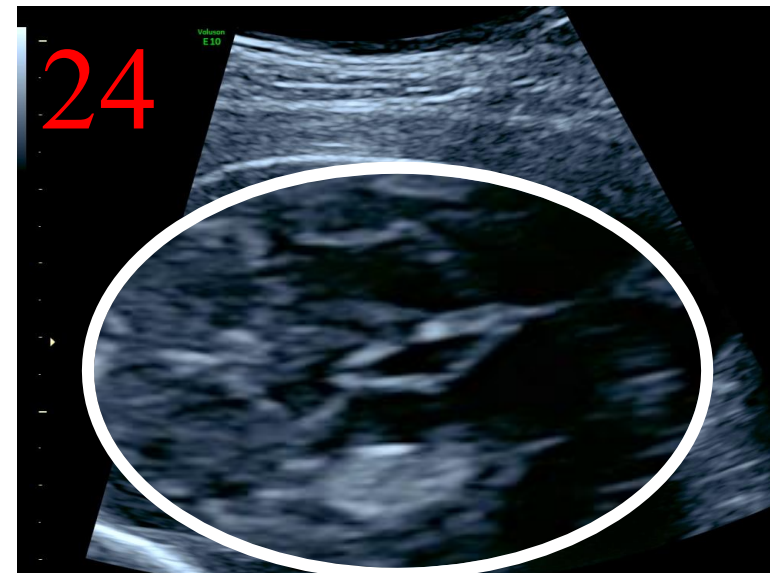
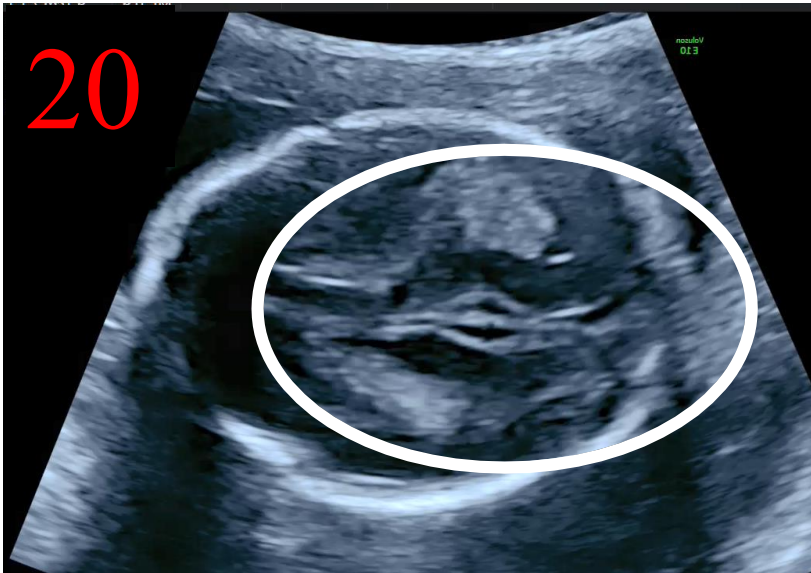
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3	Y or narrow V (depth > width) 
4	I- or J-shaped 
5	Branched 



ISUOG Guidelines for performing the 'basic examination' and the 'fetal neurosonogram'

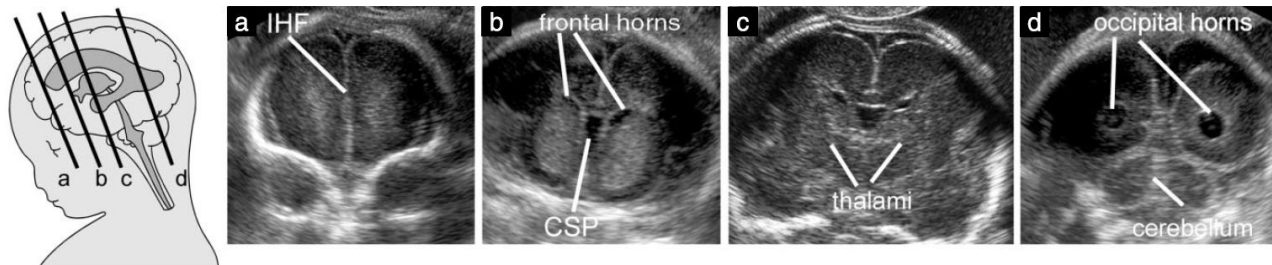
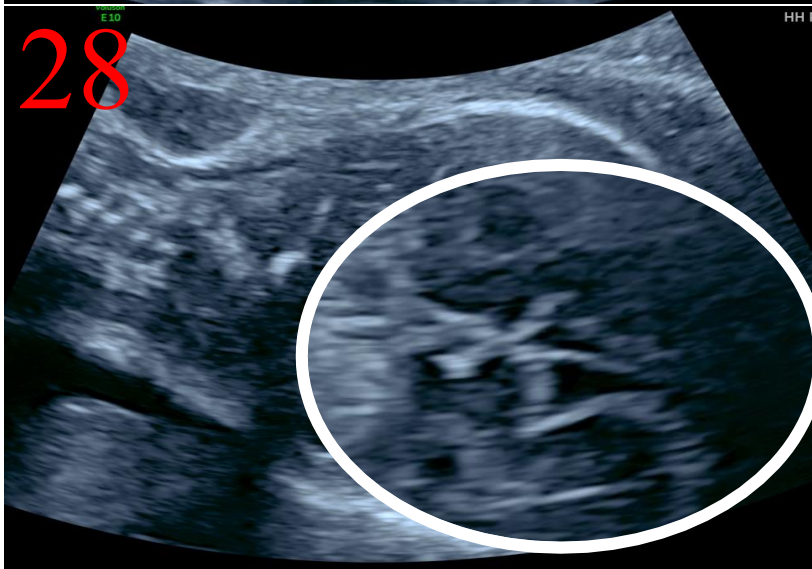
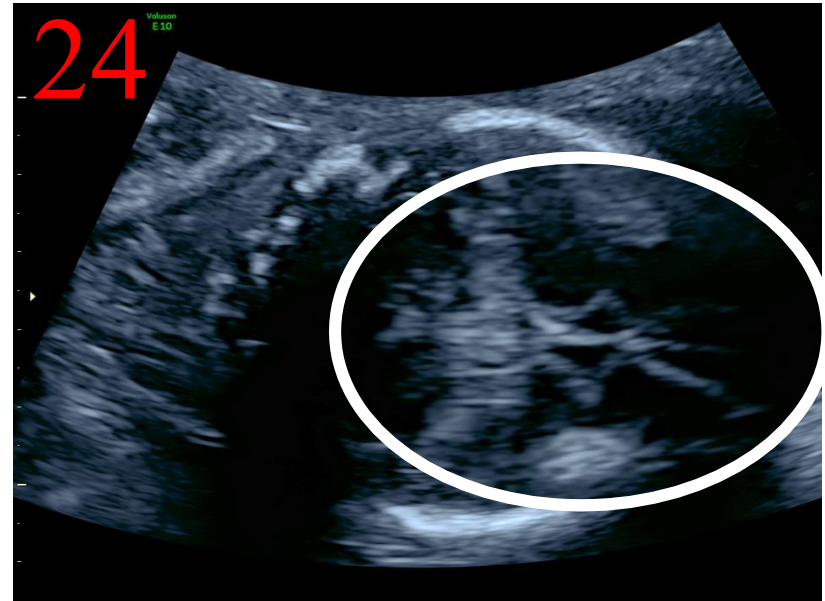
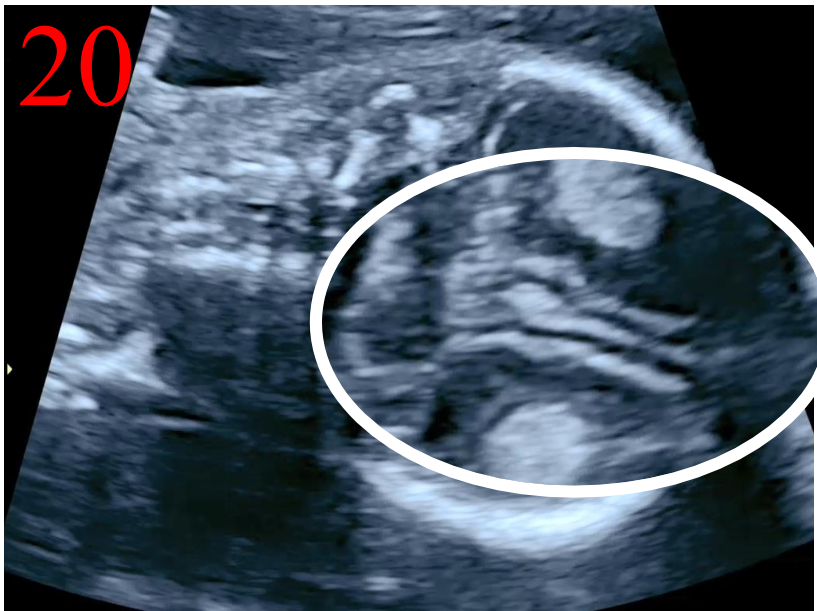
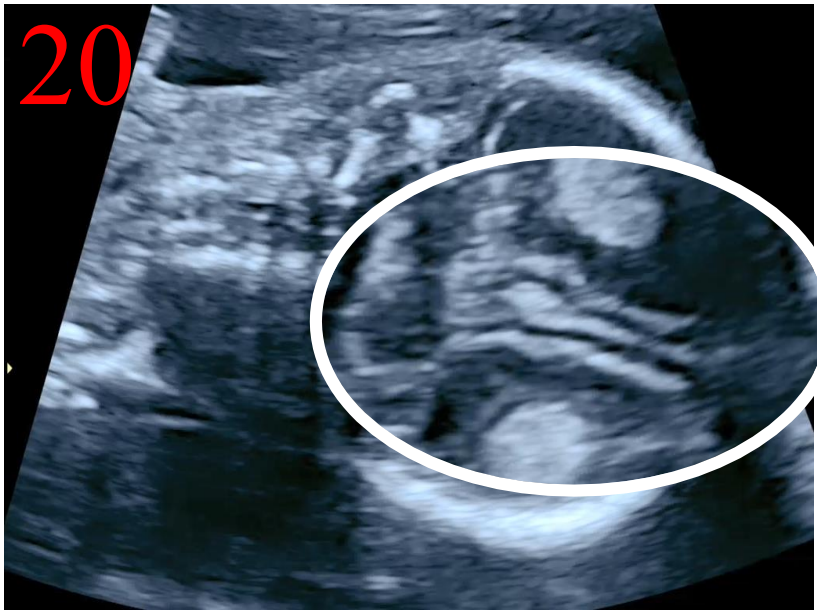


Figure 3 Coronal views of the fetal head. (a) Transfrontal plane; (b) transcaudate plane; (c) transthalamic plane; (d) transcerebellar plane. CSP, *cavum septi pellucidi*; IHF, interhemispheric fissure.

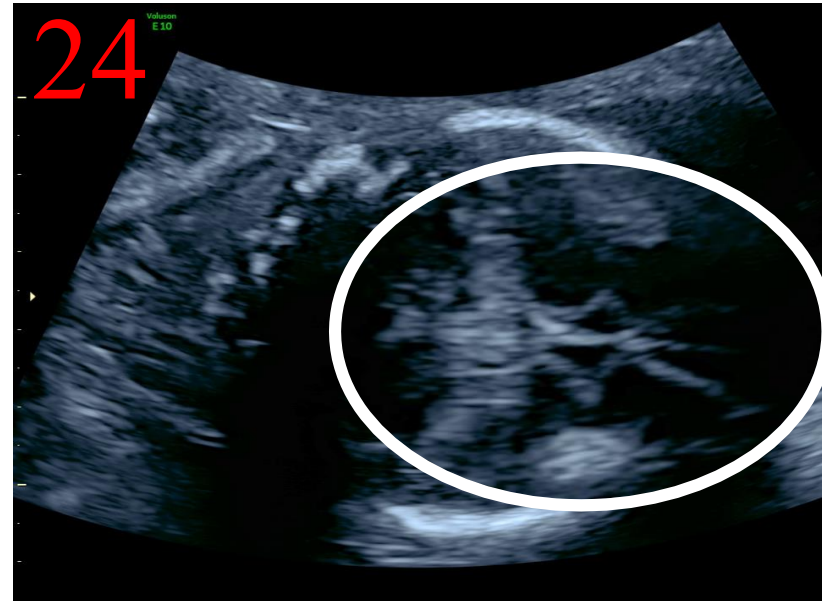
Calcarine Sulcus



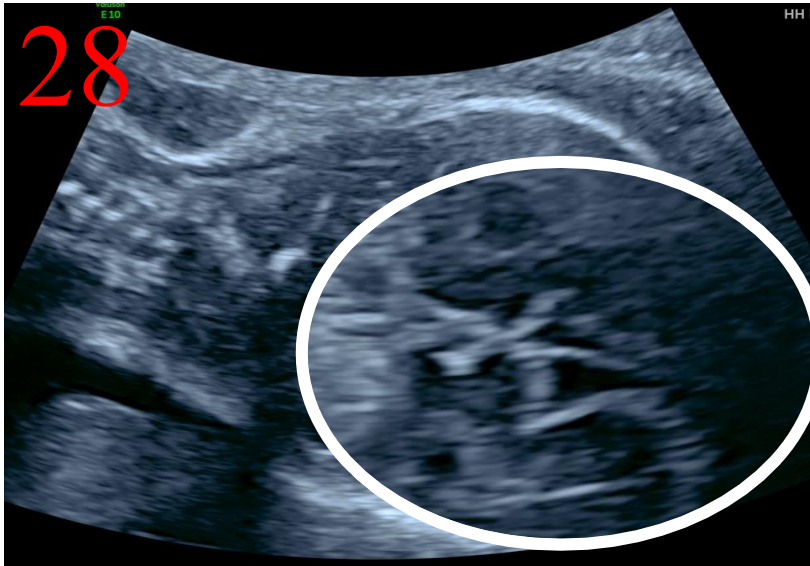
Calcarine Sulcus



Calcarine Sulcus



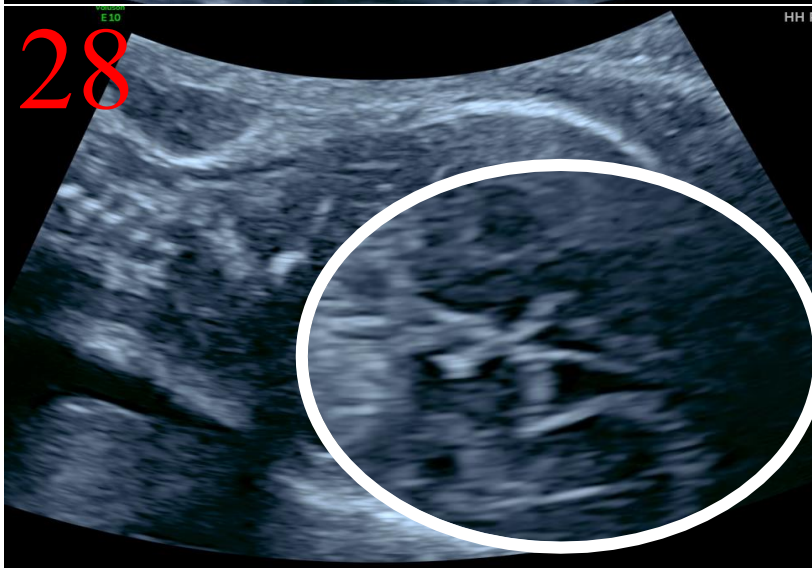
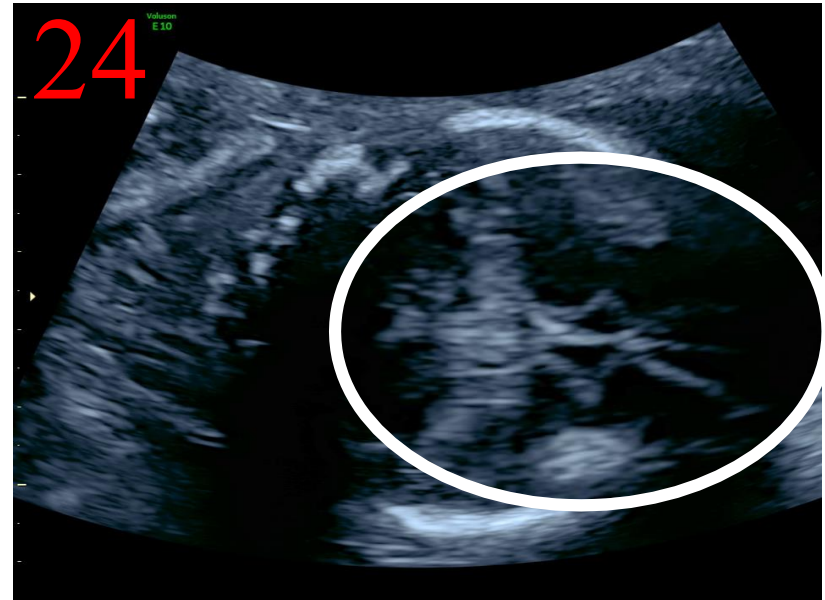
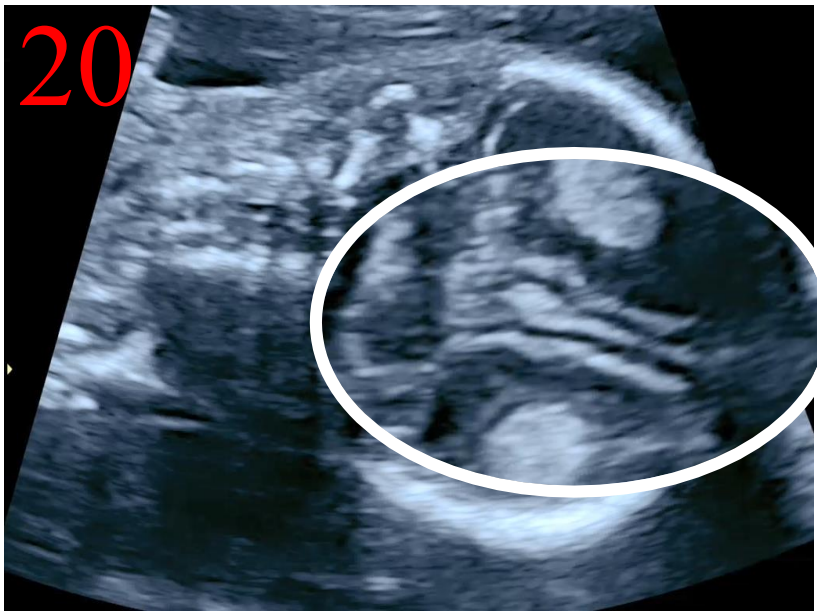
Calcarine Sulcus



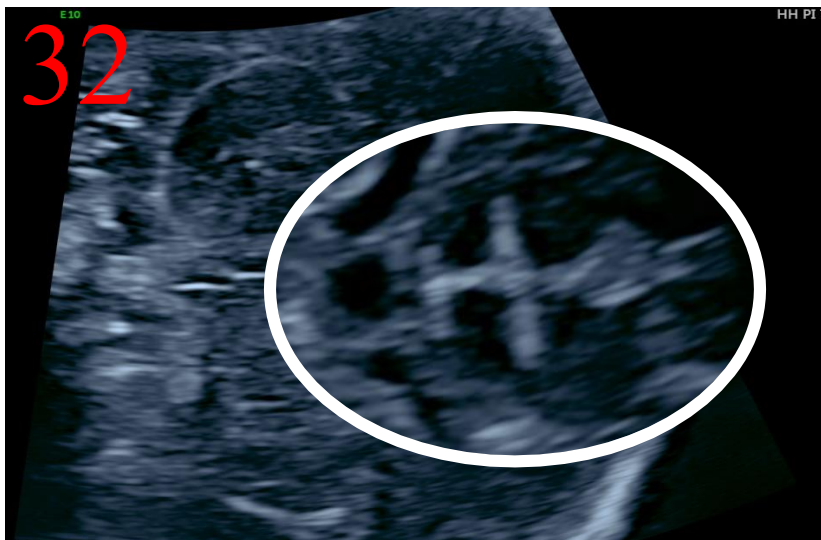
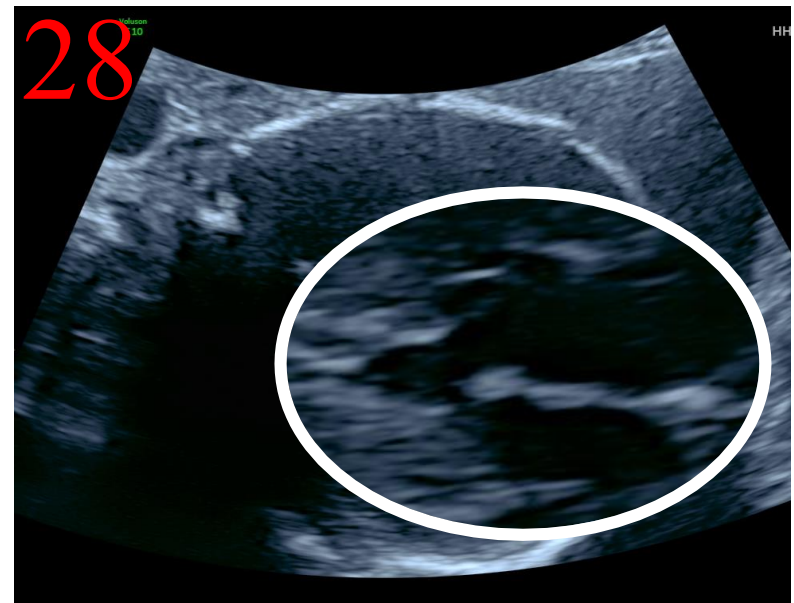
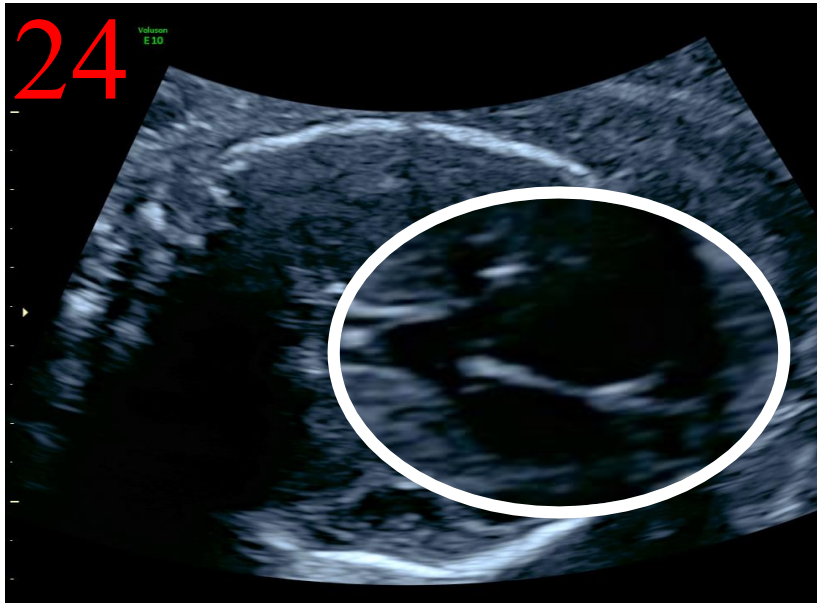
Calcarine Sulcus



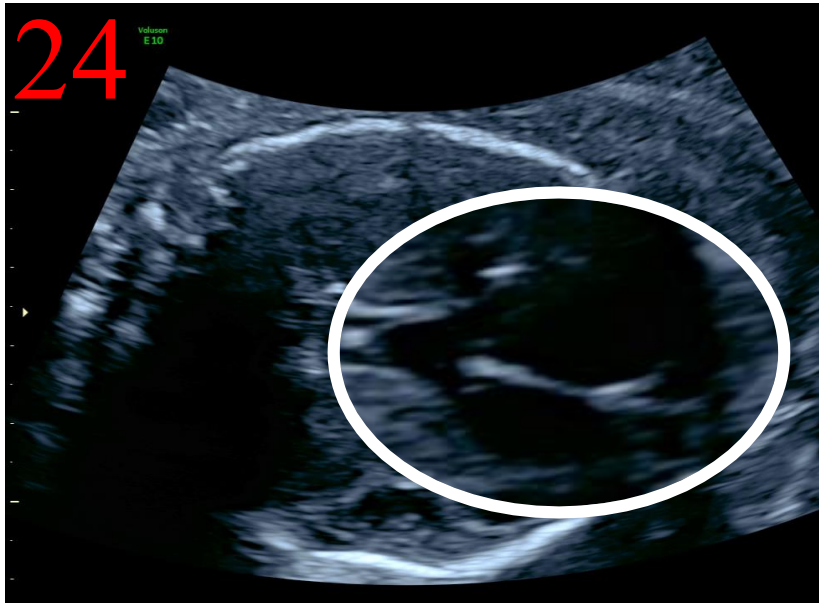
Calcarine Sulcus



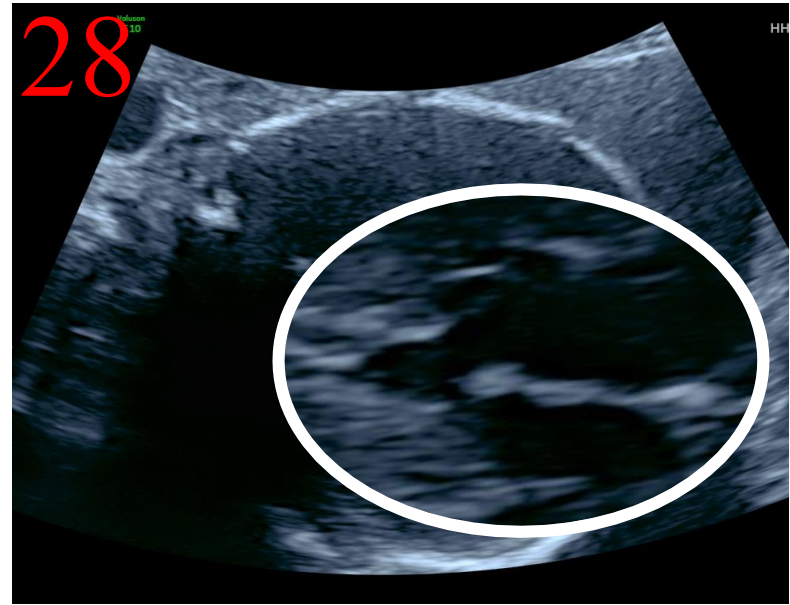
Cingulate



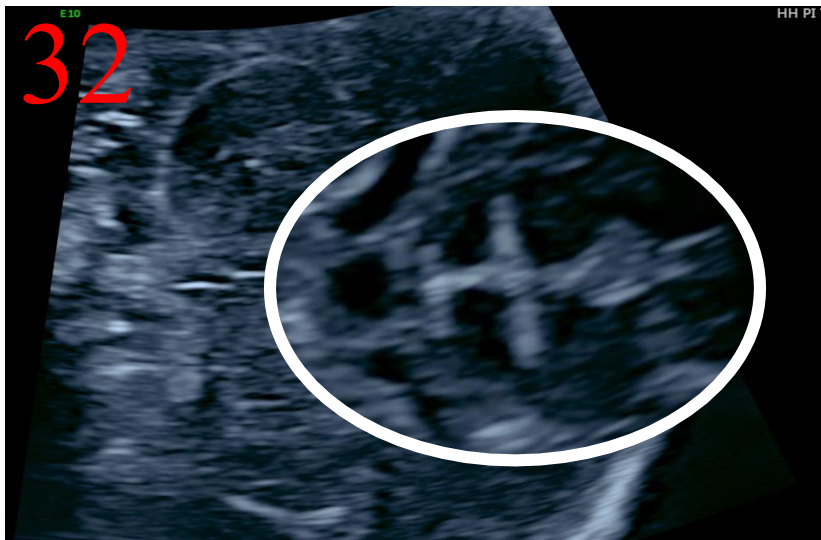
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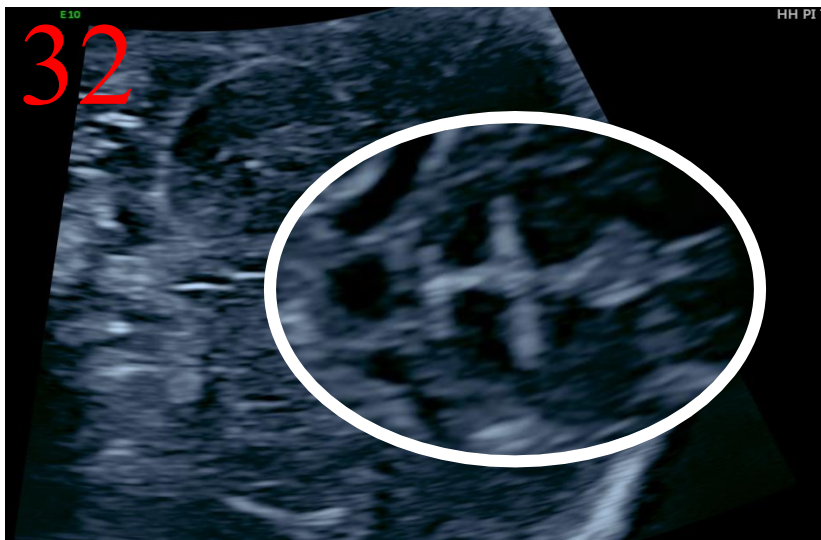
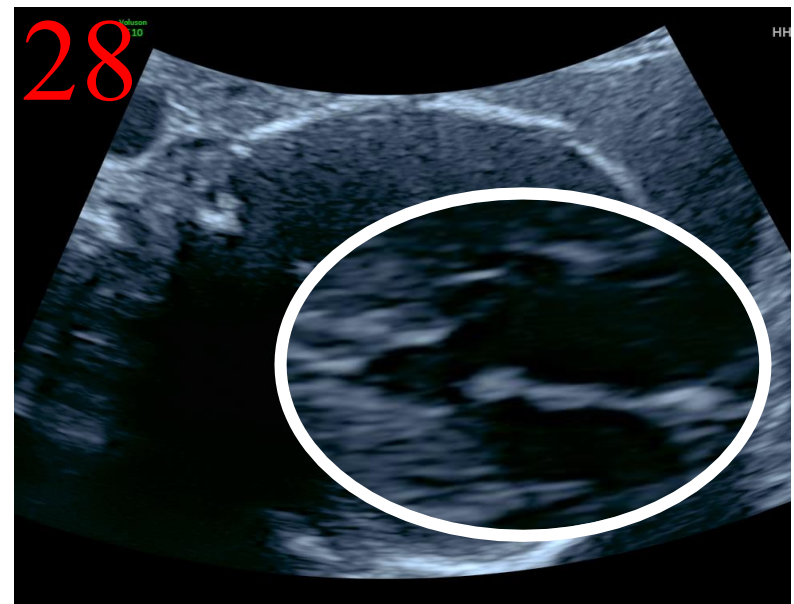
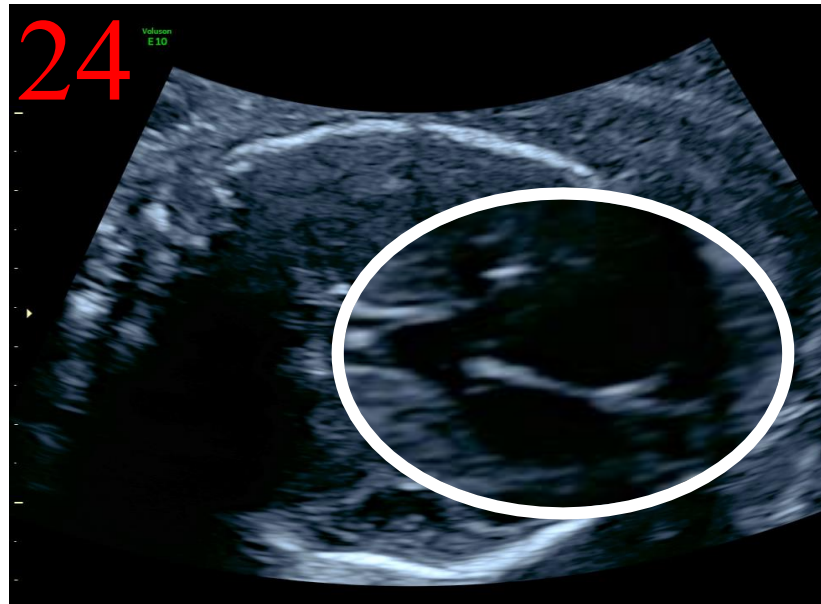
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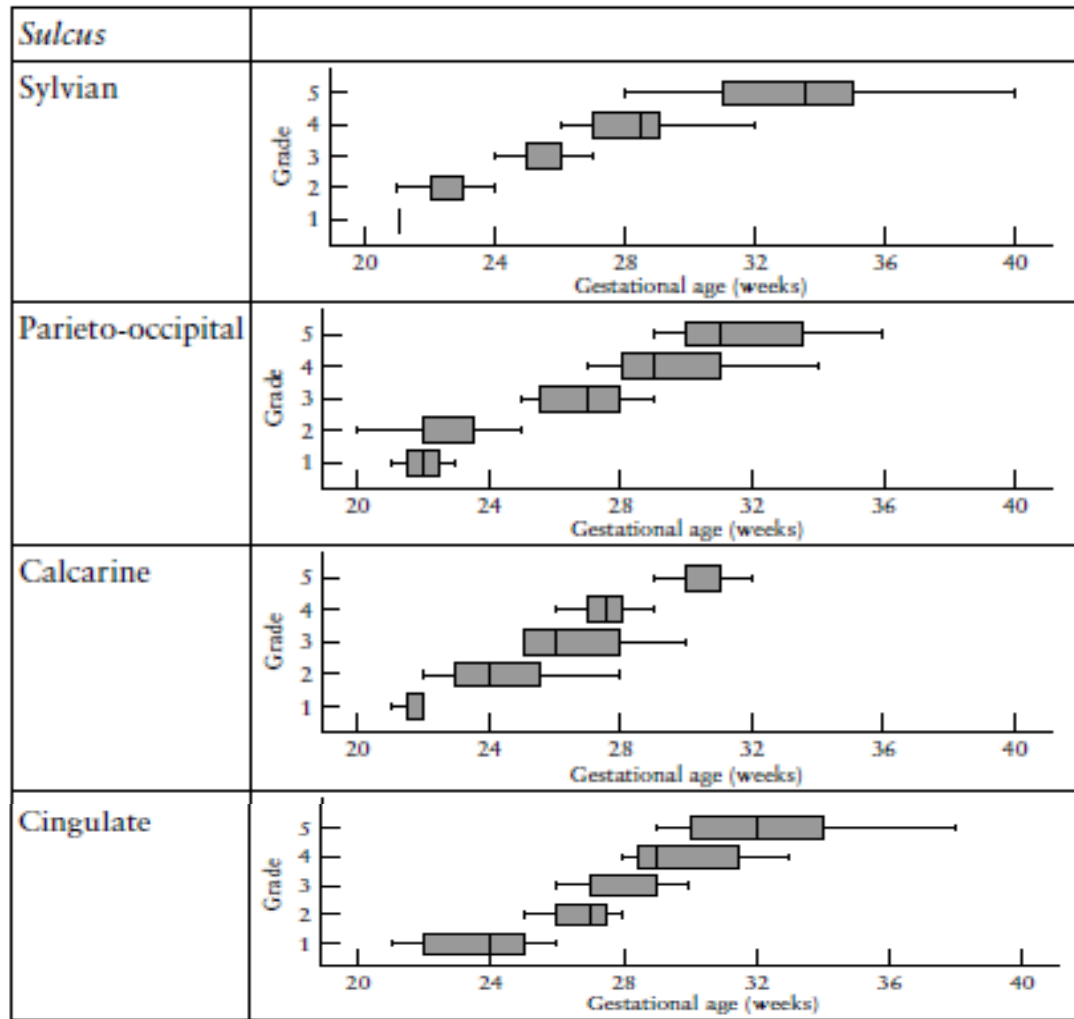
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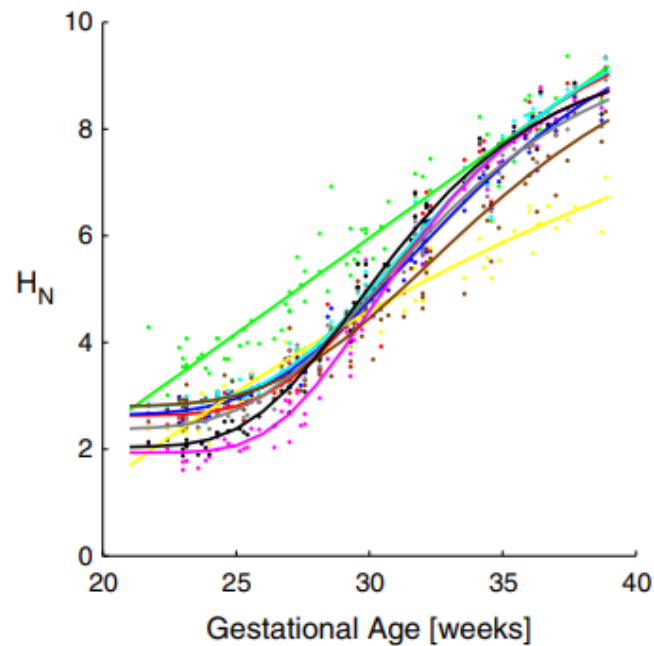
Cingulate



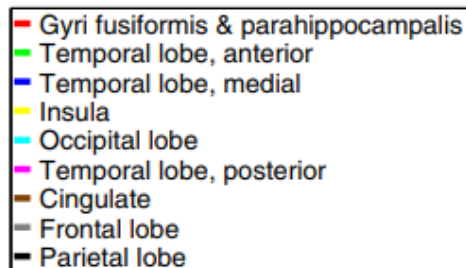
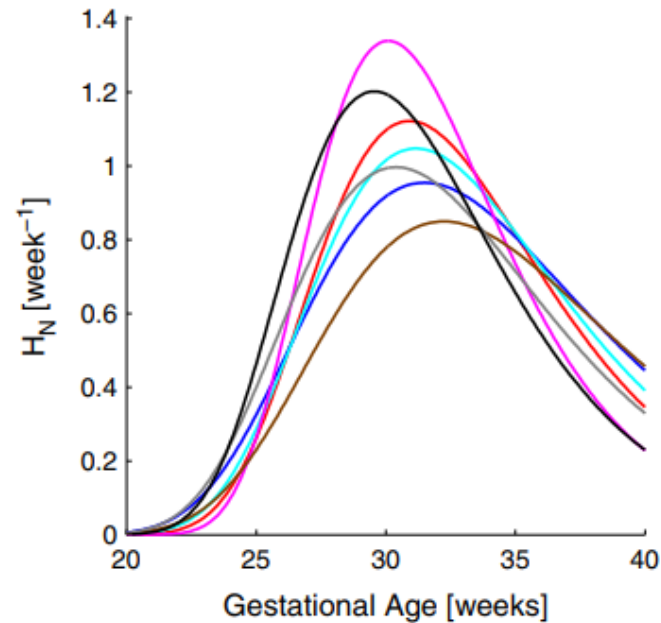
Maturatie - normaalwaarden



(a) Change of H_N over time in different regions.



(b) Rate of increase of H_N with GA.

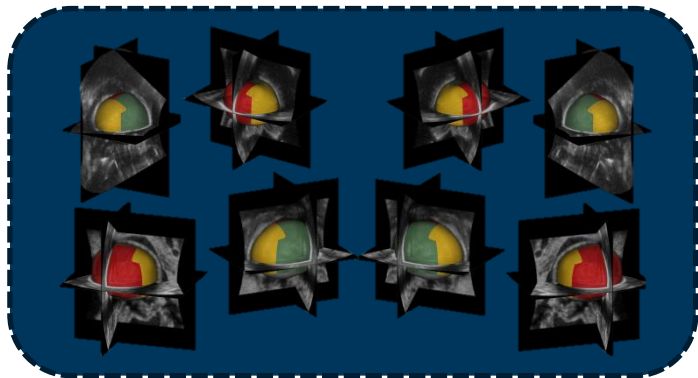


- Leeftijdspredictie dmv automatische analyse 3D volumes
- Samenwerkingsverband LUMC en Universiteit Oxford



Image-Based Age Estimation

Database Images



Training

Application

New Image

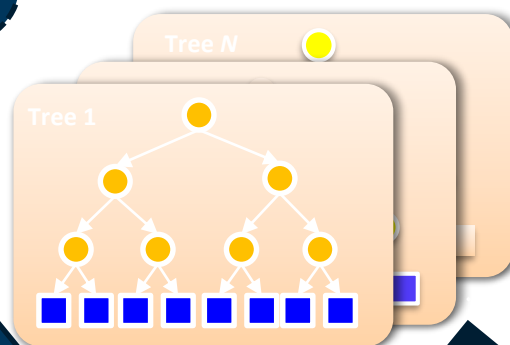
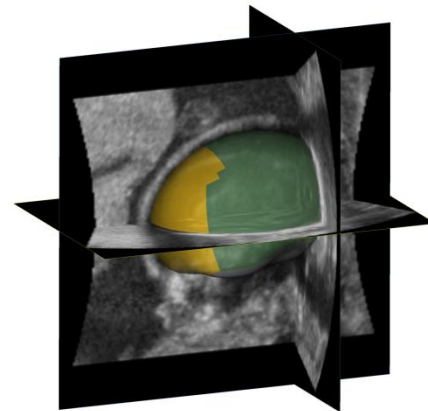
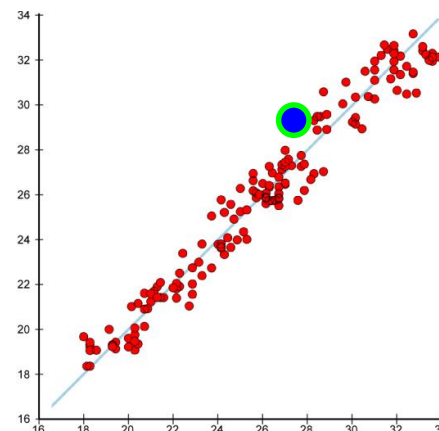
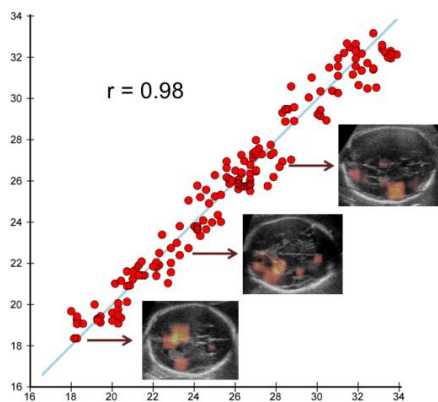
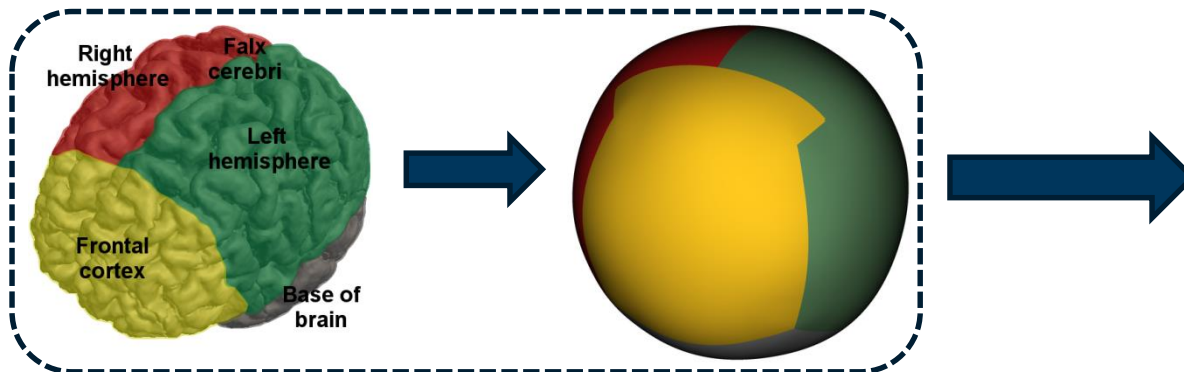


Image-Based Age Estimation



Automated age prediction software

Skull Surface Model



Aligned Images

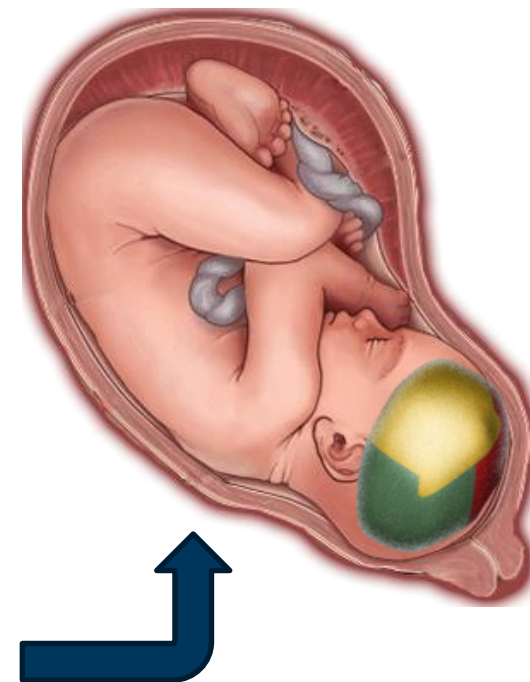
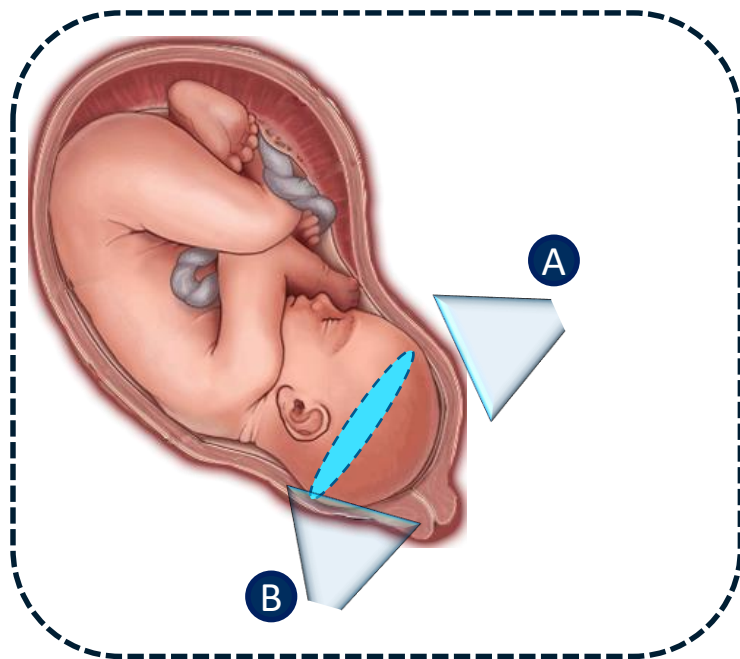
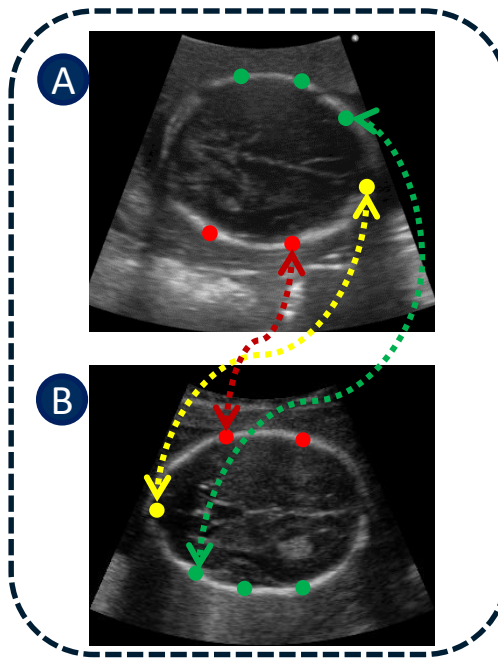


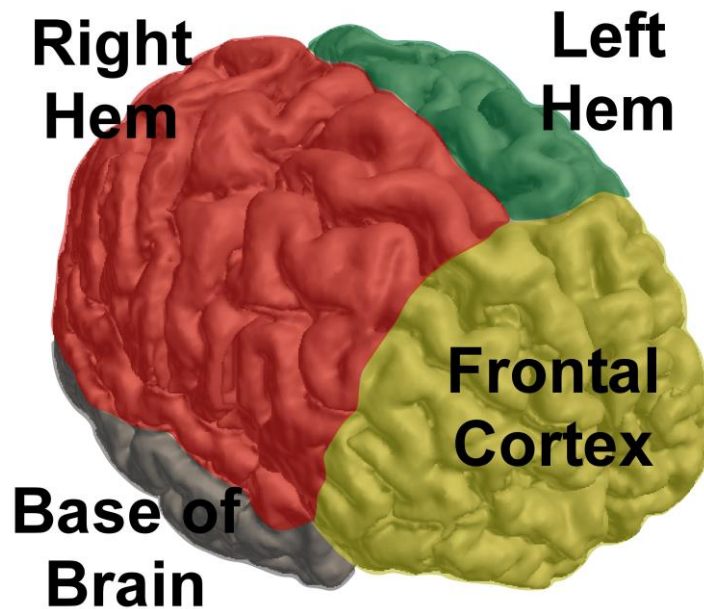
Image Acquisition



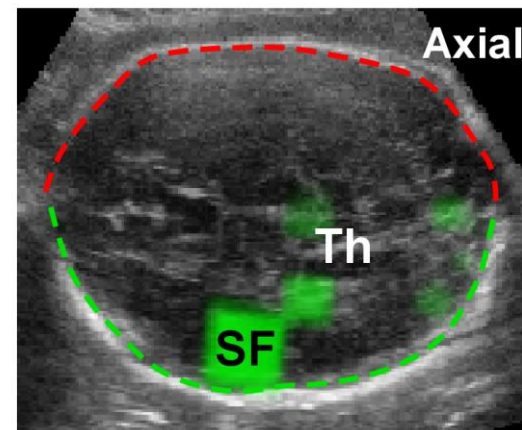
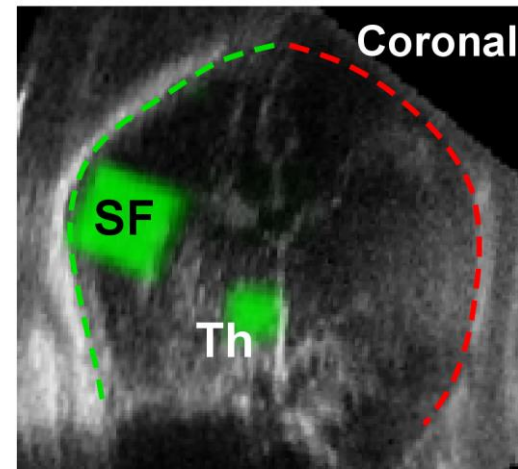
Point Matching



Age-Discriminating Brain Regions

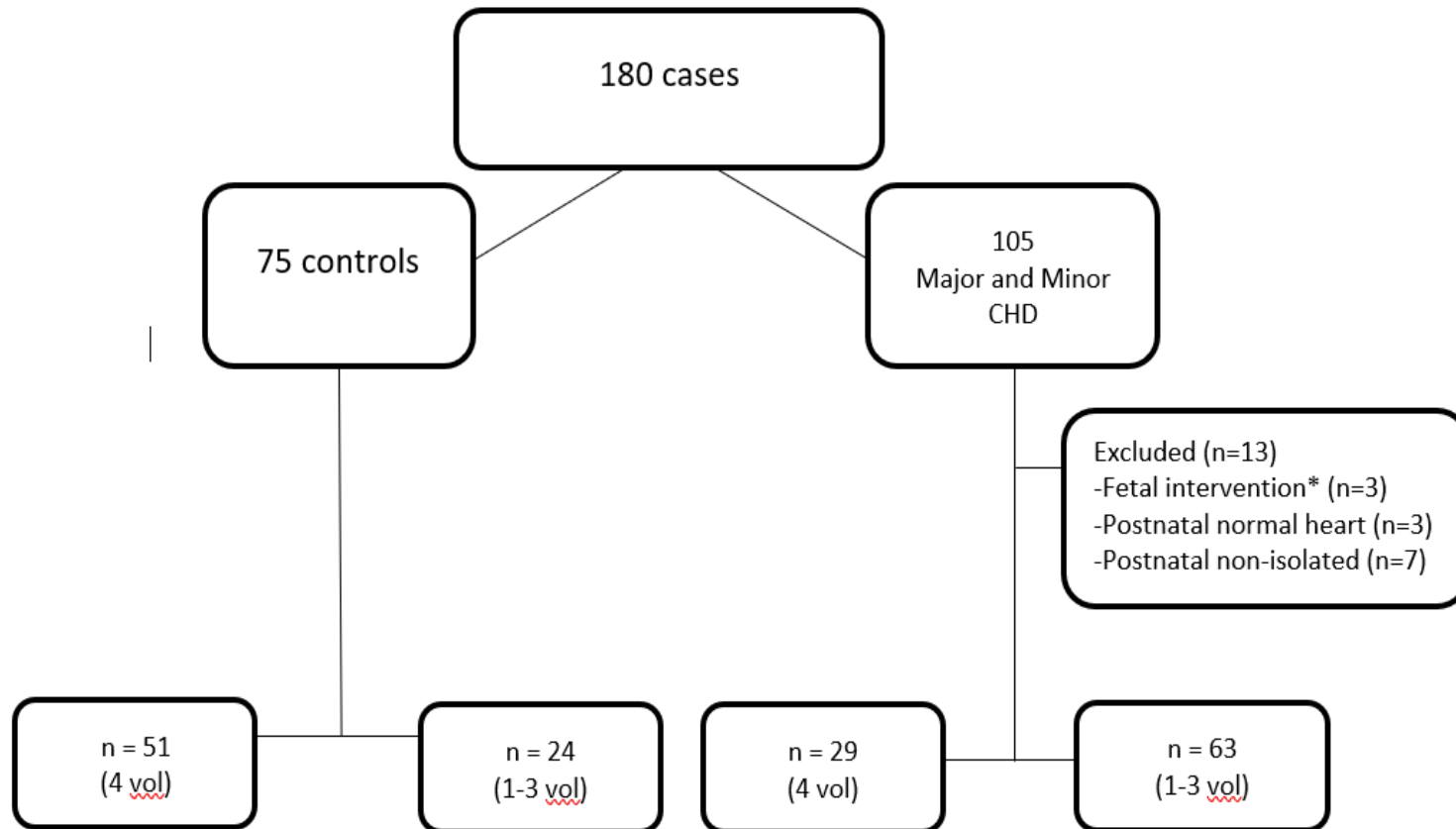


Leeftijdsonderscheidende
brein gebieden



True Age: 28^{+3} weeks
Predicted Age: 27^{+5} weeks

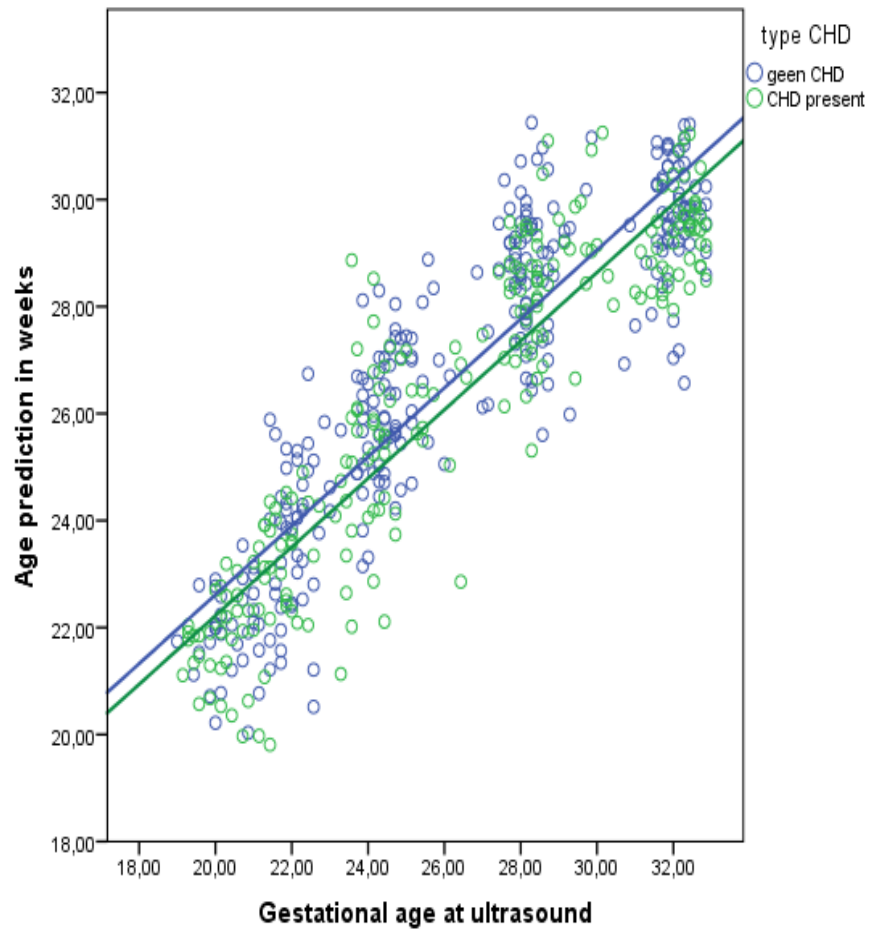
HAND-study flowchart



* Fetal intervention: in these cases of critical Aorta stenosis, an intra-uterine balloon valvuloplasty was performed.

Baseline Characteristics

Characteristics	Value		
	CHD cases	Controls	Total
No. of subjects	104	75	
No. of analyzed volumes	219 (44%)	278 (56%)	497 (100%)
Characteristics			P-value
Maternal Age in years (Mean(SD))	29.76 (4.2)	32.08 (4.39)	0.30
BMI (kg/m ²) Mean(SD)	23.79 (4.2)	23.24 (3.8)	0.11
Primigravidae (%)	44 (42%)	25 (33%)	0.28
Total no. of CHD cases	104		n.a.
HLHS	7		
Transposition of the Great Arteries	13		
Aortic Arch Hypoplasia and/or Aortic Stenosis	21		
Tricuspid or Pulmonary Atresia	11		
Tetralogy of Fallot or Fallot-like defect	15		
(un)balanced atrioventricular septal defect	7		
Ventricular Septal defect	2		
Other major CHD*	14		
Other minor CHD†	14		
Excluded Cases	14		n.a.
Fetal Intervention	3		
Postnatal non-isolated/syndromic	8		
Postnatal normal heart	3		
Pregnancy outcome			n.a.
Live birth	89 (86%)	75(100%)	
Termination of Pregnancy	15 (14%)	0(0%)	



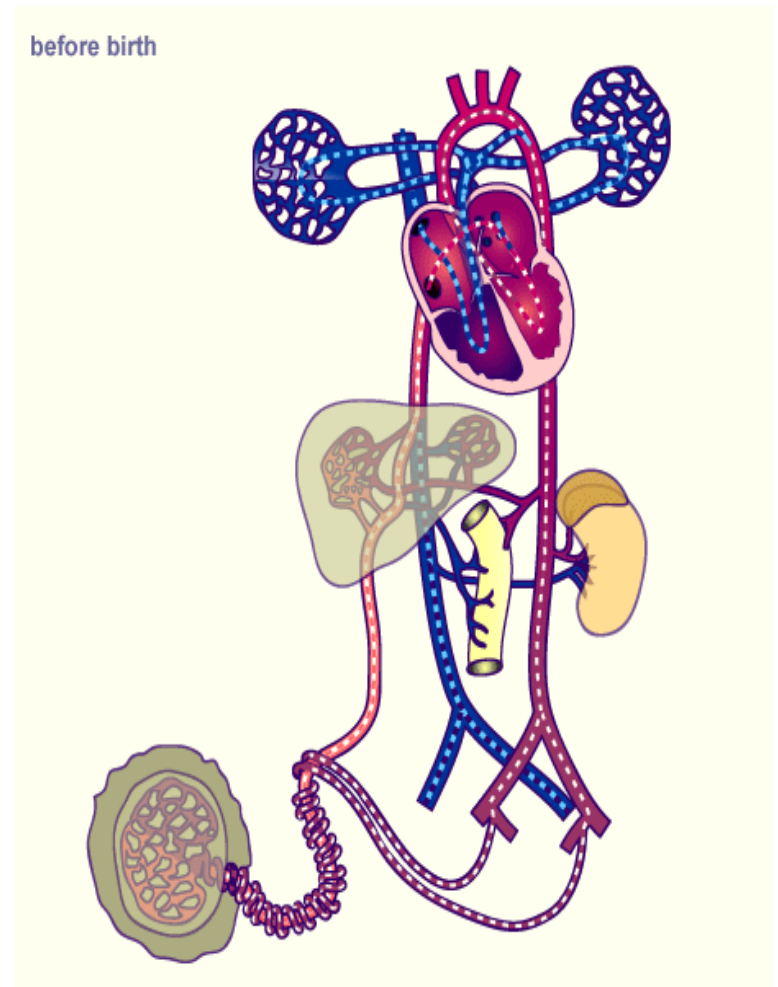
- Volumes geanalyseerd met software
- Significant verschil 2.9 dagen GA CHD groep.
- Hoeken zijn gelijk
- Discutabel of 2.9 dagen 'achterlopen' uitmaakt op latere leeftijd.

Subgroep analyse

Onderverdeling gebaseerd op:

*Flow door aortaboog
(reversed, normaal, geobstrueerd)

*O₂ Saturatie
(laag, normaal, mixed)



Hyperoxygenatie therapie

- Chronische Maternale Hyperoxygenatie(CMH) zou de flow in de Ao-ascendens toe laten nemen.
- Mogelijk zou dit kunnen leiden tot $>\text{Flow}$ en $>\text{O}_2$ in het brein.



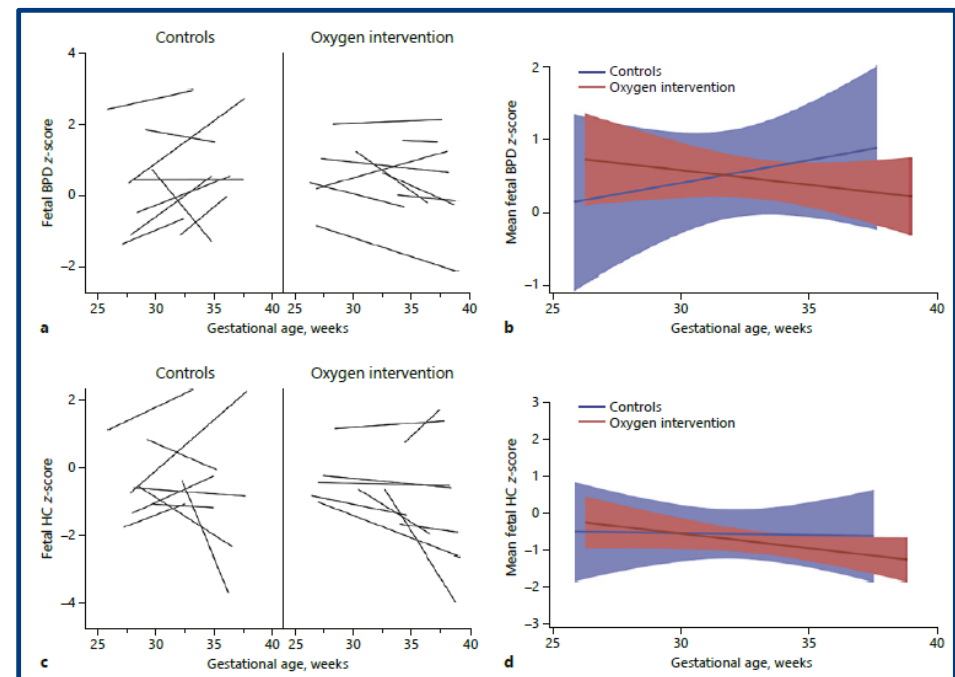
Linda Luna holds her son, Liam, who was born at Lucile Packard Children's Hospital Stanford with a rare heart defect called congenital Ebstein's anomaly.

Robert Dicks

Hyperoxygenatie therapie

Chronic Maternal Hyperoxygenation and Effect on Cerebral and Placental Vasoregulation and Neurodevelopment in Fetuses with Left Heart Hypoplasia

- 9 HLHS cases
- 9 Controls
- Hyperoxygenatie toegepast tussen 26-34 weken. Gemiddeld aantal uur 542(292-1011).
- Geen verschil in neurologische testen op leeftijd 6 en 12 maanden
- Én: aanwijzingen voor significant kleinere hoofdomtrekken....



Edwards et al. Fetal Diagnosis and Therapy; Sept. 2018.

- Automatische leeftijdspredictie is mogelijk met 3D brein volumes.
- Er lijkt een zeer klein significant verschil tussen te bestaan in de maturatie tussen CHD en controle patienten, echter is de vraag of dit klinisch relevant is.
- Analyse van subgroepen lijken significante verschillen te laten zien, echter worden nog uitgebreid met nieuwe casus
- Het is nog te vroeg om maternale hyperoxygenatie therapie te zien als oplossing, dit moet verder onderzocht worden.



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Subgroup analysis

Ascending aorta oxygen saturation				
	Low	Mixed	Normal	Total
Aortic arch flow				
Reversed	0	6(15)	0	6(15)
Obstructed	0	6(12)	23(78)	29(90)
Normal	13(51)	33(110)	11(33)	57(194)
Total	13(51)	45(137)	34(111)	92(299)

Geïsoleerd?

Prenataal vs. postnataal

- Cave extracardiale afwijkingen

Ook prenataal geïsoleerde CHD...

Kunnen chromosomale afwijkingen hebben:

- Aneuploidie:
 - 22q11 deletie syndroom(array)
- Monogenetische afwijkingen:
 - Kabuki/CHARGE etc(WES)
 - Aspecifieke genetische afwijkingen

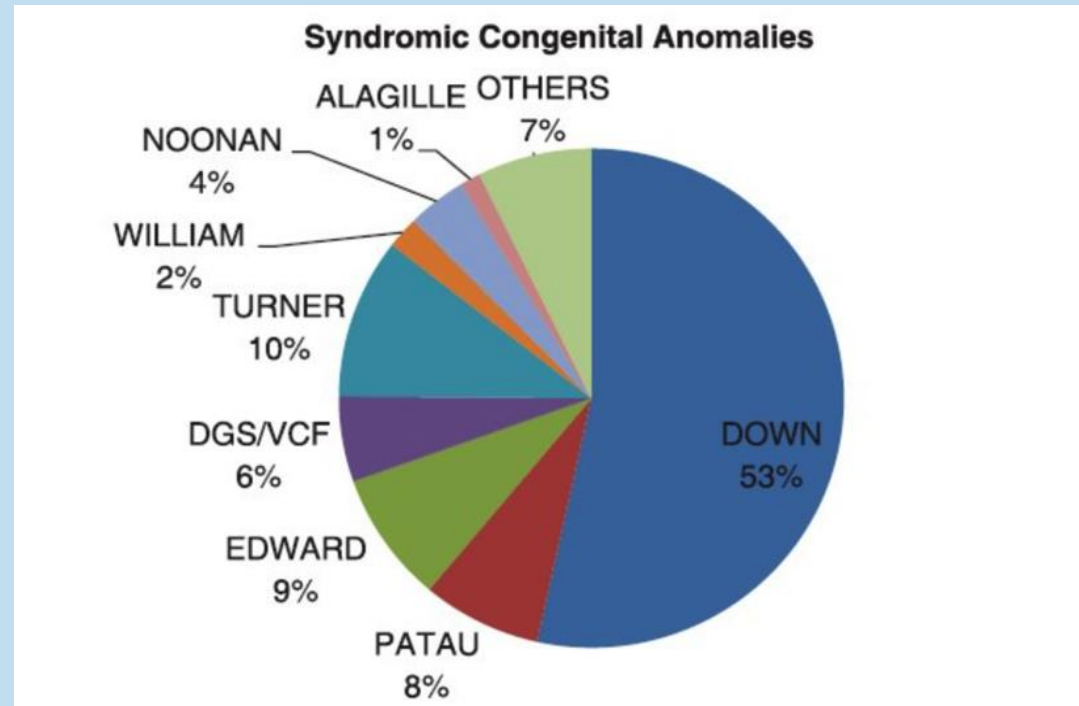


Table 3. Structural Magnetic Resonance Imaging Findings

Variable	d-TGA (n=111), n (%)	Referent (n=55), n (%)	P*
Any abnormality	37 (33)	2 (4)	<0.001
Focal or multifocal abnormality	26 (23)	0	<0.001
Focal infarction or atrophy	7 (6)	0	0.10
Brain mineralization/iron deposit	23 (21)	0	<0.001
Diffuse abnormality	3 (3)	0	0.55
Myelination delay	0	0	...
Ventriculomegaly	0	0	...
Abnormal T2 hyperintensities	3 (3)	0	0.55
Generalized abnormality	0	0	...
Developmental abnormality	9 (8)	2 (4)	0.34
Major malformation	0	0	...
Minor malformation†	9 (8)	2 (4)	0.34

d-TGA indicates d-transposition of the great arteries.

*Determined by Fisher exact tests.

†Minor malformations include Chiari malformation (n=2), arachnoid cyst, cerebellar tonsillar ectopia, enlarged empty sella, enlarged perivascular space in right parietal lobe, gray matter heterotopia in right frontal lobe, right thalamic signal abnormality (possible gliosis versus low-grade tumor), and small right hippocampus in the d-TGA group, and Chiari malformation and developmental venous anomaly in right parietal lobe in the referent group.

It is possible that, because the academic and behavioral expectations placed on children increase with advancing age, the effect of CHD on executive function becomes more apparent.