

# PERCUTANEOUS RENAL CRYOABLATION OF RENAL TUMORS IN PATIENTS WITH VON HIPPEL-LINDAU DISEASE

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## ABSTRACT

**Purpose:** We determine the feasibility and safety of performing percutaneous cryoablation of renal tumors in patients with von Hippel-Lindau disease.

**Materials and Methods:** We selected 2 men and 2 women with von Hippel-Lindau disease and radiographic determined solid renal tumors were selected to undergo percutaneous cryoablation. All patients underwent standard preoperative evaluation. An interventional magnetic resonance imaging unit was used for probe guidance and ice ball monitoring. The cryoablation procedure was performed with a 2 or 3 mm. cryoprobe using a pressurized argon gas system for ice ball formation. The patients were hospitalized overnight for observation and discharged home the following day. A followup computerized tomogram or magnetic resonance imaging scan was performed at 1 week, 1, 3, 6 and 12 months and every 6 months thereafter, along with physical examination, urinalysis, serum blood urea nitrogen and creatinine.

**Results:** A total of 5 tumors were treated ranging from 2.8 to 5.0 cm. in diameter. All patients underwent the procedure without difficulty with 2 requiring re-treatment due to residual tumor for a total of 7 treatments. At followup from 2 to 23 months there has been no radiographic evidence of recurrence at the cryoablated areas.

**Conclusions:** Percutaneous cryoablation of renal tumors in patients with von Hippel-Lindau disease proved to be successful in this initial series. Although 2 patients had residual tumor after the initial cryoablation procedure re-treatment was performed with no adverse sequela. This minimally invasive therapy may allow patients with von Hippel-Lindau disease to avoid the necessity of multiple open surgical procedures.

**KEY WORDS:** cryosurgery; carcinoma, renal cell; Hippel-Lindau disease

Patients with von Hippel-Lindau disease have a 75% chance of formation of multiple renal cell carcinomas during their lifetime. Current therapy for these tumors consists of enucleation, partial nephrectomy or radical nephrectomy.<sup>1–4</sup> Due to the natural history of this disease, patients face the prospect of multiple open surgical procedures with associated morbidity and a long convalescence period.

Renal cryoablation has been previously performed by an open, laparoscopic or percutaneous approach for the treatment of small renal cell carcinomas.<sup>5–7</sup> The development of the 0.5 Telsa open magnetic resonance imaging (MRI) unit allows the physician to operate or perform procedures while patients are positioned in the magnet.

We previously reported our technique using a percutaneous approach with MRI guidance to perform cryoablation of small renal tumors.<sup>5</sup> To date, 45 patients have been treated with minimal morbidity. This study was undertaken to assess the feasibility of a percutaneous approach using cryoablation under MRI guidance for the treatment of renal cell carcinoma in patients with von Hippel-Lindau disease.

## MATERIALS AND METHODS

All patients were treated according to an institutional review board approved protocol for human subjects. Treatment criteria were age greater than 18 years, renal tumors less than 5.0 cm. in diameter, ability to undergo MRI (no pacemaker or metallic implants) and no bleeding diathesis. The percutaneous procedure was performed in a 0.5 Telsa interventional MRI unit (General Electric Medical Systems, Milwaukee, Wisconsin) which allowed access to the patient dur-

ing scanning. The cryoablation system (Cryohit System, Galil LTD, Tel Aviv, Israel) consists of a pressurized argon system to produce a –80C freeze and heated helium gas (70C) for the thaw cycle. Before the procedure all patients underwent physical examination, including chest x-ray, EKG, complete blood count, serum electrolytes and either computerized tomography (CT) or MRI.

The technique has been reported in detail previously.<sup>5</sup> Briefly, after general anesthesia was administered the patient was placed prone in the interventional MRI unit. With a gradient imaging technique a 2 or 3 mm. cryoprobe was advanced under MRI guidance in the renal mass. A series of 3 freeze-thaw cycles were performed and the probe was repositioned as needed to ensure complete freeze of the entire mass including a 5 mm. margin beyond the mass. The patients were hospitalized overnight for observation and discharged home the following day. Followup evaluation consisted of a physical examination, serum blood urea nitrogen (BUN) and creatinine with CT or MRI at 1 week, and 1, 3, 6 and 12 months.

## CASE HISTORIES

*Case 1.* A 63-year-old male underwent right radical nephrectomy in 1986 for renal cell carcinoma with a diagnosis of von Hippel-Lindau disease. Renal insufficiency developed and he has been on hemodialysis since 1992. In 1997 CT showed a 5 cm. mass in the left kidney and left radical nephrectomy was recommended, which he refused. The patient subsequently agreed to percutaneous cryoablation which was performed in August 1999. On the 1 and 3-month post-procedure scan a 2 cm. residual mass was noted and the

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area was re-treated. CT at 18-month followup revealed no residual mass.

**Case 2.** A 62-year-old female was diagnosed with von Hippel-Lindau disease after undergoing left radical nephrectomy for renal cell carcinoma. She had a concurrent 3.8 cm. mass in the right kidney and surgery was recommended. The patient refused surgery and, after a second opinion, she underwent percutaneous cryoablation which was successful. However, a small 1.5 cm. residual mass was noted on the 6 and 12-month MRI, and the area was re-treated successfully. No residual tumor was noted on MRI scan 3 months after re-treatment.

**Case 3.** A 35-year-old female, who was the daughter of case 1 was diagnosed with von Hippel-Lindau disease in 1988. On routine surveillance ultrasound 2 renal masses measuring 3.8 and 3.5 cm. were seen in the right kidney. The patient refused surgery. Preoperative BUN and creatinine were 7 and 0.8, respectively. She underwent 2 separate cryoablation procedures with a 3-month interval between them. BUN and creatinine at 3-month followup were 8 and 0.7. The patient refused followup CT but renal ultrasound showed no residual masses at 1 year followup with von Hippel-Lindau disease.

**Case 4.** A 37-year-old male had undergone right radical nephrectomy for renal cell carcinoma. He had a 2.5 × 3.0 cm. mass in the left kidney and was referred for percutaneous cryoablation, which was performed successfully. However, approximately 2 days after the procedure the patient was rehospitalized due to abdominal pain. Repeat CT showed no evidence of abscess formation or bowel injury. Diagnosis was ileus secondary to narcotic analgesics which resolved without intervention. At 1-week followup MRI demonstrated complete ablation of the tumor. CT at 1-year followup showed no radiographic evidence of tumor.

#### RESULTS

At 3-month followup patient 1 had a residual enhancing mass in the area of cryoablation. He subsequently underwent repeat cryoablation and on 18-month followup CT there was no evidence of the residual mass. Patient 2 had a questionable area of enhancing tissue in the periphery of the previously treated tumor. On MRI at 12-month followup the area was still present and re-treatment of this area was successful. Patient 3 had no evidence of residual enhancing mass at 12-month followup. Patient 4 had no radiographic evidence of residual tumor at 1-year followup. BUN and creatinine have remained stable in all patients followup. There were no complications associated with any procedure. Figure 1 shows the pretreatment CT, and MRI of the cryoprobe entering the mass and ice ball formation, and figure 2 is the MRI at 1-year followup in case 2.



FIG. 2. Case 2. MRI 12 months after cryoablation

#### DISCUSSION

Cryoablation of renal masses has been successfully performed via the open laparoscopic and percutaneous route.<sup>6,7</sup> Biopsy of these masses 6 months after undergoing laparoscopic cryoablation has shown only fibrosis and ischemic necrosis.<sup>8</sup> Patients diagnosed with von Hippel-Lindau disease have a high incidence (75%) of renal cell carcinoma. A common feature of this disease is the development of multiple bilateral tumors. The tumors tend to be low grade and can be managed with either a wedge resection or partial nephrectomy. Frydenberg et al reported on 19 patients with renal cell carcinoma and von Hippel-Lindau disease, and 6 with low grade unilateral disease treated with either wedge resection or partial nephrectomy.<sup>1</sup> At a mean followup of 4.8 years all patients were alive without evidence of disease.

Walther et al performed partial nephrectomy on 20 patients with renal cancer and von Hippel-Lindau disease.<sup>9</sup> No patient had metastatic disease during a mean followup of 30 months. In terms of cryoablation, we have limited followup (mean 14 months) on 20 patients with no evidence of local tumor recurrence. In comparison of the technique in our study with laparoscopic cryoablation with ultrasound as described by Gill et al,<sup>6</sup> there are advantages for our approach. Ultrasonography does not allow for 3-dimensional imaging as does MRI, and it does not have the advantage of high soft



FIG. 1. Case 2. A, CT shows renal mass in solitary kidney. B, MRI reveals cryoprobe in renal mass with ice ball forming

tissue contrast resolution or real volumetric visualization that are available with MRI. Additionally, only 2 to 3, 5 mm. incisions are required for placement of the probes, which minimizes the morbidity of the procedure.

In regard to biopsy of renal masses, 3 of our 4 patients had documented renal cell carcinoma by virtue of a contralateral nephrectomy. The rate of obtaining adequate tissue samples by biopsy for making a pathological diagnosis ranges from 70% to 98%.<sup>10</sup> Even intraoperative direct vision renal biopsies were reported to have only a 75% diagnostic rate.<sup>11</sup> In light of these facts, we believed that no benefit would be gained from a biopsy of the renal mass in these patients.

Since these patients with von Hippel-Lindau disease have been treated, we now use multiple cryoprobe placements, which provides a synergistic effect in terms of a shorter freeze time required to generate an ice ball to encompass the tumor. Current laboratory study is ongoing to determine the ideal spacing and configuration of the probes but preliminary work indicates a 1 to 1.5 cm. spacing between the probes allowing for overlap on the ice balls. Since the introduction of the multiple probe technique, the number of patients requiring re-treatment should decrease. In the patients with a solitary kidney who have been treated the serum creatinine has remained stable, indicating no evidence of collateral damage to normal renal parenchymal. The ability to image the freeze front in 3 dimensions with MRI provides greater control of preventing collateral damage to the normal kidney, which is a major advantage over ultrasound or CT capability.

#### CONCLUSIONS

As patients with von Hippel-Lindau disease tend to have multiple tumors with time, the ability to treat them with a minimally invasive technique would be an advance over current therapy. The ability to minimize damage to the kidney in these patients with multiple tumors is a definite advantage for preservation of renal function. Ultimately, long-term

followup will be required to determine the effectiveness of percutaneous cryoablation. However, if this treatment proves to have long-term success, management of renal tumors in patients with von Hippel-Lindau disease will be improved with this technique.

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