Biologically Targeted Therapy for High Grade Gliomas using Inverse-planned Intensity Modulated Radiotherapy and Diffusion Tensor Imaging

Rajesh Jena[1], Stephen J. Price[2,3,4], Sarah J. Jefferies[5], Colin Baker[6], John D. Pickard[2,3], Jonathan H. Gillard[3,4], Neil G. Burnet[1]

[1]Department of Oncology. [2]Academic Neurosurgery Unit, [3]Wolfson Brain Imaging Centre, [4]University Department of Radiology, University of Cambridge, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK. [5]Oncology Centre, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK. [6]Radiotherapy Division, School of Health Sciences, University of Liverpool L69 3GB, UK.

UNIVERSITY OF CAMBRIDGE

Cambridge University Hospitals NHS Foundation Trust

SIEMENS

The Health Foundation

Background

We have demonstrated that diffusion tensor imaging (DTI) can be used to improve detection of white matter infiltration by high grade gliomas (HGG), and to individualise radiotherapy treatment planning for dose escalation.

In this study DTI is used to plan biologically optimised radiotherapy, using inverse-planned intensity modulated radiotherapy (IMRT) to deliver dose boosts to the gross tumour volume (GTV) and area of abnormality on DTI.

Methods

7 patients were included in this dosimetry study, comparing standard conformal radiotherapy (CRT) to Synchronous Boost IMRT (SB-IMRT).

Standard plans were prepared using a 2.5cm clinical target volume (CTV) margin added to the GTV, and a 0.5cm margin for the planning target volume. A dose of 60Gy in 30 fractions was specified to the PTV.

For SB-IMRT plans, a class solution was used to determine doses to GTV, DTI abnormality, and PTV, for a fixed 30 fraction schedule. Several normal tissue complication probability (NTCP) models were applied to each plan, specifically to assess the effect of biological dose transformation, and the effect of excluding the GTV from the volume of brain at risk of radionecrosis.

Morphology analysis was used to assess the eccentricity of treatment volumes, using an index of anisotropy (IA).

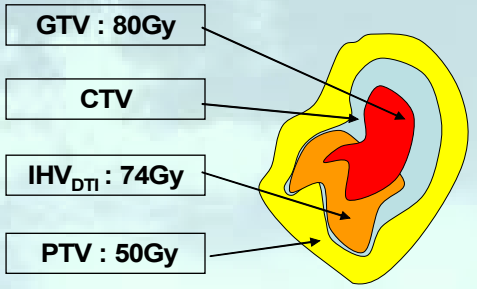
Results & Conclusions

Small (GTV < 20cc, PTV < 380cc) and medium sized (GTV < 100cc, PTV < 750cc) tumours could be boosted to doses of 80Gy and 74Gy to the GTV respectively, without violating the specified normal tissue dose constraints. In 6 out of 7 cases, the NTCP for the IMRT boost plan was lower than that of the standard CRT plan, despite the higher target dose. Excluding the GTV from the calculations resulted in a 32% mean reduction in NTCP.

Morphology analysis demonstrated that adequate spatial conformation to the treatment volumes could be achieved in all 7 cases without the need for specialist hardware such as micro-multileaf collimators. Dose inhomogeneity was observed in the outer concentric boost volumes, but at a level that compares favourably with previously published clinical studies.

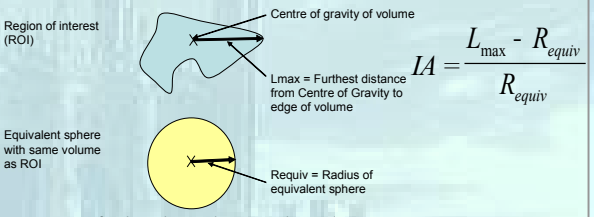
DTI based planning is a feasible technique for the implementation of IMRT based biologically targeted therapy. A clinical study based on this technique will commence later this year.

Synchronous Boost IMRT



IHV$_{DTI}$ is the volume at risk of white matter infiltration, identified using diffusion tensor imaging

Calculating index of anisotropy (IA)

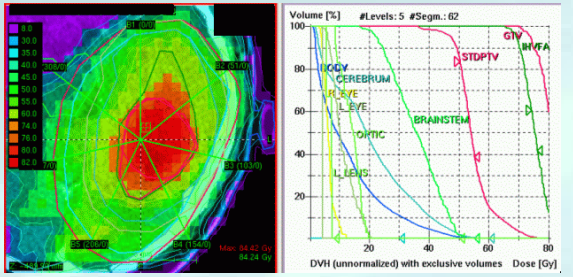


For a perfectly spherical ROI, the index is zero. As a ROI becomes more eccentric, the IA value increases.

ROIs with IA values greater than 0.9 require micro-multileaf collimators to achieve adequate dose conformation

Patient #	IA of GTV	IA of IHVDTI
1	0.44	0.67
2	0.41	0.65
3	0.5	0.57
4	0.75	0.59
5	0.41	0.74
6	0.29	0.41
7	0.49	0.71

SB-IMRT Dose Distributions



Adequate target dose conformation could be achieved using standard MLC hardware

NTCP Calculations

LKB Model				
	Physical dose		*Biological dose*	
Patient #	3DCRT to 60Gy	SB-IMRT Plan	3DCRT to 60Gy	SB-IMRT Plan
1	10.20%	11.10%	8.60%	5.20%
2	15.90%	13.20%	15.60%	6.50%
3	29.70%	18.20%	29.80%	9.40%
4	18.10%	9.60%	15.60%	4.20%
5	4.70%	4.10%	4%	3.00%
6	5.60%	2.40%	4.30%	1.00%
7	16.20%	11.80%	14.80%	5.10%

Values shown are % risk of brain necrosis at 5 years. Biological dose calculations exclude GTV from volume at risk of necrosis and make allowances for local variation in total dose and dose per fraction

References & Disclosure

Jena R, Price SJ, Baker C, Jefferies SJ, Pickard JD, Gillard JH, Burnet NG. Diffusion tensor imaging : Possible implications for radiotherapy treatment planning of patients with high grade glioma. Clin Oncol (R Coll Radiol). 2005 Dec;17(8):581-90

NGB & RJ were supported by an unrestricted educational grant from Siemens Oncology Care Systems

RJ is supported by a Health Foundation clinician scientist fellowship