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Gd-TPP-DOTA reduces cell viability in cancer cells via synchrotron radiotherapy

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High-Z elements have been proposed as radiosensitisers in X-ray photon radiotherapy due to their emission of multiple high-LET photo- and Auger electrons following X-ray irradiation. Gadolinium is a particularly attractive candidate radiosensitiser, since it can also be used as an MRI contrast agent. In this study, we report on the efficacy of Gd-triphenylphosphonium salt-DOTA (Gd(III)-TPP-DOTA) for synchrotron microbeam radiation therapy dose enhancement. The compound utilises the mitochondrial targeting moiety triphenylphosphonium (TPP) to accumulate Gd in the inner mitochondrial membrane.

Experiments were conducted using the dynamic mode option at hutch 2B of the Imaging and Medical Beamline at the Australian Synchrotron. Human glioblastoma multiforme cells (T98G cell line) were cultured to 80-90% confluence in T12.5 flasks. Approximately 24 hours prior to irradiation, the cultures were either treated with a 500 μM solution of Gd(III)DOTA-TPP or a vehicle control. Spatial dose distribution of synchrotron broad beam (BB) and single/multiple microbeams were measured using a micron-scale X-Tream dosimetry system and Gafchromic films in air and at 2 cm depth in solid water (same depth as the monolayer of cells in T12.5 flasks). A total of 96 flasks were irradiated, with doses of 0, 1, 2, 3, 4, 5, 10 and 16 Gy delivered in valley (MRT) or uniformly (BB). Post irradiation, each flask was re-seeded into 7 x 96 well-plates to perform the resazurin cell proliferation assay up to 7 days after irradiation.

Our preliminary analysis indicates that for cells irradiated by 3 Gy of BB or MRT radiation, the addition of Gd(III)DOTA-TPP results in a reduction in viable cell mass by 24.25% and 25.79%, respectively, compared with untreated flasks.

Level of Expertise

Experienced Researcher

Presenter Gender

Man

Pronouns

He/Him

Which facility did you use for your research

Australian Synchrotron

Students Only - Are you interested in AINSE student funding

No

Do you wish to take part in the Student Poster Slam

No

Condition of submission

Yes

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