

Michael A. S. Jewett · Princess Margaret Hospital, Toronto

Current limitations of radiofrequency ablation in renal cell carcinoma

For the past 50 years, the standard treatment for renal cell carcinoma (RCC) has been radical nephrectomy [1]. Apparently, equivalent cancer control is now being obtained with partial nephrectomy, or nephron-sparing surgery (NSS) for smaller tumours [2, 3, 4]. The only established curative treatment for RCC remains surgery. Although morbidity rates from surgery have decreased with improved techniques, they are still significant.

Today, most new RCCs are detected as incidental small renal masses on imaging. The natural history appears to be one of slow growth [5, 6]. The current standard approach of immediate surgery needs to be re-evaluated. A number of minimally invasive techniques designed to ablate small renal masses while preserving renal function are being investigated. Energy has been delivered percutaneously, extracorporeally or by laparoscopy and the pathophysiology of the treatment effects have been described [7]. The largest experience has been with cryotherapy. This technique appears to be safe and has short-term effectiveness and can be delivered laparoscopically. However, tumour recurrence has been described [8]. An alternative approach is localised heating. This has the ability to destroy cancerous tissues while avoiding thermal damage to surrounding healthy structures. Among the high-temperature thermal therapy modalities, microwave, interstitial laser fibre-optic, high-intensity focused ultrasound (US), high-energy shock wave and radiofrequency (RF) have been described for the ablation of small re-

nal tumours in animals and small human series with short follow-up.

RF has been tested on animals, kidney models, and some encouraging human experiences have been reported. We have: (1) developed a percutaneous RF ablation technique in an *in vivo* and *ex vivo* porcine kidney model, (2) described a potential method to ensure that critical structures surrounding the kidney are not thermally damaged during treatment, and (3) described the findings from our human experiments with this technique [9].

From our *in vivo* porcine experiment we observed that lesion size was not reproducible and that the time required to create these lesions varied considerably. We believe the variability in size is due to the effect of renal blood flow, where flow per gram of tissue is greater in the kidney than in the liver and other organs. These variations suggest that each case presents unique conditions that could impact upon the interaction between energy administration and tissue response. As opposed to liver lesions produced by RF, renal lesions were wedge-shaped. This wedge shape may be explained by the pattern of renal circulation with blood flowing segmentally from the medulla outwards to the cortex. When blood flow is occluded centrally, the rest of that segment becomes ischaemic and undergoes infarction.

Real-time monitoring of lesion progression is a very important clinical issue. Prediction of lesion size by US immediately after treatment is inaccurate; however, grey-scale US at day 7 predicted accurately lesion size. Lesion size as measured by

power Doppler US was not accurate, but it may have potential for follow-up of ablated tumours when perfusion loss is used as a marker for long-term treatment success.

Heat injury to adjacent tissues and organs was observed. This raised significant safety issues. To overcome this problem, we developed a technique to dissect the tissues surrounding the area to be treated with saline solution or CO₂. After the implementation of this adjunctive technique, no complications were observed.

Histology consistently demonstrated thermal changes in the pigs that were sacrificed immediately after RF treatment. For the lesions removed at day 7 post-RF, the findings were consistent with ischaemic-type infarction and morphologic changes ascribed to thermal injury. These findings correlate with the wedge-shaped RF lesion, which is explained by thrombosis of major vessels feeding the renal tissue from the medulla to the cortex and by the heat itself. This implies that in the kidney, the “kill zone” is not only formed by the cytomorphic correlate of thermal injury, but also by the occlusion of the segmental pattern of blood flow causing ischaemia downstream. A thin, well-defined rim of inflammation was observed in the periphery of the lesion and viable renal tissue was found beyond this rim.

As lesion size and time required to produce the lesion were not reproducible, we conducted an *ex vivo* porcine kidney experiment where different input power settings and heating times were tested to determine the optimum parameters that would make lesion formation more reproducible.

We have treated small renal masses in patients with RF [10]. Initially, the tumours were treated during surgical exposure of the kidney. In these patients the tumours were removed immediately after the RF treatment. In the remaining patients, the tumours were treated percutaneously under local anaesthesia with RF 7 days before the partial or radical nephrectomy. The approximate average of tumour ablation determined by histology was 93%. Complications due to the RF treatment can occur.

However, to date in our experiments, the efficacy of this treatment, as demonstrated by histologically proven ablation of the entire tumour volume, has not yet been observed. The inability to ablate the en-

tire tumour appears to be due to the heat sink effect of high renal blood flow and to the segmental architecture of the kidney. These factors make the kidney a unique organ and therefore preclude any extrapolation of data obtained from the treatment of liver tumours.

Percutaneous RF is a promising technique for the ablation of small renal masses; however, further investigation is required before it may be offered as definitive treatment in humans. To improve the reproducibility of RF, we have developed a phantom model in our thermal biophysics laboratory to study the relationship of renal blood flow and the delivery of thermal energy.

We are also studying methods to deliver thermotherapy with high-energy extracorporeal US.

Corresponding author

Prof. Dr. Michael A. S. Jewett

Princess Margaret Hospital,
610 University Avenue, 3-124,
Toronto ON, Canada M5G
e-mail: m.jewett@utoronto.ca

Conflict of interest: No information supplied.

References

1. Robson CJ, Churchill BM, Anderson W (1969) The results of radical nephrectomy for renal cell carcinoma. *J Urol* 101:297-301
2. Lee CT, Katz J, Shi W, et al (2000) Surgical management of renal tumors 4 cm or less in a contemporary cohort. *J Urol* 163:730-736
3. Fergany AF, Hafez KS, Novick AC (2000) Long-term results of nephron sparing surgery for localized renal cell carcinoma. *Br J Urol* 163:442-445
4. Novick AC (1998) Nephron sparing surgery for renal cell carcinoma. *Br J Urol* 82:321-324
5. Bosniak MA, Krinsky GA, Waisman J (1996) Management of small incidental renal parenchymal tumors by watchful waiting in selected patients based on observation of tumor growth rates. *J Urol* 155:584A
6. Rendon RA, Stanietzky N, Panzarella T, et al (2000) The natural history of small renal masses. *J Urol* 164:1143-1147
7. Finelli A, Rewcastle JC, Jewett MAS (2003) Cryotherapy and radiofrequency ablation: pathophysiological basis and laboratory studies. *Curr Opin Urol*
8. Gill IS, Novick AC, Soble JJ, et al (1998) Laparoscopic renal cryoablation. Initial clinical series. *Urology* 52:543-551
9. Rendon R, Gertner MR, Sherar MD, et al (2001) Development of a radiofrequency based thermal therapy technique in an in vivo porcine model for the treatment of small renal masses. *J Urol* 166:293-298
10. Rendon RA, Kachura JR, Sweet JM, et al (2002) The uncertainty of radiofrequency treatment of renal cell carcinoma: findings at immediate and delayed nephrectomy. *J Urol* 167:1587-1592

Urologe [A] 2004 · [Suppl 2]43:S123-S125 · DOI 10.1007/s00120-004-0597-3
Online publiziert: 19. May 2004 · © Springer Medizin Verlag 2004

D. A. Swanson

Department of Urology, Unit 446, The University of Texas M.D. Anderson Cancer Center,
Houston, Texas, USA

Metastasectomy for renal cell carcinoma

Although the role of surgery for metastases from renal cell carcinoma (RCC) is not yet clearly defined, we believe that it should be considered for selected patients with solitary and limited metastases, a residual mass after systemic therapy, local recurrence, and symptomatic metastases.

Metastasectomy for solitary metastasis was firmly established as potentially effective by the mid-1970s, and the 5-year survival rate is still widely quoted to be about 35%. Kavolius recently reported on 94 patients who underwent resection of a solitary metastasis as first recurrence [1]. Patients with completely respected solitary metastasis fared better than those who underwent complete resection of multiple metastases, with a 5-year overall survival rate of 52% compared with 29% ($p < 0.005$).

At The University of Texas M.D. Anderson Cancer Center, 179 (8.5%) of 2,100 patients with metastatic RCC underwent resection for an apparently solitary metastatic lesion between 1984 and 1997. Sites resected included lung (50), axial bone (29), appendicular bone (27), visceral organ (23), brain (23), locoregional location, including renal fossa or regional lymph nodes (17), and skin (10). The overall 5-year survival rate was 29%. Disease-specific 5-year survival rate for all sites was 19% and rates were dependent upon the location of the metastasis. Patients who developed a metachronous solitary metastasis fared better than those with a synchronous solitary metastasis (5-year survival rates of 39% and 22%, respectively) regardless of the site of metastasis.

Resection of multiple metastases may be worthwhile in selected patients, especially those who are anticipated to have longer survival times. However, the presence of one or more adverse prognostic indicators such as high nuclear grade (or sarcomatoid histology), poor performance status, synchronous metastases or short disease-free interval after nephrectomy, metastatic sites other than lung, and multiple organ site involvement argues against aggressive surgical resection of metastases.

Lung metastases are the most frequently diagnosed and generally most easily resected renal metastases. Typically, the size and number of lung metastases, whether they can be completely resected, and the disease-free interval are important predictors for survival. Pastorino reported on 4,572 patients who underwent complete surgical resection and compared them with 634 patients who had incomplete resections [2]. The actuarial 5- and 10-year survival rates after complete metastasectomy were 36% and 26%, respectively, compared with 13% and 7%, if incomplete.

Tanguay addressed the potential benefits from combining surgery with systemic therapy in 51 patients who had 68 thoracotomies at our institution [3]. Twenty-two patients had initial surgical resection (20 had only one or two nodules). The remaining 29 patients (20 had 4 or more residual nodules) underwent thoracotomy for residual disease after a partial response to systemic therapy. Of 22 patients who underwent initial surgery, 12 (55%) were alive after median follow-up of 48 months,