UNDERSTANDING RADIO-ENHANCEMENT WITH GADOLINIUM NANOPARTICLES FOR THERANOSTIC USE ON THE AUSTRALIAN MRI-LINAC

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Introduction: Within the context of personalised medicine, nanoparticles (NPs) are being developed as theranostic agents, incorporating both diagnostic imaging and therapeutic capabilities in the one package. This combination offers the possibility of new treatment paradigms, in particular real time image-guided targeted treatment delivery.

Gadolinium (Gd)-based nanoparticles are a promising new nano-theranostic. Gd gives excellent diagnostic contrast on MR images, and its high atomic number can be exploited to produce an enhancement of radiation dose delivery.

Gold nanoparticles have been comprehensively studied for their x-ray radiation dose enhancement properties, but Gd is less well characterised. In addition, questions remain around the mechanisms of sensitisation observed experimentally with high-energy, megavoltage photon irradiation.

Gd-based NPs are ideally suited for use on an integrated MRI-Linac system, such as that currently under development at the Ingham Institute in Sydney and our preliminary study is the first "proof of concept" study for such use. Enhanced MR image contrast enables monitoring of NP uptake location and time dependent changes in concentration. Radiotherapy delivery can thus be coordinated in real-time to achieve optimal targeting of dose and maximal enhancement by nanoparticle radiosensitisation.

Materials and methods: Our study uses simulations in GATE and Geant4 to investigate the physical mechanisms of NP dose enhancement. A range of kilovoltage beam energies were used to quantify the macroscopic dose enhancement for a sample of nanoparticles in solution compared to water. Three megavoltage beams were also simulated and dose enhancement measured – a standard clinical 6MV beam, a flattening-filter-free clinical beam, and the beam at the Australian MRI-Linac.

Further simulations explore the nano-scale pattern of dose enhancement around single and clustered nanoparticles.

Two Gd-based NPs with different nano-scale structure are investigated: AGuIX [1,2], manufactured in France and available commercially for preclinical use; a Gd NP developed in the School of Chemistry at the University of Sydney [3].

Results: Figure 1 shows the dose enhancement factors (DEF, ratio of dose in nanoparticle solution to that in pure water) obtained for clinical kilovoltage polychromatic beams.

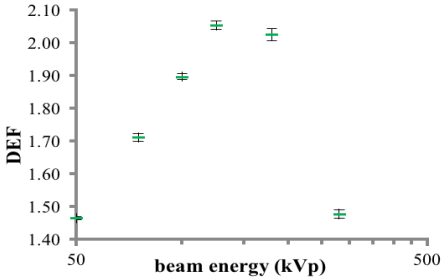

Figure 1: Simulated dose enhancement factors wth Gd NPs for a range of x-ray beam energies

Of the MV beams, the MRI-linac beam has a lower peak and average photon energy than either clinical beam, and showed the greatest DEF at ~1.3.
Experimental measurement of the dose enhancement will be run for comparison with these simulations, results not shown here.

Conclusions: Substantial physical dose enhancement with Gd NPs is predicted at the MRI-Linac and simulations show this can be attributed to the lower energy components of the beam.

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