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MRI-Based Placental Perfusion Assessment in Intrauterine Growth Restriction: Advances and Emerging Biomarkers

Ashish Kumar Shukla[1], Sachi Mall[2], Chaudhary Raj Saurabh[3], Jayant Solanki[4]

[1,2,3,4]Department of Radiodiagnosis, Santosh Deemed to be University, Ghaziabad, India

Abstract

Intrauterine growth restriction (IUGR) is a complex obstetric condition characterized by impaired foetal growth due to placental insufficiency, and it remains a leading contributor to perinatal morbidity and mortality worldwide. Early and accurate detection of placental dysfunction is essential to improve outcomes; however, conventional diagnostic methods such as Doppler ultrasound provide only indirect assessments of placental health. In recent years, advanced magnetic resonance imaging (MRI) techniques have emerged as powerful, non-invasive tools to evaluate placental perfusion and function more directly. This review highlights the current state of MRI-based placental perfusion imaging in the context of suspected IUGR, with a focus on key modalities including arterial spin labeling (ASL), dynamic contrast-enhanced (DCE) MRI, intravoxel incoherent motion (IVIM), and blood oxygen level-dependent (BOLD) imaging. These techniques allow for the quantification of critical physiological parameters such as tissue blood flow, microvascular density, and oxygenation. Additionally, we discuss recent clinical studies that validate emerging imaging biomarkers—such as perfusion fraction, ΔT2* response, and K trans—as potential tools for diagnosis, risk stratification, and monitoring of IUGR. Despite challenges such as motion artifacts and the need for standardization, MRI-based placental assessment holds significant promise for improving clinical decision-making and individualized care in high-risk pregnancies. This review aims to consolidate current evidence, identify gaps in the literature, and propose directions for future research in the field of functional placental imaging.

Keywords: Functional MRI, perfusion imaging, arterial spin labeling, blood oxygen level-dependent imaging, dynamic contrast-enhanced MRI, clinical applications, non-invasive biomarkers

Introduction

Intrauterine growth restriction (IUGR) refers to a pathological condition in which a foetus fails to reach its genetically predetermined growth potential, typically due to placental insufficiency. This condition is associated with increased perinatal morbidity and mortality, including risks of stillbirth, neonatal intensive care admission, neurodevelopmental impairment, and long-term cardiovascular and metabolic diseases in adulthood. It affects an estimated 5–10% of pregnancies worldwide, with a higher prevalence in low- and middle-income countries, where access to advanced diagnostic tools and timely obstetric care may be limited.

The underlying pathophysiology of IUGR most commonly involves abnormalities in placentation, including inadequate trophoblastic invasion and remodelling of maternal spiral arteries. These vascular deficits result in impaired utero-placental blood flow, reduced oxygen and nutrient exchange, and ultimately foetal hypoxia and malnutrition. Identifying placental dysfunction is therefore central to the diagnosis and management of IUGR.

Traditionally, foetal surveillance and IUGR diagnosis rely on serial measurements of foetal biometry and Doppler ultrasound assessment of blood flow in the umbilical artery, middle cerebral artery, and ductus venosus. While these techniques are widely available and clinically valuable, they are indirect measures of placental function and may not reflect early or subtle changes in perfusion or oxygenation (Derwig et al., 2013).

Magnetic resonance imaging (MRI) has emerged as a promising modality for placental assessment, offering detailed anatomical and functional insights without ionizing radiation. Advanced MRI techniques such as arterial spin labeling (ASL), dynamic contrast-enhanced (DCE) MRI, intravoxel incoherent motion (IVIM), and blood oxygen level-dependent (BOLD) imaging provide quantitative metrics of placental perfusion, diffusion, and oxygenation (Siauve et al., 2015; Moore et al., 2000). These functional parameters have the potential to improve the early detection and monitoring of placental insufficiency in IUGR pregnancies.

Recent studies have demonstrated correlations between MRI-derived biomarkers and both histopathological findings and clinical outcomes, supporting the translational value of these imaging tools (Sohlberg et al., 2015; Aughwane et al., 2020). Moreover, the development of non-contrast and motion-robust sequences tailored for use in pregnancy further enhances the safety and feasibility of MRI-based placental evaluation.

This review explores the current landscape of MRI techniques used to assess placental perfusion in the context of IUGR. We discuss the physiological basis of each modality, summarize recent clinical and translational studies, and examine the potential of emerging imaging biomarkers for improving diagnostic accuracy and guiding clinical management. We also address the technical and logistical challenges that remain and propose future directions for research and standardization in this evolving field.

MRI Techniques for Assessing Placental Perfusion

In recent years, various advanced MRI techniques have been developed to assess placental perfusion, offering valuable insights into maternal-foetal health. Among these, Intravoxel Incoherent Motion (IVIM) MRI has emerged as a promising non-invasive method for evaluating microcirculatory flow within the placenta by distinguishing between diffusion and perfusion components of tissue signal. IVIM-derived parameters, particularly the perfusion fraction (f), serve as surrogate markers of placental blood flow. In a seminal study by Moore et al. (2000), it was demonstrated that the perfusion fraction was significantly reduced in pregnancies complicated by intrauterine growth restriction (IUGR), indicating impaired placental perfusion. This finding highlights the potential of IVIM MRI in the early detection and monitoring of placental insufficiency, which is critical for timely intervention in high-risk pregnancies.

Diffusion-weighted imaging (DWI) is another MRI technique that has proven useful in evaluating placental abnormalities, particularly in cases of intrauterine growth restriction (IUGR). Bonel et al. (2010) utilized DWI to investigate placental tissue characteristics and reported altered diffusivity patterns in IUGR placentas, suggesting disrupted microstructural integrity and impaired placental function. These findings support the role of DWI in detecting subtle changes in placental health without the need for

contrast agents. Additionally, Dynamic Contrast-Enhanced (DCE) MRI offers detailed information on placental vascular permeability, blood flow, and volume by tracking the passage of gadolinium-based contrast agents. However, its application in pregnancy is limited due to concerns about the safety of gadolinium for the foetus. Despite this limitation, DCE MRI remains a powerful tool in research settings for studying placental perfusion and vascular function, offering high spatial and temporal resolution that can aid in understanding placental pathophysiology in complicated pregnancies.

The study by Sohlberg et al. (2015) marks a significant advancement in the non-invasive assessment of placental function, particularly through the use of Dynamic Contrast-Enhanced (DCE) MRI. Their findings demonstrated a strong correlation between DCE-derived parameters—such as placental blood flow and vascular volume—and clinically relevant outcomes, including foetal growth metrics and Doppler ultrasound measurements. This underscores the potential of DCE MRI as a powerful research and diagnostic tool for evaluating placental insufficiency and predicting adverse pregnancy outcomes like intrauterine growth restriction (IUGR). Although clinical application is limited by safety concerns related to gadolinium-based contrast agents, especially during pregnancy, the insights provided by this imaging technique are invaluable in advancing our understanding of placental pathophysiology. Complementing this, Blood Oxygen Level-Dependent (BOLD) MRI serves as a non-contrast alternative by detecting changes in deoxy haemoglobin levels, thus offering a window into placental oxygenation dynamics. Together, these techniques highlight the evolving role of functional MRI in obstetric imaging, with the potential to significantly improve prenatal care and foetal monitoring.

Recent studies by Zhou et al. (2020) and He et al. (2021) have emphasized the potential of Blood Oxygen Level-Dependent (BOLD) MRI in assessing placental oxygenation, particularly in high-risk pregnancies. They found that reduced placental T2* values—an indicator of decreased oxygenation—were consistently observed in cases of intrauterine growth restriction (IUGR), suggesting underlying hypoxic conditions. These findings highlight the clinical relevance of BOLD MRI as a non-invasive, contrast-free technique for detecting placental hypoxia. Complementing BOLD imaging, Arterial Spin Labeling (ASL) has also gained attention as a safe and effective method for evaluating placental perfusion. ASL works by magnetically labeling arterial blood water as an endogenous tracer, allowing for direct quantification of placental blood flow without the use of exogenous contrast agents. Together, BOLD and ASL represent promising tools for functional placental imaging, offering valuable physiological insights that could improve the monitoring and management of compromised pregnancies.

Goh et al. (2021) demonstrated the promising clinical value of Arterial Spin Labeling (ASL) MRI in assessing placental perfusion, particularly in pregnancies at risk for intrauterine growth restriction (IUGR). Their study showed that ASL could effectively detect reduced placental blood flow in suspected IUGR cases, underscoring its potential as a sensitive and quantitative imaging tool. Unlike traditional contrast-enhanced techniques, ASL uses magnetically labelled arterial blood as an endogenous tracer, allowing for accurate perfusion measurements without the need for exogenous contrast agents—making it entirely safe for use during pregnancy. The successful application of ASL in this context highlights its utility not only for research but also for potential integration into routine prenatal imaging protocols. By offering a non-invasive, reproducible method for evaluating placental function, ASL could play a critical role in the early identification and management of placental insufficiency, ultimately contributing to improved outcomes in high-risk pregnancies.

Emerging Biomarkers from MRI Perfusion Imaging

A growing body of research highlights the potential of MRI-derived biomarkers in the comprehensive assessment of placental function. Among these, the perfusion fraction obtained from Intravoxel Incoherent Motion (IVIM) imaging provides valuable information about microvascular blood flow within the placenta, making it a useful marker of placental perfusion. Similarly, T2* values derived from Blood Oxygen Level-Dependent (BOLD) MRI offer insights into placental oxygenation, with lower T2* values often indicating hypoxic conditions, particularly in compromised pregnancies such as those affected by intrauterine growth restriction (IUGR). Another important biomarker, K^trans^, derived from Dynamic Contrast-Enhanced (DCE) MRI, reflects the rate at which contrast agent moves from blood plasma into the extracellular extravascular space, serving as an indicator of vascular permeability and blood flow. Although the use of DCE MRI is limited in pregnancy due to safety concerns with gadolinium-based contrast agents, it remains a powerful research tool. Together, these MRI-based parameters—perfusion fraction, T2*, and K^trans^—are emerging as valuable, non-invasive surrogate indicators of placental health, with the potential to enhance early detection, monitoring, and management of placental dysfunction in high-risk pregnancies.

He et al. (2021) provided compelling evidence for the diagnostic value of MRI-derived biomarkers in evaluating placental dysfunction and predicting neonatal outcomes. In their study, both reduced perfusion fraction—measured through Intravoxel Incoherent Motion (IVIM) imaging—and decreased T2* values—obtained from Blood Oxygen Level-Dependent (BOLD) MRI—were significantly associated with adverse neonatal outcomes, including low birth weight and complications related to intrauterine growth restriction (IUGR). These findings underscore the importance of combining multiple functional MRI techniques to obtain a more comprehensive assessment of placental health. The strong correlation between these imaging markers and clinical outcomes highlights their potential role in early risk stratification and personalized management of high-risk pregnancies. By enabling non-invasive, quantitative evaluation of placental perfusion and oxygenation, these biomarkers may serve as valuable tools for identifying foetuses at risk and guiding timely interventions to improve perinatal outcomes.

In their 2017 study, Song et al. utilized a combination of diffusion-weighted imaging and magnetic resonance spectroscopy to investigate placental abnormalities in pregnancies affected by intrauterine growth restriction (IUGR). They found that IUGR placentas exhibited significantly lower apparent diffusion coefficient (ADC) values, reflecting restricted water movement likely caused by changes in placental tissue structure and reduced blood flow. Furthermore, the study identified decreased choline to lipid ratios through spectroscopy, indicating altered cellular metabolism and membrane integrity in the compromised placenta. These imaging findings suggest that both diffusion and metabolic alterations can serve as early, non-invasive markers of placental insufficiency. Such insights are crucial, as they allow for the timely detection of placental dysfunction before clinical symptoms arise, providing a window for early intervention to improve foetal health outcomes.

Aughwane et al. (2020) made a significant contribution to placental imaging by introducing an innovative approach that combines T2* mapping from Blood Oxygen Level-Dependent (BOLD) MRI with Dynamic Contrast-Enhanced (DCE) MRI metrics to create detailed oxygen saturation maps of the placenta. This technique enables a comprehensive assessment of placental oxygenation and perfusion simultaneously, providing a more complete picture of placental function than either method alone. Importantly, their study demonstrated a strong correlation between these oxygen saturation measurements and critical clinical outcomes such as birth weight and gestational age at delivery. This correlation highlights the prognostic

power of these MRI-derived biomarkers, suggesting they could serve as reliable indicators not only for diagnosing placental insufficiency but also for predicting foetal growth and timing of delivery. The ability to non-invasively quantify placental oxygenation and perfusion offers clinicians valuable information to guide timely interventions and improve management strategies in high-risk pregnancies, potentially reducing adverse neonatal outcomes and enhancing overall maternal-foetal care.

Clinical Applications and Future Directions

MRI-based perfusion imaging is gaining increasing clinical relevance in the management of pregnancies complicated by intrauterine growth restriction (IUGR), offering a non-invasive and highly informative tool for evaluating placental function. As highlighted by Roberts et al. (2022), this technique enables the early detection of placental compromise, often before clinical signs or abnormalities on ultrasound become evident. One of its key advantages lies in its ability to differentiate between constitutionally small foetuses—those who are small but otherwise healthy—and truly growth-restricted foetuses suffering from pathological placental insufficiency. This distinction is crucial, as it prevents unnecessary interventions in low-risk cases while ensuring closer monitoring and timely delivery in high-risk scenarios. Furthermore, MRI-derived perfusion metrics contribute to effective risk stratification, allowing clinicians to tailor surveillance strategies and make informed decisions regarding the optimal timing of delivery. By improving diagnostic precision and enabling personalized care, MRI perfusion imaging is emerging as a valuable asset in the prenatal management of IUGR and other placental disorders.

Longitudinal MRI imaging holds significant promise in transforming prenatal care by enabling dynamic monitoring of placental function over the course of pregnancy. This approach allows clinicians to track the progression of placental dysfunction in real time, offering critical insights into when and how interventions should be implemented to optimize foetal outcomes. Javor et al. (2013) demonstrated that MRI-derived estimates of placental volume and perfusion parameters were more accurate predictors of foetal outcomes compared to ultrasound alone. These findings underscore the added value of MRI in detecting subtle but clinically important changes in placental health that may go unnoticed on conventional imaging. By incorporating MRI into routine clinical protocols—particularly for high-risk pregnancies—there is potential for earlier identification of compromised foetuses and more individualized perinatal care planning. Such integration could lead to timely interventions, better-informed decisions regarding surveillance and delivery, and ultimately, improved maternal and neonatal outcomes. The ability to monitor placental health longitudinally represents a major step forward in prenatal diagnostics and personalized obstetric management.

Future research in placental MRI should focus on standardizing imaging protocols to ensure consistency and reproducibility across clinical and research settings. Currently, variations in scanner types, acquisition parameters, and post-processing techniques can limit the comparability of findings between studies. Establishing uniform protocols would enhance the reliability of MRI-derived biomarkers and facilitate their wider clinical adoption. Moreover, it is crucial to validate these imaging biomarkers—such as perfusion fraction, T2* values, and placental volume—across diverse populations to account for demographic and biological variability. The integration of artificial intelligence and machine learning into MRI analysis holds great promise, offering the potential to automate image interpretation, reduce observer bias, and uncover complex patterns predictive of adverse outcomes. In parallel, prospective clinical trials are needed to compare MRI findings with histopathological results and long-term neonatal outcomes, thereby confirming the clinical relevance and prognostic value of MRI-based assessments. Together, these

efforts will be key to advancing MRI from a research tool to a standardized component of prenatal care, particularly in managing high-risk pregnancies.

Challenges, Limitations, and Conclusion

While placental MRI has demonstrated significant potential in enhancing the evaluation and management of intrauterine growth restriction (IUGR), its clinical application is not without challenges. As highlighted by Siauve et al. (2015), one of the primary technical limitations is motion artifacts resulting from maternal respiration and foetal movement, which can compromise image quality and hinder accurate analysis. Additionally, the limited availability of standardized, MRI-compatible obstetric protocols, along with a shortage of trained radiologists and technicians experienced in prenatal imaging, further restricts its widespread implementation in routine clinical settings. Another critical barrier is the safety concern surrounding the use of gadolinium-based contrast agents during pregnancy, which restricts the use of dynamic contrast-enhanced (DCE) MRI—one of the most informative techniques for assessing placental perfusion and vascularity. Despite these limitations, the findings in this article underscore the importance of continuing to address these challenges through technological innovation, training, and research. Overcoming these obstacles will be essential for integrating MRI into prenatal care and fully realizing its potential to improve diagnostic precision, guide clinical decision-making, and ultimately enhance outcomes in pregnancies complicated by placental dysfunction.

Another significant limitation hindering the broader adoption of placental MRI in clinical practice is the lack of standardization across imaging platforms, acquisition protocols, and post-processing techniques. Differences in MRI machine manufacturers, field strengths, and parameter settings can lead to considerable variability in image quality and quantitative measurements, making it challenging to compare results across studies or establish universally accepted diagnostic thresholds. This inconsistency undermines efforts to validate and translate promising MRI biomarkers—such as perfusion fraction, T2*, and K^trans^—into routine use. Moreover, the high operational costs associated with MRI, including equipment, maintenance, and the need for specialized personnel, pose a substantial barrier, especially in low- and middle-income countries where access to advanced imaging is limited. These resource constraints exacerbate healthcare disparities, restricting the benefits of advanced prenatal imaging to more affluent or urban populations. Addressing these issues through global collaborative initiatives aimed at protocol harmonization, cost reduction strategies, and technology adaptation for resource-limited settings is essential to make placental MRI a viable and equitable tool for improving maternal and foetal outcomes worldwide.

Despite its current limitations, placental MRI remains a highly valuable tool due to its non-invasive, radiation-free nature and its unique ability to provide detailed, quantitative insights into placental perfusion, oxygenation, and structure. Unlike ultrasound, which may be limited in certain clinical scenarios or operator-dependent, MRI offers high-resolution functional and anatomical data that can detect subtle changes in placental health—often before clinical signs of foetal compromise emerge. This makes MRI an excellent adjunct to conventional diagnostics, particularly in complex or high-risk pregnancies such as those affected by intrauterine growth restriction (IUGR). As technological advancements continue to improve image acquisition speed, motion correction, and analytical algorithms, and as more clinical studies validate its prognostic value, MRI is expected to assume a more prominent role in prenatal care. Its integration into routine obstetric practice could significantly enhance early detection, risk stratification,

and individualized management of IUGR, ultimately contributing to better maternal and neonatal outcomes.

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