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Does whole-body in-utero MRI in those with suspected fetal abnormalities improve antenatal care? A single-centre retrospective cohort study

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ABSTRACT

Objective: To determine whether full body in-utero magnetic resonance imaging (iuMRI) rather than targeted imaging adds useful clinical information when a fetal anomaly is suspected in the brain or the body.

Design: Single-centre retrospective cohort study, from October 2011 to May 2022.

Setting: Regional Fetal MRI Service in Sheffield, UK.

Patients: All pregnant people undergoing iuMRI.

Interventions: iuMRI of the brain and body were reviewed by a fetal radiologist, and the results discussed by a multidisciplinary team.

Main outcome measures: Additional abnormalities detected on iuMRI outside of the initial area of interest on ultrasound.

Results: 1876 participants: 916 participants had a fetus with brain anomalies only on ultrasound, of which 12 (1.3%) had additional body abnormalities on iuMRI. 960 participants had body anomalies only on ultrasound, of whom 8 (0.8%) had an additional brain abnormality. The additional findings from 12 cases (0.6% of whole cohort) added useful clinical information to guide care or counselling.

Conclusion: If brain or body anomalies are found on ultrasound in the fetus, whole body iuMRI reveals additional abnormalities in a small number of cases. However, these may provide important information that changes counselling or care. Further research is required to determine how significant this impact is for clinicians and families, whether normal findings reassure families, how long whole body iuMRI adds to the MRI acquisition time, and the health economics implications.

INTRODUCTION

Ultrasound screening (USS) is a routine part of pregnancy care at 20 weeks gestation in England.[1] Where a fetal abnormality is found on ultrasound, further tests may be required, such as viral screens, genetic testing, or in-utero magnetic resonance imaging (iuMRI). When transabdominal USS detects a fetal brain abnormality, iuMRI improves diagnostic accuracy and the treating obstetrician's confidence of brain abnormalities, which can change pregnancy care.[2-7] There is no role for brain iuMRI when the fetal brain is normal on USS.[8] In-utero MRI also has a role in the evaluation of fetal respiratory, cardiac, gastrointestinal, and genitourinary systems,[9-16]. The US findings are available to the reporting clinician at the time of the MRI. Referral practices will vary across the country depending on MRI availability and experience.

In-utero MRI is typically directed towards the area of the fetus in which an anomaly is suspected and there is no available literature to guide radiologists or obstetricians on whether they should only image the area in question or the whole body. The purpose of this study was to determine whether:

1. iuMRI of the brain provided useful information when there was a fetal body abnormality on ultrasound
2. iuMRI of the body provided useful information when there was a fetal brain abnormality on ultrasound

METHODS

Ethical approval was obtained from Health and Care Research Wales (IRAS 322369), and approval from the UK Health Research Authority.

Sheffield Teaching Hospitals NHS Foundation Trust provides an iuMRI service locally and to wider areas of the UK. When a fetal anomaly is detected on ultrasound of either the body or brain and deemed appropriate by the obstetric team, a referral to the iuMRI service is made.

iuMRI is performed and all the images obtained are reported as a part of standard clinical practice (Table 1). iuMRIs performed locally are supervised by a radiologist with expertise of in-utero imaging. If an abnormality outside the targeted area is observed then additional imaging is immediately performed while the patient is in the scanner. All referrals to the iuMRI service between October 2011 to May 2022 were identified retrospectively from our local database. The initial ultrasound reports and request forms were reviewed from all cases by a single reviewer (DN), and the participants were divided into groups:

- *Group 1* – suspected fetal anomalies in the brain only (other abnormalities in the head, such as the eyes, were not considered a brain abnormality)
- *Group 2* – suspected fetal anomalies in in the body only
- *Group 3* - suspected fetal anomalies in the brain and body.

Participants in group 3 were excluded.

The nature of the suspected anomalies was collected and the results of iuMRI studied for participants in groups 1 and 2. Fetuses in Group 1 who had a body abnormality on iuMRI and in Group 2 who had a brain abnormality were identified. These cases were reviewed by a multidisciplinary team comprising a Radiologist with an expertise in in-utero imaging (EHW), a Perinatal Neurologist (ARH), a Neonatologist who provided antenatal counselling (CH) and a Fetal Medicine Obstetrician (VS). All members of the panel routinely provided antenatal counselling to families in the Fetal Maternal Unit about fetal anomalies. The panel discussed the impact the additional findings would have made to antenatal counselling or care in each case, including:

1. Whether additional information on developmental outcome was provided by iuMRI
2. Whether the information informed postnatal care, such as whether plans were needed to ensure teams were present at birth to provide resuscitation or advanced neonatal care, if palliative care should be offered to families, and whether referrals to other specialities, like neurosurgery, nephrology, or cardiology, investigations, or treatments were needed after birth

3. Whether the iuMRI results changed antenatal care, such as need for additional investigations, follow-up, or if advice on the timing or method of delivery changed.

It should be noted that images obtained of the body in a suspected brain abnormality would not be of as high a quality as a targeted body iuMRI and vice versa. The panel were asked to reach a consensus on each case's impact using one of the following categories: definitely would impact care, may impact care, or would not impact care. Some iuMRI images were reviewed to clarify the description provided in the iuMRI reports.

We present the numbers and percentage of times abnormalities were found that changed clinical practice. No further statistical analysis was performed.

RESULTS

Between October 2011 and May 2022, 2069 scans were performed on women / people who were pregnant. Group 3 consisted of 193 (9.3%) participants who were excluded from our analysis, leaving a cohort of 1876 participants. Table 2 indicates the region of the fetus primarily imaged / reason for iuMRI referral. All images were deemed diagnostic quality at the time of the scan.

Group 1 consisted of 916/1876 (48.8%) participants, of whom 12/916 (1.3%) had additional body abnormalities on iuMRI. Group 2 consisted of 960/1876 participants (51.1%), of whom 8/960 (0.8%) had a brain abnormality on iuMRI. In total, iuMRI of the whole fetus revealed abnormality in another part of the fetus in 20/1876 (1.1%) participants.

Of these 20 participants, the multidisciplinary team thought clinical care or counselling would change in 12/20 (60%), or 12/1876 (0.6%) of the whole cohort. These included: 6/916 (0.6%) participants in Group 1 and 6/960 (0.6%) in Group 2. In some cases, where the impact was categorised as 'maybe', the panel found this was due to differences in practice between

units. For example, in some units, additional referrals or investigations would be planned based on the iuMRI, and in others those investigations would have formed part of standard clinical care. In one case, consensus on impact of the iuMRI was not reached. This was a case where a tiny atretic encephalocele with no skull defect or brain tissue within the lesion was noted in addition to a congenital diaphragmatic hernia. The iuMRI 'definitely would' impact **counselling regarding management of delivery** and needed to be discussed with the family, but it was not thought to impact the risk of developmental difficulties or postnatal care.

Details of the body abnormalities found in fetuses in Group 1 (Table 3)

In three cases, there were additional eye abnormalities found that were not described on the original USS. Our a priori methodology was to consider anything not a part of the brain as a "body" abnormality. In one of these, the initial diagnosis on USS was holoprosencephaly, and the eye abnormalities on iuMRI were hypotelorism / protruding eyes. Given eye abnormalities are common with holoprosencephaly, this was not thought to impact care. In the second case, the USS suggested hydrocephalus, which was confirmed on iuMRI, which also found several other brain abnormalities suggestive of a genetic condition: enlarged posterior fossa, hypoplastic cerebellar vermis, poor formation of the Sylvian fissure. The "body" abnormalities were anophthalmia, which was a significant clinical finding that supported a genetic diagnosis and would impact on visual and cognitive development. The third case was similar: the USS showed ventriculomegaly, but the "body" abnormality was a rudimentary globe of one eye, and an abnormal palate. For both participants, these abnormalities did not require iuMRI of the body, which would not have yielded useful clinical information. For both cases, therefore, iuMRI of the body was described as "not impacting care".

The other body abnormalities not thought to impact on care included two cases with bilateral prominent renal pelvises in children with ventriculomegaly. These renal findings were not

thought to change antenatal care because it was likely there would have been additional ultrasound for the brain abnormalities, at which point any progression from prominent to dilated renal pelvises would have been detected, and the prominence was not considered significant enough to change counselling with relation to renal health. The final case was a fetus with ventriculomegaly, agenesis of the corpus callosum, a small cerebellum, and an “underdeveloped” brain on ultrasound, in whom the iuMRI confirmed the findings and found a mildly thin cervical cord. Although the c-spine is part of the neurological system, iuMRI of the body was considered important by the radiologist in diagnosing it. The thinning was not thought to be of clinical significance, compared to the other brain abnormalities. As a result, it was not thought to impact care or counselling.

In 4 cases, the body imaging findings had a significant impact on care or counselling. In one case of “brain oedema” on ultrasound, the body iuMRI showed atrophied limb musculature and significant body oedema, possible from a genetic neuromuscular or metabolic condition in which there was reduced fetal movement and / or muscle atrophy, myopathy, or muscular dystrophy. In two cases, suspected brain abnormalities (a space occupying lesion and an arachnoid cyst) on USS were found to be dural sinus fistulae on iuMRI, and the body iuMRI found enlarged mediastinum and distended jugular veins, thought to reflect the severity of the vascular abnormality and impending cardiac failure. This also would have impacted on survival and the decision of where to deliver the babies. Finally, a twin who had experienced twin to twin transfusion and received laser therapy had bilateral atrophy of the kidneys and ischaemic bowel on iuMRI. In two participants, the iuMRI of the body was considered by the MDT to “may” have an impact on clinical care: one case with a skull defect and nuchal thickening had cardiomegaly, but cardiology assessment was needed to clarify whether the heart was normal or not. The MDT considered many units would have arranged formal echocardiography for the nuchal thickness anyway, meaning the iuMRI may not have impacted care. In the second participant, the stomach was small, which was of uncertain significance.

Details on the brain abnormalities found in fetuses in Group 2 (table 4)

In four cases, iuMRI of the brain impacted on the care of a fetus who had body abnormalities on USS. One case of arthrogryposis had abnormal cortical development, likely to impact learning in addition to movement and increase the risk of epilepsy. In a second case, a cystic lesion in the sacrococcygeal region was associated with a Chiari II malformation, which would lead to a neurosurgical consultation and birth near a neurosurgical unit. The third had a large posterior fossa, and the panel thought this would lead to further imaging throughout pregnancy and probable repeat iuMRI to look for cerebellar dysplasia. The fourth case had a cystic hygroma on USS and enlarged posterior fossa, ventriculomegaly, and possible corpus callosum abnormalities on iuMRI, which would change prognostication about learning / development and genetic testing.

In one case, three of the panel thought the abnormality “may” change care and the fetal medicine consultant thought it definitely would. The brain abnormality was a tiny atretic encephalocele in a case with congenital diaphragmatic hernia (CDH). It was suspected by the MDT that the child may not survive with the CDH and the encephalocele was therefore of limited significance. If the child survived, the panel did not think that the brain findings would significantly impact on development and the neurosurgeons would not intervene surgically under anaesthetic because of concerns about the lungs. The obstetrician thought it affected delivery counselling (namely avoidance of difficult instrumental birth), given parental preference for survival-focussed care. In some units, the findings may have led to genetic testing.

In one case, the iuMRI may have impacted outcome: the USS showed an absent stomach bubble, and the iuMRI showed a fetus with reduced movements. This raised the possibility of akinesia / a neuromuscular disorder that impaired swallowing. These non-specific findings

would not necessarily have changed management given the USS findings themselves suggested a swallowing problem.

In two cases, the iuMRI findings did not impact care. One fetus with CDH had a head circumference on the lower limits of the reference range, but the published data suggests that only microcephaly between 3 and 4 standard deviations from the population mean are associated with atypical developmental outcomes,[17] and the head circumference was not that small. Postnatally, the head circumference would be measured as a part of the routine baby check, so this iuMRI was thought not to impact on care. In another participant, there was increased extra-axial CSF spaces, but normal brain structure and head circumference. This finding was not considered clinically significant and the body abnormalities on USS more important.

DISCUSSION

In this retrospective study, the incidence of iuMRI finding additional abnormalities outside the area of interest was small and, when they did occur, the abnormalities did not always impact on care. There was a flaw in our a priori methodology, in which we counted abnormalities outside the brain as “body”, when they would have been found on iuMRI of the head. As a result, it could be argued that the “true” incidence is slightly lower than we have reported.

It is tempting, therefore, to draw the conclusion that whole body iuMRI is not helpful in clinical practice and only the area of interest should be reported. Given it is likely that different radiologists would be needed to report the fetal brain and the body in most units, it could be argued that limiting the iuMRI to the area of interest reduces unnecessary use of time and resources. However, the whole of the fetal body is often caught on iuMRI, and therefore does not significantly add to imaging acquisition time. In the small number of cases where abnormalities were found and thought to be significant, this could have had an important impact on advice on pregnancy care. The importance of this information may be

sufficiently large that it is worth pursuing. Further work is needed to determine the significance of these findings for women, their families, and clinicians. It is also possible that capturing the fetal body and not reporting the findings could lead to medicolegal claims like wrongful birth when an abnormality is visible on iuMRI but missed because the images were not reviewed. We suggest a review of all images whilst the patient is still on the scanning table so that any additional views can be obtained but acknowledge this may not be logistically possible in all units.

Furthermore, our methodology assumes iuMRI results are only valuable when abnormalities are found. In fact, confirmation there are no additional fetal abnormalities may reassure both families and clinicians. For example, a normal iuMRI of the brain in the case of arthrogryposis leads a neurologist to consider neuromuscular disorders. If they are excluded on genetic testing, then a conclusion can be made that cognitive outcome could be relatively preserved. Additionally, iuMRI may have particular value when ultrasound resolution is limited (e.g. obesity, severe oligohydramnios)

There are several limitations to our work. As previously noted, our methodology of considering abnormalities to the head or eyes as “body” problems when they would be detected on targeted imaging of the brain was flawed because the imaging below the neck would not have impacted care. The panel also relied on the clinical details on request forms and imaging reports, and these may not have been accurate or complete. For example, there may have been information available to clinicians, but not our MDT, like the outcomes of prior pregnancies, family history, genetic results, or developmental outcomes in previous children. A prospective study would help address these concerns and help assess the value of normal imaging.

In conclusion, whole body iuMRI reveals additional abnormalities in parts of the fetus distant from the area of concern in relatively few cases and, of these, affects care or counselling in

around 60% of cases. However, this data would underestimate the value of normal imaging to clinicians and families. Further research would determine the impact of whole-body imaging and whether there are resource, health economic, and medicolegal arguments for or against the practice.

Table one: Standard Clinical IU MRI sequences, Siemens Avanto 1.5T

Brain:
T2 SSFSE 3 orthogonal planes
T1 Axial
DWI Axial b0,b600, b1000
Balanced GE Axial

Body:
T2 SSFSE 3 orthogonal planes
T1 Sagittal and coronal
Balanced GE axial
DWI sagittal plus additional if required b0 b600 b1000.

The centre does not use a reporting template.

Table two: Area of fetuses imaged and primary reason for imaging

Areas of abnormality on initial ultrasound
Brain (n=916) ○ VM (477) • Isolated VM = 379 • VM + other abnormalities = 98 ○ Posterior fossa abnormalities = 71 ○ Cerebrum: 156 (including ACC, cysts, holoprosencephaly) ○ Head size (micro/macrocephaly): 44 ○ Infection (CMV, toxoplasmosis, syphilis): 24 ○ CSF system 16 (including choroid plexus cysts, large 3rd and 4th ventricles) ○ Other: 128 (including family history of brain abnormalities, post TTTS laser, twin demise)
Other body regions (n=960), participants could have more than one abnormality ○ Spine (n=152) ○ Face and neck (n=51) ○ Chest (n=201) ○ Abdomen (n=523) including 188 renal cases ○ Limb and other (n=15) ○ Brain and at least 1 other body abnormality (n=193) ○ Multiple body abnormalities (n=20)

Table three: Details of fetuses with brain abnormalities on initial ultrasound where whole fetus iuMRI changed care

Initial Ultrasound Brain findings	**Gestation at iuMRI (weeks)**	**Findings on iuMRI (Extra body findings in bold)**	**Does iuMRI change practice; MDT breakdown**				How did MRI change practice
			Paed Neuro	Neonates	Radiology	FMU	
Head oedema	**32**	**Atrophied limbs and extensive oedema from scalp to body**	Yes	Yes	Yes	Yes	Genetic investigations offered in view of additional head findings
Ventriculomegaly, absent corpus callosum, small cerebellum, underdeveloped brain	**27**	**Thinning of upper cervical spine** Significant ventriculomegaly, complete agenesis of corpus callosum and increased extra-axial CSF space	No	No	No	No	Location of abnormality would also be identified on a brain MRI. No change to prognosis with additional cervical spine findings
Ventriculomegaly	**26**	**Prominent renal pelvis bilaterally,** unilateral ventriculomegaly	No	No	No	No	Distinguishment between 'prominent' but not 'dilated' led to a decision of no change.
Ventriculomegaly and dilated third ventricle	**20**	**Rudimentary globe of one eye. Abnormal palate.** Bilateral ventriculomegaly, dilated third ventricle, abnormal cerebellar hemispheres and vermis.	No	No	No	No	Location of abnormality would also be identified on a brain MRI
Space occupying lesion in brain, dural sinus fistula	**32**	**Enlarged mediastinal outline and large jugular veins**. As per ultrasound, significantly enlarged head, ventriculomegaly, extra-axial and intraventricular blood. Chiari II malformation.	Yes	Yes	Yes	Yes	Was not expecting heart failure on initial US → definitely impacts as the US day previously did not show cardiac findings An acceleration in progression which US did not demonstrate Heavily impacts counselling, prognosis and management plans – hydrops

Small cavum septum pellucidum, ventriculomegaly	**21**	**Prominent pelvicalyceal system bilaterally**. Bilateral germinal eminence cysts, bilateral ventriculomegaly.	No	No	No	No	Distinguishment between 'prominent' but not 'dilated' led to a decision of no change.
Skull defect and nuchal thickening	**22**	**Large mediastinal outline; enlarged cardiac to thoracic ratio**. Subcutaneous oedema over head, neck and upper thorax.	Maybe	Maybe	Maybe	Maybe	Agreed formal echocardiography required. Classification of 'maybe' due to differing processes between centres which leads to a difference of process. I.e. one centre would obtain echocardiography on finding of increased nuchal thickening alone due to increased risk of cardiac abnormalities.
Ventriculomegaly (of twin post laser therapy)	**23**	**Ischaemic bowel; small kidneys possibly atrophic.** Ischaemic brain damage in posterior parietal and occipital lobes	Yes	Yes	Yes	Yes	A poor prognosis with considerations of palliation and selective induction. The panel had discussions regarding fatality and the potential effects on the remaining twin including risks of brain damage as well as neonatal management. Further imaging would be indicated.
Abnormal shaped cerebellum, prominent cisterna magna	**23**	**Small fluid filled stomach.** Dandy Walker malformation	Maybe	Maybe	Maybe	Maybe	Addition of a small stomach with brain abnormalities raises suspicions of abnormalities. Classification of 'maybe' due to variation in regional guidelines regarding fluid filled stomach findings.
Cystic area superior to cerebellum; presumed arachnoid cyst	**30**	**Cardiomegaly and prominent large vessels.** Large dural sinus fistula causing displacement of brain parenchyma	Yes	Yes	Yes	Yes	Cardiac findings not consistent with usual associated abnormalities with dural sinus fistula. Poor prognosis due to late presentation of cardiomegaly and large vessels. Alterations to counselling regarding delivery and diagnosis required.
Gross bilateral hydrocephalus with dangling choroid plexus; Ventriculomegaly	**22**	**Bilateral anophthalmia.** Bilateral severe ventriculomegaly, dilated third ventricle, enlarged posterior fossa, hypoplastic cerebellar vermis, poor Sylvian fissure formation	No	No	No	No	Location of abnormality would also be identified on a brain MRI
Holoposencephaly, Frontonasal dysplasia	**20**	**Hypotelorism and protruding eyes. Absence of nasal bones; single nasal sinus and nasal cleft**	No	No	No	No	Location of abnormality would also be identified on a brain MRI

Table four: Details of cases where whole body iuMRI changed care with initial body findings on ultrasound

Initial Ultrasound Body findings	**Gestation at iuMRI (weeks)**	**Findings on iuMRI (Extra brain findings in bold)**	**Does iuMRI change practice; MDT breakdown**				How did MRI change practice?
			Paed Neuro	Neonates	Radiology	FMU	
Arthrogryposis, talipes, VSD	**21**	**Abnormal Sylvian fissure and large posterior fossa** Reduced muscle bulk of limbs and buttocks	Yes	Yes	Yes	Yes	A poorer prognosis counselled for with additional brain findings
Cystic lesion in sacrococcygeal region	**28**	**Chiari II malformation** Lipomyelomeningocele	Yes	Yes	Yes	Yes	Change in diagnosis and outcome with additional surgical involvement
Dilated large bowel	**21**	**Large posterior fossa** Abnormal bowel pattern, reduced lung volumes	Yes	Yes	Yes	Yes	Further imaging advised to investigate posterior fossa findings
Large heart, CDH	**20**	**Small head** Bilateral severe pulmonary hypoplasia	No	No	No	No	No change in counselling
Abnormal course of umbilical vein and absent stomach bubble	**30**	**Increased extra-axial CSF space** Cardiomegaly, polyhydramnios, reduced fluid in stomach	No	No	No	No	Non-specific additional finding and additional body abnormalities would be identified on iuMRI
CDH	**33**	**Atretic encephalocele** CDH	Maybe	Maybe	Maybe	Yes	Change to the route of delivery Potential involvement of further surgical specialties
Cystic hygroma	**19**	**Elevated tentorium enlarging posterior fossa, unclear corpus callosum, dilated lateral ventricles** Cystic hygroma, abnormal skull shape	Yes	Yes	Yes	Yes	Increased suspicion of genetic abnormalities – recommend whole exome sequencing if not previously offered. Additional concerns regarding progression to hydrops and cardiac defects
Absent stomach bubble	25	Very reduced movements, suspicion of oesophageal atresia or **neurological condition**	Maybe	Maybe	Maybe	Maybe	Additional brain imaging due to concerns despite a structurally normal brain regarding suspicion of a neurological problem due to reduced movements.

What is already known on this topic

- *In-utero MRI (iuMRI) demonstrates fetal brain anomalies more accurately than ultrasound.*

What this study adds

- *In Sheffield, all fetal images obtained when imaging the brain, which incorporates the fetal body, are reviewed.*
- *This is not currently routine practice in most centres in England, where iuMRI only reviews the area of abnormality suspected on ultrasound.*

How this study might affect research, practice or policy

- *We postulate this practice may miss important abnormalities that could alter antenatal counselling.*
- *We suggest a review of all images acquired when reviewing iuMRI scans*

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