Gadoxetic acid in China: a narrative review of the 15-year journey and the road ahead

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Background and Objective: Since its pivotal introduction in 2011, gadoxetic acid has fundamentally revolutionized the landscape of hepatobiliary imaging in China, shifting the diagnostic paradigm from morphological assessment toward functional hepatocyte-level evaluation. This review comprehensively summarizes its 15-year clinical evolution within the Chinese healthcare system, exploring its pharmacological benefits, advanced applications, and future integration with data-driven frameworks.

Methods: A systematic literature search was conducted across major electronic databases, including PubMed, Web of Science, and China National Knowledge Infrastructure, spanning from 2011 to 2026. The search targeted peer-reviewed articles, consensus statements, clinical guidelines, and high-impact reviews published in English and Chinese regarding gadoxetic acid-enhanced liver magnetic resonance imaging (MRI).

Key Content and Findings: Gadoxetic acid provides high sensitivity for early small hepatocellular carcinoma (sHCC) detection via specific OATP1B3 uptake. Beyond lesion detection, its quantitative mapping shows potential for estimating hepatic functional reserve (HFR) and risk stratification for post-hepatectomy liver failure. Crucially, the ongoing paradigm shift toward integrating radiomics and deep learning bridges macroscopic imaging and microscopic molecular biology, theoretically enabling a multi-dimensional profile of liver parenchyma and lesions within a single diagnostic session. However, a significant gap remains between retrospective predictive performance and clinical readiness, and these data-driven frameworks currently serve as supplementary investigational engines rather than standalone clinical decision-makers. Moving forward, integrating these high-dimensional signatures into constructs such as "digital twin" represents the next frontier. Furthermore, China's hepatitis B virus-dominant epidemiological

cohorts, comprehensive multi-modal datasets, "Med-Engineering" fusion, and collaborative networks uniquely accelerate the development and preliminary validation of these models, offering valuable insights for global precision hepatology within China's healthcare system.

Conclusions: Over the past 15 years, gadoxetic acid has evolved far beyond a conventional liver imaging tool in China. While clinical translation of advanced analytics requires rigorous, prospective multicenter validation to ensure safety, combining this functional imaging agent with data-driven frameworks represents a promising frontier to eventually optimize future radiology workflows and support personalized precision hepatology.

Keywords: Gadoxetic acid; liver magnetic resonance imaging (liver MRI); Chinese healthcare system; hepatobiliary phase (HBP); hepatocellular carcinoma (HCC)

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Introduction

Epidemiology of liver disease burden in China

As the world's second most populous country, China presents a unique epidemiology pattern of liver disease, shaped by its rapid socioeconomic transition, evolving lifestyles, and disparate healthcare access, with a prevalence of more than 400 million patients (1-3). Liver diseases, which span both acute and chronic conditions, are typically characterized by persistent hepatocyte injury and inflammation, of which its accumulation impairs liver function and induces liver hepatitis, fibrosis, cirrhosis, and ultimately, liver cancer (4). Drug-induced liver injury, a major acute pathway often triggered by the inappropriate usage of chemical drugs, biological agents, or traditional Chinese medicine, currently occurs at an incidence of approximately 23 per 100,000 in China, which is significantly higher than in developed countries (5). Hepatitis virus infection, particularly hepatitis B virus (HBV) and hepatitis C virus (HCV), remains a primary driver of chronic liver disease and its complications in China (6). *Figure 1* illustrates the geographic distribution of HBV and HCV incidence rates in the Chinese mainland, based on the latest China Health Yearbook 2024 report (7). Despite a 99.6% three-dose HBV vaccine rate—a testament to national public health efforts—approximately 75 million people (mostly aged over 30 years) remain infected. This contributed to over 360,000 new cases of liver cancer annually, accounting for more than 40% of global incidence, with a dismal 5-year survival rate of 12.1% (8-10). The longitudinal impact of these etiologies on liver cancer burden is further elucidated in *Figure 2*, which depicts the temporal trends in age-standardized death rates and disability-adjusted life years (DALYs) from 1990 to 2023, derived from the Global Burden of Disease (GBD) 2023 datasets (11). Furthermore, alongside the improving living standards, the rising prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) and alcoholic liver disease (ALD)—now affecting approximately one-quarter of the Chinese population—has emerged as a significant risk factor for liver disease burden, raising considerable public health concern (12,13).

Existing tools for liver disease management

Evaluating liver function variance provides clinicians with critical insights for disease diagnosis and management (14). Liver blood tests, also known as liver function tests, comprising serum markers such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP),

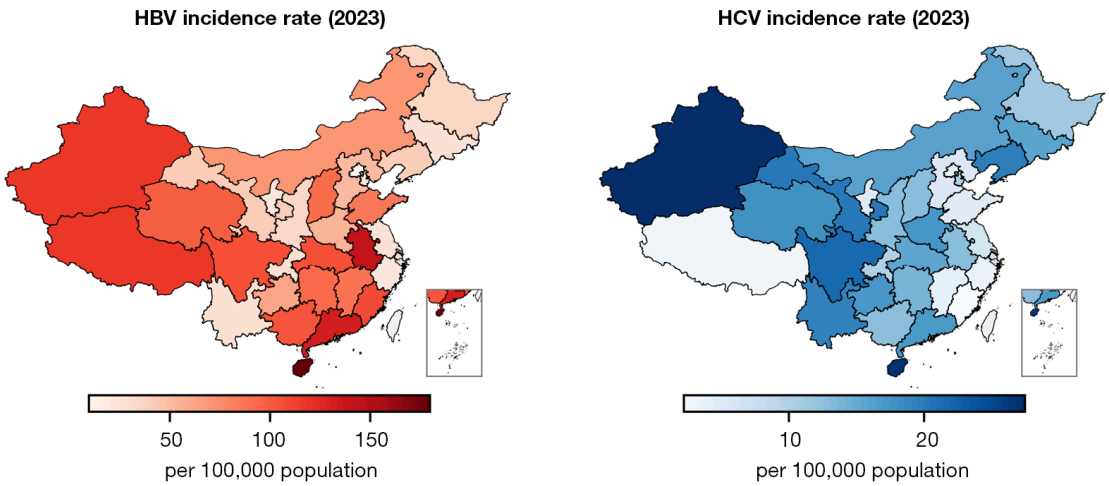


Figure 1 Geographic distribution of HBV and HCV incidence rates in the Chinese mainland. The maps represent the provincial-level incidence rates (cases per 100,000 population) for HBV and HCV based on data from the China Health Yearbook 2024. HBV, hepatitis B virus; HCV, hepatitis C virus.

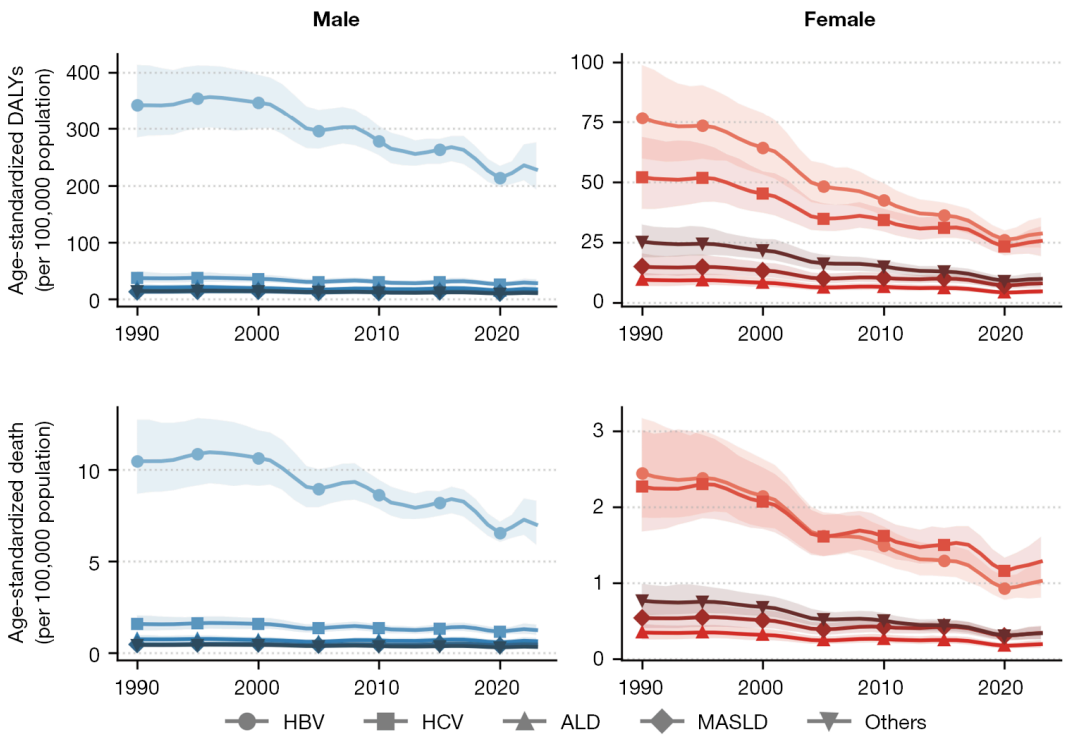


Figure 2 Temporal trends in age-standardized DALYs and death rates of liver cancer by etiology, 1990–2023. The line charts display the age-standardized DALYs and death rates (cases per 100,000 population) for liver cancer attributed to HBV, HCV, ALD, MASLD, and other etiologies. Data are derived from the GBD Study. ALD, alcohol liver disease; DALYs, disability-adjusted life years; GBD, Global Burden of Disease; HBV, hepatitis B virus; HCV, hepatitis C virus; MASLD, metabolic dysfunction-associated steatotic liver disease.

bilirubin, and albumin, serve as primary indicators of liver disease. However, their clinical utility is often limited by low sensitivity and specificity when used in isolation (15,16). Consequently, narrowing the differential diagnosis typically requires a combination of clinical history and abdominal imaging, such as ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) (17,18).

US provides a safe and cost-effective option for first-line screening, surveillance, and primary diagnosis of liver pathological changes such as fibrosis, steatosis, and focal liver lesions (FLLs). In addition to the standard B-Mode imaging, advanced techniques—including quantitative US, elastography, and contrast-enhanced US (CEUS)—allow for the evaluation of tissue attenuation, stiffness, and nodular vascular patterns. These methodologies were standardized in the (Contrast-Enhanced) Ultrasound Liver Imaging Reporting and Data System (US/CEUS LI-RADS) established by the American College of Radiology in 2017 (19-21). While CT and MRI are essential and complementary modalities that offer superior spatial resolution and less operator dependency than US (22), MRI is particularly favored for characterizing liver nodules due to its lack of ionizing radiation and superior soft tissue contrast. In contrast, CT remains a faster and more accessible solution for initial evaluation, especially when MRI is contraindicated (23).

Gadoxetic acid—a liver-specific MRI contrast agent

Since its first development in the early 1990s, gadoxetic acid (Gd-EOB-DTPA, Primovist in Europe and Eovist in the USA) has emerged as a pivotal dual-modality contrast agent, uniquely combining extracellular fluid properties with hepatocyte-specific uptake by the structural addition of a lipophilic ethoxybenzyl (EOB) group to the gadopentetate dimeglumine (Gd-DTPA) backbone (24-26). The pharmacokinetics of gadoxetic acid manifest in two distinct stages: initially, it provides an extracellular fluid distribution similar to Gd-DTPA, enabling multi-phase dynamic enhancement. Subsequently, approximately 50% of the administered contrast agent is actively absorbed by functional hepatocytes via organic anion transporting polypeptide 1B3 (OATP1B3), peaking at 10–20 minutes post-injection. It is then excreted into the bile canaliculi through multidrug resistance-associated protein 2 (MRP2). This distinct uptake mechanism defines the hepatobiliary phase (HBP), with healthy liver parenchyma exhibiting high signal intensity in T_1-weighted MRI (T_1WI), whereas most malignant FLLs—which lack functional OATP1B3 transporters—appear characteristically hypointense. This marked contrast significantly enhances the detection and differential diagnosis of FLLs, particularly for small hepatocellular carcinoma (sHCC). Furthermore, the significantly elevated relaxivity (R_1=1/T_1, Gd-EOB-DTPA *vs.* Gd-DTPA@1.5T =10.7 *vs.* 4.8 L/mmol·s) and dual clearance pathway (equally divided between hepatic and renal excretion with the half-life approximately 56 minutes in plasma in subject with normal liver function) ensure an excellent safety and efficacy profile, as the two systems can compensate for each other in patients with organ impairment (27,28).

Protocols of gadoxetic acid-enhanced liver MRI

Following its regulatory approval by the National Medical Products Administration (NMPA) in 2011, gadoxetic acid-enhanced liver MRI (EOB-MRI) has undergone rigorous standardization within the Chinese healthcare system. *Figure 3* illustrates key milestones of EOB-MRI over the past 15 years. To harmonize imaging acquisition and interpretation, the abdominal group of the Chinese Society of Radiology established the first technical expert consensus in 2016, leading to the rapid inclusion of EOB-MRI in domestic clinical guidelines by 2017. Subsequently, between 2019 and 2026, the technical standards and clinical applications were iteratively refined. These updates integrated domestic clinical feedback with evolving international standards, such as those from the American Association for the Study of Liver Disease (AASLD) and LI-RADS 2018 (29-32), culminating in the 2024 and 2026 guidelines,

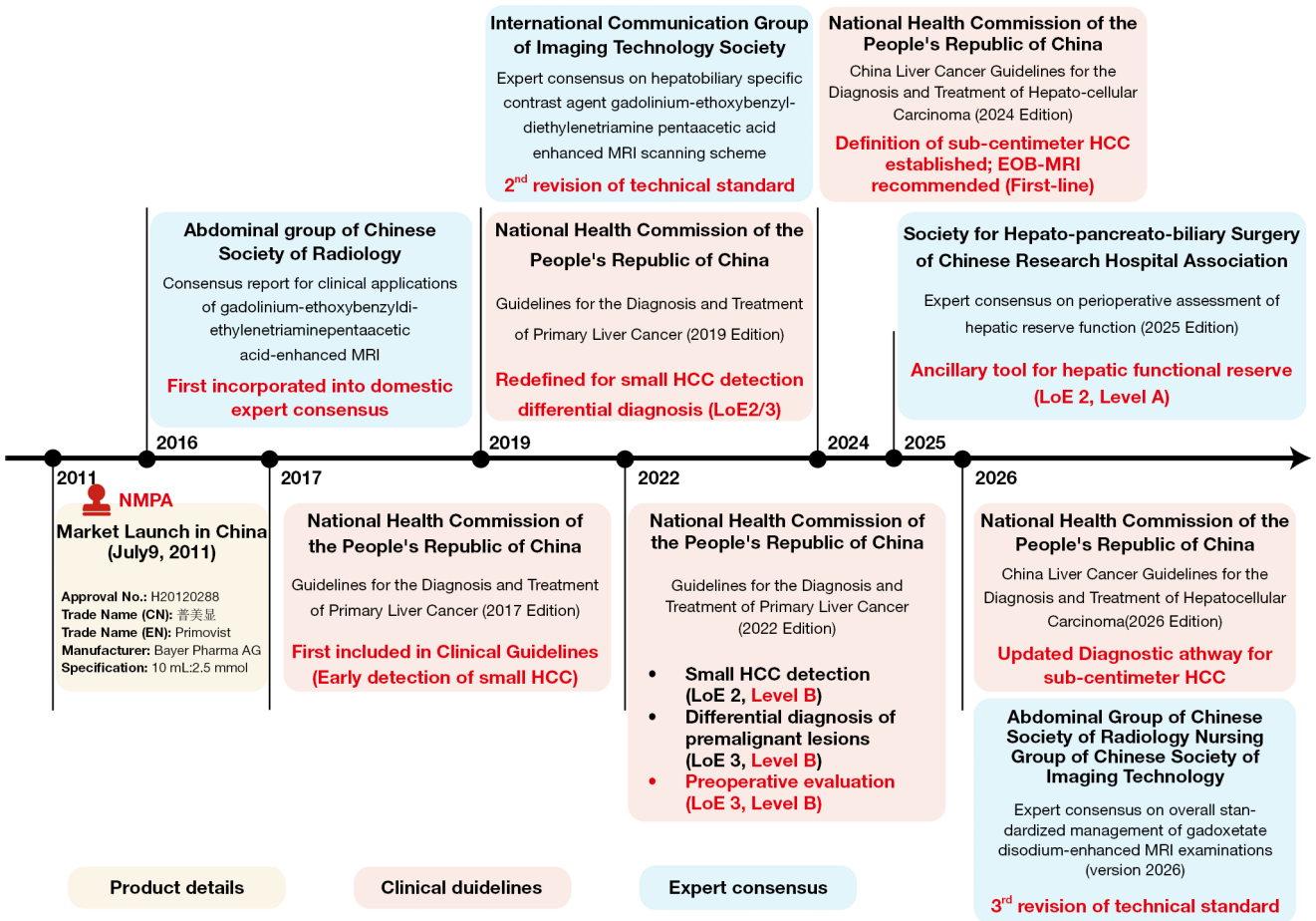


Figure 3 Timeline of development and integration of EOB-MRI into clinical practice in China. The timeline illustrates the key milestones over the past 15 years, starting from the formal market entry of EOB-MRI in 2011. It highlights the progressive adoption of EOB-MRI into major national clinical guidelines and expert consensuses from various medical societies. The increasing clinical recognition reflects its evolving role from an auxiliary tool to a core diagnostic modality for HCC in China. EOB-MRI, gadoxetic acid-enhanced magnetic resonance imaging; HCC, hepatocellular carcinoma; LoE, level of evidence.

which prioritize EOB-MRI for sub-centimeter HCC (scHCC) detection. Current standardized EOB-MRI protocols in China emphasize the following:

I. Administration: intravenous bolus injection of gadoxetic acid at a standard dose of 0.025 mmol/kg body weight (equivalent to 0.1 mL/kg body weight). A flow rate of 1 mL/s is recommended using a power injector, followed by a 20–30 mL saline flush.

II. Imaging sequences: acquisition on high-field MRI scanners (≥1.5T) with three-dimensional (3D) fat-suppressed T_1-weighted imaging (FS-T_1WI) using gradient echo sequences or 3D Dixon sequences, the latter providing a comprehensive "all-in-one" solution for simultaneous water-fat phase and proton density fat fraction (PDFF) quantification (33). In addition, respiratory-triggered fat-suppressed T_2-weighted imaging (FS-T_2WI) and diffusion-weighted imaging (FS-DWI, with b-values up to 1,000 s/mm^2) are essential components, which provide critical information to enhance diagnostic confidence (34,35).

III. Multiphasic timing: dynamic scans include pre-contrast, late arterial phase (AP, ~35 s), portal venous phase (PVP, 60–80s), and transitional phase (TP, 2–5 min). The definitive HBP is typically acquired 12–20 minutes post-injection, tailored to the patient's liver function, especially in patients with cirrhosis, where HBP may be delayed (36,37).
IV. Workflow optimization: to maximize clinical throughput, FS-T_2WI and FS-DWI are recommended for acquisition during the interval between the TP and HBP (38).

The rigorous standardization of EOB-MRI in China is dual-faceted; it combines technical adherence with proactive knowledge dissemination. Current domestic protocols strictly align with the LI-RADS 2018 definitions, ensuring that data generated across Chinese institutions are standardized for both domestic and international diagnostic interpretations and clinical decision-making (39,40). To translate these high-level standards into real-world clinical practice, systematic training and education initiatives have played a pivotal role. The Chinese Society of Radiology and various academic consortia have established nationwide workshops focusing on acquisition, artifact recognition, and structured reporting. By fostering "Center of Excellence" and mentorship programs, this educational matrix has successfully facilitated the transfer of high-end imaging expertise from tier-one medical centers to regional and community hospitals. Consequently, the diagnostic benefits of EOB-MRI are no longer confined to elite institutions but are consistently accessible throughout China's tiered healthcare system, ensuring a uniform quality of care for the nation's vast patient population.

Chinese diagnostic strategies of gadoxetic acid-enhanced liver MRI

In Chinese clinical practice, the diagnostic strategy for EOB-MRI is characterized by a high reliance on its unique functional imaging capabilities to achieve early HCC diagnosis. As guided by the domestic expert consensus of the Chinese National Liver Cancer (CNLC) guidelines, EOB-MRI is currently prioritized as a frontline diagnostic tool, sharing equal diagnostic weight with contrast-enhanced CT (CECT) and extracellular contrast media-enhanced MRI (ECCM-MRI) (41-44). The "Chinese Strategy" is rooted in a sensitivity-oriented approach, which emphasizes the critical role of HBP hypointensity as a primary indicator for identifying scHCCs (≤1 cm) and high-grade dysplastic nodules (HGDN), which may appear iso-vascular on conventional dynamic imaging. However, this proactive diagnostic framework exhibits subtle yet distinct geographic variations compared to Western strategies, e.g., the 2018 AASLD and LI-RADS guidelines (22,45), which adopt a more specificity-oriented strategy by limiting the algorithmic weight assigned to HBP findings (46). To ensure exceptional specificity and minimize false positives, Western guidelines adopt a stricter criterion for non-invasive HCC diagnosis, categorizing HBP hypointensity as an ancillary feature rather than a major diagnostic criterion (39). Nevertheless, this conservative diagnostic weighting does not diminish the extensive frontline utilization of EOB-MRI in Western clinical practice, where it is widely employed for early lesion detection, precise tumor staging, and differential diagnosis. Furthermore, a key technical divergence exists in the definition of "washout": while Chinese and other Eastern guidelines increasingly recognize the value of HBP imaging to trigger early locoregional therapies such as radiofrequency ablation (RFA), Western protocols strictly confine washout assessment to the PVP when using EOB-MRI. This restriction is designed to avoid "pseudo-washout" in the TP, thereby ensuring the high specificity required for irreversible clinical curative strategies, e.g., liver transplantation (47). Given these lingering programmatic divergences and the critical need to harmonize regional practice with emerging data-driven paradigms, a systematic retrospection is warranted. Consequently, this review comprehensively summarizes its 15-year clinical evolution within the Chinese healthcare system, exploring its pharmacological benefits, advanced applications, and future integration with data-driven frameworks. We present this article in accordance with the Narrative Review reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-2026-1127/rc).

Methods

To ensure transparency and methodological rigor, a comprehensive literature search was conducted across major electronic databases, including PubMed, Web of Science, and China National Knowledge Infrastructure, spanning from 2011 to 2026, for peer-reviewed articles published. The search strategy employed combinations of medical subject headings terms and free-text keywords, including: ("gadoxetic acid" OR "Gd-EOB-DTPA" OR "gadolinium ethoxybenzyl-diethylenetriamine pentaacetic acid" OR "EOB-MRI"), ("hepatocellular carcinoma" OR "HCC"), ("artificial intelligence" OR "deep learning" OR "radiomics"), and ("China" OR "Chinese") (*Table 1*). Literature selection prioritized original research articles, consensus statements, clinical guidelines, and high-impact reviews. Studies were included if they provided direct insights into diagnostic or prognostic performance, multi-modal integration, or clinical translation of EOB-MRI, with a specific focus on comparative data contrasting regional clinical workflows with international practice standards. Articles not published in English or Chinese, or lacking robust validation cohorts, were excluded.

Table 1 The search strategy summary

Items	Specification
Date of search	April 15, 2026
Database searched	PubMed, Web of Science, and China National Knowledge Infrastructure
Search terms used	("gadoxetic acid" OR "Gd-EOB-DTPA" OR "gadolinium ethoxybenzyl-diethylenetriamine pentaacetic acid" OR "EOB-MRI") AND ("hepatocellular carcinoma" OR "HCC") AND ("artificial intelligence" OR "deep learning" OR "machine learning" OR "radiomics") AND ("China" OR "Chinese")
Timeframe	July 9, 2011–April 15, 2026
Inclusion and exclusion criteria	Inclusion criteria: original research articles, consensus statements, clinical guidelines, and high-impact reviews
	Exclusion criteria: literature published not in English and Chinese, or lack robust validation cohorts
Selection process	Three authors (Y.L., X.C., K.Z.) conducted an independent literature search and finally determined the relevant published peer-reviewed papers

Discussion

Transformative clinical impact on the Chinese healthcare system

Over the past 15 years, EOB-MRI has redefined the clinical management of liver diseases within the Chinese healthcare system (48). As illustrated in *Figure 4*, this evolutionary impact is rooted in the unique hepatocyte-specific uptake mechanism of Gd-EOB-DTPA, which allows for a paradigm shift from traditional morphological assessment to functional evaluation at the cellular level. A pivotal milestone in this progression was the inclusion of Gd-EOB-DTPA in the 2021 national volume-based procurement program, where the mandated annual procurement volume exceeded 1.5 million units. This unprecedented scaling of clinical accessibility has solidified EOB-MRI as a standard of care. By delivering superior performance in the detection and characterization of FLLs across multiple sequences —including DWI and HBP—it holds the potential to optimize clinical pathways by facilitating early intervention. This technological superiority supports a more refined clinical framework across four key dimensions: precision oncology, individualized treatment planning, functional liver evaluation, and rigorous recurrence surveillance. Encompassing tasks from pre-operative biological risk stratification [e.g., microvascular invasion (MVI) and tumor grading] to voxel-level functional volumetric assessment,

EOB-MRI has evolved from a subsidiary diagnostic tool into a cornerstone of precision hepatology (49). This paradigm shift has not only shortened the interval from FLL detection to definitive diagnosis but also minimized the necessity for confirmatory diagnostic procedures, such as invasive liver biopsy (50). Currently, EOB-MRI is increasingly integrated into clinical workflows aligned with the "Healthy China 2030" national strategy, which sets a target of increasing the overall 5-year survival rate of cancer patients by 15% (51). Importantly, while improved diagnostic accuracy serves as a necessary prerequisite, it does not automatically guarantee superior long-term clinical outcomes. Although robust prospective data directly linking EOB-MRI to prolonged overall survival are still accumulating (52), its capability in bridging microscopic pathophysiology with macroscopic diagnostics has demonstrated an established capacity to refine therapeutic decision-making and optimize diagnostic algorithms for China's HBV-dominant population.

Precision oncology: early-stage and scHCC detection

Typically, HCC manifests as non-rim AP hyperenhancement (APHE), PVP washout, and HBP hypointensity. This signature is driven by unique tumor angiogenesis and hepatocyte dysfunction: as HCC progresses, it gradually loses portal venous supply and develops unpaired arteries, leading to the characteristics of a "wash-in, wash-out" pattern compared to the background parenchyma (53,54). Furthermore, the impaired OATP1B3-mediated uptake of gadoxetic acid—which often precedes hemodynamic shifts—results in distinct HBP hypointensity, enabling superior detection of early-stage and scHCC lesions that frequently lack the classic APHE/PVP washout features required for diagnosis via CECT and ECCM-MRI (55,56). Meta-analyses confirm that EOB-MRI achieves a significantly higher sensitivity for ≤2 cm (0.82) and ≤1 cm (0.46) compared to CECT (0.53 and 0.20, respectively) (57). In China, where HBV accounts for more than 75% of the etiological factors of liver cirrhosis, HCC predominantly evolves through classical multistep carcinogenesis, i.e., from regenerative nodule (RN) and dysplastic nodule (DN) to overt HCC. In such a distorted cirrhotic liver background, the ability of HBP hypointensity to distinguish suspicious early-stage HCC from RN or DN—especially identifying the "nodule-in-nodule" appearance—is critical for timely curative intervention (58,59). Beyond diagnostic accuracy, total diagnosis and treatment cost per patient after the initial EOB-MRI (¥30,360) evaluation demonstrates superior health economic benefits through resolving diagnostic uncertainty and reducing the additional cost for repeated imaging and invasive biopsy compared with ECCM-MRI (¥31,465) and CECT (¥30,803) (50), streamlining clinical management towards earlier, potentially curative local treatment strategies such as resection or RFA. Consequently, the adoption of EOB-MRI in China potentially expands the eligibility window for these curative therapies. While future longitudinal studies are required to systematically determine whether this staging migration definitively translates into hard survival endpoints, current evidence indicates that it substantially optimizes intermediate patient management and healthcare resource allocation by preventing "diagnostic wandering" and redundant follow-up imaging, demonstrating a substantial cost-effective advantage (60,61).

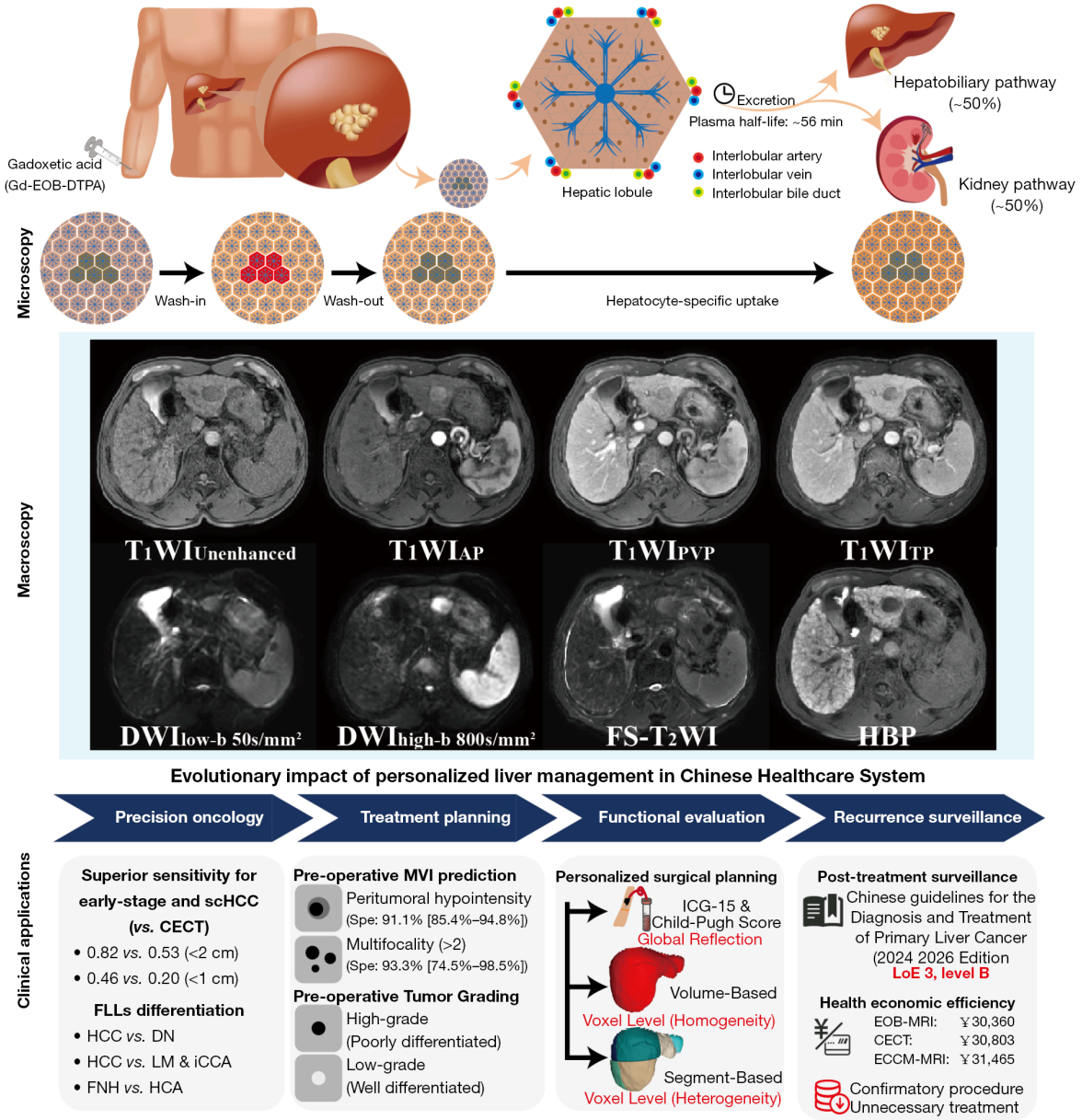


Figure 4 Transformative clinical applications of EOB-MRI in the Chinese healthcare system. The unique biphasic pharmacokinetic properties facilitate a "wash-in" and "wash-out" pattern in the dynamic phase and a characteristic hypointensity in the HBP, as shown in the representative patient (67-year-old male) with HCC (25 mm). The clinical integration of EOB-MRI extends personalized management of liver cancer through precision diagnosis; risk stratification by preoperative prediction of MVI and tumor grading; surgical planning as guided by voxel- and segment-based liver function evaluation; and recurrence surveillance adhering to domestic clinical guidelines, resulting in enhanced economic efficiency. AP, arterial phase; CECT, contrast-enhanced computed tomography; DN, dysplastic nodule; DWI, diffusion-weighted imaging; ECCM-MRI, extracellular contrast media-enhanced magnetic resonance imaging; EOB-MRI, gadoxetic acid-enhanced liver magnetic resonance imaging; FLL, focal liver lesion; FNH, focal nodular hyperplasia; FS-T2WI, fat-suppressed T2-weighted imaging; Gd-EOB-DTPA, gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid; HBP, hepatobiliary phase; HCA, hepatocellular adenoma; HCC, hepatocellular carcinoma; iCCA, intrahepatic cholangiocarcinoma; ICG-15, indocyanine green retention test at 15 minutes; LM, liver metastasis; LoE, level of evidence; MVI, microvascular invasion; PVP, portal venous phase; scHCC, sub-centimeter HCC; Spe, specificity; T1WI, T1-weighted imaging; TP, transitional phase.

Precision oncology: differential diagnosis for FLL

The clinical integration of EOB-MRI has fundamentally shifted the diagnostic paradigm for FLLs from traditional morphological assessment to hepatocyte-level functional imaging. This advancement stems from the agent's dual-property profile: dynamic vascular enhancement and hepatocyte-specific uptake mediated by OATP1B3 transporters. This synergy enables high-precision differentiation between hepatocyte-containing lesions [i.e., focal nodular hyperplasia (FNH)] and non-hepatocyte-containing or dysfunctional lesions (i.e., liver metastases or atypical hemangioma) (62).

Early HCC *vs.* DNs

In China's HBV-dominated landscape, the differentiation between DN and early HCC presents a critical diagnostic cornerstone for managing liver cirrhosis (63). This distinction is clinically imperative as it dictates the therapeutic trajectory: while DNs typically require "watchful waiting" through stringent surveillance, early HCC necessitates immediate curative intervention. Conventional extracellular MRI contrast agents often struggle with this differentiation, as they primarily rely on the "wash-in and wash-out" pattern that is frequently absent in isovascular or hypovascular early-stage lesions, leading to high false-negative rates in cirrhotic livers (64). EOB-MRI overcomes this limitation by shifting the diagnostic focus from hemodynamic changes to functional molecular alterations (65). Crucially, the downregulation of OATP1B3 transporters typically precedes the neo-angiogenesis required for arterial hyperenhancement. Consequently, most early HCCs manifest as distinctly hypointense on HBP, while low-grade DNs (LGDN) often remain iso- or hyperintense due to preserved transporter function (66). However, this biological transition is highly complex and non-linear, as a profound reduction in OATP1B3 expression can already occur during the advanced pre-malignant phase. Consequently, HGDN frequently exhibit HBP hypointensity, creating a substantial radiological overlap with early HCC that presents a recognized diagnostic challenge. Furthermore, the correlation between OATP1B3 expression and malignancy is not strictly linear: approximately 10% of well-to-moderately differentiated HCCs paradoxically retain or even overexpress OATP1B3, manifested as iso- or hyperintensity on HBP, a phenomenon driven by the abnormal activation of the Wnt/β-catenin signaling pathway (66). This molecular heterogeneity underscores that HBP signals can't be interpreted categorically; instead, they reflect a continuous spectrum of cellular dedifferentiation. This functional divergence underscores that while EOB-MRI offers superior pooled sensitivity and high diagnostic performance for identifying malignant transformation at its earliest inception, interpreting HBP signals requires a nuanced understanding of these molecular variations to guide stage-appropriate management strategies (67).

HCC *vs.* liver metastasis (LM) and intrahepatic cholangiocarcinoma (iCCA)

LM and iCCA represent major malignant burdens in hepatic oncology. Approximately 70% of patients with colorectal cancer eventually develop LM via hematogenous dissemination (68). Given their non-hepatocellular origin and the absence of OATP1B3 expression, LM lesions manifest as exquisitely "black holes" (marked hypointense) against the hyperintense liver parenchyma in HBP (69,70). This high contrast-to-noise ratio (CNR) facilitates unparalleled clinical sensitivity for detecting micro-metastases (≤1 cm), thereby refining pre-operative staging and optimizing therapy. Concurrently, the clinical landscape of iCCA in China is evolving due to the rising prevalence of metabolic syndromes and viral hepatitis, which increasingly overlaps its risk profile with HCC. Presently, iCCA is the second most common primary liver cancer (approximately 10% to 15%) after HCC (71,72). EOB-MRI transcends hemodynamic overlaps by characterizing the distinct cellular and stromal components in the HBP (73). Unlike HCC, where global hypointensity results from the malignant downregulation of OATP1B3 transporters, iCCA is characterized by its prominent desmoplastic stroma. In HBP, this distinct histological architecture typically manifests as a "targetoid appearance", which is structurally driven by a

dual-component tissue kinetic profile: the peripheral hypointense rim corresponds to the dense layer of viable tumor cells that lack functional OATP1B3 expression and thus fail to take up the agent, whereas the relatively hyperintense or progressively stained central core mirrors the fibrous stroma where the contrast agent becomes structurally sequestered within the expanded extracellular matrix due to delayed interstitial clearance (74). Although this targetoid signature is highly characteristic of iCCA, it is not entirely pathognomonic, as notable radiological overlap can occur with combined HCC-cholangiocarcinoma (cHCC-CCA) and certain hypovascular LM. Nevertheless, when contextualized with clinical biomarkers and early dynamic vascular phases, this HBP feature serves as a valuable clinical clue that substantially narrows the differential diagnosis.

FNH *vs.* hepatocellular adenoma (HCA)

FNH and HCA predominantly affect young to middle-aged women, posing a frequent diagnostic challenge in hepatology (75). FNH, the second most common benign liver tumor after hemangioma, is regarded as a regenerative response to localized vascular anomalies. Whereas HCA is a rare but clinically significant monoclonal epithelial tumor associated with prolonged oral contraceptive use. These divergent pathologies dictate distinct clinical management strategies: FNH is typically asymptomatic and requires no interventions; conversely, HCA carries a 4.2% to 10.6% risk of spontaneous hemorrhage or malignant transformation into HCC (76). Before the advent of gadoxetic acid, the differential diagnosis between FNH and HCA posed a significant diagnostic dilemma due to their shared hypervascular nature and isointense appearance on the delayed phase (equivalent to TP in EOB-MRI) in extracellular contrast agents. These radiological overlaps frequently necessitated invasive biopsies or preemptive resection to mitigate the potential risks of complications associated with HCA. The HBP manifestation facilitates superior differential diagnostic accuracy between FNH and HCA, owing to their divergent molecular and structural characteristics (77). FNH, which overexpresses OATP1B3 transporters and exhibits impaired biliary excretion, typically presents as hyper- or isointense on HBP. Conversely, significant downregulation or absence of the OATP1B3 transporters in most HCA subtypes during neoplastic transformation precludes the intracellular uptake of gadoxetic acid, resulting in HBP hypointensity. A recent meta-analysis reported excellent diagnostic performance of EOB-MRI for differentiating FNH and HCA with a pooled area under the curve (AUC) of approximately 0.98 (sensitivity 0.917, specificity 0.952) (78). By utilizing the specific HBP uptake, clinicians can confidently transition from a 'biopsy-first' to an 'imaging-first' paradigm, thereby minimizing procedural risks and morbidity while optimizing diagnostic assessment (17).

Treatment planning: pre-operative MVI prediction and tumor grading

Beyond its diagnostic utilities, EOB-MRI has emerged as a transformative tool for the preoperative prediction of MVI and tumor histological grading—both of which are pivotal determinants of HCC prognosis. Identifying microscopic tumor emboli within the portal venous system—the pathophysiological hallmark of MVI—serves as a pivotal factor in curative treatment selection, such as surgical resection *vs.* RFA. Notably, RFA has been demonstrated to be less effective for reducing the early recurrence rate for MVI-positive HCCs, with a 2-year recurrence rate reaching approximately 90% (79). While MVI status traditionally relies on post-operative histopathology, recent evidence has linked EOB-MRI features to its presence. For instance, "peritumoral hypointense" on HBP and multifocality (N2) have demonstrated remarkably high specificity of 0.911 [95% confidence interval (CI): 0.854–0.948] and 0.933 (95% CI: 0.745–0.985), respectively, for predicting MVI (79). Furthermore, EOB-MRI serves as a "virtual biopsy" for assessing tumor differentiation: low-grade (well-differentiated) HCCs may occasionally retain OATP1B3 function, appearing iso- or hyper-intense on HBP. In contrast, high-

grade (poorly differentiated) HCCs predominantly exhibit profound hypointensity due to the functional loss of hepatocyte phenotype. This predictive capability facilitates a shift toward personalized surgical oncology: patients preoperatively predicted to be at high risk for MVI-positive or harboring high-grade tumors may derive greater benefit from anatomical resection with wider margins or early consideration for liver transplantation, rather than narrow-margin non-anatomical resection. Consequently, the preoperative prediction of MVI—currently supported by regional expert consensus (Evidence Level 2)—along with EOB-MRI-based tumor grading, effectively bridges the gap between radiological features and individualized surgical intervention (80).

Functional evaluation: quantitative assessment of hepatic functional reserve (HFR)

EOB-MRI further enables comprehensive quantitative assessment of HFR, a valuable clinical adjunct for reducing the risk of post-hepatectomy liver failure (PHLF) (81,82). Traditionally, preoperative planning relies on CT- or MRI-based liver volumetry to estimate the future liver remnant (FLR) volume (83). However, these anatomical measurements assume uniform hepatocyte function, which can be misleading in patients with underlying parenchymal diseases. Unlike conventional biochemical markers [e.g., Child-Pugh score (84) or the indocyanine green (ICG) clearance rate (85)] or anatomical volumetry, which are inherently limited to providing global assessments, EOB-MRI allows for segment-specific functional mapping, capturing spatial heterogeneity within the liver. A key metric in this assessment is the relative enhancement (RE) of liver parenchyma, which exhibits a strong inverse correlation with ICG-R15, the clinical "gold standard" for HFR (86). Beyond RE, advanced quantitative parameters, such as the liver-to-muscle ratio, hepatic uptake index (HUI), and T_1 relaxation time mapping, have emerged as robust radiological surrogates for localized liver function (87-89). By integrating these functional parameters with anatomical volume, EOB-MRI enables surgeons to evaluate the functional capacity of FLR with enhanced spatial accuracy (90). This is particularly crucial for patients with heterogeneous liver diseases, such as cirrhosis or post-chemotherapy sinusoidal obstruction syndrome, where anatomic FLR volume may overestimate actual functional reserve (91). By facilitating a transition from crude volumetric estimation to functional-volumetric integration, EOB-MRI provides a sophisticated safety framework for complex hepatic resections. This integrated approach is increasingly recognized as a cornerstone of personalized surgical planning, a shift currently supported by regional guidelines with Evidence Level 2 (92).

Recurrence surveillance: enhancing surveillance in post-treatment recurrence

The clinical utility of EOB-MRI extends into the critical phase of post-treatment surveillance, where early detection of recurrence is paramount for improving long-term survival. Traditional ECCM-MRI and CECT scans often struggle to distinguish between treatment-induced alterations, such as post-RFA inflammation zones or post-chemoembolic scarring, and true tumor recurrence (93). EOB-MRI addresses these limitations by leveraging the HBP to identify "signal-void" nodules. Specifically, recurrent HCC lesions, characterized by a lack of functional OATP1B3 transporters, manifest as distinct hypointense nodules against the background of liver parenchyma that has regained contrast uptake. Moreover, EOB-MRI exhibits remarkable sensitivity for multicentric occurrence—new primary lesions arising from the field cancerization of a cirrhotic liver—which are often too small to be characterized by conventional imaging (94). The high CNR in HBP allows for the detection of sub-centimeter recurrent nodules that may be isovascular during the dynamic phase. This enhanced sensitivity facilitates early intervention through secondary resection or localized RFA, shifting the surveillance paradigm from "reaction observation" to "proactive interception". Reflecting its clinical importance, the latest Chinese

Guidelines for the Diagnosis and Treatment of Primary Liver Cancer now formally recommend EOB-MRI as a key imaging modality for rigorous postoperative surveillance every three months (Evidence Level 3, Recommendation B) (44). Consequently, the integration of EOB-MRI into standardized follow-up protocols ensures a more rigorous monitoring of the oncogenic field, providing a robust validation framework for patients after curative-intent therapies.

Health economic efficiency within the Chinese healthcare system

The widespread adoption of EOB-MRI has introduced an incremental cost-benefit advantages in the health economic landscape of liver disease management in China. Traditionally, the higher unit cost of EOB-MRI compared to CECT or ECCM-MRI was perceived as a financial barrier. However, current evidence indicates that EOB-MRI is economically justifiable when evaluated across the entire diagnostic-therapeutic trajectory (61). By increasing the sensitivity for early-stage HCC and micro-metastases, EOB-MRI helps mitigate the "diagnostic odyssey"—the costly and time-consuming cycle of indeterminate follow-up scans and invasive liver biopsies. Furthermore, its superior performance in pre-operative staging prevents expensive, ineffective surgical interventions for patients with undetected multifocal disease. At the same time, its role in functional-volumetric assessment reduces the incidence of high-cost complications such as PHLF. Within the framework of the "Healthy China 2030" initiative, the integration of EOB-MRI into standardized clinical pathways has been shown to optimize the allocation of medical resources. Importantly, while the absolute difference in total diagnostic and treatment costs per patient may appear modest at an individual level, these savings scale up to a substantial economic benefit when projected onto China's massive HBV-dominant and HCC high-risk populations. Therefore, when considering the total healthcare expenditure, including the costs of redirected treatments and avoided complications, EOB-MRI serves as a cost-effective option that balances clinical outcomes and long-term economic efficiency for the Chinese healthcare system (50,95).

This economic framework is further supported by the ongoing structural reforms in China's medical reimbursement landscape. Under the current implementation of diagnostic-related groups (DRG) and big data-applied diagnosis and intervention groups (DIP), the economic evaluation of medical technologies has shifted from single-item pricing to bundle-payment efficiency (96). In this context, the integration of EOB-MRI into clinical pathways offers an analytical tool for hospitals to optimize operational efficiency under stringent global budget management. Coupled with the nationwide volume-based procurement for contrast media—which has substantially lowered the financial threshold for high-end imaging—EOB-MRI facilitates a streamlined "One-stop-shop" diagnostic workflow. By providing high-confidence characterization in a single session, it effectively reduces the length of stay and avoids the accumulation of redundant expenses from serial indeterminate scans or invasive biopsies—costs that often exceed DGR/DIP payment thresholds. Furthermore, by mitigating the risk of high-cost post-operative complications through superior pre-operative staging, EOB-MRI helps the hepatology departments maintain economic sustainability. Consequently, EOB-MRI has become a value-congruent diagnostic modality that aligns clinical excellence with the fiscal rigor of the modern Chinese healthcare system, ensuring that the "Healthy China 2030" goals are met through both medical and economic optimization.

From visual semiotics to computational biomarkers: the data-driven paradigm shift

The landscape of diagnostic radiology is undergoing a fundamental paradigm shift, moving from traditional qualitative semiotics to high-throughput data-driven analytics (47). Historically, the interpretation of EOB-MRI relied predominantly on the "trained eye" of radiologists to identify discrete morphological features, such as enhancement patterns or border regularity. While clinically

indispensable, this traditional approach is inherently constrained by inter-observer variability and a pervasive "semantic gap"—a limitation where the profound biological heterogeneity of HCC is oversimplified into limited, subjective descriptive terms (97).

In the era of computational imaging, EOB-MRI is no longer viewed merely as visual images, but as a repository of mineable data snapshots that reflect the underlying tumor microenvironment and hepatocyte function (98). As illustrated in *Figure 5*, this data-driven framework facilitates the conversion of visual semiotics (e.g., HBP hypointensity) into high-throughput computational markers via radiomics and deep learning. By leveraging advanced computational techniques, such as radiomics and deep learning (e.g., convolutional neural network and vision transformers), research can now extract thousands of quantitative features—including spatial distribution, texture heterogeneity, and wavelet-transformed signals—that remain imperceptible to human vision. This evolution from "visual inspection" to "computational phenotyping" enables a more granular understanding of liver disease through hierarchical multi-scale frameworks: transitioning from macroscale visual semiotics and mesoscale computational markers to microscale pathology (radiopathomics) and ultimately nanoscale biological genotype (radiogenomics) (99).

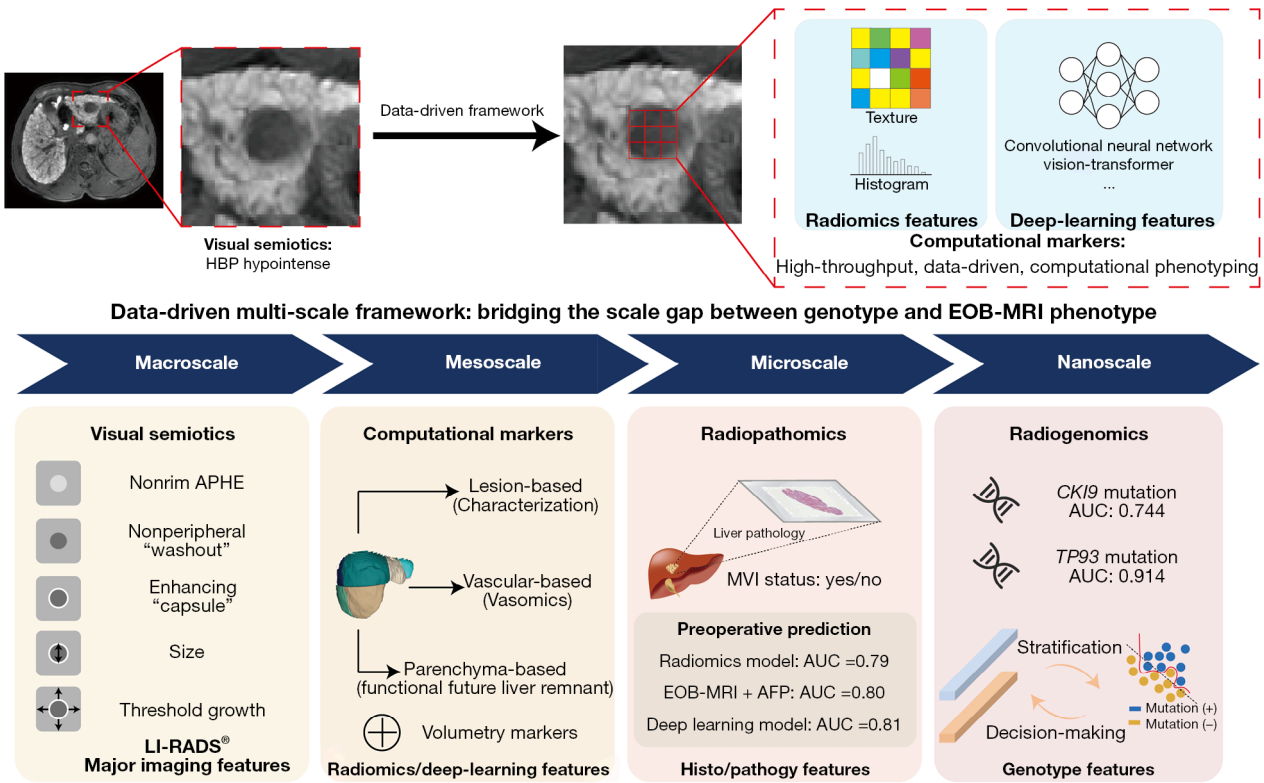


Figure 5 The comprehensive data-driven multi-scale framework for bridging the gap between EOB-MRI phenotypes and biological genotypes. Visual semiotics are converted into quantitative mesoscale computational markers via radiomics (texture/histogram) and deep-learning features (using convolutional neural networks and vision-transformer), which are hierarchically integrated with macroscale radiological semiotics (LI-RADS), microscale histopathology (e.g., MVI status), and nanoscale radiogenomics (e.g., CK19/TP53 mutations). This framework facilitates preoperative prediction and clinical decision-making through multi-dimensional patient stratification. AFP, alpha-fetoprotein; APHE, arterial phase hyperenhancement; AUC, area under the curve; EOB-MRI, gadoxetic acid-enhanced magnetic resonance imaging; HBP, hepatobiliary phase; LI-RADS, Liver Imaging Reporting and Data System; MVI, microvascular invasion.

Automatic quantitative EOB-MRI processing framework

The unique hepatocyte-specific uptake of gadoxetic acid enables it to function as both a contrast agent and a functional tracer for the direct visualization of liver metabolism. Compared to conventional markers such as the Child-Pugh score or the ICG clearance test, EOB-MRI offers superior spatial resolution —a critical advantage in cirrhotic patients where liver function is often highly heterogeneous. This capability has unlocked the potential for voxel-wise quantification, allowing for a granular assessment of localized HFR (100). By leveraging automated deep-learning segmentation tools, such as nnUNet (101), sophisticated models derived from EOB-MRI data now facilitate automated Couinaud liver segmentation and 3D liver function assessment (102). This approach allows for the precise calculation of the functional FLR (fFLR), moving beyond the crude volumetric inherent in conventional imaging. Notably, these data-driven frameworks have recently expanded to include vasomics—the high-throughput quantitative features extracted from the hepatic vascular architecture (103). By analyzing the structural remodeling of the portal and hepatic venous systems, vasomics provides a macroscopic reflection of portal hypertension and underlying parenchymal stiffness, complementing the metabolic data from EOB uptake. Most importantly, these tools are highly computationally efficient, with execution times reduced to seconds on consumer-grade graphics processing units (e.g., NVIDIA RTX 3090), representing a significant order-of-magnitude acceleration compared to the labor-intensive manual contouring, effectively eliminating a major bottleneck in clinical translation. Recently, T_1 mapping-based whole-liver histogram analysis on EOB-MRI demonstrated superior PHLF prediction and risk stratification performance over the ICG clearance test and the albumin-bilirubin scores system (104). Furthermore, the integration of EOB-MRI images-derived HUI with clinical biochemical markers to predict PHLF has demonstrated significantly higher accuracy than the traditional clinical score system (AUC: 0.802 *vs.* 0.628) (88). The synergy of these image-derived functional and vasomic parameters within automated workflows holds great promise for refining surgical decision-making and enhancing patient safety. Consequently, this transition from "static biochemical testing" to "dynamic, spatially-resolved functional mapping" represents a cornerstone of personalized surgical planning and long-term prognostic monitoring in chronic liver disease.

Radiopathomics for precision preoperative MVI prediction

MVI, a key histological indicator of aggressive biological behavior, is a critical risk factor for postoperative recurrence in HCC. Its presence often necessitates extended surgical margins, even in early-stage HCC. However, the current diagnosis of MVI remains dependent on postoperative histopathologic examination, which precludes preoperative treatment optimization. Consequently, establishing non-invasive biomarkers from preoperative imaging presents an active area of exploratory research for individualized surgical planning (105). Conventional radiological signs on EOB-MRI—such as non-smooth tumor margins, incomplete capsules, and peritumoral hypointensity on the HBP—provide valuable clues for MVI; however, their clinical utility is limited by moderate sensitivity (ranging from 31.7% to 69.8%) and inter-observer variability (ranging from 0.64 to 0.88) (106). To bridge these limitations, recent studies explored the feasibility of leveraging data-driven radiomics and deep learning architectures. By treating liver images as a high-dimensional feature space, these models attempt to capture complex, non-linear correlations between subtle imaging signatures and pathological outcomes. Specifically, Zheng *et al.* established a radiomics model leveraging EOB-MRI images from 85 patients with HCC <5 cm and achieved MVI prediction with an AUC of 0.79 (107). Furthermore, Wei *et al.* deployed a deep learning model using EOB-MRI images from 5 domestic hospitals of 750 HCCs and achieved appealing retrospective MVI prediction capability, which is significantly higher than the deep learning model developed using CECT images of the same cohort (AUC: 0.812 *vs.* 0.736) (108). Moving beyond pure imaging features, Jiang *et al.* developed an integrated MVI scoring system by combining

five EOB-MRI features with serum alpha-fetoprotein (AFP) levels. By employing a machine learning-based multivariable analysis to optimize weight factors, this synergistic approach achieved an AUC of 0.80 in an external validation set (109). These advancements underscore the potential for objective, non-invasive MVI risk stratification to guide the selection between anatomical and non-anatomical resection, ultimately holding the promise of improving long-term patient outcomes.

Radiogenomics for precision molecular phenotypes and gene expression prediction

The molecular heterogeneity of HCC significantly dictates therapeutic response and long-term prognosis (110). Specifically, Wnt/β-catenin mutations—present in approximately 25–35% of HCC cases—are characteristic of a "cold" immune microenvironment characterized by T-cell exclusion, which frequently leads to primary resistance to immune checkpoint inhibitors (111). In contrast, *TP53* mutations and the progenitor cell phenotype (e.g., *CK19* positive) typically signify aggressive tumor biology and suboptimal outcomes following conventional resection or transarterial chemoembolization (TACE) (112). While invasive needle biopsies remain the "gold standard" for confirming these molecular alterations, their clinical utility is hampered by spatial heterogeneity and procedural risks, precluding routine preoperative genomic profiling. The emergence of radiogenomics offers an exploratory, non-invasive approach by mapping high-dimensional EOB-MRI features onto the tumor's underlying molecular landscape (113). Data-driven frameworks attempt to circumvent biopsy limitations by treating the heterogeneous uptake of gadoxetic acid—governed by the expression of OATP1B3 and MRP transporters—as a macroscopic proxy for the genomic profile. For instance, Wnt/β-catenin mutation tumors often exhibit paradoxical iso- or hyper-intensity on the HBP due to OATP1B3 overexpression, whereas the progenitor cell phenotype typically shows profound HBP hypointensity reflecting functional transporter loss (114,115).

Leveraging these imaging signatures, several sophisticated models have demonstrated high predictive accuracy. Recently, Chen *et al.* developed a deep learning radiomics nomogram for non-invasive *CK19* status prediction, significantly outperforming traditional clinical-radiologic models in both internal (AUC: 0.794 *vs.* 0.614) and external (AUC: 0.744 *vs.* 0.600) validation cohorts (116). Furthermore, Jia *et al.* constructed an EfficientNetV2-based model that integrates multi-sequence data (T_1-AP, T_1-PVP, T_2WI, and HBP) to achieve excellent retrospective performance in predicting *TP53* mutation status (AUC: 0.914) (117). Such capabilities enable the preoperative identification of patients who may be refractory to immunotherapy but responsive to targeted agents, or those requiring wider surgical margins due to progenitor traits. Consequently, these findings highlight the prospective value of EOB-MRI as an investigational adjunct in precision oncology, offering a potential tool for non-invasive phenotypic research and risk stratification.

Towards data-driven personalized precision medicine: future outlook and challenges

The paradigm shift from traditional radiological semiotics to data-driven frameworks is gradually expanding the investigative scope of EOB-MRI. Emerging evidence underscores the theoretical feasibility of constructing a comprehensive, multidimensional profile of both the liver parenchyma and the FLL within a single diagnostic session. By bridging the gap between macroscopic imaging and microscopic molecular biology, the synergy of radiomics and deep learning provides a promising research scaffold that complements individual visual signs (118). However, a critical gap remains between retrospective predictive performance and established clinical utility (119). The analytical power of this data-driven evolution currently lies in its exploratory decision-support rather than real-world clinical readiness. By leveraging population-scale datasets, these models aim to facilitate individualized risk stratification that synchronizes a patient's unique HFR and vascular architecture (Section "Automatic quantitative

EOB-MRI processing framework") with tumor aggressiveness (Sections "Radiopathomics for precision preoperative MVI prediction" & "Radiogenomics for precision molecular phenotypes and gene expression prediction"). While these frameworks are envisioned to eventually aid clinicians in navigating the choice between anatomical resection and RFA or identifying candidates for neoadjuvant immunotherapy, EOB-MRI-based data-driven frameworks should currently be viewed as supplementary investigational engines rather than standalone clinical decision-makers. Looking forward, the integration of these high-dimensional imaging signatures into exploratory frameworks, such as a conceptual "digital twin" of the patient (120), represents the next frontier. Nonetheless, before these advanced analytics can be translated into standard clinical practice, they must undergo rigorous, prospective multi-center validation and formalized impact analysis to prove their safety in therapeutic decision-making and improved patient outcomes.

Strategic advantages of EOB-MRI big data research in China

Characterized by large-scale HBV-related longitudinal datasets, growing collaboration between clinical expertise and artificial intelligence (AI) methodologies, and the gradual integration of multi-regional resources, China's research landscape offers a valuable perspective on EOB-MRI. As illustrated in *Figure 6*, this collaborative framework aligns with domestic clinical resources to facilitate the evolution toward intelligent imaging. These efforts have enhanced the role of EOB-MRI, transitioning it from a routine diagnostic tool into a key component for data-intensive precision oncology. This framework is built upon four foundational dimensions at the strategic level: (I) HBV-dominant cohorts, providing substantial disease-specific datasets; (II) multi-modal data repositories, enabling a radiology-pathology-genomics analytical framework; (III) Med-Engineering integration, fostering a "physician-in-the-loop" ecosystem; and (IV) policy-driven collaboration, guided by national initiatives such as "Data Element+" and "AI+ Healthcare".

Epidemiological scale and HBV-dominant cohorts

The most distinctive epidemiological reality in EOB-MRI research within China is the large scale of its patient population, characterized by a unique disease etiology. Unlike Western cohorts, where HCC predominantly arises from HCV infection or MASLD, approximately 80% of China's HCC burden —which accounts for nearly half of the global total—is linked to chronic HBV infection (121). This etiological contrast provides researchers with extensive disease-specific cohorts. In the realm of big data, this sheer volume enables the development of diagnostic algorithms specifically optimized for the "HBV-cirrhosis-HCC" progression axis. Nevertheless, while national guidelines provide a framework for uniformity, the vast geographical expanse of China introduces significant environmental and lifestyle heterogeneity. Factors such as dietary patterns, climate, and local stressors vary remarkably across provinces. For instance, northwestern China presents a unique clinical profile, shaped by semi-arid environmental conditions and specific dietary habits that may result in metabolic signatures distinct from those on the southeastern coast. Acknowledging these regional data variations is imperative for developing robust AI models that are resilient to geographical bias and tailored to the diverse characteristics within the Chinese population.

Crucially, the distinct inflammatory and fibrotic microenvironments driven by chronic HBV infection underscore the critical role of EOB-MRI, particularly in the HBP, for identifying early-stage nodules and risk-stratifying patient populations (41). While some literature suggests potential variation in the angiogenic timelines between viral and metabolic hepatocarcinogenesis pathways, direct comparative evidence on EOB-MRI remains limited. This clinical urgency is further supported by the policy

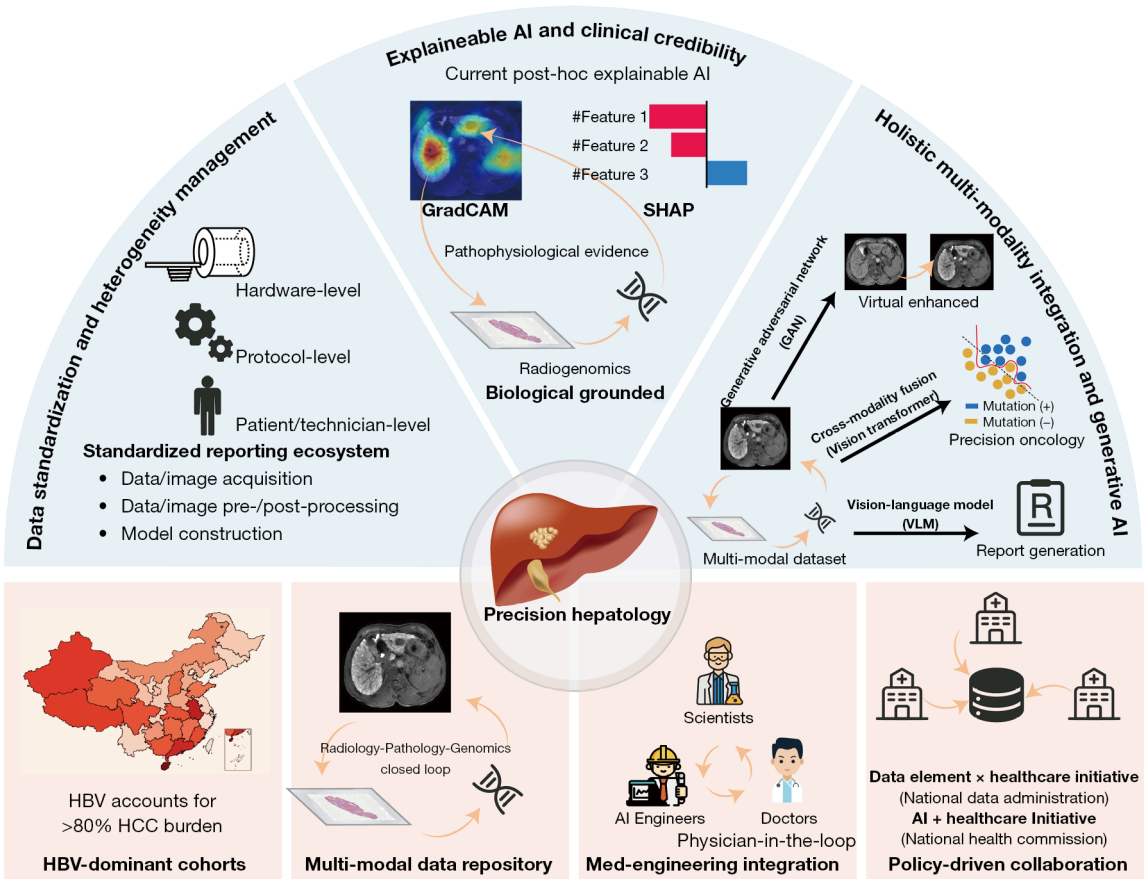


Figure 6 Strategic advantages and future directions of EOB-MRI big data research in China. China's unique research ecosystem is underpinned by four foundational strategic advantages: (I) HBV-dominant cohorts, which provide vast, disease-specific data; (II) multi-modal data repositories, enabling a radiology-pathology-genomics closed loop; (III) Med-Engineering integration, fostering "physician-in-the-loop" collaboration among clinicians, scientists, and engineers; and (IV) policy-driven collaboration, supported by the national initiatives such as "Data Element+" and "AI+ Healthcare". Building upon these foundations, three future directions are identified: (I) data standardization and heterogeneity management across multi-center protocols; (II) enhanced clinical credibility through biologically grounded explainable AI; and (III) holistic multi-modality integration leveraging generative AI, e.g., GAN and VLM, for precision hepatology. AI, artificial intelligence; EOB-MRI, gadoxetic acid-enhanced magnetic resonance imaging; GAN, generative adversarial network; GradCAM, gradient-weighted class activation mapping; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; SHAP, SHapley Additive exPlanations; VLM, vision-language model.

frameworks of the "Healthy China 2030" initiative, which promote standardized screening and expansive multi-center imaging registries linked to clinical data. Such a structured, large-scale data network has transformed the region into an active hub for hepatic AI development. By fusing radiomics and deep learning, Chinese researchers are pioneering AI tools that transcend conventional lesion detection to enable non-invasive prediction of MVI and molecular subtypes (122). Ultimately, this research paradigm not only addresses domestic clinical needs but also provides valuable insights for HBV-dominant regions worldwide, contributing to the global validation of the diagnostic and prognostic value of EOB-MRI.

Multi-dimensional data integration in the Chinese ecosystem

Beyond population scale, the horizontal and vertical integration of heterogeneous data sources creates a valuable dataset framework that characterizes contemporary EOB-MRI research within the region. Vertically, this integration seeks to connect the biological hierarchy by linking macroscopic imaging phenotypes to established proteogenomic initiatives, such as the Human Liver Proteome Project (123). By mapping EOB-MRI features—specifically peritumoral enhancement and HBP hypointensity—onto molecular landscapes, several studies have established non-invasive surrogates for critical genetic mutations (e.g., *TP53*) and distinct proteomic subtypes (124). Horizontally, this framework promotes a coordinated "radiology-pathology-genomics" analytical loop. Leveraging the massive surgical volumes in China's high-capacity centers, preoperative EOB-MRI scans are increasingly paired with digitized whole-slide imaging and longitudinal clinical records to form comprehensive multi-modal datasets. Notably, Chinese investigators have pioneered clinical-radiomic-pathomic multi-modal models, achieving encouraging performance in predicting HCC recurrence (AUC =0.863) (125). Furthermore, supported by centralized cloud-based platforms and federated learning strategies, this cross-modal fusion aims to train diagnostic algorithms that reflect the complexity of China's tiered healthcare system (126). Consequently, EOB-MRI is increasingly recognized not only as a static diagnostic tool but also a dynamic resource for whole-process management, capable of supporting clinical decision-making across diverse real-world clinical trajectories.

Rapid AI iteration driven by "Med-Engineering" fusion

The collaboration between clinical medicine and AI methodologies facilitates an active development loop between clinical expertise and algorithmic refinement. In the Chinese research landscape, this integration involves close collaboration of data scientists and clinicians within high-volume medical centers, establishing a "physician-in-the-loop" ecosystem for the annotation of nuanced EOB-MRI features. This is particularly evident in the labeling of peritumoral HBP hypointensity, a critical radiological surrogate for MVI that requires precise evaluation (127). Supported by centralized high-performance computing infrastructure and a massive surgical throughput, this synergy facilitates the rapid prototyping and prospective clinical validation of cutting-edge architectures, including vision transformers (128) and self-supervised foundation models (129). This collaborative framework accelerates the translation of raw imaging data into diagnostic tools that convert nuanced radiological expertise into objective digital biomarkers, synchronizing multi-modal evidence for precision oncology through an integrated 'detection-characterization-prognosis' pipeline, thereby narrowing the gap between bench-side algorithmic innovation and bed-side therapeutic interventions (130-132). Consequently, this "Med-Engineering" paradigm helps AI development address the specific diagnostic challenges of China's HBV-dominant population, translating localized clinical observations into reproducible methodological solutions.

Policy-driven nationwide collaborative networks: a strategic infrastructure

Driven by strategic initiatives and digital health mandates, the research landscape of China has seen increased development in multi-center EOB-MRI collaboration, aiming to connect previously isolated "data islands" through expanding networks. As depicted in *Figure 6*, this infrastructure is supported by key initiatives such as the "Data Element × Healthcare" Three-Year Action Plan [2024–2026] from the National Data Administration, and the "AI+ Healthcare" initiative from the National Health Commission (133-135). This framework encourages the standardization of imaging protocols, the formation of multi-center consortia, and the systematic connection of radiological repositories with national biobank

resources (136). By clarifying regulatory pathways for AI-based medical devices and fostering the convergence of multi-modal data, these policy frameworks help transition EOB-MRI research from fragmented pilot studies into larger, collaborative initiatives for precision hepatology (137). Ultimately, this strategic infrastructure supports the development of structured oncological data and facilitates multi-center clinical evaluation within the region.

Challenges and future directions

Despite the rapid advancements in large-scale cohort EOB-MRI research, several critical challenges remain, particularly regarding data heterogeneity across different institutions that comes from compliance of both technicians and patients in routine clinical workflow, and the interpretability of "black-box" AI models in clinical decision-making. Future research must transcend simple pattern recognition to address these hurdles before these advanced techniques are integrated into the current clinical workflow. The next frontier of AI-enabled EOB-MRI lies in data standardization for heterogeneity control, clinical credibility-driven explainable AI, the integration of generative AI, and the evolution toward holistic multi-modality AI frameworks that synchronize radiological features with biological underpinnings of liver disease. As illustrated in the upper segments of *Figure 6*, the next frontier of AI-enabled EOB-MRI is structured around three following transformative future directions:

Data standardization and heterogeneity management

The primary hurdle in large-scale EOB-MRI research is the heterogeneity of data across institutions, stemming from variation in scanner hardware, imaging protocols, technician expertise, and patient compliance. A typical clinical manifestation of this heterogeneity is transient severe motion (TSM), a phenomenon where patients experience sudden, acute dyspnea during the AP. Research indicates that the TSM occurs at a rate varying from 4.8% to 26.7%, with a pooled incidence rate of 13.0% (138), leading to severe motion artifacts that degrade image interpretation and feature extraction. Furthermore, variations in liver function and uptake time in HBP lead to inconsistent signal-to-noise ratio and CNR, ultimately complicating the standardization of deep learning features across different vendors and magnetic field strengths (139). A recent publication in *Radiology* demonstrated that only 17% (3/17) of published CT radiomic models could be properly reconstructed, and all the reconstructed models present underperformed prediction performance for programmed cell death-ligand 1 expression prediction in an independent cohort of patients with resectable non-small cell lung cancer, highlighting the sufficient information of essential items, e.g., extraction, normalization, and transformation parameters in radiomics model construction, for reproducibility (140). More importantly, when constructing data-driven radiomics or deep learning models, the clarification of data distribution, for example, the patient's liver function and the sequence timing of EOB-MRI, especially the timing of HBP, raises another critical concern regarding the "domain shift" phenomenon (141). Without granular reporting of these parameters, models trained on "optimal" data, e.g., Child-Pugh A patients with 20-minute HBP, often suffer from performance degradation when deployed in real-world cohorts with varying degrees of cirrhosis or shorter acquisition windows. This lack of transparency in data distribution hinders the development of universal harmonization techniques, such as ComBat (142) or deep learning-based domain adoption techniques (143), which require a clear understanding of the underlying site-specific variables. Therefore, future research must move beyond stagnant diagnostic performance metrics toward a standardized reporting ecosystem. This includes the mandatory disclosure of image preparation, for both data/image acquisition and data/image pre-/post-processing, and details of model constructions. Emerging research on artifact-resilient algorithms (144) and automated image quality control (145) offers

an alternative promising pathway to mitigate this data-level heterogeneity. Ultimately, the technical harmonization via advanced AI architectures with the procedural standardization of clinical variables transparency will bridge the gap between raw data variability and model robustness, paving the way for the large-scale validation and seamless clinical integration of EOB-MRI-based AI.

Explainable AI and clinical credibility

Despite the superior diagnostic and predictive performance of data-driven computational models in EOB-MRI, their inherent "black-box" nature remains a significant barrier to establishing clinical credibility. In the clinical management of liver disease, clinicians require more than a binary classification, e.g., malignant *vs.* benign or HCC *vs.* HGDN; they necessitate a transparent rationale that aligns with established radiological features, such as PVP washout or the hypointensity in the HBP. Current research primarily employs the post-hoc explainability techniques, such as gradient-weighted class activation mapping (146) or SHapley Additive exPlanations (147), to provide visual evidence of a model's focus. These tools generate saliency maps that highlight the spatial regions most influential to the model's decision, allowing radiologists to verify whether the model is focused on the lesion itself or the background noise. However, these visual explanations often lack the granularity required for subtle lesion characterization and can be susceptible to "confirmation bias", where heatmaps appear plausible but lack underlying biological logic. Furthermore, it is essential to acknowledge that AI in radiology is not a panacea. The field must balance technological enthusiasm with rigorous standardization of analysis and validation protocols (148). Modern AI models, particularly generative architectures, are susceptible to "hallucinations"—the production of plausible but anatomically incorrect features that could lead to catastrophic diagnostic errors. Moreover, models often suffer from significant performance degradation when encountering out-of-distribution data, such as images from different scanners or protocols. Therefore, moving beyond simple diagnostic accuracy metrics to emphasize real-world reliability and the detection of algorithmic failures is imperative. Future research must prioritize the development of artifact-resilient algorithms and transparent validation benchmarks to ensure that AI serves as a dependable clinical aid rather than a source of diagnostic ambiguity. To bridge this gap, future research is warranted to enhance clinical credibility through biological interpretability, which seeks to synchronize data-driven radiological features with the molecular underpinnings of liver disease. A promising research direction is the integration of radiogenomics, where EOB-MRI features are mapped to specific biological markers, such as the mutation status of the Wnt/β-catenin pathway (149). By demonstrating that the model's features correlated with the pathological grades or genetic profiles of HCC, the transition from "black-box" predictor to a biologically grounded diagnostic tool would be achieved. This synergy between data-driven intelligence and pathophysiological evidence is essential for fostering the trust of multi-disciplinary teams and ensuring the safe integration of AI models into clinical decision-making workflows.

Holistic multi-modality integration and generative AI

The final frontier of data-driven EOB-MRI research lies in the transition from unimodal pattern recognition to a holistic, multimodal diagnostic framework. While EOB-MRI provides unparalleled structural and functional insights into FLLs, clinical decisions in real-world oncology are rarely made in isolation on imaging semiotics. Future research must prioritize deep fusion strategies that synchronize radiological features with longitudinal clinical trajectories, including serum biomarkers (e.g., AFP), liver function score (e.g., Child-Pugh), and genomic expression profiles. By integrating these heterogeneous data streams, AI models such as vision transformers can evolve from simple lesion classifiers into comprehensive prognostic engines capable of predicting MVI, early recurrence, and overall survival with

improved precision. Building on this multimodal foundation, a strategic shift is occurring from "diagnostic AI" to "predictive AI". While current research primarily characterizes existing lesions, there is immense potential in leveraging computational signatures to analyze "clinically normal" livers (150). For example, applying predictive architectures to the EOB-MRI-enhanced scans of patients with chronic liver disease could help identify subtle radiomics signatures of future HCC development over medium-term follow-up periods. By monitoring the functional landscape of the liver before the onset of overt malignancy, AI could support a transition from reactive treatment to proactive risk stratification, identifying potential trajectories toward HCC before morphological changes occur, thereby contributing to personalized risk management within established screening cohorts (151).

Furthermore, the emergence of generative AI, particularly diffusion models and generative adversarial networks, is revolutionizing the data-scarce landscape of hepatobiliary imaging. Beyond data augmentation, generative AI offers transformative applications such as virtual contrast enhancement, where high-fidelity HBP-like images are synthesized from non-contrast sequences, potentially reducing costs and risks for patients with contraindications to gadoxetate disodium (152). Concurrently, the integration of multimodal large language models represents a paradigm shift in clinical workflow. These models can go beyond numerical scoring by generating structured, context-aware radiological reports and facilitating natural-language dialogue between the AI and the multidisciplinary teams (153). Ultimately, the synergy between multi-modality fusion and GenAI will bridge the gap between static image interpretation and dynamic clinical management. Moving forward, the validation of these advanced frameworks through prospective, multi-center clinical trials is essential to ensure that EOB-MRI-driven AI models remain not only technologically sophisticated but also clinically indispensable in the era of precision hepatology.

Conclusions

In conclusion, the landscape of EOB-MRI research in China has evolved far beyond conventional diagnostic imaging, emerging as a pivotal catalyst for data-intensive precision oncology. By capitalizing on unparalleled HBV-related patient cohorts and fostering a robust "Med-Engineering" synergy, China has established a unique paradigm that accelerates the translation of AI-driven diagnostic and prognostic tools. The integration of nationwide collaborative networks, supported by strategic policy frameworks, ensures that these innovations are both scalable and standardized across diverse clinical settings. Looking forward, as the field enters the era of generative AI and multimodal foundation models, the focus will shift from simple lesion characterization toward a holistic understanding of the tumor microenvironment. The "Chinese experience" in EOB-MRI big data—characterized by rapid technological iteration and deep clinical integration—offers a compelling blueprint for the global medical community. Consequently, these advancements are poised to redefine the management of liver cancer, moving toward a future where individualized, non-invasive, and high-fidelity precision medicine is accessible to all.

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Footnote

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