Oxford University Hospitals NHS
NHS Foundation Trust

THE RELATIONSHIP BETWEEN DOSE TO THE VOMITING CENTRE AND NAUSEA AND VOMITING AS A SIDE EFFECT IN FRACTIONATED STEREOTACTIC RADIOTHERAPY TO BENIGN SKULL BASE TUMOURS

Rhona Watson, Neuro-oncology Advanced Practitioner Radiographer (rhona.watson@ouh.nhs.uk),

INTRODUCTION

Oxford Cancer Centre has been using Rapid Arc™ VMAT with ExacTrac™ imaging to deliver LinAc-based fractionated stereotactic radiotherapy (FSRT) to benign skull base tumours since September 2014. Treatment-related toxicity was recorded weekly and retrospective audit of14 patient records revealed radiation induced nausea/vomiting (RIN) as the most commonly reported side effect.

Radiotherapy induces side-effects localised to the treatment area, where radiation induces DNA damage and cell death in all cells (both tumour and healthy) exposed to an ablative dose . It would therefore be reasonable to deduce that in patients treated with FSRT to the skull base, the area commonly referred to as the 'vomiting centre' (VC), comprising of the area postrema and dorsal vagal complex in the brainstem (Borison, 1986), received sufficient dose to cause RIN.

A literature review was then carried out to explore the feasibility of recommending a dose constraint to be applied to the VC at the time of physics planning while still producing an optimal treatment plan.

Having this knowledge would enable us to reduce the likelihood of RIN in this patient group and, where a plan could not be compromised, predict which patients would be more likely to develop RIN. Anti-emetic therapy could then be introduced sooner in the patient pathway if required and more detailed information could be given to patients about the likelihood of RIN as a side effect of their individual treatment plan, therefore improving patient experience and quality of life.

LITERATURE REVIEW

A number of studies have been carried out investigating VC dose in patients receiving RT for head and neck cancers. No such studies currently exist for skull base RT but it is assumed that in the context of FSRT to benign skull base lesions, given the similar anatomical region and comparative OARs, the same principles would apply

Ciura *et al* (2009)

- retrospectively contoured VC in 100 patients receiving RT to oropharyngeal cancer.
- mean dose to the VC correlated with RIN but not statistically significant.
- Only patients undergoing concurrent chemotherapy, no trend between dose and RIN in patients undergoing RT alone.

Monroe *et al* (2008)

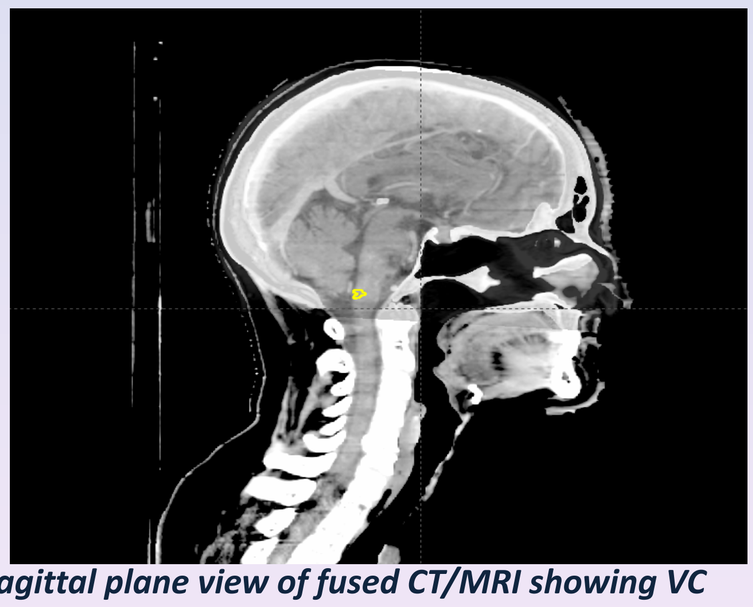
- compared dose to the VC to severity of RIN reported by patients.
- Patients reporting CTCAE grade 1 or 2 nausea were found to have a median VC dose of 26.9Gy while median dose for patients requiring anti-emetic therapy was 23.1Gy.
- Patients reporting CTCAE grade zero nausea did have significantly less VC dose (median 6.5Gy) - irrespective of whether they had received chemotherapy.

Lee *et al* (2011)

- In 49 patients receiving RT for nasopharyngeal cancer, 28.5% of patients reported either CTCAE grade 1 or 2 nausea.
- Median dose to VC was found to be 26.9Gy which correlated with RIN but was not statistically significant.
- The only predictor for RIN was found to be a dose of 40Gy or more to ≥80% of the total vestibular volume.

Wang *et al* (2012)

- retrospectively contoured the VC in 23 patients receiving RT to oropharyngeal cancer.
- Median dose to both areas was significantly higher in patients who reported CTCAE grade 1-3 nausea.
- Median max VC dose of 32.6Gy compared to 28.7Gy in asymptomatic patients.
- All 23 patients were re-planned with VC identified as avoidance structure.
- Achieved dose reduction to VC by 18%
- Median doses brought in line with those of the asymptomatic patients without significantly compromising coverage of target volumes or increasing dose to other organs at risk.



Sagittal plane view of fused CT/MRI showing VC contoured in yellow at posterior aspect of brainstem

CONCLUSION

A definitive 'safe' dose to the VC does not exist, with authors quoting a range of mean, maximum or median doses while results are clouded by the addition of concurrent chemotherapy. A degree of 'poetic licence' is required to interpret any suggested constraint, with key values ranging from 23-40Gy.

Modern planning techniques can attain stringent dose fall off therefore dose to the VC should be kept as low as reasonably achievable to optimise patient QOL.

However optimal coverage of the target and dose constraints to more critical OARS such as the optic apparatus should take priority at the time of physics planning and any suggested constraint to the VC may have to be sacrificed to a certain extent to maximise plan quality.

Patients in which the VC constraint has not been achieved should be identified and either prophylaxis or early intervention with anti-emetic therapy considered.

References:

Borison, H.L., (1986) 'Anatomy and Physiology of the Chemoreceptor Trigger Zone and Area Postrema' in Davis, J., Lake-Bakaar, G.V. and Grahame-Smith, D.G, *Nausea and Vomiting: Mechanisms and Treatment.* Berlin: Springer Berlin Heidelberg, pp. 10-17.

Ciura, K., McBurney, M., Nguyen, B., Pham, M., Rebueno, N.,Fuller, C.D., Guha-Thakurta, N. and Rosenthal, D.I., (2009) 'Effect of Brain Stem and Dorsal Vagus Complex Dosimetry on Nausea and Vomiting in Head and Neck Intensity-Modulated Radiation Therapy', *Medical Dosimetry,* 36 (1), pp. 41-45. DOI:http://dx.doi.org/10.1016/j.meddos.2009.11.002

Lee, V., Ng, S., Leung, T.W., Au, G.K.H. and Kwong, D.L.W., (2012) 'Dosimetric Predictors of Radiation-induced Acute Nausea and Vomiting in IMRT for Nasopharyngeal Cancer', *International Journal of Radiation Oncology Biology and Physics*, 84(1), pp.176-182. DOI: 10.1016/j.ijrobp.2011.10.010

Monroe, A.T., Reddy, S.C., Gibbs, G., White, G. and Peddada, A., (2008) 'Factors associated with radiation-induced nausea and vomiting in head and neck cancer patients treated with intensity modulated radiation therapy', *Radiotherapy and Oncology,* 87, pp. 188–194. DOI: 10.1016/j.radonc.2007.12.030

Wang, T., Fontenla, S., McCann, P., Young, R., McNamara, S., Rao, S., Mechalakos, J.G., and Lee, N.Y,., (2013) 'Correlation of planned dose to area postrema and dorsal vagal complex with clinical symptoms of nausea and vomiting in oropharyngeal cancer (OPC) patients treated with radiation alone using IMRT', *International Journal of Radiation Oncology Biology and Physics,* 2, pp.407–412. DOI: 10.1007/s13566-013-0094-7