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Prenatal visualisation of the torcular herophili by means of a Doppler technology highly sensitive for low-velocity flow in the expert assessment of the posterior fossa: a prospective study

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**Prenatal visualization of the torcular herophili by means of a Doppler technology highly sensitive for low velocity flow in the expert assessment of the posterior fossa: a prospective study.**

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Keywords:	DOPPLER ULTRASOUND, FETAL DIAGNOSIS AND THERAPY
Clinical Category:	FETAL MEDICINE
Abstract:	<p><b>Objective</b> To evaluate the usefulness of a Doppler technology highly sensitive for low velocity flow in the antenatal imaging of the torcular herophili (TH) in the second trimester of pregnancy.</p> <p><b>Design</b> Prospective study.</p> <p><b>Setting</b> Referral Fetal Medicine Unit.</p> <p><b>Population</b> Non-consecutive series of singleton pregnancies submitted to antenatal neurosonogram between 20 and 28 weeks of gestation.</p> <p><b>Methods</b> A midsagittal section of the fetal brain was obtained by insonating through the anterior fontanelle, then the MV-Flow™ and LumiFlow™ presets were selected in order to visualize the TH as the posterior confluence of the superior sagittal sinus and the straight sinus.</p> <p><b>Main outcome measures</b> Evaluation of the anatomic relationship of the TH with the “transpalatal line” joining the upper bony palate to the fetal skull.</p> <p><b>Results</b> 99 cases were recruited, including 1 case of open spina bifida, 1 Dandy-Walker malformation (DWM) and 2 Blake’s pouch cysts. In normal cases the TH appeared to lie on or just below the “transpalatal line”. In the</p>

	<p>cases of Blake's pouch cyst the position of the TH appeared normal if compared to controls, while in DWM a supraelevated position of the TH in respect of the transpalatal line was demonstrated. Finally, in the case of Chiari II malformation the TH was identified below the "transpalatal plane".</p> <p>Conclusions</p> <p>The prenatal US visualization of the TH by means of newly developed Doppler technologies characterized by high sensitivity for low velocity flow is feasible and allows the indirect evaluation of the insertion cerebellar tentorium in the second trimester.</p>

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Manuscripts

1 **TITLE PAGE**

2 **Prenatal visualization of the torcular herophili by means of a Doppler technology highly sensitive**  
3 **for low velocity flow in the expert assessment of the posterior fossa: a prospective study.**

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21

22 **Running title**

23 Prenatal imaging of the torcular herophili.

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24 **Abstract**

25 **Objective**

26 To evaluate the usefulness of a Doppler technology highly sensitive for low velocity flow in the  
27 antenatal imaging of the torcular herophili (TH) in the second trimester of pregnancy.

28 **Design**

29 Prospective study.

30 **Setting**

31 Referral Fetal Medicine Unit.

32 **Population**

33 Non-consecutive series of singleton pregnancies submitted to antenatal neurosonogram between  
34 20 and 28 weeks of gestation.

35 **Methods**

36 A midsagittal section of the fetal brain was obtained by insonating through the anterior fontanelle,  
37 then the MV-Flow™ and LumiFlow™ presets were selected in order to visualize the TH as the  
38 posterior confluence of the superior sagittal sinus and the straight sinus.

39 **Main outcome measures**

40 Evaluation of the anatomic relationship of the TH with the “transpalatal line” joining the upper bony  
41 palate to the fetal skull.

42 **Results**

43 99 cases were recruited, including 1 case of open spina bifida, 1 Dandy-Walker malformation (DWM)  
44 and 2 Blake’s pouch cysts. In normal cases the TH appeared to lie on or just below the “transpalatal  
45 line”. In the cases of Blake’s pouch cyst the position of the TH appeared normal if compared to  
46 controls, while in DWM a supraelevated position of the TH in respect of the transpalatal line was

47 demonstrated. Finally, in the case of Chiari II malformation the TH was identified below the  
48 “transpalatal plane”.

49 **Conclusions**

50 The prenatal US visualization of the TH by means of newly developed Doppler technologies  
51 characterized by high sensitivity for low velocity flow is feasible and allows the indirect evaluation  
52 of the insertion cerebellar tentorium in the second trimester.

53 **Funding:** none.

54 **Keywords:** Doppler ultrasound, fetal cerebellum, Dandy-Walker malformation, Blake’s pouch cyst,  
55 tentorium cerebelli.

56 **Tweetable abstract:** Prenatal imaging of the torcular herophili using a Doppler technology highly  
57 sensitive for low velocity flow.

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## 58 **Introduction**

59 The torcular herophili (TH), also known as “confluence of sinuses”, is a venous structure draining  
60 the major vessels of the intracerebral venous system, among whom the superior sagittal sinus and  
61 the straight, transverse, sigmoid, cavernous and occipital sinuses (1,2).

62 Under normal circumstances the TH is located in the middle aspect of the occipital bone and  
63 posterior to the cerebellum, just inside the cranial vault (2,3), and lies in the erosion of the occipital  
64 bone where the major venous sinus tributaries congregate (4), which is located at the junction of  
65 the falx cerebri with the tentorium cerebelli. The antenatal assessment of this latter anatomic  
66 structure is of great interest for the Fetal Medicine Specialists in the accurate classification and  
67 differential diagnosis of posterior fossa abnormalities. Indeed, the upwards displacement of the  
68 tentorium cerebelli in respect of its normal insertion on the occipital clivus is among the diagnostic  
69 criteria of Dandy-Walker Malformation (DWM) in fetuses with hypoplastic and supraelevated  
70 cerebellar vermis and abnormal communication between the fourth ventricle and the cisterna  
71 magna (1,5,6). However, the antenatal visualization of the position of the tentorium cerebelli at  
72 grey-scale ultrasound on the midsagittal plane of the fetal brain is technically challenging, and this  
73 may lead to a limited agreement in the diagnosis of DWM in fetuses with abnormal findings of the  
74 posterior fossa.

75 Due to their close anatomic relationship, the position of the TH may be assumed as a clue of the  
76 insertion of cerebellar tentorium on the fetal skull. On this basis the antenatal sonographic  
77 demonstration of the TH at Doppler imaging has been proposed as a proxy of the direct visualization  
78 of the tentorium (1). On the midsagittal view of the fetal brain at 1<sup>st</sup> trimester ultrasound (US) Volpe  
79 et al. have accurately determined the insertion of the tentorium in fetuses with normal or abnormal  
80 posterior fossa, by measuring the angle between the brainstem and the TH (7). However, the  
81 antenatal imaging of the TH at conventional Doppler imaging is also technically challenging. MV-



82 Flow™ and LumiFlow™ (Samsung Medison Co Ltd, Seoul, South Korea) are newly developed  
83 Doppler technologies that represent an alternative to Power Doppler for the visualization of slow  
84 flow microvascularized structures and vascular connections. In this study we evaluate the usefulness  
85 of MV-Flow™ technology combined with LumiFlow™ algorithm in the antenatal imaging of the TH  
86 in the second trimester of pregnancy.

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## 87 **Methods**

88 The study was conducted at two Italian Fetal Medicine referral Units (University Hospital of Parma  
89 and Carlo Poma Hospital of Mantua). The study population included a non-consecutive series of  
90 singleton pregnancies either referred from local US Departments or submitted to detailed antenatal  
91 neurosonogram due to clinical indication between 20 and 28 weeks of gestation. According to the  
92 Guidelines of the International Society on Ultrasound in Obstetrics and Gynecology, the fetal  
93 neurosonogram “usually includes the visualization of four coronal and three sagittal planes”, as well  
94 as of “the convolutions of the fetal brain that change throughout gestation” in addition to the axial  
95 views required for the basic examination (8).

96 In all the included cases, a dedicated assessment of the fetal anatomy was performed using a  
97 Samsung HERA W10 system equipped with multifrequency volumetric (4-8 MHz) transducer and  
98 MV-Flow™ and LumiFlow™ technology. For the purposes of the study, a midsagittal section of the  
99 fetal brain was obtained by insonating through the anterior fontanelle in order to visualize the  
100 corpus callosum and the cerebellar vermis on two-dimensional (2D) ultrasound. The MV-Flow™ and  
101 LumiFlow™ presets were selected and the insonation angle was adjusted in order to visualize the  
102 pericallosal arteries and the torcular herophili as the posterior confluence of the superior sagittal  
103 sinus and the straight sinus (Figure 1). The anatomic relationship of the TH with the “transpalatal  
104 line” joining the upper bony palate to the fetal skull was assessed in all cases. The mean time  
105 required to visualize the TH using the MV-Flow™ and LumiFlow™ presets was calculated in all cases.

106 The US examinations were performed for clinical or research purpose by four Authors (AD, GG, NV  
107 and TG). Exclusion criteria for the study were represented by the antenatal finding of abnormalities  
108 of the fetal central nervous system not involving the posterior fossa and by the failure to obtain a  
109 satisfactory view of the TH on the midsagittal view of the brain. Clinical data of the pregnancy and  
110 postnatal outcomes were obtained in all cases through medical records, while the ascertainment of

111 the antenatal diagnosis was performed either by neonatal ultrasound or, in the case of abnormal  
112 findings, by magnetic resonance imaging with or without pathology examination.

113 The study was conducted in the context of an unrestricted research collaboration with Samsung  
114 Medison Healthcare, Italy and approved by the local Ethics Committee of the University Hospital of  
115 Parma. Core outcome sets and patient involvement were not deemed as relevant for the research.

116 This case series was reported according to the Strengthening the Reporting of Observational Studies  
117 in Epidemiology (STROBE) guidelines (9).

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## 118 **Results**

119 Over the study period, 122 pregnant women between 20 and 28 gestational weeks were submitted  
120 to prenatal ultrasound in the two Fetal Medicine Centres involved. The study group consisted in 99  
121 (81.1%) patients, among whom 95 showed normal appearance of the forebrain and of the posterior  
122 fossa and 4 cases with abnormal findings of the posterior fossa including 1 open spina bifida, 1 DWM  
123 and 2 Blake's pouch cysts (BPC) (Figure S1). A summary of the demographic and clinical details of  
124 the study group is shown on Table S1. The median gestational age at ultrasound was 21<sup>+3</sup> weeks  
125 (20<sup>+0</sup> – 27<sup>+6</sup>).

126 In all the included cases optimal views of the TH together with the superior sagittal sinus and the  
127 straight sinus could be obtained by means of the MV-Flow™ and the LumiFlow™ presets. Among  
128 the fetuses with normal intracranial findings, at qualitative evaluation the TH appeared to lie on or  
129 just below a line drawn through the “transpalatal line” as shown in Figure 1. With regards to the  
130 three fetuses with cystic anomaly of the posterior fossa, in the cases of BPC the position of the TH  
131 appeared normal if compared to normal controls (Figure 2), while in DWM a supraelevated position  
132 of the TH in respect of the transpalatal line was demonstrated consistently with the upward  
133 displacement of the tentorium (Figure 3). Finally, in the case of Chiari II malformation the TH was  
134 identified well below the “transpalatal plane” (Figure 4). In all cases the prenatal US diagnosis was  
135 confirmed following delivery.

136 The time required to visualize the TH when the midsagittal view of the fetal brain was obtained was  
137 less than one minute in all cases.

## 138 **Discussion**

### 139 Main findings

140 This study demonstrates that the prenatal US visualization of the TH by means of newly developed  
141 MV-Flow™ and LumiFlow™ Doppler techniques is feasible, and expert US seems to represent a  
142 reliable approach for the indirect evaluation of the cerebellar tentorium insertion in the second  
143 trimester.

### 144 Strengths and limitations

145 The original design of the study and the small number of Fetal Medicine Specialists undertaking the  
146 data collection represent the major strengths of our work. On the other hand, the mixed referral  
147 population, the non-consecutive recruitment of the cases and the small number of fetuses with  
148 abnormal findings may be acknowledged as limitations as they do not allow to comment on the  
149 performance of this novel method in the antenatal diagnosis of upward or downward displacement  
150 of the tentorium cerebelli. A larger prospective study assessing the accuracy of MV-Flow™ and  
151 LumiFlow™ in the antenatal classification of cystic abnormalities of the posterior fossa is warranted  
152 before any clinical implementation of the technique may be proposed.

153 The cystic malformations of the posterior fossa represent only a proportion of the large group of  
154 midbrain and hindbrain malformations which commonly present with some degree of vermian  
155 hypoplasia or dysplasia (10), and other conditions such as arachnoid cysts may be associated with  
156 the upward displacement of the TH with a normal insertion of the tentorium. Another limitation is  
157 that we were unable to visualize the TH in 17 cases showing normal appearance of the posterior  
158 fossa, however the midsagittal view of the fetal brain is not required outside the context of the  
159 expert assessment of the fetal brain. In this present study only the persistently unfavourable  
160 position of the fetal head precluded to obtain the midsagittal view required to visualize the TH,  
161 however other conditions impairing the spread of the US beam, among whom high BMI and uterine

162 fibroids, may limit the visualization of the TH. Finally, we have not attempted any formal comparison  
163 with Doppler techniques from other manufacturers characterized by high sensitivity for slow flow  
164 (1,7,11,12), which we believe is beyond the scope of this current paper. Based on the findings of our  
165 work it is not possible to speculate that MV-Flow™ and LumiFlow™ are superior to similar Doppler  
166 techniques, therefore no specific Doppler technique is to be deemed as required as long as the  
167 prenatal visualization of the TH on a midsagittal plane including also the bony palate can be  
168 accomplished.

### 169 Interpretation

170 The evaluation of the posterior fossa on the midsagittal plane is of paramount importance for the  
171 differential diagnosis between DWM and other conditions such as BPC and vermian hypoplasia (13-  
172 15). More specifically, the height, the rotation and the morphology of the cerebellar vermis have  
173 been reported to be feasible with either 2D or three-dimensional (3D) US as the cerebellar vermis  
174 is a hyperechoic structure which can be clearly distinguished from the brainstem and fourth  
175 ventricle, which lie anteriorly, and the fluid-filled cisterna magna (16-19).

176 While the vermian anatomy and biometry is crucial for the differential diagnosis between DWM and  
177 the other cystic malformations of the posterior fossa, another important additional finding to be  
178 considered in the diagnostic workout is represented by the tentorium cerebelli insertion (6,16). It  
179 has been postulated that its supraelevation is a mandatory diagnostic requisite of DWM, while a  
180 normally inserted tentorium in fetuses with upwards rotated vermis and wide communication  
181 between the 4<sup>th</sup> ventricle and cisterna magna is compatible with BPC. On this ground, the brainstem-  
182 tentorium angle (BTA) has been proposed for the quantitative evaluation of the insertion of the  
183 tentorium cerebelli by means of 3D US (16-19). To our knowledge, there is no study evaluating the  
184 feasibility of the quantitative assessment of the BTA on 2D imaging, which can be due to the fact  
185 that the visualization of the BTA on 2D US is challenging even among experienced investigators. Very

186 recently, another technique relying on the subjective assessment of the position of the choroid  
187 plexus in relation to the roof/cyst inlet of the fourth ventricle using 3D US has been proposed for  
188 the differential diagnosis of the posterior fossa cystic malformations, however such novel approach  
189 was evaluated retrospectively, on a limited number of cases and at a single Tertiary referral centre  
190 with expertise on 3D US and prenatal neurosonology (20). In such context, fetal MRI has been shown  
191 to add in the prenatal diagnosis of abnormalities of the fetal brain compared to expert ultrasound  
192 (21), and represents a valuable tool for the differential diagnosis of the cystic malformations of the  
193 posterior fossa by enabling the accurate assessment of the lobulation and fissuration of the fetal  
194 cerebellar vermis as well as the evaluation of the position of the cerebellar tentorium and of the TH  
195 (22,23,24). However, fetal MRI is an expensive second-level test which may not be readily available  
196 in all Units; furthermore, high expertise is required in order to interpret the anatomic characteristics  
197 of the posterior fossa across gestation (25).

198 A research by Volpe et al. has demonstrated the role of the visualization of the straight and of the  
199 superior sagittal sinus by means of color or power Doppler in the identification of the tentorial  
200 insertion when measured on 2D US at a gestational age between 11 and 14 weeks in the midsagittal  
201 view used to measure the nuchal translucency (7). In our cohort of fetuses in the second trimester  
202 of pregnancy with normal intracranial findings and in the cases with BPC we found that the TH and  
203 consequently the tentorium insertion lay on or just below a line drawn tangentially above the bony  
204 palate ("transpalatal plane"). On the other hand, in the case diagnosed with DWM, the TH was  
205 demonstrated to lie above the transpalatal plane, thus confirming the upward displacement of the  
206 tentorium, while in open spina bifida the TH was clearly imaged below the "transpalatal plane",  
207 which is consistent with the caudal displacement of the posterior fossa structures which  
208 characterize the Chiari 2 malformation. Therefore, the insertion of the tentorium cerebelli may be  
209 derived from the evaluation of the TH in relation to the "transpalatal plane". Such information,

210 which can be obtained in less than one minute when the midsagittal view of the fetal brain through  
211 the anterior fontanelle is obtained, is of crucial importance for the differential diagnosis, the  
212 prognostic assessment as well as the parental counseling of cases diagnosed with cystic  
213 malformations of the posterior fossa (14). We do not envisage that MV-Flow™ and LumiFlow™  
214 Doppler techniques will allow an easy and straightforward differential diagnosis of the cystic  
215 abnormalities of the posterior fossa, however we believe that these technologies are worth to be  
216 prospectively tested in referral Fetal Medicine Units with expertise in the diagnosis and classification  
217 of such conditions.

### 218 **Conclusion**

219 In conclusion, the use of a Doppler technology highly sensitive for low velocity flow represents an  
220 easy tool enabling a comprehensive assessment of the intracranial venous system of the fetus,  
221 which has the potential to improve our capability to assess the normal anatomy and to differentiate  
222 the abnormalities of the posterior fossa. Further prospective studies are required in order to confirm  
223 the usefulness of the visualization of the TH as an indirect evaluation of the tentorium cerebelli in a  
224 clinical setting.



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227

228 **Disclosure of interest.**

229 The Authors state no financial interest related to the content of this work.

230

231 **Conflict of interest statement**

232 This work was conducted in the context of an unrestricted and unremunerated research  
233 collaboration with Samsung Medison Healthcare, Italy.

234 Dr Dall'Asta states other unrestricted and unremunerated research collaborations with Samsung  
235 Medison Korea.

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238 Dr Fabiana Sorrentino is a biomedical engineer employed by Samsung Electronics Italy, Milan, Italy.

239 She has been in charge for the optimization of the newly developed Doppler technique evaluated  
240 in this study and has actively contributed in the conceptualization and in the finalization of this work.

241

242 **Contribution to Authorship**

243 Andrea Dall'Asta – Conceptualization, data collection, manuscript writing and editing.

244 Gianpaolo Grisolia – Conceptualization, data collection.

245 Nicola Volpe – Data and outcome collection, manuscript writing and editing.

246 Giovanni Battista Luca Schera – Data and outcome collection, manuscript writing and editing.

247 Fabiana Sorrentino – Conceptualization, ultrasound assistance and setting, manuscript review.

248 Tiziana Frusca – Conceptualization, manuscript review.

249 Tullio Ghi – Conceptualization, data collection, manuscript review.

250

251 **Details of ethics approval**

252 The study was approved by the local Ethics Committee of the University Hospital of Parma on

253 19/06/2019 (Number of approval 660)

254

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257 **References**

- 2581) Karl K, Heling KS, Chaoui R. Ultrasound of the Fetal Veins Part 3: The Fetal Intracerebral Venous  
259 System. *Ultraschall Med.* 2016 Feb;37(1):6-26.
- 2602) Muthukumar N, Palaniappan P. Tentorial venous sinuses: an anatomic study. *Neurosurgery.*  
261 1998;42(2):363–371. doi:10.1097/00006123-199802000-00097
- 2623) Has R, Esmer AC, Kalelioglu I, Yuksel A, Pata O, Demirbas R. Prenatal diagnosis of torcular herophili  
263 thrombosis: report of 2 cases and review of the literature. *J Ultrasound Med.* 2013 Dec;32(12):2205-  
264 11.
- 2654) Tubbs and Oaks, *Neuroanatomy*, 2002, Volume1, Page 14. Available at  
266 <http://www.neuroanatomy.org/2002/014.pdf>
- 2675) Gardner WJ, Smith JL, Padgett DH. The relationship of Arnold-Chiari and Dandy-Walker  
268 malformations. *J Neurosurg* 1972; 36: 481–486.
- 2696) Gandolfi Colleoni G, Contro E, Carletti A, Ghi T, Campobasso G, Rembouskos G et al. Prenatal  
270 diagnosis and outcome of fetal posterior fossa fluid collections. *Ultrasound Obstet Gynecol.* 2012  
271 Jun;39(6):625-31.
- 2727) Volpe P, Persico N, Fanelli T, De Robertis V, D'Alessandro J, Boito S et al. Prospective detection and  
273 differential diagnosis of cystic posterior fossa anomalies by assessing posterior brain at 11-14 weeks.  
274 *Am J Obstet Gynecol MFM* 2019.
- 2758) International Society of Ultrasound in Obstetrics & Gynecology Education Committee. Sonographic  
276 examination of the fetal central nervous system: guidelines for performing the 'basic examination'  
277 and the 'fetal neurosonogram'. *Ultrasound Obstet Gynecol.* 2007;29(1):109–116.  
278 doi:10.1002/uog.3909

- 2799) Von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP; STROBE Initiative. The  
280 Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement:  
281 guidelines for reporting observational studies. *Lancet* 2007; 370: 1453–1457.
- 28210) Barkovich AJ, Millen KJ, Dobyns WB. A developmental and genetic classification for midbrain-  
283 hindbrain malformations. *Brain*. 2009;132(Pt 12):3199-3230. doi:10.1093/brain/awp247
- 28411) Pooh RK. Normal anatomy by three-dimensional ultrasound in the second and third trimesters.  
285 *Semin Fetal Neonatal Med*. 2012 Oct;17(5):269-77.
- 28612) Taoka T, Fukusumi A, Miyasaka T, Kawai H, Nakane T, Kichikawa K et al. Structure of the Medullary  
287 Veins of the Cerebral Hemisphere and Related Disorders. *Radiographics*. 2017 Jan-Feb;37(1):281-  
288 297.
- 28913) Garel C. Posterior fossa malformations: main features and limits in prenatal diagnosis. *Pediatr Radiol*  
290 2010; 40: 1038–1045.
- 29114) D'Antonio F, Khalil A, Garel C, Pilu G, Rizzo G, Lerman-Sagie T et al. Systematic review and meta-  
292 analysis of isolated posterior fossa malformations on prenatal ultrasound imaging (part 1):  
293 nomenclature, diagnostic accuracy and associated anomalies. *Ultrasound Obstet Gynecol*.  
294 2016;47(6):690–697. doi:10.1002/uog.14900
- 29515) D'Antonio F, Khalil A, Garel C, Pilu G, Rizzo G, Lerman-Sagie T et al. Systematic review and meta-  
296 analysis of isolated posterior fossa malformations on prenatal imaging (part 2):  
297 neurodevelopmental outcome. *Ultrasound Obstet Gynecol*. 2016;48(1):28–37.  
298 doi:10.1002/uog.15755
- 29916) Volpe P, Contro E, De Musso F, Ghi T, Farina A, Tempesta A et al. Brainstem-vermis and brainstem-  
300 tentorium angles allow accurate categorization of fetal upward rotation of cerebellar vermis.  
301 *Ultrasound Obstet Gynecol*. 2012 Jun;39(6):632-5.

- 30217) Ghi T, Contro E, De Musso F, Farina A, Conturso R, Bonasoni P et al. Normal morphometry of fetal  
303 posterior fossa at midtrimester: brainstem-tentorium angle and brainstem-vermis angle. *Prenat*  
304 *Diagn.* 2012 May;32(5):440-3.
- 30518) Katorza E, Bertucci E, Perlman S, Taschini S, Ber R, Gilboa Y et al. Development of the Fetal Vermis:  
306 New Biometry Reference Data and Comparison of 3 Diagnostic Modalities-3D Ultrasound, 2D  
307 Ultrasound, and MR Imaging. *AJNR Am J Neuroradiol.* 2016;37(7):1359–1366.  
308 doi:10.3174/ajnr.A4725
- 30919) Sun L, Guo C, Yao L, Zhang T, Wang J, Wang L et al. Quantitative diagnostic advantages of three-  
310 dimensional ultrasound volume imaging for fetal posterior fossa anomalies: Preliminary  
311 establishment of a prediction model. *Prenat Diagn.* 2019;39(12):1086–1095. doi:10.1002/pd.5549
- 31220) Paladini D, Donarini G, Parodi S, Volpe G, Sglavo G, Fulcheri E. Hindbrain morphometry and choroid  
313 plexus position in differential diagnosis of posterior fossa cystic malformations. *Ultrasound Obstet*  
314 *Gynecol.* 2019;54(2):207–214. doi:10.1002/uog.20120
- 31521) ENSO working group. Role of prenatal magnetic resonance imaging in fetuses with isolated mild or  
316 moderate ventriculomegaly in the era of neurosonography: a multicenter study [published online  
317 ahead of print, 2020 Jan 9]. *Ultrasound Obstet Gynecol.* 2020;10.1002/uog.21974.  
318 doi:10.1002/uog.21974
- 31922) Massoud M, Guibaud L. Prenatal imaging of posterior fossa disorders. A review. *Eur J Paediatr*  
320 *Neurol.* 2018;22(6):972-988. doi:10.1016/j.ejpn.2018.07.007
- 32123) Guibaud L, Larroque A, Ville D, Sanlaville D, Till M, Gaucherand P et al. Prenatal diagnosis of 'isolated'  
322 Dandy-Walker malformation: imaging findings and prenatal counselling. *Prenat Diagn.*  
323 2012;32(2):185-193. doi:10.1002/pd.3828

- 32424) Corral E, Stecher X, Malinger G, Ochoa JH, de Catte L, Sepulveda W. Thrombosis of the torcular  
325 herophili in the fetus: a series of eight cases. *Prenat Diagn.* 2014;34(12):1176-1181.  
326 doi:10.1002/pd.4453
- 32725) Lerman-Sagie T, Prayer D, Stöcklein S, Malinger G. Fetal cerebellar disorders. *Handb Clin Neurol.*  
328 2018;155:3-23. doi:10.1016/B978-0-444-64189-2.00001-9

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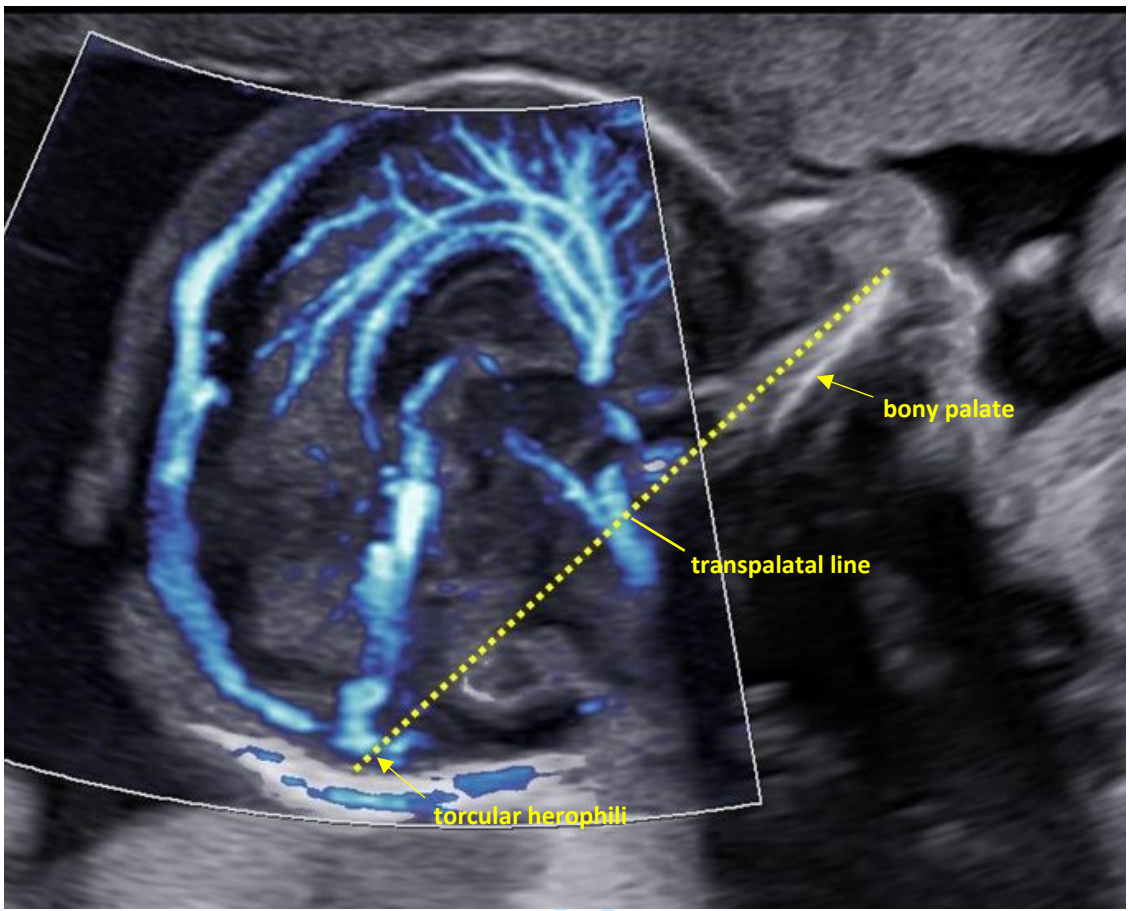
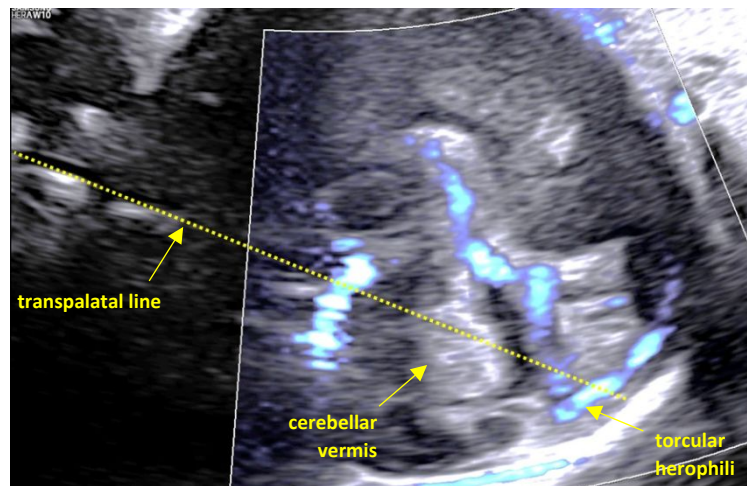


Figure 1 – Midsagittal section of the fetal brain with MV-Flow™ and the LumiFlow™ presets and visualization of the relationship between the torcular herophili and the “transpalatal line” in a 21 weeks’ normal fetus.

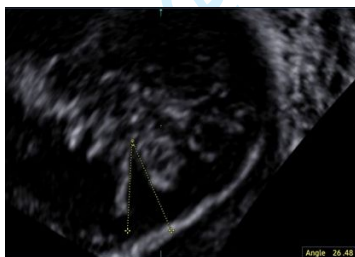
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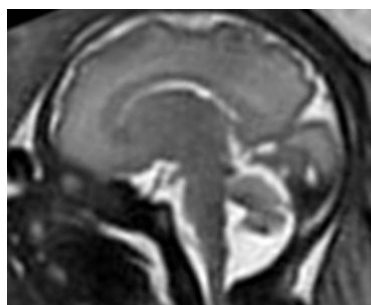
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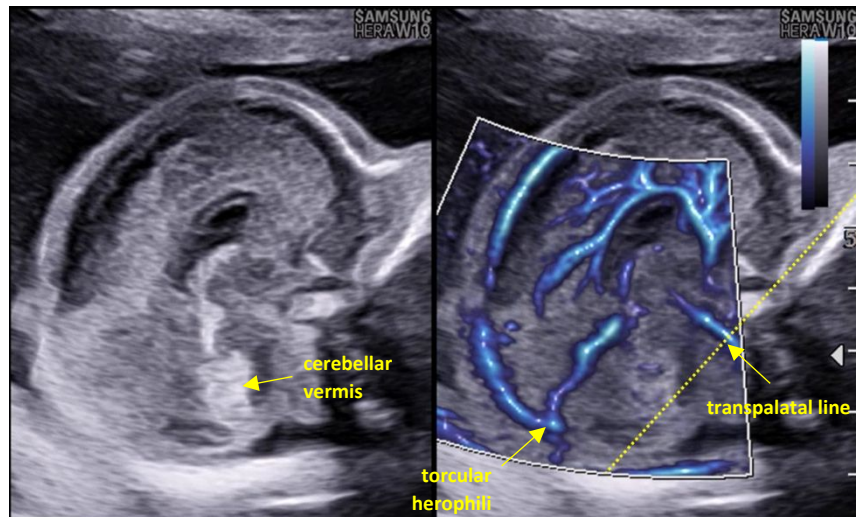
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d.

Figure 2 – a-c) Neurosonogram in a case of Case of Blake’s pouch cyst imaged at 25 weeks. a) Midsagittal section of the fetal brain with MV-Flow™ and the LumiFlow™ presets and visualization of the relationship between the torcular herophili and the “transpalatal line”; b) transcerebellar axial section on 2D gray scale and c) midsagittal view of the posterior fossa on multiplanar mode. d) Magnetic resonance imaging showing the midsagittal section of the fetal brain of the same fetus at 22 weeks of gestation.

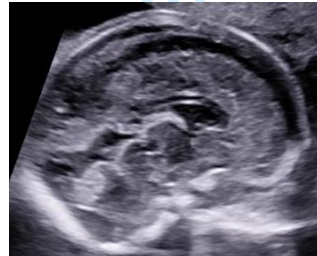




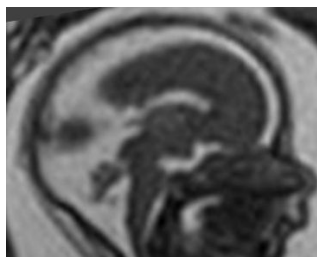
a.



b.



c.



d.

Figure 3 – a-c) Neurosonogram in a case of Dandy Walker malformation imaged at 21 weeks. a) Midsagittal section of the fetal brain with MV-Flow™ and the LumiFlow™ presets and visualization of the relationship between the torcular herophili and the “transpalatal line”; b) transcerebellar axial section on 2D gray scale and c) mid-sagittal view of the fetal brain demonstrating the upward rotation of the cerebellar vermis, which appears dysmorphic. d) Magnetic resonance imaging showing the mid-sagittal section of the fetal brain of the same fetus at 21 weeks of gestation.

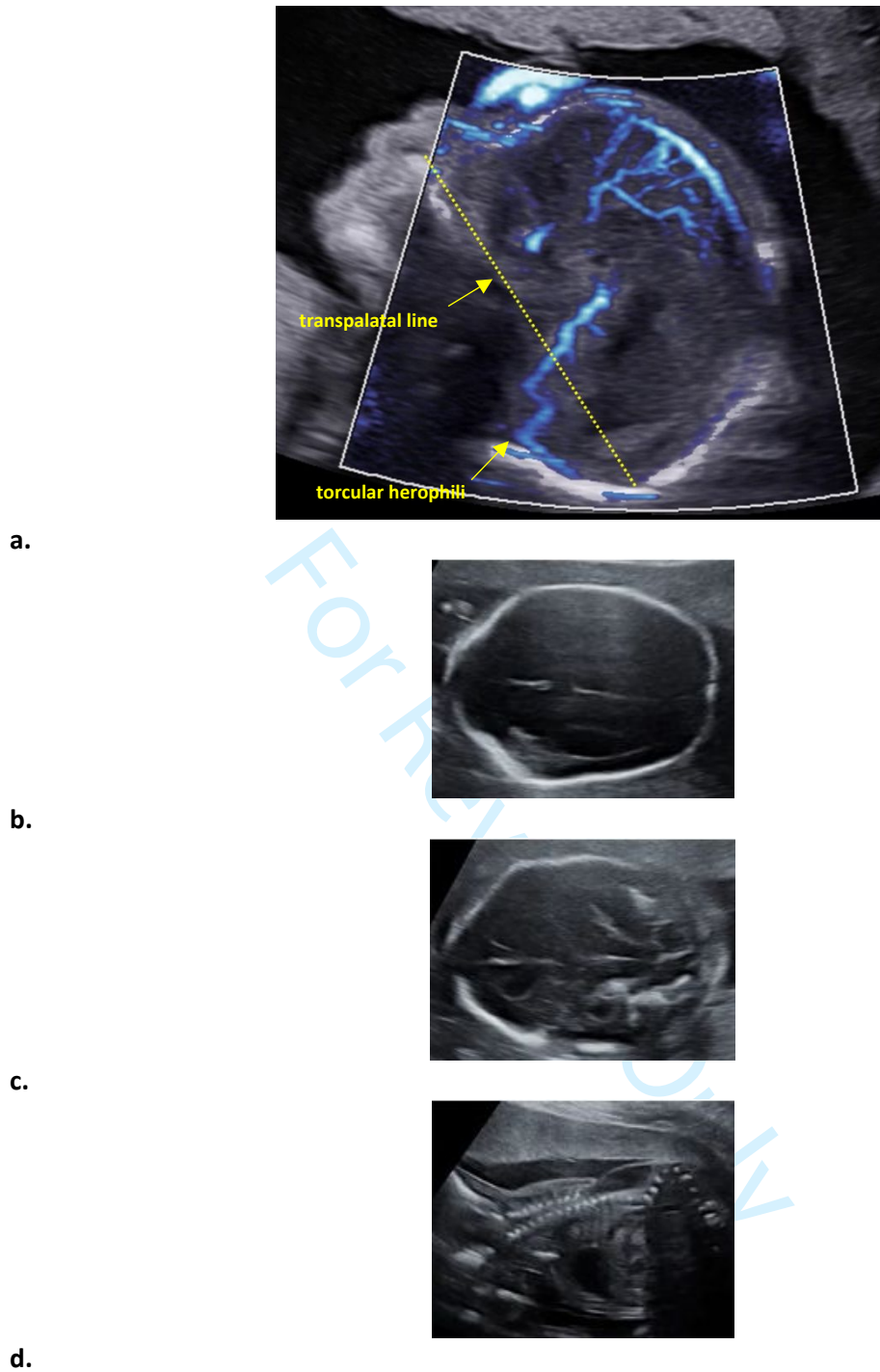


Figure 4 – a) Midsagittal section of the fetal brain with MV-Flow™ and the LumiFlow™ presets and visualization of the relationship between the torcular herophili and the “transpalatal line” in a 21 weeks’ fetus diagnosed with open spina bifida with kyphoscoliosis and Chiari II malformation; b) transthalamic axial view showing lemon shaped skull and enlarged lateral ventricles; c) transcerebellar axial view showing banana shaped cerebellum and obliteration of the cisterna magna; d) sagittal view of the spine demonstrating the vertebral defect and the myelomeningocele.

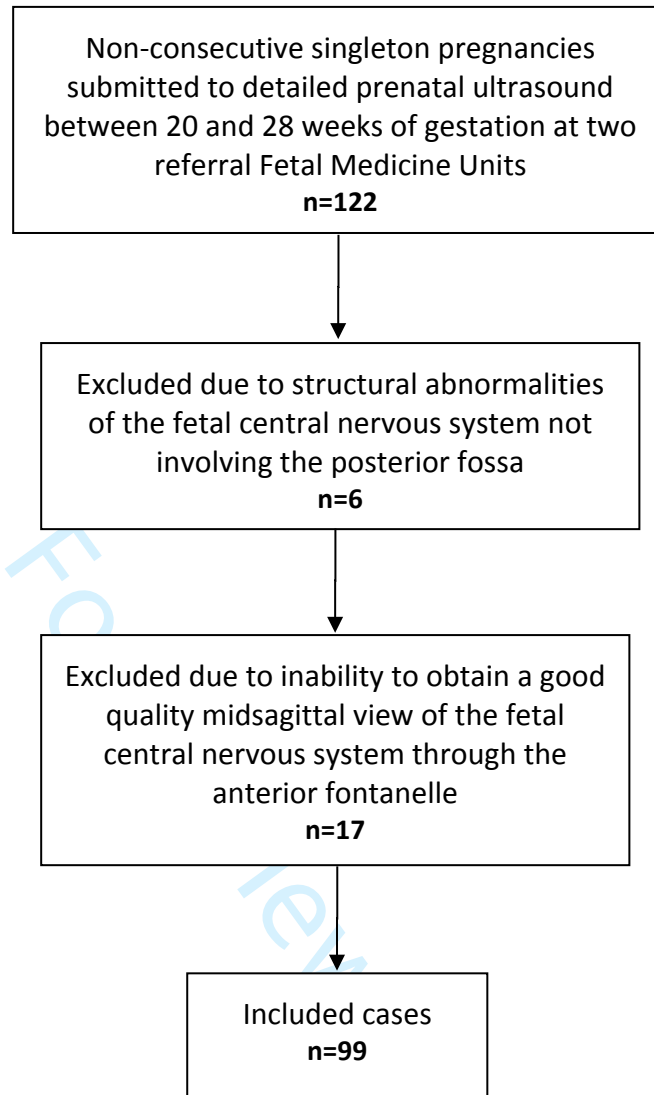


Figure S1 – Flow chart (according to STROBE guidelines) (9) for inclusion of cases.

Table S1 – Features of the included cases.

<b>Age (years), mean <math>\pm</math> SD</b>	27.0 $\pm$ 6.1
<b>BMI (kg/m<sup>2</sup>), mean <math>\pm</math> SD</b>	25.1 $\pm$ 4.7
<b>Parity, N (%)</b>	Nulliparae N 52 (52.5%)
<b>Gestation at US weeks<sup>+days</sup>, median (range)</b>	21 <sup>+3</sup> (20 <sup>+0</sup> – 27 <sup>+6</sup> )
<b>Indication for US</b>	<ul style="list-style-type: none"> <li>- High risk CST N 7 (7.1%)</li> <li>- Abnormality suspected at screening anomaly scan N 20 (20.2%)</li> <li>- Maternal or familiar past medical history N 33 (33.3%)</li> <li>- Medical complications of the pregnancy N 28 (28.3%)</li> <li>- Other (twins or higher order pregnancies, TORCH, low lying placenta) N 11 (11.1%)</li> </ul>

BMI: body mass index

US: ultrasound

CST: combined screening test

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1 **TITLE PAGE**

2 **Prenatal visualization of the torcular herophili by means of a Doppler technology highly sensitive**  
3 **for low velocity flow in the expert assessment of the posterior fossa: a prospective study.**

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21

22 **Running title**

23 Prenatal imaging of the torcular herophili.

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## 24 **Abstract**

### 25 **Objective**

26 To evaluate the usefulness of a Doppler technology highly sensitive for low velocity flow in the  
27 antenatal imaging of the torcular herophili (TH) in the second trimester of pregnancy.

### 28 **Design**

29 Prospective study.

### 30 **Setting**

31 Referral Fetal Medicine Unit.

### 32 **Population**

33 Non-consecutive series of singleton pregnancies submitted to antenatal neurosonogram between  
34 20 and 28 weeks of gestation.

### 35 **Methods**

36 A midsagittal section of the fetal brain was obtained by insonating through the anterior fontanelle,  
37 then the MV-Flow™ and LumiFlow™ presets were selected in order to visualize the TH as the  
38 posterior confluence of the superior sagittal sinus and the straight sinus.

### 39 **Main outcome measures**

40 Evaluation of the anatomic relationship of the TH with the “transpalatal line” joining the upper bony  
41 palate to the fetal skull.

### 42 **Results**

43 9983 cases were recruited, including 1 case of open spina bifida, 1 Dandy-Walker malformation  
44 (DWM) and 21 Blake’s pouch cysts. In normal cases the TH appeared to lie on or just below the  
45 “transpalatal line”. In the cases 5 of Blake’s pouch cyst the position of the TH appeared normal if  
46 compared to controls, while in DWM a supraelevated position of the TH in respect of the

47 transpalatal line was demonstrated. Finally, in the case of Chiari II malformation the TH was  
48 identified below the “transpalatal plane”.

#### 49 **Conclusions**

50 The prenatal US visualization of the TH by means of newly developed Doppler technologies  
51 characterized by high sensitivity for low velocity flow is feasible and allows the indirect evaluation  
52 of the insertion cerebellar tentorium in the second trimester.

53 **Funding:** none.

54 **Keywords:** Doppler ultrasound, fetal cerebellum, Dandy-Walker malformation, Blake’s pouch cyst,  
55 tentorium cerebelli.

56 **Tweetable abstract:** Prenatal imaging of the torcular herophili using a Doppler technology highly  
57 sensitive for low velocity flow.



## 58 Introduction

59 The torcular herophili (TH), also known as “confluence of sinuses”, is a venous structure draining  
60 the major vessels of the intracerebral venous system, among whom the superior sagittal sinus and  
61 the straight, transverse, sigmoid, cavernous and occipital sinuses (1,2).

62 Under normal circumstances the TH is located in the middle aspect of the ~~ferior to the~~ occipital  
63 bones and posterior to the cerebellum, just inside the cranial vault (2,3), and lies in the erosion of  
64 the occipital bone where the major venous sinus tributaries congregate (4), which is located at the  
65 junction of the falx cerebri with the tentorium cerebelli. The antenatal assessment of this latter  
66 anatomic structure is of great interest for the Fetal Medicine Specialists in the accurate classification  
67 and differential diagnosis of posterior fossa abnormalities. Indeed, the upwards displacement of the  
68 tentorium cerebelli in respect of its normal insertion on the occipital clivus is among the diagnostic  
69 criteria of Dandy-Walker Malformation (DWM) in fetuses with hypoplastic and supraelevated  
70 cerebellar vermis and abnormal communication between the fourth ventricle and the cisterna  
71 magna (1,4,5,6). However, the antenatal visualization of the position of the tentorium cerebelli at  
72 grey-scale ultrasound on the midsagittal plane of the fetal brain is technically challenging, and this  
73 may lead to a limited agreement in the diagnosis of DWM in fetuses with abnormal findings of the  
74 posterior fossa.

75 Due to their close anatomic relationship, the position of the TH may be assumed as a clue of the  
76 insertion of cerebellar tentorium on the fetal skull. On this basis the antenatal sonographic  
77 demonstration of the TH at Doppler imaging has been proposed as a proxy of the direct visualization  
78 of the tentorium (1). On the midsagittal view of the fetal brain at 1<sup>st</sup> trimester ultrasound (US) Volpe  
79 et al. have accurately determined the insertion of the tentorium in fetuses with normal or abnormal  
80 posterior fossa, by measuring the angle between the brainstem and the TH (67). However, the  
81 antenatal imaging of the TH at conventional Doppler imaging is also technically challenging. Among

82 ~~the limitations is the paucity of ultrasound techniques available for the imaging of the intracerebral~~  
83 ~~veins, which are characterized by low blood flow velocities and therefore require sensitive color~~  
84 ~~Doppler ultrasound in order to be reliably displayed (1). Within this context, MV-Flow™ and~~  
85 ~~LumiFlow™ (Samsung Medison Co Ltd, Seoul, South Korea) are newly developed Doppler~~  
86 ~~technologies that capable to provide a detailed view of the blood flow in relation to surrounding~~  
87 ~~tissue and~~ represents an alternative to Power Doppler for the visualization of slow flow  
88 microvascularized structures and vascular connections. In this study we evaluate the usefulness of  
89 MV-Flow™ technology combined with LumiFlow™ algorithm in the antenatal imaging of the TH in  
90 the second trimester of pregnancy.

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## 91 **Methods**

92 The study was conducted at two Italian Fetal Medicine referral Units (University Hospital of Parma  
93 and Carlo Poma Hospital of Mantua) ~~over a five-month period, between 1<sup>st</sup> July and 30<sup>th</sup> November~~  
94 ~~2019~~.

95 The study population included a non-consecutive series of singleton pregnancies either referred  
96 from local US Departments or submitted to detailed antenatal neurosonogram due to clinical  
97 indication between 20 and 28 weeks of gestation. According to the Guidelines of the International  
98 Society on Ultrasound in Obstetrics and Gynecology, the fetal neurosonogram “usually includes the  
99 visualization of four coronal and three sagittal planes”, as well as of “the convolutions of the fetal  
100 brain that change throughout gestation” in addition to the axial views required for the basic  
101 examination (87).

102 In all the included cases, a dedicated assessment of the fetal anatomy was performed using a  
103 Samsung HERA W10 system equipped with multifrequency volumetric (4-8 MHz) transducer and  
104 MV-Flow™ and LumiFlow™ technology ~~(Samsung Medison Co Ltd, Seoul, South Korea)~~. For the  
105 purposes of the study, a midsagittal section of the fetal brain was obtained by insonating through  
106 the anterior fontanelle in order to visualize the corpus callosum and the cerebellar vermis on two-  
107 dimensional (2D) ultrasound. The MV-Flow™ and LumiFlow™ presets were selected and the  
108 insonation angle was adjusted in order to visualize the pericallosal arteries and the torcular herophili  
109 as the posterior confluence of the superior sagittal sinus and the straight sinus (Figure 1). The  
110 anatomic relationship of the TH with the “transpalatal line” joining the upper bony palate to the  
111 fetal skull was assessed in all cases. The mean time required to visualize the TH using the MV-Flow™  
112 and LumiFlow™ presets was calculated in all cases.

113 The US examinations were performed for clinical or research purpose by four Authors (AD, GG, NV  
114 and TG). Exclusion criteria for the study were represented by the antenatal finding of abnormalities

115 of the fetal central nervous system not involving the posterior fossa and by the failure to obtain a  
116 satisfactory view of the TH on the midsagittal view of the brain. Clinical data of the pregnancy and  
117 postnatal outcomes were obtained in all cases through medical records, while the ascertainment of  
118 the antenatal diagnosis was performed either by neonatal ultrasound or, in the case of abnormal  
119 findings, by magnetic resonance imaging with or without pathology examination.

120 The study was conducted in the context of an unrestricted research collaboration with Samsung  
121 Medison Healthcare, Italy and approved by the local Ethics Committee of the University Hospital of  
122 Parma. Core outcome sets and patient involvement were not deemed as relevant for the research.

123 This case series was reported according to the Strengthening the Reporting of Observational Studies  
124 in Epidemiology (STROBE) guidelines (98).

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## 125 Results

126 Over the study period, ~~12205 pregnant women between 20 and 28 gestational weeks pregnant~~  
127 ~~women at a gestation between 20 and 28 weeks~~ were submitted to prenatal ultrasound in the two  
128 Fetal Medicine Centres involved. The study group consisted in ~~9983~~ (8179.10%) patients, among  
129 whom ~~9580~~ showed normal appearance of the forebrain and of the posterior fossa and ~~43~~ cases  
130 with abnormal findings of the posterior fossa including 1 open spina bifida, 1 DWM and ~~21~~ Blake's  
131 pouch cysts (BPC) (Figure ~~S12~~). A summary of the demographic and clinical details of the study group  
132 is shown on Table ~~S1~~. The median gestational age at ultrasound was 21<sup>+32</sup> weeks (20<sup>+0</sup> – 27<sup>+6</sup>).

133 In all the included cases optimal views of the TH together with the superior sagittal sinus and the  
134 straight sinus could be obtained by means of the MV-Flow™ and the LumiFlow™ presets. Among  
135 the fetuses with normal intracranial findings, at qualitative evaluation the TH appeared to lie on or  
136 just below a line drawn through the “transpalatal line” as shown in Figure 1. With regards to the  
137 ~~three~~ fetuses with cystic anomaly of the posterior fossa, in the cases of ~~BPC~~ Blake's pouch cyst  
138 the position of the TH appeared normal if compared to normal controls (Figure ~~23a~~), while in  
139 ~~DWM~~ Dandy-Walker malformation a supraelevated position of the TH in respect of the transpalatal  
140 line was demonstrated consistently with the upward displacement of the tentorium (Figure ~~33b~~).

141 Finally, in the case of Chiari II malformation the TH was identified well below the “transpalatal plane”  
142 (Figure ~~44~~). In all cases the prenatal US diagnosis was confirmed following delivery.

143 The time required to visualize the TH when the midsagittal view of the fetal brain was obtained was  
144 less than one minute in all cases.

## 145 Discussion

### 146 Main findings

147 This study demonstrates that the prenatal US visualization of the TH by means of newly developed  
148 MV-Flow™ and LumiFlow™ Doppler techniques ~~characterized by high sensitivity for low velocity~~  
149 ~~flow is feasible, and expert US in expert hands and seems to allow the visualization of the dural~~  
150 ~~sinuses lying on the midsagittal plane of the fetal brain and of the TH in all cases represent~~. The  
151 ~~findings of the study suggest that expert 2D US with the adjunct of MV-Flow™ and LumiFlow™~~  
152 ~~techniques represents a simple and a reliable approach for the indirect evaluation of the insertion~~  
153 ~~cerebellar tentorium~~ insertion in the second trimester. ~~Thanks to these newly developed Doppler~~  
154 ~~technologies, which are sensitive to slow venous flow and are capable to depict microvascularized~~  
155 ~~structures, the TH can be documented at antenatal ultrasound and, due to their close anatomic~~  
156 ~~relationship, the position of tentorium can be indirectly worked out.~~

### 157 Strengths and limitations

158 The original design of the study and the small number of Fetal Medicine Specialists undertaking the  
159 data collection represent the major strengths of our work. On the other hand, the mixed referral  
160 population, the non-consecutive recruitment of the cases and the small number of fetuses with  
161 abnormal findings may be acknowledged as limitations as they do not allow to comment on the  
162 performance of this novel method in the antenatal diagnosis of upward or downward displacement  
163 of the tentorium cerebelli. A larger prospective study assessing the accuracy of MV-Flow™ and  
164 LumiFlow™ in the antenatal classification of cystic abnormalities of the posterior fossa is warranted  
165 before any clinical implementation of the technique may be proposed.

166 The cystic malformations of the posterior fossa represent only a proportion of the large group of  
167 midbrain and hindbrain malformations which commonly present with some degree of vermian  
168 hypoplasia or dysplasia (10), and other conditions such as arachnoid cysts may be associated with

169 the upward displacement of the TH with a normal insertion of the tentorium. Another limitation is  
170 that we were unable to visualize the TH in 17 cases showing normal appearance of the posterior  
171 fossa, however the midsagittal view of the fetal brain is not required outside the context of the  
172 expert assessment of the fetal brain. In this present study only the persistently unfavourable  
173 position of the fetal head precluded to obtain the midsagittal view required to visualize the TH,  
174 however other conditions impairing the spread of the US beam, among whom high BMI and uterine  
175 fibroids, may limit the visualization of the TH. Finally, we have not attempted any formal comparison  
176 with Doppler techniques from other manufacturers characterized by high sensitivity for slow flow  
177 (1,7,11,12), which we believe is beyond the scope of this current paper. Based on the findings of our  
178 work it is not possible to speculate that MV-Flow™ and LumiFlow™ are superior to similar Doppler  
179 techniques, therefore no specific Doppler technique is to be deemed as required as long as the  
180 prenatal visualization of the TH on a midsagittal plane including also the bony palate can be  
181 accomplished.

182

### 183 Interpretation

184 The evaluation of the posterior fossa on the midsagittal plane is of paramount importance for the  
185 differential diagnosis between ~~DWMandy-Walker malformation~~ and other conditions ~~associated~~  
186 ~~with better prognosis~~ such as ~~BPCBlake's pouch cyst~~ and ~~vermian hypoplasia~~ ~~vermian hypoplasia~~  
187 (139-151). More specifically, the height, the rotation and the morphology of the cerebellar vermis  
188 ~~have~~ been reported to be feasible with either 2D or three-dimensional (3D) US as the cerebellar  
189 vermis is a hyperechoic structure which can be clearly distinguished from the brainstem and fourth  
190 ventricle, which lie anteriorly, and the fluid-filled cisterna magna (162-195).

191 While the vermian anatomy and biometry is crucial for the differential diagnosis between DWM and  
192 the other cystic malformations of the posterior fossa, another important additional finding to be  
193 considered in the diagnostic workout such is represented by the tentorium cerebelli insertion (6,16).  
194 ~~The assessment of the insertion of the tentorium cerebelli is crucial for the antenatal classification~~  
195 ~~and differential diagnosis of posterior fossa malformation (5,12).~~ It has been postulated that its the  
196 ~~supraelevation of the tentorium in respect to its normal insertion on the occipital clivus~~ is a  
197 mandatory diagnostic requisite of DWM, while a normally inserted tentorium in fetuses with  
198 upwards rotated vermis and wide communication between the 4<sup>th</sup> ventricle and cisterna magna is  
199 compatible with ~~BPCBlake's pouch cyst~~. On this ground, the brainstem-tentorium angle (BTA) has  
200 been proposed for the quantitative evaluation of the insertion of the tentorium cerebelli by means  
201 of 3D US (162-195). ~~Such measurement has been reported to be feasible and reproducible only by~~  
202 ~~means of 3D US (13).~~ To our knowledge, there is no study evaluating the feasibility of the  
203 quantitative assessment of the BTA on 2D imaging, which can be due to the fact that the  
204 visualization of the BTA on 2D US is challenging even among experienced investigators. ~~This~~  
205 ~~represents a potential limitation given that the post-processing of 3D US volumes may be time~~  
206 ~~consuming and warrants proper training~~. Very recently, another technique relying on the subjective  
207 assessment of the position of the choroid plexus in relation to the roof/cyst inlet of the fourth  
208 ventricle using 3D US has been proposed for the differential diagnosis of the posterior fossa cystic  
209 malformations, however such novel approach was evaluated retrospectively, on a limited number  
210 of cases and, ~~importantly, at a single in the context of a~~ Tertiary referral centre with expertise on  
211 3D US and prenatal neurosonology (2016). In such context, fetal MRI has been shown to add  
212 ~~acknowledged to add~~ in the prenatal diagnosis of abnormalities of the fetal brain compared to  
213 expert ultrasound (21), and represents a valuable tool for the differential diagnosis of the cystic  
214 malformations of the posterior fossa by enabling the accurate assessment of the lobulation and



215 fissuration of the fetal cerebellar vermis as well as the evaluation of the position of the cerebellar  
216 tentorium and of the TH (22,18,23,2419). However, fetal MRI is an expensive second-level test  
217 which may not be readily available in all Units; furthermore, ~~adds costs to the high expertise~~ is  
218 required in order to interpret the anatomic characteristics of the posterior fossa across gestation  
219 (25).

220 ~~Another recently published~~ research by Volpe et al. has demonstrated the role of the visualization  
221 of the straight and of the superior sagittal sinus by means of color or power Doppler in the  
222 identification of the tentorial insertion when measured on 2D US at a gestational age between 11  
223 and 14 weeks in the midsagittal view used to measure the nuchal translucency (7). ~~the role of the~~  
224 ~~BTA in the differential diagnosis between Dandy-Walker malformation and Blake's pouch cyst when~~  
225 ~~measured on 2D-US at a gestational age between 11 and 14 weeks in the midsagittal view used to~~  
226 ~~measure the nuchal translucency (6)~~. In the same work, the Authors acknowledged the role of the  
227 ~~visualization of the straight and of the superior sagittal sinus by means of color or power Doppler in~~  
228 ~~the identification of the tentorial insertion.~~

229 In our cohort of fetuses in the second trimester of pregnancy with normal intracranial findings and  
230 in the ~~single cases~~ with ~~BPC~~Blake's pouch cyst we ~~originally~~ found that the TH and consequently the  
231 tentorium insertion lay on or just below a line drawn tangentially above the bony palate  
232 ("transpalatal plane"). On the other hand, in the case diagnosed with DWM, the TH was  
233 demonstrated to lie above ~~the maxillary line~~the transpalatal plane, thus confirming the upward  
234 displacement of the tentorium, while. ~~Finally~~, in open spina bifida the TH was clearly imaged below  
235 the "transpalatal plane", which is consistent with the caudal displacement of the posterior fossa  
236 structures which characterize the Chiari 2 malformation. Therefore, the insertion of the tentorium  
237 cerebelli may be derived ~~the antenatal tracking of the TH by means of Doppler technologies enabling~~  
238 ~~the visualization of slow flow may have a major impact for the fetal medicine specialist dealing with~~

239 ~~the abnormalities of the posterior fossa, as~~ from the evaluation of the TH in relation to the  
240 “transpalatal plane” ~~the insertion of the tentorium cerebelli may be derived~~. Such information,  
241 which can be obtained in less than one minute when the midsagittal view of the fetal brain through  
242 the anterior fontanelle is obtained, is of crucial importance for the differential diagnosis, the  
243 prognostic assessment as well as the parental counseling of cases diagnosed with cystic  
244 malformations of the posterior fossa ([148](#)). We do not envisage that MV-Flow™ and LumiFlow™  
245 Doppler techniques will allow an easy and straightforward differential diagnosis of the cystic  
246 abnormalities of the posterior fossa, however we believe that ~~these these techniques which rely on~~  
247 ~~the most recent Doppler technologies~~ are worth to be prospectively tested in referral Fetal  
248 Medicine Units with expertise in the diagnosis and classification of such conditions.

#### 249 Strengths and limitations

250 ~~The original design of the study and the small number of Fetal Medicine Specialists undertaking the~~  
251 ~~data collection represent the major strengths of our work. On the other hand, the mixed referral~~  
252 ~~population, the non-consecutive recruitment of the cases and the small number of fetuses with~~  
253 ~~abnormal findings may be acknowledged as limitations as they do not allow to comment on the~~  
254 ~~performance of this novel method in the antenatal diagnosis of upward or downward displacement~~  
255 ~~of the tentorium cerebelli. A larger prospective study assessing the accuracy of MV-Flow™ and~~  
256 ~~LumiFlow™ in the antenatal classification of cystic abnormalities of the posterior fossa is warranted~~  
257 ~~before any clinical implementation of the technique may be proposed. Finally, we have not~~  
258 ~~attempted any formal comparison with other Doppler techniques characterized by high sensitivity~~  
259 ~~for slow flow microvascularized structures and vascular connections from other manufacturers~~  
260 ~~(1,6,720,218), which we believe is beyond the scope of this current paper. The properties of MV-~~  
261 ~~Flow™ and LumiFlow™ make them suitable for the antenatal evaluation of vascular structures~~  
262 ~~characterized by slow flow, however it is important to point out that based on the findings of our~~

253 ~~work it is not possible to speculate that MV-Flow™ and LumiFlow™ are superior to similar Doppler~~  
254 ~~techniques by other manufacturers.~~

## 265 **Conclusion**

256 In conclusion, ~~our study has shown that~~ the use of a Doppler technology highly sensitive for low  
257 velocity flow ~~adds substantial information over conventional Doppler imaging and~~ represents an  
268 easy tool enabling a comprehensive assessment of the intracranial venous system of the fetus,  
269 which has the potential to improve our capability to assess the normal anatomy and to differentiate  
270 the abnormalities of the posterior fossa. Further prospective studies are required in order to confirm  
271 the usefulness of ~~MV-Flow™ and LumiFlow™ technology for~~ the visualization of the TH as an  
272 indirect evaluation of the tentorium cerebelli in a clinical setting.

273 **Acknowledgements**

274 None.

275

276 **Disclosure of interest.**

277 The Authors state no financial interest related to the content of this work.

278 ~~biomedical~~

279

280 **Conflict of interest statement**

281 This work was conducted in the context of an unrestricted and unremunerated research  
282 collaboration with Samsung Medison Healthcare, Italy.

283 Dr Dall'Asta states other unrestricted and unremunerated research collaborations with Samsung  
284 Medison Korea.

285 Dr Ghi acknowledges the receipt of speaking honoraria from Samsung Medison & Co., outside the  
286 submitted work.

287 Dr Fabiana Sorrentino is a biomedical engineer employed by Samsung Electronics Italy, Milan, Italy.

288 She has been in charge for the optimization of the newly developed Doppler technique evaluated  
289 in this study and has actively contributed in the conceptualization and in the finalization of this work.

290

291 **Contribution to Authorship**

292 Andrea Dall'Asta – Conceptualization, data collection, manuscript writing and editing.

293 Gianpaolo Grisolia – Conceptualization, data collection.

294 Nicola Volpe – Data and outcome collection, manuscript writing and editing.

295 Giovanni Battista Luca Schera – Data and outcome collection, manuscript writing and editing.

296 Fabiana Sorrentino – Conceptualization, ultrasound assistance and setting, manuscript review.

297 Tiziana Frusca – Conceptualization, manuscript review.

298 Tullio Ghi – Conceptualization, data collection, manuscript review.

299

### 300 **Details of ethics approval**

301 The study was approved by the local Ethics Committee of the University Hospital of Parma on

302 19/06/2019 .(Number of approval 660)

303

### 304 **Funding**

305 None.

306 **References**

- 3071) Karl K, Heling KS, Chaoui R. Ultrasound of the Fetal Veins Part 3: The Fetal Intracerebral Venous  
308 System. *Ultraschall Med.* 2016 Feb;37(1):6-26.
- 3092) Muthukumar N, Palaniappan P. Tentorial venous sinuses: an anatomic study. *Neurosurgery.*  
310 1998;42(2):363–371. doi:10.1097/00006123-199802000-00097
- 3113) Has R, Esmer AC, Kalelioglu I, Yuksel A, Pata O, Demirbas R. Prenatal diagnosis of torcular herophili  
312 thrombosis: report of 2 cases and review of the literature. *J Ultrasound Med.* 2013 Dec;32(12):2205-  
313 11.
- 3144) Tubbs and Oaks, *Neuroanatomy*, 2002, Volume1, Page 14. Available at  
315 <http://www.neuroanatomy.org/2002/014.pdf>
- 3165) Gardner WJ, Smith JL, Padgett DH. The relationship of Arnold-Chiari and Dandy-Walker  
317 malformations. *J Neurosurg* 1972; 36: 481–486.
- 3186) Gandolfi Colleoni G, Contro E, Carletti A, Ghi T, Campobasso G, Rembouskos G et al. Prenatal  
319 diagnosis and outcome of fetal posterior fossa fluid collections. *Ultrasound Obstet Gynecol.* 2012  
320 Jun;39(6):625-31.
- 3217) Volpe P, Persico N, Fanelli T, De Robertis V, D'Alessandro J, Boito S et al. Prospective detection and  
322 differential diagnosis of cystic posterior fossa anomalies by assessing posterior brain at 11-14 weeks.  
323 *Am J Obstet Gynecol MFM* 2019.
- 3248) International Society of Ultrasound in Obstetrics & Gynecology Education Committee. Sonographic  
325 examination of the fetal central nervous system: guidelines for performing the 'basic examination'  
326 and the 'fetal neurosonogram'. *Ultrasound Obstet Gynecol.* 2007;29(1):109–116.  
327 doi:10.1002/uog.3909

- 3289) Von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP; STROBE Initiative. The  
329 Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement:  
330 guidelines for reporting observational studies. *Lancet* 2007; 370: 1453–1457.
- 33110) [Barkovich AJ, Millen KJ, Dobyns WB. A developmental and genetic classification for midbrain-  
332 hindbrain malformations. \*Brain\*. 2009;132\(Pt 12\):3199-3230. doi:10.1093/brain/awp247](#)
- 33311) [Pooh RK. Normal anatomy by three-dimensional ultrasound in the second and third trimesters.  
334 \*Semin Fetal Neonatal Med\*. 2012 Oct;17\(5\):269-77.](#)
- 3359)12) [Taoka T, Fukusumi A, Miyasaka T, Kawai H, Nakane T, Kichikawa K et al. Structure of the  
336 Medullary Veins of the Cerebral Hemisphere and Related Disorders. \*Radiographics\*. 2017 Jan-  
337 Feb;37\(1\):281-297.](#)
- 33810)13) [Garel C. Posterior fossa malformations: main features and limits in prenatal diagnosis.  
339 \*Pediatr Radiol\* 2010; 40: 1038–1045.](#)
- 34011)14) [D'Antonio F, Khalil A, Garel C, Pilu G, Rizzo G, Lerman-Sagie T et al. Systematic review and  
341 meta-analysis of isolated posterior fossa malformations on prenatal ultrasound imaging \(part 1\):  
342 nomenclature, diagnostic accuracy and associated anomalies. \*Ultrasound Obstet Gynecol\*.  
343 2016;47\(6\):690–697. doi:10.1002/uog.14900](#)
- 34412)15) [D'Antonio F, Khalil A, Garel C, Pilu G, Rizzo G, Lerman-Sagie T et al. Systematic review and  
345 meta-analysis of isolated posterior fossa malformations on prenatal imaging \(part 2\):  
346 neurodevelopmental outcome. \*Ultrasound Obstet Gynecol\*. 2016;48\(1\):28–37.  
347 doi:10.1002/uog.15755](#)
- 34813)16) [Volpe P, Contro E, De Musso F, Ghi T, Farina A, Tempesta A et al. Brainstem-vermis and  
349 brainstem-tentorium angles allow accurate categorization of fetal upward rotation of cerebellar  
350 vermis. \*Ultrasound Obstet Gynecol\*. 2012 Jun;39\(6\):632-5.](#)

- 351 ~~14~~17) \_\_\_\_ Ghi T, Contro E, De Musso F, Farina A, Conturso R, Bonasoni P et al. Normal morphometry of  
352 fetal posterior fossa at midtrimester: brainstem-tentorium angle and brainstem-vermis angle.  
353 Prenat Diagn. 2012 May;32(5):440-3.
- 354 ~~15~~18) \_\_\_\_ Katorza E, Bertucci E, Perlman S, Taschini S, Ber R, Gilboa Y et al. Development of the Fetal  
355 Vermis: New Biometry Reference Data and Comparison of 3 Diagnostic Modalities-3D Ultrasound,  
356 2D Ultrasound, and MR Imaging. AJNR Am J Neuroradiol. 2016;37(7):1359–1366.  
357 doi:10.3174/ajnr.A4725
- 358 ~~16~~19) \_\_\_\_ Sun L, Guo C, Yao L, Zhang T, Wang J, Wang L et al. Quantitative diagnostic advantages of  
359 three-dimensional ultrasound volume imaging for fetal posterior fossa anomalies: Preliminary  
360 establishment of a prediction model. Prenat Diagn. 2019;39(12):1086–1095. doi:10.1002/pd.5549
- 361 ~~17~~20) \_\_\_\_ Paladini D, Donarini G, Parodi S, Volpe G, Sglavo G, Fulcheri E. Hindbrain morphometry and  
362 choroid plexus position in differential diagnosis of posterior fossa cystic malformations. Ultrasound  
363 Obstet Gynecol. 2019;54(2):207–214. doi:10.1002/uog.20120
- 364 ~~18~~21) \_\_\_\_ ENSO working group. Role of prenatal magnetic resonance imaging in fetuses with isolated  
365 mild or moderate ventriculomegaly in the era of neurosonography: a multicenter study [published  
366 online ahead of print, 2020 Jan 9]. Ultrasound Obstet Gynecol. 2020;10.1002/uog.21974.  
367 doi:10.1002/uog.21974
- 368 ~~19~~22) \_\_\_\_ Massoud M, Guibaud L. Prenatal imaging of posterior fossa disorders. A review. Eur J  
369 Paediatr Neurol. 2018;22(6):972-988. doi:10.1016/j.ejpn.2018.07.007
- 370 ~~20~~23) \_\_\_\_ Guibaud L, Larroque A, Ville D, [Sanlaville D](#), [Till M](#), [Gaucherand P](#) et al. Prenatal diagnosis of  
371 'isolated' Dandy-Walker malformation: imaging findings and prenatal counselling. Prenat Diagn.  
372 2012;32(2):185-193. doi:10.1002/pd.3828



373~~21~~24) Corral E, Stecher X, Malinge G, Ochoa JH, de Catte L, Sepulveda W. Thrombosis of the  
374 torcular herophili in the fetus: a series of eight cases. Prenat Diagn. 2014;34(12):1176-1181.  
375 doi:10.1002/pd.4453

376~~22~~25) Lerman-Sagie T, Prayer D, Stöcklein S, Malinge G. Fetal cerebellar disorders. Handb Clin  
377 Neurol. 2018;155:3-23. doi:10.1016/B978-0-444-64189-2.00001-9

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