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Short Report

Feasibility of Hippocampal Avoidance Radiotherapy for Glioblastoma

K. Thippu Jayaprakash [*], K. Wildschut [†], R. Jena [*‡]

[*] Department of Oncology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK
[†] Department of Radiotherapy Physics, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK
[‡] Department of Oncology, University of Cambridge, Cambridge, UK

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Abstract

With improvements in survival for good performance status patients and in specific molecular subtypes of glioblastoma, some patients will survive to develop significant neurocognitive dysfunction. This retrospective planning study quantified hippocampal radiation doses in patients with glioblastoma receiving radical chemo-radiotherapy and compared this with the radiation doses that showed clinical correlation with neurocognitive dysfunction, and evaluated the potential for clinically meaningful hippocampal dose reduction using helical TomoTherapy®.

Key words: Glioblastoma; hippocampal avoidance radiotherapy; neurocognitive dysfunction

Introduction

Neurocognitive dysfunction (NCD) is an emerging survivorship issue in glioblastoma, as there has been an improvement in prognosis [1] and this is particularly relevant in patients with specific molecular subtypes who are expected to live longer [2,3]. Neurocognitive function relates to multiple pathways in the brain [4], but the principal effects of radiotherapy are on short-term memory and fine motor control. Loss of short-term memory is an early delayed radiation effect [5] and manifests as early as 4 months after radiotherapy [6] and with further improvements in survival is a realistic possibility for glioblastoma patients, the actuarial risk of a patient developing NCD is significant. There is conflicting evidence for a radiation dose volume effect for NCD in adults [7–9]. There are few established hippocampal dose volume histogram (DVH)-based constraints for hippocampal avoidance radiotherapy [8,9], which can be achieved in some glioblastoma patients with hippocampal avoidance planning [10]. The purpose of this study was to evaluate hippocampal radiation doses in a cohort of glioblastoma patients and compare them with radiation doses that showed a clinical correlation with NCD outcomes [8,11], perform hippocampal volumetric analysis and determine whether clinically relevant hippocampal avoidance radiotherapy would be feasible in glioblastoma.

Materials and Methods

Radiotherapy plan details of 25 consecutive glioblastoma patients treated with helical intensity-modulated radiotherapy (Tomotherapy HI-ART®, Accuray, USA) between October 2011 and December 2013 were obtained from institutional data archives. No specific selection criteria were used and local radiotherapy review board permission was obtained. Patients were immobilised with a thermoplastic beam direction shell. Radiotherapy planning computed tomography (slice thickness 3 mm) and magnetic resonance imaging scans were co-registered. T1 sequences with gadolinium were used to delineate the gross tumour volume (GTV). Margins (25 mm and 15 mm) were added to the GTV for 54 Gy and 60 Gy clinical target volumes (CTV)

Author for correspondence: K. Thippu Jayaprakash, Department of Oncology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Box 193, Hills Road, Cambridge CB2 0QQ, UK. Tel: +44-7891989554.
E-mail address: kthippujayaprakash@doctors.org.uk (K. Thippu Jayaprakash).

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and a 5 mm margin was added to CTVs for planning target volumes (PTV). The lens, optic pathway, pituitary gland, brainstem and cochlea were outlined as organs at risk. A simultaneous integrated boost technique was used to deliver 60 Gy in 30 fractions, five fractions per week using daily image guidance with positional correction and temozolomide chemotherapy was administered as per protocol [1].

Hippocampal image segmentation was carried out and a margin (5 mm) for the planning risk volume was added according to the RTOG 0933 trial protocol [12] and was verified by a neuroradiologist. Composite hippocampal planning risk volumes (HC-PRV) were created by combining the right and left hippocampal planning risk volumes (Figure 1A, B). The original clinical treatment dosimetry plans were overlaid to obtain hippocampal radiation dose statistics. Four patients, each one representing a cerebral lobe and one representing the posterior cranial fossa, were planned for hippocampal avoidance. The PTV coverage was not compromised and organs at risk dose constraints were not modified. The hippocampal avoidance plans were optimised using the following DVH-based parameters [8,9] to ascertain the feasibility of hippocampal avoidance planning; hippocampal maximum dose 3 Gy and HC-PRV V20 Gy $<$ 20%, V7.3 Gy and V14.9 Gy $<$ 40 % (Figure 1C, D). A data analysis was carried out using SPSS (IBM, USA) and graphs were generated with GraphPad Prism.

Results

In total there were 24 evaluable patients, as in one patient both hippocampi were within the PTV. The mean time taken for hippocampal image segmentation was 14.5 min. Fourteen tumours were located in temporal lobes and eight were in frontal lobes. One tumour arose from the parietal lobe and one from the posterior cranial fossa. The mean HC-PRV maximum dose was 54.7 Gy, which was higher than the threshold dose of 12.6 Gy above which a detrimental effect on neurocognitive function was observed [11]. The mean minimum and mean HC-PRV doses were 24.15 and 38.62 Gy, respectively.

DVH analysis showed that HC-PRV-based parameters D10, D40, D50, D80 and D100 doses were above the threshold doses that showed a significant clinical correlation with NCD [8,11] for all patients (Figure 2).

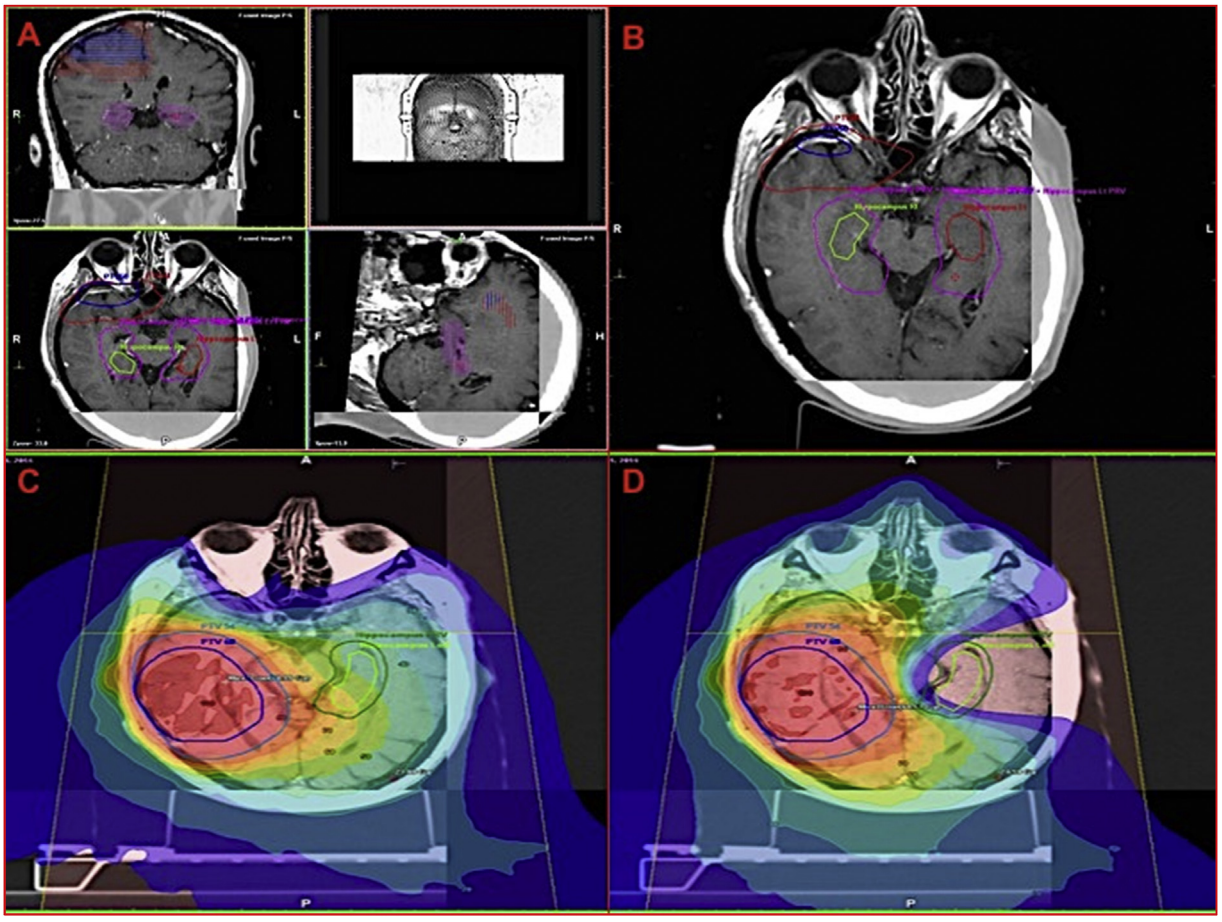

Fig 1. (A, B) Hippocampal contouring. Contour lines; pink, composite hippocampal planning risk volume (HC-PRV); red, left hippocampus; green, right hippocampus; blue and red, planning target volumes (PTV) 60 and 54. (C, D) Radiation doses shown in colour wash for original treatment plan (C) and hippocampal avoidance (D) for a right temporal tumour. Contour lines; light green, left hippocampus; dark green, HC-PRV; dark and light blue, PTV 60 and 54.

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