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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>Objective 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>Design Prospective study.</p> <p>Setting Referral Fetal Medicine Unit.</p> <p>Population Non-consecutive series of singleton pregnancies submitted to antenatal neurosonogram between 20 and 28 weeks of gestation.</p> <p>Methods 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>Main outcome measures Evaluation of the anatomic relationship of the TH with the “transpalatal line” joining the upper bony palate to the fetal skull.</p> <p>Results 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 1st 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^{+3} weeks
125 ($20^{+0} - 27^{+6}$).

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 4th 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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237 submitted work.

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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256 None.

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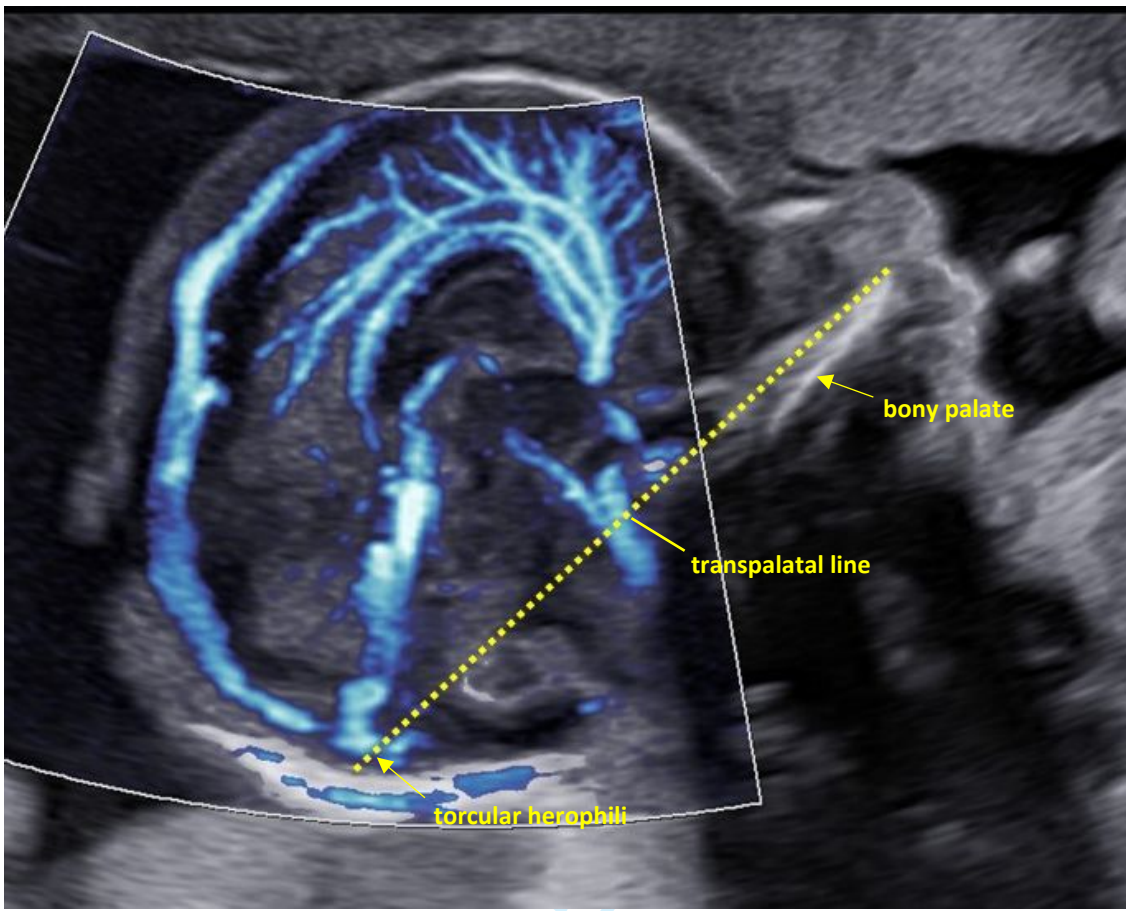
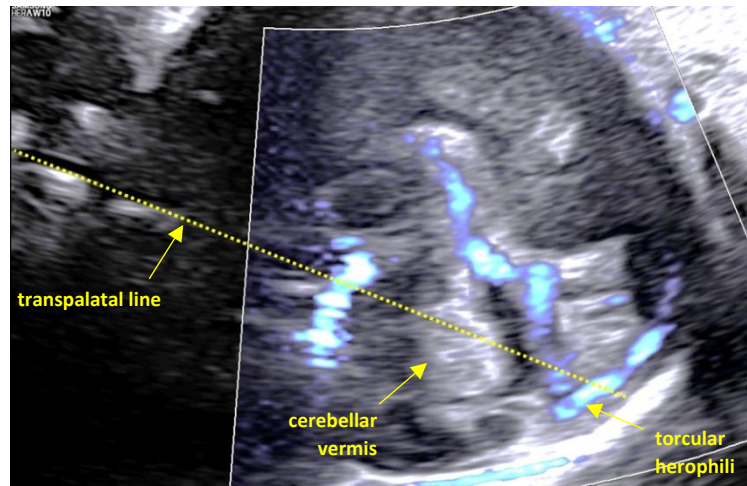
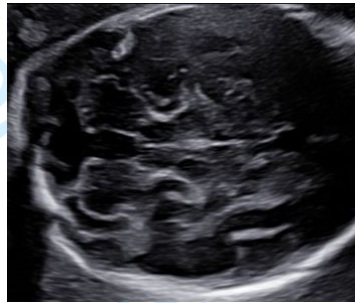


Figure 1 – Midsagittal section of the fetal brain with MV-Flow™ and the LumiFlow™ presets and visualization of the relationship between the torcular herophili and the “transpalatal line” in a 21 weeks’ normal fetus.

Only



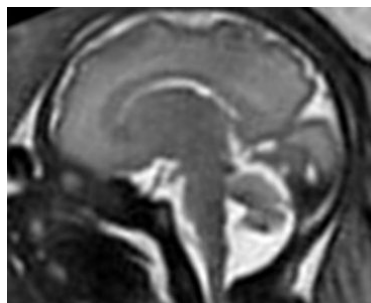
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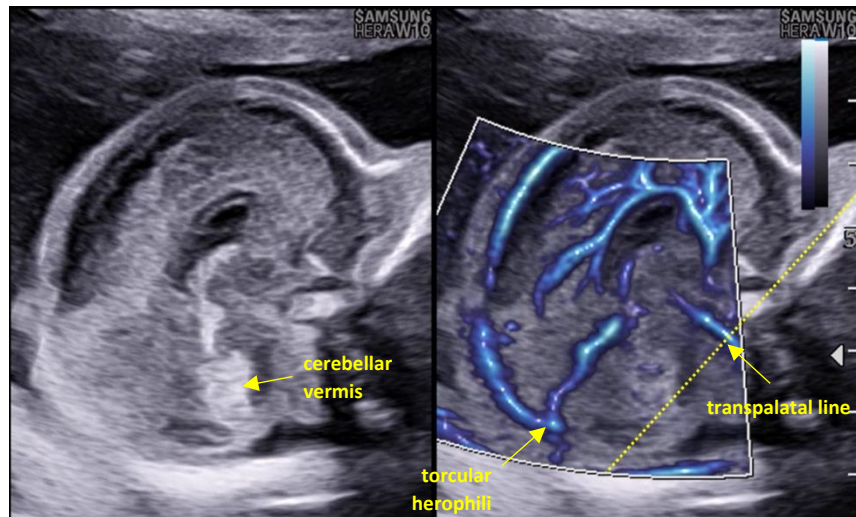


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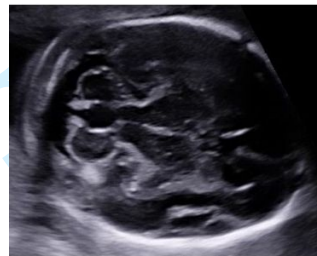


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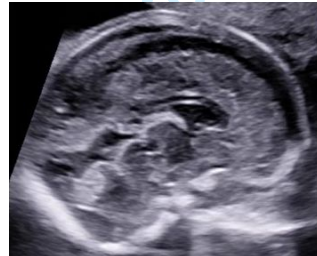
Figure 2 – a-c) Neurosonogram in a case of Case of Blake’s pouch cyst imaged at 25 weeks. a) Midsagittal section of the fetal brain with MV-Flow™ and the LumiFlow™ presets and visualization of the relationship between the torcular herophili and the “transpalatal line”; b) transcerebellar axial section 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.



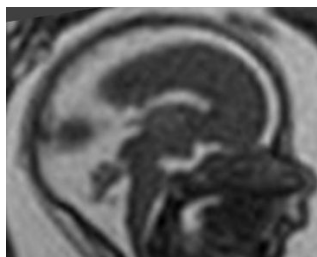
a.



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.

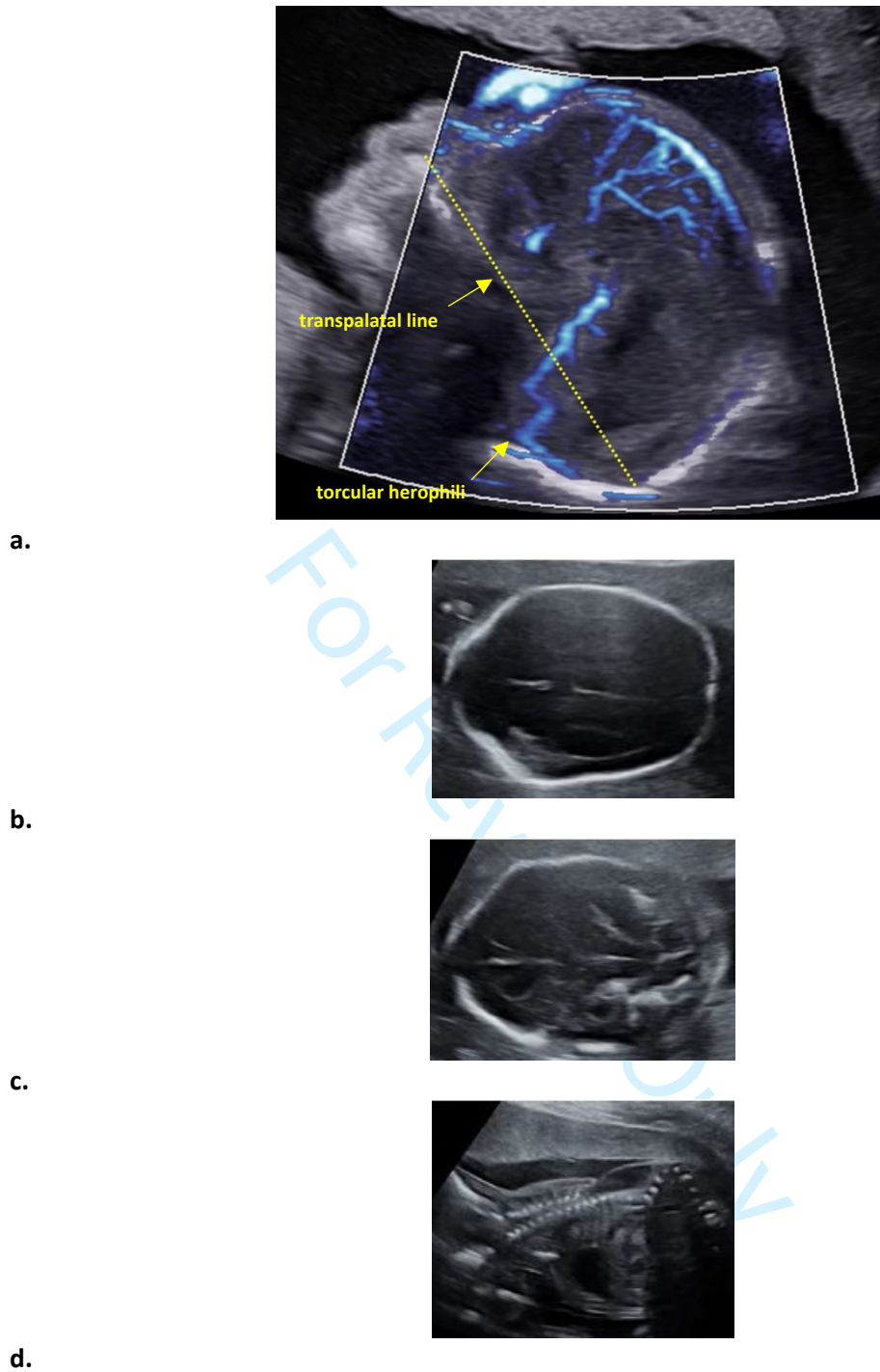


Figure 4 – a) Midsagittal section of the fetal brain with MV-Flow™ and the LumiFlow™ presets and visualization of the relationship between the torcular herophili and the “transpalatal line” in a 21 weeks’ fetus diagnosed with open spina bifida with kyphoscoliosis and Chiari II malformation; b) transthalamic 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.

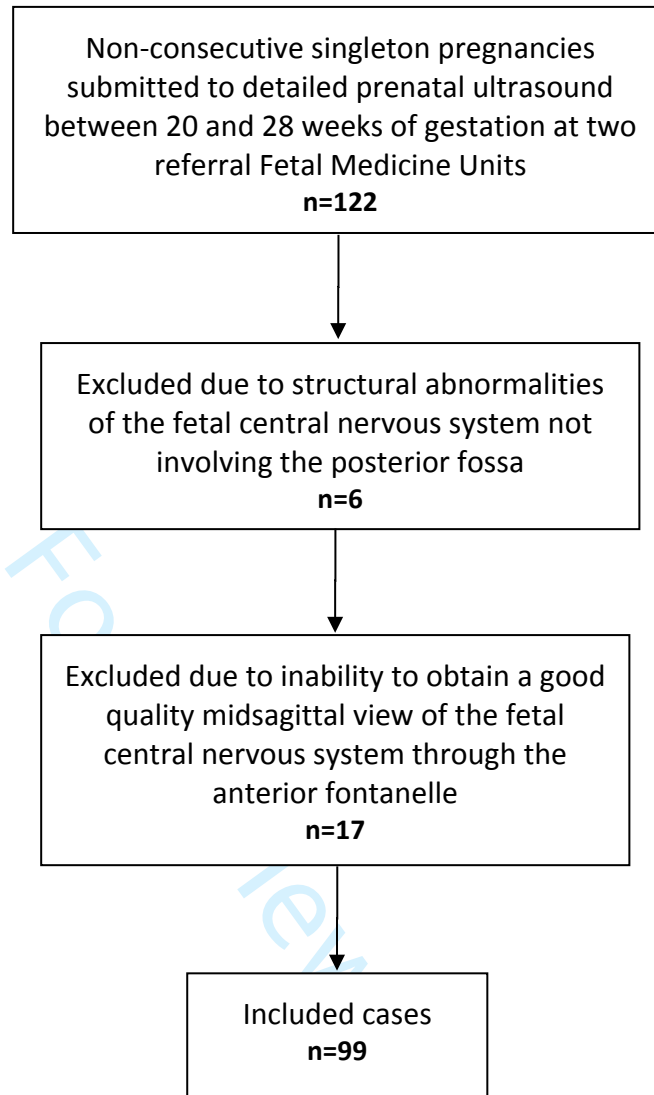


Figure S1 – Flow chart (according to STROBE guidelines) (9) for inclusion of cases.

Table S1 – Features of the included cases.

Age (years), mean \pm SD	27.0 \pm 6.1
BMI (kg/m²), mean \pm SD	25.1 \pm 4.7
Parity, N (%)	Nulliparae N 52 (52.5%)
Gestation at US weeks^{+days}, median (range)	21 ⁺³ (20 ⁺⁰ – 27 ⁺⁶)
Indication for US	<ul style="list-style-type: none"> - High risk CST N 7 (7.1%) - Abnormality suspected at screening anomaly scan N 20 (20.2%) - Maternal or familiar past medical history N 33 (33.3%) - Medical complications of the pregnancy N 28 (28.3%) - Other (twins or higher order pregnancies, TORCH, low lying placenta) N 11 (11.1%)

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 1st 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 1st July and 30th 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⁺³² weeks (20⁺⁰ – 27⁺⁶).
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 4th 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

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306 **References**

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