Istituto Nazionale di Fisica Nucleare
LABORATORI NAZIONALI DI LEGNARO

ADMIRAL
ISOLPHARM
SPES exotic beams for medicine

Laboratori Nazionali di Legnaro - INFN

Cell survival with Ag-111: data analysis

Caterina Spadetto

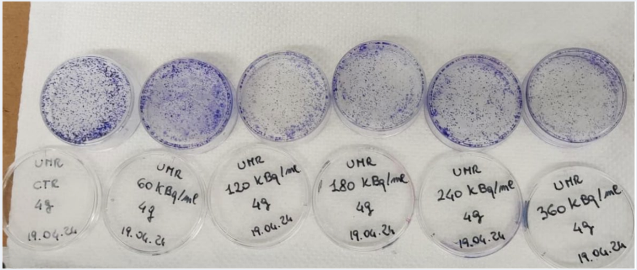
June 18, 2024

Indice

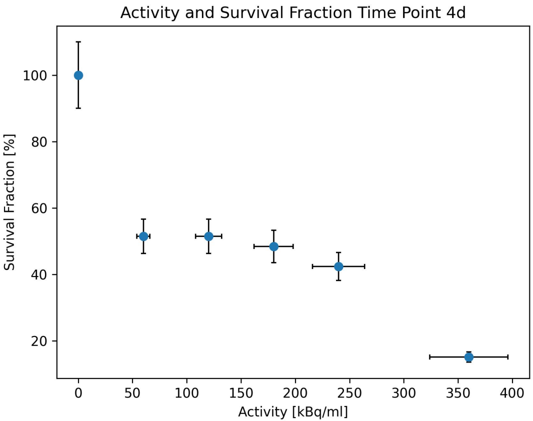
1 · Time Point 4d

Time Point 4d

Time Point 4d Foto



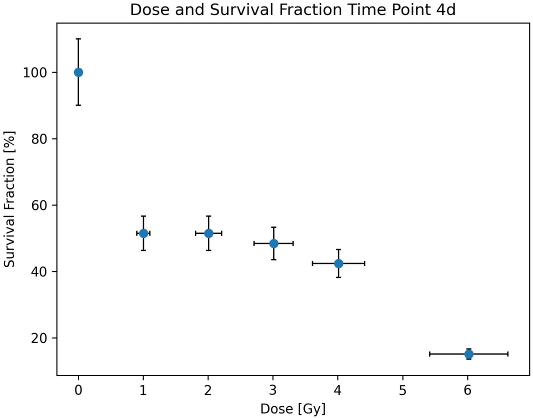
Time Point 4d



Activity [kBq/ml]	Survival Fraction [%]
–	100 ± 10
60 ± 6	52 ± 5
120 ± 10	52 ± 5
180 ± 20	48 ± 5
240 ± 20	42 ± 4
360 ± 40	15 ± 2

Activity and Survival Fraction Time Point 4d

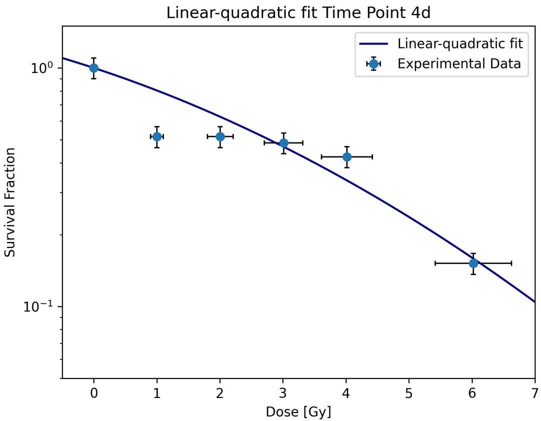
Time Point 4d



Dose [Gy]	Survival Fraction [%]
-	100 ± 10
1.0 ± 0.1	52 ± 5
2.0 ± 0.2	52 ± 5
3.0 ± 0.3	48 ± 5
4.0 ± 0.4	42 ± 4
6.0 ± 0.6	15 ± 2

Dose and Survival Fraction Time Point 4d

Linear-Quadratic Fit



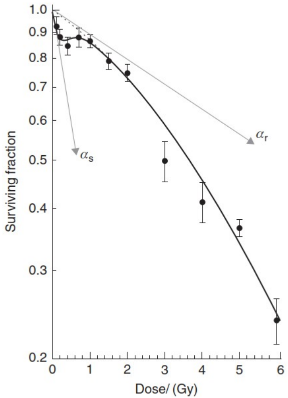
$$S(D) = e^{-\alpha \cdot D - \beta \cdot D^2}$$

- $\alpha = 0.20 \pm 0.15 \ \frac{1}{\text{Gy}}$
- $\beta = 0.02 \pm 0.04 \ \frac{1}{\text{Gy}^2}$

Low-Dose Hyper-Radiosensitivity(HRS)?

Low-Dose Hyper-Radiosensitivity

The LQ model describes cellular response to radiation above about 1 Gy. Below about 10 cGy, the cells show HRS, a phenomenon by which cells die from excessive sensitivity to low doses, due to rapid cell cycle arrest of irradiated cells in the G2 phase of the cycle. It can be characterized by a slope (α_s) that is considerably steeper than the slope expected by extrapolating back the response from high-dose measurements (α_r).[1]



[1] Joiner, M. & Van der Kogel, A. (2009). *Basic Clinical Radiobiology*, Great Britain, Hodder Arnold, 1993, pp.53-54.

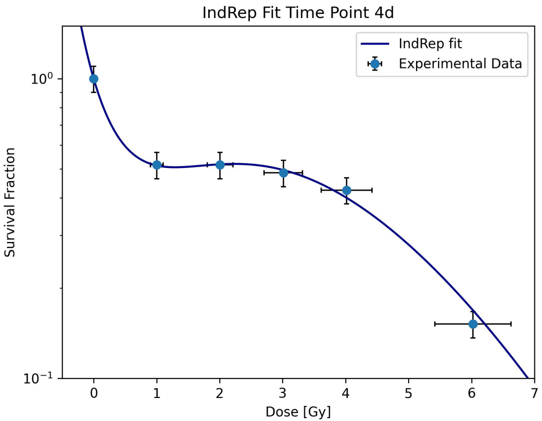
Induced-repair model

The IndRep model thus comprises two LQ models with different α sensitivities dependent on the dose given, merged into a single equation:

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

D_c	Describes the dose at which the transition from the HRS response through the IRR response starts to occur.
α_r	At very high doses ($D >> Dc$), equation above tends to a LQ model with active parameters α_r and β.
α_s	At very low doses ($D << Dc$), equation above tends to a LQ model with active parameters α_s and β.

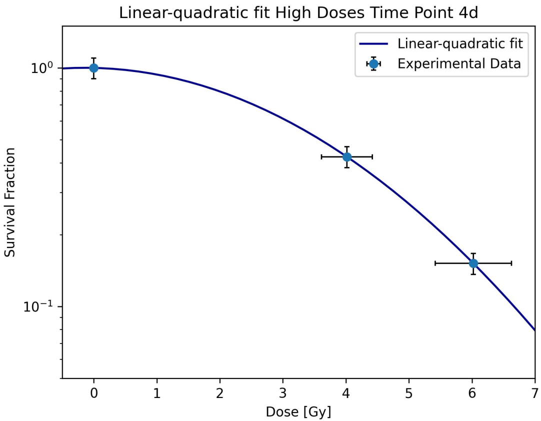
Induced-repair model Fit



Fit parameters:

- $\alpha_r = 0.01 \pm 0.11 \ \frac{1}{\text{Gy}}$
- $\alpha_s = 1.7 \pm 0.4 \ \frac{1}{\text{Gy}}$
- $D_c = 1.0 \pm 0.3$ Gy
- $\beta = 0.05 \pm 0.02 \ \frac{1}{\text{Gy}^2}$

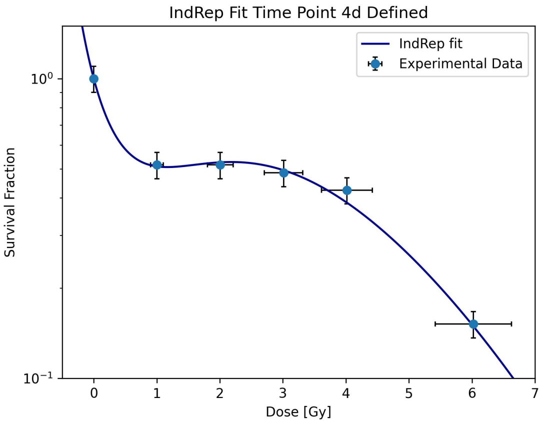
High Doses Fit



$$S(D) = e^{-\alpha \cdot D - \beta \cdot D^2}$$

- $\alpha = 0.140204 \pm 0.000009 \; \frac{1}{\text{Gy}}$
- $\beta = 0.049700 \pm 0.000002 \; \frac{1}{\text{Gy}^2}$

Induced-repair model Fit



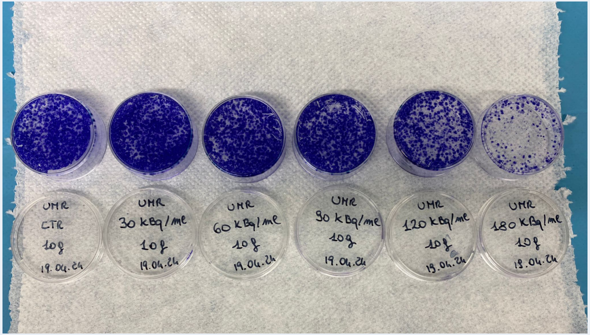
Fit parameters:

- $\alpha_s = 1.8 \pm 0.2 \ \frac{1}{\text{Gy}}$
- $D_c = 0.93 \pm 0.07$ Gy

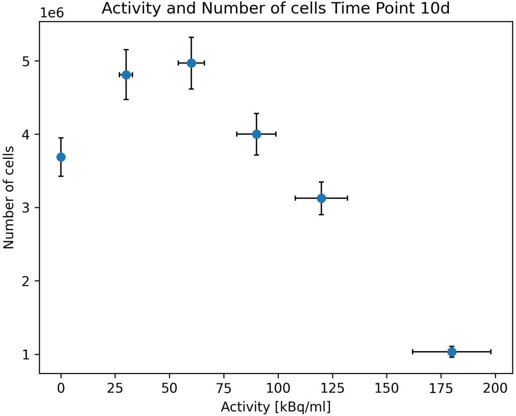
2 · Time Point 10d

Time Point 10d

Time Point 10d Foto



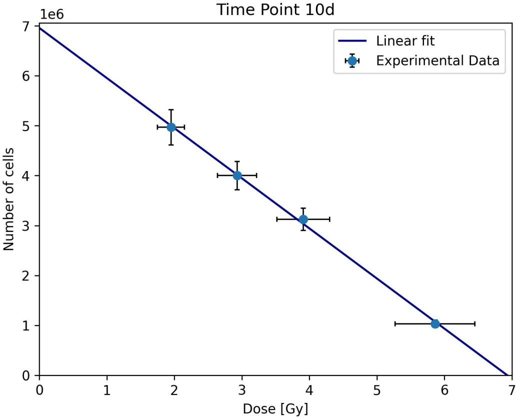
Time Point 10d



Activity[kBq/ml]	Number of Cells
–	$(3.7 \pm 0.3) \cdot 10^6$
30 ± 3	$(4.8 \pm 0.3) \cdot 10^6$
60 ± 6	$(5.0 \pm 0.4) \cdot 10^6$
90 ± 9	$(4.0 \pm 0.3) \cdot 10^6$
120 ± 10	$(3.1 \pm 0.2) \cdot 10^6$
180 ± 20	$(1.03 \pm 0.07) \cdot 10^6$

Activity and Number of Cells Time Point 10d

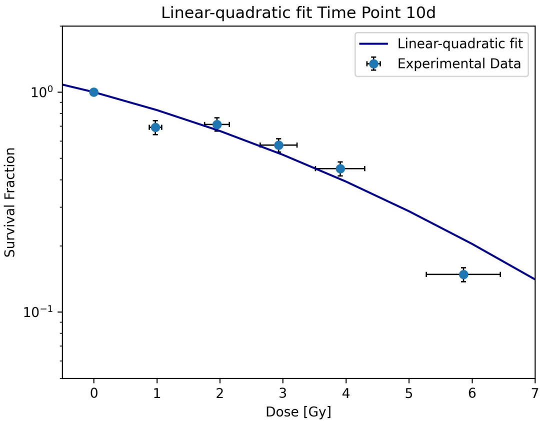
Time Point 10d



Dose [Gy]	Number of Cells
1.95 ± 0.2	$(5.0 \pm 0.3) \cdot 10^6$
2.93 ± 0.29	$(4.0 \pm 0.3) \cdot 10^6$
3.91 ± 0.39	$(3.1 \pm 0.2) \cdot 10^6$
5.86 ± 0.59	$(1.03 \pm 0.07) \cdot 10^6$

- $m = (-1.0 \pm 0.3) \cdot 10^6 \ \frac{1}{\text{Gy}}$
- $q = (70 \pm 1) \cdot 10^6$

Linear-Quadratic Fit

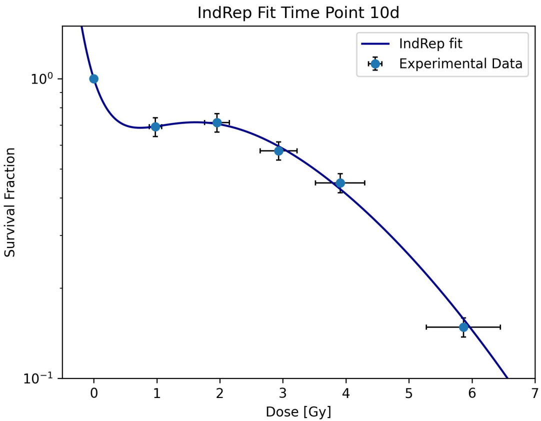


$$S(D) = e^{-\alpha \cdot D - \beta \cdot D^2}$$

- $\alpha = 0.17 \pm 0.08 \ \frac{1}{\text{Gy}}$
- $\beta = 0.015 \pm 0.02 \ \frac{1}{\text{Gy}^2}$

Low-Dose Hyper-Radiosensitivity(HRS)?

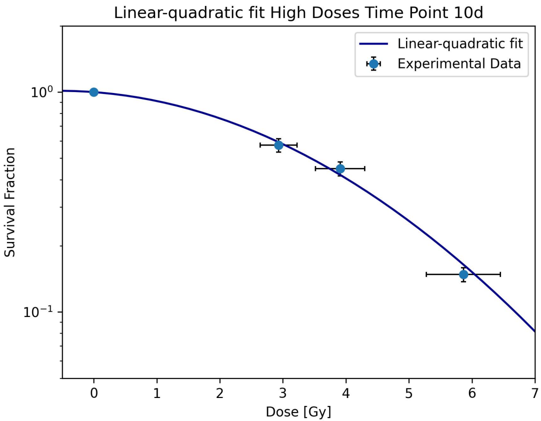
Induced-repair model Fit



Fit parameters:

- $\alpha_r = 0.013 \pm 0.06 \, \frac{1}{\text{Gy}}$
- $\alpha_s = 1.5 \pm 0.7 \, \frac{1}{\text{Gy}}$
- $D_c = 0.6 \pm 0.2\text{Gy}$
- $\beta = 0.05 \pm 0.01 \, \frac{1}{\text{Gy}^2}$

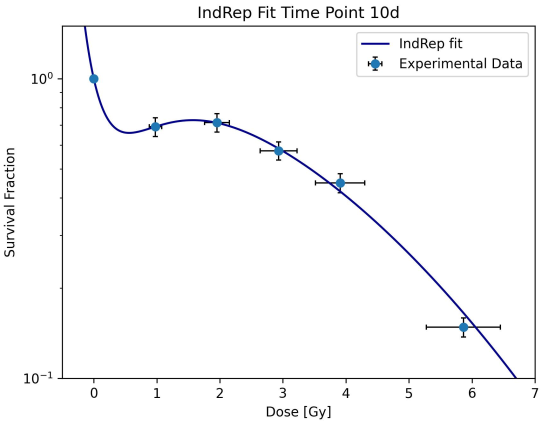
High Doses Fit



$$S(D) = e^{-\alpha \cdot D - \beta \cdot D^2}$$

- $\alpha = 0.05 \pm 0.04 \ \frac{1}{\mathrm{Gy}}$
- $\beta = 0.04 \pm 0.01 \ \frac{1}{\mathrm{Gy}^2}$

Induced-repair model Fit



Fit parameters:

- $\alpha_s = 2.2 \pm 0.7\ \frac{1}{\text{Gy}}$
- $D_c = 0.49 \pm 0.08$ Gy

Conclusions

It would be interesting to collect data at higher doses, for example 8Gy, to improve the presented analysis.

Next Steps:

1. Comparison with other beta emitters;
2. Repetition of the analysis using the S-values of the cytoplasm;
3. Time-dependent study of activities that have been administered twice.

Thanks for your attention!