Philipps Universität Marburg

THM TECHNISCHE HOCHSCHULE MITTELHESSEN

A MONTE CARLO BASED INVESTIGATION OF THE FLASH EFFECT BY EXAMINING INTER-TRACK INTERACTIONS IN RADIOBIOLOGICAL SIMULATIONS PERFORMED WITH TOPAS-NBIO

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FLASH radiotherapy

- Application of very high radiation doses in very short pulses
- FLASH dose rates ≥ 40 Gy/s
- Conventional Dosisraten: ≤ 0,03 Gy/s
- FLASH effect: reduced normal tissue toxicity while tumor control remains the same
- Reasons for the FLASH effect not yet fully identified
- Possible reasons:
  - Depletion of oxygen and inter-track interactions of radicals
  - Amount and complexity of DNA damages
  - Immune response

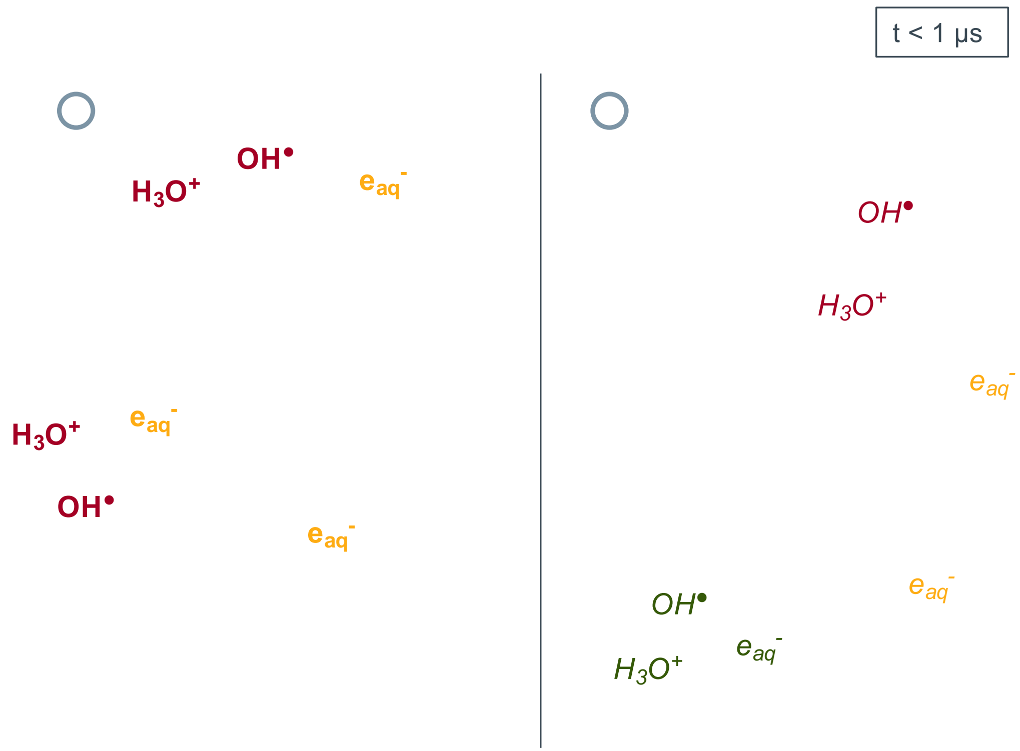
Research focus

- Investigation of effects of inter-track interactions on radical yields in radiobiological simulations (electron sources)
- Classification of DNA damages on a cell nucleus model in dependence of inter-track interactions (proton sources)

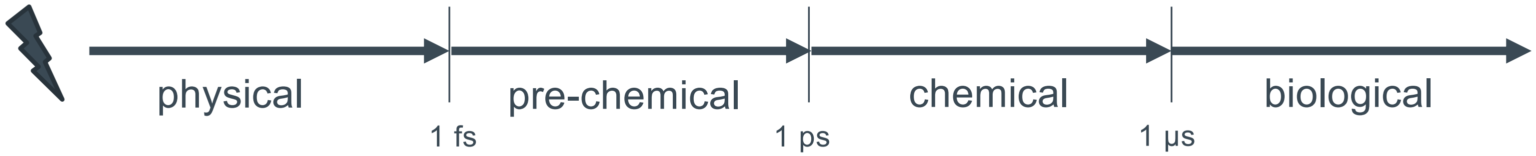
Generation of inter-track interactions in TOPAS-nBio

- Default simulations
  - Particle tracks of a primary particle, i.e. an event, are simulated <u>one after the other</u>
  - Inter-track interactions are not possible

- Simulations with inter-track interactions
  - Declaration of different primary particles as one event
  - Particle tracks are simulated <u>simultaneously</u> (use of the phase space file scorer)
  - Inter-track interactions are possible



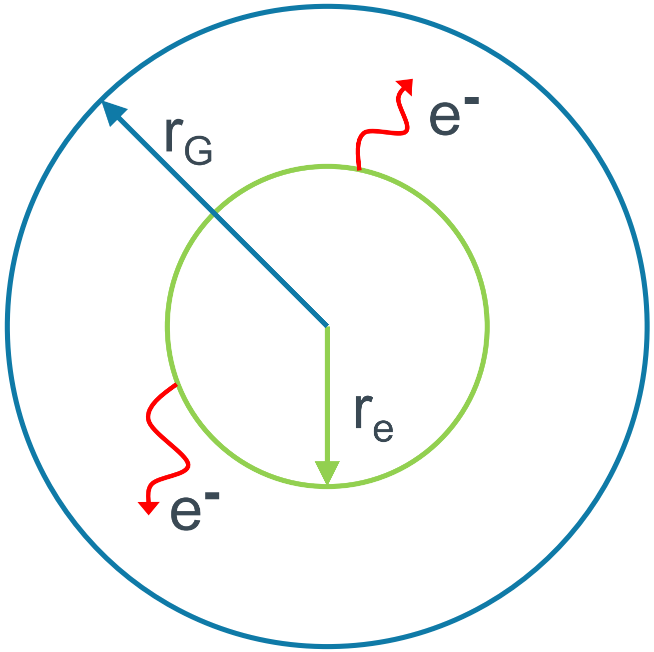
Radiobiological simulations in TOPAS-nBio



- Physical: Simulation of inelastic processes (ionization, (vib.) excitations, dissociative electron attachment) and elastic processes up to a residual kinetic energy of a few eV
- Pre-chemical: Production of radicals on the basis of inelastic processes
- Chemical: Diffusion and reaction of the chemical particles via Brownian motion
- Biological: Simulation of DNA repair kinetics

Radical yield of electron sources: simulation setup

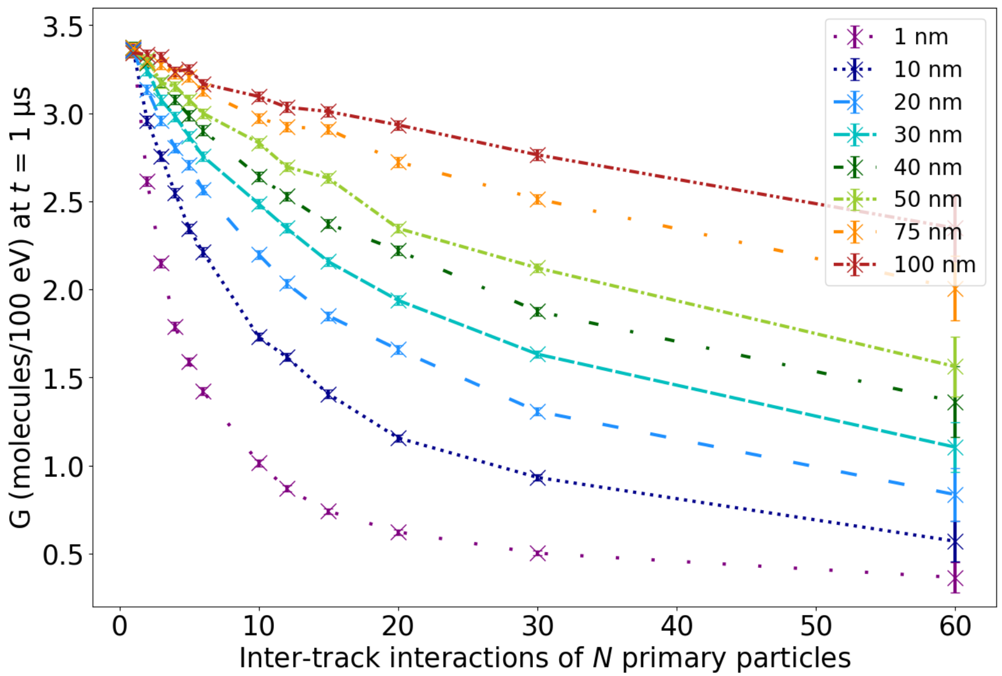
- Electrons with 60eV
  60 primary particles (100 randomseeds)
  r_e = 1-100 nm
- Inter-track interaction of *N* primary particles
  N = 2, 3, 4, 5, 6, 10, 12, 15, 20, 30, 60
- ROI radical yield: r_G = 1 µm
- End of the chemical stage: 1 µs



Simulation setup of the electron source

Radical yield of electron sources: results

Dependence of the spatial arrangement of primary particles using the example of hydroxyl (OH•)



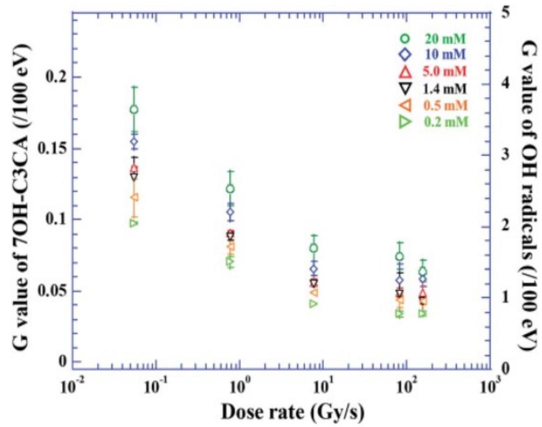


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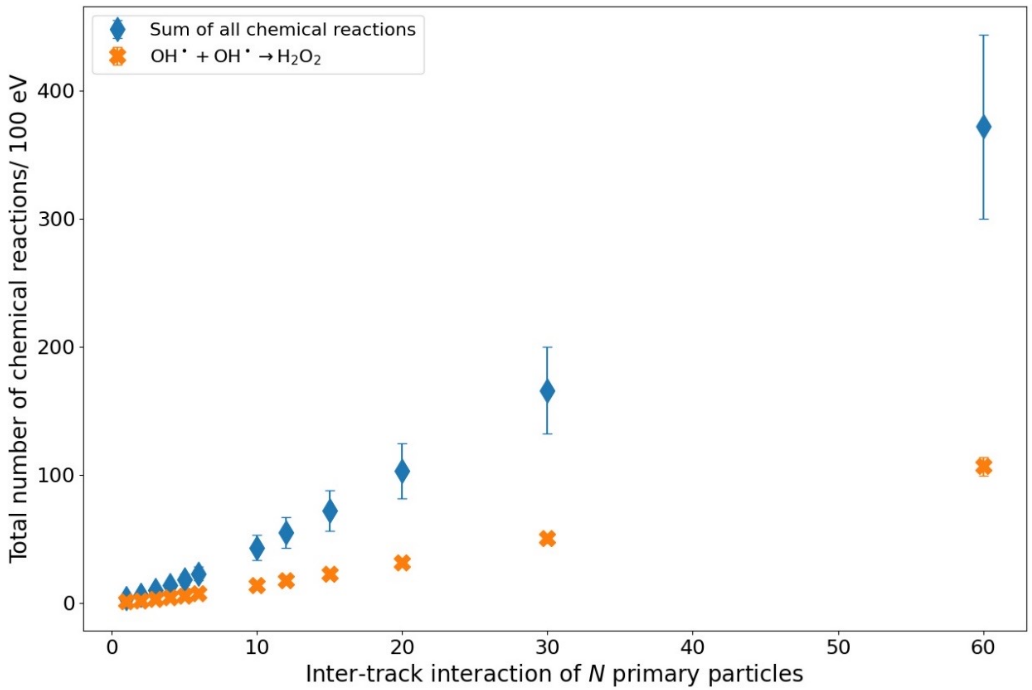
Fig. 2 *G* value of 7OH–C3CA (left axis) and that of hydroxyl radicals (right axis) as a function of dose rates. The trends of *G* values are represented at each molar concentration of C3CA solution; 20 mM: circles, 10 mM: diamonds, 5.0 mM: upward triangles, 1.4 mM: downward triangles, 0.5 mM: leftward triangles, 0.2 mM: rightward triangles.

Kusumoto, T. *et al.* (2020). Significant changes in yields of 7-hydroxy-coumarin-3-carboxylic acid produced under FLASH radiotherapy conditions. *RSC advances*, *10*(63), 38709-38714.

Radical yield of electron sources: results

Total number of reactions occurring up to the end of the chemical phase t = 1 µs as a function of *N* (for r = 1 nm).

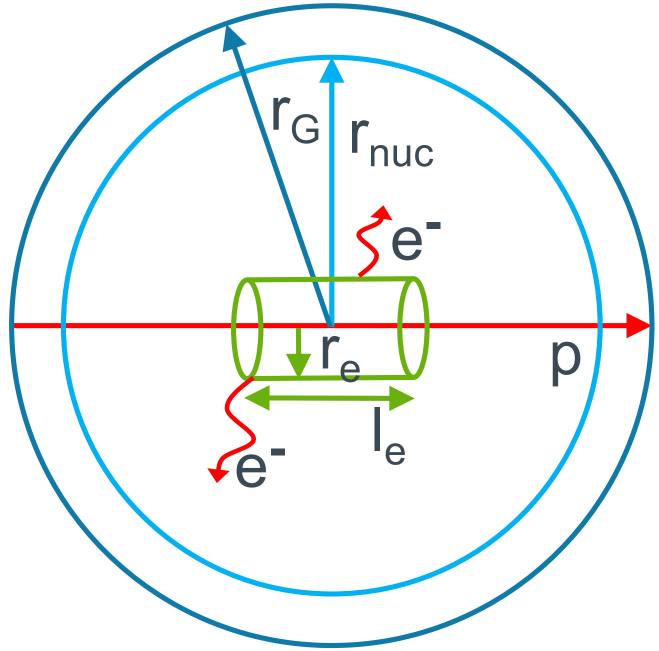


- Increasing number of reactions with *N* due to higher density of chemical molecules
- Many inter-track interactions
- Reason for the changes in G-value

DNA damage using proton sources: simulation setup

- Protons with 10/100MeV
  100 primary particles
  r_e = 1 nm, l_e = 1 µm
- N = 2, 4, 5, 10, 20, 25, 50, 100
- ROI radical yield: r_G = 5 µm
- Nucleus model: Bases, backbones, histones structered as fibers (r_{nuc} = 4,65 µm, 6,08 Gbp)

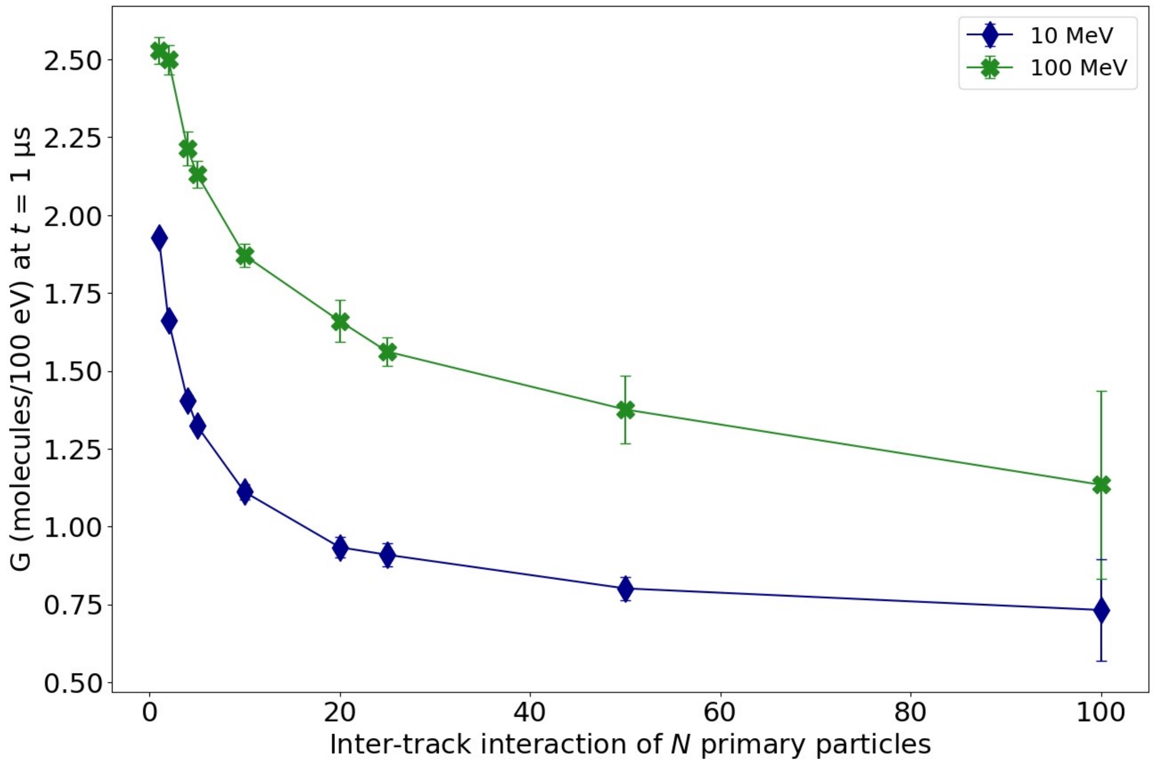
  Zhu, Hongyu, et al. "Cellular response to proton irradiation: a simulation study with TOPAS-nBio." *Radiation research* 194.1 (2020): 9-21
- End of the chemical stage: 1 µs



Simulation setup proton sources

DNA damage using proton sources: results

Comparison of the G value of hydroxyl as a function of N for 10/100 MeV protons

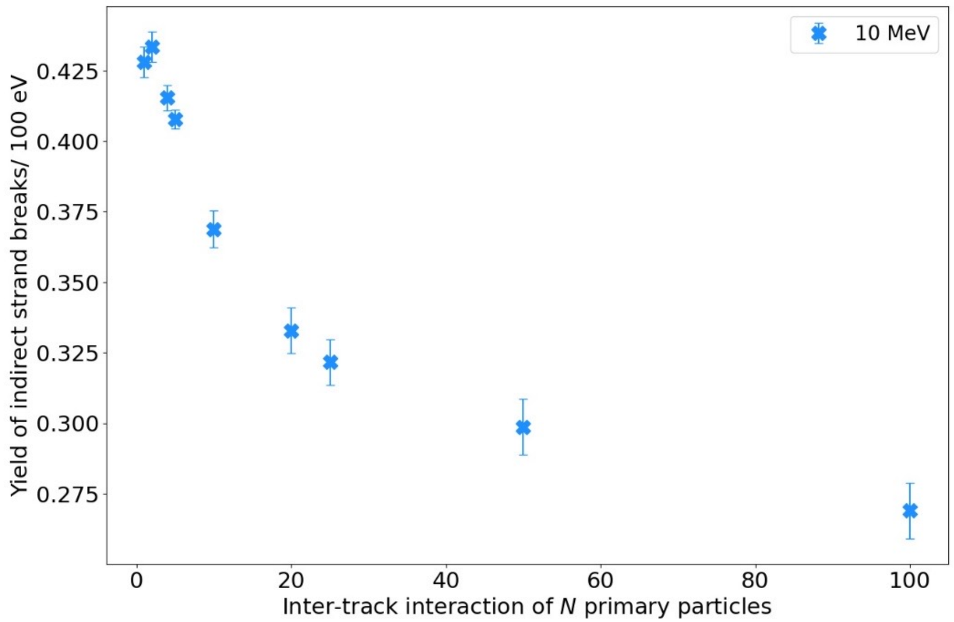


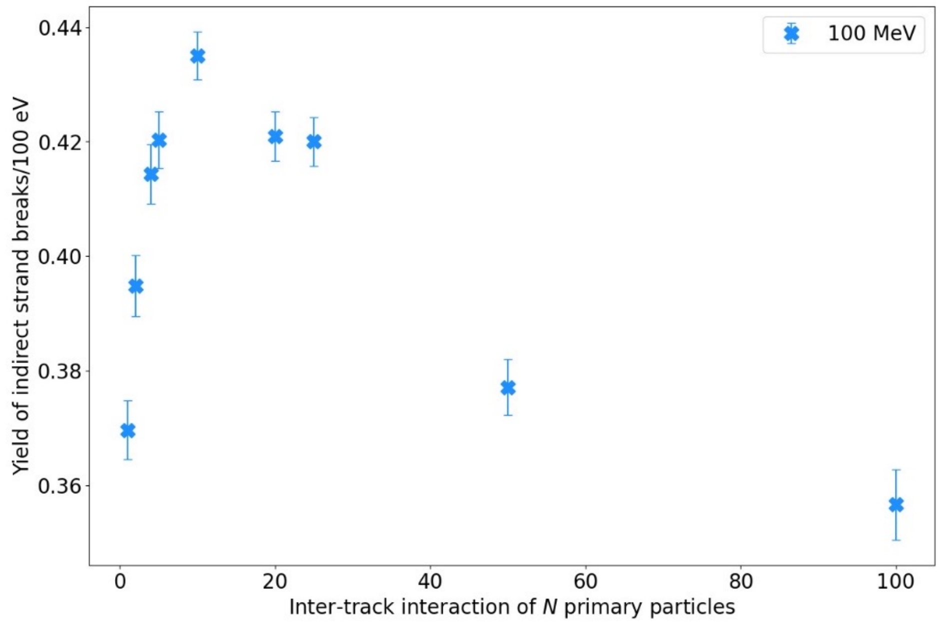
LET 10 MeV:	8,13 keV/µm
LET 100 MeV:	1,30 keV/µm

DNA damage using proton sources: results

Comparison of DNA damage as a function of N for 10/100 MeV protons

- Indirect DNA damages: by radicals produced through radiolysis (mainly OH•)
  → can be influenced by inter-track interactions





Conclusion

- Investigation of effects of inter-track interactions on radical yield in radiobiological simulations (electron sources)
  - G-value of $OH^{\bullet}$ decreases with increasing number of inter-track interactions
  - Decrease of the G-value depends on the source geometry

- Classification of DNA damages on a cell nucleus model in dependence of inter-track interactions (proton sources)
  - Variations of indirect DNA damages with inter-track interactions
  - Variations are more evident for the high LET proton source

Thank you for your attention!