In-silico calculations of DNA damage induced by DaRT for a better understanding of the radiobiological effectiveness of this treatment

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Background: Diffusing alpha-emitters radiation therapy (DaRT) is an interstitial brachytherapy technique using radium-224 seeds. Clinical trials are ongoing for treatment sites including skin and oral cavity cancer. A better understanding of the radiobiological effectiveness of the alpha particles emitted in the radium-224 decay chain is required to improve clinical outcomes for this treatment.

The aim of this work is to investigate the complexity of the direct and indirect DNA damage in the context of DaRT. DNA damage was studied by changing the base pair density, the impact of which is not well studied.

Material and Methods: Geant4-DNA [1-4] was used to simulate a simplified chromatin fibre structure repeated in a grid arrangement. The target volume and chromatin fibre spacing were varied to change the base pair density within the typical range of human cells. Alpha particles were simulated in the energy range of DaRT.

Direct strand breaks were scored using the linear damage model, with a minimum threshold of 5 eV and a maximum of 37.5 eV [5]. Indirect damage was simulated using the IRT model, with a damage probability of 40.5%. To reduce simulation time DNA molecules are only included in the chemical simulation within 9 nm of radiolysis sites. Clustering was carried out using the DBSCAN algorithm [6].

Preliminary Results: The number of strand breaks and double strand breaks per event per path length both increase approximately linearly with increasing base pair density. The cluster size of double strand breaks increases approximately linearly at lower densities and becomes constant above approximately 0.04 bp/nm^3.

The highest base pair density simulations require approximately three times as long to simulate as the lowest. However, approximately five times the number of total strand breaks are recorded, allowing for the potential to speed up simulation time by increasing the base pair density.

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