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Griffiths, P.D., Mooney, C., Bradburn, M. et al. (2018) Should we perform in utero MRI on a fetus at increased risk of a brain abnormality if ultrasonography is normal or shows non-specific findings? *Clinical Radiology*, 73 (2). pp. 123-134. ISSN: 0009-9260

<https://doi.org/10.1016/j.crad.2017.09.007>

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1 **Introduction**

2 The mid-pregnancy screening examination using ultrasonography (USS) is offered to all women in
3 the UK and is taken up by more than 95%.¹ If a structural abnormality of the fetus is recognized,
4 the woman is offered a more detailed ‘anomaly scan’ performed by a senior doctor with specialist
5 training in ante-natal USS. Structural abnormalities may be picked up for the first time later in
6 pregnancy if a woman has another USS examination because of, for example, reduced fetal move-
7 ments or poor growth. The fetal brain is a common location for such problems and there is a wide
8 range of potential abnormalities which vary massively in terms of post-natal clinical significance. A
9 woman may consider termination of pregnancy if the fetus has severe abnormalities and in such
10 cases the woman needs to be provided with the best quality information possible in order to make
11 an informed decision. The diagnostic accuracy of USS is approximately 70% as reported in several
12 publications²⁻⁸ and confirmed by a recent large prospective study.⁹ That study (MERIDIAN) was
13 designed to assess the improvement in diagnostic accuracy brought about by adding in utero MR
14 (iuMR) to the diagnostic pathway and it demonstrated a statistically significant improvement from
15 under 70% to over 92%. Similar levels of improvement has also be shown in systematic reviews
16 and meta-analyses¹⁰⁻¹³ providing compelling evidence to support the use of iuMR imaging if a fetal
17 brain abnormality is shown or suspected on USS.

18
19 Radiologists performing iuMR imaging in the UK are beginning to recognise use of iuMR imaging
20 of the brain in situations not covered by the scope of the MERIDIAN study suggesting a ‘technolo-
21 gy creep’ and this is also our experience. Specifically, iuMR is being increasingly offered to preg-
22 nant women when the fetal brain is normal on USS but the pregnancy is judged to be at ‘increased
23 risk’ of a brain abnormality. There are several clinical scenarios that may lead to that position,
24 which we outline in this paper and discuss the existing literature that either supports or contradicts

25 the use of iuMR imaging in that situation. We will also outline the future research required to guide
26 clinical management in these pregnancies.

27

28 **Why a fetus may be classified as at increased risk of a brain abnormality**

29 a) Problems concerning a sibling from an earlier pregnancy.

30 Increased risk may be based on a brain abnormality in an earlier pregnancy and may have been rec-
31 ognised either on imaging during the pregnancy or on post-natal imaging. If the brain abnormality
32 is thought to be developmental in origin a clinical geneticist may be asked to quantify the recur-
33 rence risk in future pregnancies. This can be done with some accuracy if a specific genetic abnor-
34 mality is known or strongly suspected (e.g. in many cases of lissencephaly), alternatively if a spe-
35 cific genetic abnormality is not found (e.g. most cases of agenesis of the corpus callosum) the risk
36 will be based on empirical observation from the published literature. We are aware of only one pub-
37 lication (from our group) that specifically looked at the discrepancy between USS and iuMR results
38 in this caseload.¹⁴ 100 non-selected cases were described and brain or spine abnormalities were
39 shown in 22% of fetuses of which 9% were shown only on iuMR imaging. In addition to develop-
40 mental brain abnormalities, there are an increasing number of acquired brain lesions found in chil-
41 dren on post-natal studies that are due to inheritable/genetic disorders (e.g. many metabolic disor-
42 ders) which have an increased risk of recurrence in future pregnancies.

43

44 *Agenesis of the corpus callosum*

45 It is difficult to be certain about the prevalence of agenesis of the corpus callosum in the general
46 population but most estimates are in the range of 0.3% to 0.7%, although it is seen in 2% to 3% of
47 people with a developmental disability.¹⁵ As more MR imaging examinations are performed on
48 normal people as part of research studies it will be possible to refine the prevalence estimates of
49 agenesis of the corpus callosum. We have performed many MR studies on adult volunteers from the

50 staff of our local hospital and university, including 900 brain examinations. Those adults did not
51 know which part of their body they would have scanned before volunteering (which reduces self-
52 selection bias) and we have not seen any cases of agenesis of the corpus callosum in the 900 studies
53 (unpublished but see reference¹⁶). Using the 3/n rule,¹⁷ the estimated prevalence of agenesis of the
54 corpus callosum in the general population has an upper 95% confidence interval of 0.33%. Most
55 cases of agenesis (and dysgenesis) of the corpus callosum are sporadic but it can be part of condi-
56 tions that inherit with autosomal dominant (e.g. Rubenstein-Taybi syndrome), autosomal recessive
57 (e.g. Andermann syndrome) or X-linked (e.g. Aicardi syndrome) patterns.¹⁵ If other definable ge-
58 netic abnormalities can be excluded the recurrence rate in siblings is thought to be approximately
59 5%.¹⁸ Our empirical experience shows that although the recurrence rate of isolated agenesis of the
60 corpus callosum is low, pregnant women with this family history usually ask for iuMR imaging in a
61 subsequent pregnancy. This is often supported by the fetal maternal consultant because of the
62 emerging problems of detection with USS and the high association with other brain abnormali-
63 ties.^{9,19}

64

65 *Cortical formation abnormalities*

66 The term ‘cortical formation abnormality’ covers a wide range of pathologies that result from fail-
67 ure of neuronal/glial proliferation, migration and/or organisation of the cerebral cortex.²⁰ Classic
68 (type 1) lissencephaly is characterised by under-migration of neurons and mutations of LIS1 or
69 DCX genes account for 77% of such cases (65% and 12% respectively).^{21,22} The inheritance pattern
70 is autosomal dominant for LIS1 (chromosome 17) and X-linked for (DCX) but the majority of
71 cases are *de novo* mutations. In a small number of cases there may be an identifiable parental genet-
72 ic defect, for example, if a woman with a mild phenotype carries a defective copy of the DCX gene
73 the recurrence risk may be as high as 50%. Alternatively, when one parent has a balanced transloca-
74 tion involving the LIS1 gene the recurrence risk for isolated lissencephaly sequence is thought to be

75 10 to 15%. “Cobblestone” or type 2 lissencephaly results from over-migration of neurons past the
76 basement membrane and is common in Walker-Warburg syndrome, Muscle Eye Brain disease and
77 Fukuyama muscular dystrophy.²⁰ The recurrence risk for cobblestone lissencephaly is 25% (auto-
78 somal recessive inheritance), as is the cases of lissencephaly with cerebellar hypoplasia.

79

80 A recent report from our group studied the use of iuMR in pregnancies at increased risk of lissen-
81 cephalo based on a previously affected sibling²³ and highlights a number of difficulties of studying
82 such abnormalities in the fetus, the first relating to the scarcity of the disorder. The 23 fetuses re-
83 ported in that study took 8 years to recruit despite a wide geographical coverage and in only three
84 cases did the lissencephaly recur. Secondly, when can lissencephaly be diagnosed reliably? All
85 three of the fetuses with lissencephaly were successfully recognised on iuMR with varying degrees
86 of certainty but four other fetuses were considered to be ‘possible lissencephaly’ on the 22-24 week
87 iuMR studies based on mild sulcation delay. The follow up studies performed at 28 weeks in those
88 four cases were normal and were considered to be normal after birth, which indicates a tendency to
89 report false positives in the late second trimester. We should expect similar pre-natal diagnostic
90 problems on iuMR for other cortical formation abnormalities such as polymicrogyria, which is be-
91 ing increasingly recognised as inheritable, particularly if it is bilateral and symmetrical.²¹⁻²⁴ It may
92 be difficult to diagnose polymicrogyria even if anatomically extensive and focal polymicrogyria or
93 focal cortical dysplasia is likely to be exceptionally challenging or impossible. The ability to con-
94 firm (figure 1) or exclude (figure 2) cortical formation abnormalities confidently is equally im-
95 portant to the families.

96

97 *Metabolic disorders*

98 We have discussed the problems of diagnosing some developmental brain abnormalities ante-
99 natally with iuMR because of lack of conspicuity at some stages of pregnancy and the purpose of

100 this section is to add further caution if attempting to diagnose brain abnormalities in a fetus at risk
101 of an inherited metabolic disorder. Di Mauro and Garone²⁵ describe the wide range of inheritable
102 metabolic disorders concentrating on glycogenosis and mitochondrial defects in the fetus and their
103 general observations are highly pertinent to ante-natal detection. Mendelian and maternally inherit-
104 ed disease must be present in the fetus but it does not mean that the fetus is ‘clinically’ affected.
105 Many of these metabolic disorders do not produce brain injury until infancy, childhood or even
106 adulthood and there are a number of reasons why the individual may not be affected *in utero*. For
107 example, a genetic defect may produce a mutated mature enzyme which has a fetal counterpart that
108 is not involved. In some situations, the mother is able to metabolise an abnormal gene product, or
109 the build-up of a toxic intermediate compound made by the fetus. Defects of the mitochondrial res-
110 piratory chain are amongst the most important inheritable metabolic disorders in terms of brain in-
111 volvement and impaired oxidative metabolism in the child or adult metabolically active areas. In
112 contrast, fetal tissues rely more on anaerobic glycolysis for ATP production rather than oxidative
113 mechanisms, hence providing a measure of protection.²⁶ A normal iuMR study in these situations
114 should not be used to exclude a metabolic disorder in a fetus although there are sometimes non-
115 specific finding on iuMR that may be useful (figure 3).

116

117 b) Abnormalities of the current fetus that increase the risk of a brain abnormality.

118 Other findings in the current pregnancy may indicate increased risk of brain abnormality in the fetus
119 such as the association between spine and brain malformations. Alternatively, there may be serolog-
120 ical findings that indicate a maternal infection has passed to the fetus (e.g. the ‘TORCH’ infections)
121 or chromosomal/genetic abnormalities have been recognised that may raise concern for brain in-
122 volvement. The intra-uterine environment can also adversely affect the fetal brain, particularly in
123 multi-fetal pregnancies.

124

125 *Structural abnormalities outside the brain associated with increased risk of brain abnormalities*

126 The association between ‘open’ spinal dysraphism (myelomeningocele or myelocoele) and brain
127 malformations and if that type of spinal problem is shown on ante-natal USS there is an approxi-
128 mately 90% chance that a Chiari 2 malformation will be present as well. Conversely, finding a
129 Chiari 2 malformation on USS instigates close scrutiny of the fetal spine because the vast majority
130 of Chiari 2 malformations are found in conjunction with open spinal dysraphism. There is no con-
131 sistent association between closed spinal dysraphism (skin covered abnormalities) and brain mal-
132 formations but careful assessment of the brain in such cases is still warranted on USS. There is a
133 paucity of research data about the value of iuMR imaging in the assessment of fetuses with spinal
134 abnormalities demonstrated on USS. Our group reported the results of 50 such fetuses and showed
135 disagreements between USS and iuMR imaging in 10/50 (20%) but all of those were in the descrip-
136 tion of the spinal abnormalities, not in intra-cranial findings.²⁷ Similarly, there were 21 fetuses with
137 Chiari 2 malformations in the MERIDIAN study and again extra brain abnormalities were not seen
138 on iuMR imaging in any fetus.²⁸ In spite of this low diagnostic return iuMR imaging is frequently
139 requested in a fetus with a spinal abnormality on USS and in such cases we always image the fetal
140 brain as well as the spine.

141

142 One area of interest in the recent obstetric literature is the association between congenital heart dis-
143 ease (CHD) and fetal brain abnormalities. CHD occurs in 6-8/1000 live births²⁹ and is a common
144 cause of childhood morbidity. A recent systematic review found pre-natal detection of structural
145 brain abnormalities in fetuses with CHD gave a prevalence of 28% (95% CI, 18-40%) but those
146 figures are based on three publications from only 221 cases.³⁰ Some of the reported brain abnormal-
147 ities were obvious focal abnormalities, both developmental and acquired, but the most frequently
148 reported ‘brain’ abnormality in the systematic review was ventriculomegaly (found in 8.6% of fe-
149 tuses with CHD in total). It is open to debate if ventriculomegaly should be considered as a ‘devel-

150 opmental' or 'acquired' abnormality or indeed as an anatomical variant in some cases. Other in-
151 cluded brain abnormalities were more non-specific such as reduced brain growth and maturation,
152 MR spectroscopic changes consistent with metabolic 'stress' or reduced blood flow to the brain on
153 Doppler USS. Much more detailed, prospective research is required in order to define the associa-
154 tion rate of CHD with developmental brain malformations (figure 4) and acquired brain pathology
155 and to explore the possible significance of those findings vis-à-vis the known CDH.

156

157 *Cytomegalovirus as an example of a trans-placental infection that may affect the fetal brain*

158 The acronym 'TORCH' is often used to describe the commonest infective agents that cause trans-
159 placental infection (TOxoplasmosis, Rubella, Cytomegalovirus (CMV) and Herpes), although an
160 increasing number of other viruses have been implicated. CMV infection is numerically the most
161 important in the UK but fetal infection although HIV and, more recently, Zika virus present major
162 challenges on the global scale. Leruez-Ville and Ville³¹ state that the birth prevalence of congenital
163 CMV infection in European countries with low maternal seroprevalence is around 0.4% and there is
164 a roughly equal ratio of primary CMV infections during pregnancy and reactivation of a previous
165 maternal CMV infection.^{32,33} CMV specific symptoms are found in 12.7% of new-borns with con-
166 genital CMV and approximately half of those will have permanent sequelae, many of which are
167 brain-related. Unfortunately 13.5% of infected but asymptomatic new born babies will develop
168 permanent problems relating to CMV infection.³⁴ Transplacental infection of the fetus with CMV
169 can lead to spontaneous abortion/stillbirth or result in termination of pregnancy if recognised. If the
170 infection is acquired in the early second trimester CMV seems to have a predilection for the cells in
171 the germinal matrix (ventricular zone), which interferes with normal neuro-glial proliferation, mi-
172 gration and/or organisation of the cerebral cortex. A recent article³⁵ has tried to explain the range of
173 imaging findings in relation to the timing of the infection e.g. second trimester infections at the time
174 of neuronal/glia proliferation and may produce microcephaly and/or micrencephaly, whereas agyr-

175 ia/lissencephaly is more likely to result from a failure of migration and polymicrogyria results from
176 abnormal cortical organisation (figure 5). Fetuses infected in the third trimester tend to have white
177 matter injury with calcifications.

178

179 The diagnosis of maternal CMV infection during pregnancy can be difficult. The most convincing
180 data comes from documented seroconversion in pregnancy by showing increased specific IgG but
181 this is rarely feasible because screening and prospective monitoring is not performed.³¹ In most cas-
182 es in which a fetal infection with CMV is confirmed ante-natally there was a reason to look for it
183 and this often comes from USS imaging. Leruez-Ville and Ville describe USS findings that may
184 provide clues to CMV infection under the headings of ‘severe USS brain abnormalities’ ‘mild USS
185 brain abnormalities’ and ‘extra-cerebral USS abnormalities’.³¹ Most of those are non-specific and in
186 our experience the referral information for USS usually involves some combination of ‘microceph-
187 aly’, ‘ventriculomegaly’, ‘enlarged extra-axial spaces’ or ‘germinal cysts’ (figure 6). The literature
188 comparing USS and iuMR findings in congenital CMV infection is sparse. Picone et al.³⁶ studied 38
189 fetuses (24-37 weeks gestational age) with proven congenital CMV infection and retrospectively
190 assessed the value of iuMR imaging over USS. They concluded that iuMR should be performed in
191 any situation that the USS examination is not completely normal and the major value was in cases
192 in which USS had recognised extra-cerebral manifestations of the infection but reported a normal
193 brain. Doneda and colleagues³⁷ also studied 38 fetuses with confirmed CMV infection, iuMR being
194 performed at 24-30 weeks gestational age. They reported added diagnostic value for iuMR in 18/38
195 (47%) cases and an increase in sensitivity for pathology from 38% for USS to 92% for iuMR imag-
196 ing. The sensitivity of general USS in ante-natal care should be considered as low as 35%³⁸ whilst
197 the addition of iuMR is thought to produce negative predictive values close to 90%.^{36,39}

198

199 *Brain injury in the co-twin survivor after fetal demise in monochorionic pregnancies*

200 Multiple pregnancies are generally a high risk group for both mother and fetus. This has increasing
201 importance as the rate of multiple pregnancies increase with the widespread use of assisted concep-
202 tion methods. Twins occur in about 1 in 60 pregnancies and one factor for increased risk is chorion-
203 icity.⁴⁰ Monochorionic twins make up approximately 30% of all twin pregnancies and have a single
204 placenta with shared vascular anastomotic channels between the two fetuses. In the event of demise
205 of one twin, the surviving co-twin is at increased risk of injury because of adverse effects on perfu-
206 sion or thromboembolism arising in the dead fetus or placenta. There is a 15% risk of death of the
207 co-twin in a monochorionic pregnancy and the risk of abnormal neurological development in survi-
208 vors is 26%.⁴¹ Death of one twin in a monochorionic twin pregnancy can occur spontaneously or
209 after an intervention such as laser ablation of placental vessels for twin-twin transfusion syndrome
210 (TTTS). TTTS complicates 8 to 10% of twin pregnancies and is responsible for approximately half
211 of all perinatal deaths in monochorionic twins.⁴² Again, the relative rarity of this clinical situation
212 makes properly powered, prospective studies about possible benefits of iuMR imaging over USS
213 exceptionally difficult, if not impossible without multi-centred, international trials. Our previous
214 work in the field showed brain abnormalities in 9/68 (13.2%) of co-twin survivors after demise of
215 one twin in monochorionic pregnancies and three of those abnormalities were shown correctly on
216 USS.⁴³ Examples are shown in figures 7 and 8. The small number of other publications in this area
217 support the use of iuMR imaging after single fetus demise in monochorionic twin pregnancies or
218 suggest the value of larger studies to confirm the perceived benefits of iuMR.^{44,45}

219

220 *Microcephaly*

221 Microcephaly (small skull size) is frequently found in fetuses with developmental and acquired
222 brain pathology including many of the conditions described in previous sections. Here we will dis-
223 cuss some of the issues that arise if microcephaly is the only abnormal finding on USS or if there
224 are only non-specific abnormalities such as enlarged CSF spaces or germinolytic cysts. Assessment

225 of the skull size on USS is made by measuring biparietal diameter, occipito-frontal diameter and/or
226 head circumference and compared with normative charts. This is done routinely because a small
227 head size in a fetus is considered to be an independent risk for poor neurodevelopmental out-
228 come.⁴⁶⁻⁴⁸ Important issues for research that can be answered by performing iuMR imaging along-
229 side USS include:

- 230 a) What is the accuracy of skull measurements on USS? The MERIDIAN study did not recruit
231 fetuses with microcephaly only but when it was found in conjunction with another brain ab-
232 normality there was the opportunity to compare the head sizes made on USS with those on
233 iuMR imaging. Thirty fetuses were referred with a diagnosis of microcephaly and the diag-
234 nosis was refuted on iuMR in 8/30 (false positives on USS - 27%) of cases. In addition, a
235 further 13 fetuses had microcephaly diagnosed on iuMR that was not recognised on USS
236 (false negative rate on USS 13/35 =37%). This data indicates a substantial problem in cor-
237 rectly identifying microcephaly on USS.
- 238 b) What degree of microcephaly warrants further investigation by iuMR imaging? There is lit-
239 tle agreement in the literature about what measurement constitutes microcephaly, some au-
240 thorities using <10th centile and others <3rd centile and there is little scientific justification
241 for either position. A prospective, formally powered study that recruits fetuses with varying
242 degrees of small head size diagnosed on USS followed by iuMR imaging will be able to
243 measure the proportion of cases iuMR had diagnostic and clinical impact. By this means it
244 will be possible to set a level of microcephaly which will benefit from iuMR imaging.
- 245 c) A more fundamental issue is the mismatch between head size and brain size. It is a common
246 feature of many of our iuMR studies that microcephaly was overlooked on USS but equally
247 important are the cases where the head size is not a cause for concern on either USS or
248 iuMR but the brain size is disproportionately small on iuMR imaging (micrencephaly). This

249 is coming into sharp focus now it is possible to make accurate and reproducible measure-
250 ments of fetal brain volume (figures 1 and 5 and reference⁴⁹).

251

252 **Conclusions**

253 USS will remain the mainstay of the national programme for fetal screening and anomaly scanning,
254 however, we are beginning to learn more about its limitations and that iuMR improves diagnostic
255 accuracy at a clinically significant level. Most comparative studies have concentrated on fetuses
256 with brain abnormalities visible on USS but we believe it is appropriate to perform research studies
257 on fetuses that are at increased risk of a brain abnormality but USS findings are either normal or
258 non-specific. Heightened parental and clinician anxiety is to be expected in these pregnancies and
259 we have spoken of ‘technology creep’ based on the unproven assumption that iuMR imaging will
260 provide more information and certainty but it is important for the clinical research community to
261 provide the evidence for or against this expensive resource.

262

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386 Figure legends.

387 Figure 1. A case in which recurrence of a brain malformation was confirmed on iuMR imaging. The
388 older sibling of the current fetus had a post-natal MR diagnosis of agenesis of the corpus callosum
389 (1a) and a cortical formation abnormality (lissencephaly with a posterior hemispheric predilection -
390 b). In utero MR imaging was performed at 33 weeks' gestation in the next pregnancy and agenesis
391 of the corpus callosum was confirmed (1c) along with a bilateral, symmetrical cortical formation
392 abnormality (1c and 1d), most likely to be lissencephaly although polymicrogyria could not be ex-
393 cluded on the basis of the imaging alone. The total brain volume was reduced in comparison with
394 the published reference range as described in the text (1e and reference⁴⁹).

395

396 Figure 2. A case in which recurrence of a brain malformation was excluded on iuMR imaging. The
397 older sibling of the current fetus had a diagnosis of bilateral perisylvian polymicrogyria made on
398 post-natal MR imaging (2a-2c). USS imaging in the next pregnancy showed mild ventriculomegaly
399 and iuMR was performed at 24 weeks, which confirmed mild ventriculomegaly but showed no evi-
400 dence of polymicrogyria (2d-2f). A repeat iuMR study at 31 weeks' gestational age showed resolu-
401 tion of the ventriculomegaly and cortical sulcation/gyration that was appropriate for gestational age.

402

403 Figure 3. A case in which recurrence of a metabolic disease was strongly suspected on iuMR imag-
404 ing in spite of relatively non-specific findings. Mild ventriculomegaly was detected on ante-natal
405 USS in a fetus at 20 weeks gestational age and the only history of note was an early neonatal death
406 in the previous pregnancy. iuMR imaging was performed at 21 weeks gestation and axial ssFSE T2-
407 weighted (3a) and FLAIR (3b) images confirm mild ventriculomegaly (trigones 11 and 12mm) and
408 show bilateral cysts in the germinal matrix close to the frontal horns. Cytomegalovirus infection
409 was looked for and excluded and a repeat iuMR at 30 weeks (3c axial and 3d sagittal ssFSE)
410 showed progressive ventriculomegaly (trigones 12 and 13 mm) and more extensive germinolytic

411 cysts. Pyruvate carboxylase deficiency was confirmed post-natally and similar appearances were
412 shown in the next pregnancy (3e and 3f) with the same outcome.

413
414 Figure 4. A case with associated cardiac and brain malformations confirmed on iuMR imaging.
415 Double outlet right ventricle with transposition of the great vessels and VSD had been diagnosed on
416 USS and iuMR imaging of a fetal brain was performed at 33 weeks. Hypogenesis of the cerebellar
417 vermis was demonstrated on the sagittal (4a) and coronal (4b) iuMR images. Bilateral cleft
418 lip/palate was demonstrated (4c) and had also been diagnosed on USS.

419
420 Figure 5. Post-natal MR imaging of a child with microcephaly, severe epilepsy and global devel-
421 opmental delay (6a-6d). There is an extensive bilateral cortical formation abnormality consisting of
422 polymicrogyria and bilateral schizencephaly. A subsequent diagnosis of congenital infection by cy-
423 tomegalovirus was made.

424
425 Figure 6. A case in which congenital CMV infection was made on iuMR imaging, with subsequent
426 serological/histological confirmation. A fetus referred for iuMR imaging at 31 weeks gestation be-
427 cause of ventriculomegaly on USS. The iuMR imaging (5a-5c) confirmed ventriculomegaly but al-
428 so showed microcephaly, ventricular stranding and extensive bilateral polymicrogyria. The cortical
429 formation abnormality is well shown on the model of the left lateral surface created from 3D vol-
430 ume data (5d) in comparison with an aged matched normal (5e). The brain volume was substantial-
431 ly reduced (5f).⁴⁹

432
433 Figure 7. Three cases of demise of a fetus in monochorionic pregnancies. 7a and 7b is a case of
434 spontaneous twin demise at 20 weeks and the iuMR study performed at 23 weeks. The demised
435 twin is on the right in both images. The surviving co-twin is micrencephaly from generalised en-

436 cephalomalacia. 7c and 7d show the surviving co-twin after spontaneous twin demise at 17weeks
437 and the iuMR study performed at 26 weeks. There is micrencephaly and bilateral brain injury in-
438 volving the territory supplied by middle cerebral artery on both sides. 7e and 7f are images of the
439 surviving co-twin in a monochorionic pregnancy complicated by twin-twin transfusion syndrome.
440 Laser ablation of the placental vessels was performed at 18 weeks and one twin died shortly after-
441 wards. The surviving co-twin had iuMR imaging at 25 weeks which evidence of a unilateral stroke
442 with haemosiderin staining indicating previous haemorrhage.

443

444 Figure 8. Post-natal imaging (12 weeks) of a co-twin survivor of a monochorionic pregnancy com-
445 plicated by twin-twin transfusion syndrome. There is loss of volume and abnormal cortex at the
446 posterior part of the right sylvian fissure (8a and arrowed on 8b). 8c and 8d are non-orthogonal
447 reformations of the sylvian fissures from T1 volume data showing the normal sylvian fissure on the
448 left (8c) and the abnormal posterior extension of the sylvian fissure on the right lined by abnormal
449 cortex (arrowed 8d). It is likely there was a focal infarction during the second trimester that has
450 healed by reparative polymicrogyria.^{43,45}