

# GAP

**(towards) Genome Adjusted Particle therapy**

RL – Giorgio Baiocco



# Informazioni generali

## Sezioni Coinvolte:

- TIFPA (RN)
- LNL
- RM2/RM3
- PV/CNAO
- TO
- CT

Durata del progetto:  
2026-2028

FTE 2026 sezione PV : 2.15

## Anagrafica di Pavia 2026:

|                            |        |    |
|----------------------------|--------|----|
| Giorgio Baiocco            | PA     | 50 |
| Isabella Guardamagna       | TecLab | 50 |
| Leonardo Lonati            | AdR    | 50 |
| Cecilia Riani              | PhD    | 25 |
| Pullia Marco               | CNAO   | 10 |
| Facoetti Angelica          | CNAO   | 10 |
| Charalampopoulou Alexandra | CNAO   | 10 |
| Carnevale Federica         | CNAO   | 10 |

# Goal del progetto

## Obiettivi

- **Integrate genomic data into radiobiological models** to develop a framework towards **Genomic Adjusted Particle Therapy (GAP)**.
- **Identify gene expression signatures** modulated by different radiation qualities (protons, carbon ions, and X-rays) using next-generation sequencing (NGS).
- **Develop predictive models** that combine genomic, microdosimetric, and radiobiological data to predict treatment outcomes.
- **Characterize radiation fields** using advanced new microdosimeters (MUSICA, DIODE) and reference microdosimeters (miniTEPC) to ensure precise radiation field correlation with biological effects at differential spatial scales.
- **Evaluate biological responses** across multiple cell lines (lung and pancreatic, healthy and tumor) using 2D and 3D assays, including apoptosis, senescence, and extracellular vesicle release.

## Obiettivi specifici

- INFN-Pavia section is in charge of:
  - experimental measurements on cell-culture media collected from samples from TIFPA (healthy and tumor lung cell lines) and CNAO (healthy and tumour pancreas cell lines) to isolate and characterize EV's
  - RNA extraction and RNE-seq (external service) to obtain data for bioinformatic analysis
  - Radiobiological measurements with carbon ions at the CNAO facility (starting from the 2° year) on pancreatic cells cultures in 2D and spheroids

# GARD: genomic adjusted radiation dose

## Genomic analysis at 2Gy survival fraction

Table 1. SF2 values for 48 cell lines in the database

| Cell line       | Recorded SF2 | Cell line      | Recorded SF2 |
|-----------------|--------------|----------------|--------------|
| BREAST_HS578T   | 0.79         | COLON_COLO205  | 0.69         |
| BREAST_MDAMB231 | 0.82         | COLON_HCC-2998 | 0.44         |
| COLON_HCT116    | 0.38         | COLON_HT29     | 0.79         |
| COLON_HCT15     | 0.4          | COLON_KM12     | 0.42         |
| COLON_SW620     | 0.62         | MELAN_LOXIMVI  | 0.68         |
| LEUK_CCRFCM     | 0.185        | MELAN_M14      | 0.42         |
| LEUK_HL60       | 0.315        | MELAN_MALME3M  | 0.8          |
| LEUK_MOLT4      | 0.05         | MELAN_SKMEL28  | 0.74         |
| MELAN_SKMEL2    | 0.66         | MELAN_SKMEL5   | 0.72         |
| NSCLC_A549ATCC  | 0.61         | MELAN_UACC257  | 0.48         |
| NSCLC_H460      | 0.84         | MELAN_UACC62   | 0.52         |
| NSCLC_HOP62     | 0.164        | NSCLC_EKVX     | 0.7          |
| NSCLC_NCIH23    | 0.086        | NSCLC_HOP92    | 0.43         |
| OVAR_OVCAR5     | 0.408        | OVAR_OVCAR3    | 0.55         |
| RENAL_SN12C     | 0.62         | OVAR_OVCAR4    | 0.29         |
| BREAST_BT549    | 0.632        | OVAR_OVCAR8    | 0.6          |
| BREAST_MCF7     | 0.576        | OVAR_SKOV3     | 0.9          |
| BREAST_MDAMB435 | 0.1795       | PROSTATE_DU145 | 0.52         |
| BREAST_T47D     | 0.52         | PROSTATE_PC3   | 0.484        |
| CNS_SF268       | 0.45         | RENAL_7860     | 0.66         |
| CNS_SF539       | 0.82         | RENAL_A498     | 0.61         |
| CNS_SNB19       | 0.43         | RENAL_ACHN     | 0.72         |
| CNS_SNB75       | 0.55         | RENAL_CAK1I    | 0.37         |
| CNS_U251        | 0.57         | RENAL_UO31     | 0.62         |

Abbreviation: SF2 = survival fraction at 2 Gy.

## Linear regression on selected genes

### RSI (Radiation sensitivity index)

$$\begin{aligned}
 \text{SF2} = & - 0.0098009 \cdot \text{AR} + 0.0128283 \cdot \text{cJun} \\
 & + 0.0254552 \cdot \text{STAT1} - 0.0017589 \cdot \text{PKC} \\
 & - 0.0038171 \cdot \text{RelA} + 0.1070213 \cdot \text{cABL} \\
 & - 0.0002509 \cdot \text{SUMO1} - 0.0092431 \cdot \text{CDK1} \\
 & - 0.0204469 \cdot \text{HDAC} - 0.0441683 \cdot \text{IRF1}
 \end{aligned}$$

# GARD: genomic adjusted radiation dose

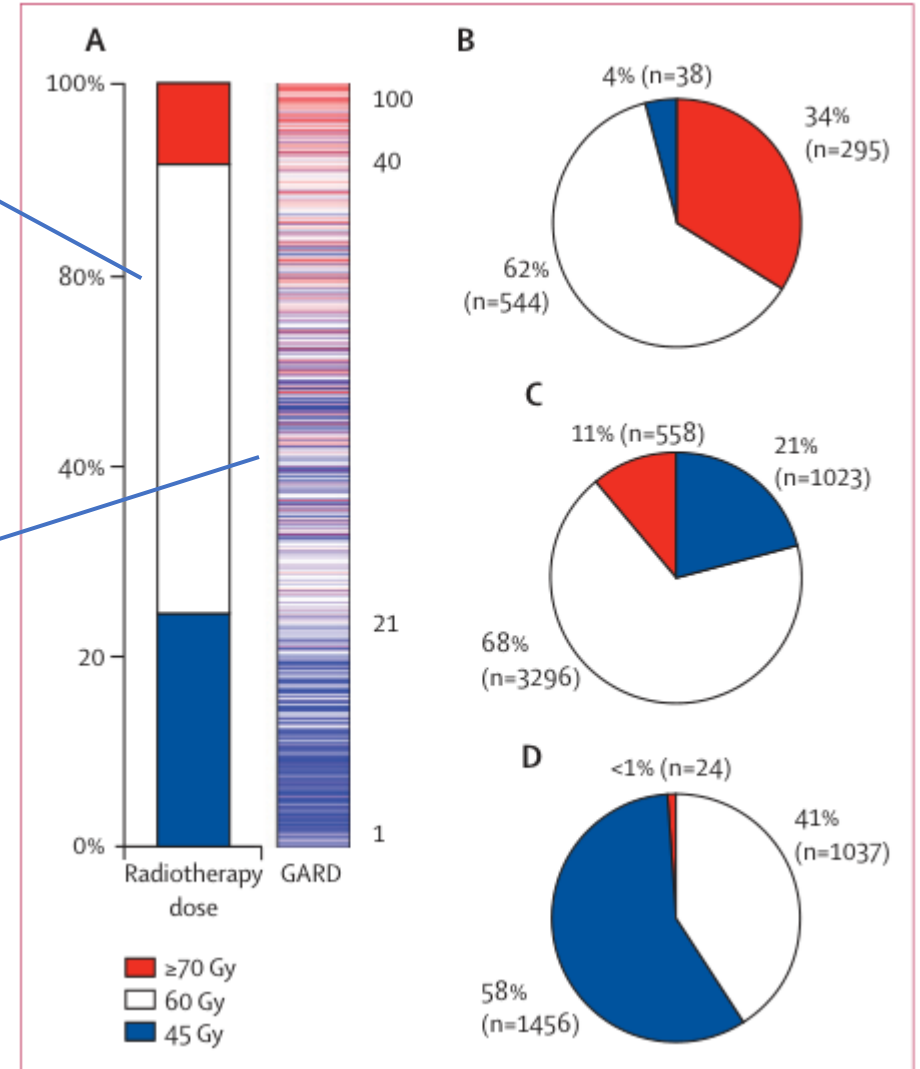
Radiosensitivity  
adjusted by patient  
specific genomic  
profiling

$$S = e^{-nd(\alpha + \beta d)}$$

$$\alpha_g = -\frac{\ln RSI}{nd} - \beta d, \quad (1)$$

Dose received by  
patient

Dose **should have  
been received** by  
patient according to  
GARD



# Preventivi

2026

|        | missioni | missioni_sj | consumo | altri_cons | inventario | spservizi | spservizi_sj | totali | totali_sj |
|--------|----------|-------------|---------|------------|------------|-----------|--------------|--------|-----------|
| LNL    | 1.5      | 1.5         | 2       |            |            |           |              | 3.5    | 1.5       |
| PV     | 7        |             |         | 7          |            |           | 14           |        |           |
| ROMA2  | 3        |             | 1.5     |            |            |           |              | 4.5    |           |
| TIFP   |          |             |         | 14.5       |            |           | 5            | 14.5   | 5         |
| TO     | 4        |             | 1.5     | 19.5       | 4          |           |              | 29     |           |
| Totale | 8.5      | 1.5         | 5       | 41         | 4          | 7         | 5            | 65.5   | 6.5       |

## INFN-Pavia section

- Consumabili per misure citometria e kit reagenti per isolamento vescicole e estrazione RNA, siero per colture cellulari di prova
- Acquisto di linee cellulari (sana e tumorale) per esperimenti di radiobiologia
- Sequenziamento RNA da ditta esterna, compreso shipment e costi di data delivery (~24 campioni)

# Previsione di budget

## 2027

- Consumabili: 61 k€;
- Missioni: 14 k€;
- Instruments: 7 k€;
- Service: 2.5 k€ [sj]
- Total: 82 + 2.5 k€ [sj]

## 2028

- Consumabili: 47 k€;
- Total: 47 k€

## Total request for year 1-2-3:

- Y1 - 65.5 k€ + 6.5 k€ [sj]
- Y2 - 82 + 2.5 k€ [sj]
- Y3 - 47 k€
- TOTAL = 194.5 + 9 [sj] k€

## INFN-Pavia section

|                                                                                | I anno | II anno | III anno | Totale | GROUP        |
|--------------------------------------------------------------------------------|--------|---------|----------|--------|--------------|
| consumabili citometria, kit reagenti per isolamento vescicole e estrazione RNA | 4      | 4       |          | 8      | PV           |
| RNA-SEQ da ditta compresa spedizione e costi di data delivery                  | 7      | 7       |          | 14     | PV           |
| linee cellulari                                                                | 3      |         |          | 3      | PV           |
| consumabili per cell culture e misure radiobiologiche presso CNAO              |        | 15      | 25       | 40     | PV e PV-CNAO |
| NGS                                                                            |        |         | 10       | 10     | PV-CNAO      |
|                                                                                | 14     | 26      | 35       | 75     |              |