

# Current Status and Future Prospects of Magnetic Resonance Imaging in Perinatal Medicine

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## ABSTRACT

Fetal magnetic resonance imaging (MRI) has become an important adjuvant to high-quality ultrasound once fetal structural anomaly is identified. There are recently developed advanced techniques such as provision of volumetric data, spectroscopy, and functional MRI. Changes in local susceptibility caused by blood breakdown products, echo-planar imaging (EPI) sequences [i.e., diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC)] are especially sensitive to hemorrhage and edema. These novel sequences are particularly useful for assessment of fetal ischemic and hemorrhagic brain lesions. Prenatal MRI has been increasingly adopted in assessment and follow-up after in utero surgeries of twin-twin transfusion syndrome, congenital diaphragmatic hernia, lower urinary tract obstruction, and myelomeningocele. Development of guidelines to better define the role of fetal MRI in relation to prenatal diagnostic ultrasound can reduce the variation of sequence protocols, magnetic field intensity, as well as the use of gadolinium performed in different centers. Novel sequences may be used for research purposes, but safety concerns of obstetric MRI cannot be overlooked. The current utilities and future prospects of MRI in perinatal medicine are updated in this article.

**Keywords:** Fetal magnetic resonance imaging, Fetal neuroimaging, Fetal therapy, Functional magnetic resonance imaging, Placental perfusion.

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## INTRODUCTION

Fetal MRI has become an important adjuvant as confirmatory and acquisition of additional information, to high-quality ultrasound once fetal structural anomaly is

identified.<sup>1,2</sup> It is not recommended to use MRI as a primary screening tool in prenatal care. Basic advantages of MRI are: (1) Provision of images in any plane or fetal position; (2) providing a large field of view; and (3) excellent soft tissue contrast resolution, even in the presence of limited liquor volume, overlying bone, or obesity.<sup>3</sup> Still, motion artifact (fetal or maternal) limits the sequences available.

Echo-planar imaging techniques have become increasingly important in cases with difficult characterization of certain fetal tissues, i.e., skeletal dysplasias and pathologies.<sup>4</sup> The recently developed advanced techniques, such as (1) Provision of volumetric data; (2) spectroscopy; and (3) functional images have expanded the lexicon to include such terms as magnetic resonance angiography, magnetic resonance spectroscopy, and functional MRI. Although there is no evidence that MRI produces long-term harmful effects regarding radiofrequency fields and the loud acoustic environment, there is still lack of consensus regarding its utility and safety.<sup>5</sup> The International Society of Ultrasound in Obstetrics and Gynecology recently suggested clinical indications and limitations of fetal MRI.<sup>6</sup> In this Editorial, we are aiming to update the current utilities and future prospects of MRI in perinatal medicine.

## Fetal Neurological MRI

Ventriculomegaly detected from prenatal ultrasound may be the most common indication for fetal MRI. Neuroimaging MR study attempts to identify morphological and functional changes in the fetal brain during its maturational course. *In utero* MR assessment of cortical convolution/gyration pattern in the presence of mild ventriculomegaly indicates the functional organization of the cortex, which may profoundly impact brain function in childhood and adult period.<sup>7</sup> Fetal MR study provides additional information mainly in those with suspected midline anomalies (i.e., posterior fossa anomalies and agenesis of corpus callosum), which may lead to complete changes of management and parental counseling. Recent systematic review suggested an up to 2.5% chance of prenatal MR to yield false results.<sup>8</sup> Maternal diabetes increases the risk of fetal neurocognitive impairment, which may be detected by prenatal MR.<sup>9,10</sup>

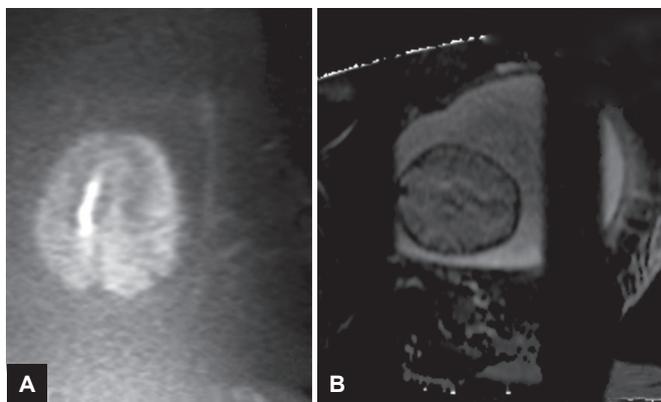
The main acquired fetal brain pathologies detected by MRI are ischemic infarctions and hemorrhage. Ischemic brain infarctions can occur in complicated monochorionic

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**Figs 1A and B:** Axial plane of brain of a fetus affected by basal ganglion hemorrhage. The DWI shows bright signal lateral to the ventricle (A). Bright signal on ADC suggests white matter edema (B)

twins; early-stage infarction shows restricted MR diffusion.<sup>11</sup> Subsequently, focal T2-weighted hyperintense lesions and a reduction of brain tissue may develop.<sup>12,13</sup> Because of changes in local susceptibility caused by blood breakdown products, EPI sequences (i.e., DWI and ADC) are especially sensitive to hemorrhage and edema, as shown in Figure 1. These sequences can also be used to detect calcifications, a consequence of many acquired fetal or maternal diseases.<sup>13,14</sup> Brain tumors or vascular malformations lead to parenchymal changes; and MR demonstration of these associated findings may direct therapeutic planning.<sup>15</sup> In addition to morphology study, microstructure, metabolism (spectroscopy), and functional connectivity (tractography) in the fetal brain can be identified.<sup>16-18</sup> The *in utero* alterations may explain neurological insults in the childhood and adult periods.<sup>19,20</sup>

### Magnetic Resonance Imaging and Fetal Surgery

Both prenatal ultrasound and MRI can be used to assess severity of congenital diaphragmatic hernia (CDH).<sup>21</sup> Fetal lung size (or lung-to-head ratio), liver and stomach position, polyhydramnios, gestational age at diagnosis, and cardiac ventricular size, which are predictive of outcome, can be assessed with ultrasound. Lung volume can be estimated using either prenatal three-dimensional ultrasound or MRI, which needs to be offset with the effect of gestational age (observed/expected total fetal lung volume). This estimation may be difficult in the case of uncertain dates or inaccurate when the fetal weight is beyond the normal range, hence, matching can be made on MR fetal body volume.<sup>22</sup> As lung volumetry is based on several slices through both lungs, and since MRI is not restricted by maternal factors, ultimately, MR volumetry is theoretically more accurate. Magnetic resonance also allows a more scaled quantification of liver “up” or “down”, although there is no standardized method for calculating the amount of liver into the thorax.<sup>23</sup> The

fetal lung-to-liver signal intensity ratio on T2-weighted images may be an accurate marker to predict fetal lung maturity.<sup>24</sup> Postnatal pulmonary hypertension can be accurately predicted with MR prenatal pulmonary hypertension index.<sup>25</sup> Fetoscopic tracheal occlusion may improve postnatal survival of CDH. The endoluminal occlusion balloon contains a metallic component that may pose MRI-related imaging issues and possible risks for the fetus and mother, such as magnetic field interactions, heating, and artifacts. An *in vitro* study showed that the balloon displayed minor magnetic field interactions and inconsequential heating. Artifacts extended approximately 10 mm from the occlusion balloon on the 3-Tesla (3-T) gradient-echo pulse sequence, suggesting that anatomy located at a position greater than this distance may be visualized on MRI.<sup>26</sup>

Fetal MRI has recently been proposed as a complementary approach for the evaluation of lower urinary tract obstruction (LUTO). Two recent studies suggest that additional diagnostic information is gained with MRI in fetuses with LUTO.<sup>27,28</sup> The DWI sequence may be useful in defining the renal parenchyma by evaluating increased signal intensity on DWI and decreased signal on ADC maps.<sup>29</sup> However, the case series are small, and further studies are necessary to fully define the benefits of MRI in evaluating and managing patients with LUTO.<sup>30</sup>

Sonographic evaluation of the posterior fossa and the spine is limited by fetal position, maternal body habitus, oligohydramnios, and ossification of the fetal skull.<sup>31</sup> In most cases, ultrasound and prenatal MRI can both delineate the dysraphic defect and the level of the placode with similar efficacy.<sup>32</sup> The MRI can allow detailed characterization of the neural tube defect and its associated anomalies, which may be contraindicated to *in utero* intervention.<sup>33,34</sup> Strong prognostic factors of open neural tube defects are the level and length of the dysraphic lesion.<sup>35</sup> Quantifying the degree of cerebellar tonsil herniation is crucial, as worsening herniation has been associated with increased postnatal risk of seizure. Open MRI has been extensively used for studies of fetal surgery for neural tube defects in animal models.<sup>36</sup>

Persistent hyperextension due to fetal neck mass can compromise the airway. Cesarean delivery with *ex utero* intrapartum treatment to secure the airway is considered or can be considered.<sup>37</sup> Detailed, high-resolution fetal MRI may serve as a valuable secondary imaging modality for clinical decision-making regarding management of pregnancy, *in utero* therapy, mode of delivery, and postnatal care.<sup>38</sup>

### MR Study of the Placenta and Umbilical Cord

Ultrasound is highly sensitive and specific in the prenatal “diagnosis” of accreta placentation when performed by

skilled operators. However, combination of ultrasound signs, such as loss of clear zone, presence of bridging vessels, subplacental hypervascularity, and placental lacunae, is not specific of “grading” the depth of invasive placentation (accreta, increta, or percreta).<sup>39</sup> Prenatal MRI should be considered as a secondary imaging tool in any case with clinical suspicion for placenta accreta, i.e., placenta previa (especially posterior previa) with previous uterine operation and discordant ultrasound findings, and in any case in which percreta is suspected.<sup>3</sup> The excellent diagnostic accuracy in identifying the depth, placental villous structure, and the topography of placental invasion came from studies that MRI performed as a secondary imaging tool in women already screened for placenta accreta on ultrasound and might not reflect its actual diagnostic performance in detecting the severity of these disorders.<sup>40,41</sup>

The improved capability of MRI to image placental villous microstructure and the increased precision of oxygen measurement within placental microcirculations allow for a research opportunity to measure placental oxygenation both *in vivo* and *ex vivo*.<sup>42</sup> Simulated cross-disciplinary approaches with mathematical modeling MR sequence data could advance our understanding of oxygen levels within the placentofetal unit, with an emphasis on dysregulated maternofetal oxygen transfer in pregnancy pathologies.<sup>43</sup> *In vivo* umbilical vein blood flow rate and fetal oxygenation rate can also be measured noninvasively with quantitative T2 MRI during the second and third trimesters of pregnancy.<sup>44</sup> Real-time *in vivo* MR tracking of placental transport for toxic nanomaterials has been studied, so that detoxification of harmful compounds can be implemented.<sup>45</sup>

### Safety Concerns of Obstetric MRI

The 3-T MRI has the potential to provide imaging with higher resolution and better signal-to-noise ratio than does 1.5 Tesla (1.5 T), while maintaining a comparable or lower energy deposition. The 3-T MRI is superior to 1.5-T MRI; as it (1) Enhances the sensitivity for deoxyhemoglobin and hemosiderin to detect hemorrhagic lesions, (2) enhances the sensitivity for calcifications for sharper delineation of bony structures, (3) enhances the quality of spectroscopy to interrogate for the presence and concentration of various metabolites in fetal tissue, and (4) enhances blood oxygen level-dependent contrast imaging for functional MRI study of fetal brain.<sup>46</sup> Although there are some theoretical concerns of MR-related heat and acoustic damage to the fetus, recent data from porcine model suggested otherwise.<sup>47</sup> With appropriate sequence adaptations, 3-T MRI may be used safely during the 2nd and 3rd trimester of pregnancy.<sup>6,48,49</sup>

Without administration of contrast media (Gadolinium), prenatal exposure to MRI is not associated with adverse fetal or long-term neurodevelopmental effects.<sup>50,51</sup> Gadolinium crosses the placenta, then filtered through fetal kidneys, and can remain in the amniotic fluid for an unknown period of time. Gadolinium-based contrast agents are not widely used in fetal imaging. Experiments in animal models showed that prenatal exposure to gadolinium at high dosage and long duration can cause fetal malformations and growth restriction, but data on the long-term consequences of *in utero* exposure of gadolinium are more limited. Data of *in utero* Gadolinium exposure in humans are still limited (Category C). Experimental exposure of gadolinium may be related to mutagenesis and carcinogenesis in postnatal life. Several small case series did not report any adverse neonatal outcomes after first-trimester exposure of gadolinium at clinical dose. This information can be used for counseling the pregnant women who unknowingly underwent MRI examination using gadolinium.<sup>52</sup>

### CONCLUSION

Although fetal MRI is being performed in many perinatal centers, the quality of imaging, sequences used, and operator experience appear to differ widely between centers.<sup>53</sup> The impact of such differences should be reduced by development of guidelines to define better the role of fetal MRI in relation to prenatal diagnostic ultrasound. The results of MRI examinations increase the positive predictive value of ultrasound alone. The two techniques appear to be complementary and should not be mutually exclusive. The MR quantification of fine and gross movements may advance our understanding of fetal anomalies with challenges in diagnosis.<sup>54-56</sup> With novel diffusion-tensor MRI and fiber tracking algorithm, quantitative assessment of microarchitecture within the cervix and its ability to resist intrauterine forces associated with pregnancy may broaden the indications of obstetric MRI.<sup>57</sup>

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