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Geant4-DNA simulation of human cancer cells irradiated with helium ion beams

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Motivation

- Tumor treatment with helium ion beams may represent an ioniz attractive trade-off between use of proton or carbon beams
- The "molecularDNA" example to simulate radiation-induced damage released June 2022 in the Geant4 11.1 BETA version



Cancers **2021**, 13, 4940

• Human cell geometry simulated in "molecularDNA", fractal-based DNA chain, straight/turned chromatin

ionization

- Create geometries of HTB177 & MCF7 cancer cells
- Simulate He⁴ irradiation to validate "molecularDNA"

K. Chatzipapas, M. Dordevic et. al

radiation

solated damage



HTB177 and MCF7 cell dimensions from morphometric analysis



lung carcinoma

- HTB177 (magn. x100): a large irregularly shaped and also ellipsoid cells nuclei
- Cell geometries modeled as ellipsoid, axes determined using ImageJ software:

$a = 8.550 \ \mu m$ $b = 2.500 \ \mu m$ $c = 6.425 \ \mu m$ (larger)

Rasband, W.S., **ImageJ**, U. S. National Institutes of Health, Bethesda, Maryland, USA, https://imagej.nih.gov/ij/, 1997-2018





breast adenocarcinoma

- MCF7 (magn. x100): big oval nuclei and with large amount of cytoplasm
- Cell geometries modeled as ellipsoid, axes determined using **ImageJ** software:

a = 7.005 μm b = 2.500 μm c = 5.300 μm (smaller)

a = 7.100 μ m b = 2.500 μ m c = 7.100 μ m ("human cell" in molecular DNA)



molecular DNA simulation of He⁴ irradiation of HTB177 & MCF7

- Creating the new cell geometries to keep N_{bp}~ 6.4Gbp
- Adjusting density w/ larger/smaller voxels or #histons
- HTB177: 77nm(38)
- MCF7: 64nm(38)





Targeting the following LET range (more in the slide 8):

LET (experimental): 4.9 +/- 0.1, 10.7 +/- 0.3, 24.7 +/- 0.4 & 39.1 +/- 1.1 keV/ μm

- MC simulation run for the following energy/LET values:
 - LET: [4, 13, 22, 31, 40 keV/µm] <=> [261, 60, 32, 21, 15 MeV] (in the exp. range)

(LET to energy correspondence from fitting ICRU Report 90 values)



molecularDNA simulation results: SSB vs LET distribution





molecularDNA simulation results: DSB vs LET distribution





molecularDNA simulation: SSB/DSB (ratio) vs LET distribution





molecularDNA simulation + experimental data: DSB vs LET

- Good agreement with the experimental data for both cell lines; scale and slope match
 - \circ the simulation is overshooting the data at high LET range but within uncertainties



HTB177



• DSB yields calculated with 10kbp distant

(These experimental results are obtained from the private communication with the authors A. Ristic, I. Petrovic et. al)



- The "molecularDNA", released in June 2022 as a Geant4-DNA extended example, was able to provide modeling of cell geometries with different sizes, and give predictions of the quantitative DNA damage following the irradiation with the He⁴ particle beams
- Further investigation of the MC simulation parameters to follow: a higher number of LET/energy points (currently only 5) with higher statistics (currently 100 events / LET)

• Also validation of the cell survival vs dose and cell repair following the He⁴ irradiation

BACKUP SLIDES



DNA solenoid geometries: 75 nm and different histone densities





molecularDNA simulation: SSB/DSB/ratio vs LET distribution





