Integrating Transcranial Ultrasound with MRI for the Diagnosis of Neonatal Hypoxic-Ischemic Encephalopathy

Ibrahim Mahmoud Eladl, Khaled Ahmed Lakouz, Eman Soliman Soliman Mohamed, Heba Fathy Tantawy

Radiodiagnosis Department, Faculty of Medicine, Zagazig University

Corresponding Author: **Eman Soliman Soliman Mohamed**

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Abstract

Background:. Neonatal hypoxic-ischemic encephalopathy (HIE) remains a leading cause of death and long-term neurodisability worldwide. Early, accurate delineation of injury pattern and burden is pivotal to triage neuroprotective therapies, counsel families, and stratify prognosis. Neuroimaging sits at the core of this care pathway. Transcranial ultrasound (TUS) is ubiquitous at the bedside, radiation-free, repeatable, and valuable for detecting intraventricular hemorrhage, ventricular size changes, perfusion surrogates, and cystic white-matter injury. Magnetic resonance imaging (MRI), including diffusion-weighted imaging (DWI) and proton MR spectroscopy (MRS), is the reference standard for lesion phenotyping, timing, and prognostication, especially for deep gray nuclei and perirolandic cortex. Yet, access, transport risk, and sedation limit same-day MRI in unstable neonates, creating a practical need for integrated imaging pathways. **Aim:** To synthesize evidence on how transcranial ultrasound integrates with MRI to improve diagnostic accuracy and prognostication in neonatal HIE. Specifically, we compare the strengths and limitations of each modality across gestational ages and injury patterns; examine the incremental value of Doppler indices and advanced MRI (DWI/MRS); and propose pragmatic, time-sensitive imaging algorithms that leverage tUS for immediate decision-making and MRI for definitive characterization.

Conclusion: TUS and MRI are complementary rather than competitive in neonatal HIE. tUS excels in availability, serial monitoring, hemorrhage screening, ventricular assessment, and detection of cystic periventricular leukomalacia; Doppler resistive indices may refine severity stratification. MRI best defines pattern, timing, and extent of hypoxic–ischemic injury, with DWI detecting early cytotoxic edema and MRS offering metabolic biomarkers predictive of outcome. An integrated, stage-appropriate approach—early and repeated tUS (including mastoid/posterior windows and targeted Doppler) followed by optimized MRI (T1/T2, DWI, SWI/T2*, and targeted MRS)—maximizes diagnostic yield within therapeutic windows, informs neuroprotective strategies such as hypothermia, and improves prognostic counseling. Standardizing acquisition, reporting, and cross-modality correlation is essential to reduce operator variability and ensure equitable, high-quality neuroimaging for neonates with HIE..

Keywords: *Transcranial Ultrasound, MRI, Hypoxic-Ischemic Encephalopathy, Neonate*

Introduction

Neonatal hypoxic-ischemic encephalopathy (HIE) is a major contributor to infant mortality and lifelong neurodevelopmental impairment, including cerebral palsy, cognitive delay, epilepsy, and visual disturbances. Despite advances in perinatal care and the adoption of therapeutic hypothermia, the global burden remains substantial, and outcomes hinge on timely recognition and stratification of brain injury within a narrow therapeutic window measured in hours rather than days [1–3]. Accurate early imaging is therefore not optional; it is foundational to clinical decision-making, prognostication, and family counseling in modern neonatal intensive care [4,5].

While MRI is widely regarded as the reference standard for characterizing HIE patterns—deep gray nuclei injury in severe sentinel events and watershed cortical–subcortical injury in partial prolonged

hypoperfusion—practical constraints limit immediate universal access. Transporting medically fragile neonates, coordinating scanner time, and avoiding sedation in unstable infants can be challenging. In contrast, bedside transcranial ultrasound (tUS) is portable, safe, fast, and repeatable, enabling real-time assessment and serial monitoring during the most dynamic phase of brain injury evolution, where treatment decisions are most time-critical [4,6–8].

tUS provides unique value in several domains: rapid screening for germinal-matrix/intraventricular hemorrhage and hydrocephalus; detection and follow-up of cystic periventricular leukomalacia (PVL); surveillance of ventricles and extra-axial spaces; and hemodynamic insight via Doppler-derived resistive indices of major cerebral arteries. In many neonatal units worldwide, these capabilities make tUS the de facto first-line modality for infants with suspected encephalopathy and the primary tool for longitudinal bedside follow-up. However, operator dependency and limited sensitivity for subtle cortical, subcortical, and deep gray lesions remain recognized constraints, underscoring the need for complementary MRI at the earliest feasible time point [7–12].

Advanced MRI techniques sharpen diagnostic precision beyond conventional T1/T2 imaging. Diffusion-weighted imaging (DWI) identifies early cytotoxic edema within 24–72 hours—often before conventional signal changes—thereby refining timing and severity estimates. Proton MR spectroscopy (MRS) adds metabolic biomarkers such as elevated lactate and reduced N-acetylaspartate that correlate with adverse outcomes, particularly when obtained within the first days of life. Susceptibility-weighted or T2* sequences enhance detection of microhemorrhage and venous congestion. Together, these sequences provide a comprehensive profile that complements tUS findings, especially for injuries involving posterior putamina, ventrolateral thalami, perirolandic cortex, hippocampi, brainstem, and superior vermis [13–16].

Despite the strengths of MRI, the clinical course of HIE is dynamic, and lesion conspicuity fluctuates with time. DWI can underestimate injury in the first 12–24 hours and pseudo-normalize after approximately 10–12 days; conversely, cyst formation in PVL and ventriculomegaly evolve over weeks. This temporality argues for an integrated pathway: immediate and serial tUS to triage, detect complications, and guide supportive care, followed by targeted MRI at the optimal window for definitive lesion mapping and prognostication. Such a strategy leverages each modality's strengths while mitigating their weaknesses, aligning imaging with the pathophysiology's timeline [4,5,13,17].

Importantly, Doppler sonography may extend tUS from structural screening to physiologic stratification. Elevated or altered resistive indices (RIs) in major cerebral arteries—most often measured in the anterior or middle cerebral artery—have been associated with encephalopathy severity and short-term outcomes, providing a bedside biomarker that can be trended during the hypothermia window. While variability in technique and thresholds exists, incorporating standardized RI assessment into tUS protocols may improve early risk stratification and selection for escalated monitoring or expedited MRI [18–21].

From a systems perspective, harmonizing acquisition and reporting across modalities is critical. Standardizing tUS windows (anterior, posterior, mastoid, and temporal), documenting vascular Doppler systematically, and using structured MRI protocols (T1/T2, DWI, SWI/T2*, and targeted short-TE MRS in deep gray nuclei and perirolandic cortex) facilitate accurate cross-modal correlation. Equally essential is a shared lexicon for lesion patterns (deep gray "central" pattern vs watershed), acknowledgment of gestational age–specific vulnerability (preterm white-matter injury versus term deep gray involvement), and explicit statements about prognostic implications. Such rigor enhances multidisciplinary communication and reduces interobserver variability—historically a limitation of ultrasound—and strengthens the evidence base for integrated care pathways [7,8,12,15,22].

Purpose of this review: We aim to provide a radiodiagnosis-centered synthesis on integrating transcranial ultrasound with MRI for diagnosing and prognosticating neonatal HIE. We (i) condense essential radiological anatomy relevant to HIE pattern recognition; (ii) summarize HIE epidemiology and pathophysiology with emphasis on imaging correlates; (iii) expand in detail the roles of US, CT, MRI,

DWI, and MRS—including timing nuances, pitfalls, and prognostic biomarkers; and (iv) elaborate technique and protocol optimization for both tUS and MRI, culminating in practical, time-sensitive imaging algorithms tailored to preterm and term neonates. Our overarching goal is to empower clinicians to deploy the right test at the right time, extracting maximal, complementary information from tUS and MRI to improve outcomes for infants with suspected HIE [13–16,18–22].

Radiological Anatomy

The neonatal brain is unique in its structural and maturational features, which strongly influence both the patterns of hypoxic-ischemic injury and their radiological appearances. The cerebral hemispheres are composed of the cortex, basal ganglia, hippocampal formation, and amygdala. The surface cortex is highly convoluted with gyri and sulci that differ between neonates and adults; in term infants, the central sulcus lies more anteriorly, and the Sylvian fissure is more oblique. These subtle maturational differences alter the topography of watershed zones and must be recognized in imaging interpretation [23–25].

The cerebral cortex is functionally organized into lobes—frontal, parietal, occipital, and temporal—each with distinct neurocognitive and motor functions. The frontal lobe includes the precentral gyrus, which serves as the primary motor cortex, while the parietal lobe contains the postcentral gyrus, the primary sensory cortex. The occipital lobe houses the visual cortex along the calcarine sulcus, and the temporal lobe contains auditory and limbic structures such as the hippocampus and amygdala. Understanding these regions is critical since selective vulnerability of perirolandic cortex, occipital lobe, and hippocampus is seen in different patterns of HIE [26–28].

The corpus callosum, the largest commissural tract, interconnects the two hemispheres and is divided into the rostrum, genu, body, and splenium. On ultrasound, the corpus callosum is best visualized in the sagittal plane through the anterior fontanelle, whereas MRI provides higher-definition views of its myelination status. Delayed or abnormal development of the corpus callosum is relevant when interpreting volume loss after HIE, particularly in cases with cystic periventricular leukomalacia or diffuse cerebral atrophy [29,30].

The basal ganglia—including the caudate nucleus, putamen, and globus pallidus—play a central role in motor regulation and are particularly vulnerable to hypoxic injury in term neonates due to their high metabolic demand. The posterior putamen and ventrolateral thalami are commonly affected in severe HIE. On cranial ultrasound, basal ganglia echogenicity can be subtle and nonspecific, while MRI, particularly T1/T2-weighted and diffusion imaging, provides greater clarity of these lesions. Damage to basal ganglia structures carries a poor prognosis with extrapyramidal motor sequelae [31–33].

The diencephalon consists of the thalamus and hypothalamus, with the thalamus serving as a sensory relay hub. In HIE, the thalami often demonstrate increased echogenicity on ultrasound and hyperintensity on MRI sequences. The brainstem and cerebellum, located in the posterior fossa, are less commonly injured in partial hypoxia but can be severely affected in profound asphyxia, especially in preterm infants. These structures are best evaluated using posterior and mastoid fontanelle sonographic windows, complemented by MRI for detailed assessment [34–36].

The ventricular system and cerebrospinal fluid (CSF) pathways are important landmarks in neonatal imaging. Each cerebral hemisphere contains a C-shaped lateral ventricle connected to the third ventricle via the foramen of Monro, with the fourth ventricle situated posterior to the brainstem. Ultrasound is excellent for evaluating ventricular size, hydrocephalus, and hemorrhage within the ventricles. MRI adds value by assessing subtle alterations in ventricular configuration secondary to periventricular white-matter loss, as commonly seen in preterm leukomalacia [37–39].

The vascular supply of the neonatal brain is derived from the anterior circulation (internal carotid system) and posterior circulation (vertebrobasilar system), forming the circle of Willis. In neonates, autoregulation of cerebral blood flow is immature, predisposing watershed regions to ischemia during systemic hypoperfusion. On Doppler ultrasound, the resistive index of the middle cerebral artery is often used as a bedside biomarker of cerebral perfusion in HIE. MRI with angiographic sequences further

delineates arterial and venous anatomy when vascular occlusion or congenital anomalies are suspected [40–42].

Neonatal Hypoxic-Ischemic Encephalopathy

Neonatal hypoxic-ischemic encephalopathy (HIE) is a leading cause of neonatal mortality and lifelong disability. Globally, its incidence is estimated between 1–3 per 1,000 live births in developed countries, with higher rates in resource-limited regions. Survivors of moderate to severe HIE remain at high risk of cerebral palsy, epilepsy, and cognitive impairment, despite advances such as therapeutic hypothermia. Early and accurate neuroimaging is central to reducing morbidity, as it helps stratify severity, guide interventions, and predict long-term outcomes [43,44].

The pathophysiology of HIE involves cerebral hypoperfusion and hypoxia, triggering anaerobic metabolism, lactate accumulation, oxidative stress, and loss of autoregulation. In preterm infants, immature oligodendrocytes are particularly vulnerable, resulting in periventricular white matter injury. In term neonates, metabolically active deep gray matter such as thalami, basal ganglia, hippocampi, and perirolandic cortex are more commonly affected. These maturational differences explain the variability in imaging patterns across gestational ages [45,46].

Clinically, HIE is graded using neurological staging systems such as the Sarnat classification, which evaluates mental status, tone, reflexes, and seizures. However, clinical assessment alone cannot reliably predict the extent or prognosis of injury. Hence, neuroimaging serves as an indispensable adjunct, not only for diagnosis but also for prognostic stratification and guiding follow-up [47].

Imaging Role in HIE

Ultrasound (US): Transcranial ultrasound is the first-line modality due to portability, lack of radiation, and ability to be performed at the bedside. It is highly effective in detecting germinal-matrix and intraventricular hemorrhage, ventricular dilatation, and cystic periventricular leukomalacia. Doppler evaluation of the middle or anterior cerebral artery can provide resistive index values that correlate with the severity of encephalopathy and outcomes. Nonetheless, US is limited by operator dependency and reduced sensitivity for cortical, subcortical, and deep gray matter injury [48,49].

CT: Computed tomography has largely been replaced by MRI but may be used in unstable neonates when MRI is not feasible. It can identify gross edema, hemorrhage, or infarction but has limited sensitivity for early hypoxic-ischemic injury and carries the risk of ionizing radiation exposure, which is especially concerning in neonates [50].

MRI (conventional sequences): MRI remains the gold standard for detailed assessment of HIE. T1- and T2-weighted images delineate cortical and white matter injury as well as basal ganglia involvement. Term infants with severe injury frequently show T1 hyperintensity in the thalami and posterior putamina. White matter injury appears as T2 hyperintensity with variable T1 signal changes. MRI performed within the first week of life provides the most prognostic value [51].

Advanced MRI techniques: Diffusion-weighted imaging (DWI) detects early cytotoxic edema within 24–72 hours, often before changes are seen on T1/T2. However, it may underestimate injury in the first 12 hours and pseudo-normalize after 10–12 days. MR spectroscopy (MRS) provides metabolic biomarkers; an elevated lactate-to-NAA ratio within the first 24 hours predicts adverse outcomes. Susceptibility-weighted imaging (SWI) or T2* sequences are valuable for detecting microhemorrhages and venous infarcts. These advanced sequences significantly enhance diagnostic accuracy and prognostic assessment [52–54].

In summary, US and MRI are complementary. Ultrasound is optimal for early bedside triage and serial monitoring, while MRI provides definitive lesion mapping, timing of injury, and prognostication. CT plays only a limited role. An integrated imaging approach maximizes diagnostic yield, reduces delays in treatment, and improves neonatal outcomes [49,52,54].

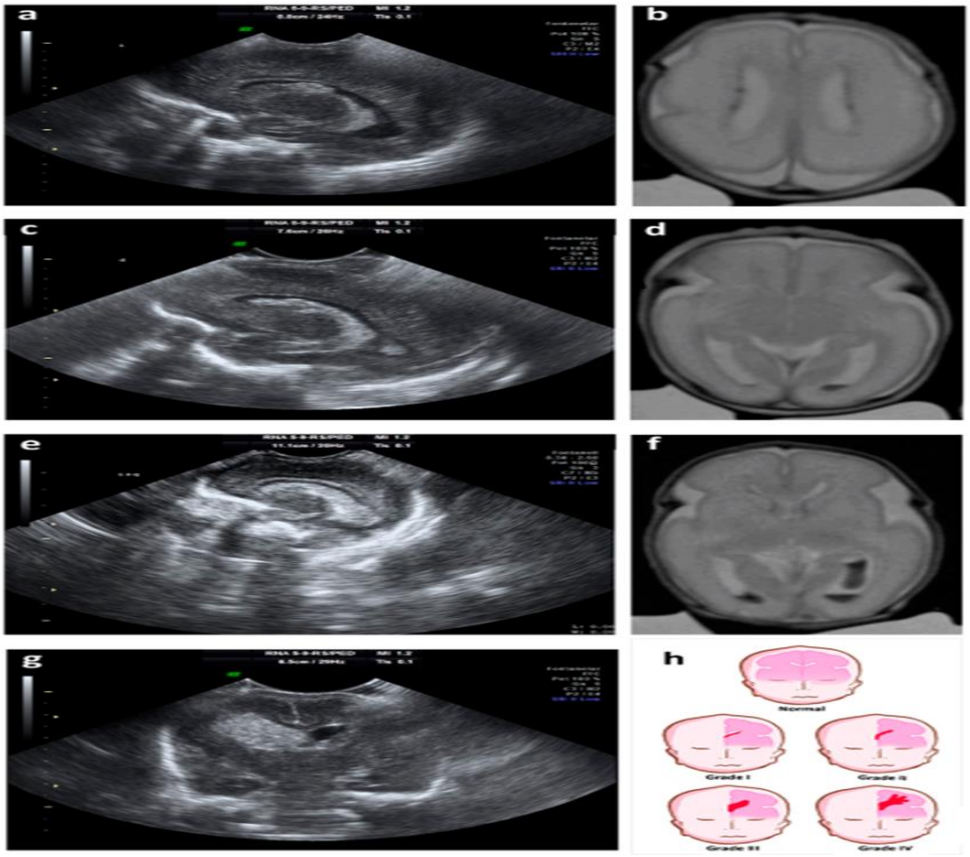

Figure 1: Ultrasound and magnetic resonance imaging (MRI) showing different grades of GM-IVH; (a) Parasagittal cerebral ultrasound through lateral ventricles shows grade I hemorrhage; (b) T2-weighted axial MRI shows grade I hemorrhage on both lateral ventricles; (c) parasagittal cerebral ultrasound through lateral ventricles shows grade II hemorrhage; (d) T2-weighted axial MRI shows grade II hemorrhage on the left lateral ventricle; (e) parasagittal cerebral ultrasound through lateral ventricles shows grade III hemorrhage; (f) T2-weighted axial MRI shows grade III hemorrhage on the left lateral ventricle and grade II hemorrhage on the right lateral ventricles; (g) coronal cerebral ultrasound shows grade IV or periventricular hemorrhagic infarction; (h) cartoon representing ultrasound classification of the germinal matrix-intraventricular hemorrhage (GM-IVH).[51].

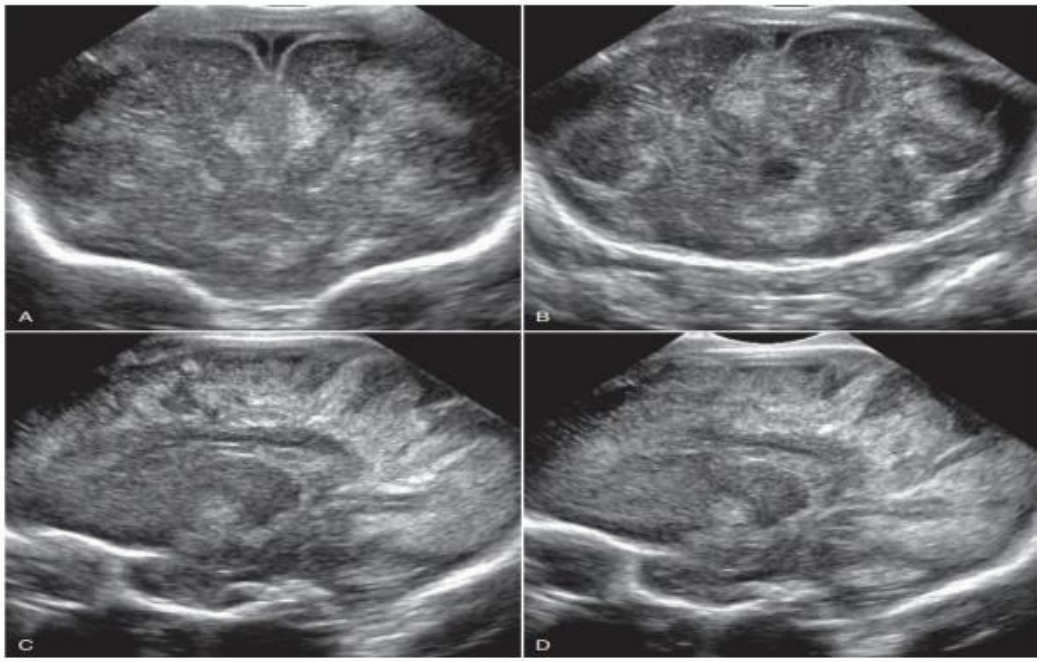

Figure :2 Cerebral Edema; (A) And (B) Coronal sonograms; (C) and (D) sagittal sonograms. Severe cerebral edema has caused effacement and silhouetting of the sulci from acute, near-total intrauterine asphyxia after placental abruption. Diffuse increased echogenicity from edema obscures sulci. Ventricles are slit-like because of the severe edema [54].

Imaging Techniques and Protocols

Sonographic Technique

Cranial ultrasound is the first-line modality for neonatal brain imaging, particularly in suspected hypoxic-ischemic encephalopathy. A high-frequency (7.5–10 MHz) transducer is recommended for preterm infants to maximize spatial resolution, whereas 5 MHz may be required for larger term infants to ensure penetration. The anterior fontanelle is the primary acoustic window and remains suitable until about 12–14 months of age. Careful thermal regulation, infection control, and gentle handling are essential during scanning to avoid physiological stress in critically ill neonates [55,56].

Coronal imaging through the anterior fontanelle provides a systematic overview from frontal to occipital lobes. At least six standardized planes are recommended, from the frontal lobes through the lateral ventricles, thalami, and posterior fossa. These planes allow evaluation of ventricular size, periventricular white matter echogenicity, caudothalamic groove, and basal ganglia echogenicity. Sagittal and parasagittal views complement this, allowing visualization of the corpus callosum, cavum septum pellucidum, and third and fourth ventricles. These systematic sweeps are crucial for consistency in reporting [57,58].

Posterior fontanelle imaging improves visualization of occipital horns and posterior white matter, particularly in cases of intraventricular hemorrhage or periventricular leukomalacia. The mastoid fontanelle provides a unique view of the posterior fossa, including the cerebellum, brainstem, and cisterna magna, which are not adequately assessed through the anterior fontanelle. This approach is particularly valuable for detecting posterior fossa hemorrhage or edema, conditions that may be underestimated otherwise [59].

The temporal window, though less commonly used, can be employed for transcranial Doppler evaluation of major intracranial vessels, including the anterior, middle, and posterior cerebral arteries. Doppler sonography allows calculation of resistive indices (RI), which are sensitive to changes in cerebral perfusion. Elevated RI values have been correlated with poor outcomes in HIE, making Doppler a valuable adjunct in early prognostic assessment [60,61].

Serial sonography is recommended: an initial scan within the first 24–48 hours to exclude hemorrhage or gross malformations, a follow-up at 7–10 days to evaluate evolving white matter injury, and a late scan around 1 month to detect cystic periventricular leukomalacia or ventriculomegaly. Such serial imaging ensures dynamic monitoring of evolving hypoxic-ischemic injury [62].

MRI Techniques and Protocols

MRI provides comprehensive evaluation of neonatal HIE but requires careful adaptation to neonatal physiology. Transport to the scanner must be coordinated with intensive care support, and sedation is minimized whenever possible. MRI protocols must balance acquisition time with diagnostic yield, often prioritizing a "shortened" protocol in unstable neonates [63].

T1-weighted imaging is essential for assessing myelination and early ischemic changes. In term infants with HIE, abnormal T1 hyperintensity in the thalami and posterior putamina is strongly associated with poor outcome. T2-weighted imaging provides superior gray–white matter contrast and is particularly valuable for identifying diffuse white matter injury in preterm infants. FLAIR sequences can highlight cystic leukomalacia and gliosis, whereas T2* or susceptibility-weighted imaging is highly sensitive to microhemorrhage and venous infarction [64,65].

Diffusion-weighted imaging (DWI) is considered indispensable in neonatal HIE. It detects restricted diffusion from cytotoxic edema as early as 12–24 hours after insult, well before conventional sequences. However, DWI must be interpreted cautiously within the first 12 hours, when false negatives can occur, and after 10–12 days, when pseudonormalization may mask injury. Apparent diffusion coefficient (ADC) mapping is therefore critical for quantifying injury severity and tracking temporal evolution [66].

Proton MR spectroscopy (MRS) enhances prognostication by providing metabolic biomarkers. A high lactate-to-NAA ratio within basal ganglia or thalami within the first 24–48 hours is a reliable predictor of poor neurological outcome. Absence of lactate and preservation of NAA correlate with favorable prognosis. MRS is particularly useful in differentiating HIE from metabolic encephalopathies, though its role in preterm infants is less standardized [67,68].

Optimized neonatal protocols usually combine axial DWI (≈45 seconds), axial T1-weighted imaging (≈4–5 minutes), and axial T2-weighted imaging (≈3 minutes). When time permits, additional sequences such as FLAIR, SWI, and targeted MRS at short echo times are strongly recommended. This structured approach ensures a balance between rapid scanning for unstable neonates and comprehensive assessment for those stable enough to tolerate longer protocols [63,69].

Integrated Approach

The most effective diagnostic strategy in neonatal HIE is integration of tUS and MRI. Ultrasound is ideal for early triage, repeat monitoring, and detection of hemorrhage or hydrocephalus, while MRI provides definitive mapping of injury pattern and severity. Doppler-derived perfusion indices extend ultrasound beyond structural imaging, while advanced MRI sequences (DWI, SWI, MRS) refine pathophysiological understanding and outcome prediction. Together, they provide a time-sensitive, complementary pathway for diagnosis and prognostication, ensuring maximal yield within the short therapeutic window available for interventions such as hypothermia [70].

The diagnostic evaluation of neonatal hypoxic-ischemic encephalopathy requires a balance between timeliness, accuracy, and safety. Transcranial ultrasound remains invaluable as a first-line modality, offering bedside accessibility, real-time monitoring, and avoidance of radiation or sedation. Its strength lies in the detection of germinal matrix hemorrhage, intraventricular hemorrhage, hydrocephalus, and cystic periventricular leukomalacia. However, its operator dependence and limited ability to detect subtle cortical or deep gray matter lesions restrict its role as a standalone tool. Thus, ultrasound should be considered an early triage and follow-up modality rather than the final diagnostic standard [71].

MRI provides unparalleled anatomical and functional insight into the neonatal brain, especially with diffusion-weighted imaging and MR spectroscopy. It is superior for lesion characterization, timing of injury, and prognostication. The ability of MRI to differentiate acute cytotoxic edema, chronic gliosis, or

white matter rarefaction makes it the gold standard for outcome prediction. Nonetheless, limitations include high cost, limited availability, and the risks of transporting critically ill neonates. These barriers explain why MRI cannot entirely replace ultrasound, but rather serves as a complementary modality [72]. An integrated imaging pathway is therefore the most effective approach. Early cranial ultrasound can screen for gross abnormalities and guide immediate management, while MRI—performed within the first week of life—provides comprehensive evaluation and prognosis. Doppler indices from ultrasound can bridge the gap by providing physiological data, complementing the structural information from MRI. This combined workflow not only improves diagnostic accuracy but also ensures that critically ill infants are not subjected to unnecessary risk while awaiting advanced imaging [73].

Future directions in neonatal neuroimaging include refinement of MRI protocols with faster, motion-robust sequences that reduce scan time and need for sedation. Quantitative techniques such as arterial spin labeling for perfusion and diffusion tensor imaging for connectivity mapping are emerging as research tools with potential prognostic value. Artificial intelligence and machine learning algorithms are also being explored to enhance ultrasound interpretation and automate lesion detection on MRI, thereby reducing interobserver variability [74].

Ultimately, the integration of ultrasound and MRI should be viewed not as a comparison but as a continuum of care. Ultrasound provides immediacy and safety, while MRI provides depth and precision. Advances in both modalities, particularly when combined with computational analytics, hold promise for earlier diagnosis, more accurate prognostication, and improved long-term outcomes in infants with HIE.

Conclusion

Neonatal hypoxic-ischemic encephalopathy remains one of the most devastating conditions in perinatal medicine, with consequences that extend far beyond the neonatal intensive care unit. Despite therapeutic advances, outcomes still depend critically on timely recognition and accurate assessment of brain injury within the first hours of life. Imaging is at the center of this challenge, guiding not only diagnosis but also prognostication and parental counseling.

Transcranial ultrasound continues to hold a vital role as the initial modality of choice. Its accessibility, safety, and ability to be performed at the bedside make it irreplaceable in the acute setting. Through anterior, posterior, mastoid, and temporal windows, it provides valuable information about ventricular size, hemorrhage, and evolving white matter changes. Doppler adds physiological insight by reflecting alterations in cerebral perfusion, offering early clues to injury severity. Yet, its limitations operator dependency and poor sensitivity for subtle cortical and deep gray lesions mean it cannot serve as the sole standard for diagnosis.

MRI, by contrast, provides unparalleled structural and metabolic detail. Conventional T1- and T2-weighted sequences characterize the extent of cortical and white matter damage, while advanced techniques such as diffusion-weighted imaging and MR spectroscopy allow detection of acute cytotoxic edema and metabolic derangements. These features make MRI the gold standard for comprehensive evaluation and outcome prediction. However, the requirement for transport, specialized equipment, and often sedation limit its routine early use, particularly in unstable neonates.

The optimal approach is therefore not one modality over another, but an integrated pathway. Ultrasound serves as the rapid, bedside screening and monitoring tool, while MRI provides definitive lesion mapping and prognostic insight. Together, they create a complementary workflow that maximizes diagnostic accuracy without compromising safety.

Looking ahead, refinements in imaging technology faster MRI protocols, automated ultrasound analysis, and the incorporation of artificial intelligence promise to further close the gap between accessibility and precision. The ultimate goal is to diagnose earlier, predict outcomes more reliably, and personalize interventions for each infant. By leveraging the complementary strengths of transcranial ultrasound and MRI, radiology continues to play a pivotal role in improving survival and long-term quality of life for neonates affected by hypoxic-ischemic encephalopathy.

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