Laboratori Nazionali di Legnaro – INFN

Cell survival measurements with free Ag-111 for the ISOLPHARM experiment

Caterina Spadetto

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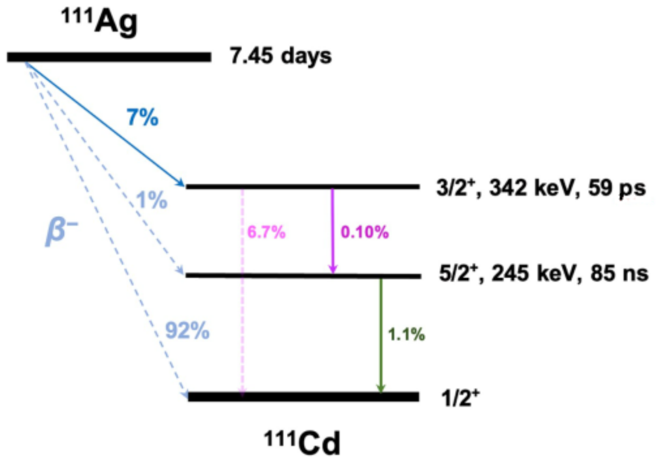
Introduction

Ag-111 is particularly suitable for **TRT** (Targeted Radionuclide Therapy), as it is:

- a β− emitter;
- the average energy of β− decay is 360 keV;
- the average tissue penetration is 1.8 mm;
- the half-life is 7.45 days.



Objective: to quantify the cell survival fraction and evaluate the most suitable biophysical model for data interpretation.

Theoretical Notes

Absorbed dose, adopting the MIRD (Medical Internal Radiation Dose) formalism:

$$\boxed{D(r_T, T_D) = \sum_{r_S} \tilde{A}(r_S, T_D)\, S(r_T \leftarrow r_S)}$$

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$$\tilde{A}(r_S, T_D) = \int_0^{T_D} A(r_S, t) dt$$

Activity of the source r_S integrated over the exposure period T_D.

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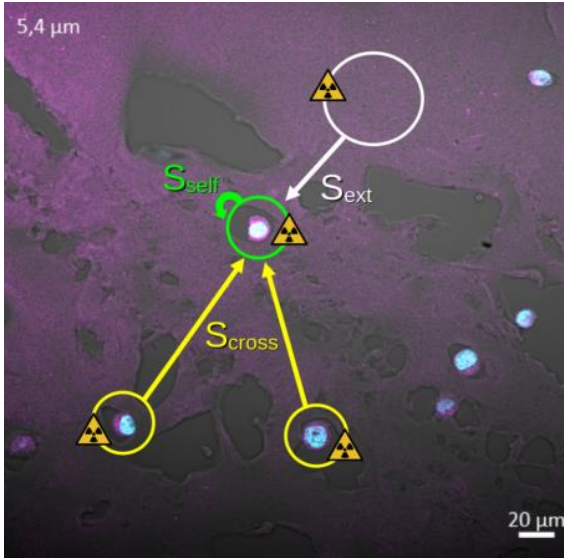
Average absorbed dose rate at the target r_T per unit of activity in the source.

Theoretical Notes

- **S_{ext}** : consider the effect of the environment on the nucleus;

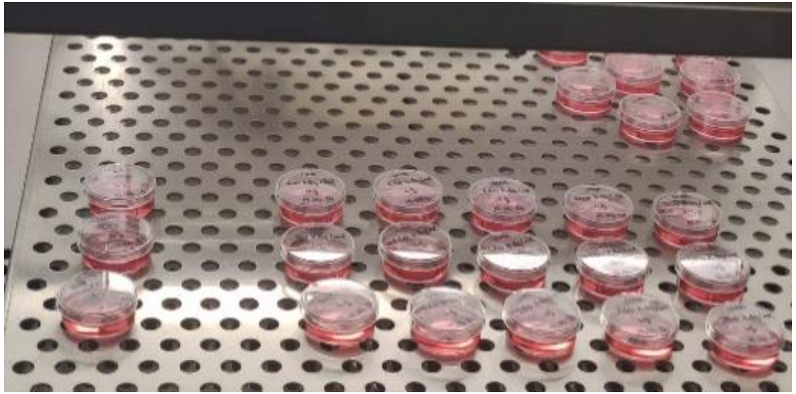
- **S_{self}** : consider the effect of cellular compartments on the nucleus, under the assumption that the radionuclide activity is in equilibrium inside and outside the cell;

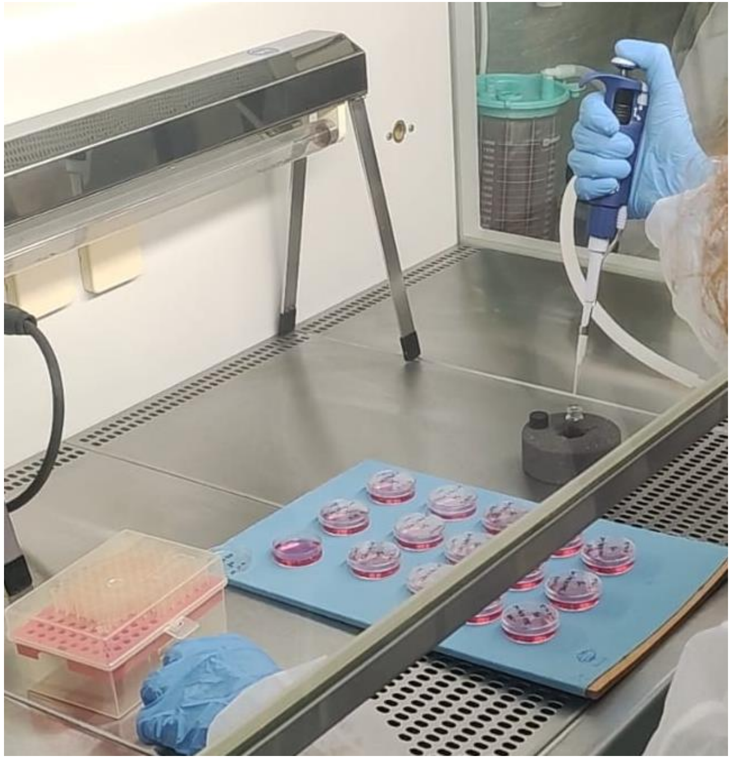
- **S_{cross}**: take into account the effect of the radionuclide internalized by other cells.



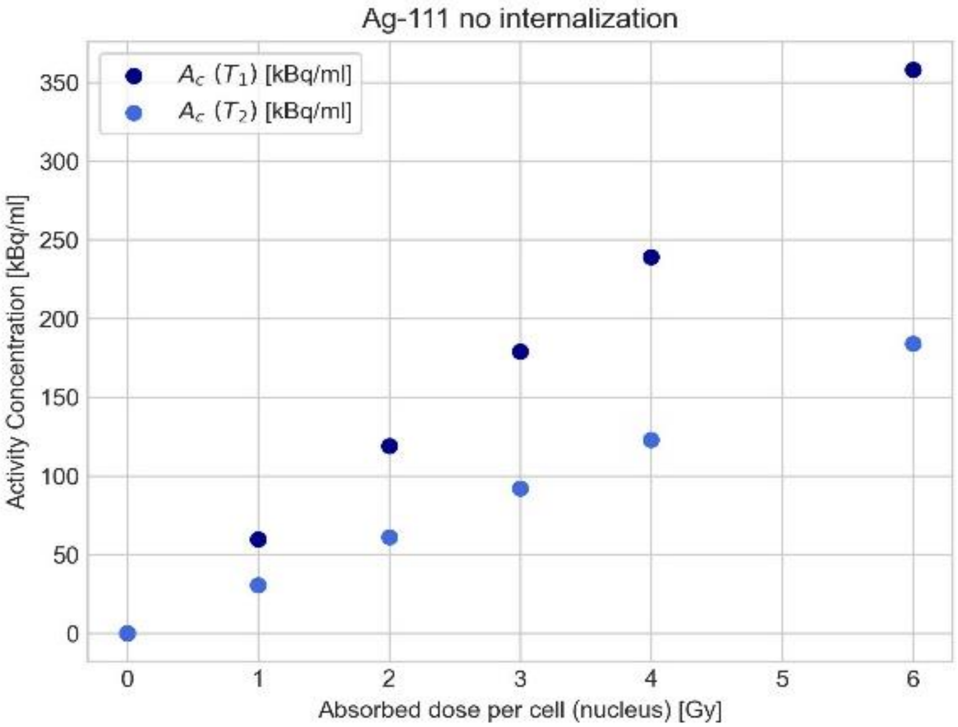
Experimental Setup

The experiment was executed on the cell line of **murine osteosarcoma UMR-106**, which grows in adhesion in DMEM medium enriched with 10% fetal bovine serum and 1% gentamicin.





Experimental Setup



Concentration of activity to be injected:

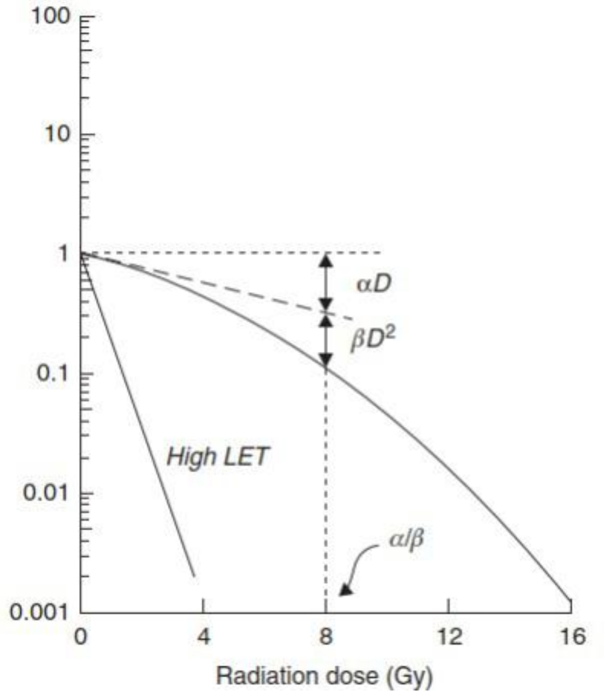
$$A_c(T) = \frac{D(T) \cdot \lambda}{S_{ext} \cdot (1 - e^{-\lambda T})}$$

Linear Quadratic Model

The **linear-quadratic** (LQ) **model** provides a simple relationship between cell survival S and absorbed dose D:

$$\boxed{S = e^{-\alpha D - \beta D^2}}$$

where α and β are two parameters that describe the cell's radiosensitivity.

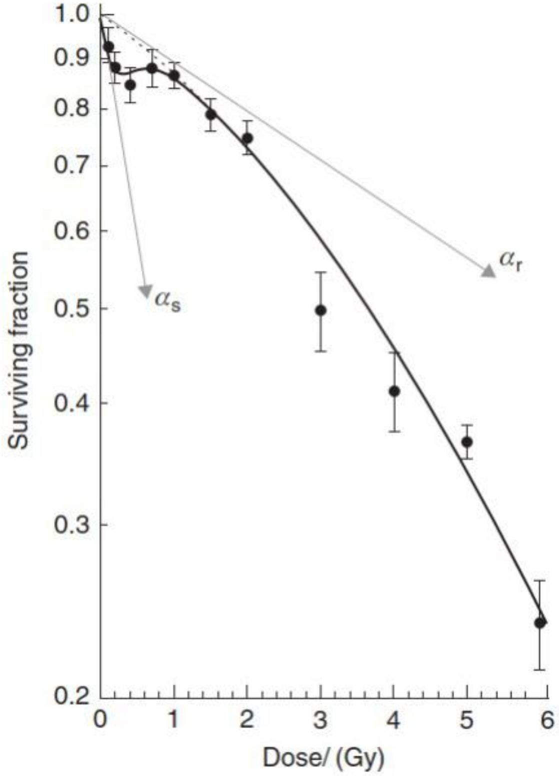


Induced Repair Model

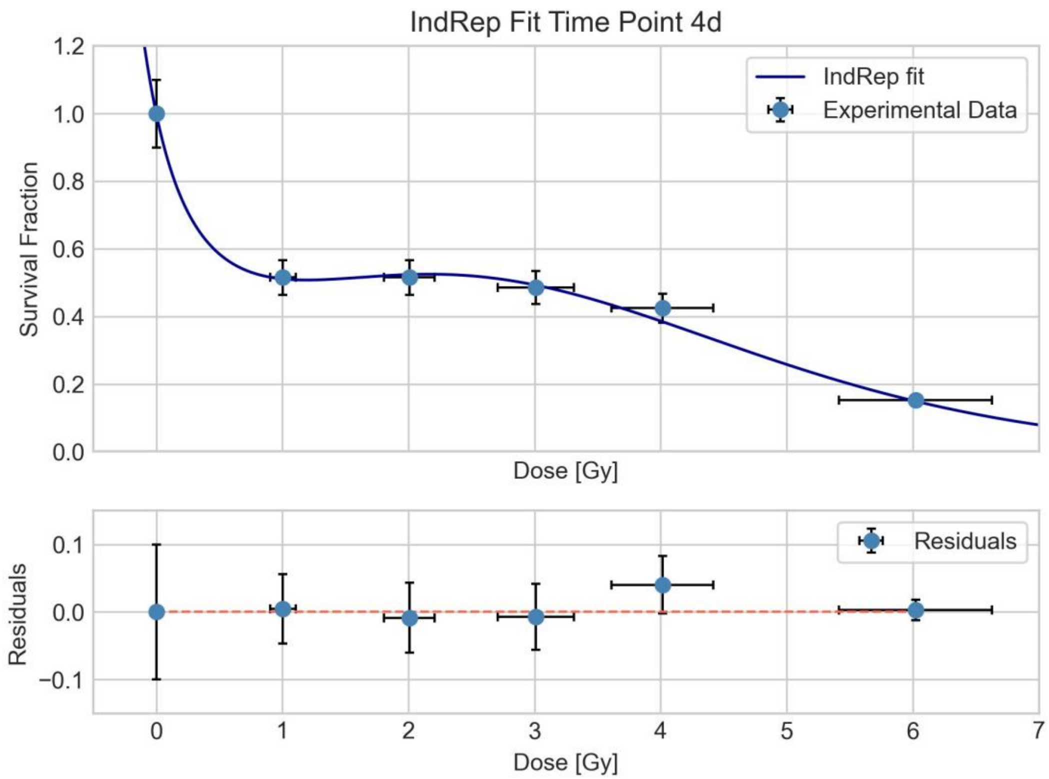
At low doses, cells can exhibit **HRS** (Low-Dose Hyper-Radiosensitivity). To describe this phenomenon is used the **induced repair model** (IndRep):

$$\boxed{S = exp\left(-\alpha_r \cdot D \cdot \left(1 + \left(\frac{\alpha_s}{\alpha_r} - 1\right)e^{-\frac{D}{D_c}}\right) - \beta \cdot D^2\right)}$$

D_c describes the dose at which the transition from the **HRS** response to the **IRR** (Increased RadioResistance) response begins to occur.



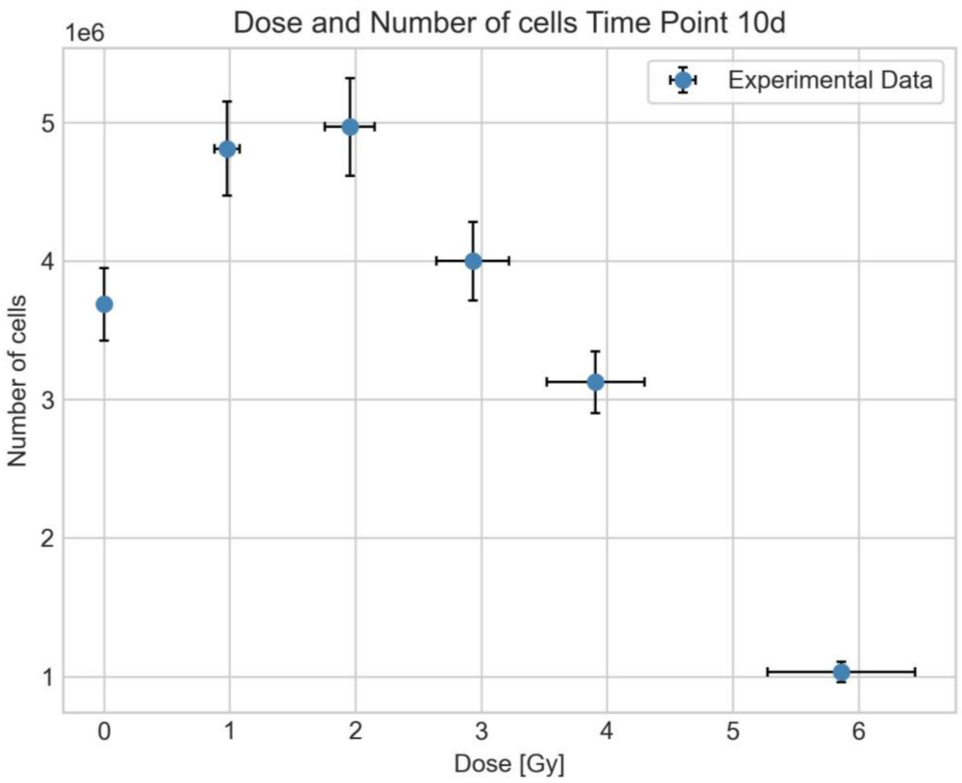
Time Point 4d – April 2024



α_r [Gy^{-1}]	β [Gy^{-2}]
$0,0140$	$0,0497$

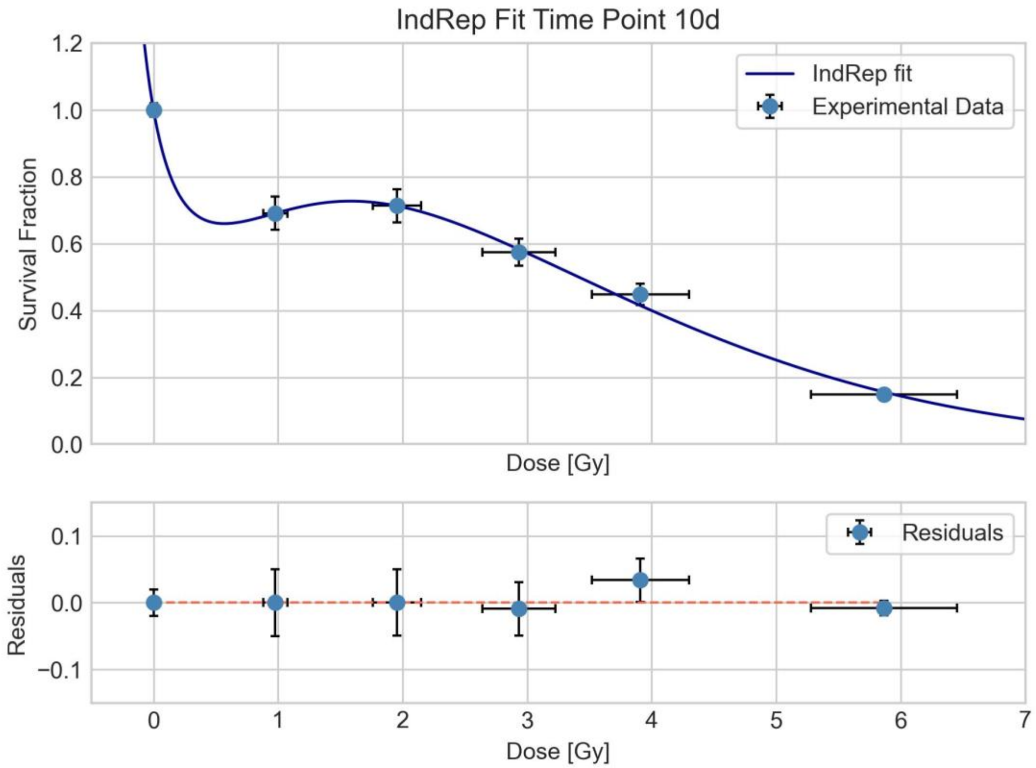
α_s [Gy^{-1}]	D_c [Gy]
$1,77 \pm 0,18$	$0,94 \pm 0,06$

Time Point 10d – April 2024



The number of counted control cells appears to be underestimated; likely, the cells have undergone stress.
Therefore, it was extrapolated through a linear fit of the data points at high doses.

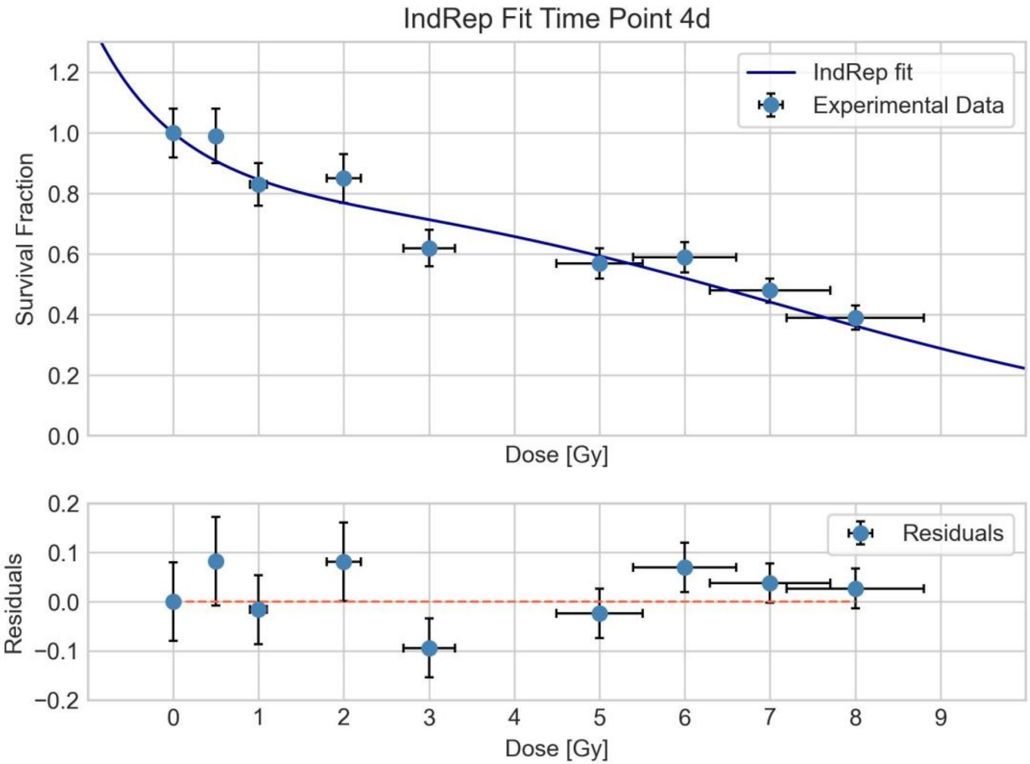
Time Point 10d – April 2024



α_r [Gy^{-1}]	β [Gy^{-2}]
$0,04 \pm 0,04$	$0,047 \pm 0,009$

α_s [Gy^{-1}]	D_c [Gy]
$2,1 \pm 0,5$	$0,50 \pm 0,06$

Time Point 4d – July 2024



α_r [Gy^{-1}]	β [Gy^{-2}]
$0,004 \pm 0,004$	$0,0143 \pm 0,0006$

α_s [Gy^{-1}]	D_c [Gy]
$0,22 \pm 0,10$	$2,4 \pm 0,8$

Conclusions

- The survival fraction decreases with increasing dose, but at low doses appears to be a region of **HRS** followed by **IRR**;
- It was not possible to conclude whether a shorter or longer exposure is more effective;
- Presence of cellular stress.

Next Steps

- Reduce the number of seeded cells to prevent cellular stress;
- To improve the accuracy and precision of the data, realize clonogenic assays;
- Comparison with other beta emitters found in the literature.

Thanks for your attention!