Bachelor Thesis 2016

Radiosensitization using gold nanoparticles

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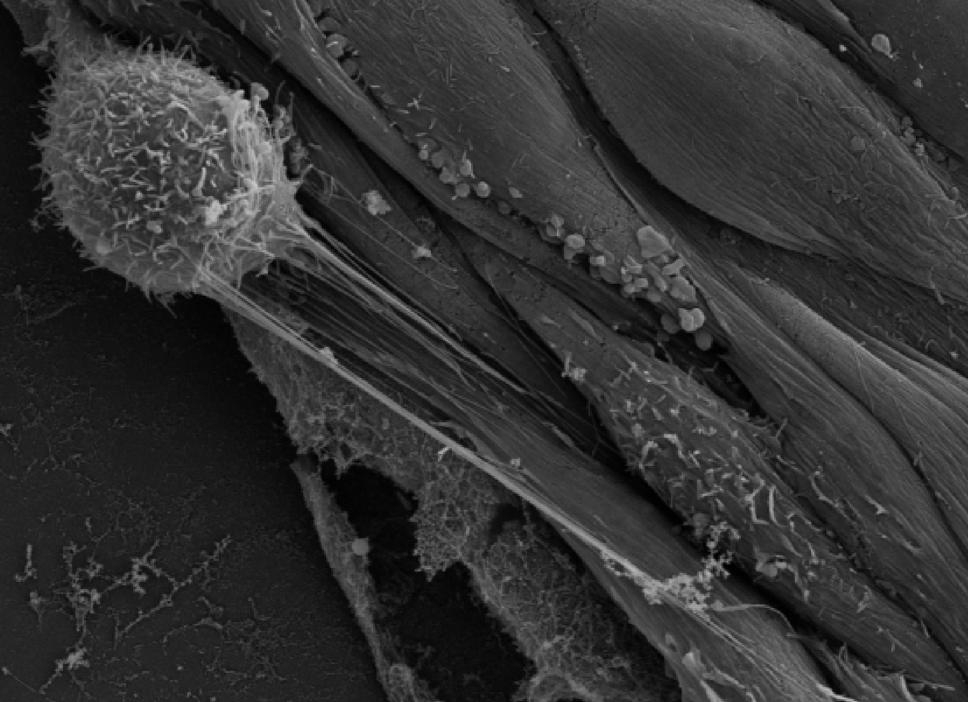
Supervisors: Bert De Roo
Mattias Vervaele
Professor: Jean-Pierre Locquet

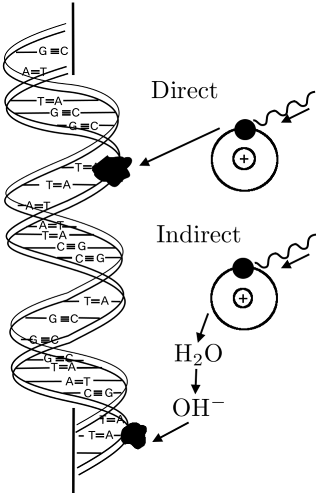


Source: Y. Connor et all. *Nature Communications* 2015,***6***

DNA damage using ionizing radiation

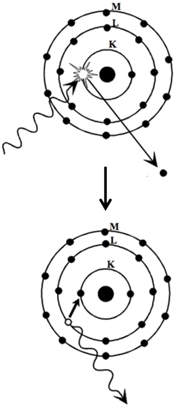
- Chemotherapy
- Surgery
- **Radiation therapy**

  Energy $\sim$ MeV

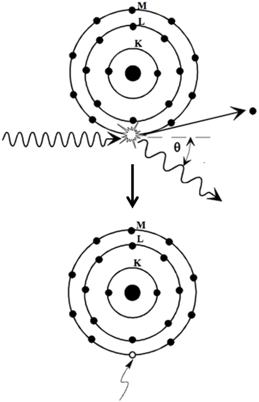


Radiosensitization of cancer cells with gold nanoparticles (GNP) E ∼ keV

Photoelectric absorption



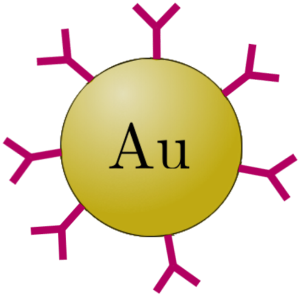
Compton effect



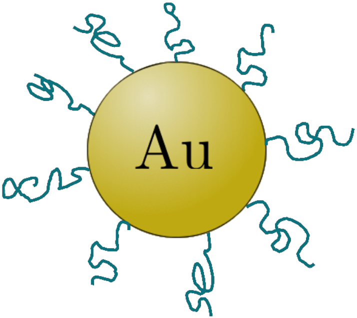
Source: `https://en.wikibooks.org/wiki/Basic_Physics_of_Digital_Radiography/The_Patient`

Targeting of the GNP to the tumor

Active targeting
Antibodies



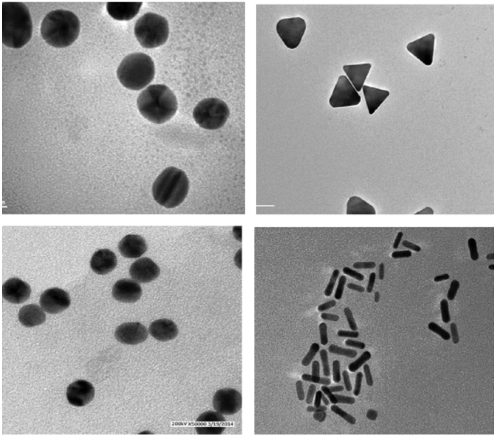
Passive targeting
PEG coating



Overview Project

Radiosensitization of DNA using gold nanoparticles

1. Synthesis
2. Characterization
    a. TEM
    b. UV-Vis
    c. DLS
3. Radiosensitization



Source: A. Chaudhary et all. *Phys. Chem. Chem. Phys., 2014* ***16***

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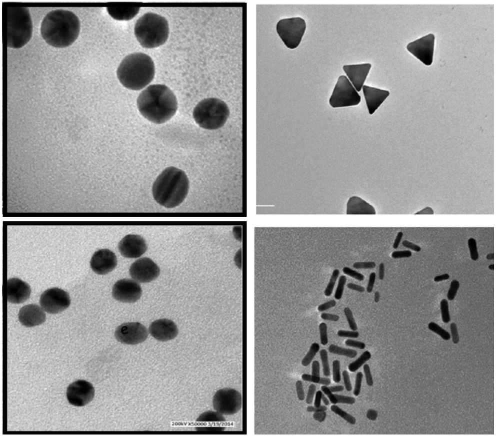

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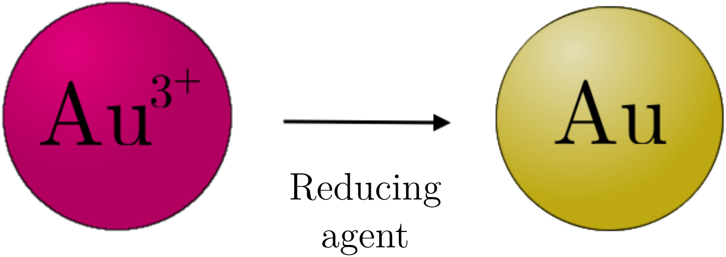
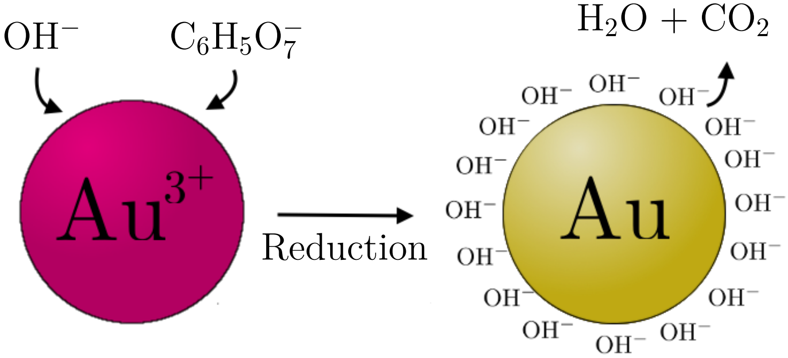
Reduction of gold ions to form GNP



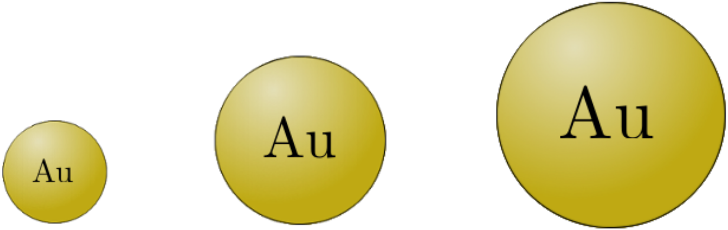
Gold ions: $HAuCl_4$ solution
Reducing agent: $Na_3C_6H_5O_7$

Reduction of gold ions to form GNP



$$6Au^{3+} + C_6H_5O_7^{3-} + 15OH^- \rightarrow Au + 6CO_2 + 10H_2O$$

The amount of citrate controls the size



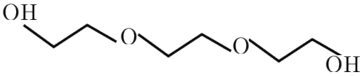
15 nm 30 nm 45 nm

2.5ml 1.24 ml 0.8 ml

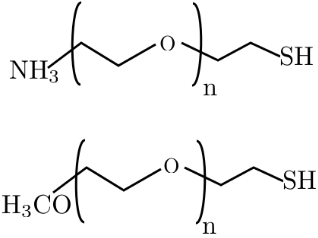
Citrate 1%

100ml $HAuCl_4$ 0.01%

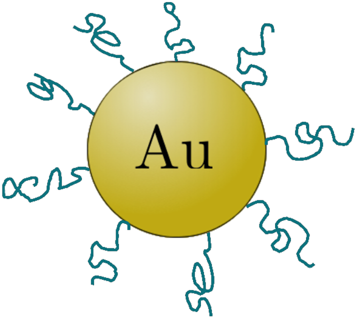
PEG for targeting and stabilization



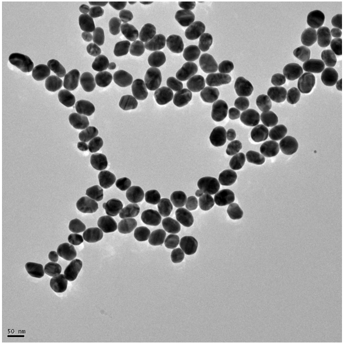
Polyethylene glycol

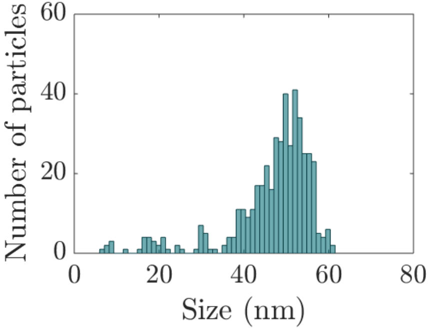


1k, 5k, 10k, 20k



TEM image analysis to determine the core diameter





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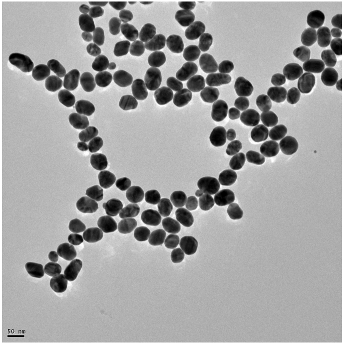
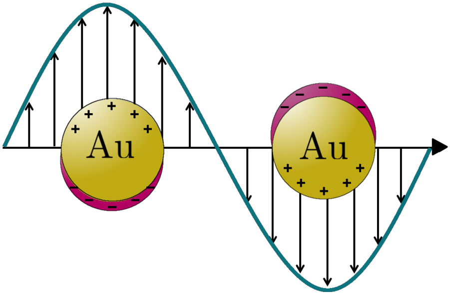
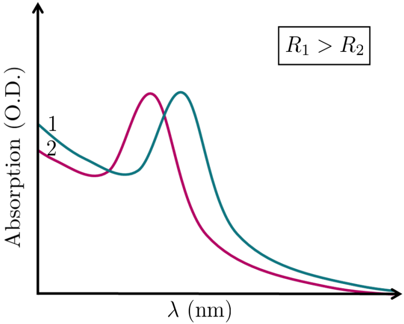


Exp. Size (nm)	Size (nm)
15	12.98 ± 0.23
	2.99 ± 0.16
30	18.29 ± 0.23
45	46.75 ± 0.47

Absorption measurements (UV-Vis) to determine the relative size





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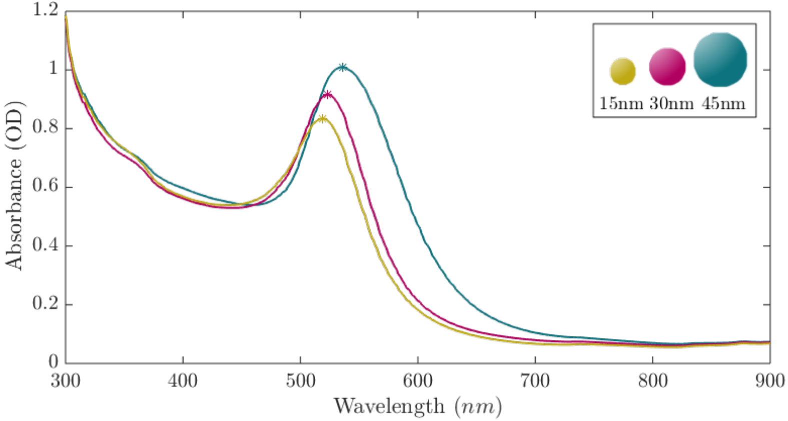
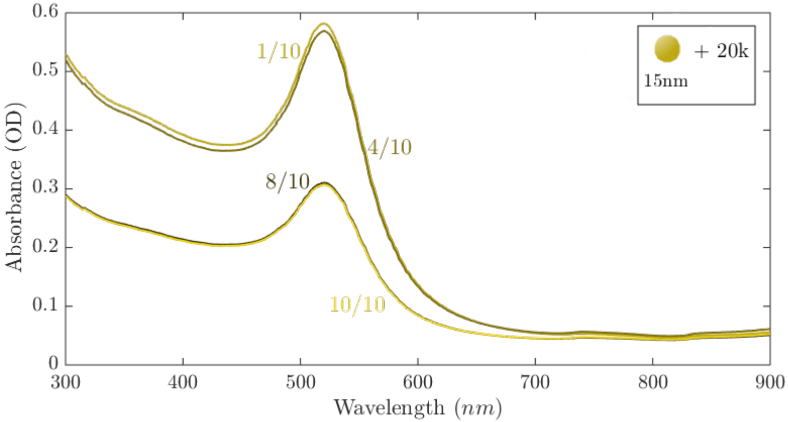


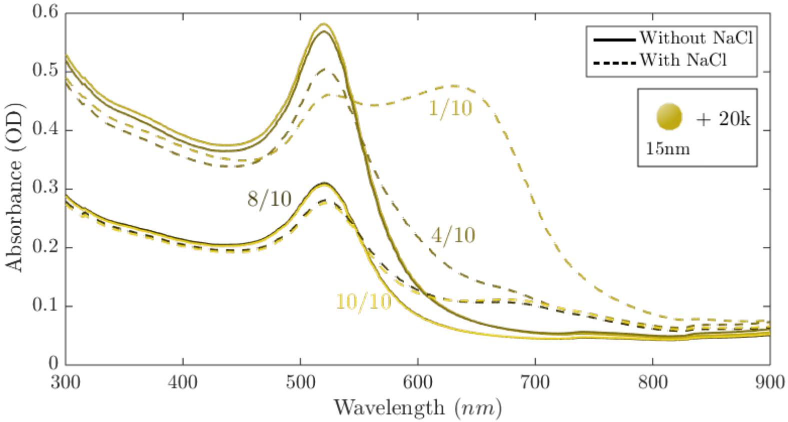
Find optimal PEG/GNP proportion

1. Add PEG and preform UV-Vis measurement

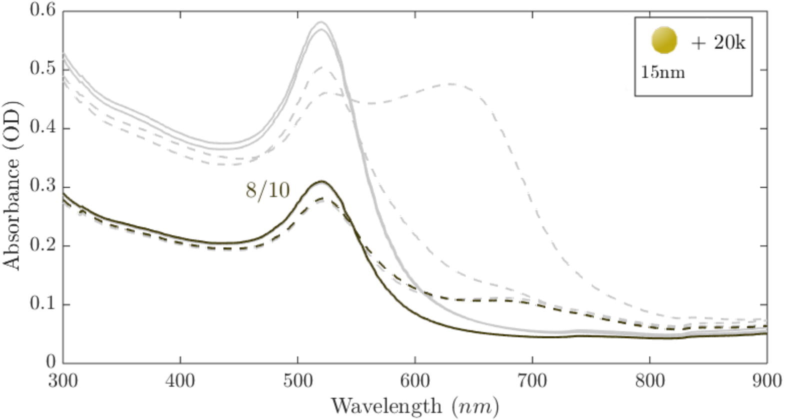


Find optimal PEG/GNP proportion

2. Add NaCl and preform UV-Vis measurement

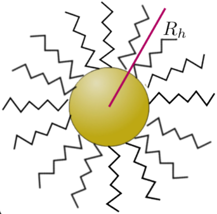


Find optimal PEG/GNP proportion



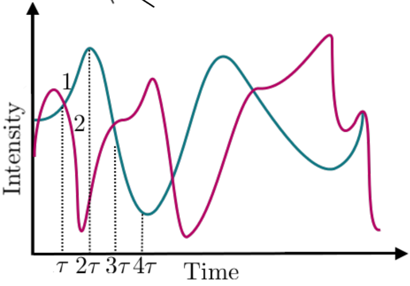
Light scattering experiments to determine the hydrodynamic radius (R_h)

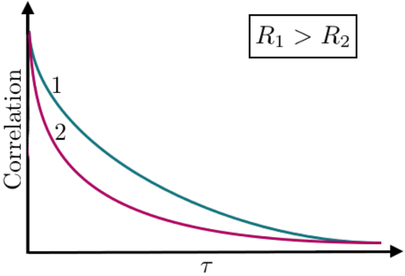
Important for diffusive properties



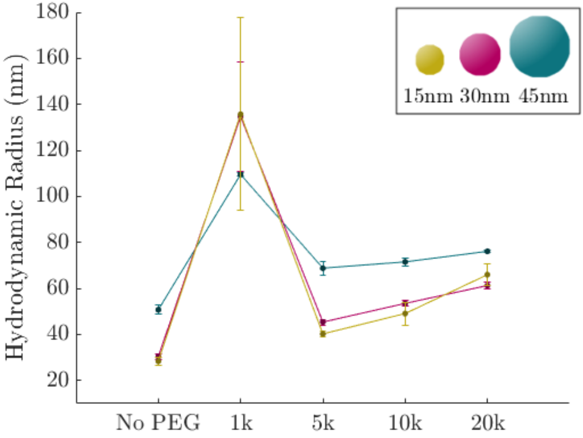
Correlation:

$$g(\tau) = \frac{\langle I(t)\rangle\langle I(t+\tau)\rangle}{\langle I(t)\rangle^2}$$

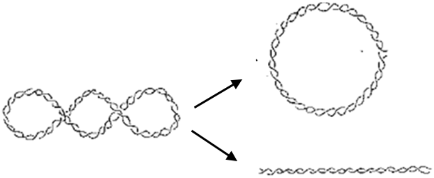




Hydrodynamic radii for the three different GNP with different functionalizations

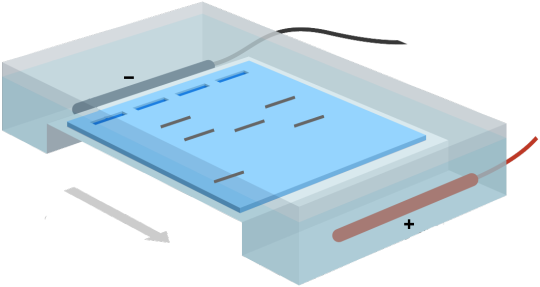


Gel electrophoresis to analyse DNA damage



Single strand break

Double strand break



Sources: https://www.quora.com/Whats-the-difference-between-a-plasmid-and-a-virus.
http://www.vce.bioninja.com.au/aos-3-heredity/molecular-biology-technique/dna-profiling.html

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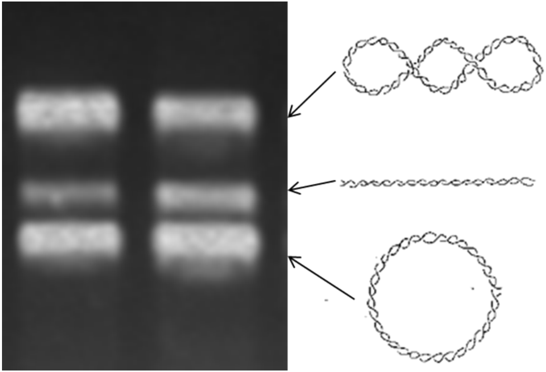
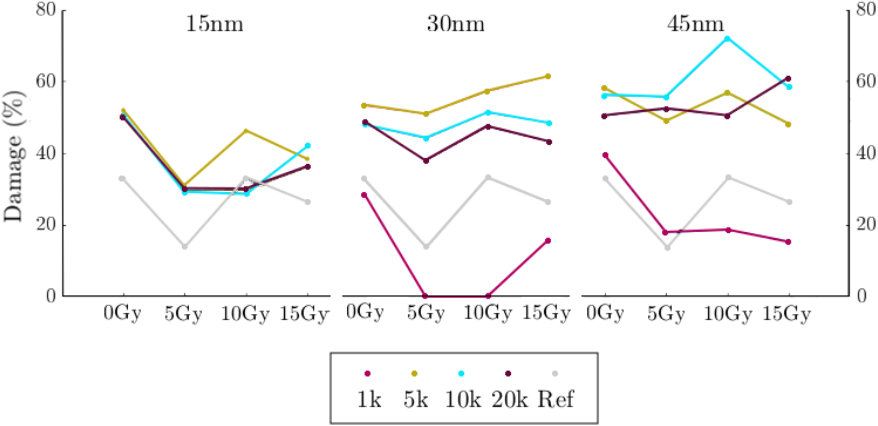


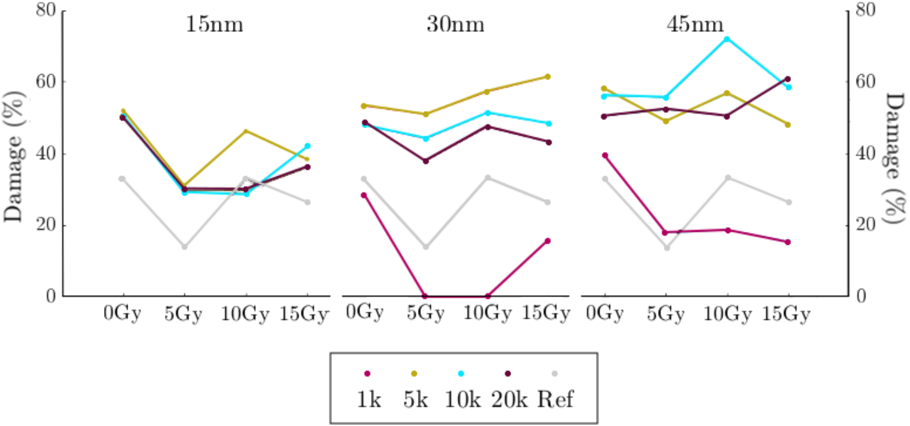
Source: Maunus R et al. Horton JR, Zhang X. Nucleic Acids Research, 34(3):939-948, 2006.

DNA damage analysis



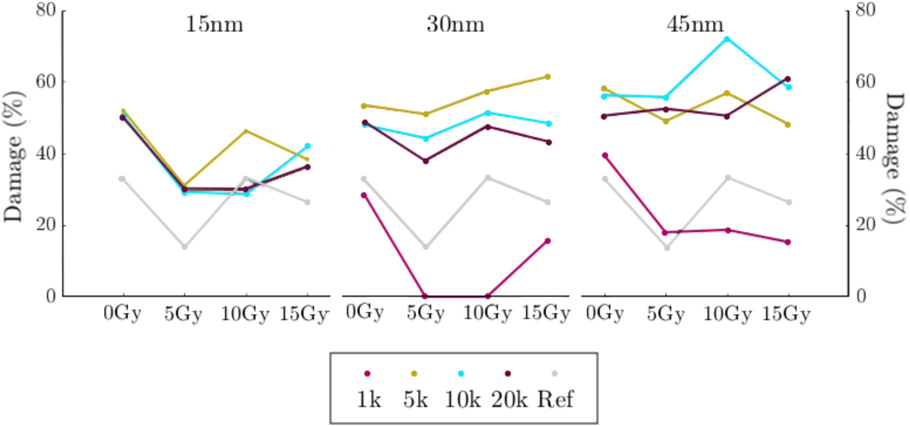
DNA damage analysis

Strange results for 1 k PEG



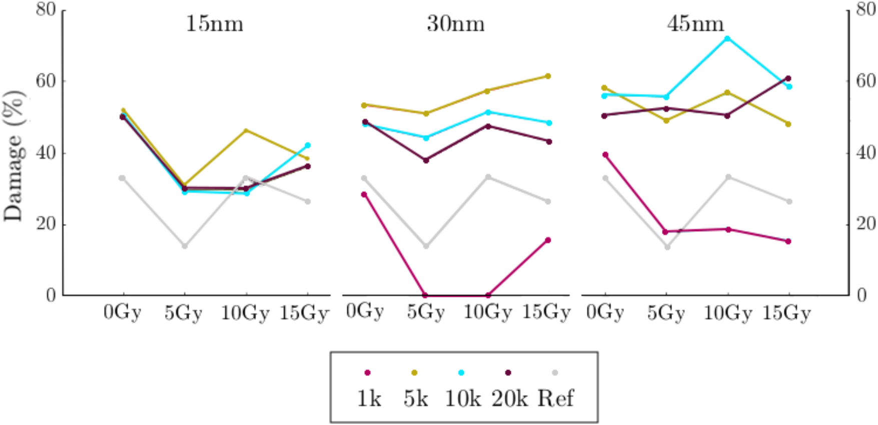
DNA damage analysis

Curves are not rising



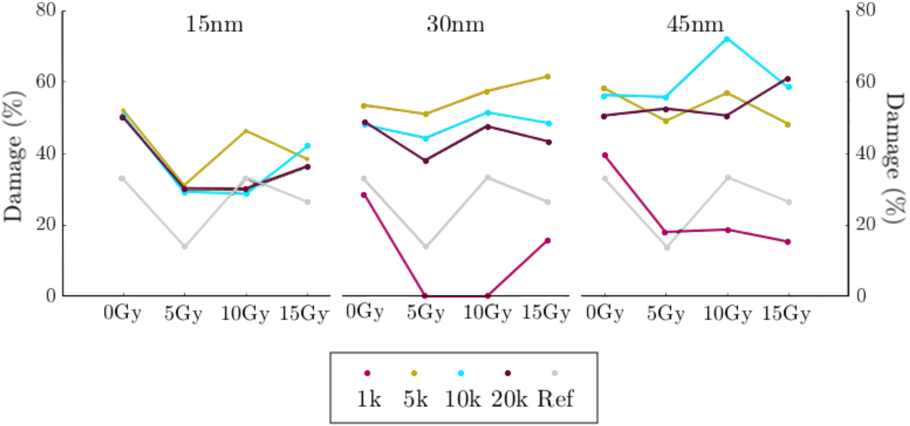
DNA damage analysis

Reference sample has an unexpected form



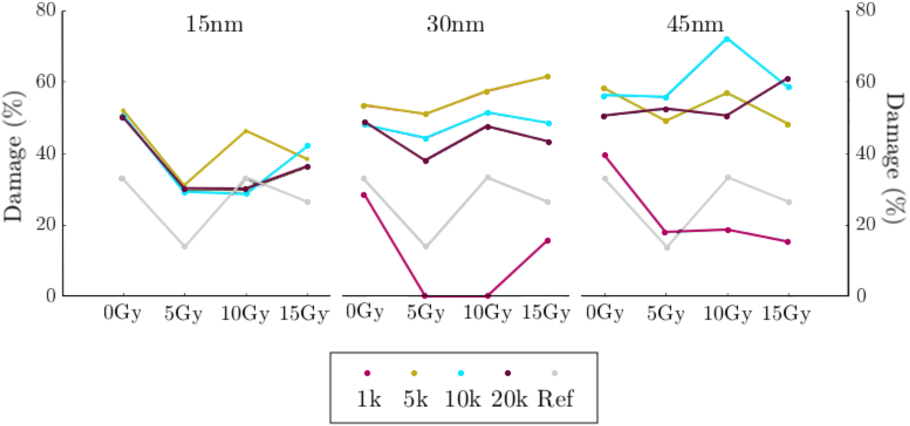
DNA damage analysis

DNA damage at 0 Gy



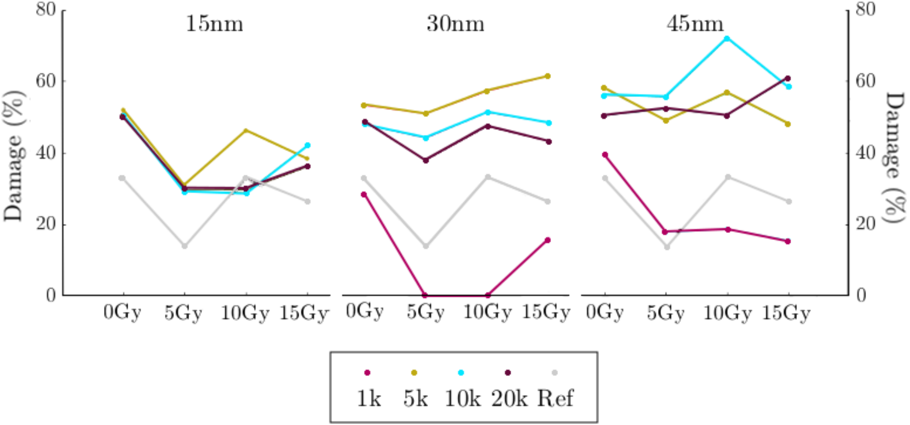
DNA damage analysis

Radiosensitization effect is present



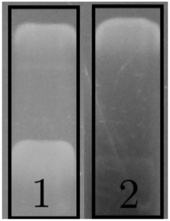
DNA damage analysis

Smaller PEG → more DNA damage
Larger GNP → more DNA damage



Conclusion DNA damage analysis

- Strange results for 1 k PEG
- Curves are not rising (except 30 nm GNP)
- Reference sample has strange form
- DNA damage at 0 Gy



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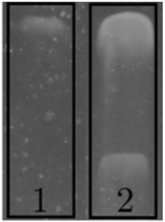

Conclusion

- Radiosensitization effect was observed
- Best results with...

  ...5k functionalization

  ...largest particles (45 nm)