

HUS Cranial Ultrasound: From Technical Innovations to Clinical Applications

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Received October 10, 2026; revision requested November 25, 2026; accepted December 18, 2026

Abstract: Conventional adult transcranial ultrasound allows bedside acquisition of cerebral structural and hemodynamic data, featuring repeatable radiation-free scanning tailored to clinical monitoring demands. Nevertheless, its clinical application is substantially limited by the adult temporal bone, which induces ultrasonic signal attenuation, wavefront distortion and reverberation artifacts. High-penetration ultrafast cranial ultrasound (HUS) effectively overcomes these skull-derived imaging limitations through synergistic integration of low-frequency single-crystal phased array detection, ultrafast plane-wave imaging, spatiotemporal clutter suppression, and high-resolution transcalvarial reconstruction. This innovative platform achieves contrast-free two-dimensional transtemporal imaging with a structural resolution of 1-2 mm, enabling clear visualization of basal anatomical landmarks, the Circle of Willis, proximal intracranial arteries, and major intracranial venous structures. This review summarizes the technical innovations of HUS and its progress in applications including the diagnosis of neurodegenerative diseases such as Parkinson's disease, noninvasive monitoring of intracranial hemorrhage and intracranial pressure in neurocritical care, integrated cervico-cerebrovascular evaluation, and psychiatric disorders. The clinical utility of HUS for refined bedside management of intracranial pathologies is discussed.

Key words: Transcranial ultrasound; Ultrafast ultrasound imaging; Bedside neuroimaging; Parkinson disease; Intracranial hemorrhage; Cerebral hemodynamics

Advanced Ultrasound in Diagnosis and Therapy 2026; 04: 346-359

DOI: [10.26599/AUDT.2026.260045](https://doi.org/10.26599/AUDT.2026.260045)

Transcranial ultrasound occupies a unique niche in neuroimaging. Unlike computed tomography (CT) and magnetic resonance imaging (MRI), which provide comprehensive anatomical visualization, the clinical utility of transcranial ultrasound lies in its capacity for real-time, repeatable bedside assessment of intracranial morphology and cerebral hemodynamics. Transcranial Doppler (TCD) acquires blood flow velocity waveforms of major intracranial arteries, whereas transcranial color-coded duplex sonography (TCCS) and B-mode transcranial ultrasound extend this capability to vascular mapping, anatomical localization, and quantitative evaluation of regional tissue echogenicity [1]. Collectively, these ultrasound modalities have established

indispensable clinical roles in neurological practice, particularly for cerebrovascular assessment, neurocritical care monitoring, and targeted brain parenchymal imaging [2]. Nevertheless, conventional transcranial ultrasound is constrained by incomplete anatomical delineation, insufficient tissue contrast, and strong dependence on qualified acoustic windows and operator experience, which substantially limits its widespread application as a structural neuroimaging modality.

The adult skull remains the predominant physical barrier to transcranial ultrasound. The temporal bone is not simply an attenuating layer but an acoustically heterogeneous structure in which the cortical tables and diploë introduce frequency-dependent absorption, reflec-

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tion, reverberation, and wavefront distortion [3-5]. Multiethnic cohort studies have demonstrated that adequate temporal acoustic windows cannot be acquired in approximately 20% of ultrasound examinations, with advanced age, female sex, and African or Asian ancestry identified as independent risk factors for imaging failure [6]. Therefore, improving transcranial acoustic penetration while preserving diagnostically reliable spatial and temporal resolution remains a core technical challenge in the field of transcranial neuroimaging.

Recent advances in high-penetration ultrafast cranial ultrasound (HUS) have introduced new approaches to addressing these limitations. In this review, HUS refers to an integrated transcranial ultrasound imaging platform that combines low-frequency single-crystal transducer technology, ultrafast plane-wave acquisition, and advanced signal processing and beamforming techniques, rather than a general category encompassing all transcranial ultrasound modalities. By integrating these technologies, HUS aims to improve the visualization of intracranial anatomical structures and cerebral hemodynamics through adult cranial acoustic windows. This review summarizes the underlying imaging principles, potential clinical applications, current limitations, and future perspectives of HUS.

HUS Cranial Ultrasound: Imaging Principles and Capabilities

Transcranial ultrasound imaging in adults is constrained by an inherent frequency-resolving trade-off: low-frequency ultrasound facilitates transcranial acoustic transmission but compromises intrinsic spatial resolution due to elongated wavelength. This technical dilemma is further exacerbated by the heterogeneous acoustic and geometrical properties of the temporal bone, which induce substantial acoustic attenuation, interface reflection, and wavefront distortion during ultrasound propagation [3,5]. Accordingly, transcranial imaging performance is determined not merely by transducer frequency, but by the synergistic interplay of transducer characteristics, skull acoustic properties, and iterative image reconstruction algorithms. Current HUS platforms adopt a 1-MHz PMN-PT single-crystal phased array, which integrates low-frequency transmission with the high electromechanical coupling efficiency and wide bandwidth unique to relaxor single-crystal materials. Supplemented by a graded acoustic matching layer that minimizes interfacial acoustic reflection and optimizes energy transfer efficiency [7], this elaborate hardware design effectively preserves adequate signal amplitude and bandwidth after transcranial propagation, enabling robust high-quality image reconstruction.

Ultrafast plane-wave imaging markedly improves spatiotemporal data acquisition capacity compared with the conventional frame-by-frame focused scanning paradigm. The HUS system achieves wide-field insonation in each single transmission and reconstructs multiple receive scan lines from one unified dataset, yielding a maximum raw frame rate of 5,000 frames per second for high-density spatiotemporal sampling of tissue and vascular signals. Coherent compounding of multi-angle steered plane waves enhances image contrast and spatial definition relative to conventional single-beam transmission, though at the expense of reduced effective temporal resolution. Such dense temporal sampling enables precise separation of low-amplitude blood-flow signals from dominant tissue and skull-derived acoustic clutter. Spatiotemporal analytical algorithms, including singular value decomposition, further discriminate vascular signals based on differential signal coherence [8], with tunable processing parameters balancing rigorous clutter suppression and faithful slow-flow preservation. Collectively, the core superiority of ultrafast acquisition lies in its high-dimensional spatiotemporal datasets, rather than superficial scanning speed.

Despite facilitating transcranial penetration, low-frequency ultrasound inherently degrades spatial resolution. HUS overcomes this limitation via coherence-adaptive beamforming and high-resolution reconstruction, which leverage inter-channel spatial and phase coherence across the phased array to refine target discrimination and anatomical localization accuracy. The HUS imaging chain achieves stepwise, systematic optimization: low-frequency single-crystal transmission preserves valid transcranial signals, ultrafast acquisition enriches spatiotemporal information density, and coherence-based reconstruction retrieves subtle anatomical spatial details. Importantly, such post-processing strategies cannot completely eliminate skull-induced phase and amplitude aberrations. Interindividual variability in skull thickness, morphology, and acoustic properties inevitably induces persistent imaging distortions, necessitating complementary aberration-correction techniques [9]. Therefore, the spatial performance of HUS should be validated under clinically realistic transcranial conditions, rather than inferred merely from sampling density or subjective image sharpness (Fig. 1).

Built on foregoing hardware and algorithmic advances, contemporary HUS achieves validated 1-2 mm transcranial structural resolution under standardized protocols. Its performance depends on acoustic window quality, target depth, and imaging geometry. By integrating low-frequency high-penetration transmission, ultrafast plane-wave compounding and real-time adaptive

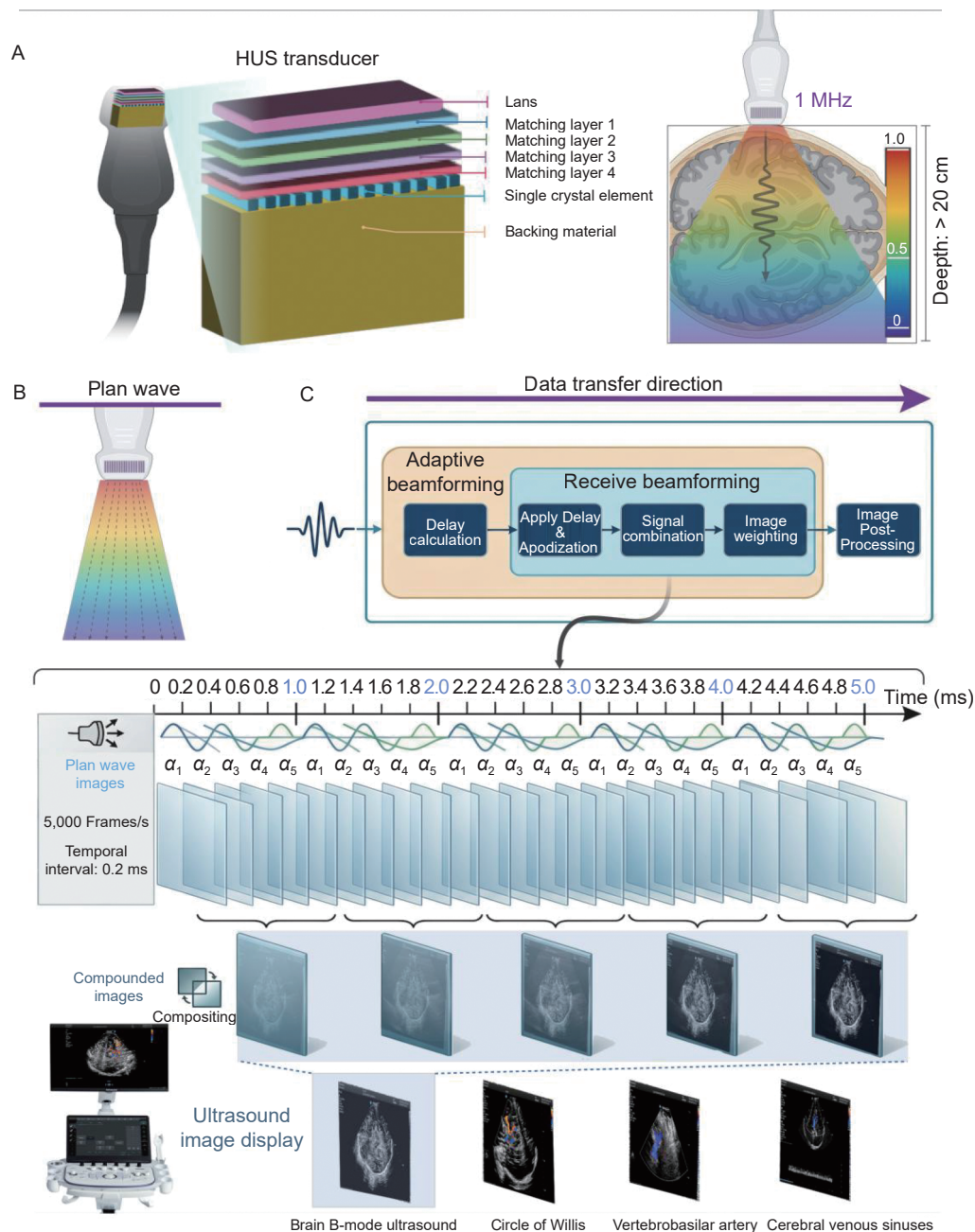


Figure 1 Transducer architecture and ultrafast plane-wave imaging workflow of HUS. (A) The HUS transducer integrates an acoustic lens, four impedance-matching layers, single-crystal piezoelectric elements and a backing material. The multilayer design improves acoustic coupling and receiving sensitivity, while the low operating frequency of approximately 1 MHz supports transcranial propagation over an imaging depth exceeding 20 cm. The colour map schematically represents the normalized acoustic field across the intracranial imaging range; (B) Broad plane-wave transmission insonifies a large field of view without sequential line-by-line scanning, enabling rapid acquisition of spatially coherent channel data; (C) The received radiofrequency signals are transferred to an adaptive beamforming pipeline. Channel-dependent delays and apodization are first calculated and applied, after which the signals are coherently combined, spatially weighted and subjected to image post-processing. In the illustrated acquisition sequence, plane waves are transmitted successively at five steering angles (α_1 – α_5) with an inter-emission interval of 0.2 ms, corresponding to a raw acquisition rate of 5,000 frames s^{-1} . Each group of five angular acquisitions is coherently compounded to improve image contrast and suppress angle-dependent artefacts while preserving high temporal resolution. Repeated compounding generates a continuous ultrafast image sequence that can support contrast-free two-dimensional structural imaging and visualization of major intracranial vessels.

phase compensation, the HUS beamforming pipeline enables robust contrast-free 2D structural imaging through thick calvaria. Compounding thousands of phase-corrected plane frames mitigates the penetration–resolution trade-off, offering a repeatable, portable, standardized tool for comprehensive intracranial neuroimag-

ing.

Despite its promising imaging capabilities, HUS faces several important technical and clinical limitations. First, although low-frequency transducers and advanced beamforming improve transcranial penetration, image quality remains influenced by individual variations in

skull thickness, acoustic properties, and temporal window accessibility. Second, the spatial resolution achieved through adaptive reconstruction should not be equated with true ultrasound super-resolution imaging, and its performance requires objective validation under clinically realistic conditions. Third, HUS-specific diagnostic thresholds and standardized examination protocols have not yet been established for many applications, particularly intracranial arterial stenosis, cerebral vasospasm, and intracranial pressure assessment. Fourth, most clinical evidence supporting these applications is derived from conventional TCD or TCCS studies, whereas direct comparative studies evaluating the incremental diagnostic value of HUS remain limited. Finally, operator dependence, equipment availability, reproducibility, and cost-effectiveness require systematic evaluation before widespread clinical implementation. Future multicenter prospective studies should establish standardized acquisition protocols, validate quantitative imaging parameters, and assess the clinical utility of HUS against established reference modalities such as CT, MRI, and angiography.

Early Screening and Long-term Follow-up Monitoring of Neurodegenerative Disorders

Neurodegenerative disorders exemplified by Parkinson's disease (PD) feature insidious prodromal symptoms and irreversible degeneration of dopaminergic neurons. Clinical diagnosis largely relies on symptomatic assessment with considerable subjectivity, highlighting an urgent unmet need for low-cost, radiation-free, repeatable imaging biomarkers for early detection and long-term dynamic monitoring. The World Federation for Ultrasound in Medicine and Biology (WFUMB) and the International Parkinson and Movement Disorder Society (2015) included transcranial ultrasound in official clinical guidelines (Level A evidence) as a standardized screening tool for early diagnosis and differential subtyping of PD versus atypical parkinsonian syndromes, while underscoring the critical roles of operator expertise and adjunct testing [2,10,11]. Nevertheless, conventional transcranial ultrasound is heavily dependent

on an adequate temporal acoustic window of the skull; up to 25%-35% of middle-aged and elderly individuals yield non-diagnostic examinations, thereby limiting its utility in large-scale PD population-based screening. The novel HUS provides a technical solution to mitigate skull-induced acoustic attenuation and allows high-resolution visualization of deep-seated midbrain anatomical structures.

Transcranial ultrasound diagnosis of parkinson's disease with HUS

Multiple meta-analyses have validated transcranial ultrasound as a non-invasive auxiliary screening modality for PD, with substantia nigra hyperechogenicity (SN+) serving as its core ultrasound marker pathologically linked to nigral iron deposition. SN+ identified on the mesencephalic plane constitutes the primary transcranial ultrasound index for PD auxiliary diagnosis (Fig. 2); a SN+ area $\geq 0.20 \text{ cm}^2$ is generally defined as a positive screening result. SN+ often presents with bilateral asymmetry and does not necessarily predominate contralateral to the clinically symptomatic limb, showing incomplete correspondence with clinical lateralization. Representing a trait-like biomarker, SN+ area does not enlarge with disease progression and bears no definite correlation with motor-symptom severity or disease duration.

According to published data, the positive detection rate of SN+ by conventional transcranial ultrasound ranges from 75% to 88% among clinically diagnosed PD patients [11]. SN+ can also be observed in some healthy elderly subjects and patients with essential tremor. Therefore, SN+ only provides supportive evidence under the Movement Disorder Society Clinical Diagnostic Criteria for Parkinson's disease and cannot independently establish a PD diagnosis.

Multi-window HUS imaging elevates the effective intracranial structural visualization rate in adults to over 90%. It permits simultaneous one-stop structural and blood-flow imaging and detects secondary PD-associated imaging alterations, such as decreased middle cerebral artery flow velocity, reduced deep-brain microcirculatory perfusion, and mild asymmetric dilatation of the

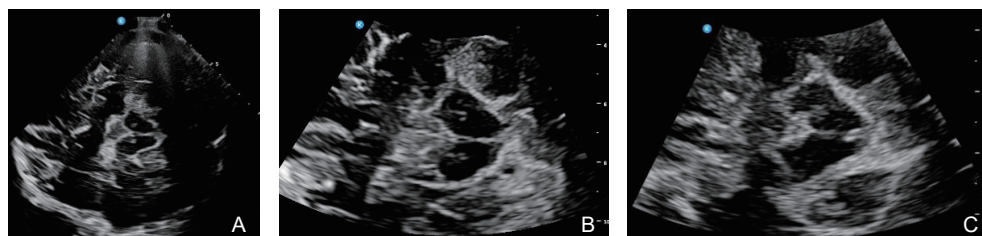


Figure 2 Clinical examination of HUS transcranial ultrasound with a probe positioned at the patient's right temporal window, transmitting the ultrasound beam through the skull toward the midbrain/substantia nigra region. (A) Normal midbrain substantia nigra; (B) magnified view; (C) PD patients display substantia nigra hyperechogenicity with an area of 0.29 cm^2 .

frontal horns of the lateral ventricles. Combined interpretation of these indices together with quantitative SN+ metrics can further improve differential-diagnostic accuracy.

Differential diagnosis

SN+ is not specific to PD. It can also occur in dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD), as well as in subsets of patients with essential tremor, healthy elderly individuals, and patients with corticobasal syndrome (CBS). By contrast, atypical parkinsonian syndromes such as multiple-system atrophy (MSA) and progressive supranuclear palsy (PSP) frequently exhibit lentiform-nucleus hyperechogenicity with normal nigral echogenicity.

According to the 2024 updated German Neurological Society PD guidelines based on systematic reviews [2], transcranial ultrasound yields a pooled sensitivity of approximately 84% and pooled specificity of approximately 85% for distinguishing PD from healthy controls or other parkinsonian disorders. Diagnostic performance deteriorates when SN+ alone differentiates PD from atypical parkinsonism, with meta-analytic pooled sensitivity of 75% and specificity of 70%. Among participants with satisfactory temporal acoustic windows, transcranial ultrasound achieves pooled sensitivity of 84.6% and specificity of 83.9% for discriminating PD from essential tremor [12,13]. Combined assessment of the substantia nigra, lentiform nucleus, and third-ventricle width markedly improves discrimination against atypical parkinsonism. Nevertheless, MRI is still recommended in early-stage disease, with transcranial ultrasound acting as a complementary imaging modality. Restricted by temporal-window quality, transcranial ultrasound performance relies heavily on standardized operator training. SN+ can neither confirm nor exclude PD in isolation; comprehensive interpretation integrating clinical phenotypes, follow-up data, and other imaging modalities is mandatory [2,14].

Clinical implications for early-stage screening and long-term follow-up

By the time patients with Parkinson's disease manifest classic motor symptoms including tremor, bradykinesia and rigidity, over 50% of nigral dopaminergic neurons have degenerated, with irreversible neuronal damage. SN+ may precede overt motor manifestations and correlates with elevated future PD risk, forming the rationale for risk-stratified screening in prior guidelines. For individuals aged above 50 years without motor impairment but with polysomnography-confirmed rapid-eye-movement sleep-behavior disorder, the co-occurrence of SN+ and verified hyposmia supports underly-

ing PD. This statement received 97.0% strong consensus in the updated German guidelines [2]. Featuring low cost, portable hardware, and simplified standardized scanning protocols, HUS cranial ultrasound is suitable for geriatric health surveys and large-scale epidemiological screening of neurodegenerative disorders in rural populations. It enables a complete clinical workflow consisting of community-based preliminary screening for prodromal high-risk individuals followed by specialized neurological work-up. Although substantia nigra hyperechogenicity may serve as a supportive imaging marker for identifying individuals at increased risk of Parkinson's disease, its echogenic area is generally considered relatively stable over time and does not reliably reflect the rate of nigral neurodegeneration or motor symptom progression. Accordingly, the potential value of longitudinal HUS assessment lies primarily in improving anatomical visualization, examination reproducibility, and multimodal evaluation rather than using changes in substantia nigra hyperechogenicity alone to monitor disease progression.

As an upgraded next-generation transcranial ultrasound platform, HUS addresses the major limitations of conventional transcranial ultrasound including poor calvarial penetration, suboptimal spatial resolution and low diagnostic yield. For Parkinson's disease assessment, its millimeter-resolution imaging provides stable anatomical references to clearly visualize the substantia nigra, lentiform nucleus, ventricles and other deep cerebral structures. This overcomes the diagnostic limitations of isolated SN+ assessment and permits multi-region deep-brain phenotyping, improving the detectability, reproducibility and diagnostic accuracy of substantia nigra hyperechogenicity. Within the care pathway for neurodegenerative diseases, this radiation-free, cost-effective multimodal imaging tool holds unique clinical value for prodromal screening, differential diagnosis, and longitudinal multimodal assessment. Complementary to MRI and positron emission tomography (PET), HUS helps refine standardized clinical workflows for PD.

Bedside Rapid Assessment of Intracranial Hemorrhage and Monitoring of Intracranial Pressure in Neurocritical Patients

Intracranial hemorrhage (ICH) is a frequent neurological emergency, and intraparenchymal hemorrhage accounts for the predominant subtype associated with an exceedingly severe disease burden [15]. As endorsed by clinical-practice guidelines, non-contrast CT constitutes the first-line imaging reference standard for patients with acute ICH. Acute ICH progresses rapidly, and

transfer of neurocritical care patients for cranial CT carries substantial safety risks [16]. Transcranial ultrasound allows rapid bedside structural screening to evaluate intracranial hematomas, ventricular morphology and cerebral midline integrity. Combined with cerebral hemodynamic parameters and optic nerve sheath diameter, it enables non-invasive assessment of cerebral perfusion and intracranial pressure fluctuation. Furthermore, serial transcranial ultrasound monitoring can dynamically track the progression of intracranial hematomas, delayed hemorrhage and progressive cerebral edema, providing continuous imaging evidence for individualized management of critically ill patients.

Bedside ultrasound for evaluation and dynamic monitoring of intracranial structures

Intracranial hemorrhage and parenchymal brain injury secondary to traumatic brain injury or other neurocritical conditions exhibit distinct ultrasound features. HUS enables visualization of intracranial hemorrhagic lesions in adults via the relatively thin temporal and occipital acoustic windows. It facilitates bedside assessment of intraparenchymal hemorrhage, intraventricular hemorrhage, subarachnoid hemorrhage, and hemorrhagic transformation secondary of ischemic stroke, acting as a valuable complementary imaging modality to CT and MRI.

In the acute phase of ICH, typical transcranial sonographic findings consist of homogeneous, well-demarcated hyperechoic lesions within the brain parenchyma. Hematoma volume can be estimated by measuring three mutually perpendicular dimensions of the hyperechoic lesion using the formula $V = A \times B \times C / 2$ ($V = \text{longitudinal} \times \text{sagittal} \times \text{coronal} / 2$), which is consistent with the volumetric algorithm adopted for CT [17] (Fig. 3). Hematomas typically exhibit uniform global hyperechogenicity during the first 1-5 days following symptom onset. In the subsequent days, echo intensity progressively diminishes beginning at the hematoma core, accompanied by gradual blurring of lesion margins. At later time-points, echo amplitude decreases further until it approximates the echogenicity of the surrounding brain parenchyma (Fig. 4).

In bedside assessment protocols, monitoring of cerebral midline structures bears critical clinical implications. Transcranial ultrasound enables identification of midline shift and ventricular width. The measured distance of midline shift demonstrates a high correlation with cranial CT measurements ($r = 0.984$, $P < 0.001$) [18,19]. Midline shift demonstrates a strong positive correlation with hematoma volume ($R = 0.90$), as validated in previous investigations [19]. A midline shift ≥ 0.5 cm signifies substantial intracranial compression and constitutes a high-risk marker for cerebral herniation.

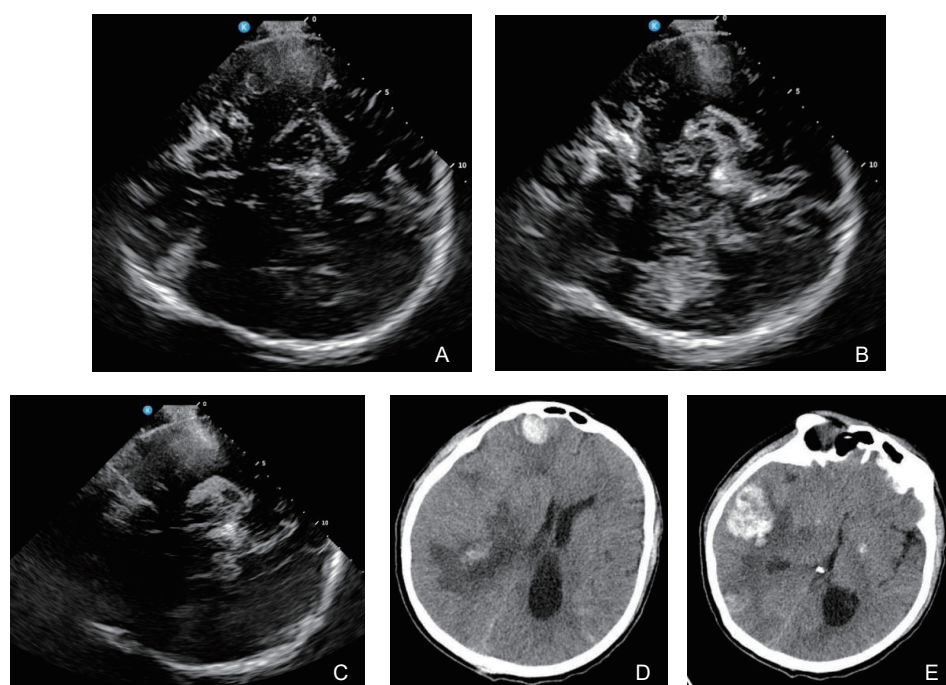


Figure 3 Representative HUS images of a patient with intracerebral hemorrhage. Male, 67 yrs, History of hypertension. Numbness in the left hand and weakness of the left lower extremity for half a day. Stuporous state with sluggish pupillary light reflex. HUS cranial ultrasound scan through the left temporal window identifies hyperechoic hematomas in the right frontal lobe (A, 2.8 mL) and right temporal lobe (B, 17.8 mL); (C) The right lateral ventricle is hyperechoic and enlarged with midline shift, suggestive of intraventricular hemorrhage extension. Non-contrast CT shows hyperattenuation in the right frontal lobe (D), right temporal lobe and right ventricle (E), confirming right frontotemporal hemorrhage extending into the right lateral ventricle, with estimated hematoma volumes of 3.6 mL and 15.6 mL, comparable to transcranial ultrasound.

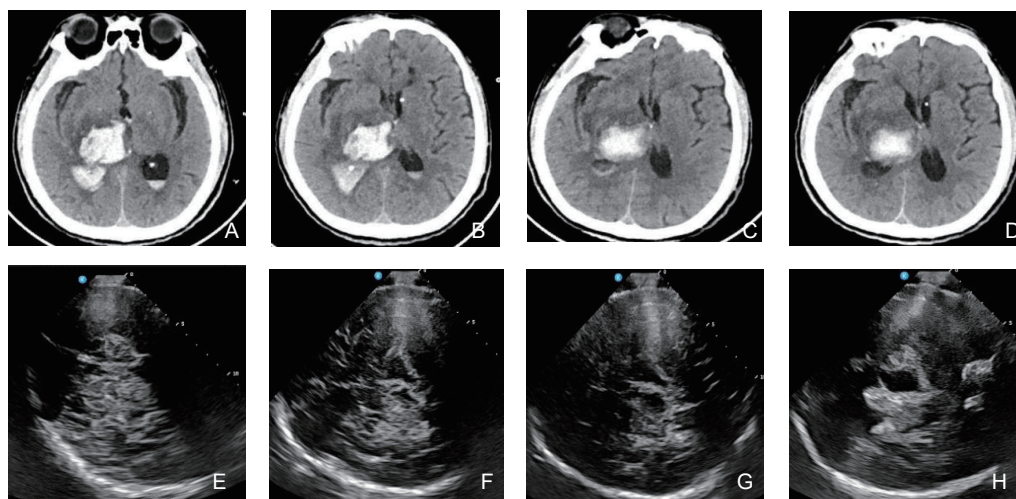


Figure 4 A 74-year-old male was admitted to the emergency department with 14 h of sudden limb weakness after a fall and urinary and fecal incontinence. (A) Baseline CT showed hyperattenuation of the right thalamus and lateral ventricle (hemorrhage), estimated hematoma volume 20.7 mL. Serial CT at day 4 (B), day 8 (C), day 11 (D) showed gradual shrinkage of the hyperattenuating lesion; (E) HUS ultrasound through the left temporal window detected hyperechoic hemorrhage in the right thalamus and lateral ventricle (23.9 mL). Follow-up ultrasound at day 4 (F) and day 8 (G) revealed progressive shrinkage and reduced echogenicity of the right intracerebral hematoma. (H) Day 11 ultrasound demonstrated substantial reduction of intraventricular hyperechoic signals, matching CT images.

Additionally, transcranial sonography enables detection of intraventricular hematoma extension and quantitative measurement of ventricular width for hydrocephalus assessment. For large-volume hemorrhage, a contralateral middle-cerebral-artery pulsatility index (PI) > 1.75 obtained via color Doppler ultrasound indicates elevated intracranial pressure. In the setting of subarachnoid hemorrhage, a mean middle-cerebral-artery flow velocity > 120 cm/s may point to cerebral vasospasm.

Intracerebral hemorrhage most commonly affects territories perfused by deep-penetrating cerebral arteries, including deep-brain regions such as the basal ganglia, thalamus and mesencephalon. These anatomical sites lie well within the effective scanning coverage of the temporal acoustic window, thereby yielding the highest lesion-detection rates on transcranial ultrasound. In contrast, superficial frontal and parietal lobar lesions, small posterior-fossa hematomas, and minimal hemorrhage confined to the occipital ventricular horn are susceptible to missed detection. Previous studies have demonstrated the feasibility of transcranial ultrasonography for detecting intracranial hemorrhage. A systematic review and meta-analysis published in 2023 reported a pooled sensitivity of approximately 88% and specificity of 81% for intracranial hemorrhage detection [18]. A more recent systematic review and meta-analysis published in 2026 reported a sensitivity of 87.8% for transcranial color-coded sonography (TCCS) in detecting hemorrhagic stroke [20]. Nevertheless, these findings were primarily derived from conventional transcranial ultrasound techniques and should not be directly extrapolated to HUS. Preliminary unpublished observations from our institu-

tion suggest that HUS may facilitate the bedside visualization of intracranial hemorrhage, particularly in deep cerebral regions. These observations remain exploratory and require validation in prospective studies using computed tomography (CT) as the reference standard. Therefore, HUS should currently be regarded as a complementary bedside imaging technique rather than a replacement for CT in the diagnosis of intracranial hemorrhage.

Non-invasive monitoring of intracranial pressure in neurocritical patients

Intracranial pressure (ICP) monitoring is an indispensable objective modality for guiding cerebral protective therapy in patients with severe craniocerebral disorders, with 22 mmHg widely accepted as the critical ICP threshold for clinical intervention. Invasive ICP monitoring remains the gold standard for the diagnosis of intracranial hypertension; however, this technique is associated with inherent risks of hemorrhage and infection, and is contraindicated in specific critically ill populations. As a promising noninvasive alternative, bedside ultrasound-based parameters including optic nerve sheath diameter (ONSD) and ultrasound-derived PI have been validated for ICP evaluation, based on the anatomical and hemodynamic correlation with intracranial cerebrospinal fluid circulation and cerebral perfusion.

Anatomically, the perioptic subarachnoid space is continuous with the intracranial cerebrospinal fluid compartment, such that elevated ICP directly distends the optic nerve sheath and increases ONSD. Hemodynamically, increased intracranial pressure and reduced

intracranial compliance elevate distal cerebrovascular resistance, which further reduces diastolic cerebral blood flow velocity and consequently increases PI. Clinically, bedside noninvasive ICP assessment primarily relies on ONSD measurement and PI calculation via middle cerebral artery flow spectrum acquisition through transcranial ultrasound. Consistent with the B-ICONIC consensus criteria, an ONSD value > 5.0 mm combined with $PI \geq 1.2$ serves as an early warning threshold for elevated ICP, whereas ONSD of 5.5–6.0 mm plus $PI \geq 1.4$ strongly suggests definite intracranial hypertension ($ICP \geq 20$ mmHg), supporting the necessity of multimodal combined interpretation for accurate judgment [21–23].

Accumulated clinical evidence has verified the diagnostic efficacy of these ultrasound parameters in traumatic brain injury patients. A systematic review encompassing eight prospective studies with 222 traumatic brain injury patients demonstrated that ONSD and transcranial ultrasound parameters yielded pooled sensitivity and specificity of both 0.82 when adopting invasive ICP monitoring as the reference standard [24]. Another meta-analysis further confirmed that ultrasound-based ICP assessment achieved a sensitivity of 92.3% and a specificity of 70%, indicating superior performance in excluding elevated ICP and monitoring progressive physiological deterioration, rather than precisely confirming intracranial hypertension.

Despite the favorable diagnostic performance, the heterogeneous diagnostic thresholds and technique-dependent measurement variations preclude the precise determination of absolute ICP values via ONSD and PI alone. Current international consensus guidelines have therefore emphasized standardized protocols for probe placement, measurement location, image quality control, and standardized result reporting to reduce operational bias [25]. Notably, ultrasound-derived Doppler indices are susceptible to multiple confounding factors, including systemic arterial pressure, arterial partial pressure of carbon dioxide, cerebral vascular lesions, and cerebral autoregulatory status, which may alter the accuracy of ICP estimation.

Clinical value of transcranial ultrasound examination

Bedside transcranial ultrasound represents a valuable monitoring tool for patients with severe craniocerebral disorders. Using multi-acoustic-window imaging, it enables rapid, repeatable, radiation-free bedside assessment of intracranial structures, midline shift, hematoma morphology and evolution, allowing dynamic surveillance of delayed hematoma expansion and progressive cerebral edema. Compared with conventional transcranial

ultrasound, HUS improves skull penetration and image quality, and achieves favorable consistency with cranial CT in determining the location and volume of ultrasound-accessible intracranial hematomas [26].

Beyond structural imaging, combined measurement of ONSD and transcranial Doppler waveform PI permits noninvasive continuous estimation of ICP and cerebral perfusion, realizing integrated bedside evaluation of intracranial structure, perfusion and ICP. Nevertheless, several constraints limit its application. ONSD measurement and Doppler hemodynamic indices should be interpreted as part of serial physiological monitoring rather than standalone quantitative surrogates for invasive ICP monitoring. Variable temporal acoustic windows and operator dependence constitute major inherent limitations, and hematoma hyper-echogenicity lacks sufficient specificity.

Despite these limitations, with the widespread clinical adoption of HUS, standardized scanning protocols, accumulating clinical evidence, and the adoption of international consensus on neurocritical care ultrasound, bedside transcranial ultrasound is expected to become a routine monitoring modality. It supports refined whole-cycle bedside management and carries substantial clinical value in severe brain injury care.

Intracranial Vascular Assessment and Integrated Cervico-Cerebral Ultrasound

The onset and progression of cerebrovascular diseases are associated not only with focal vascular abnormalities, but also with multiple factors including extracranial feeding arteries, intracranial vascular pathways, collateral circulation, and cerebral hemodynamics. Carotid ultrasound evaluates the structure and flow of the common carotid, internal carotid, and vertebral arteries, whereas TCD and TCCS assess flow direction, velocity, and spectral patterns in major intracranial arteries. Combining cervical and intracranial vascular examinations enables continuous hemodynamic assessment from extracranial feeding arteries to the primary branches of the circle of Willis, establishing an integrated cervico-cerebral ultrasound approach.

Conventional TCD infers vascular status mainly from Doppler spectra and demands substantial operator expertise in anatomical localization. TCCS identifies intracranial vessels using gray scale and color-flow guidance, yet image quality remains constrained by skull attenuation and acoustic-window quality. HUS, utilizing high-penetration probes, ultrafast and high-resolution imaging, improves visualization of major intracranial vessels and enhances reproducibility of flow measurements (Fig. 5), thereby extending integrated cervico-cerebral

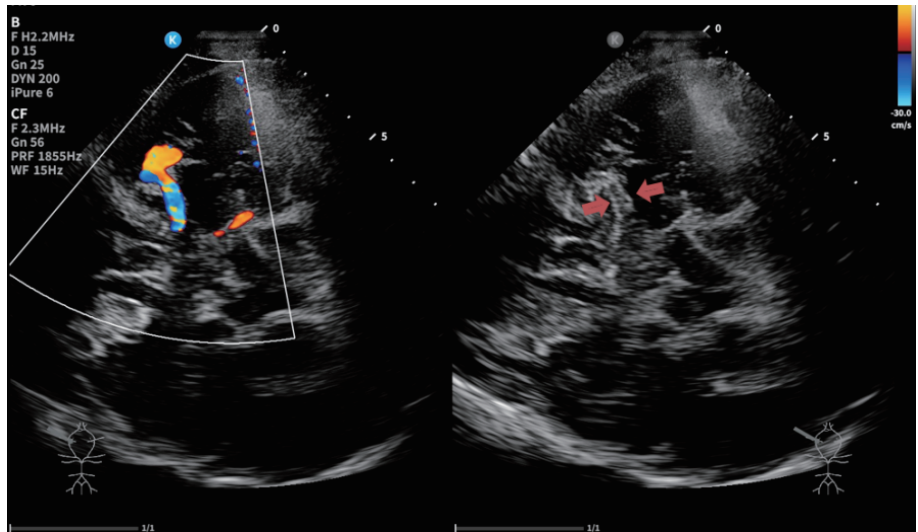


Figure 5 Dual-mode HUS imaging of the middle cerebral artery (MCA) and its anatomical localization. Left: color Doppler flow imaging shows flow in the middle MCA. Right: grayscale imaging shows the MCA groove (red arrows), an anatomical landmark for MCA localization.

ultrasound to cerebrovascular screening, critical-care monitoring, and treatment follow-up.

Integrated cervico-cerebral vascular ultrasound assessment

Integrated cervico-cerebral ultrasound is more than the simple combination of carotid and transcranial ultrasound. It evaluates the cerebral blood-supply pathway as a whole, including extracranial arterial lesions, intracranial flow changes, and collateral compensation. Examination usually begins with bilateral common carotid, internal carotid, and vertebral arteries to assess vascular structure, stenosis, and Doppler spectra [27], followed by evaluation of major vessels of the circle of Willis through the temporal, occipital, and orbital windows, including flow direction, velocity, and pulsatility index. HUS uses clearer intracranial anatomical landmarks for vessel localization and combines flow imaging with

spectral Doppler to assess major intracranial arteries. Key parameters and their clinical relevance are summarized in [table 1](#). This paradigm integrating structural visualization, vascular localization and spectral measurement facilitates intuitive intracranial vascular evaluation, which constitutes a potential strength of HUS for integrated cervico-cerebral assessment.

Combined cervical and intracranial assessment enables delineation and grading of cervico-cerebral vascular abnormalities and their hemodynamic consequences. For example, reduced MCA velocity may result from local MCA occlusion or severe ipsilateral internal carotid artery (ICA) stenosis; combined intracranial-extracranial flow integrated analysis helps localize the lesion. In ICA severe stenosis or occlusion, hemodynamic changes in ipsilateral MCA flow and collateral pathways through the anterior/posterior communicating and ophthalmic arteries can be further evaluated. Altered

Table 1 Key hemodynamic parameters and their clinical significance in integrated cervico-cerebral ultrasound assessment

Assessment	Main parameters/reference criteria	Clinical relevance
Flow velocity	PSV, EDV, MFV	Assessment of local flow velocity and hemodynamic abnormalities
MCA stenosis	50%-69%: PSV $\geq$ 180 cm/s, MFV $\geq$ 110 cm/s; 70%-99%: PSV $\geq$ 240 cm/s, MFV $\geq$ 160 cm/s*	Supports assessment of MCA stenosis and severity
Arterial occlusion	Absent flow signal or residual low-flow signal	Supports detection of occlusion and distal hypoperfusion
Peripheral resistance	PI/RI	Reflects changes in distal vascular resistance
Flow asymmetry	Velocity difference between paired vessels	Supports detection of focal hemodynamic abnormalities
Collateral circulation	Flow direction; changes in ACoA, PCoA, and ophthalmic artery flow	Assesses collateral pathways within the circle of Willis and between intracranial and extracranial circulations
Combined extracranial–intracranial assessment	Flow changes in the internal carotid and intracranial arteries	Helps localize the lesion level and assess its effect on cerebral perfusion

Note: PSV, peak systolic velocity; EDV, end-diastolic velocity; MFV, mean flow velocity; PI, pulsatility index; RI, resistance index; MCA, middle cerebral artery; ACoA, anterior communicating artery; PCoA, posterior communicating artery; TCCS, transcranial color-coded duplex sonography. *MCA velocity thresholds are based on the TCCS study by Liu et al. [28]; their applicability to HUS requires further validation.

intracranial flow direction, inter-side velocity asymmetry of paired arteries, and increased distal ICA resistance further indicate the effect on cerebral perfusion [27,29].

Assessment of intracranial arterial stenosis and occlusion

Intracranial arterial stenosis and occlusion are major causes of ischemic stroke. HUS identifies stenosis primarily by focal flow acceleration, spectral filling, turbulence, and velocity asymmetry between paired vessels. Severe stenosis typically manifests as marked focal velocity elevation, spectral broadening, and diminished distal flow. Occlusion may present as absent flow signals, a dampened low-flow spectrum, or only minimal residual flow, frequently accompanied by compensatory flow augmentation or flow reversal in adjacent vessels [30]. MCA is the most extensively studied intracranial artery in transcranial ultrasound. Using digital subtraction angiography (DSA) as the reference standard, Liu et al. analyzed 409 MCAs in 375 patients and established TCCS criteria based on peak systolic velocity, mean flow velocity (MFV), and local velocity ratios [28] (Table 1). Notably, transcranial ultrasound techniques vary in flow velocity measurements and angle correction. Thus, the above criteria may be used for HUS evaluation, yet their applicable thresholds warrant further validation.

Building on conventional hemodynamic assessment, HUS integrates anatomical localization, flow imaging, and spectral Doppler measurements, thereby enhancing

the accuracy of lesion localization and identification of abnormal blood flow. In case of MCA stenosis, the affected segment may show a narrowed or sparse flow jet, local turbulence, and increased spectral velocity (Fig. 6).

Overall, HUS builds on the established TCD/TCCS hemodynamic framework by adding anatomical localization and flow visualization, enabling bedside dynamic assessment of intracranial stenosis, occlusion, and collateral circulation. However, it cannot replace CT angiography, magnetic resonance angiography (MRA), or DSA for anatomical vascular diagnosis [31]. HUS-specific diagnostic thresholds and incremental clinical value require further study.

Dynamic monitoring of cerebral vasospasm

Cerebral vasospasm and delayed cerebral ischemia (DCI) after aneurysmal subarachnoid hemorrhage are among the best-established applications of transcranial ultrasound. The MCA is the most commonly monitored vessel. Assessment usually combines MCA MFV with the Lindegaard ratio, defined as ipsilateral MCA MFV divided by extracranial internal carotid artery MFV. An MCA MFV ≥ 120 cm/s with a Lindegaard ratio ≥ 3 supports vasospasm; an MFV > 200 cm/s with a ratio > 6 suggests severe vasospasm. In contrast, elevated MCA velocity with a Lindegaard ratio < 3 is more consistent with hyperemia [32]. The 2023 American Heart Association/American Stroke Association guideline states that TCD monitoring may help identify vasospasm and DCI risk [33].

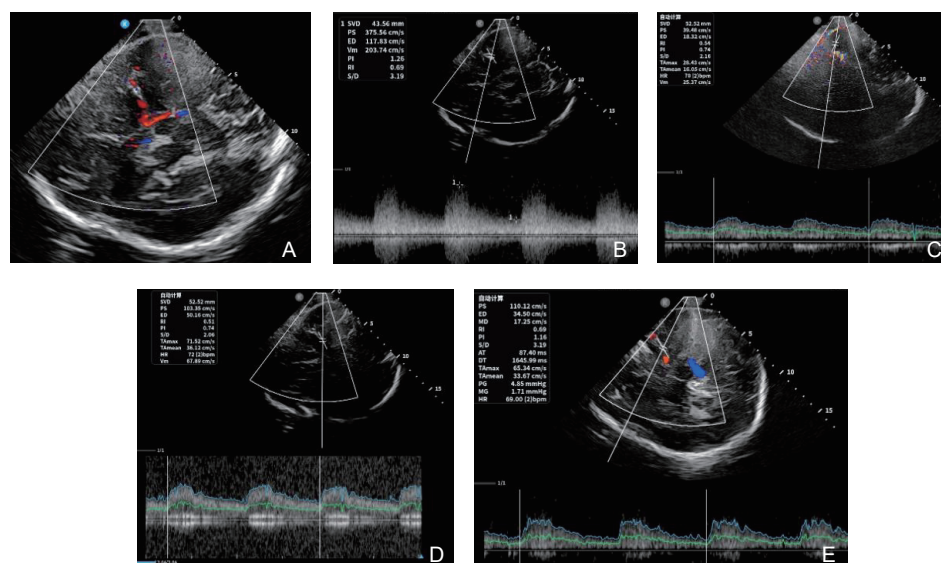


Figure 6 HUS hemodynamic findings in a patient with CT angiography-confirmed severe stenosis of the M1 segment of the left middle cerebral artery. (A) Color Doppler shows incomplete focal filling of the left MCA, suggesting restricted local flow; (B) Repeated spectral Doppler measurements show focal left MCA velocities of 332–375 cm/s; (C) Post-stenotic flow velocity is 39 cm/s, markedly lower than at the stenotic segment; (D) Pre-stenotic flow velocity is 103 cm/s, providing a reference for hemodynamic changes across the stenosis; (E) Contralateral MCA velocity is 110 cm/s, serving as a side-to-side reference.

Systematic reviews also associate TCD-detected vasospasm with DCI risk after aneurysmal subarachnoid hemorrhage. HUS can therefore use the established TCD monitoring framework, although relevant thresholds require validation on HUS platforms. A potential added value of HUS is the combined assessment of vascular morphology and hemodynamics. Ultrafast Doppler studies in neonates have shown simultaneous measurement of vessel size and hemodynamic parameters [34], suggesting that HUS may reduce reliance on velocity alone. However, high velocity is not specific to vasospasm, assessment of anterior cerebral artery, posterior cerebral artery, and distal branch vasospasm remains limited, and DCI also involves microcirculatory dysfunction. HUS findings should therefore be interpreted together with neurological status, CT angiography, CT perfusion, or DSA.

Monitoring recanalization and post-treatment hemodynamics

HUS can continuously monitor residual flow in occluded vessels and hemodynamic changes after recanalization during acute ischemic stroke treatment, although the current framework is derived mainly from TCD studies. The thrombolysis in brain ischemia (TIBI) flow grading system classifies residual flow from absent to minimal, blunted, dampened, stenotic, and normal flow patterns, describing occlusion severity and recanalization. TIBI grades correlate with angiographic recanalization and can be used for real-time monitoring during intravenous thrombolysis [35]. Compared with intermittent CTA or MRA, continuous flow monitoring may better capture rapid recanalization, reocclusion, and short-term hemodynamic fluctuations, but supporting evidence remains largely TCD-based [36].

For patients undergoing mechanical thrombectomy, DSA directly evaluates intraoperative recanalization, whereas HUS is better suited to post-procedural bedside monitoring. TCD studies indicate that recovery of ipsilateral MCA flow, together with changes in velocity, pulsatility index, and side-to-side asymmetry, may help assess post-reperfusion hemodynamics and provide information on reocclusion risk and clinical outcome [37].

Applications of HUS in Psychiatric Disorders

Psychiatric disorders are currently diagnosed primarily based on clinical manifestations, without validated objective biomarkers. While MRI and PET enable detection of structural and functional brain abnormalities, their high expense and lack of bedside repeatability restrict their utility in dynamic monitoring. Since Beck-

er et al. pioneered the application of transcranial ultrasound in psychiatric research in 1994, accumulating studies have focused on three core ultrasound domains: brainstem raphe echogenicity, ventricular morphological alterations, and cerebral hemodynamic parameters [38].

One of the most extensively investigated transcranial ultrasound findings in psychiatric research is reduced brainstem raphe echogenicity in patients with depression. As the primary origins of ascending serotonergic neural projections, the dorsal and median raphe nuclei are intimately implicated in the pathophysiological progression of depression [38]. Multiple meta-analyses including 30 studies (2,104 subjects) reported that diminished echogenicity of brainstem raphe achieved a sensitivity of 62%–66%, a specificity of 84%–85%, and an area under curve of 0.84 for depression screening, with notably higher specificity for disease discrimination [39,40]. Some studies have suggested a potential association between reduced brainstem raphe echogenicity and favorable responses to selective serotonin reuptake inhibitors (SSRIs). One study reported a positive predictive value of 88% for antidepressant treatment response among patients with reduced raphe echogenicity [41]. Nevertheless, these findings require independent validation, and the clinical utility of brainstem raphe echogenicity for predicting antidepressant treatment response remains uncertain. Furthermore, prior meta-analyses have demonstrated altered intracranial flow velocity, vascular resistance, and cerebrovascular reactivity in patients with cognitive impairment and dementia [42].

Evidence for transcranial ultrasound applications in other psychiatric conditions remains preliminary. In bipolar disorder, third ventricular enlargement suggestive of cerebral atrophy has been observed, whereas consistent alterations in brainstem raphe echogenicity have not been identified. Although large-scale MRI studies have verified that ventricular volume changes reflect cerebral and hippocampal atrophy [43], conventional transcranial ultrasound is limited by insufficient acoustic window quality and spatial resolution, precluding reliable evaluation of the lateral ventricles and hippocampus [44]. By potentially improving the visualization of intracranial anatomical structures and tissue boundaries, HUS may facilitate structural assessment in patients with bipolar disorder. However, its diagnostic value in this population remains to be established.

Due to its noninvasiveness, convenience, and radiation-free properties, transcranial ultrasound is particularly suitable for repeated assessment in children with attention-deficit/hyperactivity disorder (ADHD). Sever-

al studies have reported enlarged substantia nigra echogenic areas and a higher prevalence of nigral hyper-echogenicity in pediatric ADHD patients [45]. Some cohorts have linked increased nigral echogenicity to core ADHD symptoms, including inattention, hyperactivity, and impulsivity, while negative findings have also been documented. Accordingly, the diagnostic and clinical applicability of ultrasound markers in pediatric ADHD remains to be validated in large-scale prospective studies.

Importantly, most of the available evidence regarding transcranial ultrasound findings in psychiatric disorders is derived from conventional transcranial sonography rather than HUS-specific clinical studies. Although HUS may offer improved visualization of selected intracranial structures, its diagnostic accuracy, prognostic value, and ability to predict treatment response in psychiatric populations have not been established. Therefore, its application in this field should currently be regarded as exploratory, requiring further validation in prospective clinical studies.

Current Limitations and Future Challenges of HUS

Despite its promising potential, HUS faces several technical and clinical limitations. Transcranial imaging remains affected by skull-related acoustic attenuation, individual variations in acoustic window accessibility, and operator dependence. Furthermore, standardized examination protocols and HUS-specific diagnostic criteria have not yet been established for many clinical applications.

Most available clinical evidence is derived from conventional transcranial ultrasound studies, while direct comparisons demonstrating the incremental diagnostic value of HUS remain limited. Further multicenter prospective studies are needed to validate its diagnostic accuracy, reproducibility, and clinical utility, as well as to establish standardized imaging protocols and quantitative assessment criteria.

Conclusion and Outlook

HUS overcomes the skull acoustic attenuation limitation inherent to conventional transcranial ultrasound. Integrating high-penetration acoustic probes, ultrafast plane-wave imaging, and advanced adaptive beamforming techniques, this modality substantially improves imaging yield through the adult cranial acoustic window. It enables concurrent delineation of deep brain parenchymal anatomy and millisecond-resolved hemodynamic acquisition, exhibiting salient merits including bedside operability, radiation-free acquisition, repeat-

able scanning, and multiparametric quantitative analysis. In neurodegenerative disorders, HUS may facilitate the visualization of characteristic imaging features, such as substantia nigra hyperechogenicity in Parkinson's disease, potentially supporting clinical assessment and differential diagnosis. In neurocritical care, it enables continuous bedside surveillance of intracerebral hemorrhage, cerebral edema and intracranial pressure, conforming to the clinical paradigm of CT corroboration coupled with serial ultrasound monitoring. It supports integrated cervico-cerebrovascular assessment to underpin vascular screening, therapeutic surveillance and post-intervention follow-up for stroke cohorts. Moreover, HUS may offer potential applications in the assessment of psychiatric disorders such as depression, although its diagnostic value and ability to predict treatment response remain to be established. In summary, HUS technology expands the scope of bedside cranial imaging. With standardized scanning protocols, accumulating clinical evidence, and ongoing multicenter studies, it holds promise to facilitate refined full-cycle bedside management of intracranial diseases.

Acknowledgments

Not applicable.

Authors' Contributions

HD contributed to conceptualization of this review. GWC, WYD and HD wrote the original draft. YML, ZXZ and WYD collected and analyzed literature and prepared figures. GWC critically edited the manuscript. HD supervised the project and revised the final manuscript. All authors read and approved the final manuscript.

Funding

This work was supported by National Natural Science Foundation of China (No. 82672518).

Data Availability

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Conflict of interest

Wenyi Ding is an employee of Shenzhen Krinwave Technology Co., Ltd. and contributed to the technical aspects of the manuscript. The other

authors declare no conflicts of interest related to this work.

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