



Ultra-high dose rate irradiation induces senescence and cell cycle arrest of B16 cells

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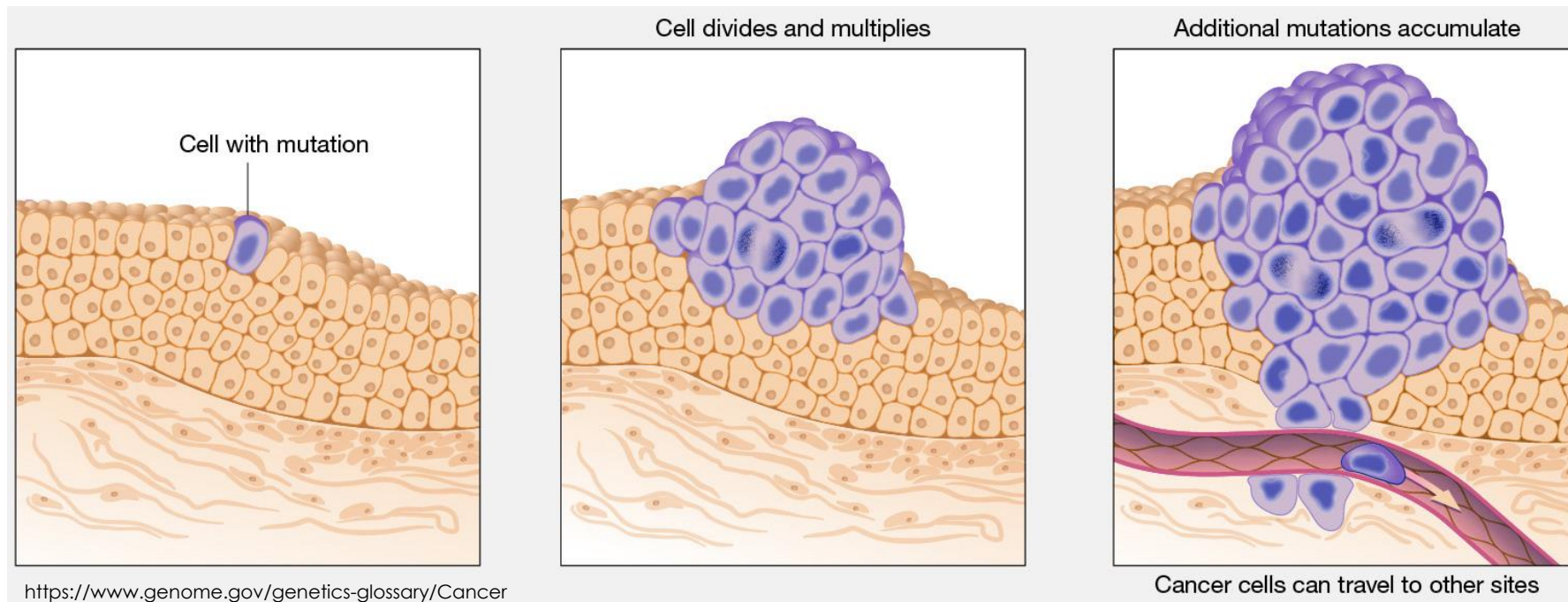
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Outlines

1. Motivation
2. IFIN-HH set-ups
3. Results
4. Conclusion and perspectives

- leading cause of death worldwide, accounting nearly one in six deaths in 2020.
- the most common cancers: breast, lung, colon-rectal and prostate cancers.
- many cancers can be cured if detected early and treated effectively.

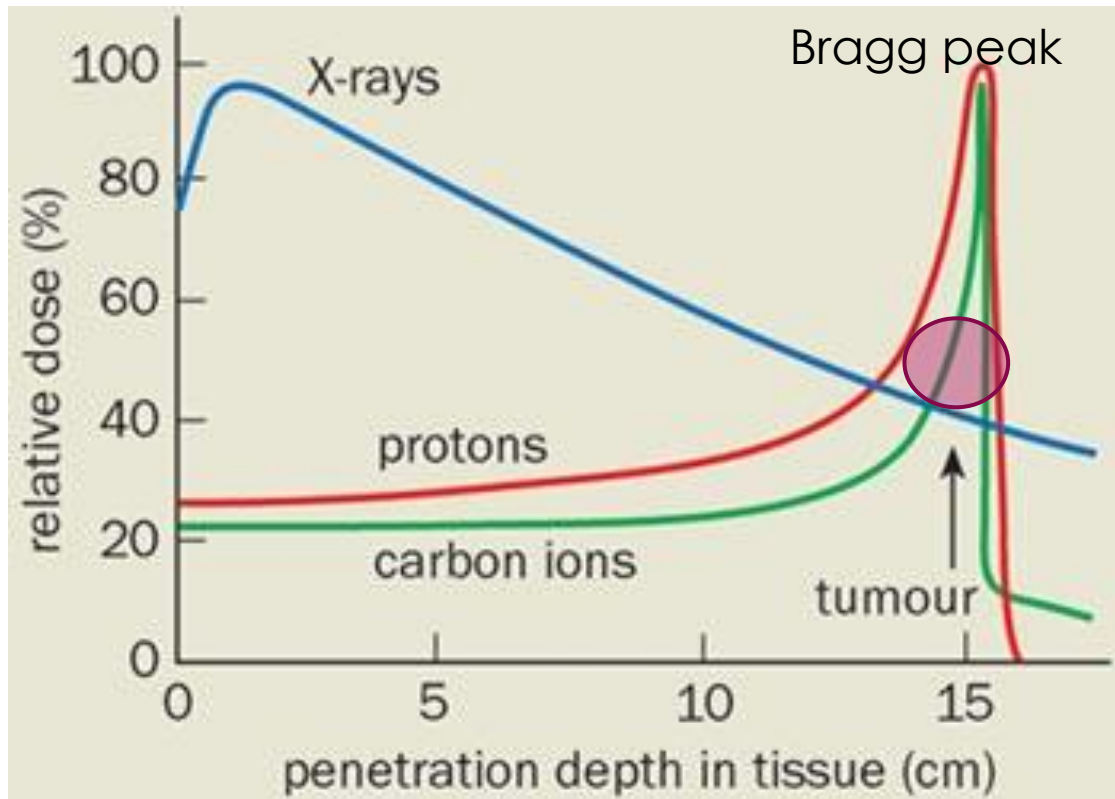




Radiation therapy

Radiotherapy dream:

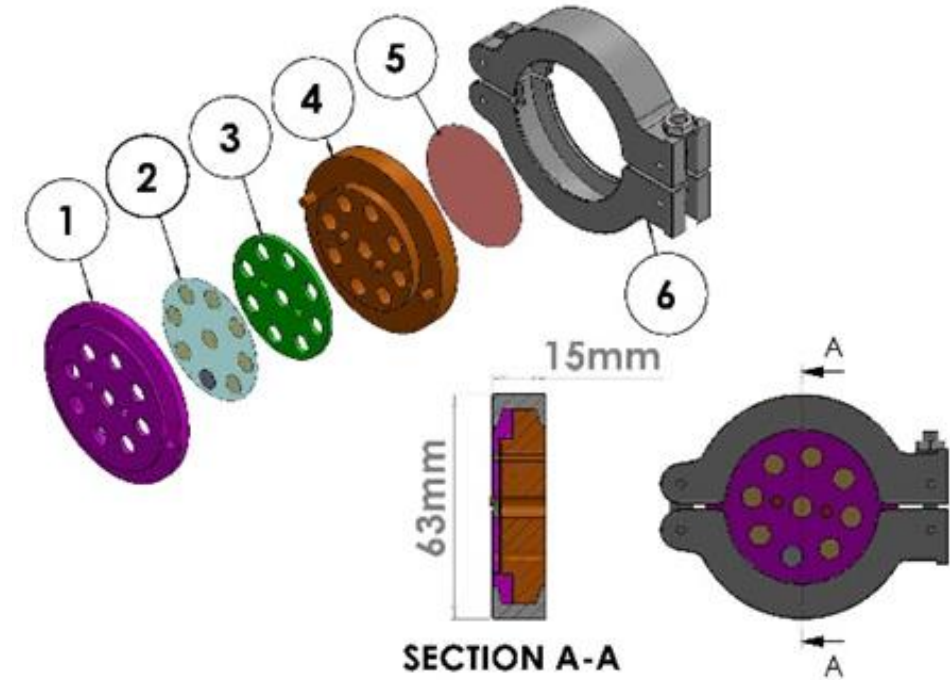
“the **key problem** is to deliver the dose in such a way that **ideally the intended target volume** (covering the tumor region) **receives 100% of the planned dose** needed to kill all cancer cells in the tumor, while the **surrounding normal tissue does not receive any dose**” (Schardt, 2016)



FLASH radiotherapy (FLASH-RT) is defined as a single ultra-high dose-rate (≥ 40 Gy/s) radiotherapy.



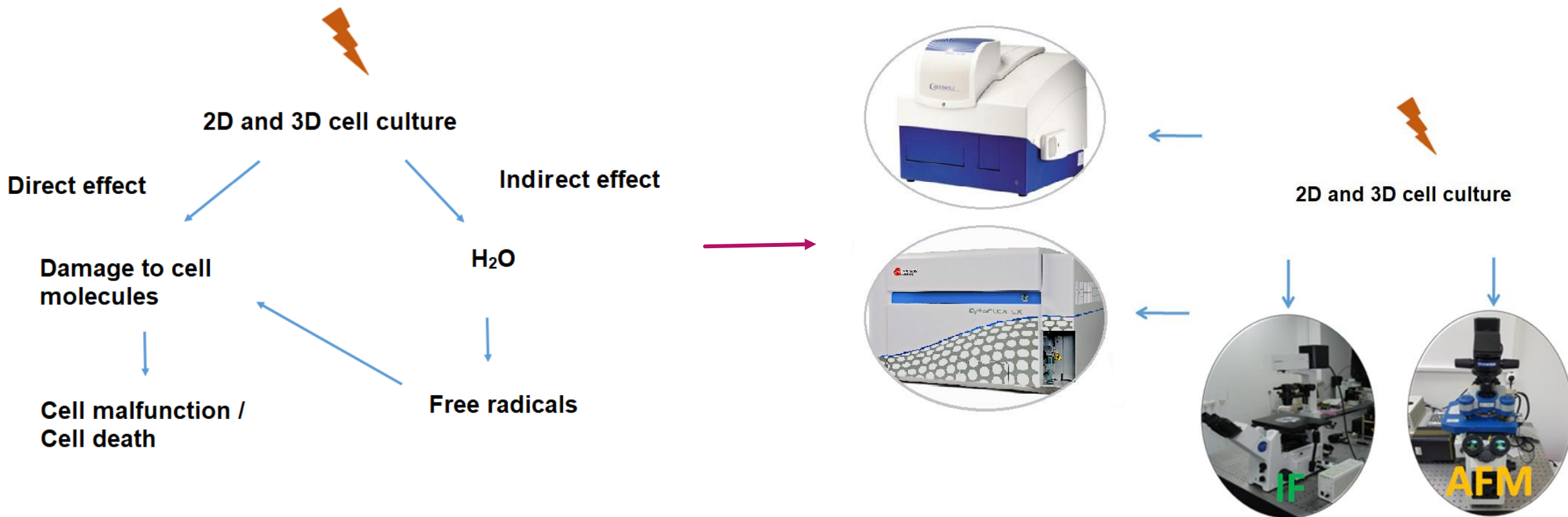
3 MV Tandatron ~ 2 MeV protons



1. Aluminum front cover;
2. Mylar foil;
3. Silicone gasket;
4. Teflon chamber;
5. Breathable sealing tape sterile;
6. KF63 vacuum clamp

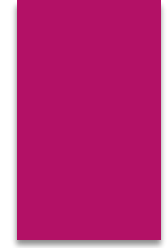


Biological investigation at IFIN-HH





Proton effects on B16 cells



- 3 MV Tandetron
- B16 cells – mouse melanoma cells
- Doses of 1 and 3 Gy with a dose rates of: 5 Gy/s, 50 Gy/s and 250 Gy/s

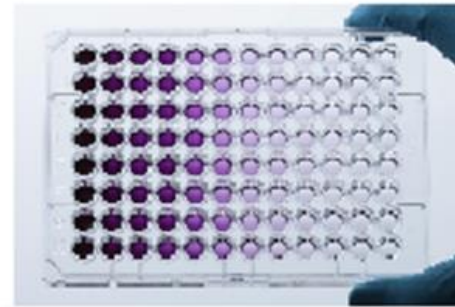
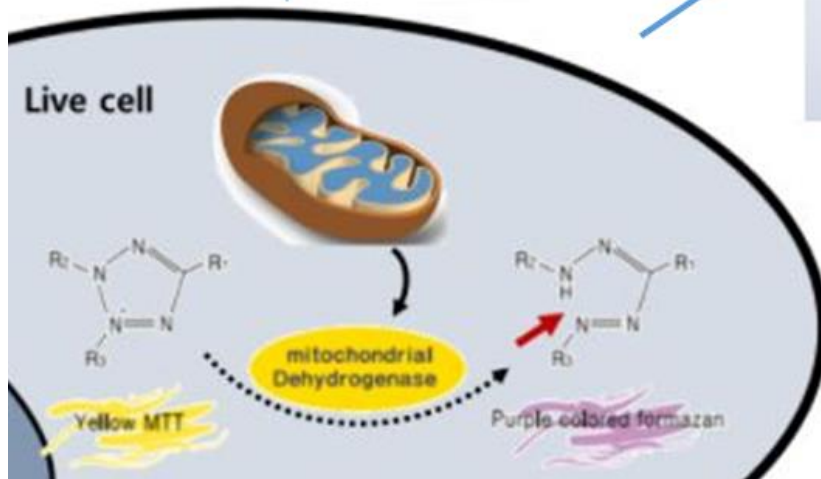


Cell viability

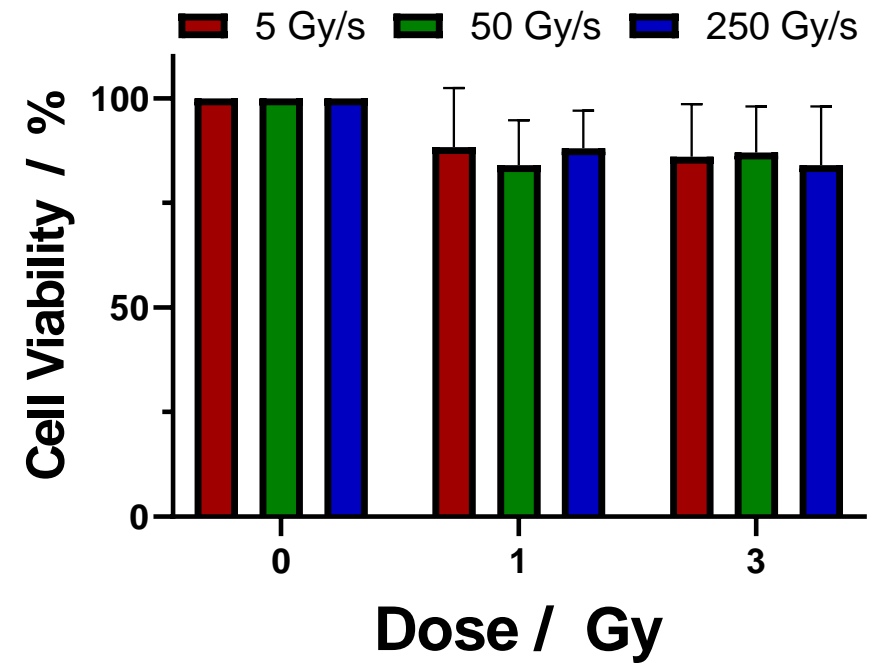


irradiated cells

after 24h
incubation with
MTT for 4h

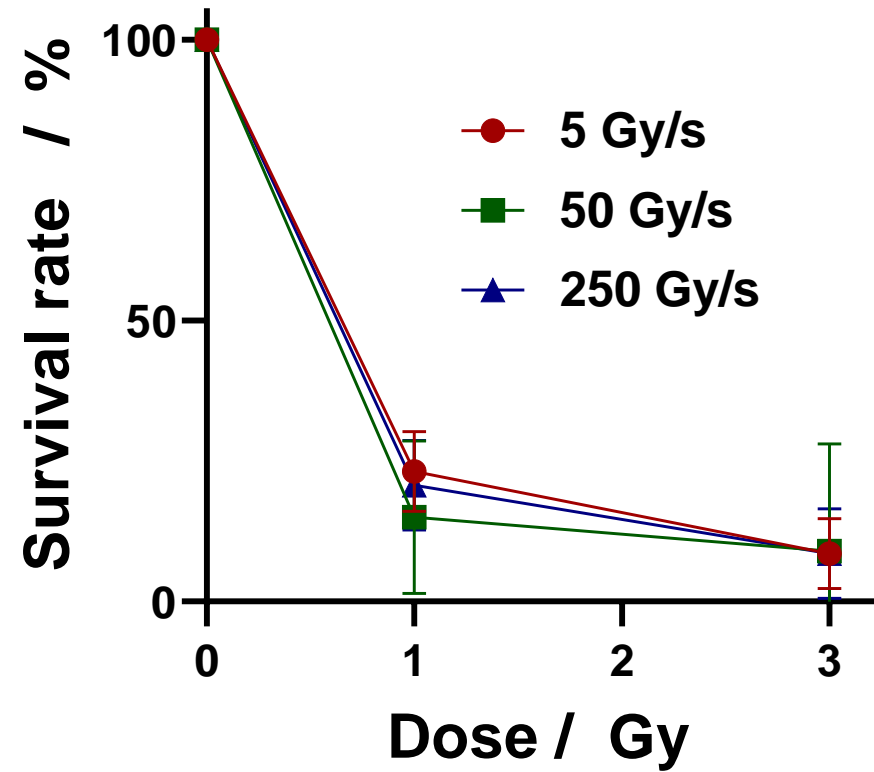
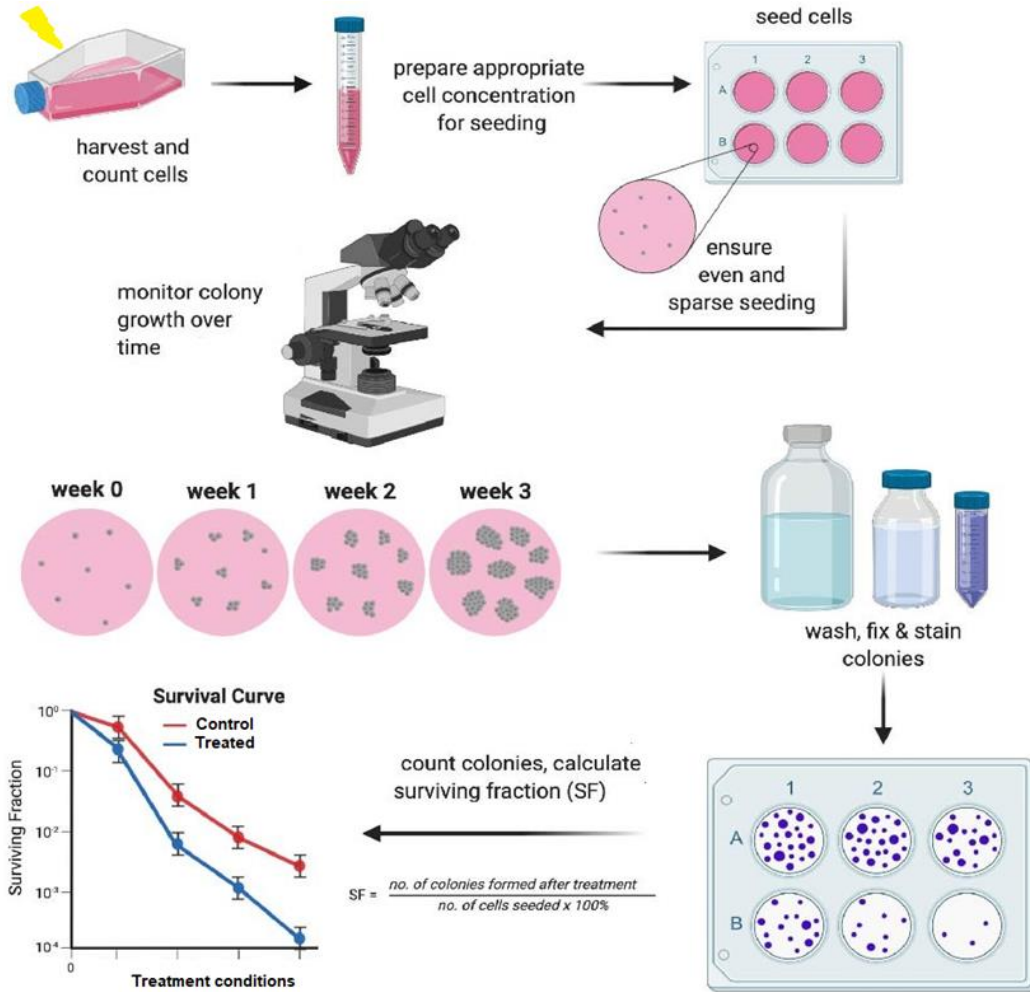


Measure absorbance
Calculate cell viability



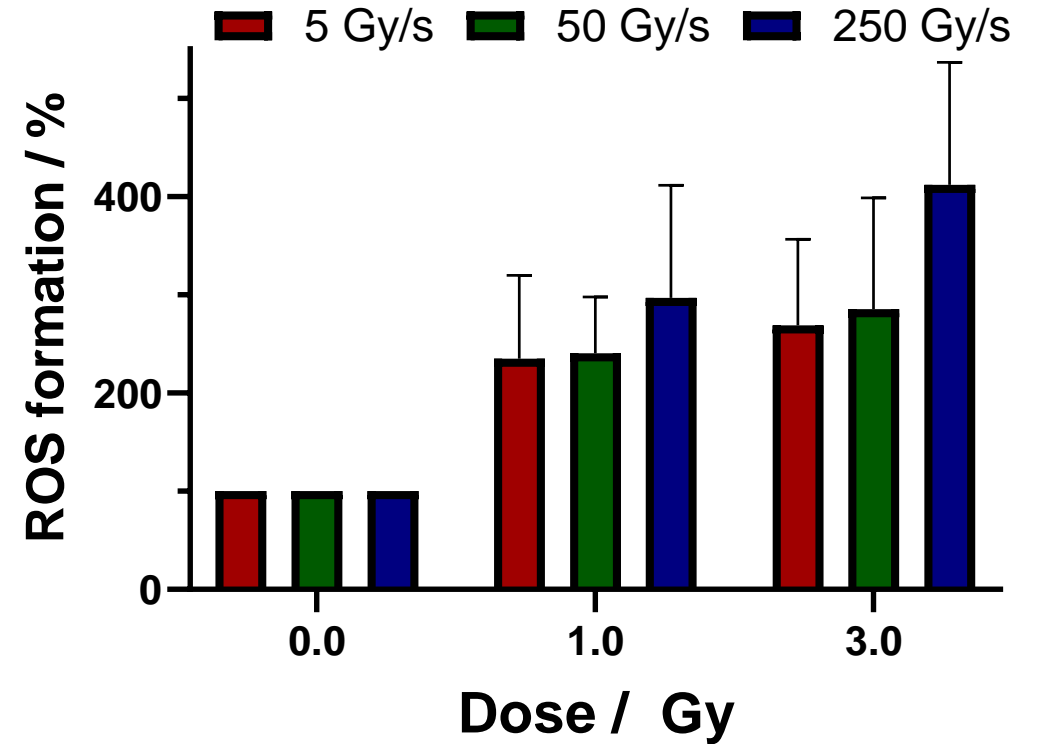
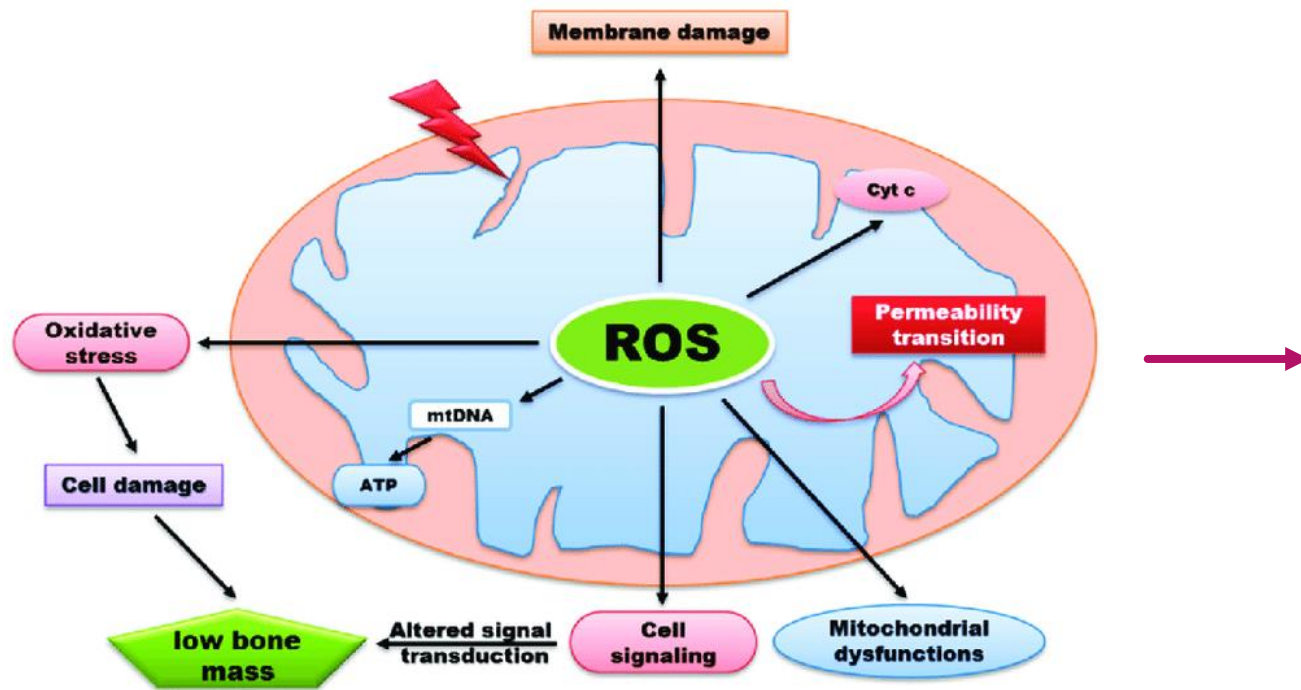


Clonogenic assay



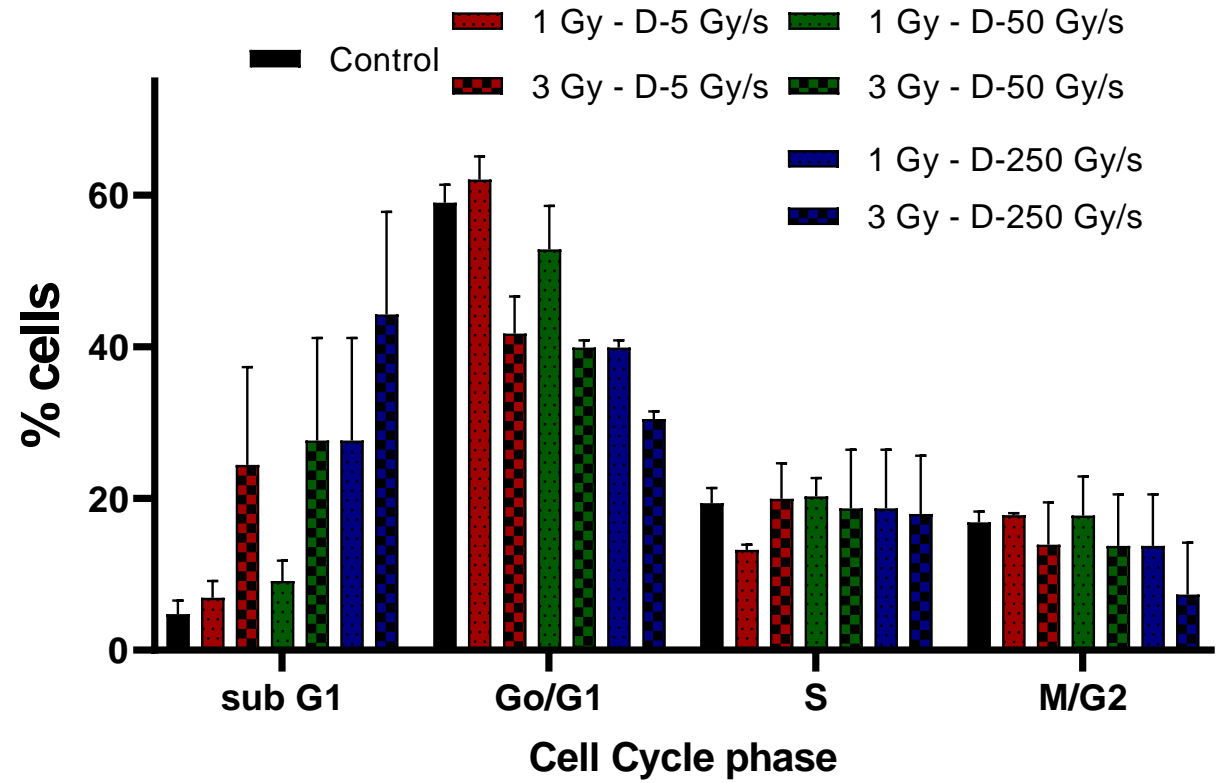
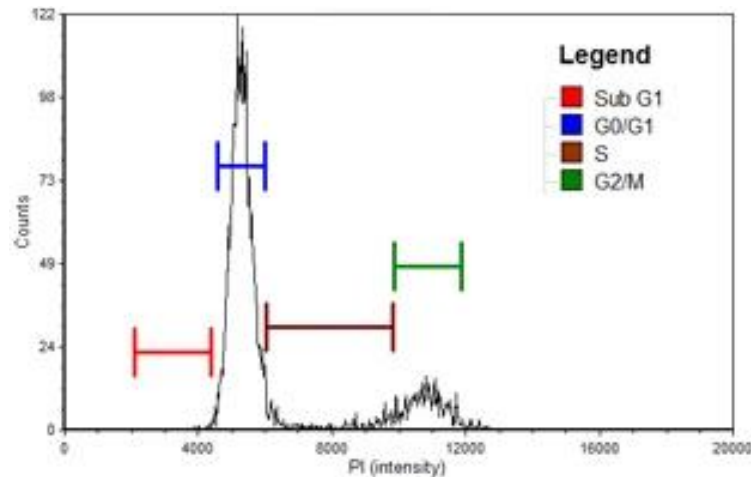
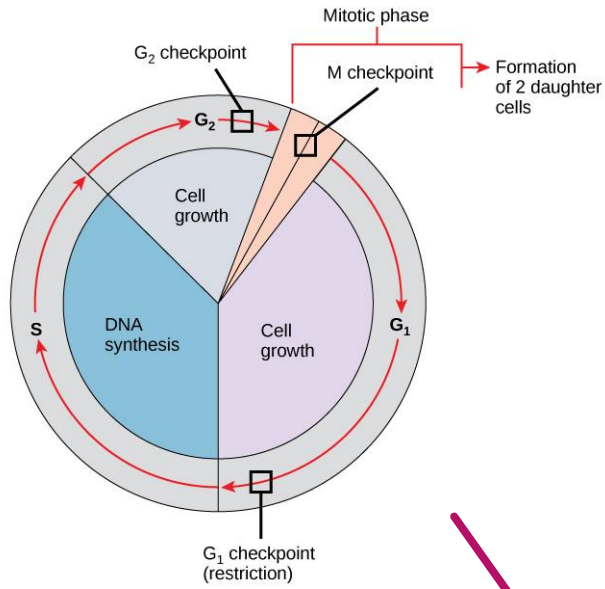


ROS formation in mitochondria



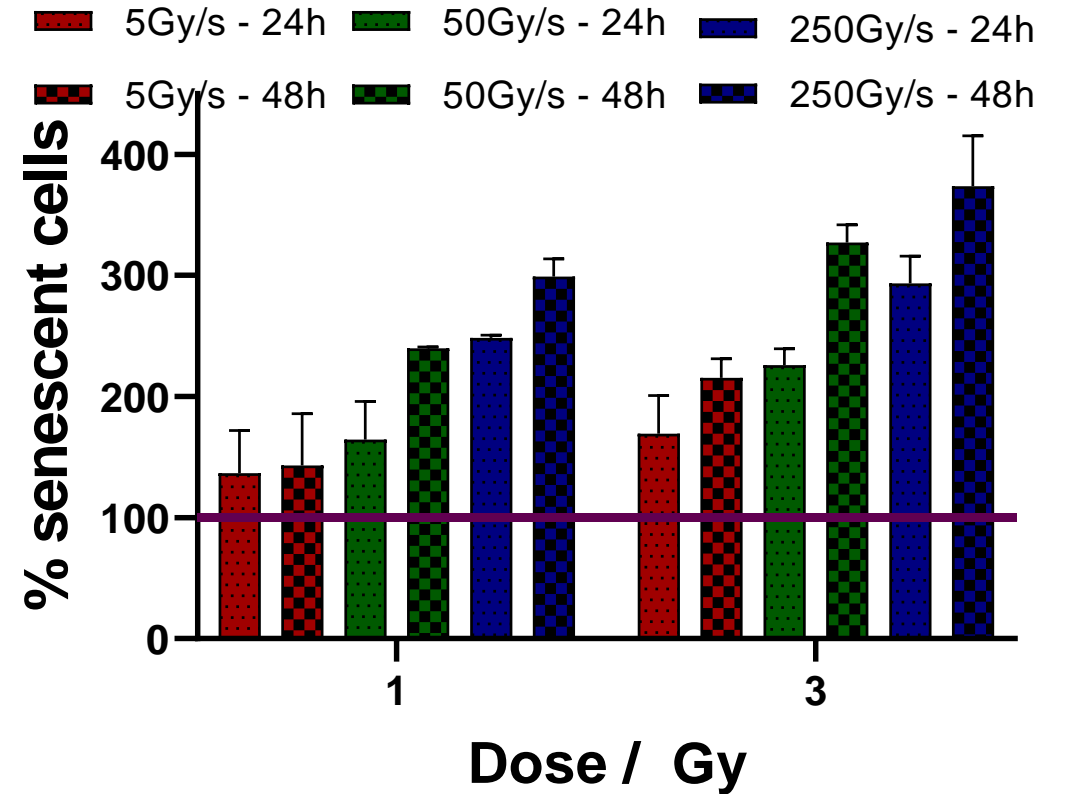
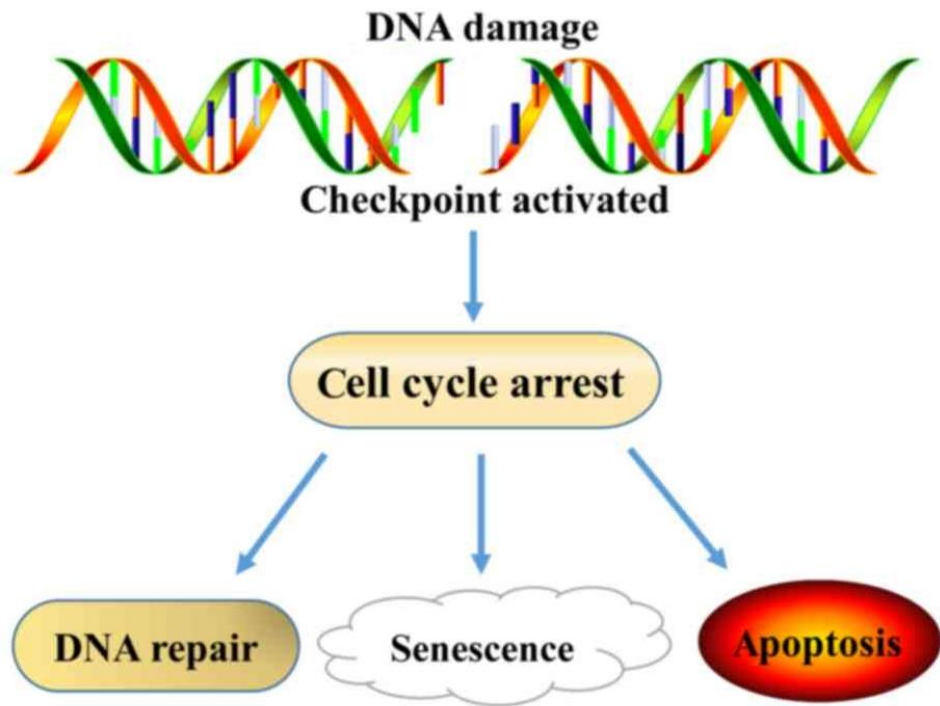


Cell cycle arrest





Senescence induction





Conclusion and perspectives

Conclusion:

- Cell viability is not significantly affected at 24h post irradiation;
- Long term survival is affected with dose increase but not with dose rate change;
- ROS formation and senescence are increasing with dose and dose rate increase;
- Cell cycle analysis show an increase of apoptotic cells with treatment.

Perspectives:

- investigation of DNA damage: gamma H2AX;
- cell death mechanism;
- investigation of morphological changes.....



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3 MV Tandetron: Mihai STRATICIUC, Radu ANDREI, Decebal IANCU

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Thank you for your attention!