

## **TITLE**

### **Fetal Body MRI and its application to Fetal and Neonatal Treatment. An illustrative review.**

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## ARTICLE SUMMARY

This illustrative review depicts the evolving role of magnetic resonance imaging (MRI) in the diagnosis and prognostication of anomalies of the fetal body (here including head and neck, thorax, abdomen and spine). A review of the current literature describing the state-of-the-art in antenatal imaging for diagnosis and prognostication of congenital anomalies is coupled with illustrative cases in true radiological planes with viewable 3D video models that demonstrate the potential of post-acquisition reconstruction protocols.

Within, we will discuss benefits and limitations of fetal MRI across the breadth of conditions included: from anomaly detection, classification and prognostication as well as defining the role of imaging in the decision to proceed to prenatal intervention. Reference will also be made to the current capabilities of ultrasound and we will explore potential ways in which the two may perform complimentary roles in the future of prenatal imaging.

## KEY POINTS (5-6 total)

- Magnetic resonance imaging (MRI) is commonly used in the classification of fetal brain anomalies; its use in fetal body anomalies is less widely adopted, recent advances have led to validation of its role in the antenatal work-up of several conditions.
- Discrimination of soft tissues by fetal MRI allows delineation of anatomy in cases of fetal tumours – this aids antenatal counselling and may change management, such as EXIT procedure in fetal neck masses.
- MRI volumetry may allow precise estimates of total lung volume, with a potential role in prognostication of congenital diaphragmatic hernia, congenital lung lesions and anterior abdominal wall defects.
- There is an important role of fetal MRI in the work-up of fetuses with spina bifida: imaging of the fetal brain is important to dictate which cases could benefit from prenatal surgery.
- MRI has a limited role in the assessment of musculoskeletal and facial anomalies, which are best appreciated on 2D or 3D USS, however its assessment of the fetal airway defines its importance in complex anatomical assessment.
- There are ongoing challenges in the antenatal diagnosis of several conditions: anorectal malformation (visualisation of the fetal pelvis, lack of a dilated rectum in many cases) and oesophageal atresia (dilated upper pouch and visualisation of distal oesophagus challenging to image)

## 1. INTRODUCTION

### BACKGROUND

Magnetic Resonance Imaging (MRI) of the fetus is a well-recognised adjunct to ultrasound (USS) for the assessment of fetal anomalies. Limitations of fetal movement-induced artefact have led to a variety of approaches including shortening of acquisition sequences – which limits the detail derived from the scan. Modern post-acquisition reconstruction techniques allow for motion-correction, three-dimensional segmentation and volumetry. The refinement of these has given fetal MRI a well-defined role in the assessment of fetal central nervous system (CNS) anomalies,<sup>1</sup> and we have more recently succeeded in reconstruction of MR images to aid in the diagnosis of fetal cardiac lesions.<sup>2</sup> New ground is also being broken in the assessment of placental pathology using MRI,<sup>3</sup> with reliable distinction of circulatory systems of mother and fetus allowing for detailed future study of placental development.<sup>4</sup>

Fetal body MRI is now also complementary to ultrasound scanning (USS) for the assessment of head and neck masses, anterior abdominal wall lesions, thoracic, abdominal pathology. Many of these body regions have been particularly challenging to image, due to fetal movement or the deformable nature of the cavity wall. This has limited the role of MRI to the assessment of contiguous but misaligned 2-dimensional slices, which has clear disadvantages in the assessment of subtle abnormalities and undersells the potential of MRI in providing 3-dimensional data. This illustrative review summarises the current state of the art of MRI for malformations of the fetal body, which may be amenable to treatment *in utero* or early postnatal life. We will use the widely recognised “gold standard” of fetal USS as a comparator and demonstrate circumstances where the two modalities may complement each other in the assessment of challenging cases.

Our review will cover lesions of the head and neck, thorax, abdomen and pelvis, and spine; each section will contain several illustrative case reports with relevant antenatal history and image-derived information. We also demonstrate new reconstruction techniques which may provide further benefits; specifically we will include illustrative examples of deformable slice-to-volume reconstruction (DSVR), which allows reconstruction of high-resolution 3D images in modifiable planes and 3D segmentation to improve accuracy of volumetry (Supplemental Figure S1A+B).<sup>5</sup>

## ETHICS APPROVALS

All cases presented were acquired through the Department for Perinatal Imaging and Health at St. Thomas' Hospital, London, the imaging departmental protocol is outlined in full (Reference to Imaging Protocols Box). The images presented have been reproduced with specific consent of patients; studies were performed either as part of the iFIND research study (National Ethics Registration 14/LO/1806) or the clinical service provided by the Perinatal Imaging Centre at St. Thomas' Hospital, London (National Ethics Registration 07/H0707/105).

## SEARCH STRATEGY AND SELECTION CRITERIA

Articles were identified through a comprehensive search of MEDLINE using terms "fetal MRI" and "antenatal MRI" with extended searches of reference lists for included articles. As a state-of-the-art review, we have referenced only the most significant or recent articles where multiple were available. Studies where current capabilities and limitations of MRI, with comparison to fetal USS were preferentially included.

### **2. HEAD AND NECK MASSES**

Most antenatally diagnosed neck masses are either lymphatic malformations (Figure 1A) or teratomas (Figure 1B), with an incidence between 1 in every 10,000 – 30,000 pregnancies.<sup>6</sup> The predominant concern is that of neonatal airway compromise and the advent of Ex-Utero Intrapartum Treatment (EXIT) has allowed life-saving measures to be performed for the fetus with a critical airway: a carefully planned airway intervention is performed whilst maintaining fetoplacental circulation until the fetus can be separated from the cord to complete the Caesarean section delivery. Identifying cases where EXIT may be necessary remains a challenge, necessitating referral to specialised centres that can coordinate the care.<sup>7</sup> Recent publications have described evaluation of the fetal airway via fetoscopy, which may be an alternative method to delineate the need for EXIT.<sup>8</sup> However, while the EXIT has proven successful in specialist centres, it is an invasive procedure with significant risks to both mother and fetus. Maternal and fetal factors alongside institutional expertise must also be considered, with accurate imaging clearly playing an important role.

MRI provides a clear advantage over conventional USS for fetal neck masses in assessing tumour extension and giving 3-dimensional visualisation of its relationship to the airway (Figure 1 and Supplemental Video 1). MRI can distinguish lymphatic malformations from teratomas by T1 and T2 contrast weightings that identify fluid, haemorrhage and fat, and anatomical relations can be precisely demonstrated. T1-weighted MRI is also able to reliably distinguish thyroid tissue,<sup>9</sup> this is important when considering the need for tracheostomy as passage of the tumour anterior to the trachea may render this infeasible. A large retrospective series demonstrates that cases requiring EXIT could be predicted using MRI measured dimensions of polyhydramnios and evidence of mass effect on the trachea, with a sensitivity of 95% and a specificity of 80%; notably, tumour size itself was not a predictive factor.<sup>10</sup>

The value of MRI in the assessment of bony defects such as orofacial clefts is generally surpassed by that of 3D ultrasound, which gives a detailed depiction of the fetal face. However there is an identified supporting role in suspected cases;<sup>11</sup> MRI may be more sensitive in detecting cases of isolated cleft palate,<sup>12</sup> where the lack of an associated labial defect may render USS diagnosis difficult.

#### ILLUSTRATIVE CASES

Figure 1A shows the T2-weighted MRI of a 31+6 weeks fetus with a lymphatic malformation of the posterolateral neck. The fetal MRI was able to exclude the diagnosis of teratoma by ruling out any solid components of the lesion, demonstrate the multicompartamental involvement, including the carotid space, and, importantly, demonstrated the preservation of the fetal airway. The baby was born asymptomatic at term and remains under observational follow-up.

Figure 1B shows the T2-weighted MRI of a fetus with a pharyngeal teratoma at 33+4 weeks gestation. 3D reconstruction measured tumour volume at 85cm<sup>3</sup>. Lateral displacement of the tongue and effacement of the oropharyngeal cavity were appreciable on the antenatal USS. MRI was able to establish the margins of the fetal airway and supported the decision to perform EXIT, where video-assisted oral intubation was performed prior to neonatal tracheostomy. Detailed illustration of the 3D reconstruction of these two lesions is provided in Supplemental Videos 1+2.

### **3. THORACIC LESIONS**

#### **LESIONS OF THE LUNG**

Bronchopulmonary foregut malformations include intestinal duplications, bronchogenic cysts, bronchial atresia, congenital pulmonary airway malformations (CPAM, illustrated in Figure 2A) and bronchopulmonary sequestrations (BPS, illustrated in Figure 2B). Incidence has previously been estimated at 1 in 20,000, however the improved detection of higher resolution USS suggests a true incidence closer to 1 in 3,000.<sup>13</sup> CPAM may be solid or cystic and fetal USS can relatively reliably define these lesions, often able to differentiate from BPS by a characteristic systemic arterial blood supply using colour doppler (shown in Figure 2B). The possibility of a “hybrid lesion” with cystic architecture and a systemic feeding vessel is also well-recognised.

Generally, these lesions are asymptomatic during fetal development; however, large lesions can lead to hydrops due to compression of adjacent structures, with an extremely poor prognosis if left untreated.<sup>14,15</sup> Postnatally, many lesions are often asymptomatic, and may even involute, but some will develop infection which is an indication for resection.<sup>16</sup> Observation of the asymptomatic lesion is a contentious issue, with some surgeons remarking on more challenging resection in those lesions affected by infection, and therefore a higher risk of surgical complications.<sup>17</sup> The amount and quality of the remaining normal lung is a key question asked of imaging in order to direct antenatal counselling. To this end, MRI-derived volumetric information may help with prognosis and surgical planning (Supplemental Videos 3-5). Moreover, MRI may better distinguish normal and abnormal lung as well as other diagnoses (such as diaphragmatic hernia), particularly in late gestation where this becomes challenging on ultrasound, this translates to an improved diagnostic accuracy suggested by studies demonstrating a re-classification of a defined diagnosis in up to 50% of cases,<sup>18</sup> thus helping to plan an appropriate delivery location if neonatal respiratory compromise is suspected.

#### **CONGENITAL DIAPHRAGMATIC HERNIA (CDH)**

CDH has an estimated incidence of one in 2,000-4,000 pregnancies and results in a herniation of abdominal viscera into the chest. Consequently, the developing lungs are abnormal in terms of airspace volume and vasculature, on both the affected and the contralateral side.

Postnatal morbidity and mortality results from ventilation difficulties, pulmonary hypertension and cardiac failure.

Antenatal measures of disease severity in expert centres have been shown to be as accurate as those taken after birth,<sup>19</sup> affirming the importance of standardisation of prenatal assessment. USS can predict outcomes in CDH with reasonable accuracy using the observed/expected Lung-Head Ratio (o/e LHR). This takes the size of the contralateral lung in a single plane as a surrogate measurement for total lung volume and remains the most commonly used antenatal prognostic indicator.<sup>20</sup> Several previous studies have failed to demonstrate the superiority of MRI in predicting outcome compared to O/E LHR,<sup>20,21</sup> however MRI is able to give more objective and reproducible estimates of total lung volume (Figure 2),<sup>22,23</sup> which has been demonstrated to be a defining measure of long-term postnatal oxygen requirement.<sup>24</sup> While fetal intervention such as Fetoscopic EndoTracheal Occlusion (FETO) is based on ultrasound measurement of observed over expected lung area to head circumference ratio (o/e LHR), MRI may soon become a more accurate modality to stratify CDH patients.<sup>25</sup>

Most published 3D reconstruction techniques for assessment of the fetal lung have been able to detect only severe cases of hypoplasia,<sup>26</sup> however novel motion-correction and reconstruction approaches such as DSVR can reliably produce volumetric measurement even from motion corrupted sequences (Supplemental Figure S1, Supplemental Videos 6-7).<sup>27</sup> Work to produce normative lung volumes throughout gestation is ongoing, as such the prognostic relevance of these measurements is anecdotal at present. Spatial anatomical relations are much more clearly demonstrated on fetal MR allowing precise localisation of lung, liver, stomach and bowel (Figure 2). This has important prognostic implications as the presence of liver within the hernia is a well-recognised poor prognostic marker.<sup>23</sup> The dimensions of the hernia defect are important determinants of operative technique and post-operative course, and MRI has even been used to print bespoke patches for defect coverage.<sup>28</sup> Looking to the future, accurate sizing of a patch would be an important step in the preparation of tissue engineered solutions.<sup>29</sup>

## ILLUSTRATIVE CASES

Figure 2A demonstrates the T2 MRI of a 24 week fetus with a lesion of left lower lung. Antenatal diagnosis is that of a microcystic CPAM. The lesion volume can be measured

(17.26cm<sup>3</sup>) along with the remaining total lung volume (TLV, 12.82cm<sup>3</sup>). There is displacement of the mediastinum, including the heart, into the right hemithorax, however there is notably no hydrops. The detailed illustrations of the 3D reconstructed image and segmentations are provided in Supplemental Videos 3-4. This lesion seemed to resolve on serial antenatal USS and postnatal CXR, the infant remains asymptomatic under ongoing follow-up.

Figure 2B demonstrates a 25+2 week fetus with a T2 hyperintense lesion behind the heart. Reorientation of planes using DSVR clearly demonstrates a systemic feeding vessel arising from the descending aorta, confirming the diagnosis of BPS. A right-sided diaphragmatic hernia was also noted, with liver and bowel herniating into the right chest. The combination of pathology results in a low TLV (7.82cm<sup>3</sup>). The detailed illustrations of the 3D reconstructed image and segmentations are provided in Supplemental Video 5. The baby was born at 30 weeks' gestation but unfortunately passed away on the first day of life.

Figure 2C demonstrates a 33 week fetus with left-sided CDH containing stomach, bowel, spleen and liver with partial herniation of the kidney. A markedly hypoplastic lung can be seen on the left side. The TLV calculated from segmentation is 23.47cm<sup>3</sup>. The patient underwent postnatal repair on Day 6 of life and is currently under follow-up at 3 years of age. Detailed illustrations of the 3D reconstructed image and segmentations are provided in Supplemental Videos 6-7.

### OESOPHAGEAL ATRESIA

Accurate antenatal diagnosis of oesophageal atresia (OA) is of particular interest to those surgeons advocating a centralisation of care for this condition. With an incidence of approximately 1 in 3,000 live births, ligation of any associated tracheoesophageal fistula is necessary in the first days of life, ideally with simultaneous repair of the atresia. At present, antenatal USS manages to identify OA in less than one third of cases. Findings of a small stomach and polyhydramnios elevating the index of suspicion but confirmation of this diagnosis is rarely possible due to the low specificity of these findings, which can be related to oropharyngeal or mediastinal masses, poor fetal swallowing or simply a normal variant.<sup>30</sup> In conjunction with USS, a recent systematic review has demonstrated MRI to provide sensitivity of more than 94% and specificity of 89%.<sup>31</sup> Findings of dilated upper oesophagus

with 'bowing' of the trachea can be readily observed on MRI (Figure 3A) and have a sensitivity of 91% and specificity of 100% in cases suspected on fetal USS.<sup>32</sup>

Our own experience with post-acquisition reconstruction has been unable to improve upon the diagnostic accuracy of two-dimensional MRI images; since the averaging process of reconstruction algorithms may potentially reduce any appearance of distension in an organ with peristalsis. We have found with improved image acquisition (Figure 3B), that the distal oesophageal lumen – recognised to be indicative of a tracheoesophageal fistula – can be seen. This may allow prediction of a long-gap oesophageal atresia, which often requires oesophageal replacement using a conduit, a procedure with both short- and long-term morbidity.<sup>33,34</sup> We anticipate that reliable and accurate diagnosis of such cases may introduce a role for tissue engineered constructs, similar to that which has been achieved in CDH.<sup>29</sup>

#### **ILLUSTRATIVE CASES**

Figure 3 demonstrates fetal MRI of two infants with oesophageal atresia. Figure 3A shows a 32+5 weeks fetus with complex foregut anatomy; the fetal MRI demonstrates a dilated oesophageal pouch displacing and bowing the trachea. The postnatal CT imaging presented alongside demonstrates the complex common channel of trachea and oesophagus and the distal oesophageal fistula relating to the left main bronchus which is hypoplastic; the complexity of the lesion prompted a redirection of care and the infant succumbed on day 2 of life. Figure 3B demonstrates a conventional type C atresia (OA with distal fistula) in a 32+5 weeks fetus. Dilated upper pouch is best appreciated on solitary coronal slices of the MRI (without reconstruction), and the bSSFP-sequence sagittal view allows a visualisation of the gap between the two ends of oesophagus (3 vertebral bodies). The baby underwent neonatal repair via thoracotomy and is well at last follow-up.

#### **4. LESIONS OF THE ABDOMEN AND PELVIS**

##### **ABDOMINOPELVIC CYST**

Abdominopelvic cysts are a relatively common finding on antenatal USS; documented in approximately one in a thousand pregnancies, they are typically ovarian in origin. The clinical, postnatal outcomes of antenatally diagnosed cysts have been well described; many will involute during antenatal or early postnatal life and are generally managed expectantly.<sup>35</sup>

However, a small proportion enlarge or may cause issues due to mass effect,<sup>36</sup> and non-ovarian cysts are still challenging to diagnose on USS.<sup>37</sup> These rarer diagnoses may require early specialist referral such as in cases of choledochal malformation, lymphatic malformation, or fetal tumour. Antenatal counselling requires reliable delineation of the cyst and its spatial and anatomical relations; the spatial resolution of MRI in three-dimensions allows for more accurate anatomical delineation, which has been shown in a small published series to improve on the diagnostic accuracy of USS.<sup>38</sup> However, caution should be taken in absolute reliance on MRI since two cases in this series were incorrectly re-classified, including a case of adrenal haemorrhage. It is worth noting that modern T2\*-weighted sequences of MRI are haemorrhage sensitive but whilst widely used in placental MR research,<sup>39</sup> these have not been optimised for fetal clinical application.

#### ABDOMINAL WALL DEFECTS

Fetal ultrasound is usually able to diagnose and distinguish between the common abdominal wall defects, exomphalos and gastroschisis; this is important as prenatal counselling and postnatal outcomes of these are markedly different. Exomphalos, with an incidence of 1 in 13,000, is commonly associated with other midline structural defects which can be demonstrated on ultrasound (cardiac, renal, spinal, diaphragmatic – note the associated CDH shown in Figure 4A). Clustering of several lesions may lead to a missed diagnosis if only ultrasound is performed; to this end, MRI has an improved detection rate for individuals with complex exomphalos, with additional anomalies being detected postnatally in twice as many fetuses that only received antenatal US imaging compared to MRI.<sup>40</sup> Accurate sizing of the defect is also an advantage of MRI, since defects of more than 5cm may be associated with prolonged respiratory and feeding-related morbidity related to the process of restoring abdominal organs and achieving abdominal closure.

Gastroschisis, by contrast, is usually an isolated lesion and occurs in one in every 6,000-10,000 pregnancies, with significant regional variation. Although outcomes are generally good, up to 25% of affected neonates however may develop significant complications but predicting this antenatally is notoriously challenging.<sup>41</sup> Complex gastroschisis may involve bowel necrosis, atresia and dysmotility, thought to be due to a combination of amniotic fluid exposure and defect constriction.<sup>42</sup> Sudden onset of stomach/bowel dilatation and polyhydramnios are used as surrogate markers of bowel atresia on antenatal USS, and there is recent published

data to evidence the value of serial 2D measurements in the prediction of complex cases.<sup>43</sup> The ability of MRI to differentiate bowel content (meconium showing bright on T1 or dark on T2, Figure 5B) may predict an associated atresia and allow an estimate of bowel viability.<sup>44</sup> Pulmonary hypoplasia is described in both gastroschisis and exomphalos, tending to be correlated to defect size in isolated defects but also related to the associated anomalies in exomphalos.<sup>45</sup> Long-term morbidity is known to be correlated to lung volumes and MR fetal lung volume assessment may be useful for counselling to this end.

### **ILLUSTRATIVE CASES**

Figure 4A demonstrates a 34+6 weeks fetus with exomphalos (arrows on axial image). The abdominal wall defect, measured in multiple planes, is approximately 5cm in width and there is significant herniation of the liver with a prominent and irregular coursing umbilical vein (highlighted on the 3D model). Associated spinal angulation and severe left CDH was also present with intrathoracic loops of bowel, spleen and stomach. The TLV was calculated as 16.61cm<sup>3</sup>. Parents elected for palliative care after delivery. The detailed illustrations of the 3D reconstructed image and segmentations are provided in Supplemental Videos 8-9.

Figure 4B shows a 24 weeks fetus with gastroschisis. Loops of bowel can clearly be seen outside the abdominal cavity without membrane coverage. The defect can be seen to originate to the right of the insertion of the umbilical cord. This pregnancy was induced, per protocol, at 37+5 weeks, the baby underwent primary cotside closure on day 1 of life and is currently well under follow-up more than 2 years later.

### **BOWEL ATRESIA, MECONIUM PERITONITIS + ANORECTAL MALFORMATION**

Intestinal atresia is found in approximately one in 3,000 pregnancies and is estimated to be associated with underlying syndrome in 20% of cases.<sup>46</sup> Antenatal ultrasound findings of echogenic and dilated bowel are associated with bowel atresia but have such low specificity that their predictive value is not useful clinically.<sup>47</sup> MRI can demonstrate progression of meconium through the fetal bowel across gestation.<sup>48</sup> Features of non-progression of meconium therefore suggests a congenital obstruction and signs of increased bowel volume may help to identify the level of atresia.<sup>49</sup> One further, albeit rare, presentation of intestinal atresia is antenatal perforation leading to meconium peritonitis. Meconium peritonitis is occasionally seen in fetuses with cystic fibrosis and such cases may not require any postnatal surgical intervention. However, there is a high mortality associated to cases of intestinal

volvulus where mesenteric ischaemia is untreatable in utero. While MRI is less able than USS to detect classical peritoneal calcifications,<sup>50</sup> it has been shown to be more reliable as an indicator of cases needing postnatal surgical intervention by the detection of proximal dilatation with micro-colorectum in a partially-blinded comparative study.<sup>51</sup>

Anorectal malformations (incidence approximately 1 in 5,000), and represent a wide spectrum of anomalies from anterior anus and perineal fistula through to persistent cloaca. Many of these are difficult to diagnose with any form of antenatal imaging. This may be due to the limited MR signal and US acoustic shadowing of the fetal pelvis as well as a lack of antenatal diagnostic features such as rectal dilatation in many cases. However, the spatial relationship of urogenital and intestinal structures in the fetal pelvis have allowed cloacal anomalies to be diagnosed using MRI with reasonable reliability.<sup>52</sup> Findings would also include abnormal signal within the bowel secondary to a mixing of urine and meconium alongside any associated Müllerian abnormalities.

## **5. SPINAL LESIONS**

### **SACROCOCCYGEAL TERATOMA**

With an incidence of around 1 in 40,000 live births, Sacrococcygeal Teratoma (SCT) is the most common tumour of the newborn. As a teratoma, SCT often contain calcified elements, whose resultant acoustic shadowing may obscure sonographic views required to delineate the internal portion of the tumour. This has clinical relevance as predominantly intra-pelvic lesions bear a worse prognosis.<sup>53</sup> Defining the consistency of the overall tumour regarding its solid/cystic proportion also carries important prognostic relevance in terms of tumour grade: solid, hypervascularized masses may lead to fetal cardiac failure, and are candidates for antenatal intervention by way of debulking, or expedited delivery.<sup>54–56</sup> MRI has proven useful to demonstrate the internal characteristics of the tumour, its intrapelvic extent and involvement of the spinal canal;<sup>57</sup> it is also particularly useful to distinguish fat tissue of the mass from surrounding pelvic side wall and the meconium content of the fetal bowel (Supplemental Figure S2 and Video 10). As tumours often enlarge rapidly during fetal life, there is clearly an ongoing role for interval imaging for the surveillance of evolving

compression, rapid growth, and fetal intervention or elective preterm delivery may be required in the most severe cases.<sup>57,58</sup>

#### ILLUSTRATIVE CASE

Supplemental figure S2, demonstrates a 24+5 weeks fetus with an SCT. The predominantly cystic structure can be seen extending into the pelvis with little external aspect (Type IV lesion), the 3D model demonstrates the close proximity to the rectum which is important in the surgical planning. This pregnancy was continued outside of our hospital region and subsequent follow-up information is not currently available.

#### SPINA BIFIDA

Open spina bifida has an estimated incidence of 1 in 2000 pregnancies with meningocele (MMC) representing the most common variant. Antenatal ultrasound diagnosis is highly accurate. The associated hindbrain herniation (Chiari malformation) leads to a typical banana shaped cerebellum with lemon-shaped sculpting of the skull, both commonly observed on mid-gestation USS. The vertebral defect and herniated content are usually also detected, and sonographic assessment of lower limb and bladder function can also be made. First trimester USS diagnosis is also feasible using the “Crash” sign which describes posterior displacement and deformation of the mesencephalon against the occipital bone in axial view(59).

In an era of fetal surgery, defining defect level and other associated abnormalities is important to select fetuses in whom prenatal MMC closure will bring functional benefit.<sup>60</sup> Here fetal MRI allows the spinal defect level to be assessed with similar accuracy to USS (Figure 5 and Supplemental Videos 11-12).<sup>61</sup> However, MRI carries the additional benefit of better defining any associated intracranial developmental anomalies such as agenesis of the corpus callosum and cortical migration anomalies that may confer a worse prognosis. Post-operative MRI to assess resolution of Chiari malformation is now used as a quality measure of surgery and allows monitoring of fetal brain development, demonstrating improvement of CSF volume in the posterior fossa, resolution of hindbrain herniation and improvement of ventricular dilatation.<sup>62</sup>

MRI is also useful to diagnose and counsel parents of a fetus with other spinal lesions such as VACTERL association or hemivertebra. It can be used to predict longer term lower limb and

bladder/bowel function and provides a useful adjunct to USS-detected closed neural tube defects in its further characterisation of spinal cord anomalies such as tethering.<sup>63</sup>

#### ILLUSTRATIVE CASES

Our figure demonstrates two cases of MMC assessed for fetal surgery. Figure 6A is a DSVR reconstructed MRI performed at 26 weeks, the sacral defect is noted at S1-S2 with sac and placode extending beyond skin level. The brain is also seen in the same scan, the lack of hindbrain herniation and relatively normal appearances of the hindbrain and posterior fossa meant that this fetus did not meet the eligibility criteria for fetal surgery and was treated postnatally. Detailed illustration and segmentations are provided in Supplemental Videos 11 and 12. Comparatively, Figure 6B represented a 23+1 weeks fetus, the hindbrain herniation can be demonstrated and is shown in the figure. Fetal surgery was performed at 24 weeks gestation, with subsequent resolution of the hindbrain herniation prior to delivery on follow-up prenatal MRI.

### **6. LESIONS OF THE KIDNEYS & URINARY TRACT**

Hydronephrosis is a common finding on antenatal imaging, with an incidence of 1% of all pregnancies. It may be self-limiting and idiopathic, however can be a consequence of a number of different abnormalities of the renal collecting system and ureter, as well as lower urinary tract obstruction (LUTO). Posterior urethral valves can be demonstrated on fetal MR with characteristic appearances of a dilated posterior urethra. Findings of a dilated bladder and/or bilateral antenatal hydronephrosis require careful work-up since fetal megacystis can present in a number of chromosomal abnormalities.<sup>64</sup> LUTO may result in a reduced amniotic fluid volume, which can make USS examination of the underlying lesion difficult. However, the paucity of amniotic fluid is of minimal consequence in MRI acquisition and reconstruction. Management is complex as not infrequently a distended bladder in the first trimester empties spontaneously, or resolves after a single USS-guided drainage.<sup>65</sup> The benefit of more invasive treatments such as bladder shunting in LUTO is unclear as demonstrated by the PLUTO trial.<sup>66</sup> There is recognition among fetal interventionalists that better patient selection for bladder

shunting is needed. This requires antenatal assessment of renal parenchyma and amniotic fluid volume, both of which can be done with modern MR image acquisition and processing.<sup>67,68</sup> While Fetal MRI does not represent a gold-standard for diagnosis, it is recognised to be a useful adjunct in the evaluation of identified pathology.<sup>69,70</sup>

Fetal MR has further prognostic use in evaluating the renal parenchyma in detail, assessing for the presence of cysts and parenchymal dysplasia, detailed in the illustrative cases below. Furthermore, MRI may play a role in measurement of lung volumes in the context of severe oligohydramnios where lung hypoplasia presents an extreme risk to newborn survival.<sup>71</sup> Diagnosis of bilateral renal agenesis is a further condition in which MRI may be useful: in the presence of anhydramnios, the adrenal glands can be mistaken for renal tissue on ultrasound whereas MRI is able to better visualise that the kidneys are absent.<sup>72</sup>

#### ILLUSTRATIVE CASES

We show two examples of hydronephrosis alongside a case of unilateral multicystic dysplastic kidney (MCDK). Supplemental Figure S3A, shows a 30 weeks fetus with unilateral hydronephrosis. Some loss of the corticomedullary differentiation can be appreciated in the affected left kidney when compared to the right. This pregnancy was referred with a known cardiac diagnosis which continued to be managed at the referring centre. In Supplemental Figure S3B, a 33+6 weeks fetus, the right kidney demonstrates calyceal clubbing and thinning of the renal parenchyma (hallmarks of severe hydronephrosis) and the left kidney shows features of moderate disease similar to the first case. Detailed 3D reconstruction can be seen in Supplemental Video 13. This pregnancy was completed at a referring centre, postnatal outcome is not currently available for this infant. Supplemental Figure S3C demonstrates a left-sided MCDK in a 20+6 weeks fetus, the accompanying image is of the referring USS, which was unable to exclude a dilated left collecting system due to acoustic shadowing. The kidney is made up entirely of communicating cysts and on MRI clearly differs from the hydronephrotic kidneys seen in previous cases. The 3D reconstruction is shown in Supplementary Video 14. The patient remains under follow-up with noted compensatory hypertrophy of the right kidney and awaits functional nuclear imaging.

## **7. CONCLUSIONS**

Fetal MRI has been demonstrated to complement fetal USS in many conditions and to be superior in others for its precise delineation of body anatomy. Wider adoption of fetal MRI may lead to reduce costs (current estimated cost to the health service approximately £400 per scan in the United Kingdom) and facilitate routine referrals through established pathways. MRI also overcomes several technical limitations of ultrasound, such as atypical fetal position, reduced amniotic fluid volume, or high maternal BMI.

Our unit has experience in performing post-acquisition reconstruction on externally acquired images, however these outputs depend on the quality of the original images and acquisition of sufficient image stacks in all three planes. While the DSVR tool is already available for download,<sup>73</sup> further technical developments are needed to support its full clinical translation: including robustness to fetal motion, and evaluation of the effects on volumetric measurements. It is important to reiterate, that reconstructed volumes should be used in conjunction with 2D images for diagnosis, as the averaging process may occlude visualisation of dynamic physiological processes such as peristalsis or cause blurring due to peristaltic motion.

A benefit common to all conditions discussed here is the 'communicability' of the images gained with MRI: three-dimensional ultrasound gives excellent spatial resolution of craniofacial and skeletal anomalies; but there is more difficulty in interpretation of soft tissue lesions within the thorax and abdomen for non-expert sonographers. The cross-sectional images obtained on conventional MR imaging are readily interpretable for the surgeon and with progress made in 3D reconstruction, are likely to guide treatment to a more precise degree.

Superiority of MRI to ultrasound in prognostication is supported by data in only a few conditions at present, reflecting the current early stage of development of fetal body MRI.<sup>74</sup> We believe that fetal MRI has the potential to aid fetal medicine, neonatal, and paediatric surgical specialists in diagnosis, prognostication, parental counselling and planning pre- and post-natal care of babies with congenital anomalies.

### **AUTHOR CONTRIBUTION STATEMENT**

JD: conceptualised and designed the review, performed the review of the literature, wrote the primary manuscript and its revision. AU, JM, AEC: identified processed original image data for inclusion as illustrative cases, performed the review of the literature and assisted in writing the primary manuscript and its revision. MD, IY, AD, PDC, JC, MR: conceptualised and designed the review, performed the review of the literature, and provided critical input in the drafting and revision of the manuscript.

### **FINANCIAL DISCLOSURES**

This review was performed independently of any directive from a funding source at any institution. The corresponding author (JD) has full access to all data presented and final responsibility for the article's submission.

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The views expressed here are those of the authors and not necessarily those of the NIHR, NHS or the Department of Health.

### **CONFLICT OF INTEREST STATEMENT**

None of the authors has any conflict of interest to disclose relevant to the content or production of this review

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