



From platforms to pathways: imaging innovation, quantitative biomarkers, and clinical translation in hepatocellular carcinoma

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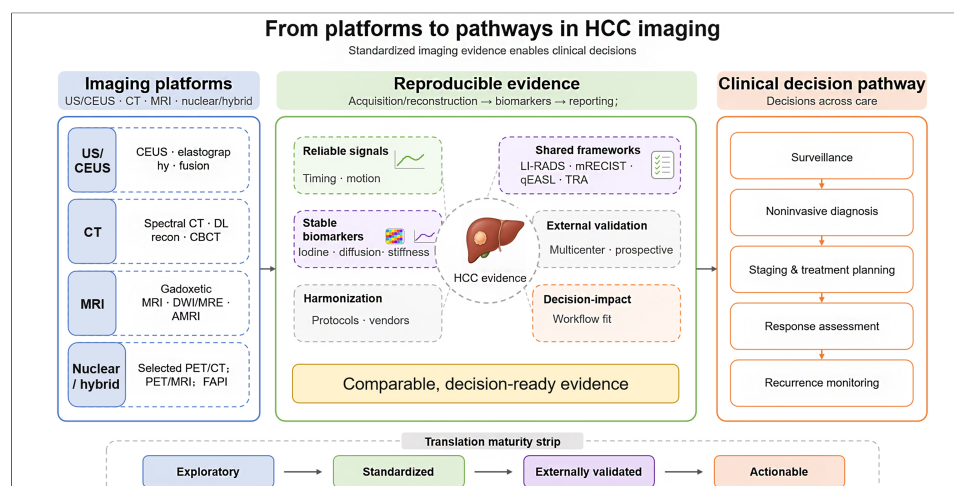
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Abstract

Imaging is central to nearly every stage of hepatocellular carcinoma (HCC) management, from surveillance and noninvasive diagnosis to staging, locoregional therapy planning, treatment response assessment, and recurrence monitoring. Recent progress begins with imaging hardware but depends just as much on acquisition design, reconstruction, quantification, harmonization, and workflow integration. This narrative review examines how ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and nuclear or hybrid imaging have changed HCC care, while separating clinically established tools from technologies that remain largely translational. Ultrasound has advanced beyond screening through contrast-enhanced ultrasound (CEUS), Kupffer-phase agents, elastography, and fusion navigation. CT has progressed through spectral imaging, deep learning reconstruction, and cone-beam guidance, whereas photon-counting CT remains promising but early. MRI has consolidated its role through 3T platforms, multichannel coils, accelerated acquisitions, hepatobiliary contrast agents, diffusion-based imaging, magnetic resonance elastography (MRE), and abbreviated protocols. Positron emission tomography remains constrained by tracer biology in early HCC, although novel tracers and positron

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emission tomography (PET)/MRI broaden selected applications. Across modalities, imaging advances are most useful when acquisition and biomarker extraction are reproducible enough to support the Liver Imaging Reporting and Data System (LI-RADS), treatment response assessment, and downstream clinical decisions. Evidence is strongest for CEUS, gadoxetic acid-enhanced MRI, MRE for selected risk questions, and image-guided interventional platforms, whereas spectral CT has growing selected-use evidence but still requires broader standardization of quantitative thresholds. By contrast, radiomics, deep learning, advanced diffusion models, photon-counting CT, and theranostic-oriented molecular imaging still face important barriers related to external validity, harmonization, and clinical qualification.

INTRODUCTION

Hepatocellular carcinoma (HCC) sits at the intersection of liver cancer biology and chronic liver disease. GLOBOCAN 2022 estimated approximately 866,000 incident liver cancers and 759,000 deaths worldwide, which keeps earlier detection and dependable follow-up at the center of HCC care^[1]. Most HCC develops in cirrhosis or other chronic liver disease, so patients often enter an imaging pathway before a tumor is confirmed^[2,3]. In selected at-risk patients, dynamic contrast-enhanced imaging can establish the diagnosis without biopsy, map tumor burden, guide locoregional therapy, and monitor response or recurrence^[4-7].

The problem is not simply whether ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET) can produce sharper images. HCC care depends on whether images are acquired at the right phase, reconstructed consistently, quantified reproducibly, and reported in language that clinicians can use. The Liver Imaging Reporting and Data System (LI-RADS), modified Response Evaluation Criteria in Solid Tumors (mRECIST), and treatment response algorithms have helped standardize parts of this pathway^[8,9]. Previous guidelines and modality-specific frameworks have often summarized HCC imaging by individual modality or reporting system^[2-4,8]. That organization is useful, but it can hide the practical question this review addresses: which platform advances actually reduce uncertainty during surveillance, diagnosis, treatment planning, response assessment, or recurrence monitoring?

Literature selection and review scope

This narrative review uses a platform-to-pathway structure to answer that question. It follows imaging progress from hardware and acquisition through reconstruction, quantitative biomarkers, standardization, and clinical translation, with attention to where the evidence is mature and where it remains early. The review was based on targeted searches of PubMed, Web of Science, and Google Scholar, prioritizing publications from January 2018 to May 2026 and earlier landmark guidelines, consensus statements, response criteria, and technical validation studies when needed. Search concepts included HCC, contrast-enhanced ultrasound (CEUS), spectral CT, photon-counting CT, gadoxetic acid-enhanced MRI, magnetic resonance elastography (MRE), PET, fibroblast activation protein inhibitor (FAPI), quantitative European Association for the Study of the Liver (qEASL), radiomics, artificial intelligence (AI), and treatment response. We prioritized clinical guidelines, consensus documents, systematic reviews, meta-analyses, multicenter or prospective studies, public datasets, and representative technical studies with clinically relevant HCC endpoints^[2-9].

WHY HCC REMAINS UNIQUELY IMAGING-DEPENDENT ACROSS THE CLINICAL PATHWAY

HCC remains uniquely imaging-dependent because each major clinical decision is conditioned on serial imaging evidence. Surveillance in high-risk populations still begins with ultrasound, often with alpha-fetoprotein (AFP) as an adjunct, despite the well-recognized sensitivity ceiling of ultrasound alone for early-stage disease^[2,3,10,11]. Once a nodule is detected, multiphasic CT, MRI, or CEUS can characterize arterial phase hyperenhancement, washout, capsule appearance, and ancillary features that drive noninvasive diagnosis in

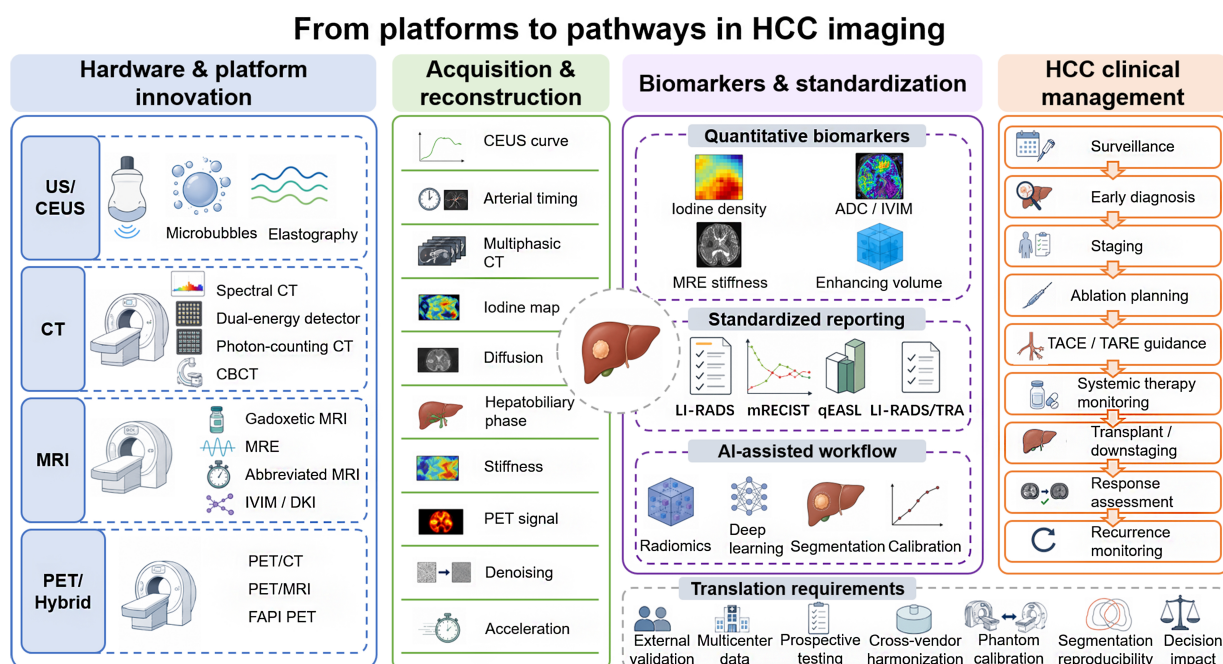


Figure 1. Conceptual pipeline for HCC imaging translation. Platform innovation at the hardware level enables acquisition and reconstruction strategies that determine whether vascular, cellular, and microenvironmental signals can be converted into quantitative biomarkers, standardized reporting, and clinically actionable decisions across surveillance, diagnosis, treatment guidance, response assessment, and recurrence monitoring. HCC: Hepatocellular carcinoma; US: ultrasound; CEUS: contrast-enhanced ultrasound; CT: computed tomography; MRI: magnetic resonance imaging; MRE: magnetic resonance elastography; IVIM: intravoxel incoherent motion; DKI: diffusion kurtosis imaging; CBCT: cone-beam computed tomography; PET: positron emission tomography; PET/CT: positron emission tomography/computed tomography; PET/MRI: positron emission tomography/magnetic resonance imaging; FAPI: fibroblast activation protein inhibitor; ADC: apparent diffusion coefficient; LI-RADS: Liver Imaging Reporting and Data System; mRECIST: modified Response Evaluation Criteria in Solid Tumors; qEASL: quantitative European Association for the Study of the Liver; TACE: transarterial chemoembolization; TARE: transarterial radioembolization; TRA: treatment response algorithm; AI: artificial intelligence.

at-risk patients^[4,5,8]. The same patient may then undergo MRI for staging, ultrasound or cone-beam CT (CBCT) guidance for therapy, and structured imaging-based response assessment after embolization, ablation, or radiation-related treatment^[6,7,9].

This longitudinal role makes HCC an instructive setting for viewing imaging as a continuum of linked steps rather than as a series of disconnected tests [Figure 1]. Upstream hardware governs whether raw data are sensitive, fast, and stable enough. Acquisition and reconstruction determine whether relevant vascular and tissue contrast is captured, while quantitative extraction and reporting determine whether findings remain comparable across readers and centers. Only then can imaging serve as a reliable basis for treatment planning or response assessment. In practice, the technologies that matter most are those that reduce uncertainty at one or more of these interfaces.

HARDWARE AND PLATFORM EVOLUTION ACROSS MAJOR MODALITIES

Platform-level advances have not affected all modalities equally, and their value is not defined by novelty alone. Representative strengths and unresolved issues are summarized in Table 1.

Ultrasound

Ultrasound remains the default entry point into the HCC pathway because it is accessible, repeatable, inexpensive, and free of ionizing radiation. The surveillance challenge, however, goes beyond visualizing the liver: small, often subtle nodules must be detected consistently enough to justify downstream work-up.

Table 1. Representative platform-level advances in HCC imaging and their clinical readiness

Modality/innovation	Main HCC decision point	Clinical readiness	Key contribution	Main limitation or implementation barrier	Representative references
US surveillance	Population-scale surveillance and first-line detection gateway	Established clinical use	Accessible surveillance gateway; US LI-RADS v2024 standardizes technique, visualization score, and triage	Operator dependence; poor acoustic windows; limited early-stage sensitivity	[2,3,5,10,11]
CEUS/CEUS LI-RADS	Problem solving for indeterminate nodules; vascular characterization	Established clinical use/Selected/emerging use	Real-time arterial capture and washout; problem solving when CT/MRI is limited	Limited whole-liver staging; variable agent access, reimbursement, and expertise	[8,16-20]
Kupffer-phase CEUS/Sonazoid workflow	Small-lesion conspicuity and selected surveillance-adjacent workflows	Selected/emerging use	Delayed Kupffer phase improves lesion conspicuity in perfluorobutane-based workflows	Not interchangeable with blood-pool agents; limited global availability and algorithm portability	[21-25]
Elastography	Background liver risk context; exploratory tumor/peritumor biology	Established clinical use/Selected/emerging use	Adds liver stiffness and microenvironmental context beyond morphology	Not a standalone HCC diagnostic test; stiffness is affected by inflammation, congestion, cholestasis, and technique	[26-29]
Fusion US/image-guided ablation	Ablation planning and intraprocedural targeting	Selected/emerging use	Improves targeting of lesions poorly visible on conventional US and links preprocedural imaging to treatment execution	Requires registration expertise, compatible equipment, and careful quality control	[30-32]
Multiphasic CT	Noninvasive diagnosis, staging, vascular mapping, and routine follow-up	Established clinical use	Fast, robust, widely available; supports arterial, portal venous, and delayed-phase assessment	Radiation and iodinated contrast exposure; phase timing and reconstruction affect quantitative biomarkers	[2-4,33,34]
Spectral/dual-energy CT	Lesion conspicuity; viable enhancement after locoregional therapy	Selected/emerging use	Low-keV images and iodine maps can improve visualization of subtle hyperenhancement and residual viability	No universal HCC thresholds; scanner/vendor dependence and harmonization remain incomplete	[35-39]
Deep learning CT reconstruction	Repeated multiphasic follow-up with lower dose or higher image quality	Selected/emerging use	Can reduce noise and dose while maintaining diagnostic confidence	Changes noise texture and edge behavior; radiomics and quantitative biomarkers require revalidation	[40-42]
Photon-counting CT	Small lesion detection; spectral/low-dose liver imaging	Research/translational stage	Higher spatial resolution and energy separation may improve small-lesion detection and dose efficiency	HCC-specific clinical evidence remains early and concentrated in expert settings	[43,44]
Perfusion CT	Tumor vascularity and antiangiogenic or locoregional response research	Research/translational stage	Can capture dynamic vascular parameters beyond static multiphasic enhancement	Radiation dose, protocol heterogeneity, and lack of harmonized thresholds limit routine use	[45,46]

CBCT-assisted TACE/TARE	TACE/TARE planning, feeding-artery detection, target coverage confirmation	Established clinical use/Selected/emerging use	Turns the angiography suite into a 3D treatment-planning environment and supports superselective therapy	Requires CBCT-equipped interventional suite, expertise, and dose/contrast management	[47-50]
Gadoxetic acid-enhanced MRI	Small-lesion diagnosis, staging, recurrence surveillance, transplant/downstaging assessment	Established clinical use	Combines vascular phases with hepatobiliary-phase biology; high sensitivity for small/equivocal lesions	Cost, time, motion artifacts, hepatobiliary-phase quality, and contrast-specific pitfalls	[2-4,54-57]
DWI/ADC	Ancillary lesion conspicuity and cellularity-related assessment	Established clinical use/Selected/emerging use	DWI is broadly available and ADC offers a simple quantitative diffusion metric	ADC thresholds vary with protocol, b-values, motion, and scanner platform	[58,59]
IVIM/DKI	Tumor biology, perfusion, microstructure, and aggressiveness research	Research/translational stage	May capture perfusion-related diffusion and non-Gaussian tissue heterogeneity	Fitting instability, acquisition burden, vendor dependence, and limited external validation	[60,61]
MRE	Liver stiffness, background liver risk, selected prognosis questions	Selected/emerging use	Highly reproducible liver stiffness biomarker; complements dynamic contrast-enhanced diagnosis	More useful for liver background and risk context than lesion diagnosis; hardware/workflow constraints	[62-64]
AMRI	Alternative surveillance in patients with inadequate US or high risk	Selected/emerging use	Workflow innovation that can bring MRI closer to surveillance-compatible use	Patient selection, cost, throughput, contrast strategy, and local availability determine feasibility	[54,65-67]
FDG/acetate/choline PET	Selected staging dilemmas, extrahepatic disease, recurrence, biologic characterization	Selected/emerging use	Whole-body biologic characterization beyond morphology; dual-tracer approaches may improve selected assessments	FDG sensitivity is low in well-differentiated HCC; tracers are not routine for early intrahepatic diagnosis	[68-71]
FAPI PET	Stromal biology, selected staging, and theranostic exploration	Research/translational stage	May visualize biology missed by FDG in selected liver tumors	FAPI uptake is not tumor-specific; HCC outcome validation and guideline qualification remain incomplete	[72,73,94]
PET/MRI	Hybrid whole-body and liver-specific problem solving	Selected/emerging use/Research/translational stage	Combines metabolic information with superior liver MRI contrast in one examination	Cost, workflow complexity, attenuation correction, and uncertain routine management impact	[74]

HCC: Hepatocellular carcinoma; US: ultrasound; CEUS: contrast-enhanced ultrasound; LI-RADS: Liver Imaging Reporting and Data System; CT: computed tomography; CBCT: cone-beam computed tomography; MRI: magnetic resonance imaging; MRE: magnetic resonance elastography; DWI: diffusion-weighted imaging; ADC: apparent diffusion coefficient; IVIM: intravoxel incoherent motion; DKI: diffusion kurtosis imaging; AMRI: abbreviated magnetic resonance imaging; PET: positron emission tomography; FDG: fluorodeoxyglucose; FAPI: fibroblast activation protein inhibitor; TACE: transarterial chemoembolization; TARE: transarterial radioembolization; mRECIST: modified Response Evaluation Criteria in Solid Tumors; qEASL: quantitative European Association for the Study of the Liver; TRA: treatment response algorithm; AI: artificial intelligence.

Contrast-specific workflows such as Sonazoid defect-reperfusion imaging show how ultrasound platforms can move beyond morphology in selected HCC settings^[12]. Contemporary Doppler and microvascular flow imaging technologies further improve sensitivity to slow flow without contrast^[13-15]. These upgrades are meaningful, but they reduce rather than eliminate operator dependence.

CEUS has been the most consequential shift because it turns ultrasound from a morphology-driven surveillance test into a real-time hemodynamic imaging tool. Continuous observation of arterial fill-in and subsequent washout is especially valuable when CT or MRI may miss the critical arterial window, or when a small indeterminate nodule requires real-time problem solving^[16-18]. CEUS LI-RADS and subsequent reviews have demonstrated high specificity in the intended at-risk population, although diagnostic behavior still depends on contrast-agent type, lesion size, and reader expertise^[8,19,20]. The 2024 CEUS nonradiation treatment response algorithm is also conceptually important because it extends ultrasound from diagnosis into structured post-treatment assessment, particularly after ablation or other nonradiation therapies^[7].

Kupffer-phase agents, especially perfluorobutane formulations, further expand ultrasound by adding a delayed reticuloendothelial phase that improves conspicuity of lesions lacking normal Kupffer cell function^[21-23]. For small or atypical nodules, this may improve detection and sometimes classification. It also complicates direct transfer of CEUS algorithms across regions, because Sonazoid-based workflows are not interchangeable with blood-pool microbubble workflows^[24,25]. Elastography adds another dimension. Liver stiffness is already clinically relevant for chronic liver disease severity, and tumoral or peritumoral stiffness has been explored as a marker of microvascular invasion, recurrence risk, or aggressive biology^[26-29]. The most durable clinical contribution of elastography in HCC is probably risk contextualization rather than lesion diagnosis.

Fusion navigation has expanded what ultrasound can accomplish during treatment. Registration of real-time ultrasound with CT or MRI, often with electromagnetic tracking, allows poorly conspicuous tumors to be targeted for ablation and shortens the distance between preprocedural planning and intraprocedural execution^[30-32]. In HCC, modern ultrasound is best viewed as a flexible platform spanning surveillance, problem solving, and intervention.

CT

Multiphasic CT remains a foundational modality for diagnosis, staging, vascular mapping, and post-treatment follow-up because it combines speed, consistency, and broad availability. Much of its clinical reliability comes from hardware evolution that is easy to overlook: faster gantry rotation, wider detector coverage, better z-axis resolution, and improved dose efficiency make it more likely that arterial, portal venous, and delayed phases are acquired at the right time and with consistent whole-liver coverage^[33,34]. For HCC, this temporal reliability matters as much as nominal spatial resolution.

Dual-energy and spectral CT have moved CT beyond attenuation measurement toward material-sensitive imaging. Low-keV virtual monochromatic images can accentuate hypervascular lesions, iodine maps can clarify viable enhancement after locoregional therapy, and virtual noncontrast images can sometimes reduce the need for true unenhanced acquisitions^[35-37]. Evidence in HCC is strongest where spectral data augment visual judgment rather than replace it. Iodine density and low-keV reconstructions can increase lesion-to-liver contrast or make subtle residual enhancement more conspicuous, but universally accepted thresholds for diagnosis or response are lacking^[38,39].

Reconstruction has been the second major CT frontier. Deep learning reconstruction and related hybrid approaches allow lower-dose multiphasic examinations while preserving or improving low-contrast detectability, an especially relevant advantage in a population requiring repeated follow-up imaging^[40-42]. The caveat is that reconstruction is no longer a neutral postprocessing step. When noise texture and edge behavior change, quantitative features and radiomics signatures may also shift, so biomarker portability cannot be assumed across reconstruction generations.

Photon-counting CT is the most visible current hardware leap. By directly counting photons and preserving energy information at the detector level, it promises higher spatial resolution, better spectral separation, and improved dose utilization^[43]. Early liver data are encouraging, including better conspicuity of small lesions and improved spectral image quality, but HCC-specific evidence remains preliminary and concentrated in expert centers^[44]. A similar caution applies to perfusion CT. It can capture tumor vascularity and antiangiogenic response more directly than static multiphasic CT, yet protocol heterogeneity, radiation exposure, and limited harmonization have kept it largely in the research domain^[45,46].

By contrast, CBCT has already shown clear procedural value. In transarterial chemoembolization (TACE) or radioembolization, intraprocedural CBCT turns the angiography suite into a three-dimensional imaging environment that can improve feeding-artery detection, confirm target coverage, and support superselective therapy^[47-50]. This may be the most clinically mature example of CT technology improving HCC care through treatment execution rather than diagnosis itself.

MRI

MRI has consolidated its central role in HCC because it combines high soft-tissue contrast with the broadest palette of structural and functional tissue characterization. Its evolution has been cumulative rather than singular. The move to 3T systems, multichannel torso coils, and parallel imaging strategies such as sensitivity encoding and generalized autocalibrating partially parallel acquisition increased signal efficiency and shortened acquisitions^[51-53]. More recent motion-robust and accelerated dynamic strategies build on this foundation, aiming to preserve arterial-phase fidelity in patients who struggle with breath-holding or have limited physiologic reserve^[54].

Hepatobiliary contrast agents, especially gadoxetic acid, are a major reason MRI frequently outperforms CT for small or otherwise equivocal lesions. By combining vascular-phase imaging with delayed hepatocyte uptake, they create a second biologic contrast mechanism that highlights lesions with reduced hepatocellular function^[55-57]. This advantage is most compelling in small HCC, borderline nodules, or patients in whom surveillance-detected lesions remain indeterminate after ultrasound or CT. At the same time, hepatobiliary-phase hypointensity is not synonymous with overt HCC, and contrast-specific artifacts or timing pitfalls can weaken arterial-phase interpretation. MRI retains its advantage when all phases, not just one, are interpreted within a standardized framework.

Diffusion-weighted imaging (DWI) is now a core sequence because it increases lesion conspicuity and provides a semiquantitative window into cellularity. Yet the more sophisticated diffusion models that followed, including intravoxel incoherent motion (IVIM) and diffusion kurtosis imaging (DKI), also illustrate how difficult quantitative MRI remains to implement clinically. These methods are biologically attractive because they attempt to separate diffusion from microperfusion or to characterize non-Gaussian diffusion behavior, and they have been associated with grading, microvascular invasion, or aggressive phenotypes in HCC^[58-61]. The challenge is robustness: parameter estimates remain sensitive to b-value design, fitting strategy, motion, and vendor implementation.

MRE is further along the maturity curve. It is one of the most reproducible imaging tools for liver stiffness assessment and has already demonstrated value in chronic liver disease and in selected HCC risk or prognosis questions^[62-64]. In practice, its most convincing role in HCC is as a background liver and microenvironment biomarker rather than a standalone tumor detection tool.

Abbreviated MRI (AMRI) represents a different type of progress, namely workflow redesign rather than new physics. By selecting a reduced sequence set, sometimes contrast-enhanced and sometimes noncontrast, abbreviated protocols aim to move MRI closer to a surveillance-compatible test for patients in whom ultrasound is likely to underperform^[65-67]. The appeal is clear, but AMRI should not be framed as universally superior surveillance. Its value depends on patient selection, local throughput, cost, and which sequences are prioritized. AMRI is therefore as much a pathway innovation as a scanner innovation.

Nuclear and hybrid imaging

Nuclear and hybrid imaging currently occupy a more selective role in HCC than ultrasound, CT, or MRI, but they remain important for biologic characterization and whole-body assessment. The well-known limitation of fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) is its relatively low sensitivity for well-differentiated HCC, which restricts its value for early intrahepatic detection^[68-70]. FDG is more useful when biology is less favorable, for example in poorly differentiated tumors, extrahepatic disease, recurrence, or prognosis-related questions.

Alternative tracers such as acetate or choline can complement FDG, and newer FAPI tracers have generated interest because they may visualize stromal biology not captured by FDG alone^[71-73]. Here again, tracer innovation has outpaced standard clinical qualification. FAPI uptake is not tumor-specific, theranostic implications in HCC remain exploratory, and most published evidence is based on small cohorts or pooled analyses.

PET/MRI illustrates both the promise and the practical limits of hybrid imaging. It combines metabolic information with superior liver MRI contrast within one examination and can be useful in selected hepatobiliary problem-solving settings, but its routine role remains constrained by cost, workflow complexity, and attenuation-correction challenges^[74]. Hardware refinements such as digital detector architectures and improved time-of-flight performance are technically favorable, yet in HCC PET usefulness still depends more on tracer biology than on scanner hardware.

ACQUISITION AND RECONSTRUCTION INNOVATIONS THAT CHANGED DIAGNOSTIC PERFORMANCE

Across modalities, the central technical question in HCC is whether acquisition and reconstruction capture the right biology at the right moment. Raw signal alone is not enough. This is most obvious in arterial-phase imaging. Hyperenhancement remains a key diagnostic and response feature, yet it is easy to miss because it depends on bolus timing, temporal resolution, and motion control. Ultrasound partly escapes this problem through continuous real-time sampling, which helps explain why CEUS is so effective for problem solving indeterminate nodules^[16,17]. CT addresses it through speed and reproducible multiphasic timing, increasingly complemented by spectral reconstructions that recover contrast when standard images are borderline^[36-39]. MRI relies less on raw speed than on acceleration, parallel imaging, and motion-robust dynamic strategies that trade sequence complexity for more reliable arterial-phase capture^[51,52,54].

Reconstruction now deserves equal attention because it changes what counts as an interpretable image. Deep learning reconstruction on CT and AI-assisted acceleration on MRI can reduce noise, shorten acquisitions, and rescue studies that would previously have been nondiagnostic^[40,42,54]. The clinical gain is greatest when decision-level performance is preserved, such as maintaining confidence in lower-dose multiphasic CT or making AMRI feasible in frail patients^[41,66]. The complication is that reconstruction can also alter texture, sharpness, or apparent enhancement patterns. Biomarkers that depend on intensity distribution, edge definition, or voxelwise heterogeneity therefore require revalidation when acquisition or reconstruction changes.

These issues explain why acquisition and reconstruction should be treated as part of the clinical evidence rather than as invisible vendor engineering. A new detector, acceleration scheme, or reconstruction network becomes clinically meaningful only when it improves the stability of diagnosis, response assessment, or intervention planning. In HCC, where serial comparison is essential, consistency may matter more than maximal image sharpness.

QUANTITATIVE IMAGING, STANDARDIZATION, AND TREATMENT RESPONSE FRAMEWORKS

Quantitative imaging is attractive in HCC because it promises to convert complex vascular and microenvironmental biology into serial, auditable measurements. CEUS time-intensity-curve parameters, CT iodine density, diffusion metrics, stiffness maps, and volumetric enhancement assessments all attempt to move interpretation beyond visual pattern recognition. The recurring problem is that quantitative data are only as useful as their technical stability. Without harmonized acquisition, reconstruction, segmentation, and reporting, thresholds drift across centers and biomarkers remain difficult to qualify for clinical decisions. Relevant standardization frameworks and biomarker classes are summarized in [Table 2](#)^[39,58,62,75-77].

It is useful to separate three related but distinct concepts in post-treatment imaging: response measurement, response categorization, and decision impact. mRECIST is primarily a measurement framework. It recognizes that viable HCC is better reflected by arterial-phase enhancement than by the total treated mass, which may remain stable or even enlarge because of hemorrhage, necrosis, edema, or treatment cavity evolution. For this reason, mRECIST remains deeply embedded in HCC trials and routine locoregional therapy follow-up. Its strengths are familiarity, simplicity, and feasibility across multicenter studies. Its limitations are geometric and biologic: a one-dimensional measurement may underrepresent irregular, infiltrative, partially necrotic, multifocal, or heterogeneously treated tumors, and mRECIST does not fully capture extrahepatic progression or mixed intrahepatic responses unless paired with broader disease assessment^[9].

qEASL and related three-dimensional enhancement-based approaches were developed to address this limitation by quantifying viable enhancing tumor volume rather than relying on a single enhancing diameter. This logic is particularly relevant after TACE, transarterial radioembolization (TARE), ablation, or combined locoregional therapy, where residual viable tumor may persist as nodular, crescentic, peripheral, or discontinuous enhancement within a complex treatment zone. qEASL is therefore best framed as a promising quantitative adjunct for selected response-assessment workflows, not as a universal replacement for mRECIST. Its main advantage is biological plausibility: it more directly represents the spatial burden of viable enhancing tumor. Its main barrier is implementation: segmentation, subtraction or registration quality, enhancement thresholds, phase timing, software platform, and local calibration all influence the final value^[78].

LI-RADS treatment response assessment (TRA) provides a complementary solution at the reporting level. Unlike mRECIST or qEASL, LI-RADS TRA is not designed primarily to compute a continuous tumor burden; it standardizes how radiologists categorize treated observations as viable, nonviable, equivocal, nonevaluable, or nonprogressing according to treatment mechanism. The 2024 CT/MRI update is useful because it separates nonradiation and radiation-based treatment response patterns, while CEUS Nonradiation TRA extends structured real-time viability assessment to appropriate nonradiation therapies and resection follow-up. In practice, these frameworks are complementary: mRECIST remains the widely used trial and clinical response metric, qEASL provides a quantitative volumetric adjunct for complex residual enhancement, and LI-RADS TRA provides standardized language for multidisciplinary communication and management decisions^[6,7].

Table 2. Standardization frameworks, quantitative biomarkers, and AI/radiomics translation requirements in HCC imaging

Framework/biomarker class	What it standardizes or measures	Main clinical task	Current readiness	Key limitation	Required next step/translational requirement	Representative references
CT/MRI LI-RADS	Major and ancillary imaging features for noninvasive diagnosis in at-risk patients	Diagnosis and multidisciplinary communication	Established clinical use	Depends on acquisition quality and intended population; limited for non-HCC malignancies and non-at-risk patients	Protocol quality assurance, education, transparent reporting, and outcome-linked updates	[4,8,76,77]
US LI-RADS	US category, visualization score, technical recommendations, and triage	Surveillance and follow-up triage	Established clinical reporting framework	Persistent operator and visualization variability; inadequate US requires alternative surveillance planning	Risk- and visualization-adapted surveillance pathways, workflow integration, and prospective validation	[5]
CEUS LI-RADS	Real-time enhancement pattern, washout timing/intensity, and CEUS category assignment	Problem solving and noninvasive diagnosis in selected at-risk patients	Established clinical use/Selected/emerging use	Agent type, lesion size, reader expertise, and regional availability affect portability	Multicenter datasets, external validation, education, and cross-region implementation studies	[8,19,20]
CT/MRI LI-RADS TRA 2024	Categorical post-LRT viability assessment; nonradiation and radiation-based therapy patterns	Response assessment, retreatment, transplant bridging/downstaging	Established/updated reporting framework	Outcome linkage varies by treatment mechanism; equivocal/nonprogressing categories need clinical validation	Prospective validation with pathology, retreatment decisions, transplant outcomes, and decision-impact studies	[6]
CEUS Nonradiation TRA 2024	Real-time CEUS assessment of viable tumor and post-treatment change after nonradiation LRT or resection	Ablation and nonradiation post-treatment assessment	Selected/emerging standardized framework	Does not cover all radiation-based therapies; local expertise and acoustic windows constrain use	Multicenter validation across ablation techniques, follow-up schedules, and workflow integration	[7]
mRECIST	One-dimensional diameter of viable arterial-enhancing tumor rather than total lesion size	Trials and routine response assessment after LRT/systemic therapy	Widely used clinical and trial metric	Geometric simplification; limited for irregular, infiltrative, partially necrotic, or heterogeneous tumors and extrahepatic disease	Harmonized use with RECIST 1.1, LI-RADS TRA, and volumetric adjuncts; decision-impact studies	[9]
qEASL/volumetric enhancement assessment	Viable enhancing tumor volume and percentage enhancement change	Quantitative response assessment after TACE/TARE/ablation; research workflows	Promising quantitative adjunct	Segmentation, subtraction registration, enhancement threshold, software, timing, and cross-center calibration dependence	Segmentation reproducibility, prespecified thresholds, external validation, model calibration, and decision-impact studies	[78,92,93]
CT iodine density/low-keV spectral CT	Iodine concentration, virtual monochromatic image contrast, and material-sensitive enhancement	Viable enhancement, lesion conspicuity, and response research	Selected/emerging use	Threshold instability across scanners, reconstruction settings, contrast timing, and vendors	Phantom calibration, cross-vendor harmonization, protocol locking, and prospective validation	[35-39]
ADC	Apparent diffusion coefficient as a simple diffusion-derived cellularity metric	Ancillary characterization and response/risk research	Established adjunct/Selected-emerging quantitative use	ADC varies with b-values, acquisition, motion, fitting approach, and scanner platform	Protocol harmonization, repeatability studies, external validation, and clinically meaningful endpoints	[58,59]
IVIM/DKI	Perfusion-related diffusion and non-Gaussian microstructural diffusion metrics	Tumor biology, aggressiveness, and response research	Research/translational stage	Longer acquisition, model instability, vendor differences, and limited multicenter evidence	Multicenter datasets, phantom calibration, cross-vendor harmonization, and prospective validation	[60,61]
MRE stiffness	Background liver stiffness and selected tissue-mechanical risk markers	Risk context, liver background assessment, and selected prognosis questions	Selected/emerging use	More informative for liver background than lesion diagnosis; hardware and workflow constraints	External validation, cross-vendor harmonization, standardized acquisition, and outcome-linked thresholds	[62-64]

Radiomics	High-dimensional shape, intensity, texture, and habitat features	MVI/grade/CK19 prediction, recurrence, response, survival, LI-RADS assistance	Research/translational stage	Retrospective single-center designs, unstable labels, data leakage risk, segmentation variability, and feature shift	IBSI-compliant extraction, patient-level splitting, external validation, model calibration, decision-curve analysis, and open reproducible code	[79-85]
Deep learning/AI prediction models	End-to-end or feature-learning models for detection, classification, biology prediction, response, and prognosis	Diagnosis assistance, tumor biology prediction, response prediction, and recurrence/survival prediction	Research/translational stage	Internal AUC often fails to generalize; labels, cohorts, scanners, and protocols vary across institutions	TRIPOD + AI, CLAIM 2024, PROBAST + AI, external validation, prospective validation, transparent reporting, fairness checks, and decision-impact studies	[82-88]
AI-assisted segmentation/volumetric response tracking	Automated liver/tumor segmentation, volume tracking, new-lesion detection, and longitudinal response support	Workflow automation and quantitative response tracking	Selected workflow tools; broader response AI remains translational	Generalization drops across scanners, contrast protocols, and institutions; difficult failure-mode auditing	Segmentation reproducibility, multicenter prospective testing, human-AI workflow integration, reader-impact studies, and safety monitoring	[84,89-91]

HCC: Hepatocellular carcinoma; CT: computed tomography; MRI: magnetic resonance imaging; US: ultrasound; CEUS: contrast-enhanced ultrasound; LI-RADS: Liver Imaging Reporting and Data System; TRA: treatment response assessment; LRT: locoregional therapy; mRECIST: modified Response Evaluation Criteria in Solid Tumors; RECIST: Response Evaluation Criteria in Solid Tumors; qEASL: quantitative European Association for the Study of the Liver; TACE: transarterial chemoembolization; TARE: transarterial radioembolization; ADC: apparent diffusion coefficient; IVIM: intravoxel incoherent motion; DKI: diffusion kurtosis imaging; MRE: magnetic resonance elastography; MVI: microvascular invasion; CK19: cytokeratin 19; IBSI: Image Biomarker Standardisation Initiative; AI: artificial intelligence; AUC: area under the receiver operating characteristic characteristic curve; TRIPOD + AI: Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis + Artificial Intelligence; CLAIM: Checklist for Artificial Intelligence in Medical Imaging; PROBAST + AI: Prediction Model Risk of Bias Assessment Tool + Artificial Intelligence.

Treatment response imaging in HCC is moving from diameter-only measurement toward mechanism-aware and volume-aware assessment, but these tools are not at the same stage of use. mRECIST is familiar and trial-ready; LI-RADS TRA provides a reporting language for post-locoregional therapy communication; qEASL remains a quantitative adjunct that still needs automated reproducible segmentation, harmonized thresholds, multicenter validation, and prospective decision-impact studies before broad implementation^[6,7,9,78].

Taken together, mRECIST, qEASL, and LI-RADS TRA should be viewed as complementary rather than interchangeable tools. mRECIST remains the most familiar clinical and trial metric, qEASL provides a volumetric enhancement-based adjunct for complex residual viable tumor, and LI-RADS TRA provides standardized post-treatment reporting language for multidisciplinary communication^[6,7,9,78].

COMPUTATIONAL IMAGING BIOMARKERS, RADIOMICS, AND AI

Radiomics and AI in HCC are better treated as task-specific tools than as a single technology class. For diagnosis, AI may support lesion detection, arterial-phase timing quality control, LI-RADS feature extraction, and risk stratification of indeterminate observations such as LI-RADS category 3 or 4. For tumor biology, models have been explored for microvascular invasion, histologic grade, cytokeratin 19 (CK19) or Ki-67 expression, molecular subtype, immune microenvironment, and recurrence risk. For treatment planning and follow-up, computational imaging may help estimate ablation margins, tumor territory, residual viable volume, new-lesion detection, and longitudinal response^[79-84].

The most mature near-term application is likely workflow support rather than autonomous diagnosis. Automated or semi-automated liver and tumor segmentation can reduce measurement burden, improve volumetric consistency, and enable qEASL-like or volume-based response workflows. Longitudinal deep learning systems that combine segmentation, tumor volume tracking, and new-lesion detection illustrate

how AI could eventually complement RECIST/mRECIST-style workflows. However, such systems should be framed as decision-support and measurement-assistance tools until external validation and clinical impact data show that they improve management decisions or patient outcomes^[84].

The barriers to clinical translation are substantial. Many HCC radiomics studies remain retrospective, single-center, and small relative to the dimensionality of the feature space. Labels such as microvascular invasion, treatment response, recurrence, and progression-free survival are clinically meaningful but can be unstable across institutions because they depend on pathology sampling, treatment selection, follow-up interval, and competing risks. Imaging inputs are also heterogeneous: arterial timing, hepatobiliary phase quality, CT reconstruction kernel, MRI field strength, b-values, contrast agents, and scanner vendors can all shift radiomic features or deep learning representations. Segmentation is another major source of variability, particularly for infiltrative tumors, multifocal disease, necrotic regions, and post-treatment cavities^[85].

For these reasons, the key question is no longer whether an HCC imaging AI model achieves a high internal area under the receiver operating characteristic curve (AUC), but whether it remains calibrated, reproducible, and clinically useful outside the development environment. Essential prerequisites include patient-level data splitting, prevention of data leakage, external multicenter validation, prospective or temporal validation, complete reporting of preprocessing and model selection, assessment of calibration and decision-curve net benefit, subgroup testing across etiology and scanner platforms, and evaluation of how the model changes decisions in a real multidisciplinary workflow. Phantom calibration and cross-vendor harmonization are especially important for quantitative biomarkers and radiomic features; explainability and failure-mode analysis are especially important for deep learning systems^[85-88].

Methodological frameworks should be part of this translation pathway. The Image Biomarker Standardization Initiative (IBSI) provides a foundation for radiomic feature standardization. The Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis-Artificial Intelligence (TRIPOD + AI) statement supports transparent reporting of AI-based prediction models. The Checklist for Artificial Intelligence in Medical Imaging (CLAIM) 2024 is tailored to medical imaging AI reporting, and the Prediction model Risk Of Bias Assessment Tool-Artificial Intelligence (PROBAST + AI) helps evaluate risk of bias and applicability. These frameworks do not prove clinical utility by themselves, but they define the minimum level of transparency needed before HCC imaging AI can be compared across centers or considered for clinical deployment^[85-88].

At present, radiomics and AI are more defensible as radiologist-supervised workflow tools than as autonomous diagnostic systems. They may help with HCC diagnosis assistance, tumor biology prediction, treatment response evaluation, recurrence prediction, and workflow automation, but most models remain at a research or translational stage. Their near-term value is likely to come from consistency, efficiency, and quantitative traceability inside established reporting workflows^[84-91].

IMAGE-GUIDED INTERVENTION AND WHOLE-COURSE MANAGEMENT

The clinical value of imaging innovation is easiest to appreciate during intervention, where technical gains can be mapped directly to procedural success. Fusion ultrasound and electromagnetic tracking make it possible to target lesions that are inconspicuous on gray-scale ultrasound alone, thereby expanding candidacy for percutaneous ablation^[30-32]. CEUS can then be reused immediately after ablation to assess residual perfusion and to direct same-session retreatment when needed^[7].

For transarterial therapy, CBCT integrates preprocedural and intraprocedural information into a common coordinate system. Feeding-artery identification, tumor territory mapping, and confirmation of target coverage can all be improved within the angiography suite itself^[47-50]. This is one reason HCC is an especially

useful model for image-guided oncology: the same technological ecosystem that detects disease also helps deliver and verify therapy.

Response assessment closes the loop. mRECIST remains deeply embedded in trials and clinical practice, but structured CT/MRI and CEUS treatment response algorithms provide a more explicit language for classifying viable, equivocal, or nonviable disease after therapy^[6,7,9]. As volumetric quantification becomes more practical, the next step will likely be better alignment between acquisition, segmentation, response criteria, and retreatment decisions, rather than wholesale replacement of existing frameworks.

CURRENT LIMITATIONS, STANDARDIZATION GAPS, AND TRANSLATIONAL BARRIERS

Seen from the pathway level, the remaining problem is less a lack of imaging tools than a lack of dependable translation across settings. Access is the first constraint. CEUS agents, spectral CT, 3 Tesla MRI, CBCT-equipped suites, PET/MRI, and new radiotracers are not distributed evenly across regions or reimbursement systems. A technology that works in a tertiary center will not improve HCC outcomes at population scale unless it can be placed into a realistic referral, reporting, and treatment workflow^[2,3,66].

Technical variability is the second constraint. Iodine maps, diffusion metrics, stiffness measurements, and radiomic features all depend on acquisition, reconstruction, segmentation, and software choices. Deep learning reconstruction and new detector platforms can improve images, but they can also change texture, edge definition, or apparent enhancement. Thresholds developed on one scanner or protocol therefore require phantom calibration, cross-vendor harmonization, and transparent reporting before they are used as clinical decision rules^[39,60,85].

Evidence maturity is the third constraint. CEUS, gadoxetic acid-enhanced MRI, MRE for selected risk questions, and CBCT-assisted transarterial therapy have enough clinical experience to guide current practice in appropriate settings^[18,49,62]. Spectral CT has selected-use evidence but still needs broader threshold standardization. Photon-counting CT, FAPI-oriented molecular imaging, IVIM/DKI metrics, and many radiomics or deep learning models should remain labeled as translational until multicenter and prospective studies link them to patient management or outcomes^[43,44,60,61,72,73,85-88].

Governance is the fourth constraint. AI prediction models are often reported with incomplete preprocessing, unclear label definitions, or only internal test performance. The TRIPOD + AI statement, CLAIM 2024, and PROBAST + AI now make these weaknesses easier to identify^[86-88]. For HCC imaging, a credible translation pathway has to evaluate technical performance, clinical utility, workflow fit, and failure modes together.

FUTURE DIRECTIONS

The next useful advances will probably be those that connect one step of the pathway to the next. Ultrasound can remain the surveillance gateway if visualization scoring, CEUS problem solving, and fusion guidance are used to triage patients rather than to duplicate CT or MRI. CT progress should focus on calibrated spectral and photon-counting measurements for lesions and treated tumors, not only image appearance. MRI development should make hepatobiliary contrast, motion-robust dynamics, diffusion, elastography, and abbreviated protocols easier to deploy in patients who need repeated examinations. PET and hybrid imaging should be reserved for biologic or whole-body questions that CT and MRI cannot answer.

Across modalities, four priorities follow from this logic: multicenter protocol harmonization, prospective decision-impact studies, response frameworks that connect segmentation to retreatment decisions, and AI systems that improve consistency within existing standards. The aim is not to replace expert interpretation

with one model or one modality. It is to make HCC imaging more comparable across centers, more explicit about uncertainty, and more useful at the point where management decisions are made^[10].

This review addresses a specific problem in HCC imaging: how to judge whether a platform advance has moved far enough along the pathway to support clinical decisions. The synthesis separates established tools, selected or emerging uses, and translational technologies, and links them to surveillance, diagnosis, treatment planning, response assessment, and recurrence monitoring. That framing makes the maturity gap clearer. CEUS, gadoxetic acid-enhanced MRI, selected MRE, and CBCT-assisted therapy already support clinical care in defined settings, whereas spectral CT, photon-counting CT, FAPI PET, advanced diffusion metrics, radiomics, and many AI models still need standardization and decision-impact evidence. For the wider HCC field, the main contribution is a practical way to align technical development with clinical pathways. Better images matter, but reproducible measurements, common reporting language, and evidence that changes management will matter more for the next stage of HCC imaging.

DECLARATIONS

Authors' contributions

Made substantial contributions to the conception and design of the review: Xie Y, Cai J

Performed literature search and drafted the manuscript: Huang Y

Prepared the figures and tables: Huang Y

Critically revised the manuscript for important intellectual content: Xie Y, Cai J

All authors read and approved the final manuscript.

Availability of data and materials

Not applicable.

AI and AI-assisted tools statement

During the preparation of this manuscript, the AI tool ChatGPT (GPT-5.5, released 2026-04-23) was used solely for language editing. The tool did not influence the study design, data collection, analysis, interpretation, or the scientific content of the work. All authors take full responsibility for the accuracy, integrity, and final content of the manuscript.

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Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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