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Optimizing Microbeam Radiation Therapy with High-Z Nano-structured Ceramic Particles

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Microbeam radiation therapy (MRT) implements spatially-fractionated kilovoltage x-rays for deep-seated tumour treatment [1,2] to provide better normal tissue sparing [3]. However, tumour treatment with MRT can be further optimized with high-Z nanoparticles (NPs), which have been shown to enhance the dose delivered by conventional radiotherapies [4]. Tantalum pentoxide (Ta2O5) NPs are novel nano-structured ceramic particles that are non-toxic [4] and show optimal x-ray absorption in kilovoltage energies [5,6]. This research assesses the ability of ceramic NPs, including Ta2O5 NPs, to selectively raise the tumour valley dose in MRT. This multi-modal approach is named: Synchrotron Microbeam Activated Radiation Therapy (SMART).

Geant4 [7,8] simulations investigated the physical dose enhancement of Ta2O5 NPs to a population of cells due to monoenergetic broad-beams and microbeams (50-200 keV).

Simulation results were correlated to in-vitro experiments obtained in hutch 1B and 2B at the Imaging and Medical Beamline (IMBL), Australian Synchrotron, using tumorous 9L gliosarcoma and normal Madin Darby Canine Kidney cells. NPs were added to cells in T12.5cm2 flasks 24hrs before 90-100% confluence. Cells were irradiated using a 1.4T or 3T wiggler field to produce 50μm/400μm or 50μm/200μm microbeams with weighted average energies of 42 keV and 95 keV respectively. Cell survival following treatment was evaluated with clonogenic assays after 15 doubling times.

Ta2O5 NPs improved the MRT and broad-beam selectivity towards tumour cells, due to the NPs clustering about the nucleus of 9L tumour cells. Other ceramic NPs such as bismuth oxide, with more homogeneous NP distributions, also saw improvement to the MRT treatment efficiency.

Simulations confirmed that NP clusters produced the most selective dose enhancement to MRT. Modelling micro- and broad-beams showed that NP dose enhancement is energy dependent. For Ta2O5 NPs, 40 keV x-rays are optimum for dose enhancement in broad-beam cases, and microbeam energies greater than 100 keV produce better NP dose enhancement with more secondary electrons that raise the valley dose (>100 μm from the microbeam).

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Microbeam Radiation Therapy, Nanoparticles, Dose Enhancement, Radiobiology, Monte Carlo

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Primary author(s) : Prof. LERCH, Michael (University of Wollongong)

Co-author(s) : Prof. ROSENFELD, Anatoly (Centre for Medical Radiation Physics, University of Wollongong); Mr DIPUGLIA, Andrew (University of Wollongong); Dr STEVENSON, Andrew (Australian Synchrotron/CSIRO); Ms ENGELS, Elette (University of Wollongong); Dr DAVIS, Jeremy (University of Wollongong); Mr CAMERON, Matthew (CMRP University of Wollongong); Dr TEHEI, Moeava (University of Wollongong); Dr LI, Nan (University of Wollongong); Ms ROBERTS, Natalia (University of Wollongong); Ms MCKINNON, Sally (University of Wollongong); Dr OKTARIA, Sianne (University of Wollongong); Dr CORDE-TEHEI, Stephanie (Prince of Wales Hospital, UOW); Dr GUATELLI, Susanna (University of Wollongong)

Presenter(s) : Prof. LERCH, Michael (University of Wollongong)

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