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Can we Cure Resistant Cancers?

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Editorial

A paradigm shift is required to address the cancers that were considered incurable and resistant to either radiation or chemotherapy till recently. Renal Cell Carcinoma (RCC) is one such entity that was considered a radio and chemo resistant tumor till the turn of century. After the advent of tyrosine kinase inhibitors (targeted therapy) the outlook for systemic therapy for metastatic disease has changed with patients surviving longer than 9-12 months. High dose hypo fractionated radiation precisely targeted by Stereotactic Body Radio Therapy (SBRT) can result in long-term cure of primary as well as oligometastaic renal cell cancers. The management of Stage Ia renal tumors (<4cm, limited to kidney) is partial nephrectomy or ablative techniques (radiofrequency ablation, cryoablation or SBRT) for non surgical patients. The management of renal metastasis with SBRT followed by Sorafenib/Sunitinib can provide >24cm months with a good quality of life. Radiofrequency ablation and /or cryotherapy (RFA/CA are Indicated in clinically localized RCC especially in elderly patients not amenable to surgery due to medical comorbidities or patients with solitary kidney. Favorable results have been achieved with <4cm tumors located at the periphery. The relative contraindications of RFA/CA include a tumor size >5cm, tumor location near renal hilum, collecting duct or renal vessels.

In contrast to RFA & cryotherapy, SBRT is capable of treating larger tumours, adjacent to collecting vessels as well as ureteric ducts. It can achieve high control rates >90% in so called "resistant RCC", both the primary and metastasis. Thus SBRT has role in stage IA RCC where an ablative technique has been recommended which includes localized stage – medically unfit for surgery, RCC in only 1 functioning kidney, bi-lateral kidney lesions, recurrent disease either in the tumor bed or para-aortic nodes; skeletal or vertebral metastases, brain, liver, lung and adrenal metastasis from RCC. SBRT may represent a novel non-invasive, nephron-sparing option for the treatment of primary RCC. Experiments have shown that RCC cells are radio resistant at low dose but a clear dose response relation is seen with a higher cell kill beyond 8Gy as reported by Zelefsky et al. [3] Radio resistance is overcome at high doses per fraction (SBRT) delivered by the accurate delivery methods through Cyberknife or Linear accelerators.

Dose to Overcome Radio Resistance

Ning et al. [1] performed clonogenic survival assays with two human RCC cell lines. The cells were irradiated with 0 – 15 Gy and surviving fractions were calculated. They observed that at 1.8–2 Gy per fraction there was a small proportion of cell kill which increased exponentially at more that 6Gy per fraction. This has been proven to be true in the well established stereotactic literature for RCC metastases to the brain also. Stinauer et al. [2] studied the dose for local control in RCC with SBRT. Single fraction equivalent dose (SFED) >45Gy was a predictor of local control (LC) providing a >90% chance of LC. SFED 44.3Gy is equivalent to 48Gy/3 fraction that translates to a biologically equivalent dose (BED) of 126 Gy. In their study median Overall Survival (OS) of 22.2 months was reported and the median OS had not been arrived at for RCC.

Siva S et al. [4] published a review of 10 studies with 126 patients treated for primary RCC. A dose of 40Gy/5 fractions had been used with a follow up of 9-57.5 months. The crude weighted local control rate and 2-year estimated weighted local control rate were 93.1% and 92.9% respectively. Commonly reported toxicities were fatigue and nausea, followed by radiation dermatitis and enteritis recovering within 2-3 weeks post treatment. Rates of severe toxicity (grade 3+) were very low.

It is postulated that there is inter-mitotic death of the tumour cells besides vascular shut down and stromal breakdown at such high doses resulting in a cascade of ceramide, sphingomyelin and cytokine production that are presented to the T-cells through antigen presenting cells. This sets up the un-masking of the circulating tumour cells and an immune response from the host resulting in long term control in oligo-metastaic renal cell cancers.

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A combination of stereotactic radiation followed by tyrosine kinase inhibitors may result in keeping the patients disease free longer than either of them alone. The way forward for in-operable or metastatic renal cell cancers is to address loco-regional as well as metastatic disease with multi-modality therapy and aim towards achieving a cure for the tumour that was considered lethal till two decades ago.

References

1. Zelefsky MJ, Greco C, Motzer R, Magsanoc JM, Pei X, Lovelock M, et al. Tumor control outcomes after hypofractionated and single-dose stereotactic image-guided intensity-modulated radiotherapy for extracranial metastases from renal cell carcinoma. Int J Radiat Oncol Biol Phys. 2012; 82: 1744-1748.
2. Ning S, Trisler K, Wessels BW, Knox SJ. Radiobiologic studies of radioimmunotherapy and external beam radiotherapy *in vitro* and *in vivo* in human renal cell xenografts. Cancer. 1997; 80: 2519-2528.
3. Stinauer MA, Kavanagh BD, Schefter TE, Gonzalez R, Flaig T, Lewis K, et al. Stereotactic body radiation therapy for melanoma and renal cell carcinoma: impact of single fraction equivalent dose on local control. Radiat Oncol. 2011; 6: 34.
4. Siva S, Pham D, Gill S, Corcoran NM, Foroudi F. A systematic review of stereotactic radiotherapy ablation for primary renal cell carcinoma. BJU Int. 2012; 110: E737-E743.