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Local Treatment Strategies in Renal Cell Carcinoma: Current Evidence and Future Directions

Ye Tian[1] & Hongbin Deng[1]

[1] Department of Oncology, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China
Correspondence: Hongbin Deng, Department of Oncology, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China.

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Abstract

The role of local treatment in renal cell carcinoma has been substantially refined in recent years. In localized disease, partial nephrectomy remains the standard treatment because it offers durable oncologic control, complete pathological assessment, and nephron preservation. With the development of cryoablation, radiofrequency ablation, microwave ablation, and stereotactic body radiotherapy, non-surgical local therapies have become important options for selected patients. Percutaneous ablation is best supported in small and technically accessible tumors, whereas stereotactic body radiotherapy provides a noninvasive alternative for patients unsuitable for surgery or invasive procedures. In metastatic renal cell carcinoma, cytoreductive nephrectomy has shifted from a routine upfront strategy to a selective intervention determined by patient selection and treatment sequencing. In oligometastatic and oligoprogressive disease, metastasis-directed local therapy may delay systemic treatment initiation, maintain the benefit of ongoing systemic therapy, and prolong disease control. Overall, local treatment for renal cell carcinoma has moved from isolated technical application toward stage-specific and precision-based integration. Future studies should further clarify indication boundaries, patient selection, treatment timing, long-term renal outcomes, and prospective comparative evidence.

Keywords: renal cell carcinoma, local treatment, partial nephrectomy, stereotactic body radiotherapy, cytoreductive nephrectomy

1. Introduction

The scope of local treatment in renal cell carcinoma has expanded in recent years. In localized disease, partial nephrectomy remains the core treatment, while non-surgical modalities such as thermal ablation and stereotactic body radiotherapy have broadened treatment options beyond surgically fit patients. The 2025 European Association of Urology guideline recommends partial nephrectomy for T1 tumors and considers tumor ablation or stereotactic body radiotherapy for cT1 tumors requiring treatment but unsuitable for surgery. (Bex A, Ghanem YA, Albiges L, et al., 2025) In metastatic renal cell carcinoma, local treatment is also being redefined. The 2024 ESMO guideline states that upfront cytoreductive nephrectomy is no longer the standard initial strategy for advanced clear-cell renal cell carcinoma, and that local treatment

should be considered within the broader therapeutic pathway. (Powles T, Albiges L, Bex A, et al., 2024)

Accordingly, the key clinical question is no longer simply whether local treatment should be used, but which patients should receive which modality, in what setting, and for what purpose. This review summarizes recent advances in nephron-sparing surgery for localized disease, non-surgical local treatment for localized disease, the changing role of cytoreductive nephrectomy in metastatic disease, and metastasis-directed local therapy in oligometastatic and oligoprogressive settings.

2. Advances in Nephron-Sparing Surgery for Localized Renal Cell Carcinoma

Despite the diversification of local treatment, partial nephrectomy remains the most mature and best-supported standard strategy for localized renal cell carcinoma. Its value lies in achieving tumor control, pathological assessment, and nephron preservation simultaneously. Current research has therefore extended beyond perioperative safety to long-term survival, competing mortality, and postoperative renal function.

Recent comparative studies continue to support the oncologic and functional advantages of partial nephrectomy in appropriately selected patients. Kohada et al. showed that overall survival was worse after radical nephrectomy than after partial nephrectomy, and that this difference was driven mainly by non-cancer mortality rather than renal cancer-specific death. (Kohada Y, Shikuma H, Goto K, et al., 2025) In a SEER-based study of T1b renal cell carcinoma, Liu et al. likewise found that partial nephrectomy maintained stable long-term oncologic control and was associated with better overall survival than radical nephrectomy. (Liu H, Wang J, Tao L, et al., 2025) These findings indicate that procedure selection should take into account not only tumor removal, but also renal reserve, competing mortality, and comorbidity burden.

Evidence on postoperative renal function further supports the standard role of partial nephrectomy. Cao et al. found that partial nephrectomy was oncologically safe and associated with a persistently higher postoperative estimated glomerular filtration rate than radical nephrectomy, with a more pronounced difference in patients with diabetes. (Cao Y, Cui Y, Li R, et al., 2025) At the same time, advances in minimally invasive surgery have expanded the applicability of nephron-sparing procedures. Liu et al. reported that in highly complex tumors, robotic-assisted partial nephrectomy was associated with improved perioperative outcomes and less warm ischemia-related injury than laparoscopic partial nephrectomy. (Liu S, Zhang B, Weng B, et al., 2024) This suggests that some tumors previously treated with radical nephrectomy on the basis of anatomical complexity may still be candidates for nephron-sparing surgery.

Overall, partial nephrectomy remains the preferred treatment for localized renal cell carcinoma because it provides the most established balance among oncologic control, pathological information, and renal preservation. Radical nephrectomy remains appropriate when nephron-sparing surgery cannot be performed safely or is unlikely to offer meaningful overall benefit.

3. Non-Surgical Local Treatment for Localized Renal Cell Carcinoma

Evidence supporting non-surgical local treatment for localized renal cell carcinoma has increased substantially. Its role has evolved from an alternative for elderly or frail patients to a stratified strategy defined by tumor size, anatomical location, baseline renal function, and feasibility of invasive intervention. The main approaches are percutaneous ablation and stereotactic body radiotherapy. Percutaneous ablation, including cryoablation, radiofrequency ablation, and microwave ablation, is characterized by minimal invasiveness and preservation of renal parenchyma, whereas stereotactic body radiotherapy provides local ablation through high-precision image guidance without requiring a puncture route. (Huang RS, Chow R, Benour A, et al., 2025; Siva S, Bressel M, Sidhom M, et al., 2024) However, evidence remains based mainly on systematic reviews, cohort studies, and single-arm prospective studies rather than randomized head-to-head comparisons with surgery.

Percutaneous ablation is currently the most established non-surgical local treatment, particularly in cT1a disease, small peripheral tumors, technically feasible lesions, and patients in whom renal preservation is critical. A recent meta-analysis comparing non-surgical ablative strategies showed that these modalities can achieve consistently high local control with low

rates of severe adverse events, supporting their role in selected localized tumors. (Huang RS, Chow R, Benour A, et al., 2025) In a propensity score-matched SEER-based study of cT1a solid renal cell carcinoma, Guo et al. found shorter overall survival with heat-based thermal ablation than with cryoablation, although cancer-specific outcomes did not differ significantly. (Guo RQ, Peng JZ, Sun J, et al., 2024) A systematic review of percutaneous cryoablation further showed that renal functional decline was generally small, including in patients with T1b disease. (David-Dimitris Chlorogiannis, Anargyros Chlorogiannis, Dimitrios K. Filippiadis, Alexis Kelekis, Gregory C. Makris & Christos Georgiades, 2024) Together, these findings support a relatively well-defined role for percutaneous ablation, especially cryoablation, in selected small renal masses.

At present, however, the indications for ablative treatment remain concentrated in patients with small, technically accessible lesions who are not suitable for surgery. Long-term oncologic evidence and the ability to obtain complete pathological assessment remain inferior to surgery. Ablation is therefore better regarded as an important alternative rather than a replacement for standard surgical treatment.

Compared with percutaneous ablation, stereotactic body radiotherapy entered the local treatment framework later. Renal cell carcinoma was previously considered relatively insensitive to conventionally fractionated radiotherapy, but advances in image guidance, motion management, and dose delivery have enabled high biologically effective doses to achieve meaningful local ablation. (Siva S, Louie AV, Kotecha R, et al., 2024) Current evidence from systematic reviews, practice guidelines, and prospective studies supports its feasibility and local efficacy, although direct comparative evidence against surgery remains limited.

Prospective studies have strengthened the clinical role of SBRT for primary renal tumors. FASTRACK II reported excellent short-term local control and favorable intermediate clinical outcomes in patients with primary kidney cancer who were unsuitable for surgery. (Siva S, Bressel M, Sidhom M, et al., 2024) Long-term follow-up data also suggest that renal functional decline after primary tumor SBRT is generally moderate, with a low incidence of dialysis, including in patients with a solitary kidney. (Vivian S. Tan et al., 2024) These results support SBRT as a noninvasive local treatment option for elderly patients, those with substantial comorbidity, and those with anatomical features unfavorable for surgery or percutaneous ablation.

Percutaneous ablation and SBRT should therefore be viewed as complementary rather than competitive. Percutaneous ablation remains more established for small peripheral tumors with a safe puncture route, whereas SBRT offers an important noninvasive option for larger tumors, lesions near the renal hilum, bowel, or major vessels, tumors with high puncture-related risk, or patients unable to tolerate anesthesia or invasive procedures. The clinical question is not which modality is universally superior, but how to match each modality more precisely to tumor burden, anatomy, and patient condition.

In addition to local ablation, SBRT may also exert immune-modulating effects. High-dose radiotherapy can promote tumor antigen release and alter the tumor microenvironment, thereby enhancing antitumor immune responses. Existing reports have suggested a potential interaction between radiotherapy and immunotherapy, including occasional observations of the abscopal effect. (Feinaj A, Fox E, Sinibaldi V, et al., 2024; Hori K, Hirohashi Y, Aoyagi T, et al., 2020) However, in renal cell carcinoma this evidence remains limited to mechanistic inference and case-based observations. The present role of SBRT is therefore supported primarily by its local control, tolerability, and increasingly defined indications, whereas its potential systemic immune effects remain to be validated.

Taken together, non-surgical local treatment in localized renal cell carcinoma has become increasingly stratified. Percutaneous ablation remains a mature option for patients who are not surgical candidates or who require maximal nephron preservation, while the evidence supporting primary tumor SBRT continues to strengthen for larger tumors, lesions unsuitable for puncture, or patients requiring a fully noninvasive pathway. Future studies should focus on direct comparisons among techniques, long-term renal and quality-of-life outcomes, and more precise definition of indications by tumor size, location, and baseline renal function.

4. The Evolving Role of Cytoreductive Nephrectomy in Metastatic Renal Cell Carcinoma

In metastatic renal cell carcinoma, the role of

cytoreductive nephrectomy has shifted from broad routine use to selective application. This change reflects the combined influence of randomized trials, systematic reviews, and retrospective evidence from the immunotherapy era. Local surgery is no longer viewed as a fixed initial step for all patients with synchronous metastatic disease, but as an intervention that must be interpreted within the context of systemic therapy, disease burden, performance status, and treatment goals.

In the phase III CARMENA trial, sunitinib alone achieved survival outcomes that challenged the traditional paradigm of immediate nephrectomy followed by systemic therapy. (Méjean A, Ravaud A, Thezenas S, et al., 2018) In SURTIME, a deferred strategy after initial systemic treatment was associated with more favorable overall survival than immediate cytoreductive nephrectomy, supporting the value of treatment sequencing and response-based patient selection. (Bex A, Ghanem YA, Albiges L, et al., 2025) These studies indicate that initial systemic therapy can identify patients most likely to benefit from subsequent surgery while avoiding ineffective operations in rapidly progressive disease.

A 2024 Cochrane systematic review concluded that the highest-level evidence, derived mainly from the targeted therapy era, supports a cautious and selective rather than routine use of cytoreductive nephrectomy in patients requiring systemic therapy. (Dahm P, Ergun O, Uhlig A, et al., 2024) Retrospective evidence from the immunotherapy era suggests that cytoreductive nephrectomy may still provide benefit in selected patients. Fallah et al. reported better outcomes among patients treated with immune checkpoint inhibitors plus antiangiogenic therapy who underwent cytoreductive nephrectomy, while also emphasizing the persistent impact of prognostic selection factors that cannot be fully controlled in retrospective analyses. (Fallah J, Gittleman H, Weinstock C, et al., 2024) Recent reviews have similarly argued that the role of cytoreductive nephrectomy should now be interpreted in relation to patient selection, systemic treatment background, and timing rather than as a routine upfront procedure. (Hara T & Miyake H., 2025)

Overall, cytoreductive nephrectomy remains part of the treatment framework for metastatic renal cell carcinoma, but its role has fundamentally changed. It is no longer a relatively fixed treatment step, but a selective local intervention requiring careful patient selection and timing judgment. It appears most appropriate in patients with symptomatic primary tumors, disease control after initial systemic therapy, good performance status, and limited metastatic burden. The key question has therefore shifted from whether cytoreductive nephrectomy should be performed to which patients should undergo it, when it should be undertaken, and how it should be integrated into the overall treatment sequence.

5. Metastasis-Directed Local Treatment in Oligometastatic and Oligoprogressive Disease

Metastasis-directed local treatment has become an increasingly important component of oligometastatic and oligoprogressive renal cell carcinoma management. In contrast to widely metastatic disease, where systemic therapy remains central, the main value of local treatment in this setting lies in regulating treatment tempo and extending the duration of benefit. Interpretation therefore depends not only on local control, but also on the specific therapeutic objectives of different clinical scenarios.

In oligometastatic disease, prospective studies suggest that metastasis-directed radiotherapy can produce durable local control and prolong the interval before systemic therapy is required. Tang et al. reported encouraging progression-free and systemic therapy-free outcomes with metastasis-directed radiotherapy in oligometastatic clear-cell renal cell carcinoma. (Tang C, Sherry AD, Seo A, et al., 2025) In a phase IIb study of systemically untreated oligometastatic kidney cancer, Hannan et al. further showed that most patients had still not initiated systemic therapy at 1 year and that local control remained excellent. (Hannan R, Assadi R, Christie A, et al., 2026) Although these studies are mainly single-arm, they support the conclusion that carefully selected patients with low-volume disease may achieve a prolonged systemic therapy-free interval after metastasis-directed local treatment.

In oligoprogressive disease, the value of local treatment lies primarily in maintaining the benefit of ongoing systemic therapy. Current evidence suggests that the clinical goals of oligometastatic and oligoprogressive disease are distinct: the former focuses on delaying systemic therapy initiation, whereas the latter aims to eradicate a limited number of resistant lesions and prolong the efficacy of the current regimen.

(Tang C, Sherry AD, Seo A, et al., 2025) This distinction also explains the use of different endpoints across studies, including progression-free survival, systemic therapy-free survival, and time to next-line treatment.

Despite consistent directionality, the evidence still relies heavily on single-arm and retrospective studies, and its conclusions remain strongly influenced by patient selection. Hoffer et al. reported better outcomes among patients receiving local therapy in addition to systemic treatment, but eligibility for local treatment was itself closely related to lesion number, metastatic site, general condition, and prior treatment response. (Hoffer S, Eggers H, Fröhlich T, et al., 2025) Metastasis-directed local treatment therefore appears most relevant in patients with low disease burden, controllable lesions, good performance status, and multidisciplinary confirmation that delaying treatment escalation is clinically meaningful. It should not be extrapolated directly to patients with widely metastatic disease.

Overall, current evidence suggests that metastasis-directed radiotherapy or metastasectomy may prolong the systemic therapy-free interval or delay switching systemic regimens in selected patients with low-volume disease. In oligoprogressive disease, local treatment appears particularly useful for preserving an effective systemic treatment pathway. Future research should standardize the definitions of oligometastatic and oligoprogressive disease, clarify patient selection criteria, and define the incremental value of local treatment across metastatic sites and systemic treatment contexts.

6. Current Limitations and Future Directions

Although research on local treatment for renal cell carcinoma has increased substantially, the maturity of evidence remains uneven across clinical scenarios. In localized disease, partial nephrectomy is already established as standard therapy. By contrast, although the value of ablation and SBRT is becoming clearer, evidence still depends largely on non-randomized comparisons, systematic reviews, and single-arm prospective studies. A recent ISRS systematic review and practice guideline confirmed that primary renal SBRT has achieved a meaningful level of technical maturity and clinical feasibility, but its long-term efficacy boundaries relative to surgery remain insufficiently defined. (Siva S, Louie AV, Kotecha R, et al., 2024)

In metastatic disease, the main controversy surrounding cytoreductive nephrectomy is no longer whether it has lost all value, but how to select patients and sequence treatment in the immunotherapy era. Current randomized evidence derives mainly from the targeted therapy era. Although retrospective studies suggest benefit in selected patients, selection bias remains difficult to eliminate. Future prospective studies should therefore focus on strategies that reassess surgical value after response to systemic therapy and incorporate variables such as risk stratification, disease burden, symptom control, and systemic treatment background.

In oligometastatic and oligoprogressive disease, a major challenge is incomplete standardization of the study population itself. The core issue is not merely to accumulate more survival data, but to determine how metastatic site, disease burden, tumor biology, and systemic treatment context shape the benefit of local treatment. Another important direction is to move beyond technique selection toward full-course treatment integration. Image-guided metastasis-directed therapy, molecular and imaging biomarkers, and more refined coordination with systemic therapy are increasingly relevant. (Vandaele S, Albersen M, Beuselinck B, et al., 2025) Future research should therefore focus less on technical feasibility alone and more on precisely defining treatment goals at different disease stages.

7. Conclusion

The role of local treatment in renal cell carcinoma continues to evolve. In localized disease, partial nephrectomy remains the central nephron-sparing treatment. Percutaneous ablation and SBRT provide established alternative pathways for elderly patients, those with substantial comorbidity, and those unsuitable for surgery. At present, the role of SBRT is supported mainly by high local control and favorable tolerability, whereas its potential systemic immune effects still require higher-level validation. In metastatic disease, cytoreductive nephrectomy has entered an era of selective use, and metastasis-directed local therapy in oligometastatic and oligoprogressive disease is acquiring clearer strategic significance. Overall, local treatment is shifting from isolated technical intervention toward precision-based and stage-specific integration, although evidence level, indication boundaries, and long-term outcomes still require

further clarification. Future evidence on patient selection, treatment timing, long-term functional outcomes, and prospective comparative studies will determine the ultimate role of local treatment in full-course renal cell carcinoma management.

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