Universidad Nacional de San Martín

Dan Beninson
Instituto de Tecnología Nuclear

UNIVERSITÀ DI PAVIA

CNEA

Computational and experimental studies for space radiation and hadrontherapy

Ezequiel Canay
Supervisors: Francesca Ballarini, Ricardo L. Ramos
Abroad supervisors: Agustina M. Portu, Andrés Arazi

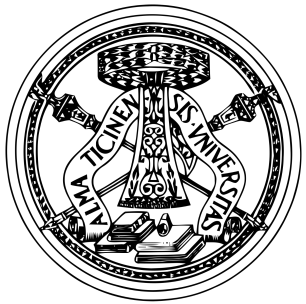
Presentation

Biomedical Engineer

PhD in CO-TUTELA

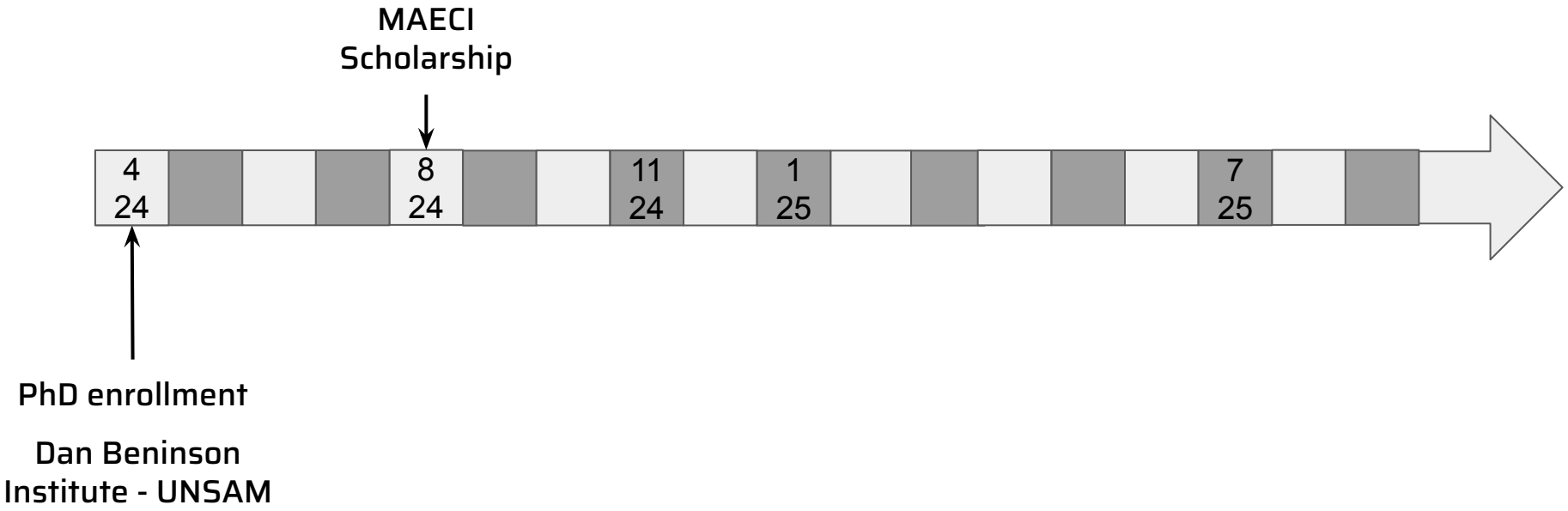
LA UNIVERSIDAD NACIONAL DE SAN MARTÍN
(nuclear technology)

and

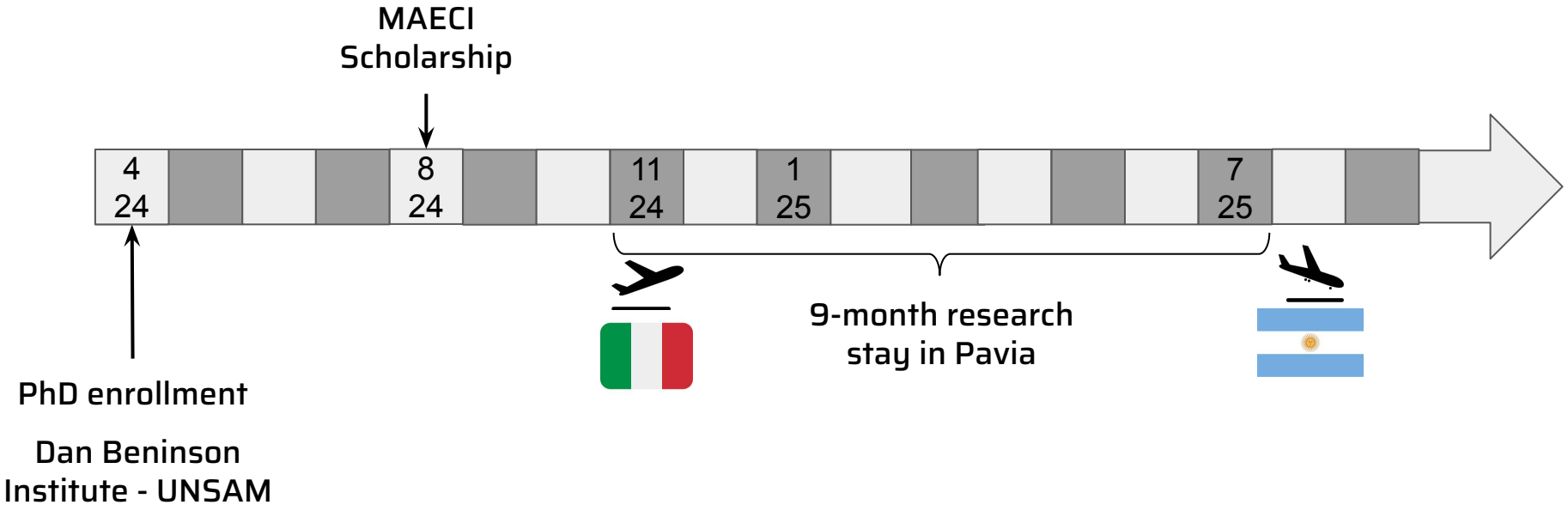


LA UNIVERSITÀ DEGLI STUDI DI PAVIA
(Physics)

Chronology of My PhD



Chronology of My PhD



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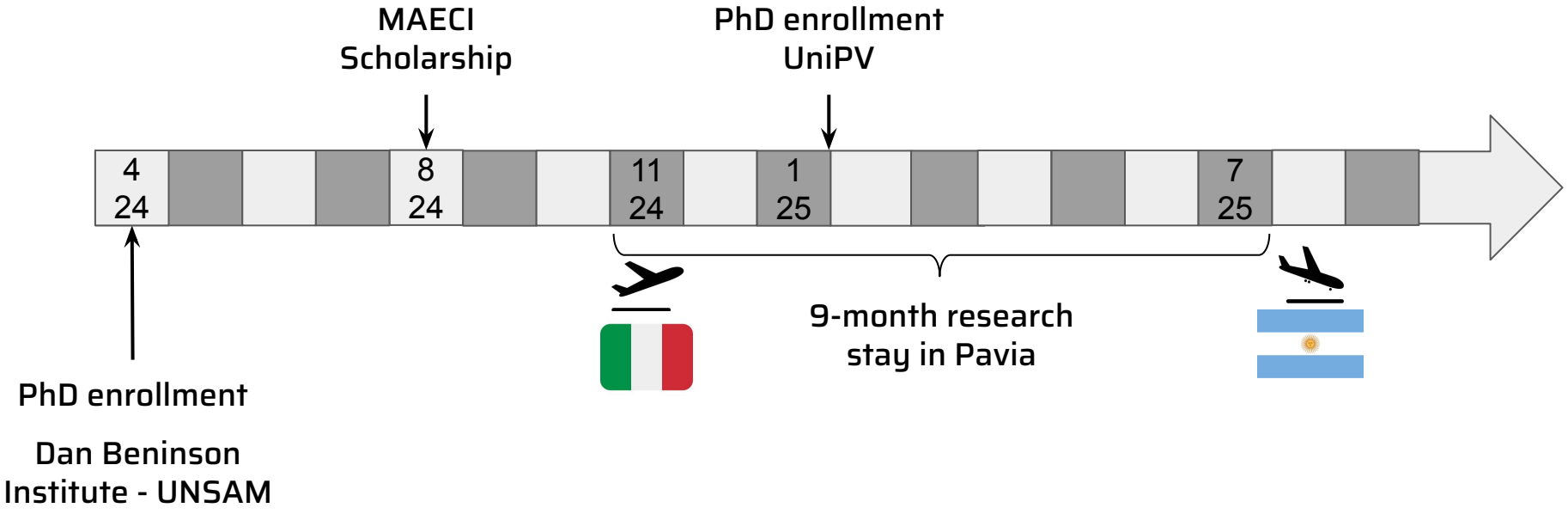
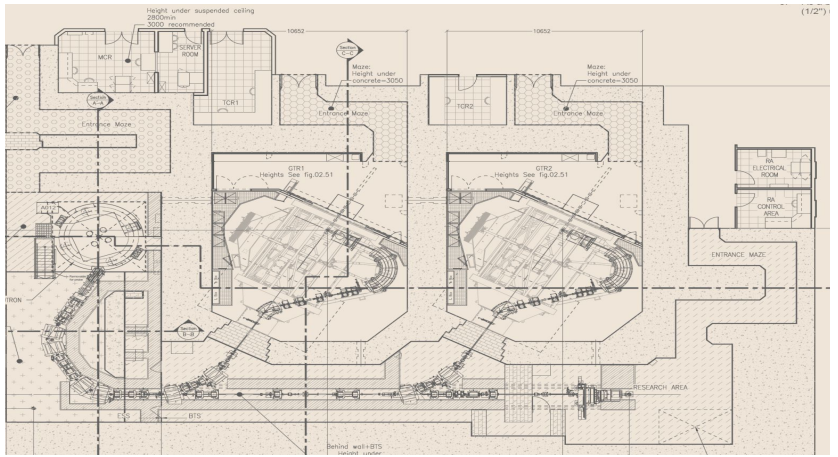


Proton therapy in Argentina

CeArP



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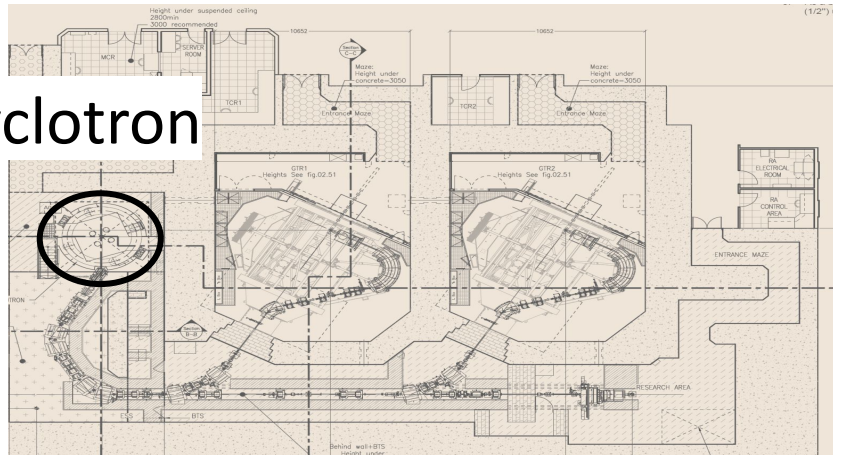
CeArP

Cyclotron



Proton therapy in Argentina

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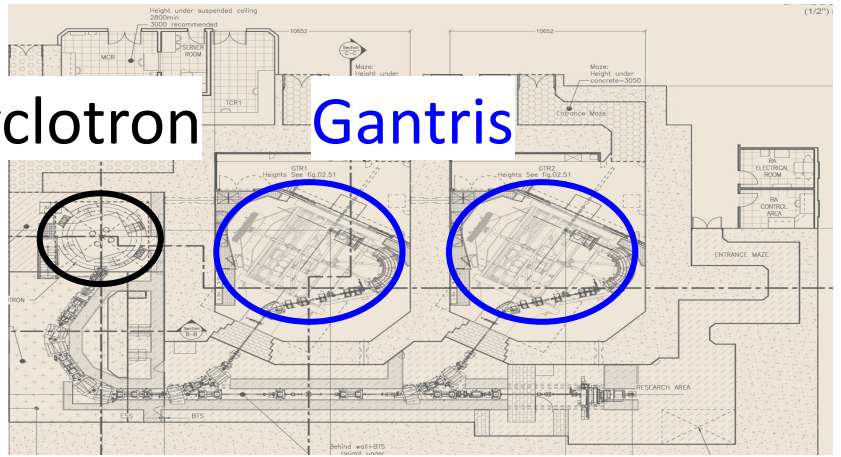
Cyclotron

Gantris



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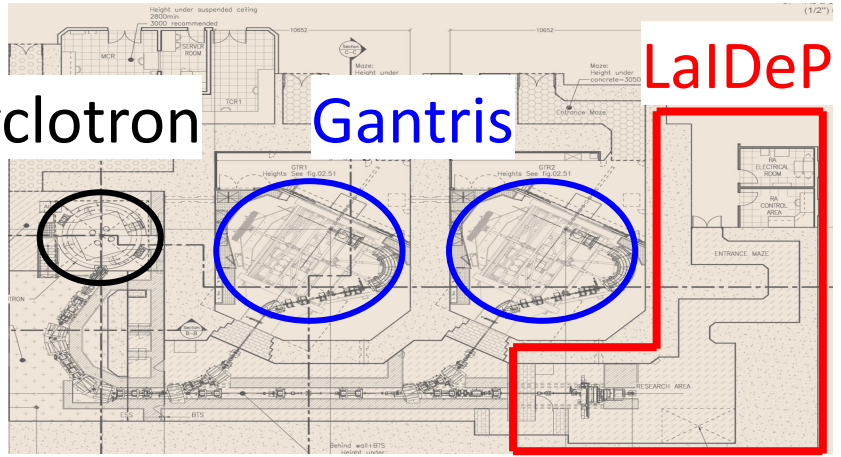
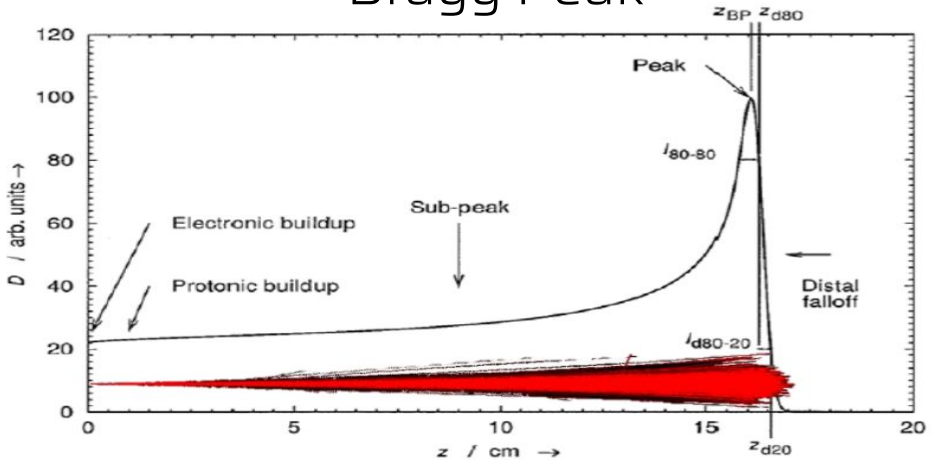


Proton therapy

Non-conventional Radiotherapy

External Radiotherapy with Proton Beams

Bragg Peak



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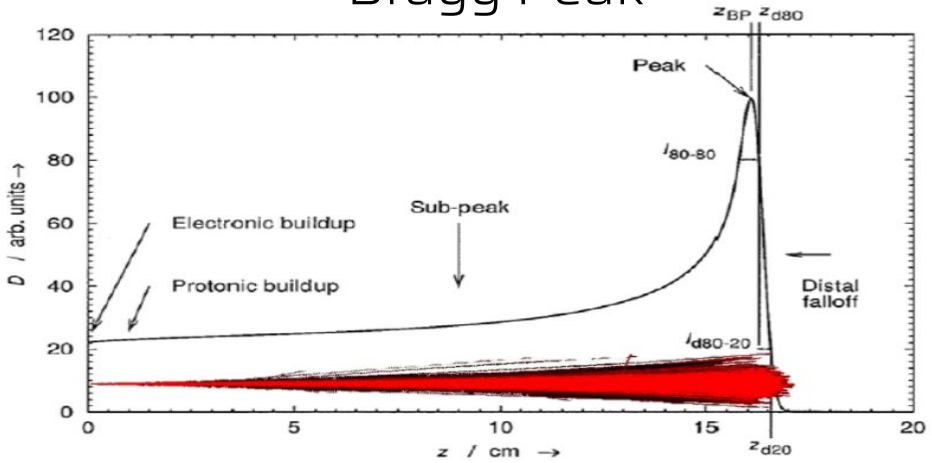
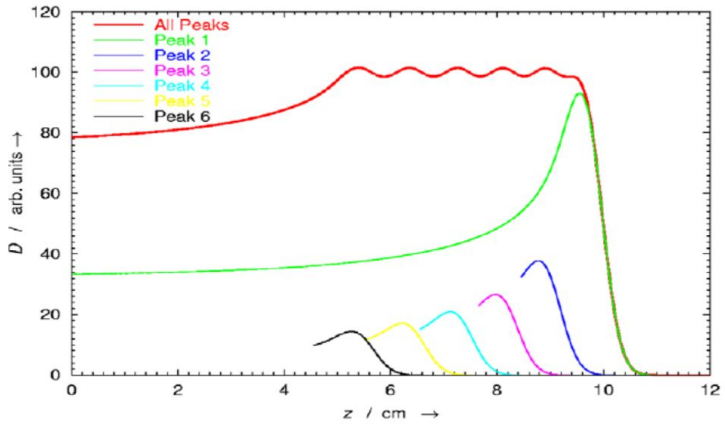


Spread-Out Bragg Peak



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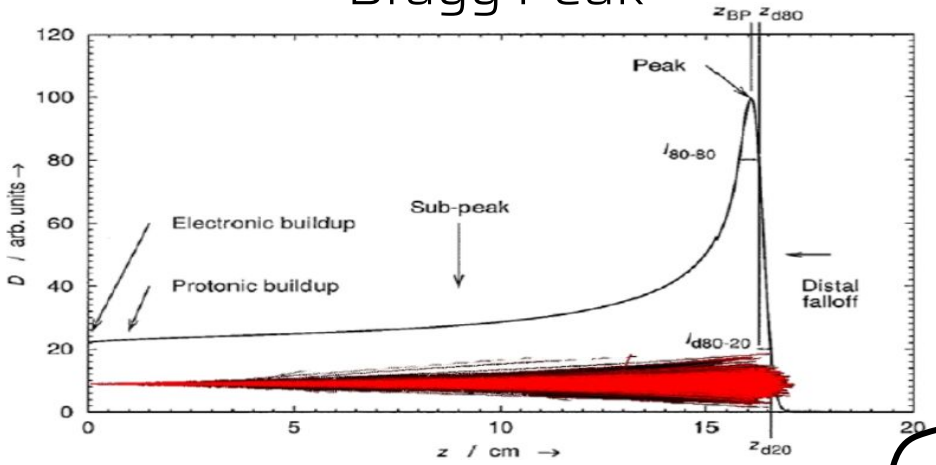
External Radiotherapy with Proton Beams

Bragg Peak



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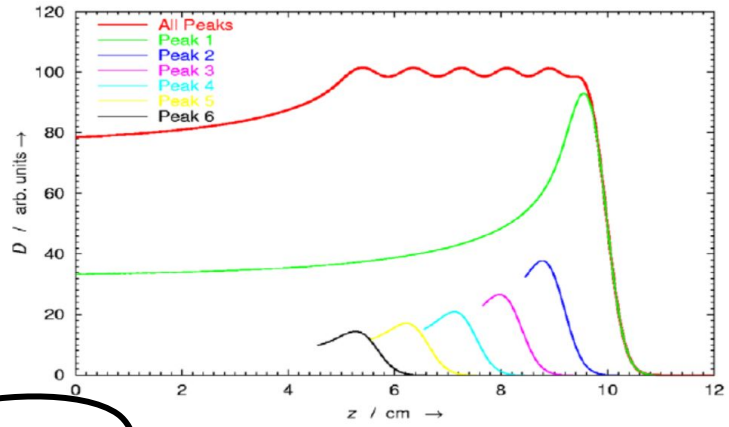

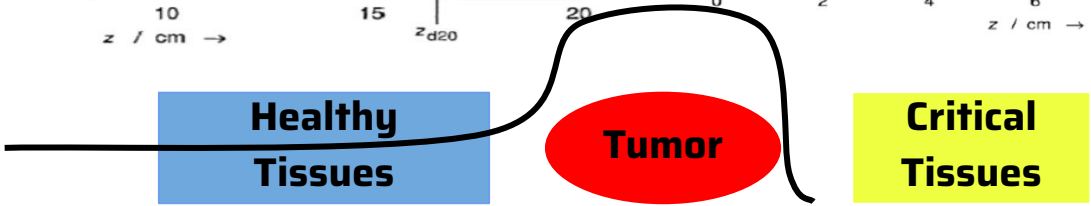

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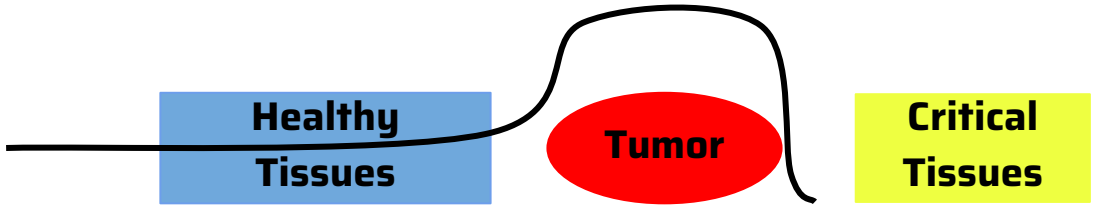
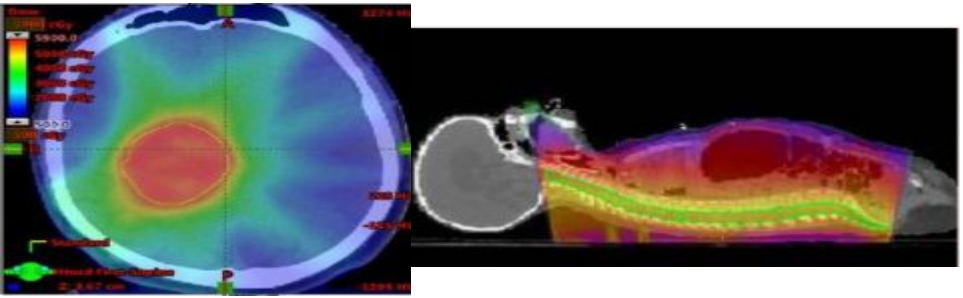


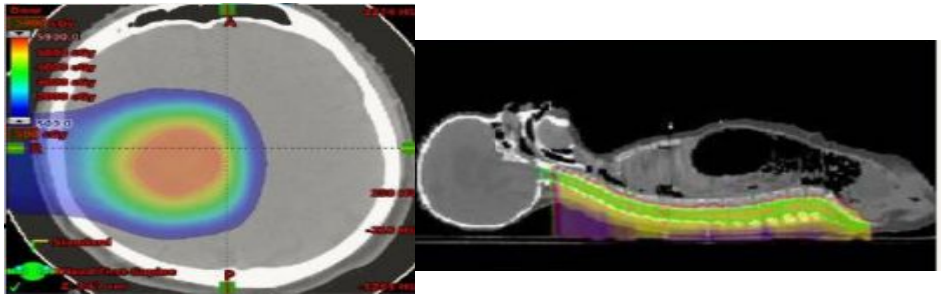
X-rays



brain tumor

spinal cord

Proton



brain tumor

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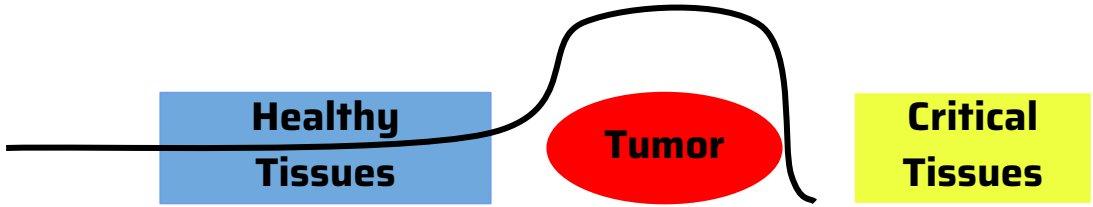

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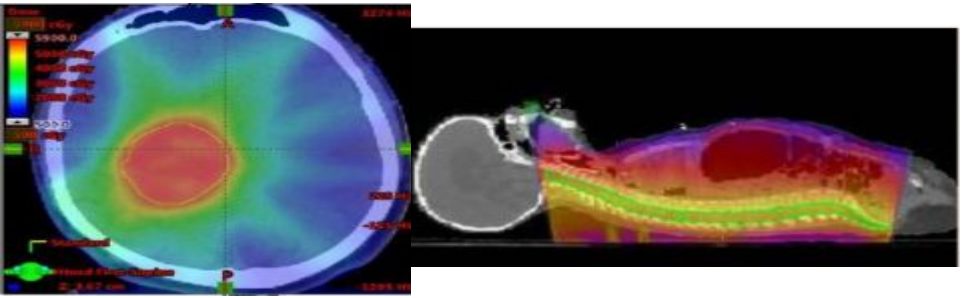

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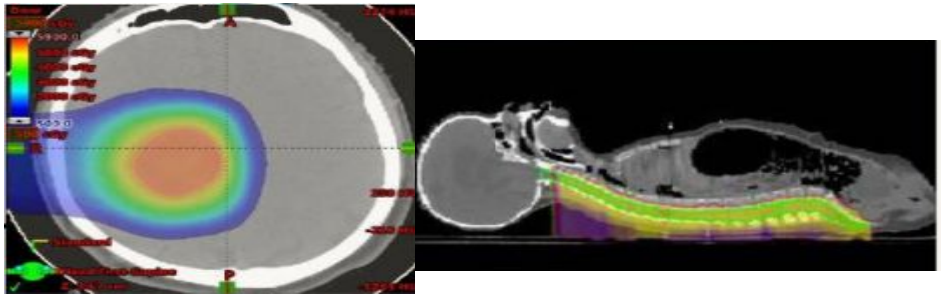
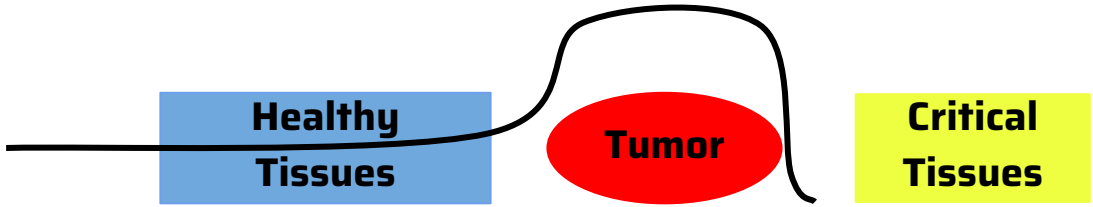


- Little to no radiation behind the tumor

Proton therapy

Spread-Out Bragg Peak



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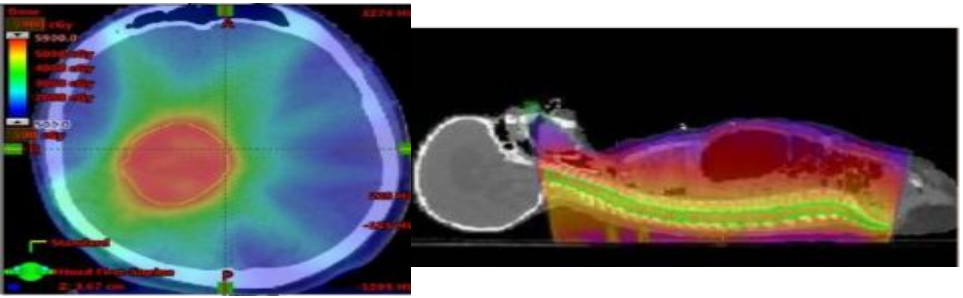
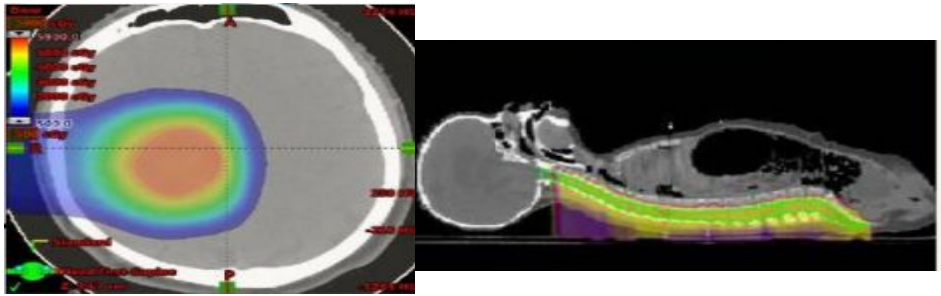


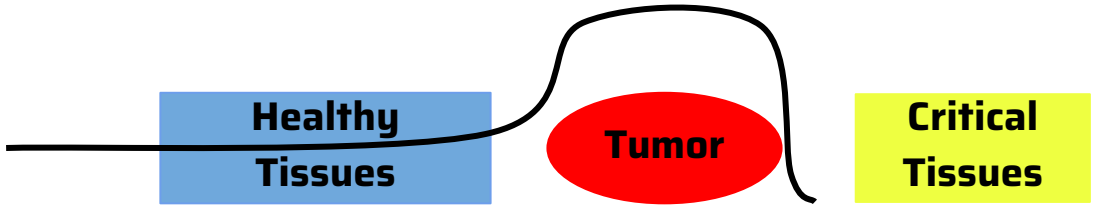
Proton



- Little to no radiation behind the tumor
- Low integral dose per treatment

Proton therapy

Spread-Out Bragg Peak



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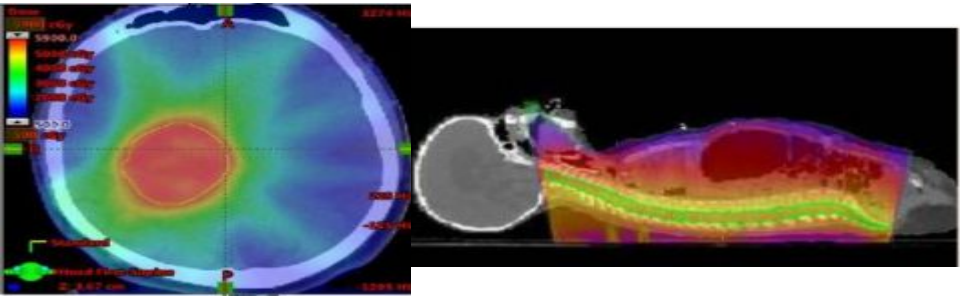
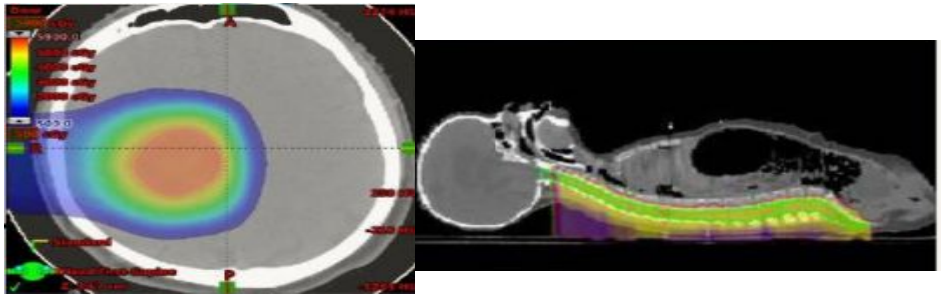


Proton



- Little to no radiation behind the tumor
- Low integral dose per treatment
- Can reduce side effects

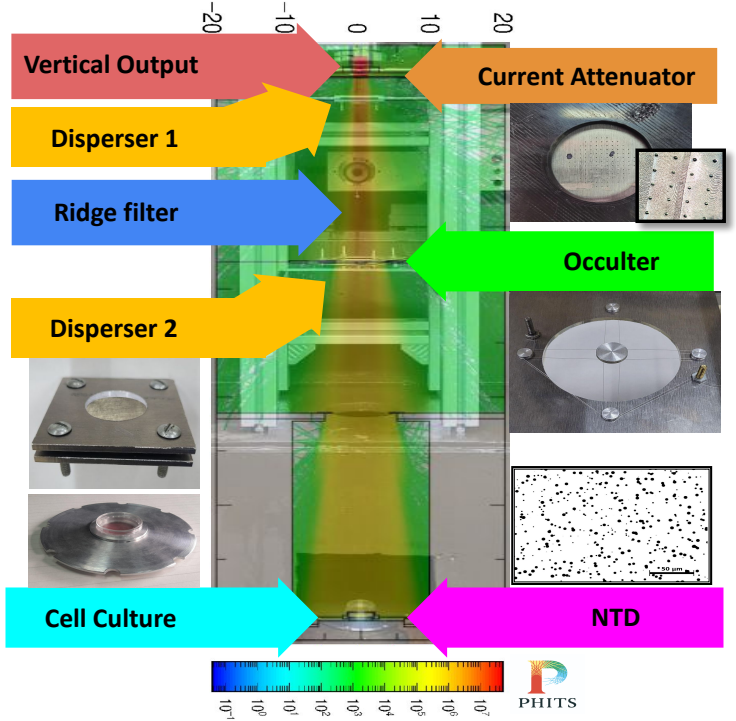
Implementation of vertical proton beam

TANDAR

External Vertical Beam for radiobiological studies in Proton Therapy

Implementation of vertical proton beam

Shaping systems

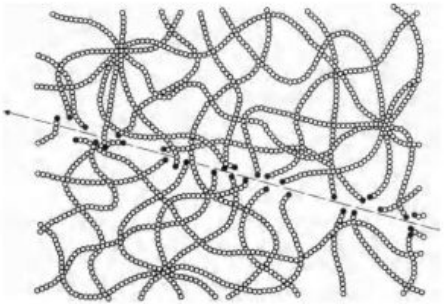


TANDAR

External Vertical Beam for radiobiological studies in Proton Therapy

Characterization of vertical proton beam

nuclear track detectors (NTD)



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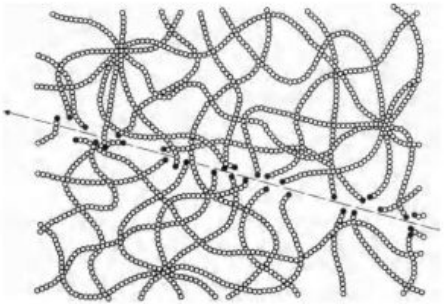

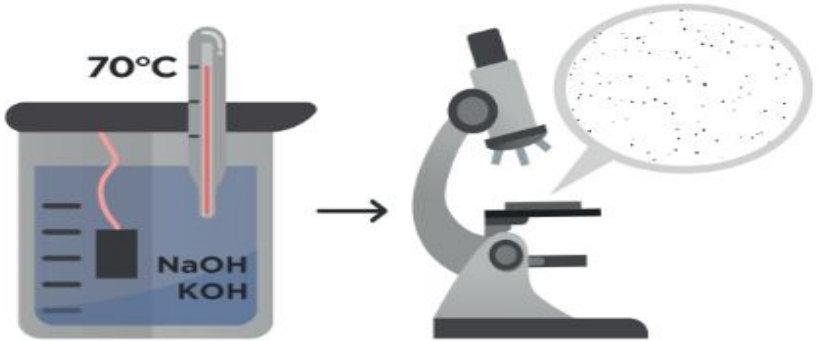

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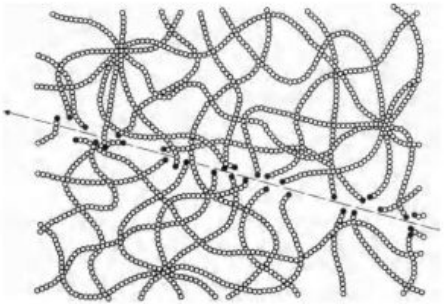

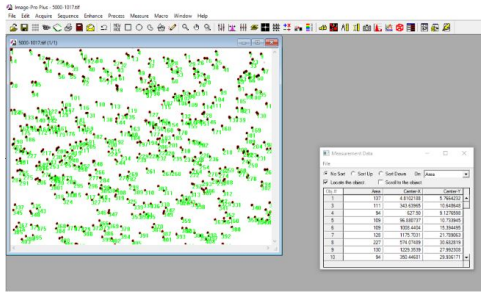

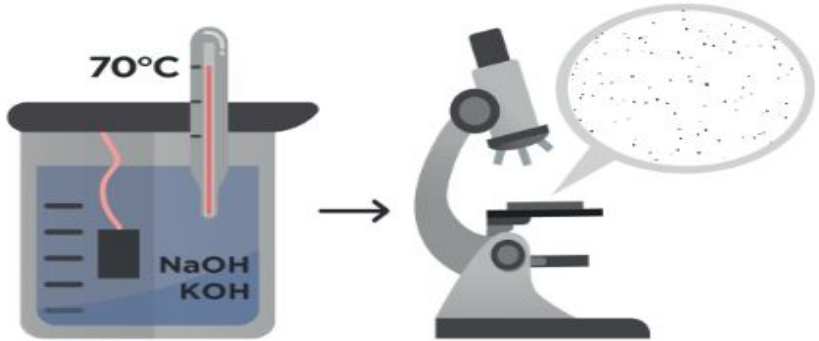

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External Vertical Beam for radiobiological studies in Proton Therapy

Radiobiological studies

CeArP

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Radiobiological studies

CeArP

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Study of biophysical models of radiation damage

Proton therapy

Radiobiological studies

CeArP

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Study of biophysical models of radiation damage

Proton therapy and more

Extrapolation of Proton Therapy Models

Space Radiation for Astronauts

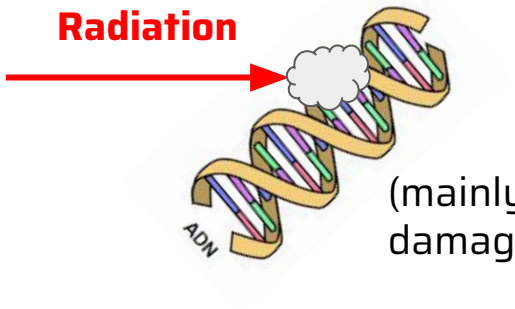
Biological risks: cancer, cardiovascular diseases, central nervous system damage, and other degenerative effects.

Extrapolation of Proton Therapy Models

Space Radiation for Astronauts

Biological risks: cancer, cardiovascular diseases, central nervous system damage, and other degenerative effects.

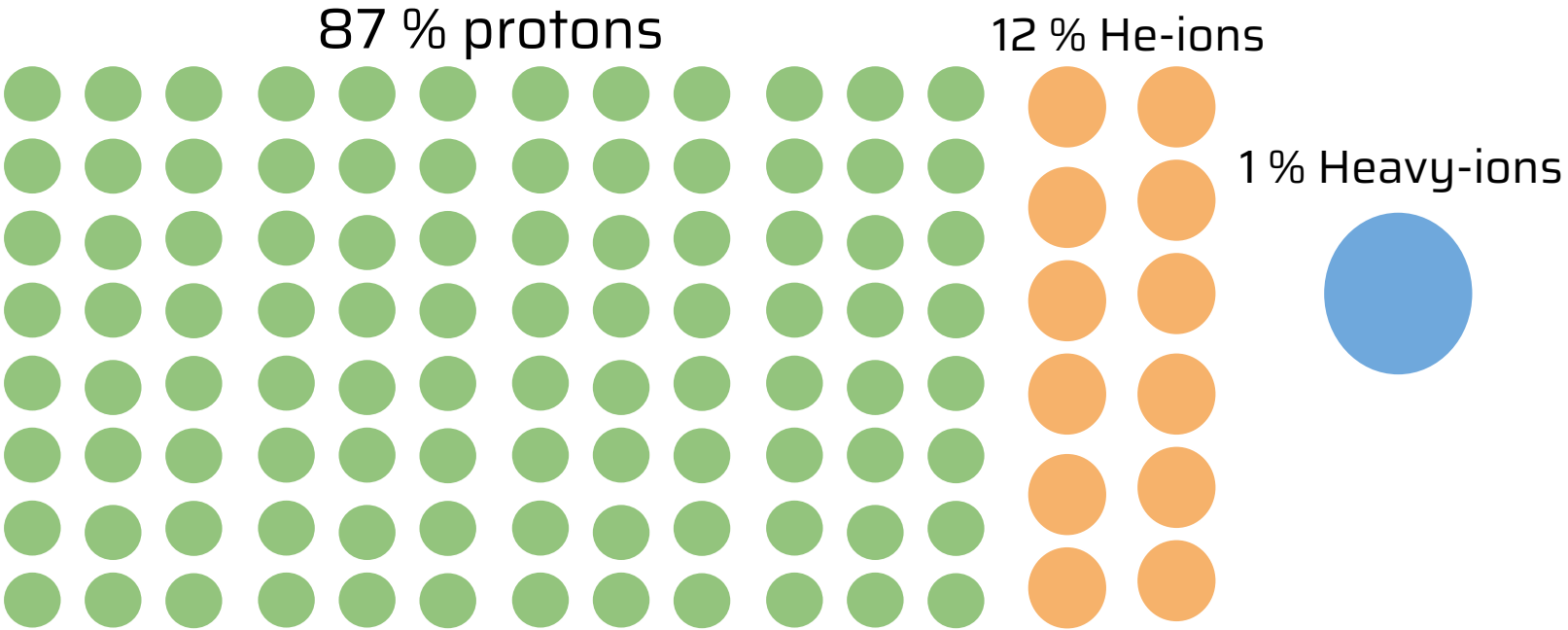
Biological damage



(mainly, cell death and chromosome damage)

Space Radiation in free space

Galactic Cosmic Rays (GCR)



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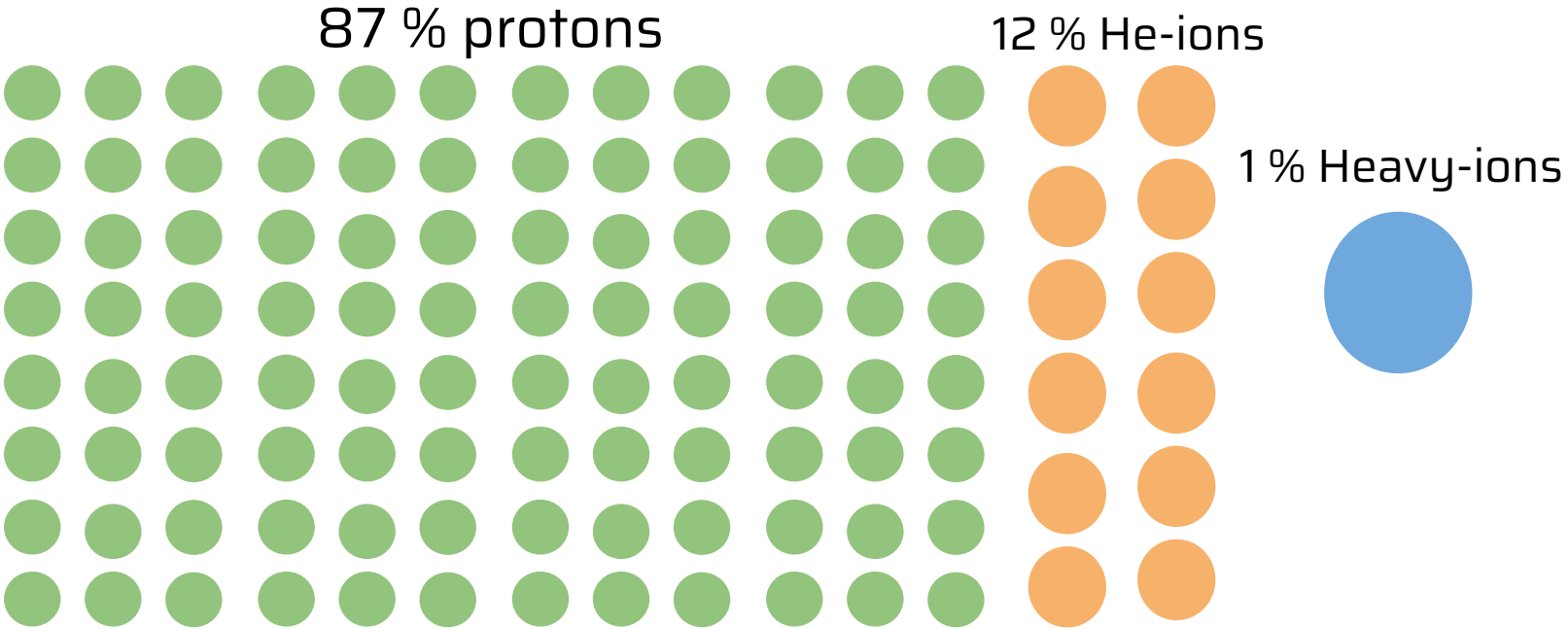
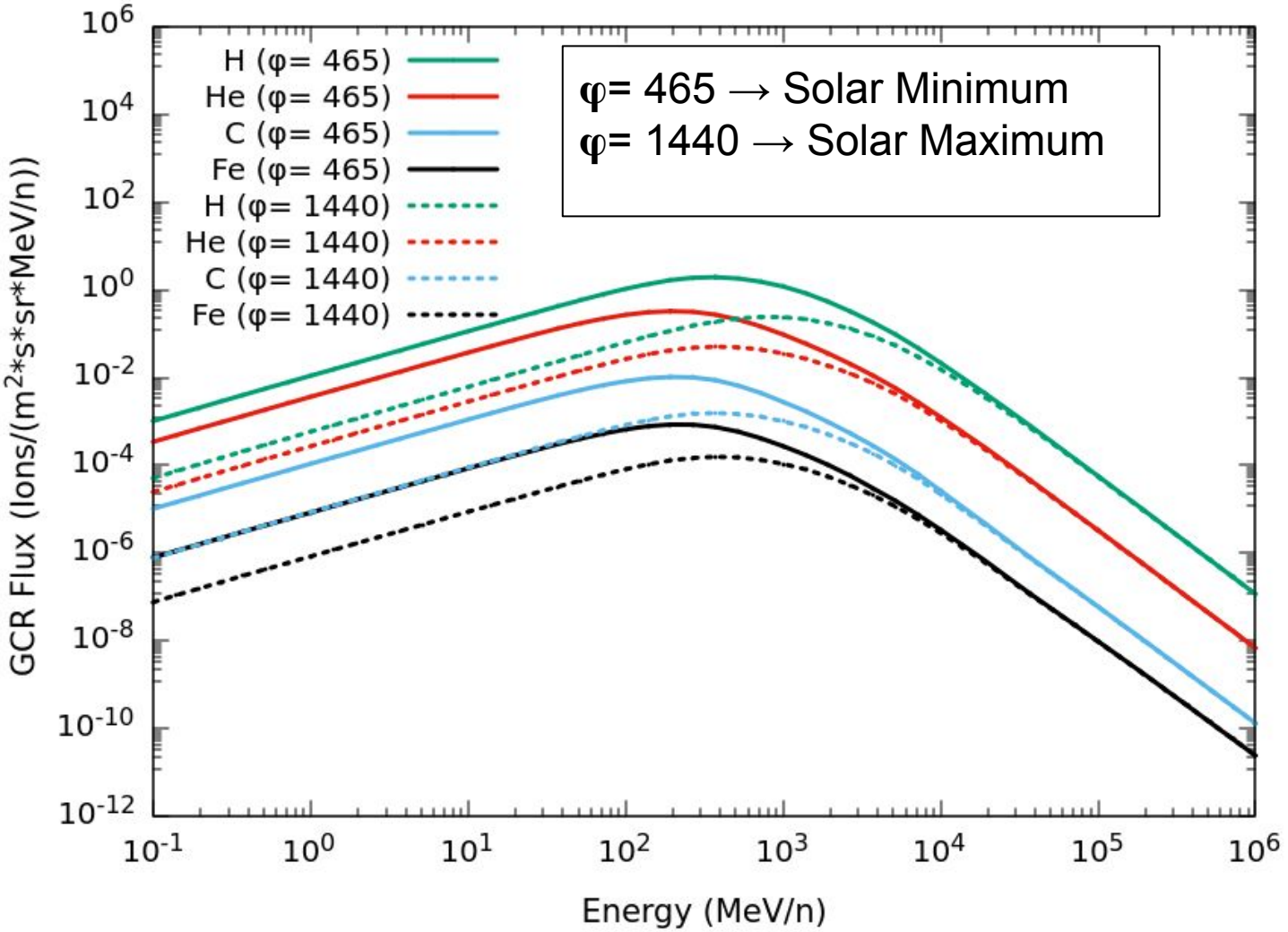
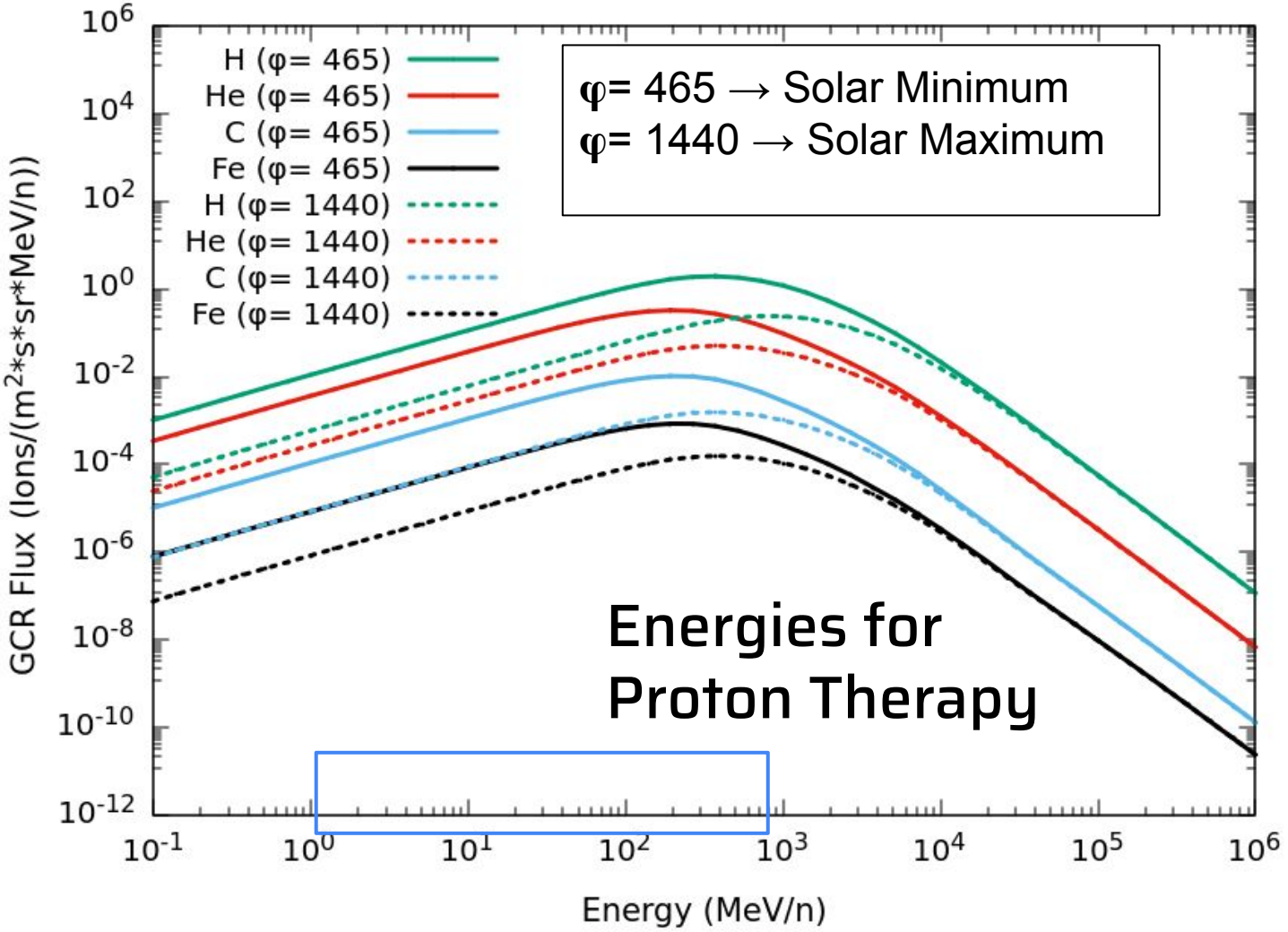


Maximum Dose Rate = 0.5 mGy/day


H (φ= 465)
He (φ= 465)
C (φ= 465)
Fe (φ= 465)
H (φ= 1440)
He (φ= 1440)
C (φ= 1440)
Fe (φ= 1440)
φ= 465 → Solar Minimum
φ= 1440 → Solar Maximum
GCR Flux (Ions/(m2*s*sr*MeV/n))
Energy (MeV/n)
10^6
10^4
10^2
10^0
10^-2
10^-4
10^-6
10^-8
10^-10
10^-12
10^-1
10^0
10^1
10^2
10^3
10^4
10^5
10^6


H (φ= 465)
He (φ= 465)
C (φ= 465)
Fe (φ= 465)
H (φ= 1440)
He (φ= 1440)
C (φ= 1440)
Fe (φ= 1440)
φ= 465 → Solar Minimum
φ= 1440 → Solar Maximum
Energies for Proton Therapy
GCR Flux (Ions/(m2*s*sr*MeV/n))
Energy (MeV/n)
10^6
10^4
10^2
10^0
10^-2
10^-4
10^-6
10^-8
10^-10
10^-12
10^-1
10^0
10^1
10^2
10^3
10^4
10^5
10^6

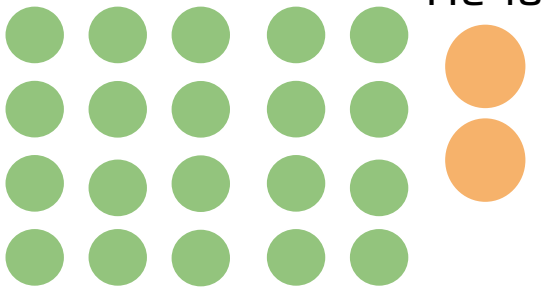
Space Radiation in free space

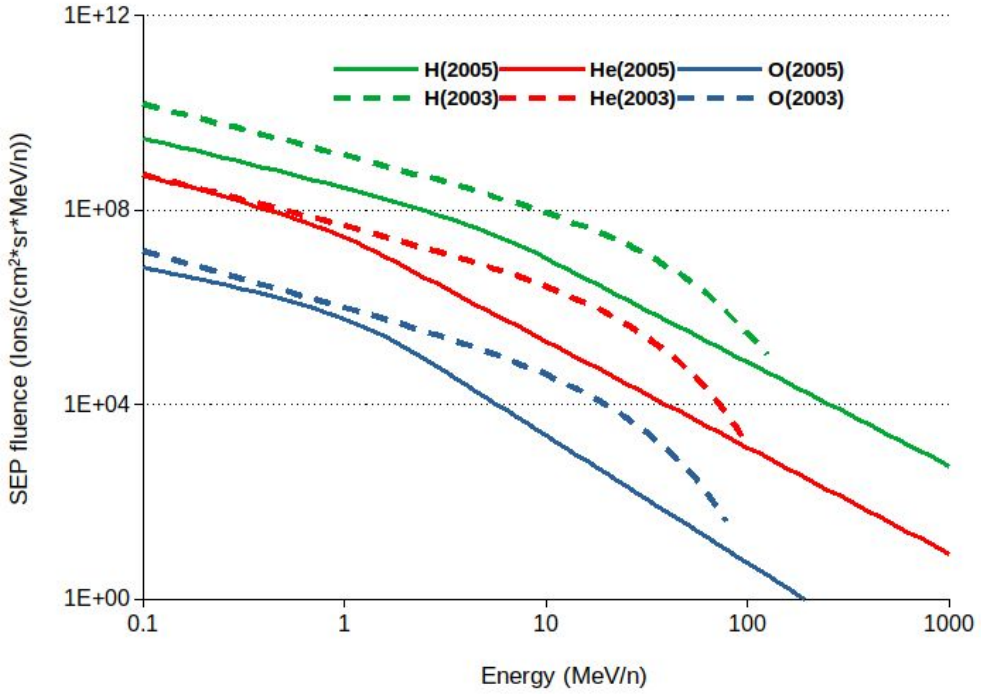
Solar Particle Events (SPE)

- Up to 10^{11} particles.cm^{-2} in few hours, mainly protons

Protons

He-ions





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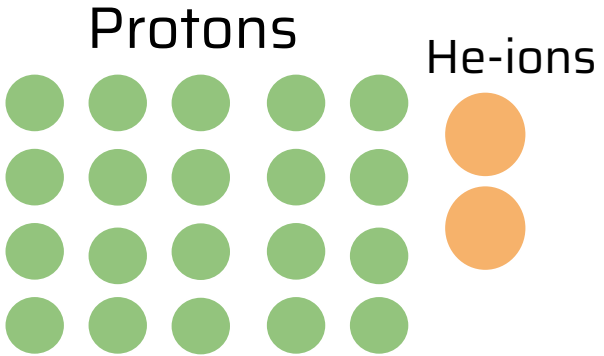

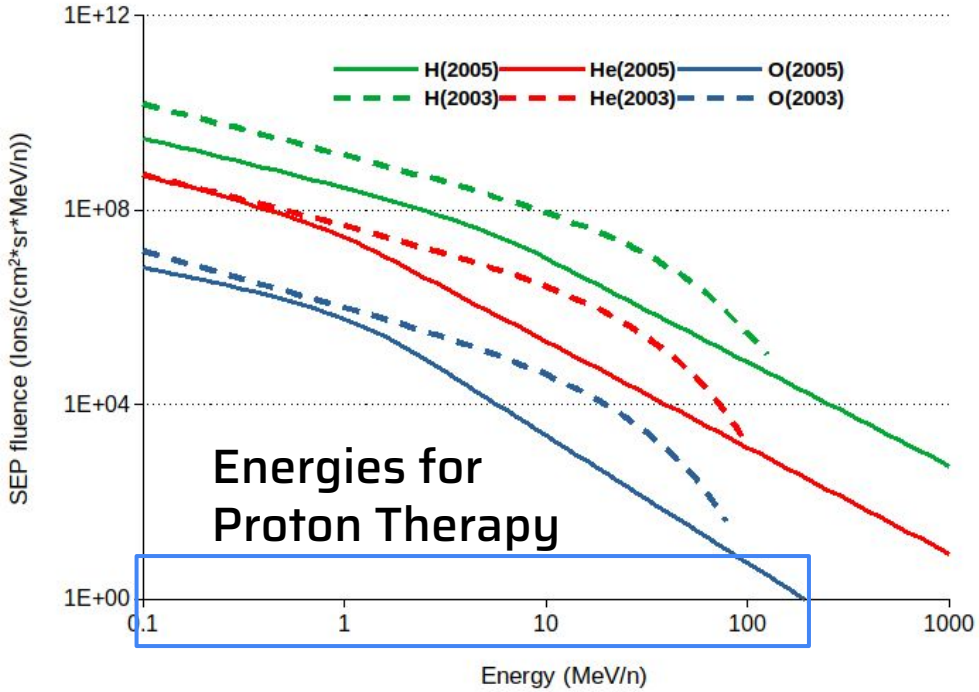

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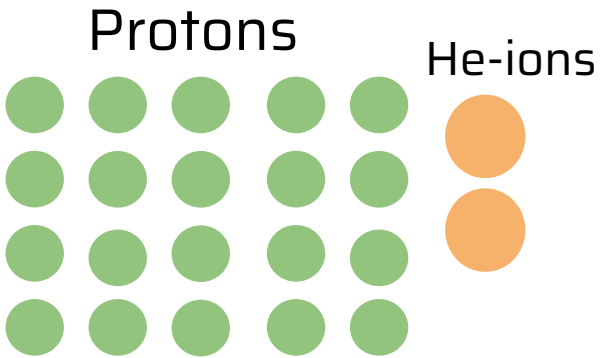
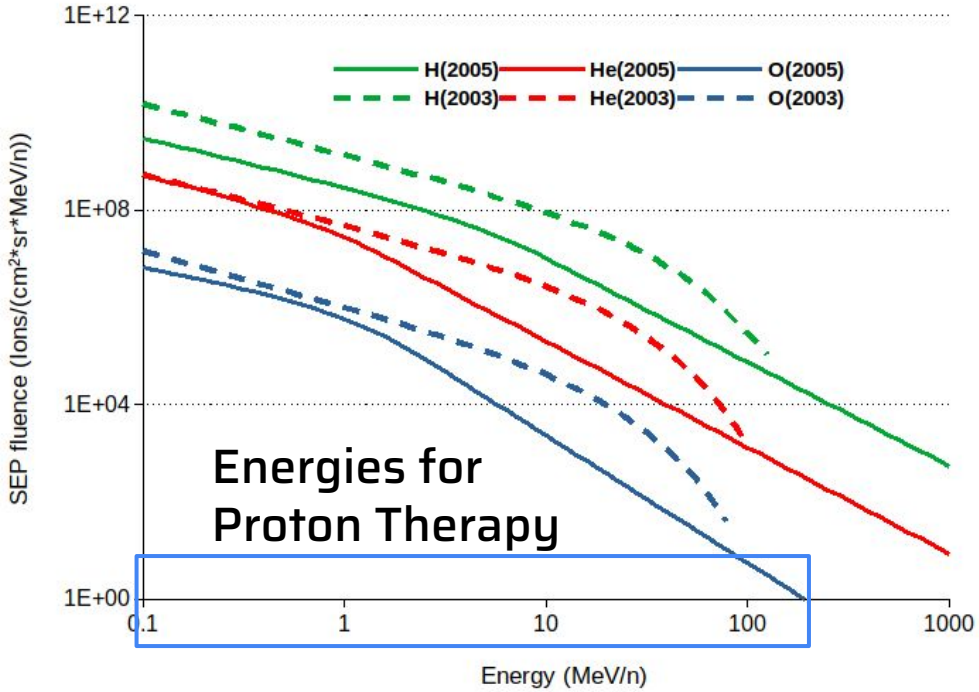


Dose → 1 Gy/event



Similarities

proton therapy and space radiation

Particle: Proton

Energy range: (0-260 MeV)

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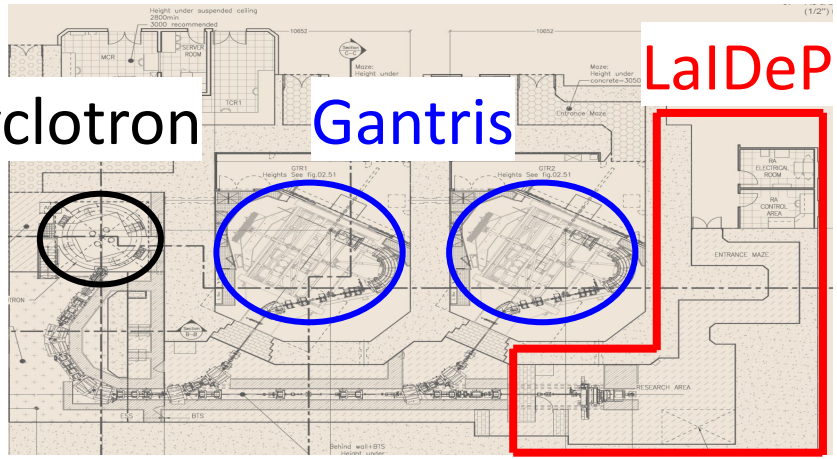
CeArP



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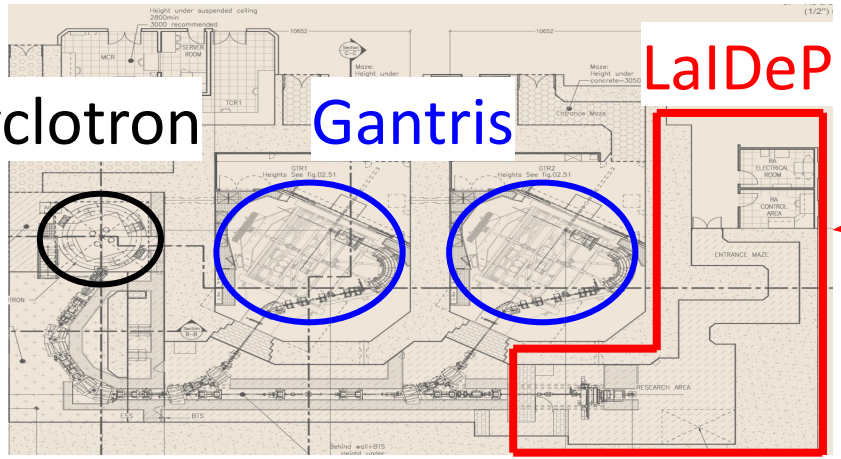

Dose Rate

Solar Particle Events (SPE)

Dose→ Gy/event (≈ 1Gy/h)

Proton Therapy

Dose Rate ≈ 1 Gy/min

Dose Rate

Solar Particle Events (SPE)

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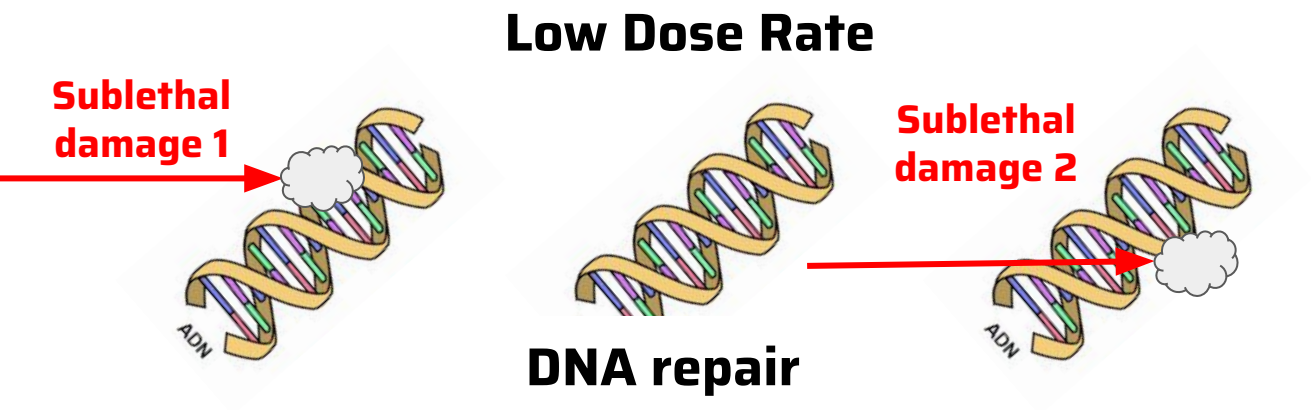
Proton Therapy

Dose Rate ≈ 1 Gy/min



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Proton Therapy

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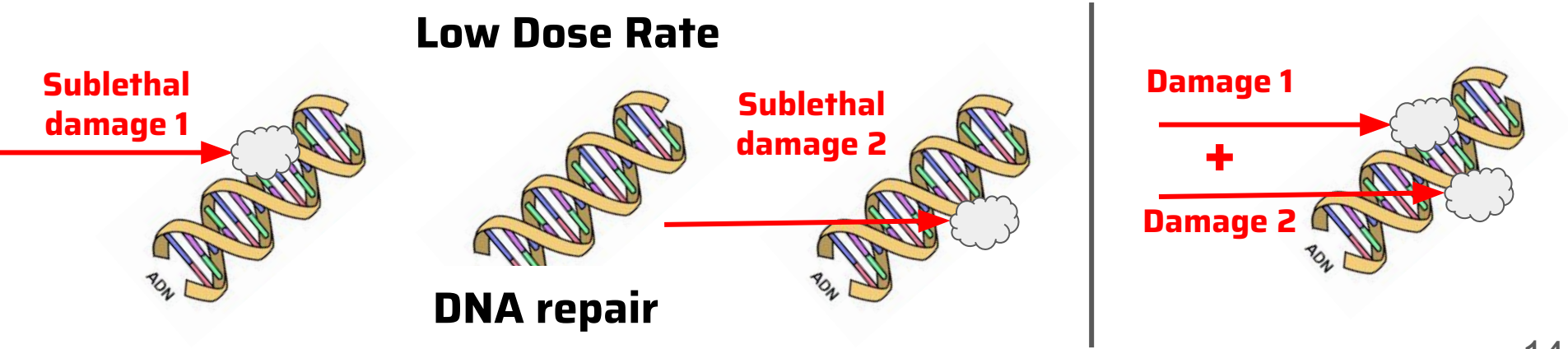


Research in Pavia

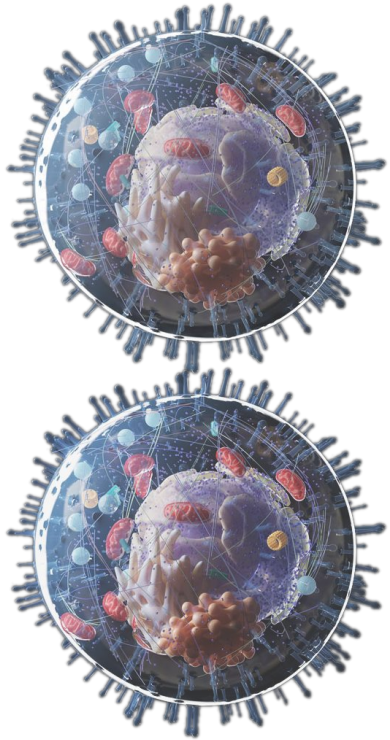
“Incorporation of dose-rate effects into the BIANCA biophysical model and application for space radiation risk assessment”

ARES project
Istituto Nazionale di Fisica Nucleare

which investigates the biological risks associated with space radiation exposure of astronauts.

Relative biological effectiveness

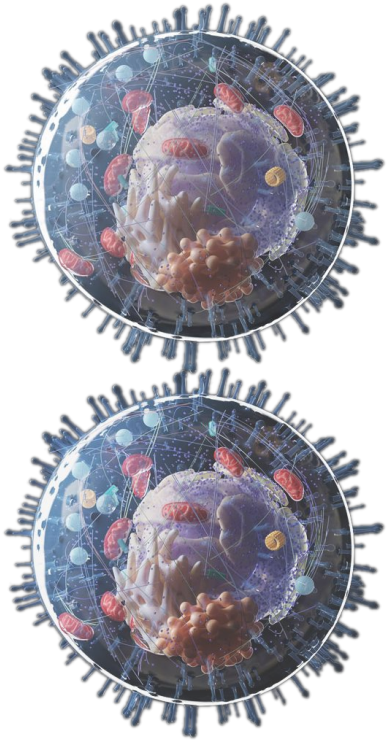
$$RBE = \frac{Dose_{photons}}{Dose_{space\ radiation}}$$



Same biological effect

Relative biological effectiveness

$$RBE = \frac{Dose_{photons}}{Dose_{space\ radiation}} = 1.5$$



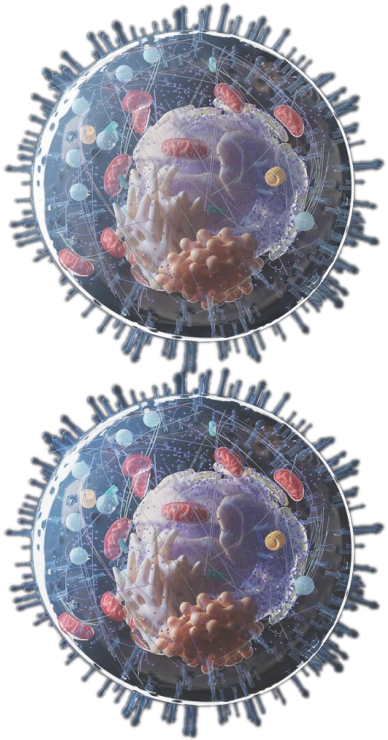
Same biological effect

Relative biological effectiveness

$$RBE = \frac{Dose_{photons}}{Dose_{space\ radiation}}$$

1.5

1 Gy



Same biological effect

Relative biological effectiveness

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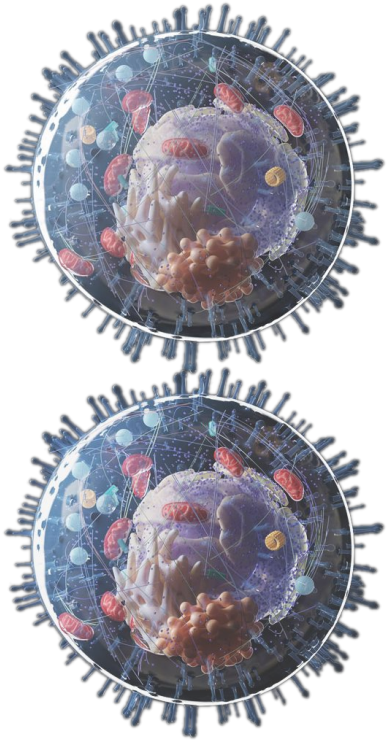
1.5

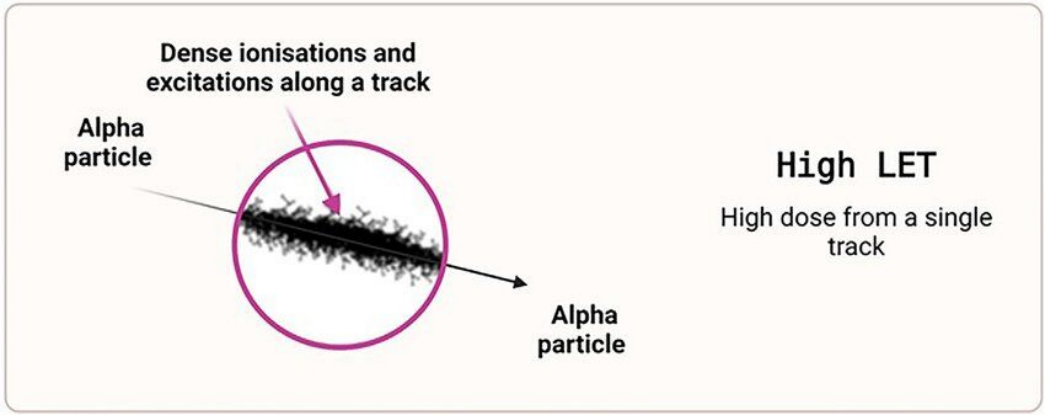
1.5 Gy

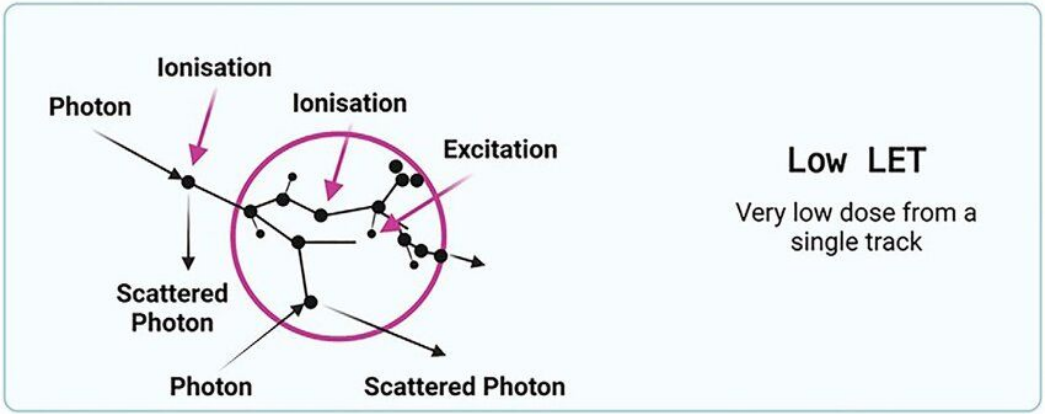
1 Gy



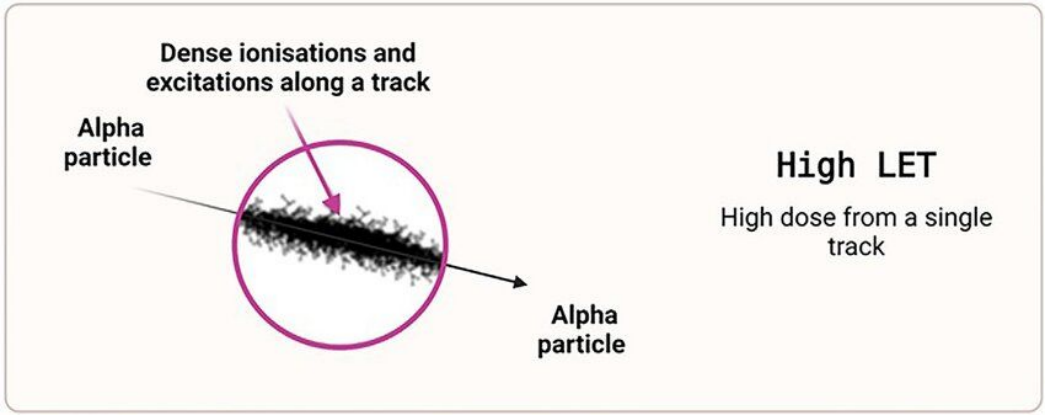
Same biological effect

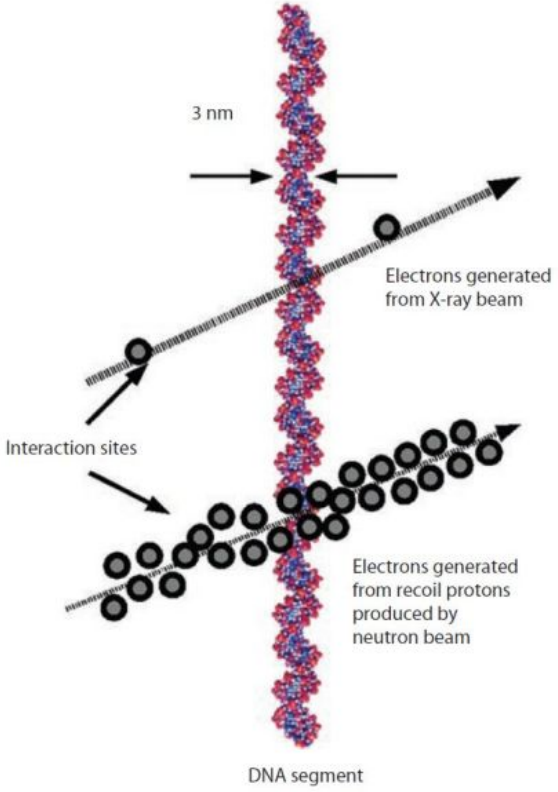
Linear Energy Transfer (LET)





Linear Energy Transfer (LET)





NCRP recommendations on the RBE values for non-cancer effects.

Radiation Type	Recommended RBE	Range
1 to 5 MeV neutrons	6.0	4-8
5 to 50 MeV neutrons	3.5	2-5
Heavy ions	2.5	1-4
Protons > 2 MeV	1.5	-

Fixed values

NCRP recommendations on the RBE values for non-cancer effects.

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Fixed values

WP1 – Space radiation effects computational studies

ARES Project

Grant Giovani in CSN5 – 2023/2024

PI: Ricardo Ramos

WP1 – Space radiation effects computational studies

Particle transport Code

Physics

ARES Project

Grant Giovani in CSN5 – 2023/2024

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WP1 – Space radiation effects computational studies

Particle transport Code + BIANCA Model

Physics

Biological damage

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WP1 – Space radiation effects computational studies

Particle transport Code + BIANCA Model → RBE depending on LET, particle and dose

Physics

Biological damage

ARES Project

Grant Giovani in CSN5 – 2023/2024

PI: Ricardo Ramos

WP1 – Space radiation effects computational studies

Particle transport Code + BIANCA Model → RBE depending on LET, particle and dose

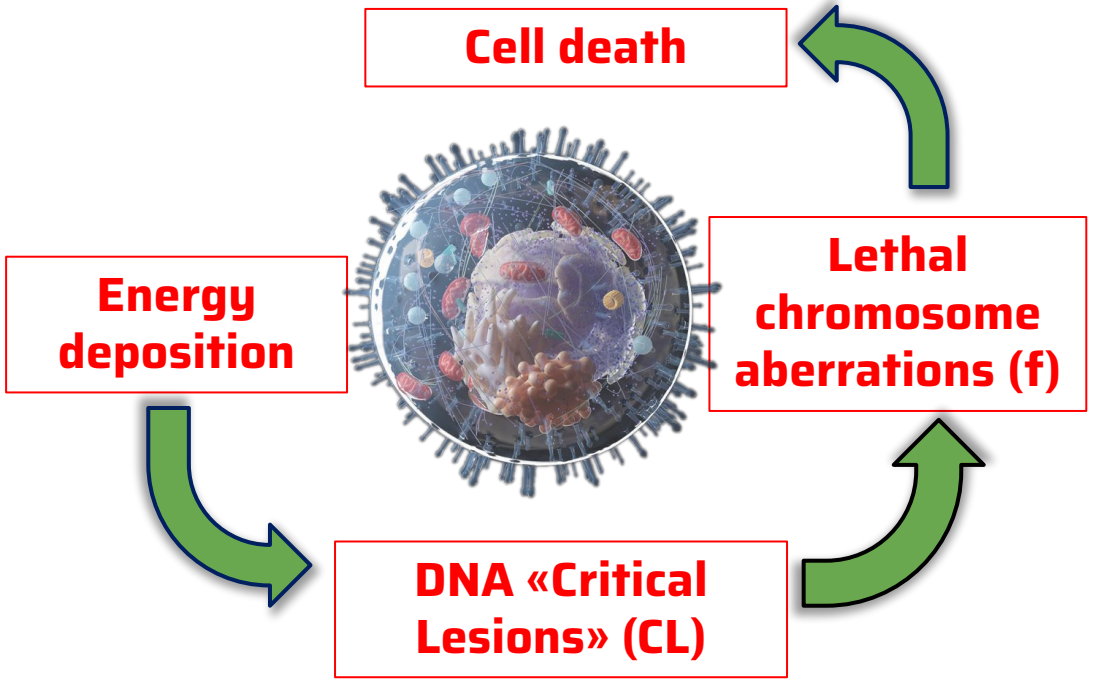
Physics

Biological damage

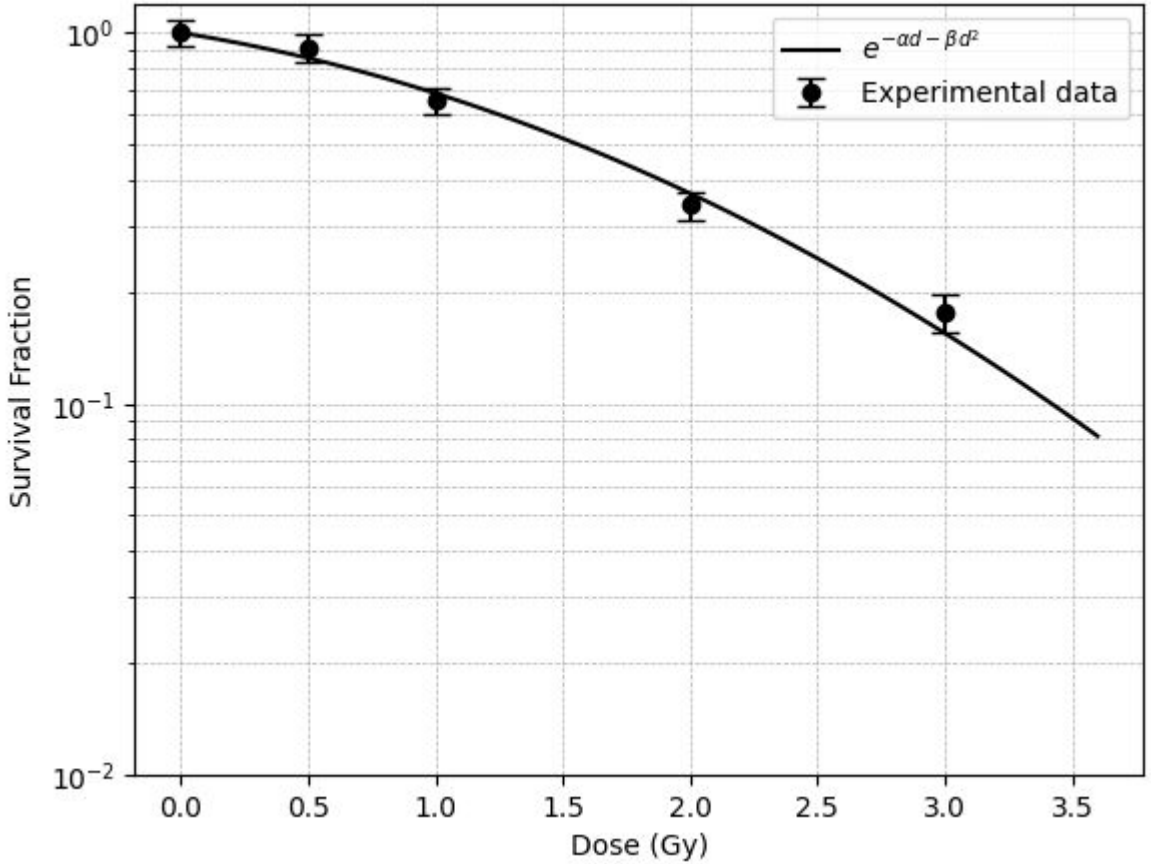
+ dose rate

BIANCA model developed in Pavia

Main assumption: DNA “critical lesions” lead to chromosome aberrations, and some chromosome aberrations (e.g., dicentrics) lead to cell death



Linear-quadratic cell survival model



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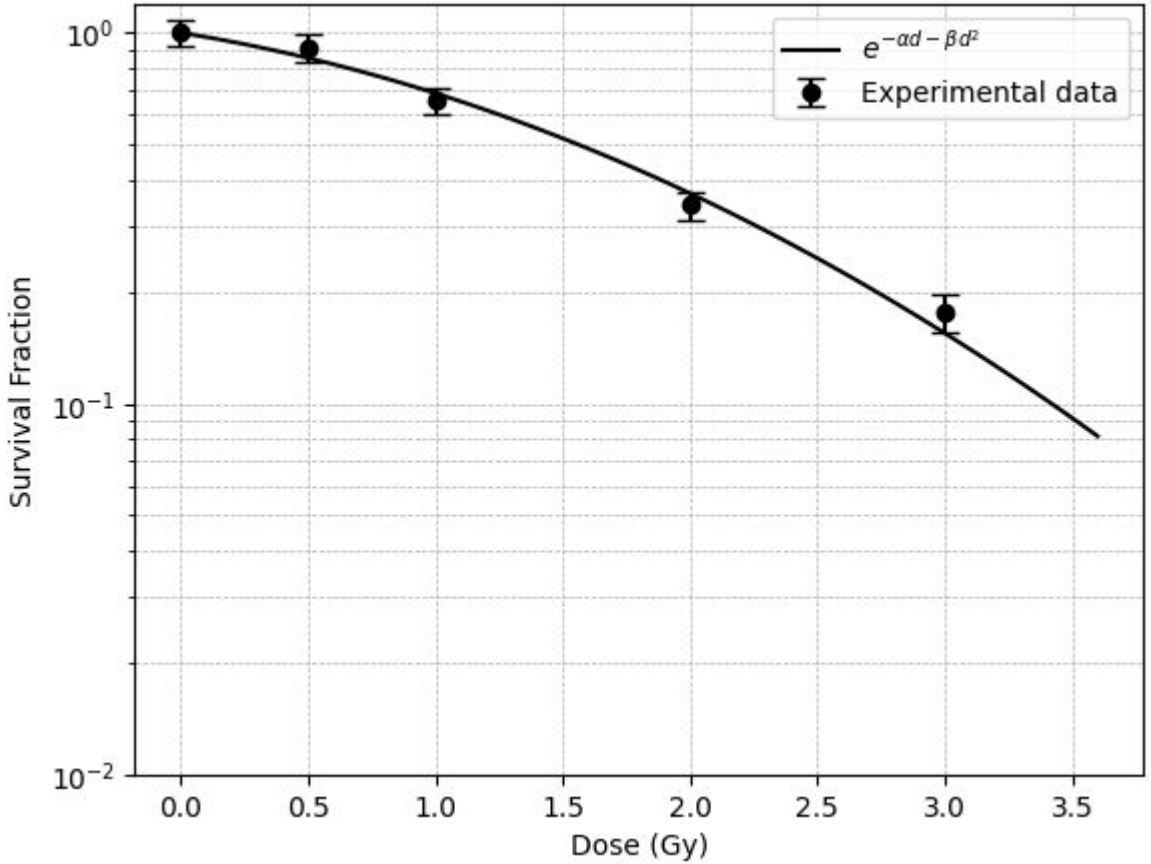
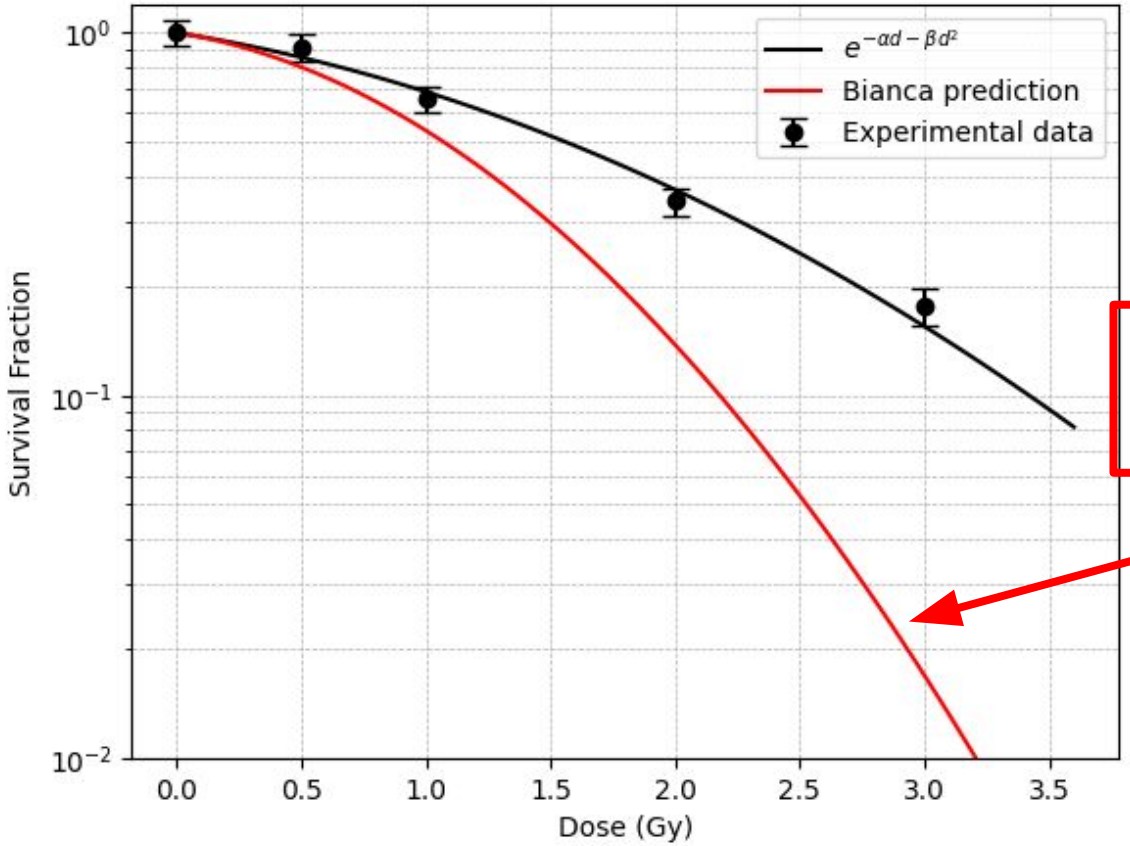


$$S(D_i) = \exp -(\alpha_i D_i + \beta_i D_i^2)$$

Linear-quadratic cell survival model



$$S(D_i) = \exp -(\alpha_i D_i + \beta_i D_i^2)$$

Prediction for Different LET

BIANCA model

Example of radiobiological database for V79:

```
Z=1 A=1,2,3
LET     alfa                beta
5      0.161168003608071 0.034227925863557
7.5    0.219155512347106 0.031807059167825
10     0.277730304065006 0.026062986984213
12.5   0.324223249128924 0.031963531745716
15     0.370061833526514 0.032195025167274
17.5   0.421451839190716 0.031121716722449
20     0.482515824349661 0.028525693688078
22.5   0.560520033338037 0.018863044675061
25     0.613244623202487 0.019486893814967
27.5   0.670278414247874 0.018719108913174
30     0.723636950773347 0.019048357687813

Z=2  A=3 (He3)
LET     alfa                beta
5    0.134484868252636 0.033328267759041
10   0.144914045351193 0.039167916406686
20   0.195309536204132 0.055766427339300
30   0.254263496879065 0.086614721872234
40   0.346232798363745 0.110820821623133
50   0.461751927355611 0.125899692117198
60   0.577156328111620 0.149414730517834
70   0.688177599469057 0.170307321062664
80   0.831202131850177 0.173711239896555
90   0.958976414546513 0.178987749762615

Z=2 A=4 (He4)
LET     alfa                beta
5    0.122919965474113 0.0282243396663055
10   0.164742642147497 0.0320256389518587
```

Cell death for each ion and LET:

$$S(D_i) = \exp -(\alpha_i D_i + \beta_i D_i^2)$$

Lea-Catcheside Model

$$S(D_i) = \exp -(\alpha_i D_i + \mathbf{G(\mu T)} * \beta_i D_i^2)$$

Lea-Catcheside Model

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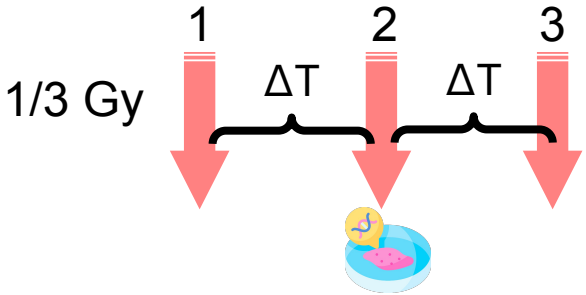
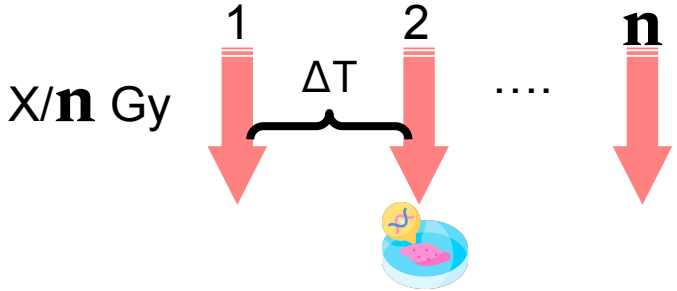
High-dose-rate fractions

1 Gy Triple fraction



X Gy **n** fraction



Lea-Catcheside Model

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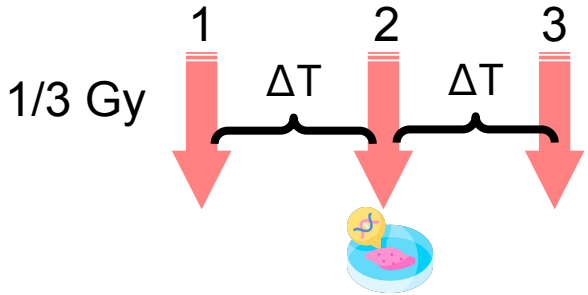
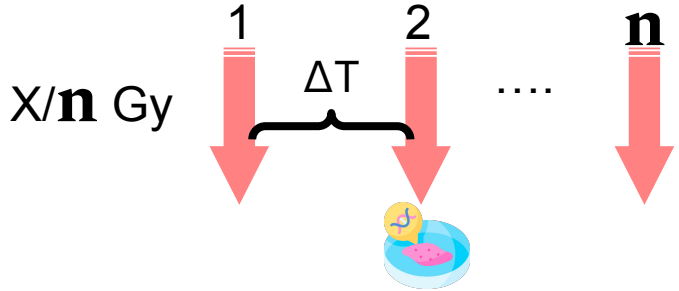


X Gy **n** fraction



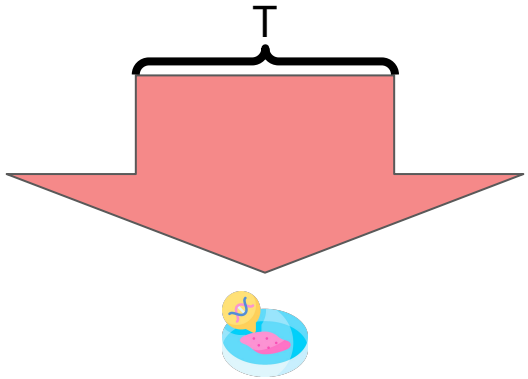
High-dose-rate fractions → $\mathbf{G} = \frac{1}{n}\left[1 + \frac{2}{n}\frac{\theta}{1-\theta}\left(n - \frac{1-\theta^n}{1-\theta}\right)\right]$ $\theta = e^{-\mu\,\Delta T}$

μ is the DNA repair rate constant

Lea-Catcheside Model

$$S(D_i) = \exp -(\alpha_i D_i + \mathbf{G(\mu T)} * \beta_i D_i^2)$$

Continuous low-dose rate



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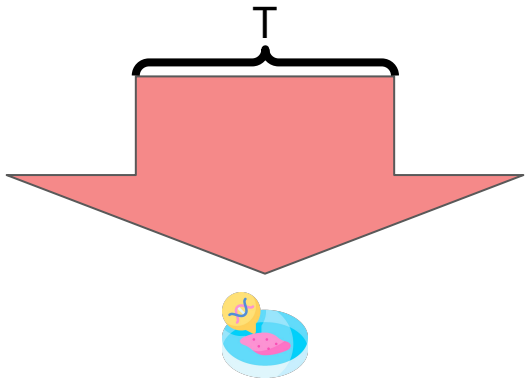

Continuous low dose rate → $\mathbf{G} = \frac{2}{\mu T}\left(1 - \frac{1 - e^{-\mu T}}{\mu T}\right)$

T is the irradiation duration

μ is the DNA repair rate constant

BIANCA (α_i,β_i) + Lea-Catcheside

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```
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Z=2 A=4 (He4)
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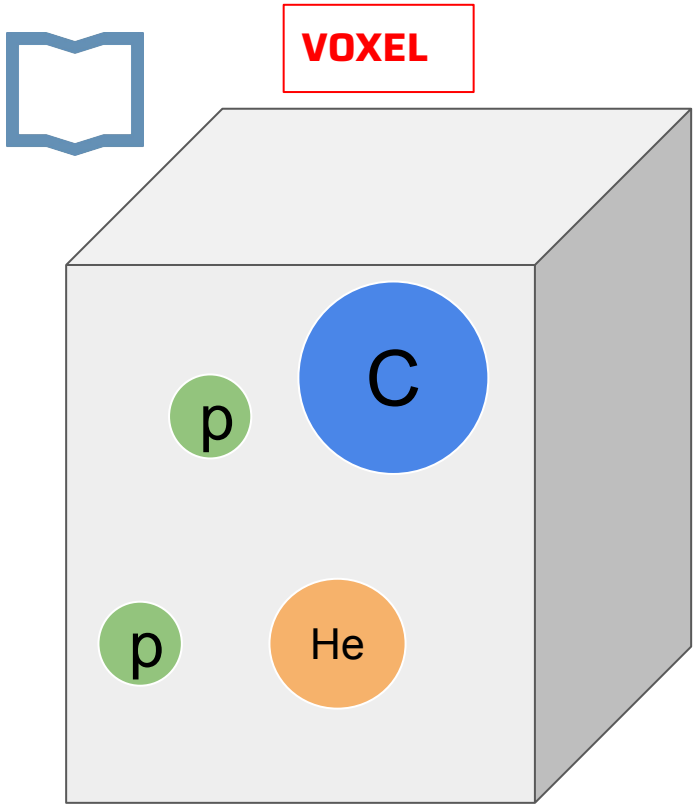
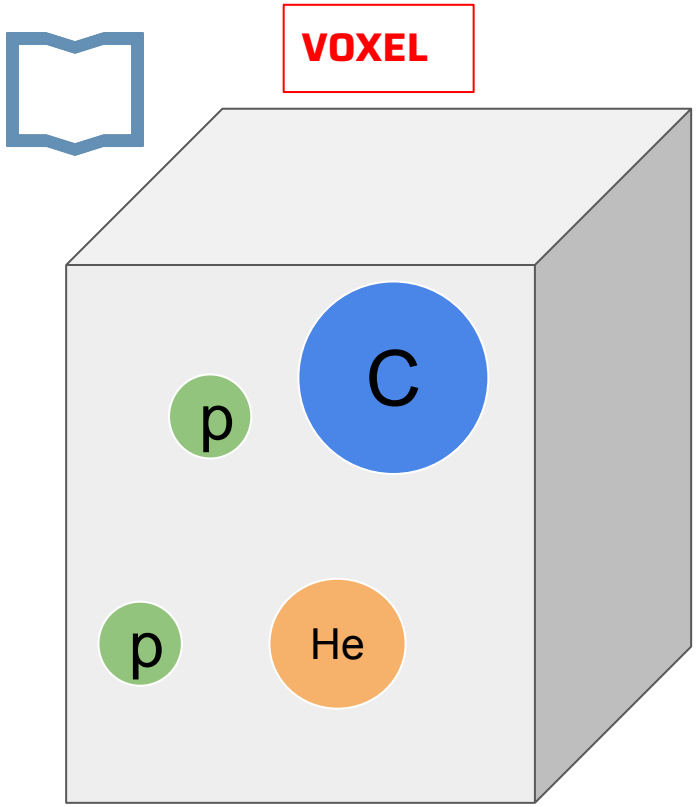


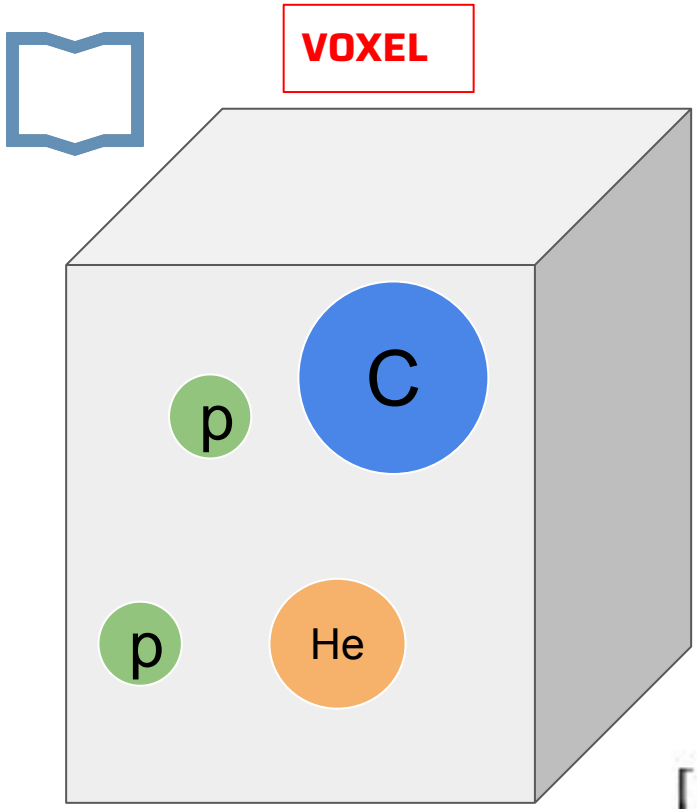
Particle Transport Code
Dose (D_i), LET, particle



Particle Transport Code
Dose (D_i), LET, particle

BIANCA (α_i,β_i) + Lea-Catcheside

$$\alpha = \frac{\sum_i \alpha_i D_i}{\sum_i D_i} \qquad \sqrt{\beta} = \frac{\sum_i \sqrt{\beta_i} D_i}{\sum_i D_i}$$



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$$D_X = \frac{\left[-\alpha_X + \sqrt{\alpha_X^2 + 4\beta_X \ln S}\right]}{2\beta_X}$$

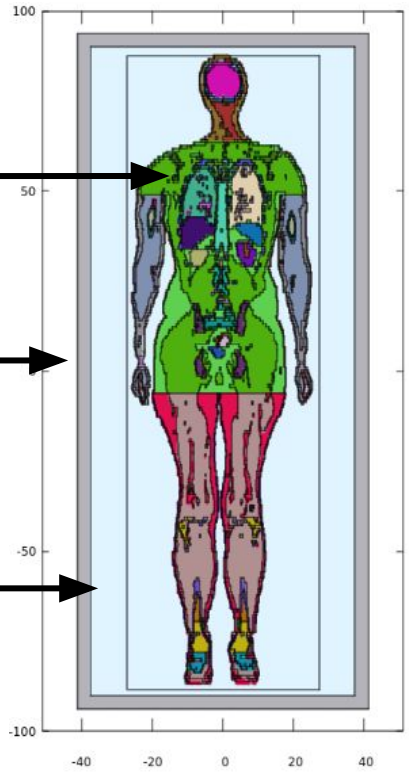
RBE= D_x/D **VOXEL**

SPE: DOSE and RBE calculations

Male and female ICRP phantoms

Cylindrical Al shielding (r=38cm, h=180cm)

Variable thickness (from 0 to 30 g/cm^2)



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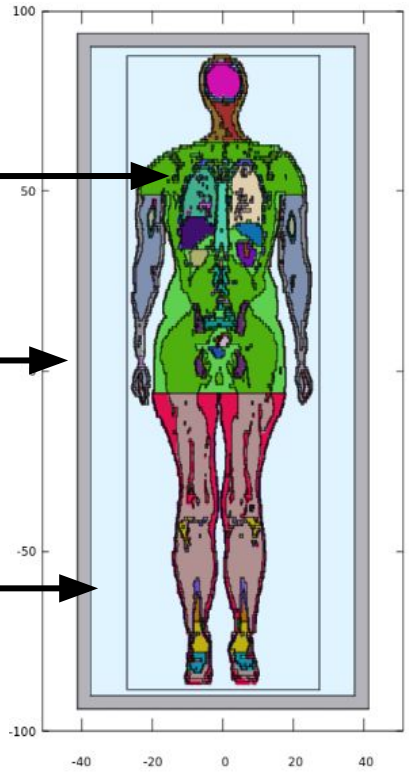

Solar Particle Events of August 1972

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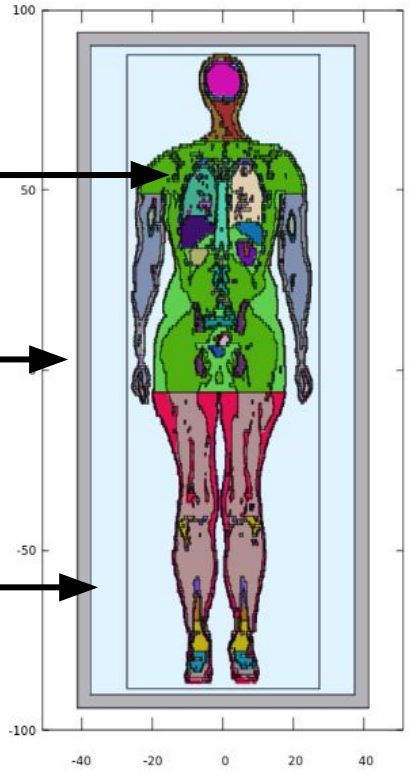


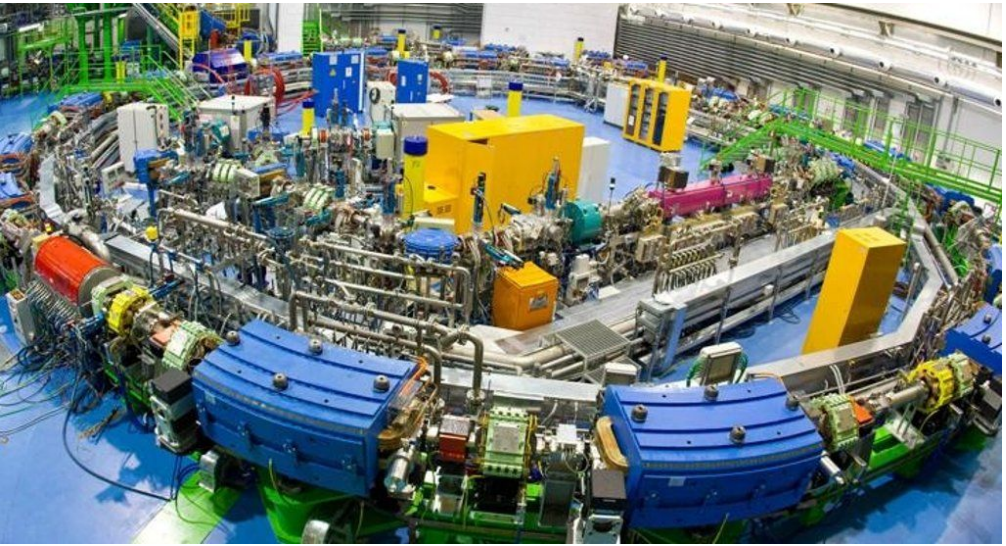
Solar Particle Events of August 1972

Organ	D (mGy)	RBE	G (mGy-eq)	H (mSv)
Av. Skin	444.62	1.47	655.43	669.79
BFO	129.69	1.57	203.14	210.45
Colon	121.24	1.58	191.56	196.91
Lung	150.15	1.56	234.45	239.67
Stomach	113.81	1.58	180.25	186.29
Breast	343.03	1.49	512.62	545.75
Heart	110.05	1.59	174.58	181.03
Bladder	122.50	1.57	192.58	195.00
Oesophagus	110.05	1.59	174.58	181.03
Liver	121.86	1.58	192.37	197.80
Uterus/Cervix	64.25	1.68	108.20	118.08
Ovaries	64.02	1.68	107.44	11

Model validation

CNAO

The National Center for Oncological Hadrontherapy

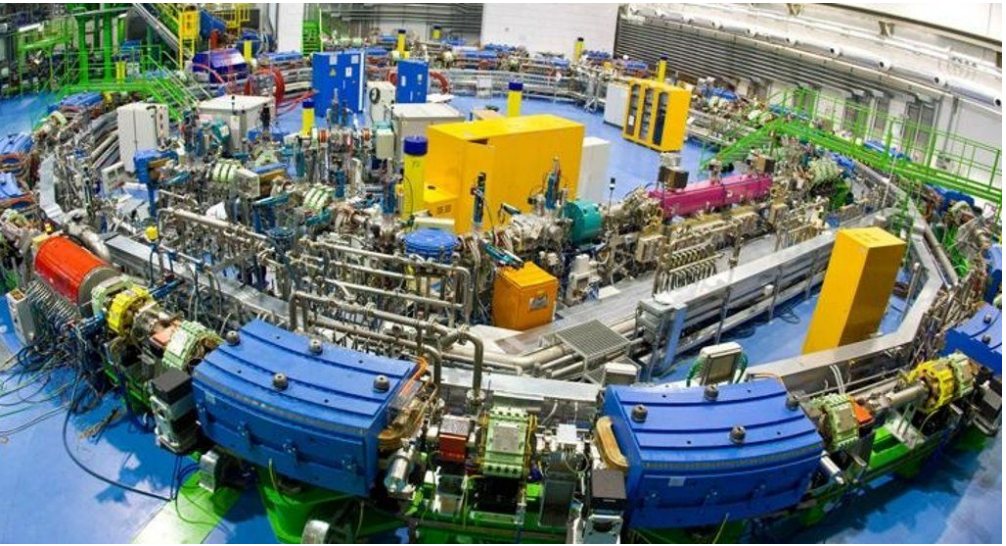


Irradiation of **AG01522** human fibroblast cells with different dose fractionations

Model validation

CNAO

The National Center for Oncological Hadrontherapy

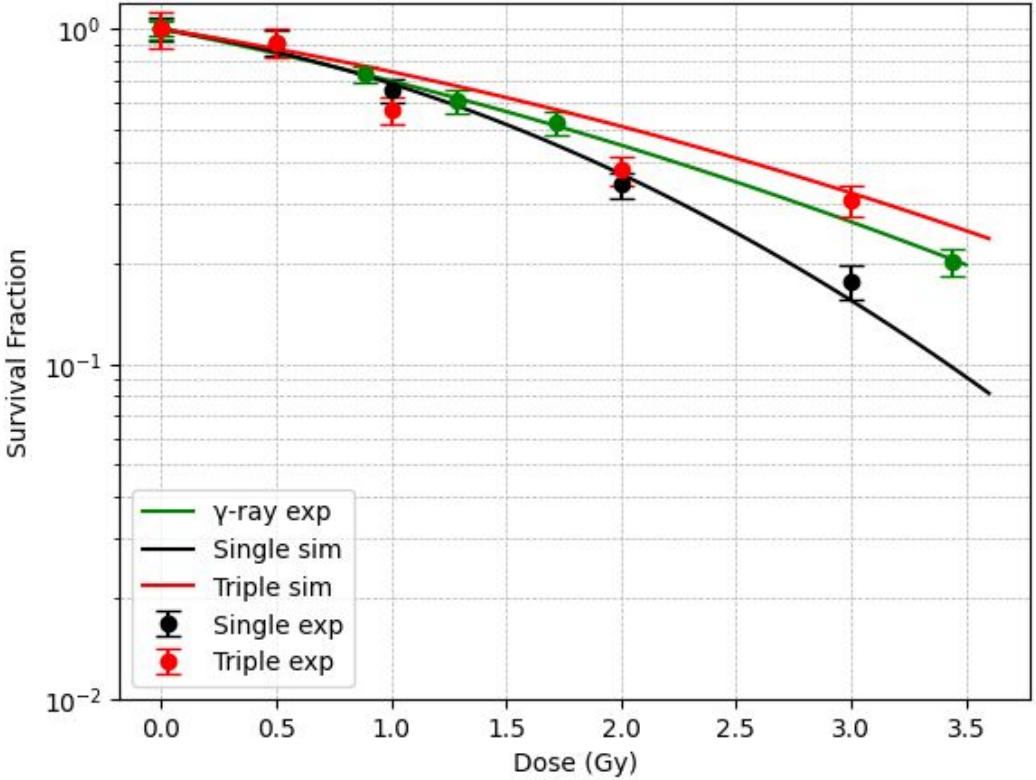


Irradiation of **AG01522** human fibroblast cells with different dose fractionations

combined with experimental data from the literature

Lea-Catcheside Model validation

AG01522 human fibroblast cells irradiated at the **CNAO** center, 0.70 keV/µm proton



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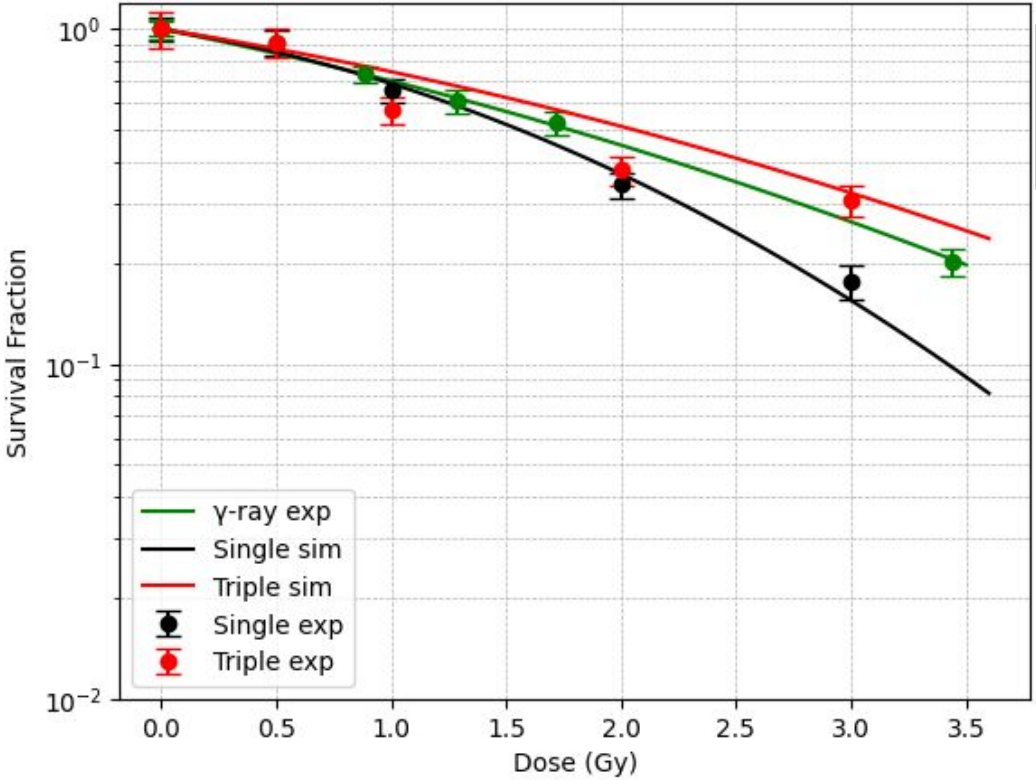

Single fraction experimental data
— Coefficients α and β for single fraction irradiation were obtained using BIANCA

Lea-Catcheside Model validation

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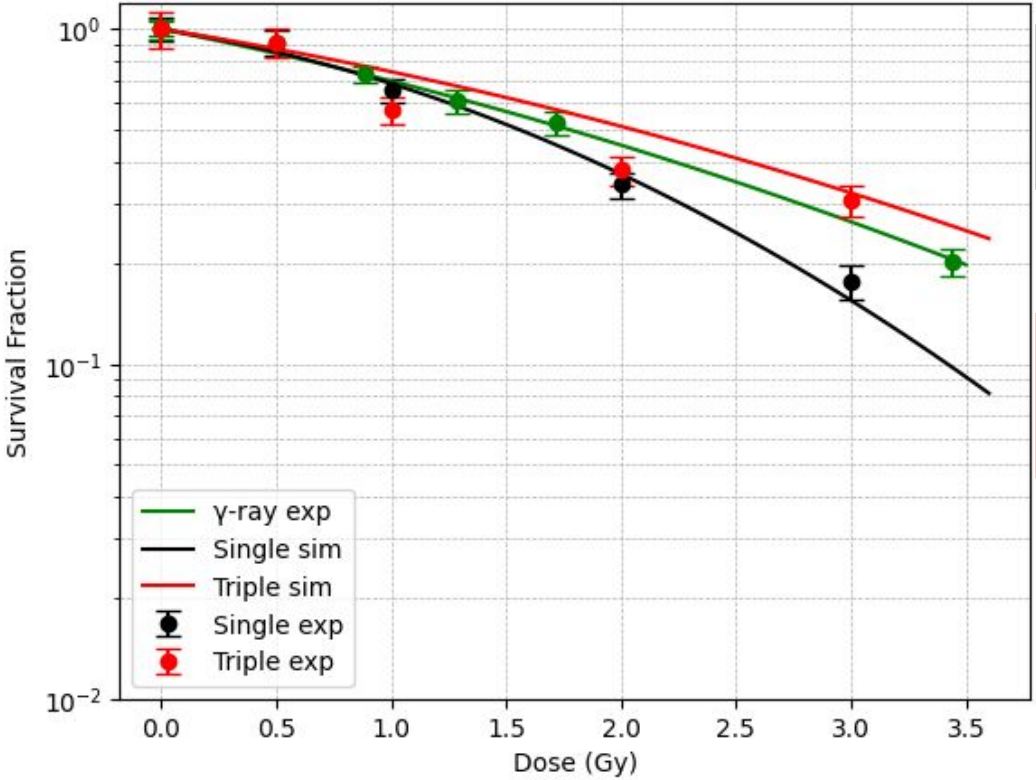


Single fraction experimental data

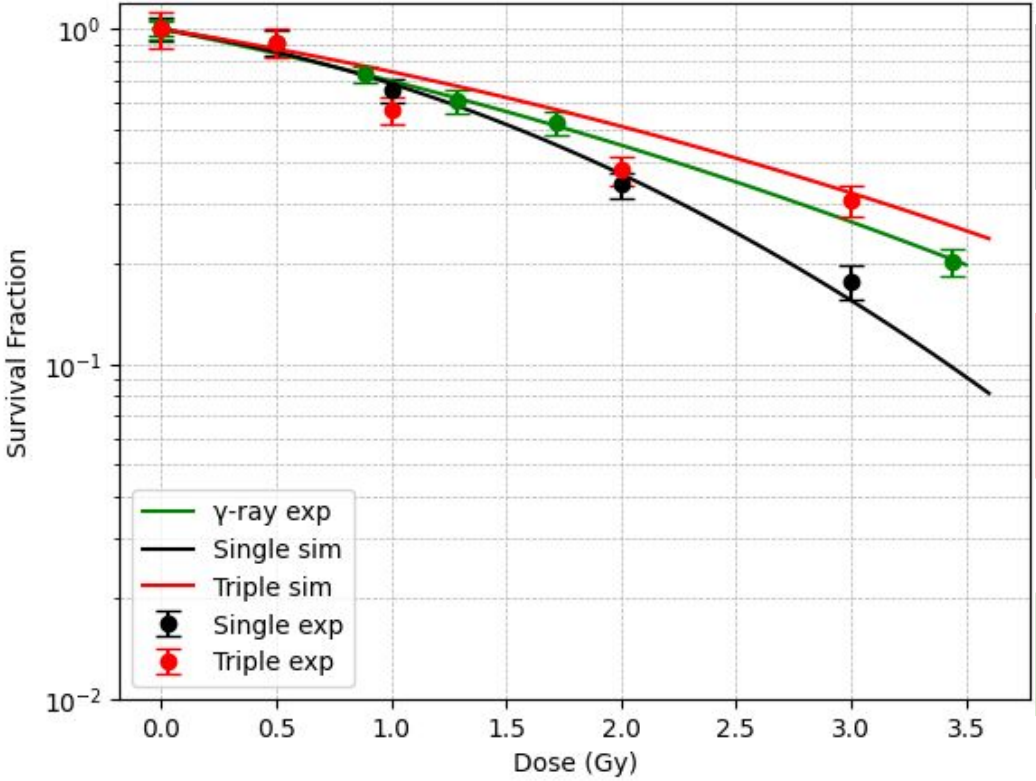
— Coefficients α and β for single fraction irradiation were obtained using BIANCA

— Coefficient β was modified according to the Lea-Catcheside Model for dose fractionation.

Triple fraction experimental data

Lea-Catcheside Model validation

AG01522 human fibroblast cells irradiated at the **CNAO** center, 0.70 keV/μm proton



Single fraction experimental data
— Coefficients α and β for single fraction irradiation were obtained using BIANCA

— Coefficient β was modified according to the Lea-Catcheside Model for dose fractionation.
Triple fraction experimental data

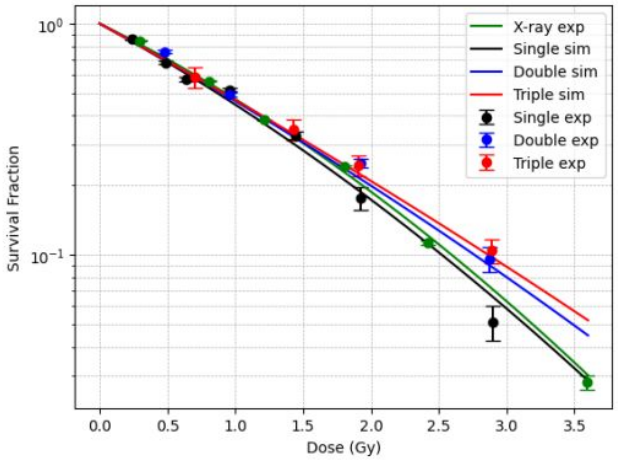
Green gamma-ray acute irradiation obtained in this work at LENA are also reported for comparison.

Single fraction experimental data
— Coefficients α and β for single fraction irradiation using BIANCA

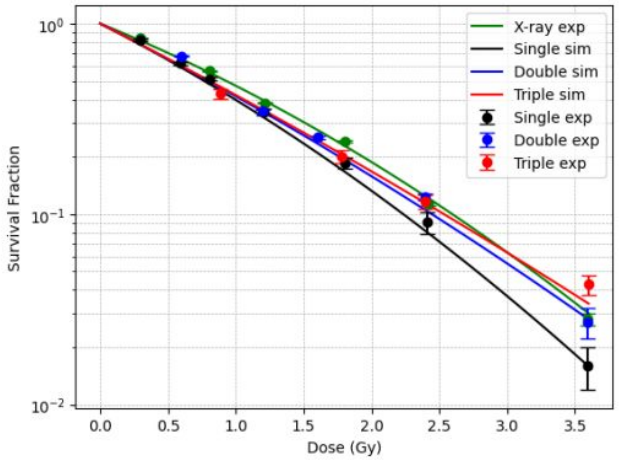
— Coefficient β was modified according to the Lea-Catcheside Model for dose fractionation.
Double fraction experimental data

— Coefficient β was modified according to the Lea-Catcheside Model for dose fractionation.
Triple fraction experimental data

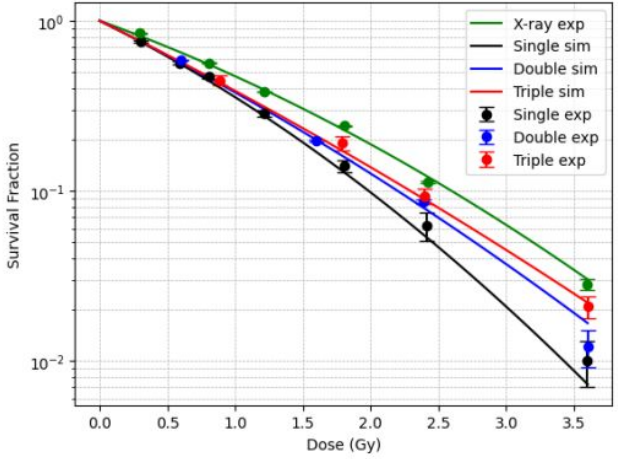
Green gamma-ray acute irradiation are also reported for comparison.



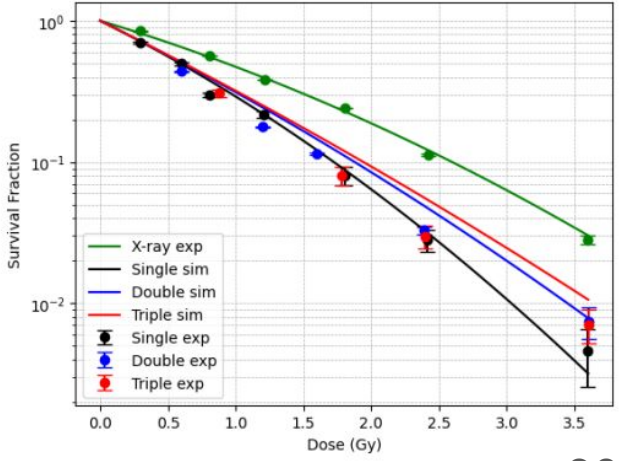
(a) LET values 0.63 keV/µm



(b) LET values 1.68 keV/µm

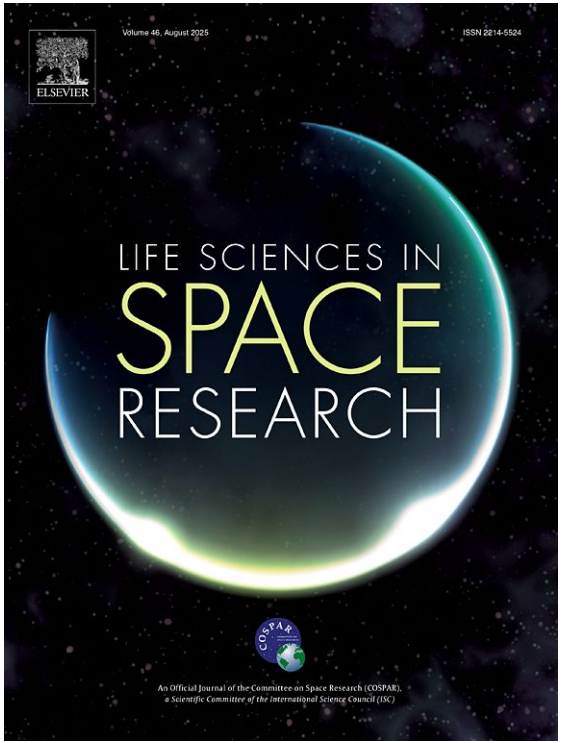


(c) LET values 2.45 keV/µm



(d) LET values 7.5 keV/µm

Publication of Research Article



ELSEVIER

Life Sciences in Space Research

Available online 9 September 2025

In Press, Journal Pre-proof ⓘ What's this?

Incorporation of dose-rate effects into the BIANCA biophysical model and application for space radiation risk assessment

E.I. Canay [1 2 3], M. Carante [3 4], A. Casali [3 4], E. Bernardini [5], D. Dondi [6 4], Dhanalakshmi Vadivel [6 4], L. Cansolino [7 4], E. Delgrosso [8], C. Ferrari [7 4], M. Pullia [9 4], F. Bonforte [9 4], J. Riback [1 10], S. Gonzalez [1 2 10], V. Vercesi [4], F. Ballarini [3 4] ✉, R. Ramos [3 4]

Universidad Nacional de San Martín

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ecanaycnea@gmail.com
National Atomic Energy Commission (CNEA) — UNSAM — UniPV