Imaging Modalities Used in the Assessment of Liver Cancer: A Review

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Abstract

Liver cancer, particularly hepatocellular carcinoma (HCC), remains a major cause of morbidity and mortality worldwide. Early detection and accurate staging are crucial for improving patient outcomes and guiding therapeutic decisions. Imaging plays a central role in the assessment of liver cancer, not only for diagnosis but also for treatment planning and follow-up. This review outlines the key imaging modalities currently employed in liver cancer evaluation, including ultrasonography, computed tomography (CT), and PET imaging techniques and diagnostic techniques Emerging Techniques in Liver Cancer Imaging Comparison of Traditional Imaging Features, Radiomics, and Deep Learning Their respective strengths, limitations, and future directions are also discussed.

Keywords: Liver cancer imaging; computed tomography; magnetic resonance imaging; ultrasonography; positron emission tomography, diagnostics techniques.

Introduction

Hepatocellular carcinoma (HCC), in particular, is a fatal form of liver cancer that continues to be a major global health concern [1]. Although it can arise without chronic liver illness, this aggressive tumor frequently develops in people with such diseases [2]. Liver cancer is the sixth most prevalent type of cancer diagnosed globally, according to Global Cancer Statistics 2020. About 830,000 people died from it in 2020, making it the third most common cause of cancer-related fatalities [3]. Males are typically more likely than females to have HCC [4]. The World Health Organization (WHO) estimates that liver cancer will cause more than one million deaths by 2030 [5]. HCC and cholangiocarcinoma, sometimes referred to as primary liver cancer (PLC), are the two principal forms of liver cancer [6]. Angiosarcoma and hepatoblastoma are rare types of liver cancer [7]. There are multiple steps in the HCC procedure. Hepatocyte cells, the primary parenchymal cells of the liver, are the source of it. Liver fibrosis is brought on by these cells' constant regeneration and damage, which ultimately raises the risk of cirrhosis. Cirrhosis may eventually develop into HCC, occasionally spread to neighboring tissues, and result in metastatic events [8]. Due to the advanced state of the disease, certain contemporary medications are only available for local therapy and palliative care. However, since cancer cells proliferate quickly, and healthy liver cells are primarily at rest, cell cycle-based therapies present exciting new possibilities [9]. Bile duct cancer,

also known as cholangiocarcinoma, is a type of epithelial cell cancer that starts in the bile ducts that connect the liver to the gallbladder and small intestine. It is divided into three categories based on anatomical location and is the second most common primary liver cancer after HCC: Intrahepatic CCA develops inside the liver, perihilar CCA happens at the bile duct junction where it enters the liver, and distal common carotid artery in the bile duct close to the small intestine [10]. Approximately 10% of all cholangiocarcinoma's are intrahepatic. It is common for combined HCC-ICC tumors to display the more aggressive behavior trait. Furthermore, ICC is usually discovered at an advanced stage, either with local invasion or metastatic dissemination. With an incidence of 0.85 per 100,000, ICC can make up as much as 20% of all cholangiocarcinoma cases worldwide [11]. When cancer cells from a primary malignancy, such as those that start in the colon, breast, or lungs, migrate to the liver and cause metastatic lesions, it is known as secondary or metastatic liver cancer. Through blood or lymphatic channels, these cancer cells spread to the liver, where they multiply to become secondary liver cancer, which advances the course of the illness [12]. The most frequent location for metastases from colorectal cancer (CRC) is the liver. The bulk of metastases, which affect more than half of CRC patients, involve the liver. After liver metastases are surgically removed, the 5-year survival rate is between 24% and 40%. The difficulties in treating advanced-stage metastases are highlighted by the fact that overall survival rates for colorectal liver metastases are still low, especially in patients with incurable disease [13]. Accurate diagnosis and successful treatment planning are complicated by the unique etiology, histology, and treatment regimen of each kind of liver cancer. Growth factors, receptors, cellular changes, and associated signaling pathways have all been found to exhibit aberrant expression or exertion in HCC [10]. Hepatitis B, hepatitis C, alcoholic cirrhosis, diabetes, and non-alcoholic steatohepatitis are among the major risk factors, albeit they differ greatly between cases and geographical areas [14]. Hepatitis can cause liver fibrosis and eventually cirrhosis, which is the leading cause of death for those who have it [15]. The main treatment options for HCC are surgical procedures like liver transplantation and resection, which are frequently limited by the advanced stage of the disease at diagnosis. Radiofrequency ablation (RFA) has become a crucial treatment option, especially in the early stages of PLC, and locoregional and systematic therapies have greatly improved patient outcomes [16]. Recent research has connected the morphological characteristics of HCC to inheritable genetic mutations and dysregulation of important natural biological pathways, such as Wnt/β-catenin and P53, which control cell growth and apoptosis. These inherited abnormalities and disruptions of pathways can lead to uncontrolled cell proliferation and tumor development in HCC [17].

Imaging Modalities

Ultrasound

The British Society of Gastroenterologists (BSG) guidelines for the diagnosis of both HCC and cholangiocarcinoma in adults specify the use of B mode ultrasonography (US), which is frequently the first line of investigation in liver illness [18,19].

CEUS, or contrast-enhanced ultrasound:

The development of ultrasound contrast agents (UCAs) and technological advancements by ultrasound manufacturers have enabled UCAs to transition from Doppler rescue agents to diagnostic agents, offering a real-time assessment of contrast enhancement patterns of liver lesions.

The microbubble structure of UCAs utilized in diagnostic US is made up of gas bubbles that are held in place by a shell [20]. Perfluorocarbons with a phospholipid membrane serve as the basis for current generation microbubbles, which have low solubility and advantageous resonance behavior at low acoustic pressures. Because they are too big to penetrate the interstitial fluid and too small to be filtered by the lungs, microbubbles, which normally have diameters between 3 and 5 μm, stay in the vascular compartment for several minutes after being injected intravenously. Continuous real-time imaging is made possible by these compounds' strong non-linear harmonic responses when insonated with low acoustic pressure and their ability to generate particular signals without being destroyed when insonated at low mechanical index (MI).

The arterial phase, portal venous phase, and late phase are three overlapping vascular phases that can be defined and seen because to UCAs' function as blood pool agents. These phases continue until the UCA is removed from the hepatic parenchyma. This late phase may be a reflection of sinusoid pooling, reticuloendothelial system (RES), or Kupffer cell uptake, and it deviates from the equilibrium phase of extracellular computed tomography (CT) and magnetic resonance imaging (MRI) agents [21,22].

Less than 5% of people experience minor side effects from UCAs, which usually include vasovagal episodes, taste abnormalities, and temporary discomfort at the injection site. Because UCAs are not nephrotoxic, renal function does not need to be assessed before taking them. Compared to modern X-ray contrast agents, the incidence of severe hypersensitivity or allergic reaction is lower and on par with that of MR contrast agents [23].

Computer Tomography

Focused liver lesions can now be better detected and described thanks to the introduction of multidetector row helical computed tomography (MDCT), which offers greater spatial and temporal resolution [24]. The whole liver can be photographed in 10 seconds or less with MDCT since numerous data sets are acquired with each rotation of the x-ray tube, as opposed to 25–30 seconds with single slice helical CT technology. Multiple trips through the liver at various vascular phases after bolus are made possible by the brief time required to scan the liver. Superior spatial resolution and the capacity to display data in different planes are achieved by using contrast injection and thin-section collimation to create volume data sets with isotropic or nearly isotropic voxel dimensions. A "dual-phase" approach is frequently used with single-slice helical CT, acquiring images in both the portal venous-dominant phase and the hepatic arterial-dominant phase. The early arterial phase of the "triple-phase" method is photographed 18–25 seconds after a contrast bolus injection [25]. It is possible to obtain a 3D CT hepatic-mesenteric angiography by using multiplanar reconstructions.

Since they exhibit the greatest amplification in comparison to the background liver parenchyma, hypervascular liver lesions are best seen in the late arterial phase. Hepatic vein opacification and greatest parenchymal enhancement occur during the portal venous-dominant phase.
The entire abdomen and, based on the clinical indication, the pelvis are included in this phase. In order to better characterize focal liver lesions, a delayed or equilibrium phase conducted three to five minutes after contrast delivery may be useful.

Magnetic Resonance Imaging (MRI)

Given the current advancements in multi-detector CT technology, it is likely arguable whether MRI is still the most sensitive and specific method for assessing the liver [26,27]. However, the flexibility and variety of pulse sequences offered by MRI offer a major benefit over CT, and lesion/liver contrast is higher with MRI than with CT. Multiple magnetic resonance pulse sequences are used in hepatobiliary MRI, and each one generates pictures that offer distinct details about the liver and biliary tree. A T1-weighted in-phase/out-of-phase spoiled gradient echo sequence and one or more T2-weighted sequences are included in the majority of exams. It is also possible to identify patterns of tumor enhancement by combining these sequences with extracellular injectable contrast agents, typically with a fat-saturated spoiled gradient echo sequence. Additionally, better liver tumor detection and characterization are made possible by the introduction of tissue-specific contrast agents as super paramagnetic iron oxide [28–30]. Pacemakers, cochlear implants, implanted cardiac defibrillators, and metallic orbital foreign bodies are among the conditions that preclude MRI.

Agents for intravenous MR contrast:

Clinically accessible liver contrast agents fall into the following categories: non-specific extracellular contrast, liver-specific hepatocyte-specific and RES-specific categories, and agents that combine early blood pool and late RES-specific characteristics.
For liver MRI, extracellular gadolinium chelates are widely utilized. Three stages of contrast enhancement are usually observed after an intravenous infusion of a gadolinium-based agent: the arterial, portal venous, and equilibrium phases. Since the portal vein provides the majority of the liver's blood supply, the majority of the liver does not enhance during the arterial phase. Liver lesion enhancement patterns are comparable. to those shown on contrast-enhanced CT and CEUS. For detecting late enhancement of liver lesions, the equilibrium phase, also known as the delayed phase, is helpful. Furthermore, distinctive results on delayed imaging include peripheral or heterogeneous washout from liver metastases and washout of contrast from HCC. Imaging procedures may need to be modified in light of recent concerns regarding nephrogenic systemic sclerosis in renal insufficiency after intravenous gadolinium [31,32].

Contrast agents targeted to the liver

Contrast drugs that selectively target hepatocytes:

Hepatocytes absorb hepatocyte-selective contrast chemicals, which are then excreted by the kidneys and biliary system [33]. They are all T1-relaxation boosting drugs that intensify the signal in both malignancies that contain hepatocytes and normal liver tissue. Hemangiomas and metastases are examples of non-hepatocyte-containing tumors that do not absorb these drugs and are made more noticeable by the background liver's increased signal on delayed aging. Like gadolinium chelates, agents like Gd-BOPTA (Multihance) also display early perfusional information.

Reticuloendothelial agents:

These compounds reflect the quantity of active macrophages and target the RES, specifically the liver and spleen [34]. Superparamagnetic iron oxide (SPIO) particles are among the reticuloendothelial agents that are presently being used in therapeutic settings. When employed alone or in conjunction with gadolinium, SPIO particles function as a negative contrast agent [35,36]. The majority of liver cancers, whether benign or malignant, lack SPIO particle absorption and are deficient in Kupffer cells [37,38]. Because the backdrop liver darkens preferentially after SPIO injection, the majority of liver tumors seem somewhat hyperintense. The most precise method for identifying liver tumors may be a "dual contrast" MRI that combines gadolinium and SPIO-enhanced images [39].

Diffusion-weighted MRI:

Diffusion-weighted imaging (DWI) increases the visibility of numerous hepatic and extrahepatic cancers by using pulse sequence techniques that are sensitive to the microscopic mobility of water protons on a very tiny scale [40].

PET stands for Positron Emission Tomography.

The idea of functional imaging in disease management has been completely transformed by the development of molecular imaging with PET, especially in the field of oncology, which accounts for 90% of PET applications. PET imaging has better spatial resolution and image clarity than gamma camera SPECT radiopharmaceuticals, and it can identify even tiny lesions more effectively [41]. PET offers whole body imaging, which enables the diagnosis of multifocal and metastatic diseases, which is an advantage over cross-sectional anatomical imaging. The fluorinated glucose derivative is the most often utilized of several radiopharmaceuticals based on labeled short-lived positron emitters.

18F-FDG (fluorodeoxyglucose). Improvements in other cross-sectional imaging methods, namely MRI and US, have made the employment of traditional nuclear medicine techniques, such as colloid scintigraphy, in the imaging of liver cancer virtually obsolete [42].

Diagnostic techniques

High morbidity and mortality are characteristics of hepatocellular carcinoma, a particularly deadly and severe kind of cancer [43]. It is important to diagnose HCC in its early stages because most patients do not exhibit any symptoms at all. In order to identify the disease early on, diagnostic methods are essential. A key element of diagnostic methods is the histology of liver cancer, especially when it comes to differentiating between early-stage and more advanced instances. Based on the size of the tumor and the level of cellular differentiation, HCC is categorized into early and advanced stages by the WHO and international consensus criteria [44]. Early HCC is frequently linked to cirrhotic livers and is characterized by hypovascularity. It is usually less than 2 cm with poorly defined edges. On the other hand, advanced HCC can exhibit a variety of macroscopic shapes, including diffuse, massive, or nodular patterns [45]. Well-vascularized tumors, broad trabecular or pseudoglandular structures, cytologic atypia, and other histological characteristics are important indicators of HCC.

The reticulin network is lost. Accurate diagnosis, staging, and therapy of liver cancer depend on an understanding of these differences, which makes more efficient and specialized treatment plans possible. Liver cancer is diagnosed using a variety of invasive and non-invasive diagnostic methods.

Invasive Techniques

For the diagnosis of HCC, a biopsy is an invasive procedure that offers many benefits over imaging methods. A biopsy is used to obtain a tiny sample of tissue, which yields crucial data, especially for the diagnosis of well-differentiated HCC [46]. There are several ways to get biopsy samples, including tissue and liquid biopsy techniques. A liquid biopsy is a less intrusive technique that looks for cancerous cells or pieces of tumor DNA in a sample of blood or other bodily fluids. This method examines the blood's extracellular vesicles, non-coding RNAs, cell-free DNA, and circulating tumor cells [47].

An additional method that may be used for HCC detection, minimal residual illness identification, treatment selection, and therapeutic response monitoring is liquid biopsy [48]. By facilitating non-invasive, real-time tumor monitoring, the quickly developing field of liquid biopsy is revolutionizing cancer care [49]. Using a needle, endoscope, or surgical technique, a little sample of tissue is taken from the body for examination under a microscope during a tissue biopsy. The outcome aids physicians in making well-informed choices regarding available treatments. Tissue biopsies are still a vital diagnostic technique for cancer [50]. This approach of tumor sample analysis yields important information for identifying the type and presence of malignancy [51]. Tissue biopsies can have certain dangers, though, such as the potential for consequences including discomfort and bleeding, especially in cirrhosis patients. About 5.9% of cases had modest problems, and 0.5% of cases have substantial bleeding. In the end, tissue and liquid biopsies both play significant roles in the diagnosis and treatment of HCC [52]. While liquid biopsies are anticipated to play complimentary roles in early HCC identification and treatment response monitoring, tissue biopsies may become essential in matching patients to appropriate treatments [53].

Non-invasive Techniques

The foundation for early HCC identification and surveillance is non-invasive diagnostic methods, which reduce patient pain while yielding crucial diagnostic data. Since non-invasive methods are currently the preferred method, biopsies of HCC are rarely needed. MRI, computed tomography (CT), and ultrasound are the most widely utilized diagnostic methods [54]. Imaging is crucial for HCC screening and monitoring, diagnosis, staging, and assessing response to treatment [55]. For the surveillance, diagnosis, staging, and post-treatment monitoring of HCC, imaging methods such USG, CT scans, MRIs, and positron emission tomography (PET) are essential [56]. These cutting-edge imaging techniques offer useful data to support clinical judgment and patient care [57].

The **Liver Imaging Reporting and Data System (LI-RADS)** provides a standardized framework for interpreting liver imaging in high-risk individuals. It complements clinical findings and histopathological evaluation, thereby improving diagnostic accuracy and staging. LI-RADS plays a crucial role in differentiating benign from malignant hepatic lesions and guiding therapeutic strategies [58].

Ultrasonography is a widely applied, real-time imaging modality that uses high-frequency sound waves to visualize internal organs, tissues, and vascular flow, making it valuable in detecting and monitoring liver pathologies, including hepatocellular carcinoma (HCC) [59]. Both the **American Association for the Study of Liver Diseases (AASLD)** and the **European Association for the Study of the Liver (EASL)** endorse ultrasound as the primary surveillance tool for individuals at elevated risk of HCC. This includes patients with cirrhosis, chronic HBV infection with additional risk factors (e.g., male sex, older age, family history), HCV infection with advanced fibrosis or cirrhosis, and those with non-alcoholic fatty liver disease (NAFLD) associated with significant fibrosis [60].

The introduction of **contrast-enhanced ultrasound (CEUS)** agents, such as Levovist and Sonazoid (commonly used in Japan), has markedly advanced HCC diagnosis and management [61]. CEUS enables superior lesion characterization, earlier detection of small tumors, and more precise interventional guidance, ultimately improving therapeutic planning [62]. These technological innovations have significantly enhanced the clinical management of HCC, offering better outcomes for patients.

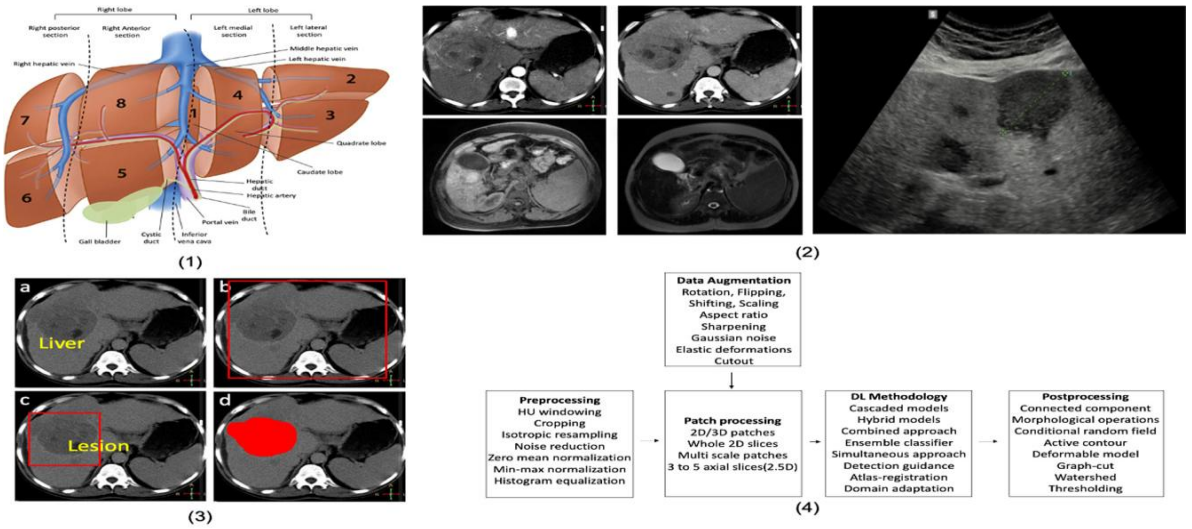
Similarly, **computed tomography (CT)**, a cross-sectional imaging modality based on computerized X-ray acquisition, remains integral to accurate diagnosis and treatment planning [63]. Using multiphase sequential acquisitions, CT provides high-resolution images of the liver. Historically, contrast-enhanced helical CT was considered a dependable method for detecting and staging HCC .

Recent **advances in CT imaging** have introduced techniques such as angiographic mapping of key vascular structures, which further enhance diagnostic precision [64]. Novel approaches—including **perfusion CT, dual-energy CT, and hepatocyte-specific contrast imaging**—represent major innovations in radiology [65]. These methods improve lesion detection, facilitate more accurate staging of hepatocellular carcinoma (HCC), and help guide individualized treatment strategies.

Magnetic resonance imaging (MRI) provides several advantages over CT, the most important being the absence of ionizing radiation exposure [66,67]. MRI offers superior soft-tissue contrast, which aids in the detailed visualization and characterization of liver lesions [68]. It also has the benefit of sometimes avoiding contrast use, and when contrast is required, smaller amounts are generally sufficient compared to CT [69]. Moreover, hepatocyte-specific contrast agents can be utilized in MRI, offering unique diagnostic insights [70].

A comprehensive liver MRI protocol incorporates multiple advanced techniques: **T2-weighted imaging** highlights areas of fluid, edema, or inflammation; **T1-weighted imaging** delivers detailed anatomical resolution; and **diffusion-weighted imaging with apparent diffusion coefficient mapping** assists in tumor detection by measuring water diffusion. Additionally, **contrast-enhanced sequences** improve the assessment of tumor vascularity, liver perfusion, and hemodynamic changes [71,72]. Beyond lesion characterization, newer MRI technologies allow **quantitative assessment of hepatic fat, iron load, and stiffness via MR elastography** [73]. Dynamic contrast-enhanced MRI further provides valuable information on hepatic perfusion and functional status [74]. Altogether, MRI stands out as a versatile modality for comprehensive evaluation and management of HCC.

Positron emission tomography (PET) represents another important advancement. PET employs the radiotracer **18F-fluoro-2-deoxy-D-glucose (FDG)**, which accumulates in cancer cells due to their increased glucose metabolism. Following phosphorylation by hexokinase, FDG becomes trapped intracellularly, enabling visualization of tumor metabolism [75]. While PET is highly sensitive for detecting extrahepatic metastases, its relatively low sensitivity for primary HCC lesions limits its role in initial staging [76]. Consequently, **PET-CT is best used as a complementary tool** alongside CT, MRI, and bone scintigraphy, particularly in patients considered for curative approaches such as resection or transplantation. The metabolic data provided by PET add valuable dimensions to staging accuracy and treatment planning in HCC [77].



Collage of (1) Liver anatomy, (2) Imaging modalities (CT, MR, US) for liver analysis, (3) Liver analysis tasks, (4) Overview of the methods used in selected papers.

Figure:1 Collage of liver images [78]

Comparison of Traditional Imaging Features, Radiomics, and Deep Learning

Conventional imaging modalities such as CT and MRI provide valuable non-invasive biological and pathological information, and have been shown to serve as independent predictors for preoperative assessment of CK19-positive hepatocellular carcinoma (HCC). However, their use is constrained by subjectivity, reliance on radiologists' visual interpretation, and relatively limited predictive performance. Radiomics has emerged as a way to overcome these limitations by extracting a large number of high-dimensional, often imperceptible, quantitative features from medical images using advanced computational techniques. In oncology, radiomics has demonstrated potential in capturing tumour characteristics such as histological grade, disease progression, and genetic expression, offering non-invasive evaluation across multiple time points and improving both diagnosis and prognostication. Nonetheless, challenges remain, including insufficient biological interpretability of radiomic features, lack of standardization in feature extraction and model development, and the time-consuming manual segmentation of regions of interest (ROIs) by radiologists. Deep learning, a sophisticated branch of machine learning, addresses some of these issues by automatically identifying and learning the most relevant imaging features for a given task, eliminating manual feature extraction and reducing observer variability. It allows the discovery of more complex and informative imaging biomarkers while saving time and labor. Despite these advantages, deep learning models are often criticized for their "black-box" nature, making clinical interpretation difficult [79,80]. Moreover, studies applying deep learning to predict CK19 expression in HCC remain limited, highlighting the need for further research to validate their clinical utility.

Discussion

Early detection and accurate characterization of hepatic malignancies—particularly HCC—remain central to improving patient outcomes, and imaging is the clinical backbone for screening, diagnosis, staging, treatment selection, and response assessment. No single modality answers all clinical questions: ultrasound (US), contrast-enhanced multiphasic CT, contrast-enhanced MRI (including hepatobiliary agents), and PET/CT each have complementary strengths and limitations. International practice guidelines and reporting systems (most notably LI-RADS) emphasize multiphasic CT or MRI for definitive noninvasive diagnosis in at-risk patients while positioning US primarily for surveillance; this multimodality paradigm both maximizes diagnostic yield and reduces unnecessary biopsies.Ultrasound remains the most widely used modality for HCC surveillance because it is noninvasive, inexpensive, and widely available; however, its sensitivity is highly operator- and patient-dependent and decreases substantially for lesions <2 cm and in patients with steatosis or obesity. Contrast-enhanced ultrasound (CEUS) improves lesion characterization, provides real-time vascular information, and can be a valuable problem-solving tool in experienced centers; recent systematic reviews and updated US-LI-RADS guidance support CEUS as an important second-line technique, particularly when CT/MRI are inconclusive or contraindicated. Nevertheless, US/CEUS is less useful for whole-liver staging compared with cross-sectional modalities. Multiphasic, contrast-enhanced CT is widely available and provides rapid, reproducible assessment of arterial phase hyperenhancement, washout, and capsule — the classic imaging hallmarks used in noninvasive HCC diagnosis and staging. CT's strengths include excellent spatial resolution, speed, and broad accessibility; its limitations include ionizing radiation, lower intrinsic soft-tissue contrast compared with MRI, and potential nephrotoxicity from iodinated contrast. CT is often the first cross-sectional test used in many centers and is fully integrated into LI-RADS/clinical pathways when MRI is unavailable or contraindicated. MRI offers the highest soft-tissue contrast and a wide array of sequences (T1, T2, diffusion-weighted imaging [DWI], dynamic multiphasic imaging) that improve detection and characterization of small lesions, assessment of tumor biology (cellularity, necrosis), and evaluation of vascular invasion. Hepatocyte-specific contrast agents (e.g., gadoxetate disodium) further increase sensitivity for early and small HCCs by exploiting differential hepatocyte uptake in the hepatobiliary phase, thereby improving lesion conspicuity and characterization; MRI also enables functional assessment (DWI, perfusion) that increasingly informs prognosis and therapy planning. These advantages make MRI the preferred cross-sectional modality when available and feasible. PET/CT has a more limited role in primary HCC detection because conventional ^18F-FDG PET shows variable uptake in HCC (sensitivity depends on tumor differentiation and metabolic phenotype). However, PET provides unique whole-body staging capability, can identify extrahepatic disease missed on conventional imaging, and has prognostic value (FDG-avid tumors often have worse outcomes). Emerging PET tracers and dual-tracer strategies (e.g., combining FDG with other tracers, and novel probes such as FAPI or PSMA for selected indications) are showing promise for improved detection, lesion characterization, and therapy planning, but these remain adjuncts rather than primary diagnostic tests in routine practice. Beyond

modality choice, standardized reporting systems (LI-RADS for CT/MRI and updated US LI-RADS for surveillance) and algorithmic approaches improve diagnostic consistency across centers, reduce unnecessary biopsies, and guide management decisions. Problem-solving combinations—such as CT/MRI backed by CEUS when results are equivocal or MRI with hepatobiliary contrast when CT is non-diagnostic—have been shown to increase sensitivity while preserving specificity. Additionally, computational advances including radiomics and artificial intelligence are rapidly maturing and offer potential to extract prognostic imaging biomarkers, automate detection, and reduce reader variability; these tools are complementary and are likely to be increasingly integrated into clinical workflows pending robust validation. Despite substantial progress, several important limitations and research needs remain. Surveillance sensitivity for early HCC is imperfect (US performance varies), small lesion characterization still relies heavily on MRI availability, and CT involves radiation and contrast risks. PET approaches and novel tracers require broader validation and cost-effectiveness studies before routine use. Prospective multicenter studies are needed to define optimal modality sequences in different risk strata, to standardize CEUS use across platforms, and to validate radiomic/AI signatures across vendor and population heterogeneity. Finally, equitable access to high-quality multiphasic MRI remains a global challenge that affects the generalizability of guideline recommendations. In summary, a pragmatic, patient-centered imaging strategy for liver cancer leverages ultrasound for surveillance, multiphasic contrast-enhanced CT or MRI (preferably MRI when available) for diagnosis and staging using LI-RADS-based criteria, CEUS as a targeted problem-solving technique, and PET for selected staging or prognostic questions. Emerging tracers and computational imaging promise further gains but must be adopted thoughtfully after prospective validation. Combining modalities and standardized reporting maximizes diagnostic accuracy while minimizing invasive procedures—an approach supported by contemporary practice guidelines and the evolving evidence base.

Conclusion

The assessment of liver cancer relies on a multimodal imaging approach, with each technique contributing unique strengths and compensating for the limitations of others. Ultrasound remains a cost-effective and widely available first-line modality, particularly valuable for screening and guiding interventions, though its diagnostic accuracy is operator-dependent and limited in obese patients or those with advanced cirrhosis. Computed tomography (CT) offers excellent spatial resolution and is pivotal in staging and vascular evaluation, yet it carries the risk of radiation exposure and nephrotoxic contrast effects. Magnetic resonance imaging (MRI), especially with hepatocyte-specific contrast agents, provides superior soft-tissue characterization and functional information, making it one of the most sensitive techniques for lesion detection and characterization. Positron emission tomography (PET), though limited in detecting well-differentiated hepatocellular carcinoma, is valuable for identifying extrahepatic spread and monitoring treatment response .

Importantly, the integration of imaging with diagnostic techniques, such as biopsy and molecular profiling, ensures a more comprehensive evaluation of tumor biology, which is essential for precision medicine. The complementary role of these modalities highlights the importance of individualized imaging strategies tailored to clinical context, tumor characteristics, and therapeutic planning. Future directions include the incorporation of radiomics and artificial intelligence to enhance diagnostic accuracy, improve risk stratification, and enable non-invasive tumor phenotyping. Ultimately, a multidisciplinary, multimodal approach remains crucial for the accurate diagnosis, staging, and management of liver cancer.

References

1. Chacko S, Samanta S: Hepatocellular carcinoma: a life-threatening disease. Biomed Pharmacother. 2016, 84:1679-88. 10.1016/j.biopha.2016.10.078
2. Craig AJ, von Felden J, Garcia-Lezana T, Sarcognato S, Villanueva A: Tumour evolution in hepatocellular carcinoma. Nat Rev Gastroenterol Hepatol. 2020, 17:139-52. 10.1038/s41575-019-0229-4
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F: Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021, 71:209-49. 10.3322/caac.21660
4. Ferlay J, Soerjomataram I, Dikshit R, et al.: Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015, 136:E359-86. 10.1002/ijc.29210
5. Sayiner M, Golabi P, Younossi ZM: Disease burden of hepatocellular carcinoma: a global perspective . Dig Dis Sci. 2019, 64:910-7. 10.1007/s10620-019-05537-2
6. Wu CH, Chiu NC, Yeh YC, et al.: Uncommon liver tumors: case report and literature review. Medicine (Baltimore). 2016, 95: e4952. 10.1097/MD.0000000000004952
7. Liver and bile duct cancer. (2024). Accessed: July 30, 2024: https://www.cancer.gov/types/liver.
8. Tunissiolli NM, Castanhole-Nunes MM, Biselli-Chicote PM, Pavarino EC, da Silva RF, da Silva RC, Goloni Bertollo EM: Hepatocellular carcinoma: a comprehensive review of biomarkers, clinical aspects, and therapy. Asian Pac J Cancer Prev. 2017, 18:863-72. 10.22034/APJCP.2017.18.4.863
9. Brindley PJ, Bachini M, Ilyas SI, et al.: Cholangiocarcinoma. Nat Rev Dis Primers. 2021, 7:65. 10.1038/s41572-021-00300-2
10. Wu B, Sodji QH, Oyelere AK: Inflammation, fibrosis and cancer: mechanisms, therapeutic options and challenges. Cancers (Basel). 2022, 14:552. 10.3390/cancers14030552
11. Tsilimigras DI, Brodt P, Clavien PA, et al.: Liver metastases. Nat Rev Dis Primers. 2021, 7:27. 10.1038/s41572-021-00261-6
12. Liu LX, Zhang WH, Jiang HC: Current treatment for liver metastases from colorectal cancer. World J Gastroenterol. 2003, 9:193-200. 10.3748/wjg. v9. i2.193

13. Quaglia A: Hepatocellular carcinoma: a review of diagnostic challenges for the pathologist. J Hepatocell Carcinoma. 2018, 5:99-108. 10.2147/JHC.S159808
14. Gaddikeri S, McNeeley MF, Wang CL, et al.: Hepatocellular carcinoma in the noncirrhotic liver. AJR Am J Roentgenol. 2014, 203: W34-47. 10.2214/AJR.13.11511
15. Fattovich G, Stroffolini T, Zagni I, Donato F: Hepatocellular carcinoma in cirrhosis: incidence and risk factors. Gastroenterology. 2004, 127:S35-50. 10.1053/j.gastro.2004.09.014
16. Kinsey E, Lee HM: Management of hepatocellular carcinoma in 2024: the multidisciplinary paradiagram in an evolving treatment landscape. Cancers (Basel). 2024, 16:666. 10.3390/cancers16030666
17. Wu MC: Clinical research advances in primary liver cancer. World J Gastroenterol. 1998, 4:471-4. 10.3748/wjg.v4.i6.471
18. Ryder SD. Guidelines for the diagnosis and treatment of hepatocellular carcinoma (HCC) in adults. Gut 2003; 52 Suppl 3: iii1-iii8
19. Khan SA, Davidson BR, Goldin R, Pereira SP, Rosenberg WM, Taylor-Robinson SD, Thillainayagam AV, Thomas HC, Thursz MR, Wasan H. Guidelines for the diagnosis and treatment of cholangiocarcinoma: consensus document. Gut 2002; 51 Suppl 6: VI1-VI9
20. Cosgrove DO, Eckersley R. Contrast-enhanced ultrasound: Basic physics and technology overview. In: Lencioni R. Enhancing the role of ultrasound with ultrasound contrast agents. Pisa: Springer, 2006: 3-14
21. Kono Y, Steinbach GC, Peterson T, Schmid-Schonbein GW, Mattrey RF. Mechanism of parenchymal enhancement of the liver with a microbubble-based US contrast medium: an intravital microscopy study in rats. Radiology 2002; 224: 253-257
22. Yanagisawa K, Moriyasu F, Miyahara T, Yuki M, Iijima H. Phagocytosis of ultrasound contrast agent microbubbles by Kupffer cells. Ultrasound Med Biol 2007; 33: 318-325
23. Piscaglia F, Bolondi L. The safety of Sonovue in abdominal applications: retrospective analysis of 23188 investigations. Ultrasound Med Biol 2006; 32: 1369-1375
24. Weg N, Scheer MR, Gabor MP. Liver lesions: improved detection with dual-detector-array CT and routine 2.5-mm thin collimation. Radiology 1998; 209: 417-426
25. Foley WD, Mallisee TA, Hohenwalter MD, Wilson CR, Quiroz FA, Taylor AJ. Multiphase hepatic CT with a multirow detector CT scanner. AJR Am J Roentgenol 2000; 175: 679-685
26. Glockner JF. Hepatobiliary MRI: current concepts and controversies. J Magn Reson Imaging 2007; 25: 681-695
27. Teefey SA, Hildeboldt CC, Dehdashti F, Siegel BA, Peters MG, Heiken JP, Brown JJ, McFarland EG, Middleton WD, Balfe DM, Ritter JH. Detection of primary hepatic malignancy in liver transplant candidates: prospective comparison of CT, MR imaging, US, and PET. Radiology 2003; 226: 533-542
28. Semelka RC, Helmberger TK. Contrast agents for MR imaging of the liver. Radiology 2001; 218: 27-38

29. Bellin MF. MR contrast agents, the old and the new. Eur J Radiol 2006; 60: 314-323
30. Gandhi SN, Brown MA, Wong JG, Aguirre DA, Sirlin CB. MR contrast agents for liver imaging: what, when, how. Radiographics 2006; 26: 1621-1636
31. Kuo PH, Kanal E, Abu-Alfa AK, Cowper SE. Gadolinium based MR contrast agents and nephrogenic systemic f ibrosis. Radiology 2007; 242: 647-649
32. Board of the faculty of the Royal College of Radiologists.Gadolinium-based contrast media and nephrogenic systemic sclerosis. 2007. Royal College of Radiology, UK. Available from: URL:http://www.rcr.ac.uk/docs/radiology/pdf/BFCR0714_Gadolinium_NSF_guidanceNov07.pdf
33. Hamm B, Vogl TJ, Branding G, Schnell B, Taupitz M, Wolf KJ, Lissner J. Focal liver lesions: MR imaging with Mn DPDP--initial clinical results in 40 patients. Radiology 1992; 182: 167-174
34. Ferrucci JT, Stark DD. Iron oxide-enhanced MR imaging of the liver and spleen: review of the first 5 years. AJR Am J Roentgenol 1990; 155: 943-950
35. Ward J, Guthrie JA, Scott DJ, Atchley J, Wilson D, Davies MH, Wyatt JI, Robinson PJ. Hepatocellular carcinoma in the cirrhotic liver: double-contrast MR imaging for diagnosis. Radiology 2000; 216: 154-162
36. Halavaara J, Tervahartiala P, Isoniemi H, Hockerstedt K. Efficacy of sequential use of superparamagnetic iron oxide and gadolinium in liver MR imaging. Acta Radiol 2002; 43: 180-185
37. Kim YK, Kwak HS, Kim CS, Chung GH, Han YM, Lee JM. Hepatocellular carcinoma in patients with chronic liver disease: comparison of SPIO-enhanced MR imaging and 16-detector row CT. Radiology 2006; 238: 531-541
38. Araki T. SPIO-MRI in the detection of hepatocellular carcinoma. J Gastroenterol 2000; 35: 874-876
39. Ward J, Robinson PJ, Guthrie JA, Downing S, Wilson D, Lodge JP, Prasad KR, Toogood GJ, Wyatt JI. Liver metastases in candidates for hepatic resection: comparison of helical CT and gadolinium- and SPIO-enhanced MR imaging. Radiology 2005; 237: 170-180
40. Chow LC, Bammer R, Moseley ME, Sommer FG. Single breath-hold diffusion-weighted imaging of the abdomen. J Magn Reson Imaging 2003; 18: 377-382
41. Meikle SR, Dahlbom M. Positron emission tomography (PET). In: Ell PJ, Gambhir SS. Nuclear medicine in clinical diagnosis and treatment. Edinburgh: Churchill Livingstone, 2004: 1827-1843
42. Choi BY, Nguyen MH. The diagnosis and management of benign hepatic tumors. J Clin Gastroenterol 2005; 39: 401-412
43. Chidambaranathan-Reghupaty S, Fisher PB, Sarkar D: Hepatocellular carcinoma (HCC): epidemiology, etiology and molecular classification. Adv Cancer Res. 2021, 149:1-61. 10.1016/bs.acr.2020.10.001
44. Schlageter M, Terracciano LM, D'Angelo S, Sorrentino P: Histopathology of hepatocellular carcinoma. World J Gastroenterol. 2014, 20:15955-64. 10.3748/wjg.v20.i43.15955

45. Karadag Soylu N: Update on hepatocellular carcinoma: a brief review from pathologist standpoint . J Gastrointest Cancer. 2020, 51:1176-86. 10.1007/s12029-020-00499-5
46. Di Tommaso L, Spadaccini M, Donadon M, Personeni N, Elamin A, Aghemo A, Lleo A: Role of liver biopsy in hepatocellular carcinoma. World J Gastroenterol. 2019, 25:6041-52. 10.3748/wjg.v25.i40.6041
47. Jain D: Tissue diagnosis of hepatocellular carcinoma. J Clin Exp Hepatol. 2014, 4:S67-73. 10.1016/j.jceh.2014.03.047
48. Lee YT, Tran BV, Wang JJ, et al.: The role of extracellular vesicles in disease progression and detection of hepatocellular carcinoma. Cancers (Basel). 2021, 13:3076. 10.3390/cancers13123076
49. Osho A, Rich NE, Singal AG: Role of imaging in management of hepatocellular carcinoma: surveillance, diagnosis, and treatment response. Hepatoma Res. 2020, 6:55. 10.20517/2394-5079.2020.42
50. Lone SN, Nisar S, Masoodi T, et al.: Liquid biopsy: a step closer to transform diagnosis, prognosis and future of cancer treatments. Mol Cancer. 2022, 21:79. 10.1186/s12943-022-01543-7
51. Martins I, Ribeiro IP, Jorge J, Gonçalves AC, Sarmento-Ribeiro AB, Melo JB, Carreira IM: Liquid biopsies: applications for cancer diagnosis and monitoring. Genes (Basel). 2021, 12:349. 10.3390/genes12030349
52. Mouliere F, Thierry AR: The importance of examining the proportion of circulating DNA originating from tumor, microenvironment and normal cells in colorectal cancer patients. Expert Opin Biol Ther. 2012, 12 Suppl 1:S209-15. 10.1517/14712598.2012.688023
53. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD: Liver biopsy. Hepatology. 2009, 49:1017-44. 10.1002/hep.22742
54. Lehrich BM, Zhang J, Monga SP, Dhanasekaran R: Battle of the biopsies: role of tissue and liquid biopsy in hepatocellular carcinoma. J Hepatol. 2024, 80:515-30. 10.1016/j.jhep.2023.11.030
55. El Jabbour T, Lagana SM, Lee H: Update on hepatocellular carcinoma: pathologists' review . World J Gastroenterol. 2019, 25:1653-65. 10.3748/wjg.v25.i14.1653
56. Hoshida Y: Correction to: hepatocellular carcinoma. Hepatocellular Carcinoma: Molecular and Translational Medicine. Hoshida Y (ed): Humana, Cham; 2019. 71-92. 10.1007/978-3-030-21540-8_17
57. Hennedige T, Venkatesh SK: Imaging of hepatocellular carcinoma: diagnosis, staging and treatment monitoring. Cancer Imaging. 2013, 12:530-47. 10.1102/1470-7330.2012.0044
58. Chernyak V, Fowler KJ, Kamaya A, et al.: Liver imaging reporting and data system (LI-RADS) version 2018: Imaging of hepatocellular carcinoma in at-risk patients. Radiology. 2018, 289:816-30. 10.1148/radiol.2018181494

59. Kanzaria HK, McCabe AM, Meisel ZM, et al.: Advancing patient-centered outcomes in emergency diagnostic imaging: a research agenda. Acad Emerg Med. 2015, 22:1435-46. 10.1111/acem.12832
60. Sheu JC, Sung JL, Chen DS, et al.: Early detection of hepatocellular carcinoma by real-time ultrasonography. A prospective study. Cancer. 1985, 56:660-6. 10.1002/1097-0142(19850801)56:33.0.co;2-f
61. Bota S, Piscaglia F, Marinelli S, Pecorelli A, Terzi E, Bolondi L: Comparison of international guidelines for noninvasive diagnosis of hepatocellular carcinoma. Liver Cancer. 2012, 1:190-200. 10.1159/000343833
62. Kudo M: New sonographic techniques for the diagnosis and treatment of hepatocellular carcinoma . Hepatol Res. 2007, 37 Suppl 2:S193-9. 10.1111/j.1872-034X.2007.00184.x
63. Piscaglia F, Lencioni R, Sagrini E, Pina CD, Cioni D, Vidili G, Bolondi L: Characterization of focal liver lesions with contrast-enhanced ultrasound. Ultrasound Med Biol. 2010, 36:531-50. 10.1016/j.ultrasmedbio.2010.01.004
64. Hussain S, Mubeen I, Ullah N, et al.: Modern diagnostic imaging technique applications and risk factors in the medical field: a review. Biomed Res Int. 2022, 2022:5164970. 10.1155/2022/5164970
65. Scaglione M, Pinto A, Romano S, Scialpi M, Volterrani L, Rotondo A, Romano L: Using multidetector row computed tomography to diagnose and stage pancreatic carcinoma: the problems and the possibilities. JOP. 2005, 6:1-5.
66. Pandharipande PV, Krinsky GA, Rusinek H, Lee VS: Perfusion imaging of the liver: current challenges and future goals. Radiology. 2005, 234:661-73. 10.1148/radiol.2343031362
67. Ehman EC, Johnson GB, Villanueva-Meyer JE, Cha S, Leynes AP, Larson PE, Hope TA: PET/MRI: where might it replace PET/CT?. J Magn Reson Imaging. 2017, 46:1247-62. 10.1002/jmri.25711
68. Semelka RC, Armao DM, Elias J Jr, Huda W: Imaging strategies to reduce the risk of radiation in CT studies, including selective substitution with MRI. J Magn Reson Imaging. 2007, 25:900-9. 10.1002/jmri.20895
69. Bryant TH, Blomley MJ, Albrecht T, et al.: Improved characterization of liver lesions with liver-phase uptake of liver-specific microbubbles: prospective multicenter study. Radiology. 2004, 232:799-809. 10.1148/radiol.2323030596
70. Richardson L: Radiation exposure and diagnostic imaging. J Am Acad Nurse Pract. 2010, 22:178-85. 10.1111/j.1745-7599.2010.00494.x
71. The Basics of mri Interpretation. (2023). Accessed: August 24, 2024: https://geekymedics.com/the-basics of-mri-interpretation/.
72. Jacobs MA, Ouwerkerk R, Petrowski K, Macura KJ: Diffusion-weighted imaging with apparent diffusion coefficient mapping and spectroscopy in prostate cancer. Top Magn Reson Imaging. 2008, 19:261-72. 10.1097/RMR.0b013e3181aa6b50

73. França M, Alberich-Bayarri Á, Martí-Bonmatí L, et al.: Accurate simultaneous quantification of liver steatosis and iron overload in diffuse liver diseases with MRI. Abdom Radiol (NY). 2017, 42:1434-43. 10.1007/s00261-017-1048-0
74. Tan CH, Venkatesh SK: Magnetic resonance elastography and other magnetic resonance imaging techniques in chronic liver disease: current status and future directions. Gut Liver. 2016, 10:672-86. 10.5009/gnl15492
75. Schrevens L, Lorent N, Dooms C, Vansteenkiste J: The role of PET scan in diagnosis, staging, and management of non-small cell lung cancer. Oncologist. 2004, 9:633-43. 10.1634/theoncologist.9-6-633
76. Wudel LJ Jr, Delbeke D, Morris D, et al.: The role of [18F]fluorodeoxyglucose positron emission tomography imaging in the evaluation of hepatocellular carcinoma. Am Surg. 2003, 69:117-24; discussion 124-6.
77. Lu RC, She B, Gao WT, Ji YH, Xu DD, Wang QS, Wang SB: Positron-emission tomography for hepatocellular carcinoma: current status and future prospects. World J Gastroenterol. 2019, 25:4682-95
78. Survarachakan, S., Prasad, P. J. R., Naseem, R., de Frutos, J. P., Kumar, R. P., Langø, T., ... & Lindseth, F. (2022). Deep learning for image-based liver analysis—A comprehensive review focusing on malignant lesions. *Artificial Intelligence in Medicine*, *130*, 102331.
79. Lambin P, Rios-Velazquez E, Leijenaar R, et al. Radiomics: extracting more information from medical images using advanced feature analysis. Eur J Cancer. 2012;48(4):441–446. doi:10.1016/j.ejca.2011.11.036
80. Lambin P, Leijenaar RTH, Deist TM, et al. Radiomics: the bridge between medical imaging and personalized medicine. Nat Rev Clin Oncol. 2017;14(12):749–762. doi:10.1038/nrclinonc.2017.141