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The Role of Fetal Brain Magnetic Resonance Imaging in Current Fetal Medicine

THESIS SUMMARY

MICHAEL AERTSEN

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ABSTRACT

In open spina bifida we studied the use of MRI for the assessment of the posterior fossa and prevalence of supratentorial anomalies before and after in utero repair. New postprocessing techniques were applied to evaluate fetal brain development in this population compared to controls. In fetuses with congenital diaphragmatic hernia, we evaluated the brain development in comparison to controls. Diffusion weighted imaging was applied to study difference between fetuses with proven first trimester cytomegalovirus infection and controls. Finally, we investigated the value of third trimester fetal brain MRI after treatment for complicated monochorionic diamniotic pregnancies.

CORRESPONDING AUTHOR:

Michael Aertsen

KU Leuven, BE

michael.aertsen@uzleuven.be

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INTRODUCTION

Fetal magnetic resonance imaging (MRI) has become an important adjunct to prenatal ultrasound in the assessment of fetal abnormalities of the central nervous system. It has become clear that both modalities are complementary, allowing better understanding of the disease process, classification of abnormalities, and determination of prognosis and management options [1, 2, 3]. Over the last decades, several in utero treatment options have been proven beneficial and effective, including laser coagulation in monochorionic pregnancies complicated by twin-to-twin transfusion syndrome (TTTS), in utero closure of spina bifida aperta and, most recently fetoscopic endoluminal tracheal occlusion in congenital diaphragmatic hernia (CDH). Furthermore, there have been some recent developments in the prenatal therapy of cytomegalovirus (CMV) infection. The role of imaging of the fetal brain in this population has been recognised widely with an important role for fetal MR [4, 5, 6].

FETAL BRAIN MRI IN SPINA BIFIDA APERTA

Because of the efficacy of fetal surgery for spina bifida aperta, accurate prenatal imaging of fetuses with spina bifida aperta has become crucial to select eligible fetuses [7]. We investigated the use of fetal MRI in patients being assessed for fetal surgery for spina bifida.

First, we demonstrated that the majority of measurements that are used on postnatal MR images cannot be reliably made around the time of fetal surgery. These measurements include brain stem measurements, and foramen magnum diameter, tentorial length and cisterna magna width. Conversely, assessment of the posterior fossa dimensions and the level of cerebellar herniation were shown reproducible [8]. The latter has been used as a secondary outcome measure in the landmark study on fetal surgery for spina bifida, in other words the Management of Myelomeningocele Study, before and after fetal surgery [9]. Recently the *interpeduncular angle* (IPA) was proven significantly lower in fetuses with open spinal dysraphism, similar to observations in adults with intracranial hypotension [10]. The authors suggest that a reduced IPA is an early sign of CSF-leakage, causing intracranial hypotension, and later followed by frank cerebellar descent.

In the same study we demonstrated that already within seven days, in the majority of fetuses, there is reappearance of fluid cisterns in the posterior fossa8, Figure 1]. Earlier studies, such as the one from Sutton [11]), also reported such changes between three and six weeks after the surgery in all fetuses where this

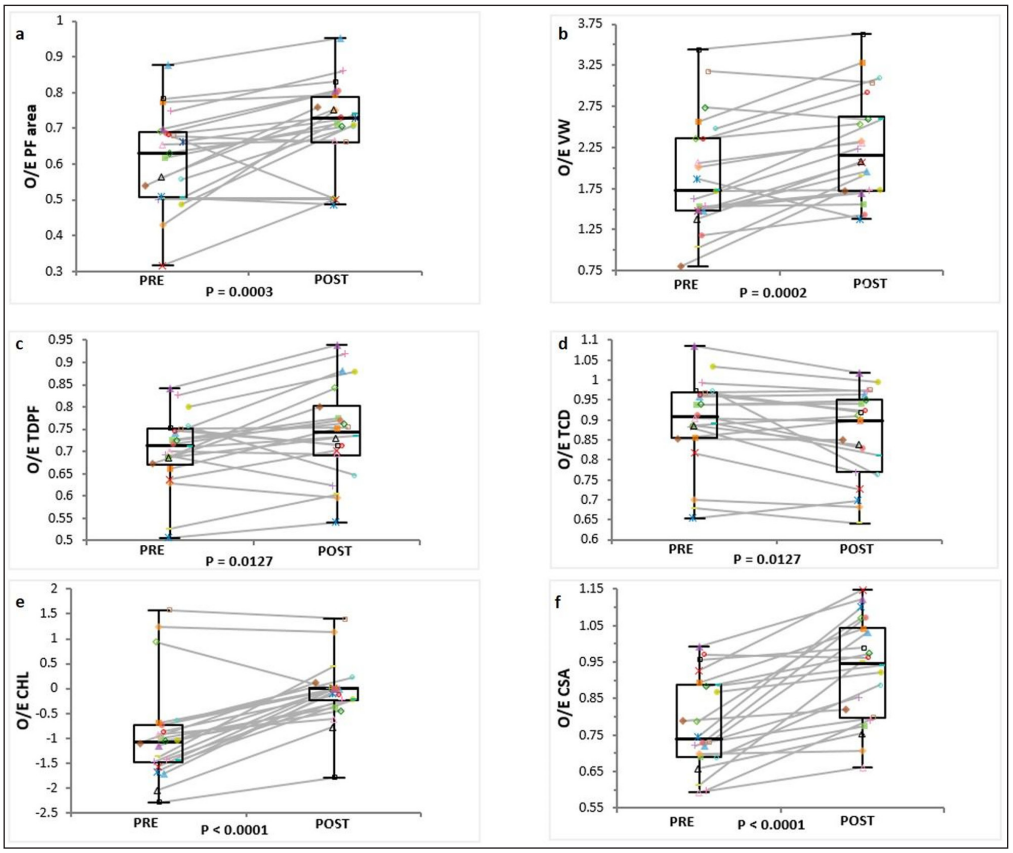

Figure 1 Boxplot demonstrating the minimum, first quartile, median, third quartile and maximum of the observed over expected ratio (O/E) in preoperative open spinal dysraphism (OSD) fetuses and postoperative OSD fetuses at one week for the posterior fossa area (PF area) **(a)**, ventricular width (VW) **(b)**, transverse diameter of the posterior fossa (TDPF) **(c)**, transverse cerebellar diameter (TCD) **(d)**, cerebellar herniation level (CHL) **(e)** and clivus- supraocciput angle (CSA) **(f)**.

was measured. The re-accumulation of intracranial CSF can be an interesting proxy of the efficacy of spinal closure [12].

A follow-up MRI later in pregnancy was shown to predict the need for postnatal hydrocephalus treatment [13]. Another reason to perform a postoperative MRI, such as six weeks following surgery, is that the fetal brain can be better documented. For instance, periventricular nodular heterotopia will be more frequently picked up [14, 15]. The question is obviously how that information would be used in the further clinical management of the pregnancy, given the advanced gestational age.

Second, we described the nature and occurrence of supratentorial abnormalities in fetuses with spina bifida [16]. Proper assessment is important for counselling women about fetal surgery [17]. Besides ventriculomegaly, evidence of damage to white matter tracts and abnormalities of the corpus callosum [18] or indications of abnormal neuronal migration are frequently observed in fetuses with open spina bifida [14, 15, 19–22]. When using MRI in fetuses meeting the criteria for fetal surgery on ultrasound findings, half of them were found to have corpus callosum abnormalities and/or ventricular wall abnormalities [16]. This number is in line with findings in a recent systematic review by our group [23]. Whether MRI is essential for this, hence adds information to US, has to our knowledge not been proven. In our own hands, US also detected a whole range of supratentorial abnormalities. At our center, US findings inform the MRI, and thus we cannot truly measure what would be the theoretical added value of one imaging modality above the other.

Third, we used a new 3D SVR algorithm [24] and an automated segmentation method [25] to document perioperative changes in fetal brain development in fetuses with spina bifida as compared to fetuses without the conditions [26]. Documenting in utero changes following surgery is important, as increasingly fetal surgery is being practiced, and it is expected that more of these operations will be done when minimally invasive methods will be widely implemented [27–29]. The shift towards prenatal repair is, at this moment changing the 'natural history' of open spina bifida 8, 16, 30–33].

In our cohort we did not find any difference in cerebellar volume with that of controls but demonstrated that the cerebellar shape changed importantly after fetal surgery, eventually becoming more comparable to that of controls [26]. The fact that we found cerebellar volumes to be *comparable to that of controls*, needs further investigation. In a prior study, we have found that posterior fossa dimensions in spina bifida prior to 26 weeks were very variable [8]. Others have demonstrated that infants who were not operated in utero, but postnatally, have different white matter and cerebellar volumes. The authors tied this to the mechanical compression and ventricular dilatation present prior to (postnatal) surgery [34–36]. The widely accepted theory of McLone and Knepper explains this as follows. The ongoing leakage of CSF at the spinal defect prevents ventricular distention and normal development of the bony structures of the posterior fossa [37]. In turn, the limited growth of the bony posterior fossa limits the cerebellar development, leading to cerebellar compression [35, 36].

We also evaluated the white matter in our fetal surgery population, and, again, no differences in volume or shape were found compared to normal controls [26]. These fetuses however had a variable degree of ventriculomegaly prior to fetal surgery; after the operation, the ventricular width continued to increase, in concordance with the observations of others [8, 12, 16, 26]. To us, it remains unclear how the white matter volume evolves during the remainder of the pregnancy and in postnatal life in this subset of patients.

In the same study, we used spectral matching to document cortical folding. We demonstrated an increased shape index prior to fetal surgery, and a decreased shape index seven days after fetal surgery, both compared to the index in normal controls [26]. This is, to our knowledge, the first study specifically documenting cortical development in fetuses before and after fetal surgery. Postnatal studies demonstrated that children with open spina bifida (who underwent postnatal repair) have a different cortical folding pattern in comparison to normal age-matched controls [38, 39]. Longitudinal analysis of the cerebellar and white matter development, both volume and shape, as well as cortical folding with spectral matching, will allow us to document the impact of prenatal surgery during the remainder of the pregnancy and potentially also postnatally.

Fourth, we applied the new 3D SVR algorithm [24] to create the first spatio-temporal atlas of the fetal brain in spina bifida aperta [40, Figures 2a, 2b]. The application of our atlas for automated segmentation of fetal brain MRIs with open spinal dysraphism did result in a more accurate segmentation compared to those based on other atlases that used normal fetal brains. This illustrates, as suggested by Jakab et al. [41]. the potential of 3D SVR techniques with automated segmentation. They may eventually provide new outcome predictors for fetuses with this condition based on quantitative research.

FETAL BRAIN MRI IN CONGENITAL DIAPHRAGMATIC HERNIA

CDH is another congenital malformation for which fetal surgery has been shown to be beneficial in given circumstances [42–44]. Imaging studies in infants with

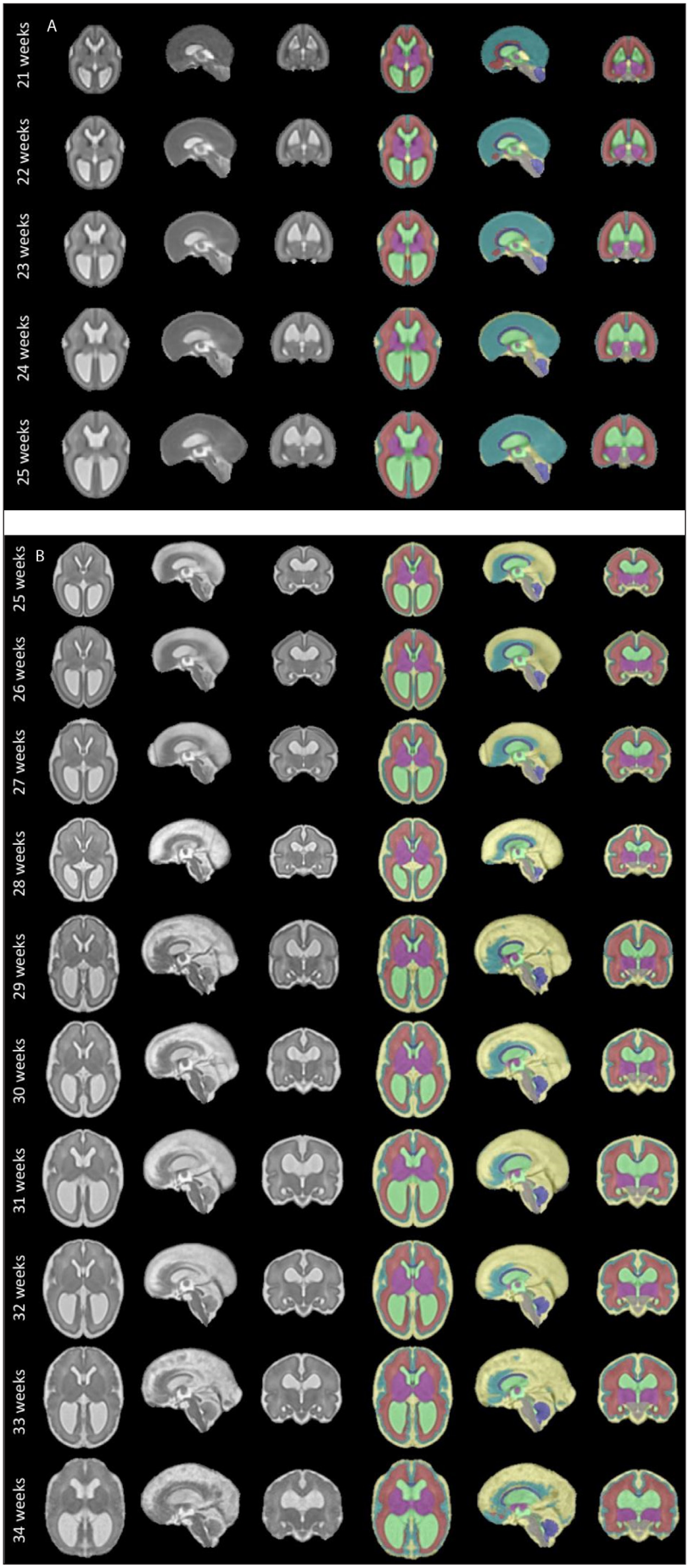

Figure 2 Overview of our Spatio-temporal atlas in fetuses with open spina bifida before **(a)** and after **(b)** in utero spina bifida repair. These include the overview of the eight fetal brain segmentation regions. Yellow: extra-axial cerebrospinal fluid, turquoise: cortex, red: white matter, purple: deep grey matter, grey: brainstem, green: intra-axial cerebrospinal fluid, light blue: cerebellum, dark blue: corpus callosum.

CDH have demonstrated several abnormalities, including increased extra-axial space, delayed sulcation and white matter injury, but the exact mechanisms remain unclear, and studies reporting on the neurodevelopmental outcome in isolated CDH are limited [45–47]. Fetuses with CDH have variable degrees of hemodynamic dysfunction. We have previously reported a decline of more than 20% in the middle cerebral artery peak systolic velocity, hence in brain perfusion in fetuses with CDH [48]. There may be similarities to the circulatory disturbances in fetuses with congenital heart defects where there are recognized alterations in antenatal brain development. In left-sided CDH, herniation of abdominal structures may result in mild to moderate cardiac hypoplasia, which in turn may compromise cardiac output [49]. Cardiac compression in CDH fetuses may also compromise venous return [49, 50]. This may, in turn, cause venous congestion and lead to decreased CSF resorption [51], and an overall increase of intracranial fluid.

We reported on a significant delay in brain development in fetuses with isolated CDH at 28 weeks of gestation and to a lesser extent at 33 weeks of gestation. This is in line with earlier observations by ultrasound and the first MRI data demonstrating an altered brain development in utero in CDH fetuses. Others have not found such differences [50], and those looking only at postnatal data hypothesized that postnatal events may eventually cause altered brain development [50, 52–56].

FETAL BRAIN MRI IN CONGENITAL CYTOMEGALOVIRUS INFECTION

In fetuses infected with CMV in the first trimester, there is an increased risk of sensorineural hearing loss and impaired cognitive development [1, 2, 57–61]. Neurosonography (NSG) is the most important modality in the follow-up of fetuses with confirmed first-trimester CMV-infection [59]. We found an added value of fetal MRI in the third trimester in fetuses with proven first-trimester CMV infection [3]. Moreover, there is a correlation between grading of abnormalities found at NSG [62] and those found at MRI [5]. The importance of white matter abnormalities for the outcome is reflected in a new brain MRI score for postnatal evaluation [63]. The only prenatal grading system for brain abnormalities on fetal MRI [5] also includes abnormal white matter hyperintensities. Yet, white matter hyperintensity remains a controversial finding on fetal MRI, especially in cCMV [64, 65]. It is probably the most known false-positive finding in CMV because of its subjectivity [5, 66]. Recently, Roee et al. [67] have demonstrated MRI detects more subtle findings in CMV-infected fetuses. But more importantly, they found 66% false positive findings in fetuses with an unknown infective status undergoing imaging, the majority being detected on MRI only, emphasizing the importance of amniocentesis in this population [67]. In our study, we evaluated the routine application of diffusion weighted imaging (DWI) in fetuses with proven first-trimester cCMV to evaluate the white matter. Despite a failure rate of >10%, DWI should be implemented in routine fetal MRI for CMV as we found a significant higher ADC value in the brain of cCMV-infected fetuses compared to controls, and our findings suggested a correlation with the severity of abnormalities found on anatomical sequences [3] The higher ADC is in line with a postnatal study comparing cCMV with periventricular leukomalacia (PVL) in children [68].

FETAL BRAIN MRI IN FETUSES TREATED FOR TWIN-TO-TWIN TRANSFUSION SYNDROME

In twin pregnancies, there is an increased risk of abnormal postnatal neurological development in fetuses surviving TTTS [69–71]. Others showed a benefit of fetal brain MRI for the detection of brain abnormalities in TTTS [72, 73]. The ISUOG practice guidelines on the role of ultrasound in twin pregnancy do not encourage fetal brain MRI at 30 weeks in survivors after laser ablation TTTS [74]. Nonetheless, we offer our patients a routine fetal brain MRI in the third trimester. In our retrospective study, compared to ultrasound, we found that MRI detected an additional brain lesion in 6% (4/69) [75]. Although the number of abnormalities in our study, as in other studies, was rather small, their consequences however were very important. Of the four pregnancies, the only one that was continued showed cerebral palsy of the affected twin postnatally. The abnormalities only detected on MRI were disorders of cortical development (Table 1), known to be often missed on US and detected more easily on MRI (Table 1) [17, 73, 76]. Migrational disorders are difficult to diagnose [20, 76]. Furthermore, they are more difficult to diagnose on neurosonography, increasing the value of the MRI in these cases [77], (Figure 3). Righini et al. [76] presented their experience in the detection of abnormalities of cortical malformation prior to 24 weeks and described different cortical patterns [76]. Glenn et al. [20] showed that the accuracy of MRI is highest when the abnormality is seen in at least two planes [17]. In addition, we often perform a repeat MRI after 10–14 days for confirmation in these cases. This practice of course is not always feasible if the legislation regarding continuation of the pregnancy is more limited compared to our country [76]. Our results suggest routine third trimester MRI in survivors of TTTS after laser ablation seems justified.

	INTERVENTION (WEEKS)	SINGLE IUFD CO-TWIN	DIAGNOSIS	GA MRI (WEEKS)	MAIN LESION	OUTCOME AFFECTED TWIN
Case 1	26.3	No	MRI	29.5; 31.5	Parietotemporal white matter heterogeneity with foci of bleeding; evolution to atrophy on follow-up	Spontaneous in utero demise of donor at 34.5 weeks
Case 2	20.2	No	MRI	30.1	Focal polymicrogyria frontal right	Birth at 34 weeks, cerebral palsy at 5 years
Case 3	16.4	No	MRI	28.2; 31.1	Bilateral focal polymicrogyria	Cord occlusion
Case 4	24.1	Cord occlusion for recurrent TTTS	MRI	27.4	Focal polymicrogyria	Termination of pregnancy
Case 5	19.5	Spontaneous demise day 5 post laser	US + MRI	29.5	Bilateral cortical atrophy secondary to bleeding	Comfort care after birth at 30 weeks because of brain anomaly and prenatal bowel perforation–neonatal demise
Case 6	21.2	No	US + MRI	29.2	Cortical atrophy	Cord occlusion

Table 1 Characteristics of the six fetuses with brain lesions on third-trimester MRI after laser coagulation of the anastomoses.

Legend: GA = gestational age; MRI = magnetic resonance imaging, US = ultrasound; TTTS = twin-to-twin transfusion syndrome; IUFD: Intra-uterine fetal death.

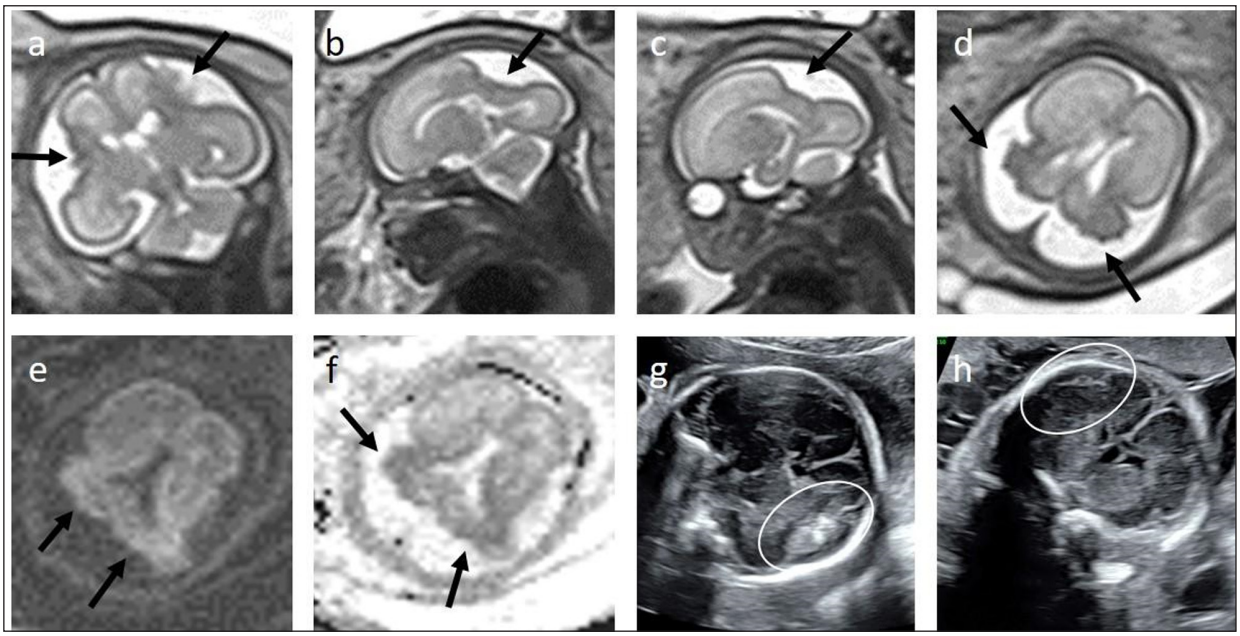

Figure 3 T2-weighted MRI images **(a–d)** and DWI **(e)** with corresponding ADC map **(f)** of an ex-donor at a gestation of 28 weeks (w) in a monochorionic diamniotic pregnancy complicated by TTTS with laser intervention at 20 w (Case 5 in Table 1). Prior US at 24 w **(g)** and 26 w **(h)** are also shown. Fetal MRI was performed for further evaluation of suspected subdural bleeding on the right, which appeared to remain stable in extension but with decreasing echogenicity (white circle in g and h). In addition, the fetus was also monitored closely with US for necrotizing enterocolitis with bowel distension and complicated ascites with peritoneal hyperechoic nodules (not shown). MRI at 28 w (a–f) demonstrates symmetrical bilateral cortical atrophy with irregular lining and hypo-intense signal on T2 (black arrow in a-d), in keeping with old ischemia. On b-1000 of DWI (e) and ADC (f) no acute ischemia was seen; only the same atrophy (black arrow in e and f) was evident.

CONCLUSION

Although we have demonstrated the added value of fetal brain MRI in several fetal conditions, it remains a challenging technique that needs to be performed upon proven indications and in centers with the necessary expertise in fetal imaging [78]. Not only will this allow maximized exposure in these specialized centers, this will also permit to interpret the findings on fetal imaging (neurosonography and fetal MRI) in a multidisciplinary setting (including fetal specialist, radiologist, pediatric neurologist, geneticist, pathologist) as recommended [78–81].

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COMPETING INTERESTS

The author has no competing interests to declare.

AUTHOR AFFILIATION

Michael Aertsen orcid.org/0000-0003-1994-5365
KU Leuven, BE

REFERENCES

1. **Elkan Miller T, Weisz B, Yinon Y,** et al. Congenital cytomegalovirus infection following second and third trimester maternal infection is associated with mild childhood adverse outcome not predicted by prenatal imaging. *Journal of the Pediatric Infectious Diseases Society*. 2021; 10(5): 562–8. DOI: https://doi.org/10.1093/jpids/piaa154
2. **Kyriakopoulou A, Serghiou S, Dimopoulou D,** et al. Antenatal imaging and clinical outcome in congenital CMV infection: A field-wide systematic review and meta-analysis. *The Journal of infection*. 2020; 80(4): 407–18. DOI: https://doi.org/10.1016/j.jinf.2020.02.012
3. **Aertsen M, Dymarkowski S, Vander Mijnsbrugge W, Cockmartin L,** et al. Anatomical and diffusion-weighted imaging abnormalities of third-trimester fetal brain in cytomegalovirus-infected fetuses. *Ultrasound Obstet Gynecol*. 2022; 60(1): 68–75. DOI: https://doi.org/10.1002/uog.24856
4. **Leruez-Ville M, Ghout I, Bussieres L,** et al. In utero treatment of congenital cytomegalovirus infection with valacyclovir in a multicenter, open-label, phase II study. *Am J Obstet Gynecol*. 2016; 215(4): 462 e1–e10. DOI: https://doi.org/10.1016/j.ajog.2016.04.003
5. **Cannie MM, Devlieger R, Leyder M,** et al. Congenital cytomegalovirus infection: contribution and best timing of prenatal MR imaging. *European Radiology*. 2016; 26(10): 3760–9. DOI: https://doi.org/10.1007/s00330-015-4187-0
6. **Leruez-Ville M, Ren S, Magny JF,** et al. Accuracy of prenatal ultrasound screening to identify fetuses infected by cytomegalovirus which will develop severe long-term sequelae. *Ultrasound Obstet Gynecol*. 2021; 57(1): 97–104. DOI: https://doi.org/10.1002/uog.22056
7. **Heuer GG, Moldenhauer JS, Scott Adzick N.** Prenatal surgery for myelomeningocele: review of the literature and future directions. *Childs Nerv Syst*. 2017; 33(7): 1149–55. DOI: https://doi.org/10.1007/s00381-017-3440-z
8. **Aertsen M, Verduyckt J, De Keyzer F,** et al. Reliability of MR Imaging–Based Posterior Fossa and Brain Stem Measurements in Open Spinal Dysraphism in the Era of Fetal Surgery. *American Journal of Neuroradiology*. 2019; 40(1): 191–8. DOI: https://doi.org/10.3174/ajnr.A5930
9. **Adzick NS, Thom EA, Spong CY,** et al. A Randomized Trial of Prenatal versus Postnatal Repair of Myelomeningocele. *New England Journal of Medicine*. 2011; 364(11): 993–1004. DOI: https://doi.org/10.1056/NEJMoa1014379
10. **Sepulveda F, Quezada F, Montoya F, Sepulveda W.** Interpeduncular angle: A new parameter for assessing intracranial hypotension in fetuses with spinal dysraphism. *Prenat Diagn*; 2021. DOI: https://doi.org/10.1002/pd.5905
11. **Sutton LN.** Improvement in Hindbrain Herniation Demonstrated by Serial Fetal Magnetic Resonance Imaging Following Fetal Surgery for Myelomeningocele. 1999; 282(19): 1826. DOI: https://doi.org/10.1001/jama.282.19.1826
12. **Joyeux L, Van der Merwe J, Aertsen M,** et al. Neuroprotection is improved by watertightness of fetal spina bifida repair in fetal lamb. *Ultrasound Obstet Gynecol*; 2022. DOI: https://doi.org/10.1002/uog.24907
13. **Zarutskie A, Guimaraes C, Yepez M,** et al. Prenatal brain imaging for predicting need for postnatal hydrocephalus treatment in fetuses that had neural tube defect repair in utero. *Ultrasound Obstet Gynecol*. 2019; 53(3): 324–34. DOI: https://doi.org/10.1002/uog.20212
14. **Rethmann C, Scheer I, Meuli M,** et al. Evolution of posterior fossa and brain morphology after in utero repair of open neural tube defects assessed by MRI. *Eur Radiol*. 2017; 27(11): 4571–80. DOI: https://doi.org/10.1007/s00330-017-4807-y
15. **Nagaraj UD, Peiro JL, Bierbrauer KS,** et al. . Evaluation of Subependymal Gray Matter Heterotopias on Fetal MRI. *AJNR Am J Neuroradiol*. 2016; 37(4): 720–5. DOI: https://doi.org/10.3174/ajnr.A4585
16. **Trigo L, Eixarch E, Bottura I,** et al. Prevalence of supratentorial anomalies assessed by magnetic resonance imaging in fetuses with open spina bifida. *Ultrasound Obstet Gynecol*. 2022; 59(6): 804–12. DOI: https://doi.org/10.1002/uog.23761
17. **Crombag N, Sacco A, Stocks B,** et al. 'We did everything we could'- a qualitative study exploring the acceptability of maternal-fetal surgery for spina bifida to parents. *Prenat Diagn*. 2021; 41(8): 910–21. DOI: https://doi.org/10.1002/pd.5996
18. **McLone DG, Dias MS.** The Chiari II malformation: cause and impact. *Childs Nerv Syst*. 2003; 19(7–8): 540–50. DOI: https://doi.org/10.1007/s00381-003-0792-3
19. **Blondiaux E, Sileo C, Nahama-Allouche C,** et al. Periventricular nodular heterotopia on prenatal ultrasound and magnetic resonance imaging. *Ultrasound Obstet Gynecol*. 2013; 42(2): 149–55. DOI: https://doi.org/10.1002/uog.12340
20. **Glenn OA, Cuneo AA, Barkovich AJ,** et al. Malformations of cortical development: diagnostic accuracy of fetal MR

imaging. *Radiology*. 2012; 263(3): 843–55. DOI: https://doi.org/10.1148/radiol.12102492

21. **Miller E, Widjaja E, Blaser S,** et al. The old and the new: supratentorial MR findings in Chiari II malformation. *Childs Nerv Syst*. 2008; 24(5): 563–75. DOI: https://doi.org/10.1007/s00381-007-0528-x
22. **Mitchell LA, Simon EM, Filly RA, Barkovich AJ.** Antenatal Diagnosis of Subependymal Heterotopia. 2000; 21(2): 296–300.
23. **Mufti N, Sacco A, Aertsen M,** et al. What brain abnormalities can magnetic resonance imaging detect in foetal and early neonatal spina bifida: a systematic review. *Neuroradiology*. 2022; 64(2): 233–45. DOI: https://doi.org/10.1007/s00234-021-02853-1
24. **Ebner M, Wang GT, Li WQ,** et al. An automated framework for localization, segmentation and super-resolution reconstruction of fetal brain MRI. *Neuroimage*. 2020; 206. DOI: https://doi.org/10.1016/j.neuroimage.2019.116324
25. **Fidon L, Ourselin S, Vercauteren T.** Distributionally Robust Deep Learning using Hardness Weighted Sampling 2020; 2020 January: [arXiv: 2001.02658 p.]. https://ui.adsabs.harvard.edu/abs/2020arXiv200102658F.
26. **Mufti N, Aertsen M, Ebner M,** et al. Cortical spectral matching and shape and volume analysis of the fetal brain pre- and post-fetal surgery for spina bifida: a retrospective study. *Neuroradiology*. 2021; 63(10): 1721–34. DOI: https://doi.org/10.1007/s00234-021-02725-8
27. **Danzer E, Joyeux L, Flake AW,** et al. Fetal surgical intervention for myelomeningocele: lessons learned, outcomes, and future implications. *Dev Med Child Neurol*. 2020; 62(4): 417–25. DOI: https://doi.org/10.1111/dmcn.14429
28. **Joyeux L, Belfort MA.** Fetal surgery for spina bifida: a great success story in surgical innovation. *Dev Med Child Neurol*. 2021; 63(11): 1243–4. DOI: https://doi.org/10.1111/dmcn.15019
29. **Sanz Cortes M, Chmait RH, Lapa DA,** et al. Experience of 300 cases of prenatal fetoscopic open spina bifida repair: report of the International Fetoscopic Neural Tube Defect Repair Consortium. *Am J Obstet Gynecol*. 2021; 225(6): 678 e1–e11. DOI: https://doi.org/10.1016/j.ajog.2021.05.044
30. **Nagaraj UD, Bierbrauer KS, Stevenson CB,** et al. Prenatal and postnatal MRI findings in open spinal dysraphism following intrauterine repair via open versus fetoscopic surgical techniques. *Prenat Diagn*. 2020; 40(1): 49–57. DOI: https://doi.org/10.1002/pd.5540
31. **Nagaraj UD, Bierbrauer KS, Stevenson CB,** et al. Spinal Imaging Findings of Open Spinal Dysraphisms on Fetal and Postnatal MRI. *AJNR Am J Neuroradiol*. 2018; 39(10): 1947–52. DOI: https://doi.org/10.3174/ajnr.A5760
32. **Nagaraj UD, Bierbrauer KS, Stevenson CB,** et al. Myelomeningocele Versus Myelocele on Fetal MR Images: Are There Differences in Brain Findings? *AJR Am J Roentgenol*. 2018; 211(6): 1376–80. DOI: https://doi.org/10.2214/AJR.18.20088
33. **Nagaraj UD, Bierbrauer KS, Zhang B,** et al. Hindbrain Herniation in Chiari II Malformation on Fetal and Postnatal MRI. *AJNR Am J Neuroradiol*. 2017; 38(5): 1031–6. DOI: https://doi.org/10.3174/ajnr.A5116
34. **Del Bigio MR.** Neuropathology and structural changes in hydrocephalus. *Developmental Disabilities Research Reviews*. 2010; 16(1): 16–22. DOI: https://doi.org/10.1002/ddrr.94
35. **Juranek J, Dennis M, Cirino PT,** et al. The cerebellum in children with spina bifida and Chiari II malformation: Quantitative volumetrics by region. *Cerebellum*. 2010; 9(2): 240–8. DOI: https://doi.org/10.1007/s12311-010-0157-x
36. **Juranek J, Salman MS.** Anomalous development of brain structure and function in spina bifida myelomeningocele. *Developmental Disabilities Research Reviews*. 2010; 16(1): 23–30. DOI: https://doi.org/10.1002/ddrr.88
37. **McLone DG, Knepper PA.** The cause of Chiari II malformation: a unified theory. *Pediatric neuroscience*. 1989; 15(1): 1–12. DOI: https://doi.org/10.1159/000120432
38. **Juranek J, Fletcher JM, Hasan KM,** et al. Neocortical reorganization in spina bifida. *Neuroimage*. 2008; 40(4): 1516–22. DOI: https://doi.org/10.1016/j.neuroimage.2008.01.043
39. **Treble A, Juranek J, Stuebing KK,** et al. Functional significance of atypical cortical organization in spina bifida myelomeningocele: relations of cortical thickness and gyrification with IQ and fine motor dexterity. *Cerebral Cortex* (New York, NY: 1991). 2013; 23(10): 2357–69. DOI: https://doi.org/10.1093/cercor/bhs226
40. **Fidon L, Viola E, Mufti N,** et al. A spatio-temporal atlas of the developing fetal brain with spina bifida aperta [version 1; peer review: 1 approved]. 2021; 1(123). DOI: https://doi.org/10.12688/openreseurope.13914.1
41. **Jakab A, Payette K, Mazzone L,** et al. Emerging magnetic resonance imaging techniques in open spina bifida in utero. *European Radiology Experimental*. 2021; 5(1): 23. DOI: https://doi.org/10.1186/s41747-021-00219-z
42. **Russo FM, Cordier AG, Basurto D,** et al. Fetal endoscopic tracheal occlusion reverses the natural history of right-sided congenital diaphragmatic hernia: European multicenter experience. *Ultrasound Obstet Gynecol*. 2021; 57(3): 378–85. DOI: https://doi.org/10.1002/uog.23115
43. **Deprest JA, Nicolaides KH, Benachi A,** et al. Randomized Trial of Fetal Surgery for Severe Left Diaphragmatic Hernia. *N Engl J Med*; 2021. DOI: https://doi.org/10.1056/NEJMoa2027030
44. **Deprest JA, Benachi A, Gratacos E,** et al. Randomized Trial of Fetal Surgery for Moderate Left Diaphragmatic Hernia. *N Engl J Med*; 2021. DOI: https://doi.org/10.1056/NEJMoa2026983
45. **Van der Veeken L, Vergote S, Kunpalin Y, Kristensen K, Deprest J,** et al. Neurodevelopmental outcomes in children with isolated congenital diaphragmatic hernia: A systematic review and meta-analysis. *Prenat Diagn*; 2021. DOI: https://doi.org/10.1002/pd.5916

46. **Danzer E, Hoffman C, D'Agostino JA,** et al. Neurodevelopmental outcomes at 5 years of age in congenital diaphragmatic hernia. *J Pediatr Surg*. 2017; 52(3): 437–43. DOI: https://doi.org/10.1016/j.jpedsurg.2016.08.008
47. **Danzer E, Kim SS.** Neurodevelopmental outcome in congenital diaphragmatic hernia: Evaluation, predictors and outcome. *World J Clin Pediatr*. 2014; 3(3): 30–6. DOI: https://doi.org/10.5409/wjcp.v3.i3.30
48. **Van Mieghem T, Sandaite I, Michielsen K,** et al. Fetal cerebral blood flow velocities in congenital diaphragmatic hernia. *Ultrasound Obstet Gynecol*. 2010; 36(4): 452–7. DOI: https://doi.org/10.1002/uog.7703
49. **Vogel M, McElhinney DB, Marcus E,** et al. Significance and outcome of left heart hypoplasia in fetal congenital diaphragmatic hernia. *Ultrasound Obstet Gynecol*. 2010; 35(3): 310–7. DOI: https://doi.org/10.1002/uog.7497
50. **Radhakrishnan R, Merhar SL, Su W,** et al. Prenatal Factors Associated with Postnatal Brain Injury in Infants with Congenital Diaphragmatic Hernia. *AJNR Am J Neuroradiol*. 2018; 39(3): 558–62. DOI: https://doi.org/10.3174/ajnr.A5500
51. **Miyajima M, Arai H.** Evaluation of the Production and Absorption of Cerebrospinal Fluid. *Neurol Med Chir (Tokyo)*. 2015; 55(8): 647–56. DOI: https://doi.org/10.2176/nmc.ra.2015-0003
52. **Danzer E, Hoffman C, D'Agostino JA,** et al. Short-Term Neurodevelopmental Outcome in Congenital Diaphragmatic Hernia: The Impact of Extracorporeal Membrane Oxygenation and Timing of Repair. *Pediatr Crit Care Med*. 2018; 19(1): 64–74. DOI: https://doi.org/10.1097/PCC.0000000000001406
53. **Danzer E, Zarnow D, Gerdes M,** et al. Abnormal brain development and maturation on magnetic resonance imaging in survivors of severe congenital diaphragmatic hernia. *Journal of Pediatric Surgery*. 2012; 47(3): 453–61. DOI: https://doi.org/10.1016/j.jpedsurg.2011.10.002
54. **Radhakrishnan R, Merhar SL, Burns P,** et al. Fetal brain morphometry on prenatal magnetic resonance imaging in congenital diaphragmatic hernia. *Pediatric Radiology*. 2019; 49(2): 217–23. DOI: https://doi.org/10.1007/s00247-018-4272-z
55. **Radhakrishnan R, Merhar S, Meinzen-Derr J,** et al. Correlation of MRI Brain Injury Findings with Neonatal Clinical Factors in Infants with Congenital Diaphragmatic Hernia. *AJNR Am J Neuroradiol*. 2016; 37(9): 1745–51. DOI: https://doi.org/10.3174/ajnr.A4787
56. **Lucignani M, Longo D, Fontana E,** et al. Morphometric Analysis of Brain in Newborn with Congenital Diaphragmatic Hernia. *Brain Sci*. 2021; 11(4). DOI: https://doi.org/10.3390/brainsci11040455
57. **Navti OB, Al-Belushi M, Konje JC.** Cytomegalovirus infection in pregnancy – An update. *European Journal of Obstetrics, Gynecology, and Reproductive Biology*. 2021; 258: 216–22. DOI: https://doi.org/10.1016/j.ejogrb.2020.12.006
58. **Buca D, Di Mascio D, Rizzo G,** et al. Outcome of fetuses with congenital cytomegalovirus infection and normal ultrasound at diagnosis: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2021; 57(4): 551–9. DOI: https://doi.org/10.1002/uog.23143
59. **Leruez-Ville M, Foulon I, Pass R,** et al. Cytomegalovirus infection during pregnancy: state of the science. *Am J Obstet Gynecol*. 2020; 223(3): 330–49. DOI: https://doi.org/10.1016/j.ajog.2020.02.018
60. **Lipitz S, Yinon Y, Malinger G,** et al. Risk of cytomegalovirus-associated sequelae in relation to time of infection and findings on prenatal imaging. *Ultrasound Obstet Gynecol*. 2013; 41(5): 508–14. DOI: https://doi.org/10.1002/uog.12377
61. **Dreher AM, Arora N, Fowler KB,** et al. Spectrum of disease and outcome in children with symptomatic congenital cytomegalovirus infection. *J Pediatr*. 2014; 164(4): 855–9. DOI: https://doi.org/10.1016/j.jpeds.2013.12.007
62. **Leruez-Ville M, Ville Y.** Fetal cytomegalovirus infection. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2017; 38: 97–107. DOI: https://doi.org/10.1016/j.bpobgyn.2016.10.005
63. **Lucignani G, Rossi Espagnet MC, Napolitano A,** et al. A new MRI severity score to predict long-term adverse neurologic outcomes in children with congenital Cytomegalovirus infection. *The Journal of Maternal-Fetal & Neonatal Medicine: the Official Journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet*. 2021; 34(6): 859–66. DOI: https://doi.org/10.1080/14767058.2019.1620725
64. **Doneda C, Parazzini C, Righini A, Rustico M,** et al. Early cerebral lesions in cytomegalovirus infection: prenatal MR imaging. *Radiology*. 2010; 255(2): 613–21. DOI: https://doi.org/10.1148/radiol.10090749
65. **Yaniv G, Hoffmann C, Weisz B,** et al. Region-specific reductions in brain apparent diffusion coefficient in cytomegalovirus-infected fetuses. *Ultrasound Obstet Gynecol*. 2016; 47(5): 600–7. DOI: https://doi.org/10.1002/uog.14737
66. **Diogo MC, Glatter S, Binder J,** et al. The MRI spectrum of congenital cytomegalovirus infection. *Prenat Diagn*. 2020; 40(1): 110–24. DOI: https://doi.org/10.1002/pd.5591
67. **Roee B, Adi W, Michael B,** et al. Subtle findings on fetal brain imaging in CMV infected pregnancies: What is the clinical significance? A retrospective analysis with outcome correlation. *Prenat Diagn*. 2020; 40(4): 447–53. DOI: https://doi.org/10.1002/pd.5634
68. **Van der Voorn JP, Pouwels PJ, Vermeulen RJ,** et al. Quantitative MR imaging and spectroscopy in congenital cytomegalovirus infection and periventricular leukomalacia suggests a comparable neuropathological substrate of the cerebral white matter lesions. *Neuropediatrics*. 2009; 40(4): 168–73. DOI: https://doi.org/10.1055/s-0029-1243228

69. **Lopriore E, Van Wezel-Meijler G, Middeldorp JM,** et al. Incidence, origin, and character of cerebral injury in twin-to-twin transfusion syndrome treated with fetoscopic laser surgery. *Am J Obstet Gynecol*. 2006; 194(5): 1215–20. DOI: https://doi.org/10.1016/j.ajog.2005.12.003
70. **Sananès N, Gabriele V, Weingertner AS,** et al. Evaluation of long-term neurodevelopment in twin-twin transfusion syndrome after laser therapy. *Prenat Diagn*. 2016; 36(12): 1139–45. DOI: https://doi.org/10.1002/pd.4950
71. **Schou KV, Lando AV, Ekelund CK,** et al. Long-Term Neurodevelopmental Outcome of Monochorionic Twins after Laser Therapy or Umbilical Cord Occlusion for Twin-Twin Transfusion Syndrome. *Fetal Diagn Ther*. 2019; 46(1): 20–7. DOI: https://doi.org/10.1159/000491787
72. **Griffiths PD, Sharrack S, Chan KL,** et al. Fetal brain injury in survivors of twin pregnancies complicated by demise of one twin as assessed by in utero MR imaging. *Prenat Diagn*. 2015; 35(6): 583–91. DOI: https://doi.org/10.1002/pd.4577
73. **Stirnemann J, Chalouhi G, Essaoui M,** et al. Fetal brain imaging following laser surgery in twin-to-twin surgery. *BJOG : An International Journal of Obstetrics and Gynaecology*. 2018; 125(9): 1186–91. DOI: https://doi.org/10.1111/1471-0528.14162
74. **Khalil A, Rodgers M, Baschat A,** et al. ISUOG Practice Guidelines: role of ultrasound in twin pregnancy. *Ultrasound Obstet Gynecol*. 2016; 47(2): 247–63. DOI: https://doi.org/10.1002/uog.15821
75. **Aertsen M, Van Tieghem De Ten Berghe C, Deneckere S,** et al. The prevalence of brain lesions after in utero surgery for twin-to-twin transfusion syndrome on third-trimester MRI: a retrospective cohort study. *Eur Radiol*. 2021; 31(6): 4097–103. DOI: https://doi.org/10.1007/s00330-020-07452-x
76. **Righini A, Parazzini C, Doneda C,** et al. Early formative stage of human focal cortical gyration anomalies: fetal MRI. *AJR Am J Roentgenol*. 2012; 198(2): 439–47. DOI: https://doi.org/10.2214/AJR.11.6662
77. **Paladini D, Quarantelli M, Sglavo G,** et al. Accuracy of neurosonography and MRI in clinical management of fetuses referred with central nervous system abnormalities. *Ultrasound Obstet Gynecol*. 2014; 44(2): 188–96. DOI: https://doi.org/10.1002/uog.13243
78. **Prayer D, Malinger G, Brugger PC,** et al. ISUOG Practice Guidelines: performance of fetal magnetic resonance imaging. *Ultrasound Obstet Gynecol*. 2017; 49(5): 671–80. DOI: https://doi.org/10.1002/uog.17412
79. **Malinger G, Ben-Sira L, Lev D,** et al. Fetal brain imaging: a comparison between magnetic resonance imaging and dedicated neurosonography. *Ultrasound Obst Gyn*. 2004; 23(4): 333–40. DOI: https://doi.org/10.1002/uog.1016
80. **Paladini D, Malinger G, Pilu G,** et al. The MERIDIAN trial: caution is needed. *Lancet*. 2017; 389(10084): 2103. DOI: https://doi.org/10.1016/S0140-6736(17)31337-5
81. **Pistorius LR, Hellmann PM, Visser GH,** et al. Fetal neuroimaging: ultrasound, MRI, or both? *Obstet Gynecol Surv*. 2008; 63(11): 733–45. DOI: https://doi.org/10.1097/OGX.0b013e318186d3ea

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