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Rethinking Dose Point Kernels for Radionuclides in Cancer Treatment

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The advent of Radio-Pharmaceutical Therapy (RPT) marks an impactful advancement in radiation oncology, offering the potential to treat tumours with cellular precision while minimising adverse effects. Evaluating the efficacy of this treatment relies on accurate dosimetry, which is traditionally informed by absorbed dose, but absorbed dose alone overlooks the spatial complexity of radiation-induced damage and is likely an incomplete predictor of cell damage. Linear Energy Transfer (LET), which quantifies microscopic particle track structure, has been correlated with higher rates of complex and lethal DNA damage [1,2]. Therefore, this work moved to improve RPT treatment planning by generating a library of LET point kernels alongside standard dose point kernels.

A custom application was developed using the Geant4 particle simulation toolkit [3,4] to model monoenergetic alpha particles and electrons in a water phantom. Dose and LET point kernels were generated for energies from 2.5 keV to 10 MeV. The dose point kernels demonstrate that absorbed dose is deposited locally, within 0.02 times the particle's CSDA range. The corresponding LET point kernels show highest LET regions located significantly further, with LET peaking at 0.4-1.2 times each particle's CSDA range. For alpha particles, this is expressed as a characteristic high-LET Bragg peak at the end of the particle's track, illustrating a high incidence of DNA damage far from the maximum dose region.

These findings highlight that conventional dose-based planning may largely underestimate biologically significant cell damage. Instead, LET point kernels could be used generate 3D LET distributions alongside clinical dose maps, paving the way for more and biologically driven RPT treatment planning.

[1] Wang et al. Int. J. Radiat. Oncol. Bio. Phys. 107(3), (2020).
[2] Guerra Liberal et al. Sci. Rep. 13(1), (2023).
[3] Agostinelli et al. NIMA 506(3), (2003).
[4] Allison et al. NIMA 835, (2016).

Author: LENGERER, Ella (Swinburne University of Technology)

Co-authors: BROWN, Jeremy (Swinburne University of Technology); RUSSELL, Sarah (Peter MacCallum Cancer Centre)

Presenter: LENGERER, Ella (Swinburne University of Technology)

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