A review of acute toxicity and plan adaption robustness from magnetic resonance guided radiotherapy to renal and adrenal tumours.

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Introduction

Stereotactic ablative radiotherapy (SABR) for adrenal and renal tumours has been shown to have promising local control with low toxicity.[1] This is challenging to achieve due to the tolerance and close proximity of the organs at risk (OARs). As noted by Stemkens et al.[2] it was found that with standard linac based renal SABR there was a risk of dosimetric errors due to a variation in intra-fraction respiratory motion. This can be prevented by the use of real-time treatment planning adaptation and tumour tracking using Magnetic Resonance – guided radiotherapy (MRgRT).[3] Further dose escalation strategies and techniques are recommended to improve patient outcomes[4], using MRgRT.

Methods

Eight patients were treated with extreme hypofractionated MRgRT ranging from 40-45Gy in 5 fractions or 36Gy in 3 fractions, to a kidney tumour, renal bed recurrence or adrenal gland metastasis. A fully adaptive workflow was used for each fraction, for both re-contouring of the gross target volume (GTV) and nearby OARs, by a Consultant Clinical Oncologist (CCO). Treatment plans were then re-optimisation based on interfractional changes.

A post-treatment CT scan was completed to assess local progression. Toxicity scores were recordedusing the Common Terminology Criteria for Adverse Events (CTCAE) grading system [5&6]. Retrospective analysis was completed on the V100 and V95 PTV coverage, Visceral OAR doses and interfractional tumour change, where Visceral OAR is a combined volume encompassing; stomach, duodenum, small bowel and large bowel.

Results

Patient	PTV coverage (%)				Visceral OAR dose received (cc)					
	V95		V100		V33Gy		V30Gy		V25Gy	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
1	98.72	0.73	94.83	0.30	0.00	0.00	0.03	0.01	4.72	0.13
2	98.13	0.64	94.97	0.25	0.00	0.00	0.00	0.00	0.00	0.00
3	85.92	1.44	78.86	1.99	0.00	0.00	0.00	0.00	0.05	0.06
4	96.83	3.25	93.26	6.36	0.31	0.21	1.24	0.78	6.93	4.37
5	96.62	1.50	89.76	3.68	0.00	0.00	0.09	0.07	4.87	0.43
6	96.00	0.90	93.79	1.19	0.06	0.03	0.32	0.07	2.81	0.58
7	95.98	1.46	89.95	4.07	0.00	0.01	0.09	0.17	2.91	2.79
8	97.66	2.01	94.19	1.72	0.04	0.04	0.16	0.11	1.04	0.33

Table 1: The mean and standard deviation (SD) for all fractions, of PTV coverage and Visceral OAR dosimetry.

In this patient group the average (± standard deviation (SD)) of the PTV V95% and V100% dose coverage was 95.58 ± 4.21% and 91.01 ± 5.94% respectively. Target PTV coverage of V100 ≥ 95% was achieved in 14/38 fractions. All fractions complied with visceral OAR dose constraints and the average V33Gy, V30Gy and V25Gy volumes received were 0.05 ± 0.12cc, 0.25 ± 0.48cc and 2.82 ± 2.94cc respectively (see table 1).

The GTV size changed >10% in volume in 3/8 patients. Figure 1 shows an example where the GTV size from the simulation planning MR was smaller compared to the latter fractions. The same image sequence (TRUEFISP) was used for all imaging.

Median follow-up was 3.2 months, with no confirmed cases of disease progression. One patient was lost to follow up. Reported toxicity was limited to fatigue and nausea. All patients reported ≤ Grade 1 toxicity except one patient who reported Grade 2 toxicity for both fatigue and nausea (see table 2).

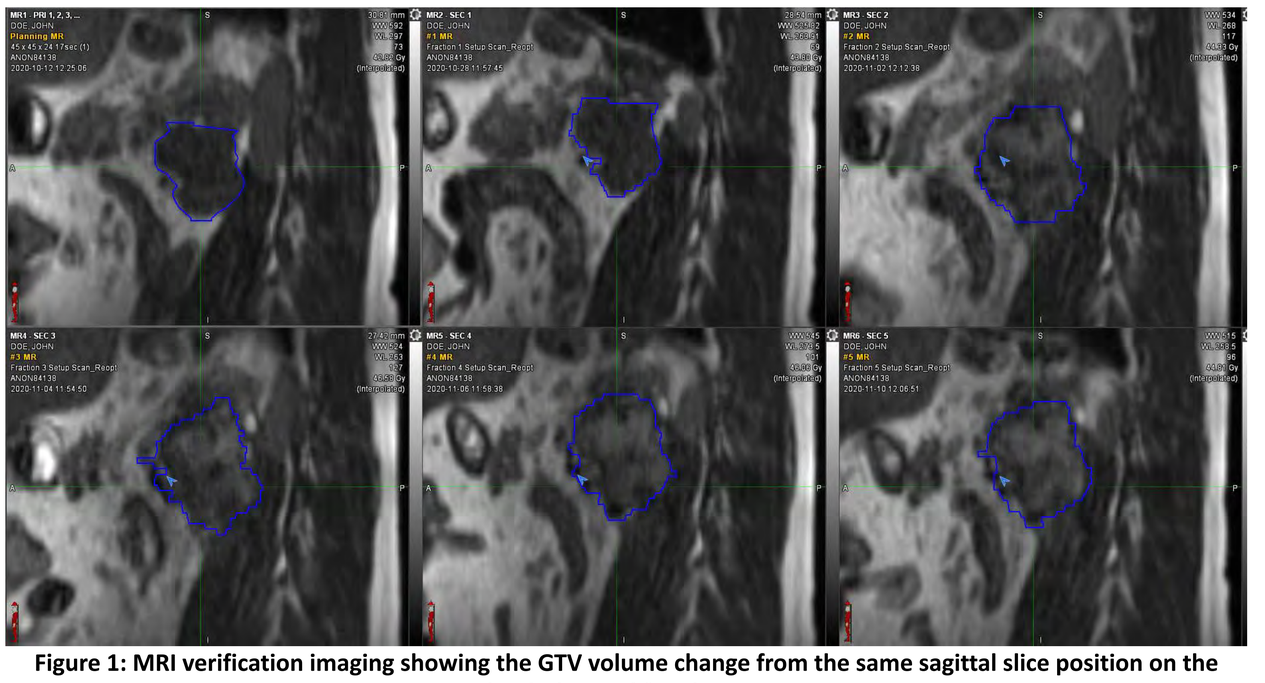
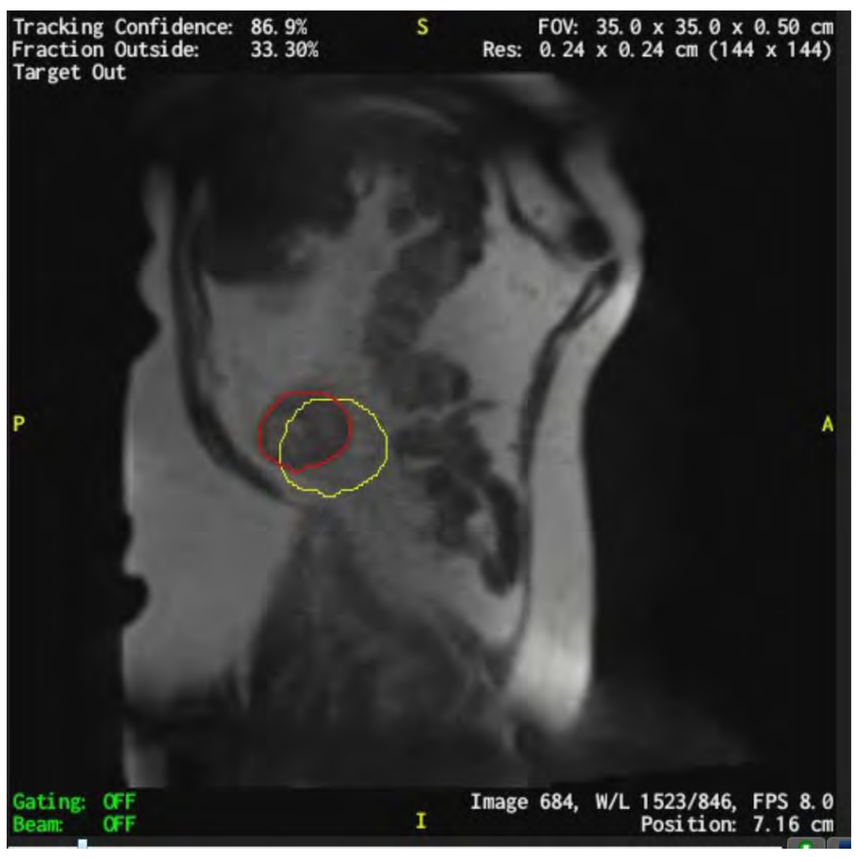


Figure 1: MRI verification imaging showing the GTV volume change from the same sagittal slice position on the simulation and fractions 1-5

Patient	Tumour target site (primary)	Dose fractionation	Local progression	Fatigue grade	Nausea grade	Follow up time post Rt (days)
1	L kidney (RCC)	36Gy/3#	No	0	0	129
2	L renal bed recurrence	40Gy/5#	No	1	0	184
3	R kidney (RCC)	40Gy/5#	N/A	0	1	0
4	L renal bed recurrence	40Gy/5#	No	1	1	304
5	L kidney (RCC)	40Gy/5#	No	2	2	192
6	R adrenal met (breast)	40Gy/5#	N/A	1	1	35
7	L adrenal met (lung)	40Gy/5#	N/A	0	0	65
8	L adrenal met (L kidney)	45Gy/5#	N/A	1	1	0

Table 2: Patient post treatment follow-ups. Local progression was assessed from CT imaging ad toxicity scores were graded using CTCAE. Patient 7 was unavailable to contact and lost to follow-up



Video 1: A 2-D cine-MRI image series during beam irradiation

Discussion/Conclusion

A consistently high PTV coverage was achieved despite interfractional changes. Interestingly, re-optimsation based on interfractional changes allowed for improved PTV coverage compared to the initial base plan in 27/38 and 22/38 fractions for the V95% and V100% respectively. The use of 2D cine-MRI image gating allowed for small PTV margins of 3mm. A study by Palacios et al, showed that abdominal OARs have considerable movement, even during patient breath hold. The online daily adaption and use of gating is therefore advantageous in ensuring as accurate treatment delivery as possible.[7] Video 1 shows an example of this, where the GTV is deformed onto the image and gated so that the beam irradiation is only delivered during a consistent shallow breath hold.

Interfractional re-contouring of the GTV showed how it can change size and shape compared to a baseline simulation scan taken 2 weeks prior to the first fraction. For one patient, the GTV size increased after fraction 1 for the remaining fractions by 26-42cc (51-82%). This highlights the benefit of both re-adaption of contours and MRI to MRI imaging from simulation to fractional verification. Re-contouring was completed by multiple CCOs resulting in inter-observer variations.

The results from follow-up showed no severe toxicity scores with a single patient having both Grade 2 fatigue and nausea. Local progression information is not yet available for all patients, however 4/8 patients had no evidence of local progression by CT criteria. Median follow up in this study is just 3.2 months, a longer follow up period is required to give more meaningful tumour control results.

This small study concludes therefore that the use of daily adaptive MRgRT for the treatment of renal and adrenal tumours is accurate and allows for safe delivery of dose escalation. The use of daily recontouring of the GTV, as well as the OARs surrounding the target area ensures precise adjustment for any GTV changes, as well as adaption for positional changes in the OARs including stomach, bowel and duodenum. This study is limited by the small sample size and short period of follow-up.

References

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