

Towards the estimation of neutron RBE for mutagenesis by simulating clustered DNA damage

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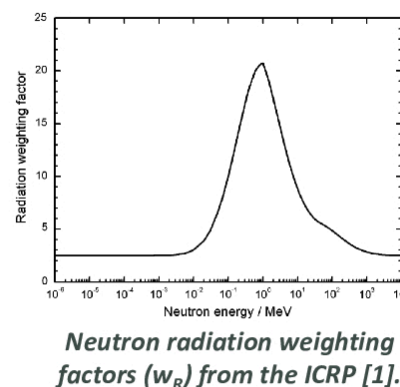
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INTRODUCTION

- Secondary neutrons pose a carcinogenic risk to radiotherapy patients.
- Carcinogenic risk varies with neutron energy, as evidenced by the neutron radiation weighting factors (w_R).
- w_R , based on RBE data, are used in radiation protection but are unsuited for risk estimates.
- Need a better metric to assess risk!

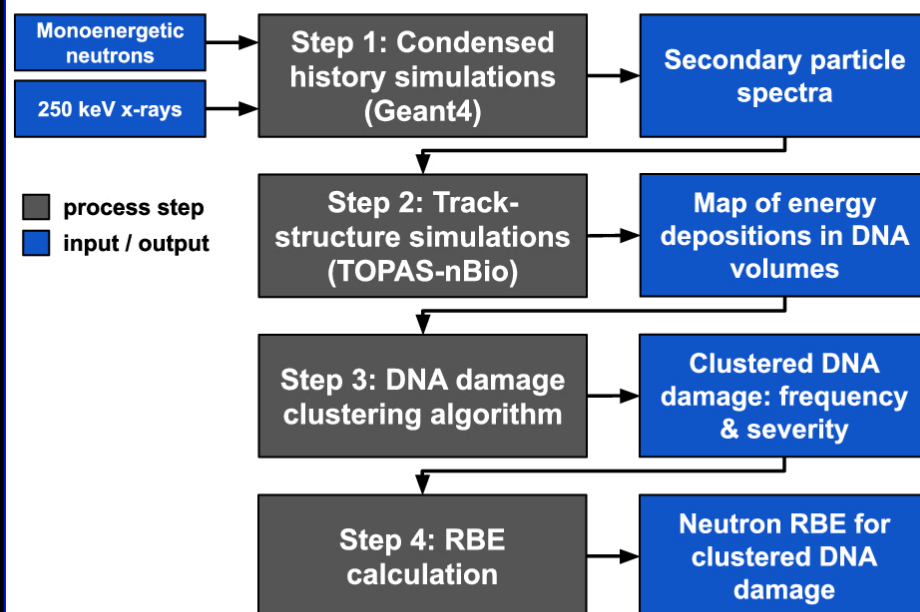


OBJECTIVE

- Estimate neutron RBE for mutagenesis, one possible cause of carcinogenesis, by simulating clustered DNA damage in a geometric model of nuclear DNA

METHODOLOGY – OVERVIEW

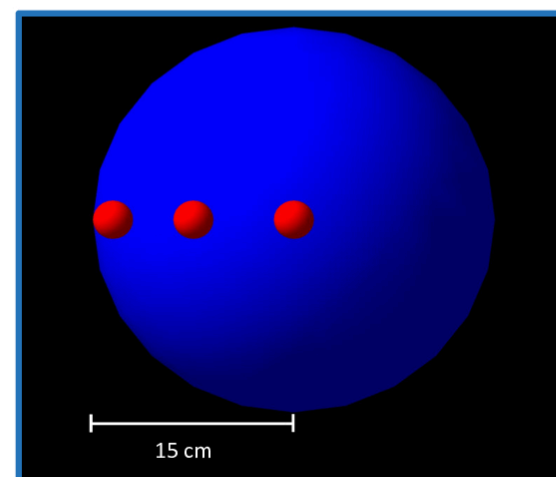
- The simulation and analysis pipeline of this project can be broken into four steps, which are detailed in the accompanying panels.



Schematic of the Monte Carlo simulation and analysis pipeline used to determine neutron RBE for clustered DNA damage.

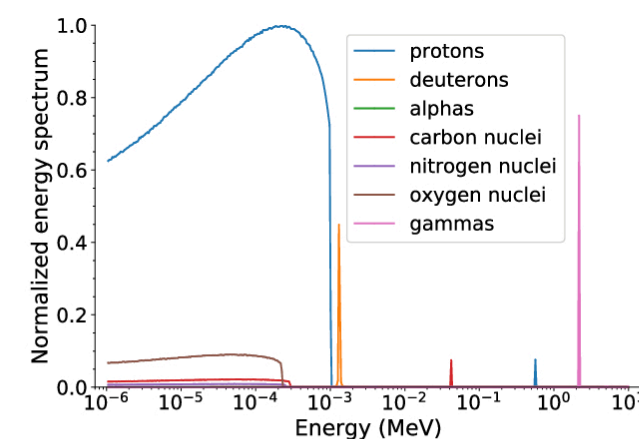
STEP 1: CONDENSED HISTORY SIMULATIONS

- Following the method of Lund et al. (2020) [2]:
- A model of the ICRU-4 tissue phantom [2] was created using the Geant4 Monte Carlo toolkit [3].



ICRU-4 tissue phantom containing 3 scoring volumes [2].

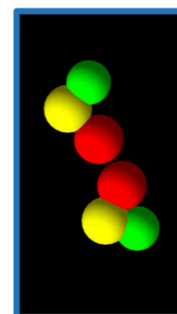
- The phantom was irradiated with monoenergetic neutrons and 250 keV reference photons.
- The energy spectra of secondary particles were recorded in 3 scoring volumes of increasing depth.



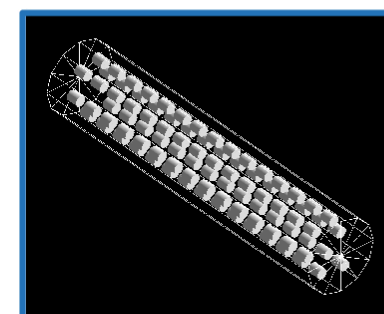
Example secondary particle spectra obtained for 1 keV neutrons in the outermost scoring volume

STEP 2: TRACK-STRUCTURE SIMULATIONS

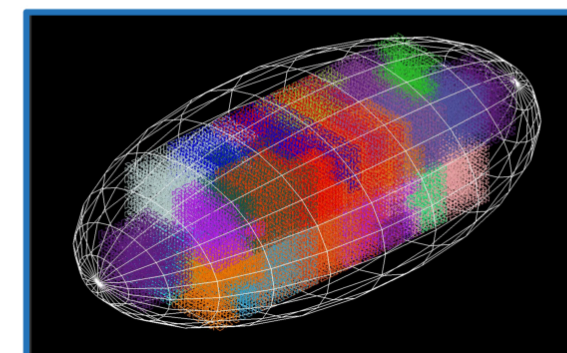
- Using the open-source model of whole-nuclear DNA developed by McNamara et al. (2018) [4]:
- Individual elements of DNA base pairs (i.e. nitrogenous bases and deoxyribose sugar-phosphate backbone) are modelled as spheres.
- Chromatin strands of the DNA double helix are arranged in a fractal pattern to fill an ellipsoidal nucleus.



DNA base pair.



Chromatin fibre containing 20,000 base pairs.

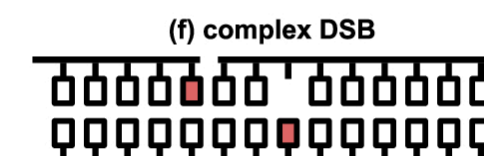
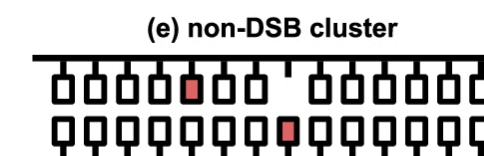
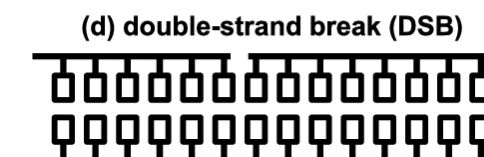
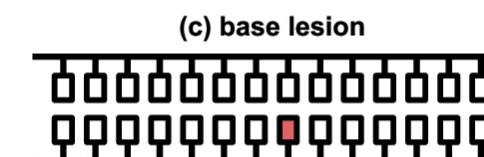
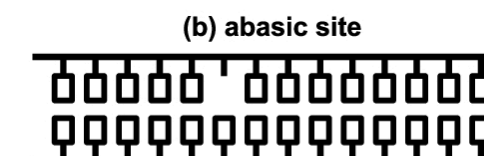
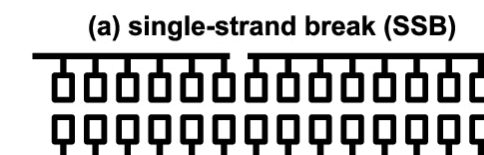


Nucleus containing over 300,000 fibres and 6 billion base pairs. Reproduced from McNamara et al. [4].

- Particle tracks were stochastically sampled from the energy spectra obtained in Step 1.
- The particle tracks were imposed on the nuclear DNA model using TOPAS-nBio [5].
- Energy deposits in the DNA volumes were accumulated on a track-by-track basis and recorded.
- Maps of energy deposits were imported into the clustering algorithm in Step 3.

STEP 3: DNA DAMAGE CLUSTERING ALGORITHM

- Simple (i.e. single-site) DNA damage is recorded according to adjustable energy-thresholds.
 - e.g. 17.5 eV to induce a single-strand break.
- Simple DNA damage is clustered according to adjustable distance-thresholds.
 - e.g. double-strand break = single-strand breaks on opposing strands within 10 base pairs.



Types of DNA damage. (a-c): examples of simple damage, (d-f): examples of clustered damage.

STEP 4: RBE CALCULATION

- Yields of clustered DNA damage are scaled by the complexity of the damage (i.e. # of lesions per cluster).
 - Y_N = neutron-induced clustered DNA damage yield
 - Y_X = photon-induced clustered DNA damage yield
- $RBE = \frac{Y_N}{Y_X}$
- Plot RBE as a function of neutron energy.

RESULTS / CONCLUSIONS

- Aim to report neutron RBE for clustered DNA damage and compare with the neutron weighting factors & published neutron RBE from literature.
- All our data & code will be made open source.
 - Data will be made compatible with Standard DNA Damage format [6].

REFERENCES

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- [6] Schuermann et al. A New Standard DNA Damage (SDD) Data Format. 2019.

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