Pegem Journal of Education and Instruction, Vol. 14, No. 3 , 2024 (pp. 467-473)

RESEARCH ARTICLE WWW.PEGEGOG.NET

Evolving Radiologic Approaches in Monitoring Hepatocellular Carcinoma After Locoregional Therapy

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ABSTRACT

***Background*:** Hepatocellular carcinoma (HCC) represents a major global health challenge, particularly in regions with high prevalence of chronic liver disease. Locoregional therapies (LRTs), including transarterial chemoembolization (TACE), radiofrequency ablation (RFA), microwave ablation (MWA), and radiation segmentectomy, are widely adopted for patients with unresectable HCC. Accurate and timely radiologic assessment following LRT is critical for determining therapeutic efficacy, detecting residual or recurrent disease, and guiding subsequent management. This review aims to comprehensively explore the evolving radiologic strategies used to monitor hepatocellular carcinoma after locoregional therapy. Emphasis is placed on conventional imaging modalities such as contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI), as well as advanced functional techniques including diffusion-weighted imaging (DWI), hepatobiliary phase imaging, and dynamic contrast enhancement. The role of structured interpretation systems like LI-RADS Treatment Response Algorithm (TRA) and modified RECIST (mRECIST) is also examined.

Conclusion:

Imaging plays a pivotal role in the post-treatment surveillance of HCC. While traditional anatomical assessments based on lesion size have been foundational, the current era favors functional imaging and standardized response criteria that incorporate tumor viability, vascular enhancement patterns, and ancillary features. MRI, especially when combined with hepatospecific contrast agents and diffusion-weighted sequences, has shown superior performance in detecting viable tumor tissue. The LI-RADS TRA and mRECIST criteria have standardized interpretation and improved interobserver consistency. However, challenges remain, including post-treatment imaging artifacts, variations in therapeutic response, and overlap with benign post-ablative changes. Continuous refinements in imaging protocols, consensus guidelines, and radiologic-pathologic correlation are essential for optimizing outcomes. A multimodal, structured approach tailored to the type of LRT and individual patient context remains the cornerstone of accurate HCC monitoring.

Keywords: Radiologic Approaches, Hepatocellular Carcinoma, Locoregional Therapy

INTRODUCTION

Hepatocellular carcinoma (HCC) ranks as the sixth most common malignancy worldwide and remains a leading cause of cancer-related mortality, particularly in patients with chronic liver disease and cirrhosis [1]. While surgical resection and liver transplantation offer curative potential, the majority of HCC cases are diagnosed at intermediate or advanced stages, where locoregional therapies (LRTs) such as transarterial chemoembolization (TACE), radiofrequency ablation (RFA), and microwave ablation (MWA) are the mainstay of treatment [2,3].

In this therapeutic landscape, radiologic assessment plays an indispensable role in both initial treatment planning and post-treatment monitoring. Historically, treatment response was gauged primarily by changes in tumor size, as defined by conventional Response Evaluation Criteria in Solid Tumors (RECIST) [4]. However, this size-based approach often fails to reflect the true biological response of HCC to LRT, where tumor necrosis and lack of enhancement—rather than shrinkage—may indicate successful therapy [5].

To address this limitation, newer imaging-based criteria such as modified RECIST (mRECIST) and the Liver Imaging Reporting and Data System Treatment Response Algorithm (LI-RADS TRA) have emerged. These systems emphasize tumor viability through contrast-enhancement behavior, thereby improving the accuracy of treatment response evaluation [6,7]. At the same time, advances in imaging modalities—especially multiphase contrast-enhanced MRI and diffusion-weighted imaging (DWI)—have enhanced the detection of residual viable tumor tissue and early recurrence [8].

This review aims to explore the evolving radiologic landscape for HCC monitoring post-LRT, highlighting both conventional and emerging imaging tools, the diagnostic performance of structured reporting systems, and current clinical challenges. An emphasis is placed on tailoring imaging follow-up protocols to the type of LRT administered and ensuring that radiologic interpretation accurately guides subsequent clinical decisions.

Conventional Imaging Modalities for Response Assessment

Radiologic surveillance following locoregional therapy (LRT) in hepatocellular carcinoma (HCC) initially relied on conventional imaging techniques such as contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI). These modalities remain fundamental in post-treatment assessment due to their widespread availability and established diagnostic performance.

CT Imaging

Contrast-enhanced multiphasic CT is commonly used in routine follow-up of HCC. It involves imaging during arterial, portal venous, and delayed phases, providing dynamic evaluation of lesion vascularity—a crucial feature for detecting viable tumor [9]. Residual viable HCC typically demonstrates arterial phase hyperenhancement (APHE) followed by washout in the portal or delayed phase, a hallmark of tumor activity [10]. Despite its advantages, CT has limitations in detecting small residual tumors or distinguishing post-treatment changes such as coagulative necrosis, hemorrhage, or inflammation from viable neoplasia [11].

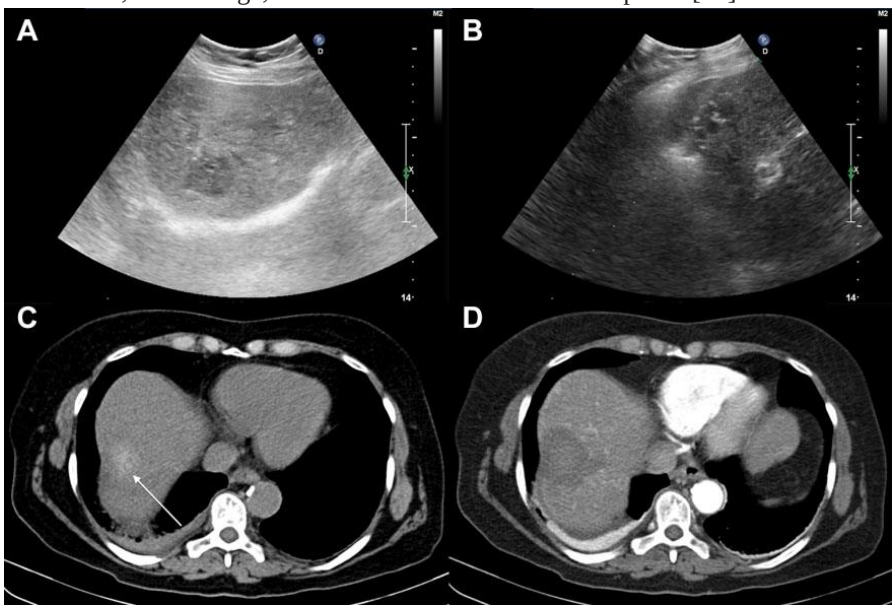

Figure (1): Pre (**A**) and post (**B**) microwave ablation (MWA) ultrasound (US) images, post MWA unenhanced (**C**) and (**D**) arterial computed tomography (CT) images of a 76-year-old man with hepatocellular carcinoma (HCC), showing signs of coagulative necrosis

appearing as central hyperintensity in the context of hypointense-treated area (**C**). No enhancing areas were demonstrated on arterial CT images (**D**) suggesting the complete ablation of the HCC nodule. [11].

MRI and Dynamic Imaging

Dynamic contrast-enhanced MRI using extracellular or hepatobiliary-specific contrast agents offers superior soft-tissue contrast resolution and functional information, making it more sensitive than CT in detecting subtle residual tumor enhancement [12]. MRI sequences, including T1-weighted, T2-weighted, and dynamic post-contrast imaging, allow for multiparametric assessment. The presence of APHE, intralesional signal alterations, and washout features help determine viability [13]. Additionally, MRI is less affected by beam-hardening artifacts, which can hinder CT interpretation in post-ablation zones.

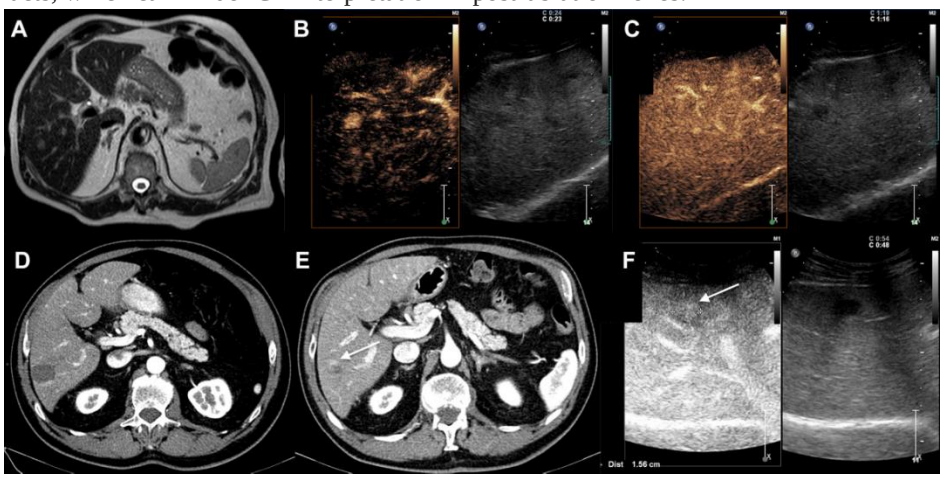

Figure (2): Pre-radiofrequency ablation (RFA) magnetic resonance (MR; **A**), and contrast-enhanced US (CEUS; **B and C**) images and post-RFA computed tomography (CT; **D and E**) and CEUS (**F**) images of 73-year-old man with hepatocellular carcinoma (HCC). Pre RFA T2-weighted (T2w) MR images demonstrated a mild-T2w hyperintense mass (**A**) showing arterial phase hyperenhancement (APHE) and washout appearance on CEUS images (**B and C**). On 1-month follow-up arterial-phase (**D**) CT images, no residual tumor was demonstrated suggesting a complete ablation. On 6-month follow-up arterial phase CT (**E**) and CEUS (F) images, a residual HCC nodule showing APHE was appreciable in the cranial portion of the treated area (*white arrow* in **E and F**).[13].

Response Criteria in Conventional Imaging

Traditional RECIST criteria, based solely on changes in tumor size, have been largely supplanted by modified RECIST (mRECIST), which incorporates viability indicators like contrast enhancement patterns [6]. These enhancements allow more accurate characterization of response post-TACE or ablation, particularly when necrosis occurs without measurable shrinkage.

While CT and MRI remain cornerstones of radiologic evaluation, emerging techniques and structured response algorithms now complement and refine the utility of these modalities, aiming to improve early detection of recurrence and inform therapeutic decisions more accurately.

Structured Response Criteria: mRECIST and LI-RADS Treatment Response Algorithm

To standardize interpretation and enhance diagnostic consistency in assessing hepatocellular carcinoma (HCC) after locoregional therapy (LRT), structured radiologic response criteria have evolved, notably the modified Response Evaluation Criteria in Solid Tumors (mRECIST) and the Liver Imaging Reporting and Data System Treatment Response Algorithm (LI-RADS TRA).

Modified RECIST (mRECIST)

mRECIST refines the original RECIST by shifting the focus from overall tumor size to viable tumor tissue, defined by the presence of arterial phase hyperenhancement (APHE) on dynamic imaging. This adjustment is critical for assessing response to therapies like transarterial chemoembolization (TACE) or ablation, where necrotic tumor tissue may remain unchanged in size despite effective treatment [14]. mRECIST categorizes treatment response as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD) based on the reduction or persistence of enhancing viable tissue [15].

LI-RADS Treatment Response Algorithm (TRA)

The American College of Radiology introduced the LI-RADS TRA to provide a standardized framework tailored specifically for patients at risk for HCC undergoing LRT. TRA builds upon the strengths of mRECIST but offers additional granularity through distinct diagnostic categories: viable, nonviable, and equivocal. "Viable" lesions show APHE, washout, or enhancement similar to pretreatment imaging, while "nonviable" lesions show no such enhancement. The "equivocal" category reflects uncertainty in enhancement patterns,

prompting short-term follow-up or further imaging [16].

LI-RADS TRA has shown higher interobserver agreement and diagnostic accuracy compared to mRECIST, especially when used with MRI [17]. Its adoption improves reproducibility in both clinical practice and research, aiding multidisciplinary decision-making regarding further treatment or surveillance.

As structured response algorithms evolve, their integration into daily radiologic workflow continues to enhance the precision of post-treatment monitoring and improve long-term outcomes in patients with HCC.

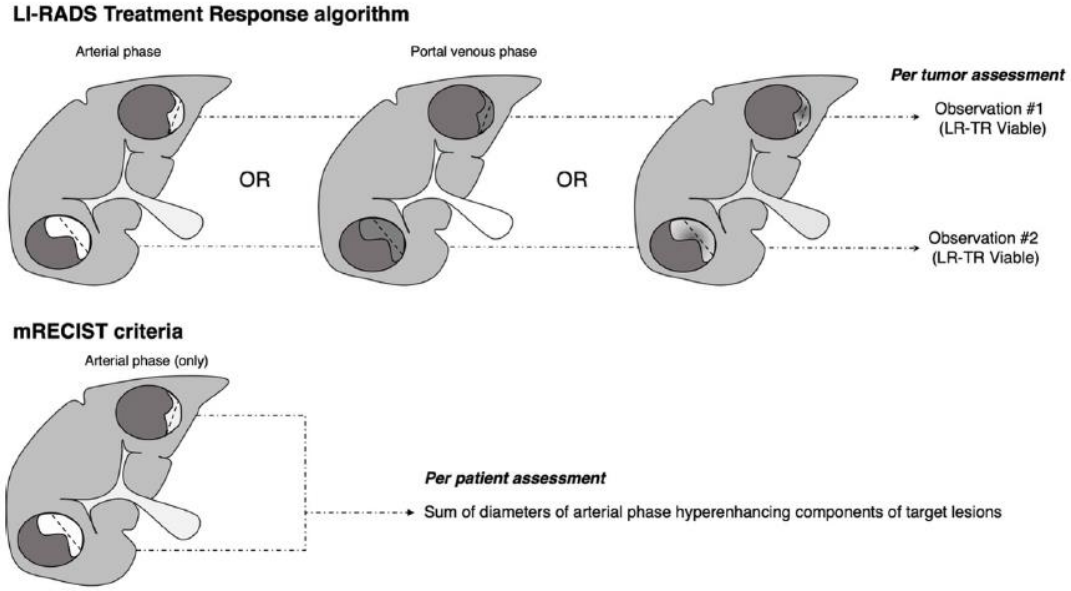

Figure (3): Comparison between Liver Imaging Reporting and Data System (LI-RADS) treatment response algorithm and modified Response Evaluation Criteria in Solid Tumors (mRECIST) to assess response. In the LR-Treatment response algorithm (LR-TRA), viable tumor is characterized by the presence of residual nodular or thick rim arterial phase hyperenhancement, or nodular or thick rim washout, or any enhancement that is similar to the pretreatment tumor characteristics in any imaging phase. In mRECIST, only residual arterial phase hyperenhancement is considered viable tumor. In both systems, residual tumor is measured as the longest diameter of the enhancing component of a treated tumor. In the LR-TRA, response is assessed on a per lesion basis, whereas in mRECIST, response is assessed on a per patient basis. [16].

Advanced MRI Techniques and Functional Imaging Tools

Recent advancements in MRI technology have introduced functional imaging sequences that enhance the evaluation of hepatocellular carcinoma (HCC) response after locoregional therapy (LRT). These techniques provide insights into tumor physiology beyond conventional morphologic assessment.

Diffusion-Weighted Imaging (DWI)

DWI leverages the random motion of water molecules to detect changes in tumor cellularity. Treated HCCs exhibiting necrosis typically show increased apparent diffusion coefficient (ADC) values, reflecting decreased cellular density, whereas residual viable tumor maintains lower ADC values [18]. Multiple studies have demonstrated that early post-treatment ADC measurements can predict long-term treatment outcomes more accurately than size-based criteria alone [19].

Perfusion MRI

Dynamic contrast-enhanced (DCE) MRI perfusion studies quantify parameters such as blood flow, blood volume, and permeability-surface area product. These metrics correlate with tumor angiogenesis and viability. After LRT, a significant reduction in perfusion parameters often precedes detectable changes in enhancement patterns, allowing earlier identification of nonresponders [20].

Hepatobiliary-Specific Contrast Agents

Gadoxetic acid–enhanced MRI provides combined dynamic and hepatocyte-specific imaging. Residual viable HCC typically appears hypointense on the hepatobiliary phase due to reduced expression of transporters, whereas treated necrotic areas may retain contrast longer [21]. This dual-phase approach improves lesion conspicuity and differentiation of post-treatment changes.

Radiomics and Quantitative Image Analysis

Although still primarily research tools, radiomic analysis extracts high-dimensional quantitative features (e.g., texture, shape) from imaging data. Early studies suggest that radiomic signatures derived from DWI and DCE sequences can stratify responders versus nonresponders and may predict recurrence risk [22].

Incorporating these advanced MRI techniques into routine follow-up protocols holds promise for more precise, earlier assessment of therapeutic efficacy, potentially guiding personalized retreatment strategies.

Emerging Roles of Computed Tomography and Dual-Energy Imaging

Computed tomography (CT), a cornerstone in oncologic imaging, continues to evolve with advanced technologies such as perfusion CT and dual-energy CT (DECT), offering added value in post-locoregional therapy (LRT) assessment for hepatocellular carcinoma (HCC).

Perfusion CT

Perfusion CT measures dynamic tissue vascularity by evaluating parameters like hepatic blood flow (HBF), hepatic blood volume (HBV), and mean transit time (MTT). These functional parameters are particularly useful in detecting early residual disease after TACE or ablation, even when no morphological enhancement changes are evident. Treated HCCs generally show a significant decline in perfusion metrics, while persistent hyperperfusion may indicate viable tumor [23].

Dual-Energy CT (DECT)

DECT utilizes two different X-ray energy spectra, enabling material decomposition and generation of iodine maps and virtual non-contrast images. This technique improves lesion conspicuity and enhances sensitivity in detecting residual enhancement post-treatment, especially in complex post-ablative changes or lipiodol-rich TACE zones [24]. DECT has also been shown to improve inter-reader agreement in assessing treatment response.

Volumetric and Quantitative CT Analysis

Post-treatment CT volumetry, especially using semi-automated software, allows precise tracking of tumor shrinkage or progression over time. 3D quantitative analysis tools provide reproducible metrics for tumor volume reduction, necrotic fraction, and enhancement intensity, which may correlate better with patient outcomes than diameter-based criteria alone [25].

Although CT remains inferior to MRI in soft-tissue characterization, its speed, availability, and newer functional applications such as DECT and perfusion imaging make it a valuable complementary tool in post-LRT surveillance, particularly when MRI is contraindicated or unavailable.

Radiologic Adaptations in Monitoring Systemic Therapy Response in Hepatocellular Carcinoma

As systemic therapies, including tyrosine kinase inhibitors (TKIs), immune checkpoint inhibitors (ICIs), and combination regimens, become integral to hepatocellular carcinoma (HCC) management, the need for refined radiologic strategies to evaluate treatment response has grown. Traditional anatomic criteria such as RECIST 1.1 are often insufficient in the immunotherapy era, as tumor shrinkage is not always a reliable surrogate for clinical benefit.

Modified Response Criteria: mRECIST and Beyond

The **modified RECIST (mRECIST)** framework addresses this limitation by emphasizing changes in **viable tumor**—defined by arterial phase enhancement—rather than tumor size alone. This is especially important for therapies that induce necrosis without immediate size reduction. While mRECIST is validated for locoregional therapies, its application has been extended to systemic treatments, showing better correlation with patient outcomes compared to RECIST 1.1 [26].

Atypical Response Patterns with Immunotherapy

Checkpoint inhibitors may elicit **pseudoprogression**, where tumors initially enlarge due to immune cell infiltration before regressing. This phenomenon necessitates cautious interpretation of early post-treatment imaging. **iRECIST** has been proposed to address this, allowing continued therapy beyond initial progression if the patient is clinically stable, with a requirement for confirmation on follow-up scans [27].

Functional Imaging as a Biomarker

Functional imaging modalities, including **diffusion-weighted imaging (DWI)** and **dynamic contrast-enhanced MRI (DCE-MRI)**, have shown promise in capturing early cellular or perfusion changes following systemic therapy. Decreased apparent diffusion coefficient (ADC) values or alterations in perfusion parameters may precede morphological changes, providing an early indicator of treatment response [28].

Additionally, **PET-CT**, though limited in HCC due to variable FDG uptake, can be useful in selected cases, particularly in poorly differentiated tumors or in the setting of systemic metastases [29].

Challenges and Future Directions

Despite advances, variability in imaging protocols and lack of standardization across institutions remain key challenges. Emerging techniques such as **radiomics** and **quantitative imaging biomarkers** offer potential but require further validation. Integration of imaging findings with serological markers (e.g., AFP kinetics) and clinical context is essential for accurate interpretation and management.

Conclusion

The evolving landscape of hepatocellular carcinoma (HCC) therapy—spanning locoregional interventions, systemic treatments, and immunotherapy—has driven a corresponding transformation in radiologic monitoring strategies. Traditional size-based criteria such as RECIST 1.1 have proven inadequate in capturing the nuanced treatment responses seen with newer modalities, especially immunotherapy. In response, more functional and enhancement-focused frameworks such as mRECIST and LI-RADS Treatment Response Algorithm (TRA) have gained traction for evaluating viable tumor burden, rather than relying solely on anatomic changes.

MRI, particularly when incorporating dynamic contrast and diffusion-weighted imaging, has emerged as a central tool in post-treatment evaluation, providing superior soft-tissue characterization and early detection of residual viable tumor. The adoption of LI-RADS TRA has standardized reporting across institutions and improved the reproducibility of radiologic assessments. Furthermore, newer modalities such as perfusion imaging, quantitative biomarkers, and radiogenomics are under investigation for their potential to predict response and guide personalized management.

With the advent of immunotherapy, atypical response patterns such as pseudoprogression have necessitated the development of new criteria like iRECIST. These address the limitations of conventional imaging by allowing continued therapy in the setting of initial apparent progression, pending confirmatory imaging.

Ultimately, optimal radiologic monitoring in HCC requires an integrative approach—balancing radiological findings with serological markers (e.g., alpha-fetoprotein), clinical context, and treatment modality. Standardization of imaging protocols, validation of novel biomarkers, and multidisciplinary collaboration will be pivotal in refining response assessment and improving patient outcomes in HCC care.

How to cite this article: Magdy Mohamed Alfawal, Hossam Eldin Mansour Abdelrahman, Ahmed Abd-Elazim Ismail, Finan Abdulrhman Shabrawy Abbas (2024). Evolving Radiologic Approaches in Monitoring Hepatocellular Carcinoma After Locoregional Therapy. Pegem Journal of Education and Instruction, Vol. 14, No. 3, 2024, 467-473

Source of support: None.

Accepted: 25.05.2024 **Received** 10.05.2024 **Published :** 28.06.2024

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