Feasibility and Oncologic Control after Percutaneous Image **Guided Ablation of Metastatic Renal Cell Carcinoma**

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Purpose: We assessed the safety, local control and oncologic efficacy of percutaneous ablation in the treatment of metastatic renal cell carcinoma.

Materials and Methods: A retrospective review was performed of 61 patients who underwent 74 ablation procedures to treat 82 metastatic renal cell carcinoma lesions with the intent of local eradication. Technical success, local tumor control, complications and patient survival were analyzed according to standard criteria.

Results: Four (4.9%) technical failures were observed while 2 patients were lost to followup. Time to recurrence was assessed for the subset of 76 (93%) tumors that were followed after ablation. Six (of 76, 7.9%) tumors recurred at a mean of 1.6 years after ablation (median 1.4, range 0.6 to 2.9). Thus, known overall local tumor control was achieved in 70 of 80 (87.5%) tumors. Estimated local recurrence-free survival rates (95% CI, number still at risk) at 1, 2 and 3 years after ablation were 94% (88–100, 41), 94% (88–100, 32) and 83% (70–97, 17), respectively. Estimated overall survival rates (95% CI, number still at risk) at 1, 2 and 3 years after ablation were 87% (79-97, 42), 83% (73-94, 31) and 76% (63-90, 19), respectively.

Conclusions: Image guided ablation of metastatic renal cell carcinoma is a relatively safe procedure with acceptable local control rates. Ablation may offer patients a minimally invasive option of local tumor eradication and warrants a role in the multimodal treatment approach for select patients.

> Key Words: carcinoma, renal cell; neoplasm metastasis; ablation techniques

Renal cell carcinoma is a malignancy with increasing incidence due to the wider application of imaging techniques for clinical diagnosis.^{1,2} More than 65,000 new cases of RCC will be diagnosed this year in the United States alone.³ Moreover, approximately 1 in 3 patients will initially present with metastatic renal cell carcinoma with a further 1 in 3 in whom metachronous metastatic disease is likely to develop. This suggests that up to 50% of patients diagnosed with renal cell carcinoma will, at some point, harbor mRCC.4 Recently the treatment of mRCC, a traditionally cytotoxic and radiotherapy resistant disease, has moved from cytokine based therapy to targeted agents.^{5–10} The treatment of mRCC has evolved in recent years with the widespread introduction of targeted therapies

Abbreviations and Acronyms

CT = computerized tomography mRCC = metastatic renal cellcarcinoma

RCC = renal cell carcinoma

RFA = radio frequency ablation

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against the vascular endothelial growth factor and its receptor axis, as well as the mammalian target of rapamycin. Indeed, since 2005, 7 novel agents for the treatment of mRCC have been approved by the Food and Drug Administration. These therapies have increased the 2-year survival probability for patients with advanced stage disease from 44% (95% CI 41–47) to 51% (CI 46–55).¹¹

Despite advancements in systemic therapies for the treatment of mRCC, surgical metastasectomy continues to have an important role in patient treatment. Patients who undergo complete metastasectomy experience significantly improved survival.5,12 Alt et al have recently shown that complete surgical resection of oligometastatic RCC is also associated with a survival benefit. 13 Tosco et al have also demonstrated that Leuven-Udine clinical prognostic groups may represent a novel patient stratification tool and prognostic indicator in mRCC treatment algorithms, while confirming the important role of metastasectomy in patients with resectable disease and good performance status. 14,15 Unfortunately, novel systemic therapies are associated with a minimal complete response rate, and only immunotherapy, via interleukin-2, has been associated with a durable complete response in 7%. 16 Systemic therapy can also portend significant adverse effect rates between 10% for tyrosine kinase inhibitor monotherapy to more than 50% for combination systemic therapy. 16 The best potential opportunity for mRCC cure is with local tumor eradication through surgical resection and, more recently, image guided ablation.

Percutaneous image guided ablation has evolved into an effective and established method of treating primary RCC with an acceptable safety profile and local control rates. 17-20 Moreover radio frequency ablation and cryoablation have been effectively used to treat neoplasms of the liver, adrenal, lung, bone and soft tissue. ^{21–26} However, a paucity of studies have systematically examined the risk and efficacy benefit of image guided ablation in the treatment of mRCC for cure, local control or palliation. Initial reports by Bang et al have suggested cryoablation for mRCC has a low morbidity and risk of tumor recurrence with possible survival benefit. We report the feasibility, technical success, oncologic outcomes and adjunctive survival of image guided ablation for mRCC in our 12-year ablation experience.

MATERIALS AND METHODS

This retrospective review was approved by the institutional review board and was compliant with the Health Insurance Portability and Accountability Act of 1996. Adult patients with renal cell carcinoma metastases who underwent percutaneous image guided ablation of a metastatic site

for local control between June 2000 and September 2012 were identified from the radiology hospital based registry. Patients with mRCC tumors were selected to undergo image guided ablation based on a multidisciplinary treatment approach involving members of medical oncology, radiology, urology and radiation oncology.

The purpose and intent of referral by the multidisciplinary team for intervention to the metastatic site was discerned before any ablation procedure, and those patients undergoing ablation for local control were included. Final patient and tumor characteristics are shown in table 1. The clinicopathological characteristics of age (mean 67 years, range 38 to 91), gender, primary lesion treatment, primary RCC characteristics (T stage, Fuhrman grade and histology), metastatic onset, age at first metastasis, disease-free interval, ECOG (Eastern Cooperative Oncology Group) performance status at ablation²⁷ and metastatic burden at ablation were included. A detailed description of ablative sites and thermal technique is also included in table 1. TNM staging was assigned according to the 2009 TNM guidelines.²⁸ Importantly 82 mRCC tumors ablated during 74 procedures in 61 patients were included for analysis. Pathological confirmation of mRCC was achieved before the treatment of 79 lesions (96%). Cementoplasty was performed after ablation of 5 bone/spine lesions to provide mechanical stabilization of the treated metastasis. Additional systemic and immunotherapeutic treatments specific to the index patient and radiation treatment of the index treated tumor were recorded.

Ablation Procedure Methods

All cases were performed with patients under general anesthesia. The choice of RFA or cryoablation was based on operator preference, although all hepatic lesions were treated with RFA and, in general, larger extrahepatic masses were treated with cryoablation.

The Precise™ (Galil Medical Inc., Arden Hills, Minnesota) or Endocare (Healthtronics/Endocare Inc., Irvine, California) systems were used in all cryoablation treatments. Since 2000 we have used 2 RFA devices. From 2000 to 2002 we primarily used the RITA device (Angiodynamics). Since 2002 we have used an impedance based internally cooled RFA device (Cool-tipTM). Computerized tomography and/or ultrasound guidance was used to place the cryoprobe or electrode into the metastasis. For cryoablation the total number of probes placed was based on size, location and morphology of the tumor with a goal of providing an iceball that would completely encompass the tumor with 5 mm or greater margins. CT monitoring of the iceball was performed with a Siemens Somatom Sensation open 40-slice CT system (Siemens AG, Munich, Germany). Diagnostic CT of the ablation site was performed immediately after ablation while the patient remained under general anesthesia. This served to assess for complications and, particularly after RFA, determine the success of the ablation.

After the ablation procedure patients were admitted to the hospital for overnight observation. Procedural complications were evaluated based on accepted standardized criteria set forth in the CTCAE (Common Terminology Criteria for Adverse Events) IV guidelines. ²⁹ Routine imaging followup via contrast enhanced CT or magnetic

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