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**Future directions of image-guided thermal ablation in colorectal cancer lung oligometastases**

Wang YY *et al.* IGTA outlook of CRC lung metastases

## Abstract

Colorectal cancer (CRC) with lung oligometastases, particularly in the presence of extrapulmonary disease, poses considerable therapeutic challenges in clinical practice. We have carefully studied the multicenter study by Hu *et al*, which evaluated <sup>1</sup>the survival outcomes of patients with metastatic CRC who received image-guided thermal ablation (IGTA). These findings provide valuable clinical evidence supporting IGTA as a feasible, minimally invasive approach and underscore the prognostic significance of metastatic distribution. However, the study by Hu *et al* has several limitations, including that not all pulmonary lesions were pathologically confirmed, postoperative follow-up mainly relied on dynamic contrast-enhanced computed tomography, no comparative analysis was performed with other local treatments, and the impact of other imaging features on efficacy and prognosis was not evaluated. Future studies should include complete pathological confirmation, integrate functional imaging and radiomics, and use prospective multicenter collaboration to optimize patient selection standards for IGTA treatment, strengthen its clinical evidence base, and ultimately promote individualized decision-making for patients with metastatic CRC.

**Key Words:** Colorectal cancer; Lung oligometastases; Extrapulmonary metastases; Image-guided thermal ablation; Dynamic contrast-enhanced computed tomography; Functional imaging

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**Core Tip:** Colorectal cancer with lung oligometastases, especially when accompanied by extrapulmonary lesions, remains a major therapeutic challenge. Image-guided thermal ablation is a potentially effective minimally invasive local therapy, but current practice has several limitations: The absence of pathological confirmation for some metastatic

sites, follow-up dependency on dynamic contrast-enhanced-computed tomography and vulnerability to inflammatory interference, a lack of control groups receiving other standard local treatments, and small sample sizes in certain subgroups. Future studies should improve pathological sampling, incorporate functional imaging, such as fluorodeoxyglucose positron emission tomography/computed tomography, and increase the sample size to provide more reliable evidence for individualized therapy.

### **TO THE EDITOR**

We read with great interest the recent paper entitled “<sup>1</sup>Extrapulmonary metastases impact survival outcomes of thermal ablation for colorectal lung oligometastases: A multicenter study”[1]. In this study, Hu *et al*[1] conducted a multicenter study of significant academic and clinical importance. The authors systematically evaluated survival outcomes in patients with metastatic colorectal cancer (CRC) who underwent image-guided thermal ablation (IGTA) and focused on prognostic differences among lung oligometastases combined with various patterns of extrapulmonary metastases, providing key real-world data and valuable clinical insights for this special population.

CRC is among the most common lethal malignancies worldwide and frequently metastasizes to the lungs[2,3]. Local treatment strategies for lung oligometastases include surgical resection, stereotactic body radiotherapy (SBRT), and IGTA[4,5]. However, for patients who also have extrapulmonary metastases, clinical decision-making is particularly complex. Traditional approaches generally recommend systemic therapy as the primary treatment, and high-quality evidence regarding the true value and candidate population for local therapy remains unclear[3,6-8]. In this context, the multicenter study by Hu *et al*[1], which used strict inclusion criteria and a standardized core procedural protocol, demonstrated the feasibility and safety of IGTA in clinical practice and provided strong real-world support for its application in patients with colorectal lung oligometastases. The authors further analyzed the relationship between metastatic distribution and prognosis and reported that patients with liver-only metastases had significantly better overall survival and progression-free survival than those with other

extrapulmonary metastases did. These findings highlight metastatic distribution as an independent prognostic factor, guiding whether IGTA should be incorporated into comprehensive treatment and laying the foundation for future prospective research. However, after careful review, we found that the study has several limitations that may affect the rigor of its conclusions and its clinical applicability. Therefore, we propose and discuss possible solutions to guide improvements in future research.

First, some pulmonary metastatic lesions lacked pathological confirmation. Imaging features of benign and malignant nodules can overlap, whereas histology or cytology remains the diagnostic gold standard[9,10]. Relying solely on computed tomography (CT) findings may introduce diagnostic bias, influence the choice of local treatment, and reduce the reliability of survival analyses[11]. Second, postoperative follow-up and efficacy assessment depended on dynamic contrast-enhanced CT (DCE-CT). Notably, DCE-CT may cause certain adverse reactions, including allergic responses to iodinated contrast agents, contrast-induced nephropathy in patients with impaired renal function, and potential thyroid dysfunction[12,13]. Severe renal insufficiency, known iodine allergy, and pregnancy are also considered major contraindications for this examination[14]. Although DCE-CT is recommended by the European Society of Medical Oncology and is valuable for assessing local control, postoperative inflammation, scarring, and nonmalignant changes following ablation are difficult to distinguish from recurrent or residual tumors when DCE-CT alone is used, which may lead to false-positive or false-negative results[15-18]. Functional <sup>2</sup>imaging modalities such as fluorodeoxyglucose positron emission tomography (FDG-PET)/CT and <sup>6</sup>diffusion-weighted magnetic resonance imaging have demonstrated high sensitivity and specificity for evaluating local treatment response, and previous studies suggest that combining volumetric and functional imaging can further improve accuracy[19-22]. Therefore, the exclusive reliance on DCE-CT in this study may limit the ability to fully reflect lesion activity and treatment response. Third, this study did not include other local treatment modalities as control groups. Recent studies have shown that IGTA achieves similar efficacy to surgery or SBRT in treating CRC lung metastases[23-25]. These

findings highlight the need for future large-scale prospective randomized trials to clarify the relative advantages and indications of IGTA in multimodal therapy. Fourth, the imaging analysis focused mainly on the number and size of metastases while neglecting malignant features that indicate tumor aggressiveness, such as margin infiltration, necrosis extent, and morphological irregularities. Recent studies have confirmed that these features are associated with early recurrence and prognosis after IGTA[26-29]. The incorporation of such imaging characteristics can significantly improve predictive modeling performance and help accurately identify high-risk patients[26,30]. Finally, some extrapulmonary metastatic subgroups had relatively small sample sizes. For example, few patients had bone or abdominopelvic metastases, which may introduce selection bias and reduce the stability of hazard ratio estimates in multivariable analysis. Although the authors performed center-specific sensitivity analyses, the small sample size inevitably limited the statistical power.

To address these shortcomings, future research should strengthen the evidence base and further define the clinical value of IGTA in patients with metastatic CRC. Pathological confirmation of all metastatic lesions should be incorporated at enrollment, percutaneous biopsy or surgical sampling should be used, and molecular pathology and genomic testing should be combined to support precision therapy and targeted drug selection[31]. Follow-up assessments should integrate multimodal functional imaging, including <sup>5</sup>FDG-PET/CT and PET/magnetic resonance imaging, to achieve more comprehensive and objective surveillance[10,32]. For treatment comparison, prospective studies should add patient cohorts receiving surgical resection or SBRT as control groups to clarify the advantages and indications of IGTA within a multidisciplinary framework[33]. Moreover, with the rapid development of artificial intelligence and radiomics, combining high-dimensional imaging features such as lesion morphology, texture, and spatial distribution and using deep learning methods to construct predictive models are recommended. This approach may help identify potential high-risk lesions before treatment, predict postoperative local control and long-term recurrence risk, and guide individualized therapeutic decisions[10,34,35]. Expanding the overall sample size

and increasing subgroup numbers through multiregional and multinational collaboration will further improve statistical robustness and allow the exploration of additional prognostic factors and practical stratified treatment strategies.

In conclusion, the multicenter study by Hu *et al*[1] demonstrates that IGTA, as a minimally invasive, repeatable, and well-tolerated local treatment, can achieve effective local control while reducing complications, providing important clinical evidence for patients with CRC and lung oligometastases. However, limitations in pathological confirmation, imaging follow-up, study design, and subgroup sample size may weaken the reliability and generalizability of the conclusions. Future research combining pathological verification with advanced <sup>4</sup>functional imaging technologies such as FDG-PET/CT and PET/magnetic resonance imaging, together with optimized study design and larger sample validation, will significantly improve the accuracy of IGTA efficacy assessment and optimize patient selection for CRC treatment. We believe that implementing these improvements will offer higher-quality evidence for individualized therapy in patients with CRC and lung oligometastases and represent an important step forward in advancing translational medical research.

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