On the simulation of neutron-induced indirect DNA damage using TOPAS-nBio to estimate neutron relative biological effectiveness

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Introduction

- Photoneutrons of varying energies are liberated during high-energy photon EBRT.
- Photoneutrons contribute to the whole-body radiation dose and pose a carcinogenic risk.
- Recent work has shown that DNA strand breaks (SBs) due to indirect action occur up to three times more often than SBs due to direct action(1).

Objectives

- **Develop and validate a pipeline to simulate and score indirect action** in a DNA model.
- Use this pipeline to **quantify the risk of neutron-induced mutagenesis related to indirect action** by estimating neutron RBE as a function of energy.

Methods

- TOPAS framework and the low-energy TOPAS-nBio extension were used to simulate physical and chemical interactions.
- DNA model from a parallel study on neutron-induced direct clustered DNA damage(2) was used.
- **[Step 1] Code implementation** of indirect action.
- **[Step 2] Benchmarking of the model** with published results by comparing SB yields of monoenergetic protons (similar simulation parameters but different DNA models).
- **[Step 3] Estimation of neutron RBE** by comparing indirect SB yields of monoenergetic neutrons (1eV to 10 MeV) and 250 keV reference X-rays.

DNA Model

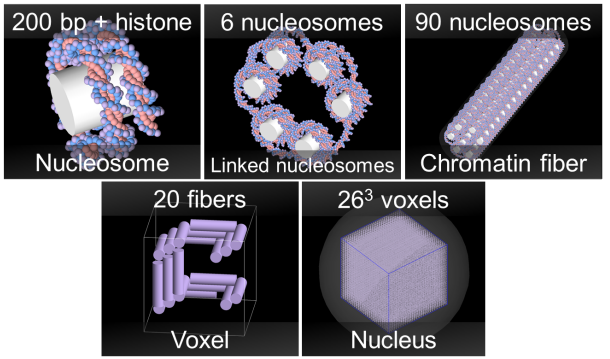

Fig 1. Components of the DNA model(2) with 6.33 Gbp.

Results – [Step 1]

- Implemented features in our code for indirect action simulations:
  - Only interactions between OH· and DNA backbone volumes were considered to lead to SBs with a 40% probability, as used by Zhu *et al.*(1).
  - Molecules were not allowed to be generated inside DNA and histone volumes.
  - Histones are scavengers of OH·, e^-_{aq}, and H· species.
- Other features:
  - Parameters related to indirect action can be easily modified by the user via the TOPAS parameter file.
  - Compatible with scoring direct action, including recording hybrid damage.

Results – [Step 2]

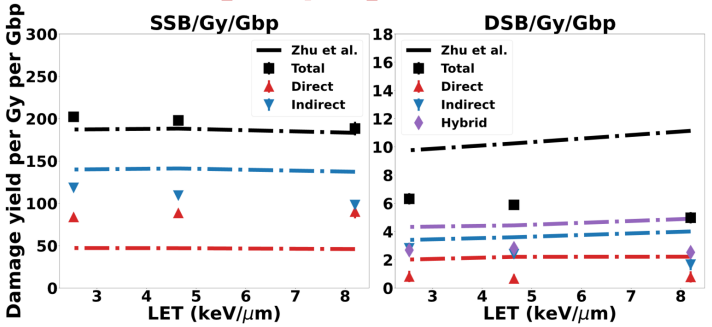

Fig 2. Comparison of damage yields by monoenergetic protons in our work (markers) versus published data(1) (broken lines).

Discussion

- SSB and DSB yields are on the expected order of magnitude.
- Discrepancies are consistent with what we expect from differences in DNA models.
- **[Step 3]** We are currently running simulations to expose our DNA model to monoenergetic neutrons and 250 keV X-rays to compare clustered DNA damage yields.

Conclusions & Ongoing Work

- A validated implementation of indirect action has been developed.
- It is currently being used to collect necessary data to produce neutron RBE curves for indirect action that can be compared with our existing RBE curves for direct action.

Acknowledgements

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References

1) *Zhu H. et al.* 2020 Cellular response to proton irradiation: a simulation study with TOPAS-nBio
2) *Montgomery L. et al.* 2021 Modeling the carcinogenic effects of neutron radiation by simulating clustered DNA damage using TOPAS-nBio (YIS talk)