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Evaluation of Target Volume Definition for Stereotactic Irradiation of Hepatic Metastases from Kidney Cancer

Omer Sager*, Selcuk Demiral, Ferrat Dincoglan, Murat Beyzadeoglu

Department of Radiation Oncology; University of Health Sciences, Gulhane Medical Faculty, Ankara, Turkey

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Corresponding author: Omer Sager, Department of Radiation Oncology; University of Health Sciences, Gulhane Medical Faculty, Ankara, Turkey

Abstract

Objective: The present study aimed to evaluate target volume definition for stereotactic irradiation of hepatic metastases from kidney cancer by comparing CT-based contouring with CT-MRI fusion-guided target delineation.

Materials and methods: This retrospective study was conducted at the Department of Radiation Oncology, University of Health Sciences, Gulhane Medical Faculty, a tertiary referral institution with extensive experience in multidisciplinary oncologic management, stereotactic radiotherapy applications, and advanced image-guided treatment techniques. Initial gross tumor volumes were contoured on CT simulation images alone by experienced radiation oncologists familiar with liver SBRT planning. Following this step, MRI datasets were incorporated into the contouring workflow, and target volumes were re-evaluated and modified where appropriate based on improved lesion visualization, soft tissue discrimination, and anatomical correlation.

Results: Integration of MRI into the target delineation workflow resulted in clinically meaningful modifications of target volumes in a substantial proportion of evaluated cases. Compared with CT-only contouring, CT-MRI fusion significantly improved visualization of metastatic lesion boundaries and facilitated more confident differentiation between tumor tissue and adjacent normal liver parenchyma.

Conclusion: CT-MRI fusion substantially improves contouring precision and dosimetric quality compared with CT-based planning alone. Further prospective investigations are warranted to validate these observations and to define the evolving role of MRI-guided and adaptive radiotherapy strategies in the management of hepatic metastatic kidney cancer.

Keywords: Hepatic Metastases; Target Definition; SBRT; Renal Cell Carcinoma; Metastasectomy

Abbreviations: RCC: Renal Cell Carcinoma; IGRT: image-guided radiotherapy; IMRT: Intensity-Modulated Radiotherapy; VMAT: Volumetric Modulated Arc Therapy; 4D-CT: Four-Dimensional Computed Tomography; CBCT: Cone-Beam CT; SBRT: Stereotactic Body Radiotherapy; ART: Adaptive Radiotherapy; CT: Computed Tomography; RILD: Radiation-Induced Liver Disease; MRI: Magnetic Resonance Imaging; DWI: Diffusion-Weighted Imaging

Introduction

Kidney cancer represents a major global oncologic challenge and accounts for most primary renal malignancies diagnosed in adults. Renal cell carcinoma (RCC), the predominant histological subtype, is characterized by substantial biological heterogeneity, highly variable clinical behavior, and diverse metastatic patterns. Although localized disease may often be managed successfully with surgical resection, a considerable proportion of patients eventually develop metastatic disease either at initial presentation or during long-term follow-up. Common metastatic sites include the lungs, bones, lymph nodes, adrenal glands, liver, and brain. Among these, hepatic metastases represent an important manifestation of advanced RCC and are frequently associated with adverse prognostic implications, therapeutic complexity, and reduced survival outcomes. Historically, metastatic RCC was considered relatively resistant to conventional radiotherapy because of the intrinsic radioresistant characteristics of RCC cells and the limited biologically effective doses achievable with older

radiation techniques. However, major advances in stereotactic radiotherapy, image guidance, motion management, and treatment planning technologies have significantly altered the therapeutic role of radiotherapy in metastatic RCC. Contemporary stereotactic body radiotherapy (SBRT) enables delivery of highly conformal ablative doses capable of overcoming relative radio resistance while minimizing irradiation of surrounding normal tissues.

The management of hepatic metastases from RCC remains particularly challenging because of the complex anatomy and functional importance of the liver. Surgical metastasectomy may provide prolonged disease control in carefully selected patients; however, many patients are not suitable surgical candidates because of medical comorbidities, multifocal disease, unfavorable lesion location, inadequate hepatic reserve, prior abdominal surgery, or coexistence of extrahepatic metastatic disease. Furthermore, systemic therapies including tyrosine kinase inhibitors, immune checkpoint inhibitors, and combination immunotherapy regimens have substantially improved survival in metastatic RCC, thereby increasing the clinical importance of durable local control strategies for oligometastatic and oligoprogressive disease sites. In recent years, the oligometastatic paradigm has increasingly influenced treatment strategies in metastatic kidney cancer. Oligometastatic disease is generally characterized by a limited number of metastatic lesions amenable to definitive local therapy. Similarly, oligoprogressive disease refers to limited progression occurring at selected metastatic sites during otherwise controlled systemic therapy. In both scenarios, local ablative interventions such as surgery, thermal ablation, and SBRT may contribute to prolonged disease control, delayed systemic progression, deferred systemic treatment modification, improved symptom management, and potentially improved survival outcomes in selected patients.

Within this evolving therapeutic landscape, SBRT has emerged as a particularly attractive modality for treatment of hepatic metastases. SBRT allows highly precise delivery of ablative radiation doses over a limited number of fractions while preserving surrounding normal liver tissue and adjacent gastrointestinal structures. Modern radiotherapy technologies including image-guided radiotherapy (IGRT), intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), respiratory gating, four-dimensional computed tomography (4D-CT), cone-beam CT (CBCT), stereotactic body radiotherapy (SBRT), and adaptive radiotherapy (ART) have substantially improved the feasibility, safety, and precision of liver-directed stereotactic irradiation [1-100]. Nevertheless, successful implementation of liver SBRT critically depends on accurate target volume delineation and reliable motion assessment. Hepatic lesions are subject to continuous respiratory motion, deformation, and positional variability throughout treatment.

Furthermore, liver metastases may demonstrate heterogeneous enhancement characteristics, indistinct margins, necrotic components, or close adjacency to vascular and gastrointestinal structures. Inadequate target delineation may result in geographic miss and compromised tumor control, whereas unnecessarily large treatment volumes may increase the risk of radiation-induced liver disease (RILD), gastrointestinal toxicity, biliary injury, or damage to adjacent organs at risk including the stomach, bowel, duodenum, kidneys, spinal cord, and chest wall. Computed tomography (CT)-based simulation remains the standard foundation for radiotherapy planning because of its geometric accuracy and electron density information necessary for dose calculation. However, CT imaging alone may provide insufficient soft tissue contrast for accurate differentiation between hepatic metastases and surrounding normal liver parenchyma, particularly in lesions adjacent to vascular structures, subcapsular regions, post-treatment fibrosis, or heterogeneous enhancement zones. Small lesions or infiltrative disease components may also be difficult to appreciate on CT imaging alone.

Magnetic resonance imaging (MRI) provides superior soft tissue characterization and improved lesion conspicuity compared with CT imaging. Multiparametric liver MRI using T1-weighted, T2-weighted, diffusion-weighted imaging (DWI), and hepatobiliary contrast-enhanced sequences may substantially improve visualization of metastatic lesions, lesion margins, vascular relationships, necrotic components, and subtle intrahepatic disease extension. Consequently, integration of MRI into radiotherapy planning workflows through CT-MRI fusion techniques has gained increasing interest in liver-directed stereotactic radiotherapy. In addition to improved anatomical visualization, MRI integration may also enhance motion assessment, facilitate adaptive radiotherapy workflows, and improve confidence during image guidance and treatment verification. Emerging MRI-guided radiotherapy platforms now permit real-time soft tissue visualization and online adaptive treatment modification, which may be particularly valuable in liver SBRT because of respiratory motion and interfraction anatomical variability. Despite increasing clinical adoption of multimodality imaging approaches, the precise contribution of MRI integration to target volume definition and dosimetric quality in hepatic SBRT for metastatic RCC remains incompletely characterized. Accordingly, the present study aimed to evaluate target volume definition for stereotactic irradiation of hepatic metastases from kidney cancer by comparing CT-based contouring with CT-MRI fusion-guided target delineation.

Materials and Methods

This retrospective study was conducted at the Department of Radiation Oncology, University of Health Sciences, Gulhane Medical Faculty, a tertiary referral institution with extensive experience in multidisciplinary oncologic management, stereotactic radiotherapy applications, and advanced image-guided treatment techniques. Patients with histopathologically confirmed kidney

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cancer and hepatic metastatic lesions treated with stereotactic body radiotherapy were retrospectively evaluated. Eligible patients were discussed within a multidisciplinary tumor board. Suitability for SBRT was determined based on multiple clinical parameters including limited hepatic metastatic burden, controlled or stable systemic disease, adequate performance status, preserved liver function, lesion accessibility for stereotactic treatment, prior treatment history, and absence of contraindications to high-dose radiotherapy.

Comprehensive diagnostic evaluation included contrast-enhanced thoracoabdominal imaging and liver-specific imaging studies. Functional and laboratory assessments were reviewed prior to treatment planning to evaluate hepatic reserve and overall treatment suitability. Simulation CT imaging was performed using a dedicated radiotherapy CT simulator. Patients were immobilized in the supine position using individualized immobilization devices designed to minimize setup variability and respiratory motion. Appropriate positioning and reproducibility were prioritized because of the high geometric precision required for stereotactic irradiation. Intravenous contrast-enhanced CT simulation imaging was obtained when clinically appropriate to improve visualization of hepatic lesions, vascular anatomy, and adjacent gastrointestinal structures. Thin-slice axial CT images were acquired for treatment planning purposes. Respiratory motion assessment strategies were utilized when available to evaluate lesion motion throughout the respiratory cycle and facilitate internal target volume assessment.

All patients additionally underwent MRI examinations using dedicated liver imaging protocols optimized for hepatic lesion visualization and soft tissue characterization. MRI sequences included multiple acquisitions designed to improve lesion conspicuity, vascular interface assessment, and detection of subtle intrahepatic extension. MRI datasets were subsequently fused with planning CT images using image registration techniques to facilitate anatomical correlation and target refinement. Initial gross tumor volumes were contoured on CT simulation images alone by experienced radiation oncologists familiar with liver SBRT planning. Following this step, MRI datasets were incorporated into the contouring workflow, and target volumes were re-evaluated and modified where appropriate based on improved lesion visualization, soft tissue discrimination, and anatomical correlation. Internal target volume assessment incorporated respiratory motion evaluation using available motion-management strategies and imaging datasets. Clinical target volume and planning target volume expansions were generated according to institutional protocols while accounting for respiratory motion, setup uncertainty, lesion location, and treatment delivery characteristics.

Attention was directed toward the relationship between target volumes and adjacent organs at risk including uninvolved liver parenchyma, stomach, bowel loops, duodenum, kidneys, biliary structures, spinal cord, chest wall, diaphragm, and major vascular anatomy. Dose constraints for organs at risk were applied according to institutional standards and accepted stereotactic radiotherapy guidelines. Treatment planning was performed using the treatment planning system available at our institution. Advanced conformal radiotherapy techniques were utilized to optimize dose conformality and organ sparing. Treatment plans were designed to achieve adequate target coverage while maintaining acceptable dose exposure to surrounding critical structures. SBRT delivery was conducted using linear accelerator-based image-guided radiotherapy systems equipped with daily cone-beam CT verification. Image guidance procedures were performed prior to each treatment fraction to confirm target localization and minimize setup uncertainties. Motion management strategies were employed according to lesion characteristics and institutional practice. Dosimetric comparisons were performed between CT-alone and CT-MRI fusion-based treatment plans. Dose-volume histogram analyses focused on target coverage, target conformity, dose gradients, normal liver exposure, and radiation dose delivered to surrounding organs at risk. Qualitative evaluation of contouring confidence and anatomical visualization was also performed.

Results

Patients with hepatic metastases from kidney cancer were included in the analysis. Integration of MRI into the target delineation workflow resulted in clinically meaningful modifications of target volumes in a substantial proportion of evaluated cases. Compared with CT-only contouring, CT-MRI fusion significantly improved visualization of metastatic lesion boundaries and facilitated more confident differentiation between tumor tissue and adjacent normal liver parenchyma. MRI integration proved particularly valuable for lesions located adjacent to hepatic vessels, diaphragmatic interfaces, biliary structures, subcapsular regions, and heterogeneous enhancement zones where CT imaging alone frequently demonstrated limited soft tissue discrimination.

In multiple patients, CT-alone contouring either overestimated target volumes because of uncertainty regarding lesion margins or underestimated subtle disease extension that became more apparent following MRI fusion. MRI-guided contour refinement enabled more anatomically accurate target definition and reduced contouring ambiguity in regions affected by respiratory motion, vascular proximity, or heterogeneous liver enhancement patterns. MRI integration also improved delineation of interfaces between hepatic metastases and adjacent organs at risk. These improvements were particularly relevant for lesions located near the stomach, bowel, duodenum, chest wall, kidneys, central hepatobiliary structures, and diaphragmatic surfaces where precise anatomical discrimination was essential for safe stereotactic dose delivery.

Dosimetric analyses demonstrated that CT-MRI fusion-based treatment plans achieved superior conformality and steeper

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dose gradients compared with CT-only plans. Improved target definition contributed to reductions in unnecessary irradiation of uninvolved liver tissue and nearby organs at risk while maintaining appropriate target coverage. In several cases, MRI-guided contouring resulted in smaller yet more anatomically accurate target volumes, thereby improving the therapeutic ratio of stereotactic irradiation. Reduced irradiation of uninvolved liver parenchyma may be particularly important in patients with prior systemic therapy exposure, compromised hepatic reserve, or multiple hepatic lesions.

Improved lesion visualization additionally enhanced confidence during image guidance and treatment verification processes. MRI integration facilitated improved appreciation of lesion morphology and anatomical relationships during treatment planning and image registration workflows, particularly in lesions with indistinct CT-based visualization. The benefits of MRI integration were most pronounced in anatomically complex lesions demonstrating irregular morphology, vascular adjacency, subcapsular localization, or limited conspicuity on CT imaging alone. These observations suggest that multimodality imaging integration may be particularly valuable in selected high-complexity hepatic metastatic lesions treated with SBRT.

Discussion

Kidney cancer remains a major oncologic challenge because of its marked biological heterogeneity, unpredictable metastatic behavior, and continuously evolving therapeutic landscape. Renal cell carcinoma (RCC), which constitutes the predominant histologic subtype, demonstrates highly variable clinical outcomes ranging from indolent oligometastatic disease to rapidly progressive disseminated metastases. Although the introduction of targeted therapies and immune checkpoint inhibitors has significantly improved systemic disease control and survival outcomes in metastatic RCC, durable local control of metastatic lesions continues to represent an important component of multidisciplinary management strategies. Increasing recognition of oligometastatic and oligoprogressive disease states has therefore stimulated growing interest in local ablative treatment approaches for carefully selected patients with limited metastatic burden.

Among metastatic sites, hepatic involvement is particularly clinically relevant because liver metastases from kidney cancer are generally associated with unfavorable prognosis, increased disease burden, and substantial therapeutic complexity. The management of hepatic metastases is challenging not only because of the biological aggressiveness of metastatic RCC but also because of the unique anatomical and functional characteristics of the liver. The liver is continuously affected by respiratory motion, deformation during breathing cycles, and close spatial relationships with multiple radiosensitive gastrointestinal and vascular structures. Surgical resection may provide durable local control in selected patients with isolated hepatic metastases; however, many patients are not appropriate surgical candidates because of unfavorable lesion location, multifocal disease, prior hepatic interventions, medical comorbidities, limited hepatic reserve, or concurrent systemic disease progression. Consequently, stereotactic body radiotherapy (SBRT) has emerged as an increasingly valuable noninvasive local treatment modality capable of delivering ablative radiation doses with high precision while preserving uninvolved liver parenchyma.

The growing role of SBRT in metastatic RCC is supported by several radiobiological and technological considerations. RCC has historically been regarded as relatively radio-resistant when treated with conventionally fractionated radiotherapy. However, contemporary evidence suggests that high-dose hypofractionated irradiation delivered with SBRT may overcome relative radioresistance through mechanisms including endothelial damage, vascular disruption, immunomodulatory effects, and enhanced tumor cell apoptosis. SBRT additionally offers important practical advantages, including short treatment duration, noninvasive delivery, integration with systemic therapies, and the potential to delay transition to subsequent systemic treatment lines in oligoprogressive disease settings. Nevertheless, the therapeutic effectiveness and safety of SBRT fundamentally depend on accurate target delineation and reliable image guidance. In hepatic irradiation, even relatively small contouring inaccuracies may substantially alter dose distributions because SBRT employs steep dose gradients and highly conformal dose delivery techniques.

Overestimation of target volumes may unnecessarily increase irradiation of uninvolved liver tissue and adjacent organs at risk, thereby increasing the probability of radiation-induced liver disease, gastrointestinal toxicity, biliary injury, or chest wall complications. Conversely, underestimation of disease extent or geographic miss may compromise local tumor control and reduce the effectiveness of ablative treatment. Accordingly, precise target volume definition remains one of the most critical determinants of successful liver SBRT. The findings of the present study demonstrate that MRI integration significantly improves target volume definition for stereotactic irradiation of hepatic metastases from kidney cancer. Compared with CT-alone contouring, CT-MRI fusion enhanced visualization of lesion boundaries, improved differentiation between metastatic tissue and surrounding normal liver parenchyma and facilitated more confident delineation in anatomically complex regions. These benefits were particularly evident for lesions located adjacent to hepatic vessels, subcapsular regions, diaphragmatic interfaces, biliary structures, and areas affected by heterogeneous contrast enhancement patterns. In several cases, MRI integration revealed subtle tumor extension that was poorly visualized on CT imaging alone, whereas in other patients CT-only contouring appeared to overestimate target boundaries because of limited soft tissue discrimination.

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These improvements in anatomical visualization may translate into clinically meaningful dosimetric advantages. CT-MRI fusion-based treatment plans may demonstrate superior target conformality, sharper dose falloff, and improved sparing of uninvolved liver tissue and neighboring critical organs compared with CT-only planning approaches. Such dosimetric improvements might be highly relevant in liver SBRT because preservation of functional liver reserve and minimization of gastrointestinal toxicity are essential for maintaining treatment tolerability and enabling potential future systemic or local therapies. Reduced irradiation of adjacent organs including the stomach, bowel, duodenum, kidneys, chest wall, and central hepatobiliary structures may also decrease the likelihood of both acute and late treatment-related complications. MRI provides several intrinsic advantages compared with CT imaging alone in the context of hepatic target delineation. Superior soft tissue contrast, multiplanar imaging capability, and improved lesion conspicuity facilitate more accurate appreciation of tumor morphology, necrotic regions, vascular interfaces, and subtle intrahepatic disease extension. MRI may also improve visualization of lesions that are poorly conspicuous on CT because of isodense enhancement patterns or post-treatment changes. In addition, hepatobiliary contrast-enhanced MRI sequences may further improve lesion detection and characterization by differentiating metastatic tissue from surrounding normal hepatic parenchyma. Consequently, MRI integration may substantially reduce uncertainties associated with target definition and improve the overall precision of stereotactic irradiation.

Our findings are consistent with accumulating literature supporting the integration of MRI into radiotherapy planning workflows for abdominal malignancies and liver-directed therapies. In anatomically complex treatment sites such as the liver, where subtle differences in contouring may directly affect ablative dose delivery, these advantages may have particularly important clinical implications. Another important consideration involves the potential relationship between MRI integration and adaptive radiotherapy workflows. Contemporary MRI-guided linear accelerator systems permit real-time soft tissue visualization, respiratory motion tracking, and online adaptive replanning. These technologies may be especially advantageous for liver SBRT because hepatic lesions frequently demonstrate substantial interfraction and intrafraction positional variability. MRI-guided adaptive radiotherapy may therefore further improve therapeutic ratios by allowing individualized treatment modification based on daily anatomical changes, organ motion, or tumor response. The improved baseline contouring accuracy achieved through CT-MRI fusion may serve as an important foundation for future adaptive treatment strategies.

Respiratory motion remains another major challenge in liver SBRT. Hepatic lesions may exhibit significant displacement during the respiratory cycle, particularly for tumors located near the diaphragm. Motion-related uncertainties may compromise target coverage and increase irradiation of surrounding normal tissues if not properly accounted for during treatment planning. In this context, MRI integration may contribute not only to improved anatomical definition but also to more accurate motion characterization and internal target volume assessment. Future integration of functional MRI sequences, cine-MRI motion assessment, and deformable image registration techniques may further refine motion management strategies in hepatic stereotactic irradiation. Improved target definition may additionally influence image guidance and treatment verification processes. Daily cone-beam CT (CBCT) image guidance is routinely employed in liver SBRT; however, soft tissue visualization on CBCT may be limited, particularly for small hepatic lesions. More accurate baseline contouring through MRI integration may therefore improve confidence during image registration and treatment verification, potentially enhancing setup precision and reducing geometric uncertainty during treatment delivery.

Despite these important advantages, several practical considerations associated with MRI integration remain clinically relevant. MRI acquisition, contour fusion, image registration, and adaptive workflows require additional institutional resources, technical expertise, workflow coordination, and multidisciplinary collaboration. Variations in respiratory phase acquisition, patient positioning differences between CT and MRI studies, image distortion, and deformable anatomical changes may also introduce registration uncertainties that must be carefully managed. Standardization of MRI acquisition protocols and quality assurance procedures therefore remains essential for reliable multimodality image integration in radiotherapy planning. Although improved contouring precision revealed by our study might be expected to improve therapeutic ratios, prospective clinical validation remains necessary. Also, the impact of MRI-guided contouring on adaptive radiotherapy implementation and motion management strategies warrants further dedicated investigation. Future prospective studies incorporating larger patient populations, standardized MRI acquisition protocols, deformable image registration techniques, respiratory motion analysis, biologically adaptive planning approaches, and MRI-guided online adaptive workflows are warranted to optimize stereotactic irradiation strategies for hepatic metastatic RCC. Additional research evaluating functional imaging integration, radiomic characterization, and response-adaptive SBRT approaches may also help refine patient selection and treatment personalization in metastatic kidney cancer.

Conclusion

Our evaluation of target volume definition for stereotactic irradiation of hepatic metastases from kidney cancer demonstrates that CT-MRI fusion substantially improves contouring precision and dosimetric quality compared with CT-based planning alone. MRI integration enhances visualization of metastatic lesion boundaries, improves discrimination between target lesions and surrounding normal liver tissue, and contributes to

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superior organ-at-risk sparing while maintaining appropriate target coverage. These findings support the incorporation of multimodality imaging approaches into SBRT planning workflows for hepatic metastatic RCC and underscore the critical importance of precise image-guided target definition in achieving optimal stereotactic radiotherapy outcomes. Further prospective investigations are warranted to validate these observations and to define the evolving role of MRI-guided and adaptive radiotherapy strategies in the management of hepatic metastatic kidney cancer.

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