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Differential response of Diffuse Intrinsic Pontine Glioma cell lines to microbeam versus conventional radiotherapy

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Background: Diffuse Intrinsic Pontine Glioma (DIPG) is a devastating paediatric brainstem tumour with extremely poor prognosis and limited treatment options. Radiotherapy is the mainstay treatment but is limited to palliative use. Microbeam Radiotherapy (MRT) is a promising pre-clinical synchrotron radiotherapy modality which could improve the therapeutic ratio between normal tissue toxicity and tumour control through radiobiological mechanisms that are a radical departure from those of conventional radiotherapy (CRT).

Objectives: The aim of this study was to compare the cellular response of two human DIPG cell lines to MRT and conventional broad-beam radiotherapy and compute dose equivalence between the two modalities. We hypothesised that MRT would elicit a different cellular response to CRT, and that different DIPG cell lines would have different intrinsic radio-sensitivities.

Methods: Two human DIPG cell lines, SF7761 and JHH-1, were exposed to MRT (112 to 560 Gy) or CRT (2 to 8 Gy) in vitro to produce clonogenic cell-survival curves. Equivalent CRT doses were interpolated for each MRT dose. Apoptosis induction and cell-cycle response assays were performed five days after irradiation via flow cytometry to assess differences in cellular response between the cell lines and radiotherapy modalities at equivalent doses.

Results: The SF7761 cell line, which originated from a patient with no prior history of radiation treatment, was significantly more radiosensitive to both CRT and MRT compared to the JHH-1 cell line, which originated from a six year old male who had previously undergone combined chemotherapy and radiotherapy (Figure 1). JHH-1 formed polyploid cells and exhibited delayed G2/M arrest following both CRT and MRT. Furthermore, apoptosis and cell cycle assays demonstrated that at equivalent doses, MRT induced more unrepaired DNA damage that was detrimental to the cell-cycle and cell viability for both cell lines five days following irradiation.

Conclusion: This is the first study to compare the response of DIPG cell lines to MRT and CRT. Although MRT caused more DNA damage that was detrimental to the cell cycle compared to CRT, the JHH-1 cell demonstrated radio-resistance regardless of the radiation modality used. The findings of this study support the use of MRT as a potential alternative to CRT for patients with radiosensitive tumours and also contribute to our understanding of the differential response of cancer cells to MRT and CRT.

Keywords or phrases (comma separated)

Microbeam Radiotherapy, Brain tumour, Dose equivalence, Radiobiology

Are you a student?

Yes

Do you wish to take part in the Student Poster Slam?

Yes

Are you an ECR? (<5 yrs</br>since PhD/Masters)

No

What is your gender?

Male

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