Small renal tumors: natural history, observation strategies and emerging modalities of energy based tumor ablation

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With further advances in the technology of non-invasive imaging modalities as well as their utilization, diagnosis of incidental renal tumors has increased considerably. A large proportion of these renal tumors have been small (<4 cm) masses, for which nephron sparing surgery has been proven to be effective for. The trend toward minimally invasive options in the management of renal tumors has prompted interest in energy-based ablation techniques as a possible alternative to radical or partial nephrectomy in select patients. This article will review the natural history of small renal neoplasms and the emerging modalities of energy based energy ablation such as cryoablation, radiofrequency ablation, interstitial photon radiation, interstitial laser technology, microwave ablation, and Cyberknife extracorporeal renal tissue ablation.

Key Words: renal cell carcinoma, tumor, natural history, energy ablation

Introduction

The diagnostic rate of small, "incidental" tumors which are amenable to local excision or ablation has increased significantly due to widespread use of non-invasive body imaging tests. Concomitantly, the role of nephron-sparing surgery has expanded beyond the traditional circumstances of neoplasms in solitary/functionally solitary kidneys or tumors present bilaterally. However, there are patients who are poor surgical candidates and those with hereditary based renal tumors who are at risk of multiple renal operations and who may benefit from a less invasive treatment modality, which further reduces surgical morbidity and better preserves renal function. We will review the existing literature on the natural history of small renal tumors, data on observational strategies, and on emerging modalities of energy ablative

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nephron sparing surgery, including cryoablation, radiofrequency ablation, interstitial photon radiation, interstitial laser technology, microwave ablation, and Cyberknife extracorporeal renal tissue ablation.

Natural history of small renal tumors

Traditionally, renal cell carcinoma (RCC) has been seen as a single entity that expressed a variety of histological appearances. With advent of the advances in genomics, today RCC is more accurately recognized as a family of neoplasms resulting from distinct genetic abnormalities with unique morphological features but a common derivation from the renal tubular epithelium.[1] The most common subtypes of RCC include clear cell carcinoma, which is the most common type of malignant renal tumor, papillary RCC and chromophobe RCC, which account for approximately 70%, 10%,[2] and 5%,[3] of cases, respectively. However, with the exception of a few very rare variants, the question of whether different histological variants of renal cell carcinoma portend different survival outcomes remains controversial.[4-8]

Also as a consequence of the advances in the molecular understanding of the pathology of RCC, other tumor parameters, such as ploidy,[9] nuclear morphometry[10,11] and molecular markers,[12] have also been evaluated as potential predictors of outcome in patients with renal cell carcinoma. Numerous biomolecular factors are currently under investigation to determine their usefulness and correlation with diagnosis, stage and prognosis for RCC.

With increasing availability and utilization of improved abdominal imaging modalities, including ultrasound, computerized tomography (CT) and magnetic resonance imaging (MRI), incidentally discovered small renal masses less than 4 cm in diameter are being reported more frequently.[13,14] Most of these incidentally discovered renal masses are low stage renal cell carcinoma.[15-17] and indeed, clinical stage migration with renal cell carcinoma (RCC) has been observed at most centers during the last 30 years.[17-20]

RCC is most commonly discovered in the seventh decade of life,[17] and therefore many patients are older and have significant co-morbid disease with an increased risk of perioperative mortality and morbidity. Although morbidity from nephrectomy has decreased with improved techniques, it is still significant and reported in 11% to 40% of cases.[21]

In recent retrospective studies Bosniak et al suggested that tumors less than 3.5 cm in diameter rarely metastasize and have a slow growth rate,[22,23] suggesting a role for surveillance with properly selected patients. Metastases were not reported by Bosniak et al for tumors of this size at nephrectomy.[22,23] Furthermore, Bosniak et al described the growth rate of renal tumors as a mean of up to 0.36 cm per year change in diameter based on serial imaging.[22,23] Most tumors demonstrated little or no change in diameter with a small proportion accounting for most of the growth. They hypothesized that these same fast growing tumors are those that are not curable, even with early detection and removal.

In contrast, Oda et. al.,[24] retrospectively reviewed the records of 16 patients with a mean tumor size of 2 cm whose lesions were found incidentally and who did not undergo immediate surgical treatment for renal solid masses that were later proven to be RCC. They found that the median growth rate of growth rates primary lesions was 0.54 (range 0.10 to 1.35 cm/year, significantly higher that those reported by Bosniak et al. who demonstrated an overall growth rate for renal tumors of 0–1.10 cm/year (mean 0.36 cm/year).[22,23] This may have been due to the difference in the clinicopathological features of the patients of the two studies. While the study by Bosniak et al.[23] included oncocytoma and unknown pathological findings of renal masses. Oda et al.[24] included patients with hostopathologically proven RCC. In the latter case, the authors concluded that initial clinical and pathological features cannot always predict subsequent clinical behavior of incidentally found RCC, suggesting that candidates for 'watchful waiting' should be selected very carefully.

In the literature, only one report exists in which patients were followed prospectively after diagnosis with a small renal mass. Rendon et al.[25] prospectively followed 13 patients with radiologically detected solitary small renal masses that were unfit for or refused surgery. Median patient age was 69 years and mean lesion volume at 2.95 cm in diameter and patients were followed with abdominal imaging for a median of 42 months. Of the 13 patients five underwent surgery during the follow up period because of tumor enlargement and/or onset of symptoms, all five of whom demonstrated RCC on pathological analysis. No patient had metastases. Only two tumors were fast growing and these were the only two cases in which symptoms developed. When these patients were excluded from analysis, average growth rate was 0.216 cm per year which was not statistically significantly different from 0 slope or no growth. While acknowledging the limitations of small sample size, the authors concluded that the growth rate of small renal tumors is variable, with

those tumors that are destined to grow progressively and possibly metastasize doing so early and most small tumors growing at a low rate or not at all, with the implication that the standard practice of immediate partial or radical nephrectomy for incidentally detected small renal masses in the elderly or infirm would need to be reviewed.

It seems reasonable to suggest, given the absence of large series of prospective studies evaluating the natural history of small renal neoplasms in the context of strategies aimed at tumor surveillance, that patient selection for "watchful waiting" be based on a combination of patient co-morbidity as well as tumor size, and that given the heterogeneity of renal tumors, radiographic follow up need be intermittent and long standing.

Emerging modalities of energy ablative nephron sparing surgery

Incidental detection of a small, solid or complex renal mass is an increasingly frequent clinical scenario.[20] Depending upon the clinical situation, treatment alternatives include tumor surveillance (watchful waiting), radical nephrectomy, or increasingly, partial nephrectomy. Although long term cancer cure rates and functional efficacy of partial nephrectomy is well documented in the literature,[26] the procedure itself is associated with the potential morbidity of open surgery. With the increasing application of minimally invasive surgery, several energy based tissue ablation technologies are being investigated in the laboratory and/or clinically. These technologies include cryosurgery, radiofrequency ablation, microwave thermotherapy, interstitial laser, and interstitial photon radiation.

Cryoablation

Cryoablation, a targeted tissue ablation technique used for the treatment of a wide variety of neoplasms, including—liver,[27] prostate,[28] and kidney,[29]—is the most well investigated and clinically utilized energy based ablation technology.

On the tissue level, cryoablation causes tissue necrosis by the deposition of intracellular and extracellular ice—an event which leads to the disruption of the cell membrane, organelles, proteins and local microvasculature.[30] In addition, there is an increase in intracellular osmolarity which adds further injury. Eventually, this leads to coagulation necrosis followed by fibrosis and scarring.[30,31]

Investigations in animal models have demonstrated that renal cryoablation produces predictable and reproducible tissue destruction.[30] In swine, Chosy et al.[32] demonstrated that complete renal tissue ablation occurred at temperatures of –19.4°C. For cancer cells however, lower temperatures may be required and a temperature of –40°C has been recommended to insure cancer cell death. Baust et al.[33] found that a temperature of –40°C is found 5-6 mm inside the edge of the forming iceball. Therefore, extension of the iceball 1 cm beyond the tumor edge should ensure adequate tissue ablation. Current techniques involve insertion of 1 or more cryo probes into the target tissue and rapid cooling by circulating pressurized Nitrogen or Argon. A core temperature of –180–C or –195–C is achieved to ensure a temperature of at least –40°C at the tumor margin. To maximize cell death, a double freeze-thaw cycle is frequently used with rapid freezing and slow thawing. In addition, though continuous renal perfusion has raised concerns regarding dissipation of the cold temperatures during cryoablation, in a canine model, Campbell et al.[31] demonstrated that renal artery clamping during cryoablation provides no additional advantages with respect to more efficient freezing. Real time monitoring of the advancing iceball during cryoablation is essential to guarantee safe and effective cryoablation. To that end, ultrasound has been most valuable, where intraoperatively, the evolving iceball has been described as a hyperechoic advancing crescent with a posterior acoustic shadow.[34] MRI has also been reported as a monitoring modality for percutaneous applications.[35]

Uchida et al.[36] reported the initial experience with cryoablation of renal tumors, performed percutaneously on two patients. Delworth et al.[37] subsequently reported open cryoablation in two patients with solitary kidneys and larger patient series have subsequently been reported.[38]

Although open and percutaneous approaches have been successfully performed, the laparoscopic approach offers distinct delivery advantages. Like open surgery and unlike the percutaneous approach, laparoscopy allows for direct visualization as well as complete mobilization of the kidney, while minimizing injury to adjacent organs. In addition, while percutaneous access to anterior or medially located tumors may be difficult, laparoscopy provides direct access to such tumors transperitoneally. For posterior renal tumors, the retroperitoneal approach is effectual. Furthermore, intraoperative ultrasound using a flexible, steerable laparoscopic ultrasound probe passed through a laparoscopic port, can provide a real time image for precise insertion the cryo probe and for monitoring of the advancing iceball.[31]

The Cleveland Clinic reported the initial series of laparoscopic renal cryoablation in 1998.[39] Subsequently, Gill et al.[29] reported their experience on 32 patients, all of whom had small (<4 cm), circumscribed, renal tumors which were remote from the collecting system. Indications for laparoscopic cryoablation were: tumor size <4 cm (15 patients), solitary kidney (4), renal dysfunction (2), calculus disease (21), and metastasis to the kidney (2). Mean patient age was 65.4 years (range 35-93) and mean tumor size on preoperative CT scan was 2.3 cm. Operatively, 22 patients were approached retroperitoneally and 10 transperitoneally. Intraoperative pre cryoablation needle biopsy revealed renal cell carcinoma in 20 patients. Cryoablation time with a double freeze-thaw cycle averaged 15.1 min, with a total surgical time averaged 2.9 hours and a mean blood loss of 66.8 cc (range 10-200). Sequential MRI scans demonstrated a gradual contraction in the mean diameter of the cryolesions, with five out of the 20 patients demonstrating no visible tumor by 1 year follow up. Of the initial series at 3 and 6 month follow up, the biopsy was negative for cancer in all 23 patients. The only intraoperative complication in this series, a superficial liver laceration secondary to a fan retractor, resolved spontaneously. Hospital stay averaged 1.8 days (and less than 23 hours in 69% of patients) and there were two postoperative complications, both of which were managed conservatively (a perirenal hematoma and herpes esophagitis).

Recently, the Cleveland Clinic reported a 3-year follow up of 50 patients (24 of whom with greater than a 4 year follow-up).[40] With a of tumor size of 2.1 cm (range 1-4 cm) and biopsy confirmed renal cell carcinoma in 61% of cases, it was noted that there were two recurrences in the period of follow-up: one positive biopsy for recurrent renal cell carcinoma at 9 months which subsequently underwent radical nephrectomy and another patient who had an enhancing mass at 18 month with biopsy confirmed recurrent renal cell carcinoma, who also underwent a radical nephrectomy.

Shingleton and Sewell[35] recently reported a series utilizing open MRI guided percutaneous cryoablation with a mean follow-up of 9 months (range 3 to 14 months). Twenty patients with 22 tumors were treated, and the authors used a triple freeze thaw cycle of -180°C with 5 mm margin for a mean tumor size of 3 cm. Operative time of 1.5 hours, there was one intraoperative complication (a perirenal hematoma which required blood transfusion), and hospital stay was 23 hours for 95% of the patients treated. Though one patient demonstrated radiographic evidence of persistent tumor which required retreatment, surgery was required in none, and there were no reported metastases during the period of follow up.

Laparoscopic cryoablation seems to be an effective treatment modality for small peripheral renal tumors. The technique is minimally invasive, has a rapid learning curve, results in minimal blood loss and morbidity, and, to date, has demonstrated precise reliable ablation of small renal neoplasms. However, while renal cryoablation is technically safe and early results are encouraging, longer term follow-up to prove the oncological efficacy of cryoablation awaits.

Radiofrequency ablation

Radiofrequency interstitial tissue ablation (RFA) has been recently applied as a minimally invasive strategy for the ablation of select renal tumors. The vast majority of human experience with RFA has been in the treatment of liver metastases but renal tumor radio frequency ablation is still in infancy.[41,42]

On the tissue level, the cytotoxic mechanism involves desiccation due to high intracellular temperatures. Radio frequency ablation induces ionic agitation, frictional heat and cell death by coagulative necrosis.[43] Pathological analysis done in 24 hours of renal tumor radio frequency ablation demonstrates pyknosis, stromal edema, and loss of nucleoli and nuclear detail in the treatment zone.[44] Energy is delivered to tissues via specially designed needles resulting in heating tissues to 105°C -110°C, and monitoring is accomplished by temperature probe, impedance feedback and ultrasonography. Immediate temperature and impedance monitoring provide predictable real-time control of tissue ablation while ultrasonography demonstrates a hyperechoic blush.[43]

De Baerre et al.[45] reported preliminary results following percutaneous RFA of five patients with five biopsy proven renal tumors and a median follow up of 9 months.[45] Using a triple needle electrode and sonographic or CT guidance, with an application time of 15 minutes, only one tumor required more than one application during treatment. At follow up, all patients were deemed recurrence-free based on CT imaging criteria of hypoattenuating area with no contrast enhancement at the RFA sites. Three minor complications including a subcapsular hematoma in one patient and transient gross hematuria in two were observed and managed expectantly without clinical sequelae.

Ogan et al.[46] utilized radiographic criteria to evaluated outcomes post RFA treatment. They treated 15 patients with small (less than 4 cm) renal tumor

and followed patients with interval computed tomography scans at 6 weeks and 3, 6, and 12 months, and every 6 months thereafter. They defined their criteria for successful ablation as a lesion along with a margin of normal parenchyma that no longer enhanced (less than 10 Hounsfield units) on follow-up contrast imaging. With a mean tumor size of 2.4 cm, the average procedure time was 95 minutes (range 60 to 150) and all patients underwent the procedure without any major complications. At a mean follow-up of 4.9 months, and utilizing their criteria, they noted that 12 (93%) of 13 tumors were no longer enhanced. The procedure was aborted in three patients however, because of intervening bowel or lung parenchyma.

Pavlovich et al.,[44] reported on their experience with percutaneous RFA treatment of small hereditary tumors in 21 patients. Treatment eligibility criteria for percutenous RFA were: tumor diameter less than 3.0 cm, evidence of tumor growth over a 1 year period, and solid appearance with contrast enhancement on CT. Efficacy of treatment was assessed by lack of enhancement on follow-up CT scan. A total of 24 ablations were performed and at 2 month follow up, a majority of tumors (19 of 24, 79%) ceased to enhance on contrast CD. Five tumors, were however, still enhancing at a 2 month follow up, though a number of these were thought to have been inadequately treated. Overall, four minor complications were encountered (two episodes each of transient psoas pain and skin paresthesia).

Gervais et al.[47] recently reported their updated clinical experience with percutaneous RFA for RCC. They treated 34 patients with a total of 42 tumors over a period of follow up of 3.5 years and performed a univariate analysis of the results to assess the effect of tumor size and location on technical success. Technical success was defined as absence of CT enhancement on follow up scanning. All 29 exophytic tumors (mean size, 3.2 cm; size range, 1.1-5.0 cm) were completely ablated, as were two parenchymal tumors. The remaining 11 tumors had a component in the renal sinus. For large (>3.0 cm) tumors, presence of a tumor component in the renal sinus was a significant negative predictor of technical success (P =.004); only five of these 11 tumors were completely treated, compared with 11 of 11 tumors without a renal sinus component. A similar analysis was not possible for small tumors because no small tumors involved the renal sinus. Four complications occurred in a total of 54 ablation sessions: one minor hemorrhage, two major hemorrhages, and one ureteral stricture.

More troubling however, have been the results, which have utilized direct inspection of resected tumor tissue as a measure of a successful outcome.

Rendon et al.[48] reported their experience of RFA for the treatment of small renal tumors followed by immediate or delayed nephrectomy in 10 patients[48] with a mean tumor size of 2.4 cm. Mean total ablation time was 17 minutes. In the first group, five tumors in four patients were treated with RFA followed immediately by radical or partial nephrectomy. In the other group, six renal tumors were initially treated with percutaneous RFA followed by partial or radical nephrectomy 7 days later. The authors found it difficult to achieve complete tumor destruction in their specimens, as on pathologic examination, 4 of the 5 tumor specimens in the immediate nephrectomy group and 3 of the 6 tumor specimens in the delayed nephrectomy group demonstrated persistent viable cancer cells. The authors reported one patient with perioperative complications (subcapsular hepatic hematoma, biliary fistula and pneumonia).

Michaels et al.[49] conducted a prospective study to assess the effectiveness of RFA in the treatment of small renal tumors. They treated 20 tumors in 15 patients with RFA through an open surgical approach immediately before partial nephrectomy. Tumor size ranged from 1.5 cm to 3.5 cm in diameter (mean 2.4 cm), tumors were heated to 90 to 110ºC for 6 to 16 minutes (mean 9.1 minutes) following which open partial nephrectomy was performed. They found that all 20 specimens had evidence of morphologically unchanged tumor and normal renal parenchyma. Complications included 2 postoperative caliceal leaks treated by stent placement and 1 intraoperative renal pelvic thermal injury requiring pyeloplasty.

Matlaga et al.[50] also conducted a prospective pathological evaluation of RFA efficacy. They treated 10 patients with histologically confirmed RCC by RFA followed by immediate nephrectomy. Mean tumor size was 3.2 cm. (range 1.4 to 8.0 cm) and all tumors underwent RFA ablation for 12 minutes prior to tumor excision by partial or radical nephrectomy. Of the 10 tumors treated, 8 were completely ablated with a mean treatment margin of 6.75 mm. (range 2 to 13 mm). Of the two tumors that were incompletely treated one never attained a temperature sufficient for tissue destruction and the other measured 8 cm in diameter.

The authors in the abovementioned three studies, which utilized direct tissue examination and histological and biochemical criteria to examine tissue viability,[48-50] have demonstrated that current RFA regimens are ineffective for total destruction of renal tumor tissue in a significant proportion of the time.

Though other authors have postulated with longer term follow up, the full effect of RFA may reach completion, the data from these three studies suggest that RFA, at this present time, remains experimental until consistent and duplicable long-term oncologic efficacy is demonstrated. Therefore at this time, this technology should be reserved and applied to select patients with contraindications to surgery. Furthermore, in comparison to cryoablation, the other well-reported energy based method of tissue ablation for kidney tumors, the data presented thus far in show cryoablation to result in more consistent and reliable renal tumor tissue destruction.

Interstitial photon radiation ablation

A miniature interstitial photon radiosurgery system has been described as an alternative to surgical resection and external-beam radiation for tumors and may now offer an alternative for ablation of renal lesions. Interstitial photon radiation has been extensively used for brain tumors,[51] and brain metastases.[52] It's mechanism of action essentially induces a radiation dose dependent metabolic cell death, with loss of membrane integrity preceeding lethal morphological changes consistent with cellular necrosis and apoptosis.[51]

Experience with interstitial photon radiation with renal tissue is largely investigational and preclinical. Chan et al.[53] evaluated the feasibility of ablation by PRS in a normal parenchyma canine model. Delivery of 15 Gy of local radiation at a radius of 1.3 cm over 10 minutes was carried out to peripheral and central areas of both kidneys, and the animals were followed with for a 6 month period. Histologic analysis at sacrifice demonstrated an average lesion size was 2.5 cm in diameter, and biopsy confirmed coagulative necrosis with sharp demarcation from the surrounding parenchyma.

From the same group, Solomon et al.,[54] defined the radiographic characteristics of interstitial photon radiation renal ablation in a canine model. They noted that ablated lesions though visible at 1 month following therapy, consistently decreased in size over the 6 months of follow-up, with size being proportional to dose delivered. Overall, renal lesions were low in attenuation with frequent rim enhancement that diminished over time and were thus similar in CT appearance to lesions produced by other ablative techniques.

Interstitial laser ablation

Interstitial laser ablation is another emerging thermoablative minimally invasive modality that has been investigated as a treatment option for a variety of neoplasms, including brain[55] and breast.[56] Interstitial laser ablation utilizes optical fibers to deliver a high-energy laser to the target lesion. MR imaging is used both for placement of the laser in the tumor and for monitoring progress of thermocoagulation caused by the laser. Success of interstitial laser ablation is dependent on the delivery of the optical fibers to the target area, real-time monitoring of the effects of the treatment, and subsequent evaluation of the extent of thermal damage.

Working with a porcine model, Gettman et al.[57] investigated the safety and efficacy of laparoscopically applied interstitial laser ablation of renal tissue, with and without renal hilar clamping. The animals were then sacrificed at immediately or at 2 or 4 weeks, followed by a biochemical and histological examination. It was noted that grossly, parenchymal lesions appeared firm and white with a central zone of carbonization, cavitation, or both. Histopathology examination revealed cellular inflammation in acute lesions; chronic lesions demonstrated coagulative necrosis with progressive fibrosis. However, NADH staining demonstrated residual viable cells within the treatment zone of survival animals but not in acutely sacrificed animals. Hilar occlusion resulted in a slightly, but statistically insignificantly, larger lesion.

De Jode et al.[58] reported the first cases in the literature involving the use of interstitial laser ablation for RCC. Under MRI guidance, three patients with metastatic disease who required palliation were treated using a percutaneous technique with real-time MR guidance in an open access interventional MR scanner. Laser therapy was delivered using a neodymium-YAG source via a water-cooled applicator system. Thermal lesions were monitored in real time using a color thermometry sequence. All patients were discharged the following day with no complications. Follow-up with gadolinium-enhanced MRI in a conventional high-field system confirmed necrosis in the targeted tissue.

Though interstitial laser ablation is an emerging technique, evidence of viable cells within treatment zone of benign parenchyma of an animal model[57] mandates refinement of the technique before further application in humans.

Microwave ablation

Though the initial report of investigation of microwave energy on renal tissue was reported in 1969,[59] there was a paucity of investigative citations on microwave on renal tissue. In 1995, Kagebayashi et al.[60] reported

the first case of clinical utilization of microwave thermotherapy in the treatment of RCC. The reported a case of a 4.5 cm multilocular cystic RCC detected incidentally which was treated with a microwave tissue coagulator. Follow up of 1.5 years with serial imaging failed to demonstrate any tumor recurrence or metastases.

Kigure et. al.[61] investigated the effectiveness of laparoscopically delivered microwave thermotherapy on implanted renal VX-2 tumors in a rabbit model. A comparison was made between a group that received no treatment, a group that underwent nephrectomy and a group that underwent laparoscopic microwave thermotherapy. They noted that the survival rate in the laparoscopic microwave thermotherapy group was significantly higher than that in the no-treatment group, and was the same as that in the nephrectomy group and the serum creatinine level did not increase after microwave therapy.

These results indicate that ultrasound-guided microwave thermotherapy has the potential of being a nephron-salvaging treatment for small renal tumors.

Cyberknife extracorporeal radiosurgical tissue ablation

The Cyberknife is a frameless, image-guided radiosurgical device,[62] originally developed for the treatment of treatment of brain tumors.[63] Recently, this technology has also been clinically investigated for the treatment of lung tumors[64] and at the Cleveland Clinic, a preclinical animal model has also been recently investigated for possible treatment of renal tumors.[65]

Rather than using rigid immobilization, the Cyberknife combines two different technologies to deliver conformal radiosurgery doses without a frame: firstly, it relies on an image-to-image correlation algorithm for target localization. Furthermore, the system utilizes a novel, light-weight, high-energy radiation source, which combines a linear accelerator mounted on a highly maneuverable robotic arm.[62] The Cyberknife is unique in that it divides the high-dose radiation necessary to ablate the lesion completely into up to 1200 beams. Each one of these beams of radiation has a significantly reduced dose. Therefore, the individual dose of each beam is essentially benign to the pathway and surrounding tissue. However, at the focal point of these beams, the dose is additive, and the desired ablative dose is attained.[65]

Ponsky et al.[65] examined the in vivo effectiveness of cyberknife technology on a porcine kidney model. A total of 16 radiographically specified areas by a pretreatment CT scan were designated as "lesions" in the kidneys of eight pigs. All animals were treated under general anesthesia with no complications and histologic evaluations were completed at 4, 6, or 8 weeks. The authors noted that the degree of tissue change increased with time, and after 8 weeks, the treated areas showed complete fibrosis characterized by dense, connective tissue completely devoid of all normal kidney architecture. As a result of the demonstration of the cyberknife as a safe, efficacious and reproducible tissue ablation technology in kidneys, plans are underway to investigate its efficacy in the clinical setting. □

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