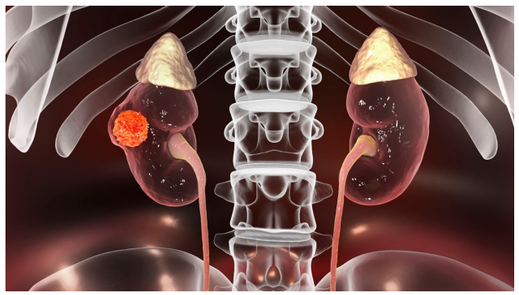
SBRT offers hope for Inoperable Kidney Cancer

Renal cell carcinoma is the most common malignancy of the kidney. Its incidence has been steadily increasing over the past few decades. There are several reasons for this. Firstly, abdominal scans for screening or investigation of symptoms are being carried out with increasing frequency. As a result, more incidental kidney tumours are being detected.

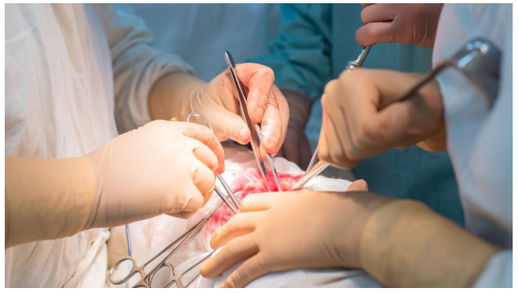


Hypertension and obesity both increase the risk of development of renal cell carcinoma. These risk factors have been increasing in prevalence over the years.

Conventional Treatment Modalities and Their Limitations

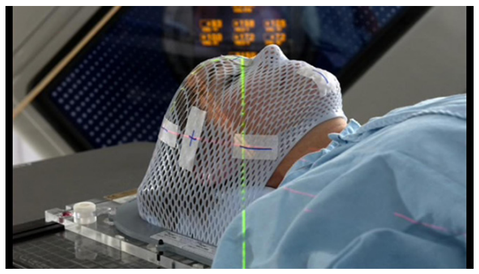
Surgical resection of the tumour or kidney has the preferred method of treatment for many years. In patients without metastasis, surgery can lead to cure. Partial nephrectomy can be carried out for smaller tumours. For larger tumours, radical nephrectomy is the treatment of choice. Cryotherapy and radiofrequency ablation have also been used, but this is restricted to small tumours less than 3cm. The local control rates are also inferior to that of surgery.

For older patients, or those with co-morbidities, surgery entails peri-operative mortality risk, from both anaesthesia-related difficulties and post-operative complications. Patients with poor or borderline renal function may not have adequate kidney reserves following nephrectomy. Therefore, there is an unmet need for a treatment modality to address patients will renal cell carcinoma who are medically or surgically inoperable.



Role of Radiotherapy in RCC

Conventional radiotherapy involves giving small doses at repeated intervals. It is a common belief that RCC is relatively radio-resistant, compared to other cancer types. So, while conventional radiotherapy can still deliver palliate symptoms caused by the tumour, like bleeding, it is unlikely to offer long lasting control of the tumour. However, when radiotherapy is delivered in large doses over 1 to 5 treatments to RCC, control rates are much improved. These large doses must be precisely delivered to avoid damaging the surrounding tissue. This treatment concept has been applied effectively and safely to ablate RCC brain metastases using Stereotactic Radiosurgery (SRS).



Frameless SRS using a thermoplastic mask together with an advanced digital navigation system

Stereotatic Radiosurgery (SRS) is a highly targeted and focused radiation treatment which delivers extremely high doses of radiation directly to the target to destroy it. It involves customization of immobilization device ie radiosurgery facemask, CT simulation as well as computer- aided planning.

The challenge of radiating RCC with ablative radiotherapy

The brain is an organ fixed in position in the skull and thus brain metastases within are easily targeted with external immobilization like a head frame or a thermoplastic mask. The kidney on the other hand moves with respiration. This presents a challenge in a) localising the treatment area according to motion, and b) minimizing the potential for significant collateral damage to functional kidney tissue if this treatment area is too large. Thus, radiotherapy to the kidney previously had been restricted to conventional radiotherapy in small doses which are less effective.

Stereotactic Body Radiation Therapy (SBRT)

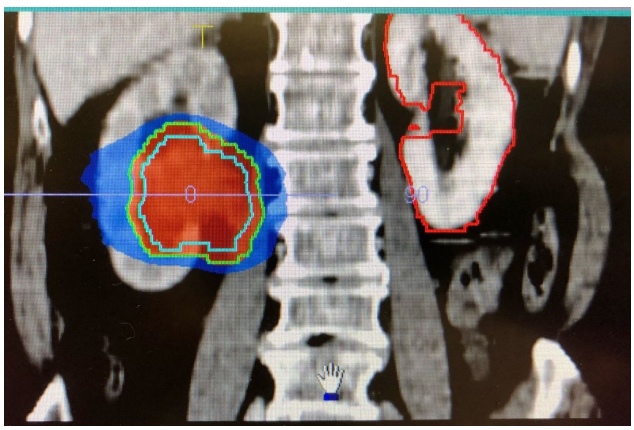
SBRT has is an advanced radiotherapy technique that in recent years has allowed non-invasive ablation of tumours in the body. SBRT brings the same concepts of SRS to treatment of tumours outside the brain – high doses in up to 5 treatments, sharp dose fall-off beyond the tumour to spare normal tissue and a specialised 3D-coordinate system to target the tumour. In addition, motion management measures are used to account for movement of the tumours within the body.

Biological and Physical Basis of SBRT in RCC

As previously mentioned RCC is relatively radioresistant. High doses of radiation per treatment overcome this through alternate tumour cell death pathways like ceramide-mediated apoptosis instead of p53-mediated mitotic death, and effects on the blood vessel endothelium of the typically vascular RCC. The sharp dose falloff beyond the target tumour allows optimal sparing of neighbouring nephrons, to minimise reduction in post-SBRT renal function.

Techniques of Administering SBRT

A CT scan is used to localize the tumour. There are two ways to deal with motion of the kidney – either reducing motion through external immobilization, and accounting for it, or eliminating it through breath hold. In the former method, motion is reduced through external abdominal compression and a 4D-CT that charts the location of the kidney in all phases of respiration is used to localise the treatment area. In the latter method, patients hold their breath during the CT scan and subsequent treatments to eliminate motion. The depth of breath hold is monitored in real time by a spirometry device which will automatically cut off treatment if the depth correlated to kidney position is not maintained. Whichever the localisation technique, the delivery of the radiation is through computer planned, high conformal intensity modulated radiotherapy (IMRT) or volumetric arc therapy (VMAT).



Coronal view of Right Kidney SBRT Plan showing high doses (red wash) concentrated on tumour (light blue line) with a small margin (green line). Blue wash shows low doses; it can be seen that renal parenchyma superior and inferior to it are spared from them.

Clinical Efficacy of SBRT in RCC

An International Radiosurgery Oncology Consortium for Kidney (iROCK) was formed to study and document implementation of SBRT for Kidney Cancer. A multi-institutional analysis of 223 patients was published in 2018, showing that, up to 4 years, SBRT was highly effective, controlling the primary kidney tumour more than 95 percent of the time. Severe long term side effect rate was low at 1.3 percent. There was an expected deterioration in overall renal function, but it was acceptable with decreased GFR of 5.5 +/- 13.3ml per minute. This compares favourably to partial nephrectomy (mean loss 16.6 mil per min) or total nephrectomy (mean loss 25.5ml per min). Also, the mean size of tumours treated was more than 4cm, larger than the less than 3cm tumours that can be treated by radiofrequency or cryoablation.

The consortium further studied the use of SBRT in patients with patient with a solitary kidney in an analysis of 81 patients across 9 institutions. Similar results to the previous analysis, in regard to tumour control and overall renal function, were achieved if the tumour was less than 4cm in diameter.

Conclusion

SBRT will occupy an important niche in the treatment of primary kidney cancer. It is non-invasive and can thus be used in older patients, or patients with co-morbidities, who are medically inoperable. It does not have the same size limitations as radiofrequency or cryoablation. Patients with a solitary kidney can also be safely treated with SBRT if the tumour is not too big. With the addition of SBRT, there is hope for curative treatment even with patients who cannot have surgery.

References:

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