Attività Gruppo V - RM3: FRIDA & MICROBE-IT

A. Attili - Roma Tre - July 4, 2022

FRIDA - FLASH Radiotherapy with hIgh Dose-rate particle beAms

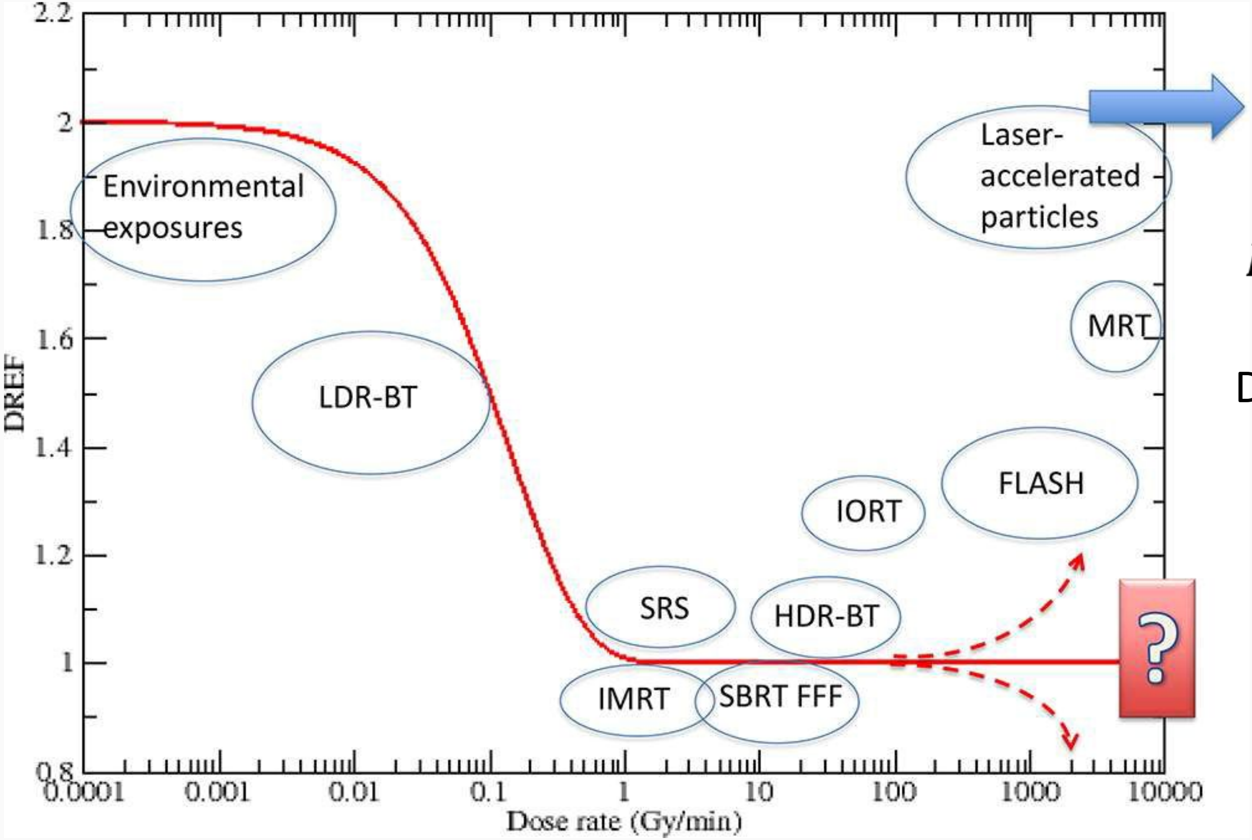
Research area:

Radiation biophysics / Radio Therapy / Particle Therapy / Medical Applications / Accelerators

Working Packages (3 years):

1. WP1: **FLASH effect understanding** (TIFPA, RM3, PI, LNS, MI)
2. WP2: **FLASH beam delivery** (LNS, RM1, MI, PI)
3. WP3: **FLASH beam monitoring & dosimetry** (TO, LNS, RM1, PI)
4. WP4: **FLASH treatment planning** (RM1, TIFPA, MI, PI)

The "FLASH" effect

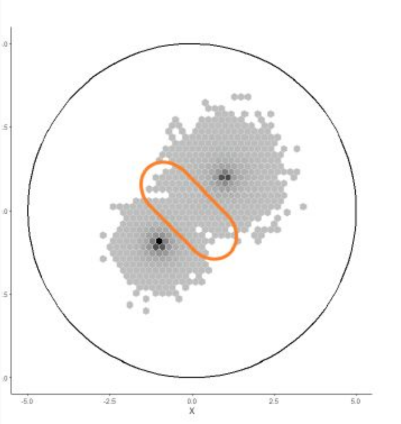


$$DREF = \left.\frac{D(\dot{D})}{D(\dot{D}_{ref})}\right|_{same\ effect}$$

Dose-Rate Effectiveness Factor

Durante, M., BräUer-Krisch, E., & Hill, M. (2018). Faster and safer? FLASH ultra-high dose rate in radiotherapy. British Journal of Radiology, 91(1082), 6–9. https://doi.org/10.1259/bjr.20170628

DNA damage modeling in FLASH conditions



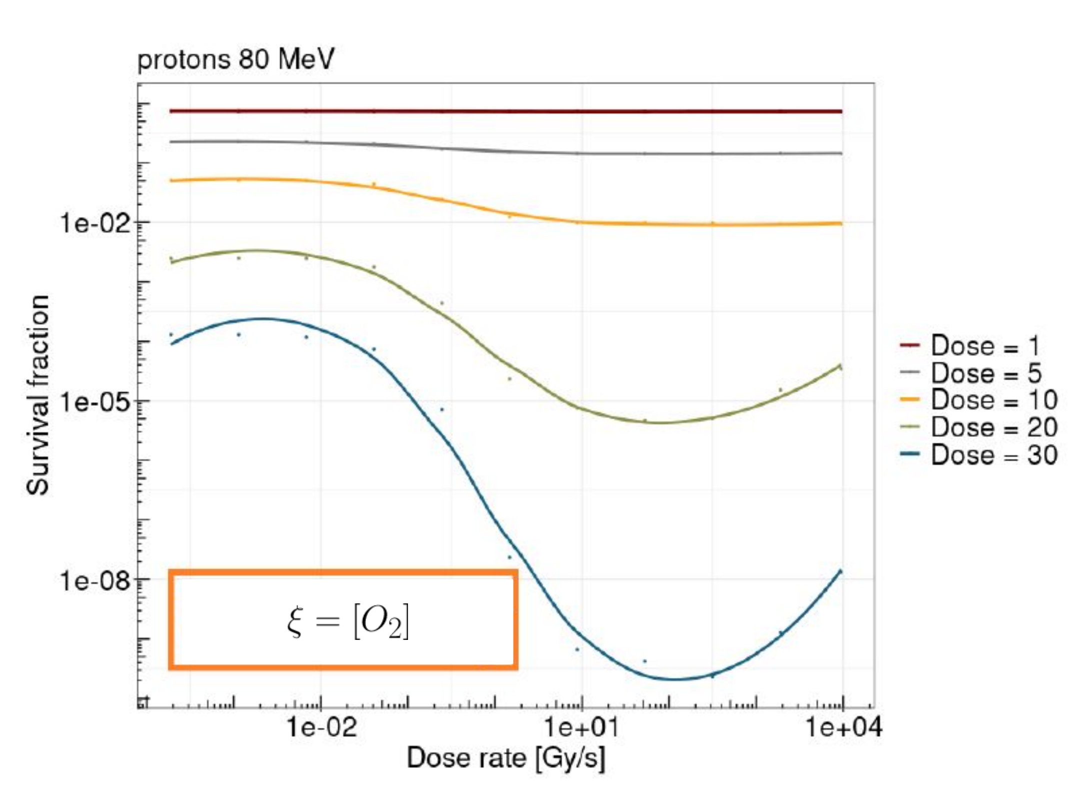
In the track overlap region the presence of free radicals reduces the yield of DNA damages induced by radiation

$$
\begin{cases}
Y(t) &= Y_0 + \mathcal{P}^a\left(\int_0^t aX(s)ds\right) + \mathcal{P}^b\left(\int_0^t bX(s)(X(s)-1)ds\right) + \\
 &\quad + Z_Y(\xi(t))\mathcal{P}^d\left(\int_0^t \dot{d}\, ds\right) \\
X(t) &= X_0 - \mathcal{P}^a\left(\int_0^t aX(s)ds\right) - \mathcal{P}^r\left(\int_0^t rX(s)ds\right) + \\
 &\quad -2\mathcal{P}^b\left(\int_0^t bX(s)(X(s)-1)ds\right) + Z_X(\xi(t))\mathcal{P}^d\left(\int_0^t \dot{d}\, ds\right), \\
\hline
\frac{d}{dt}\left[e^-_{aq}\right](t) &= f_{e^-_{aq}}(\xi(t)) + G_e\rho\dot{z}, \\
\frac{d}{dt}[O_2](t) &= f_{O_2}(\xi(t)), \\
\frac{d}{dt}C_{H_2O_2}(t) &= f_{H_2O_2}(\xi(t)) + G_{H_2O_2}\rho\dot{z}, \\
\frac{d}{dt}C_{OH^\bullet}(t) &= f_{OH^\bullet}(\xi(t)) + G_{OH^\bullet}\rho\dot{z}, \\
\frac{d}{dt}[H^\bullet](t) &= f_{e^-_{aq}}(\xi(t)) + G_{H^\bullet}\rho\dot{z}, \\
\frac{d}{dt}[H_2](t) &= f_{e^-_{aq}}(\xi(t)) + G_{H_2}\rho\dot{z}, \\
\frac{d}{dt}C_{O_2^{\bullet-}}(t) &= f_{O_2^{\bullet-}}(\xi(t)), \\
\frac{d}{dt}[R^\bullet](t) &= f_{R^\bullet}(\xi(t)) + G_{R^\bullet}\rho\dot{z}, \\
\frac{d}{dt}[ROO^\bullet](t) &= f_{ROO^\bullet}(\xi(t)), \\
\xi &= \left(\left[e^-_{aq}\right], [O_2], C_{H_2O_2}, C_{OH^\bullet}, [H^\bullet], [H_2], C_{O_2^{\bullet-}}, [R^\bullet], [ROO^\bullet]\right).
\end{cases}
$$

Reaction Table from:

Labarbe, R., Hotoiu, L., Barbier, J., & Favaudon, V. (2020). A physicochemical model of reaction kinetics supports peroxyl radical recombination as the main determinant of the FLASH effect. Radiotherapy and Oncology, 153, 303–310.

DNA damage modeling in FLASH conditions



Abstract submitted at FRPT 2022:

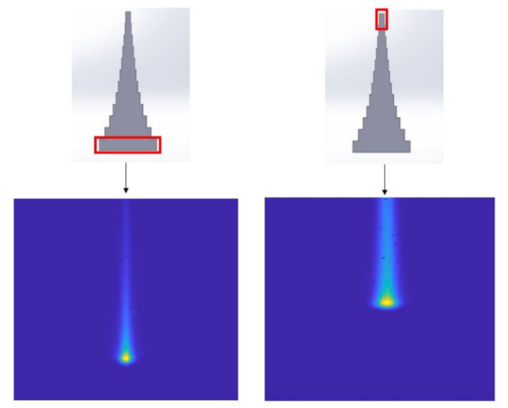
"Across the stages: merging the chemical stages to the Generalized Stochastic Microdosimetric Model (GSM2) as an insight in ultra-high dose rate biological mechanism" (Cordoni et al.)

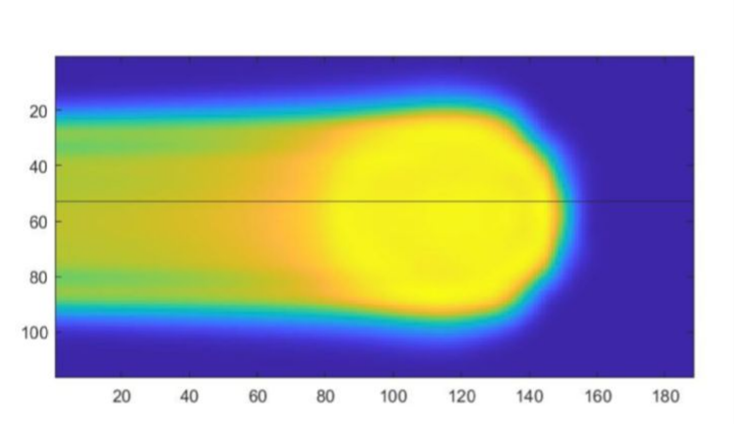
Submitted proposals:

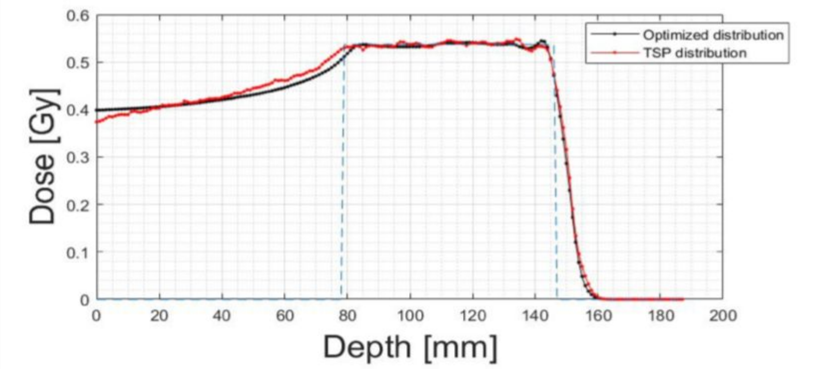
- **AIRC** 2021 → 2022: “*Mechanistic insights in preclinical FLASH radiotherapy through advanced dosimetry and biophysical modeling*” (A. Spinelli)
    - Photons/electrons
    - 5 years
- **AIRC** 2022 (‘MFAG’): “*Development and validation of 3D beam range modulators for FLASH proton therapy*” (F. Tommasino)
    - Protons
    - 5 years - 1 PhD grant (3 yrs), 2 post-doc (2 yrs)
- **PRIN** 2022: “*Proton therapy with 3D beam range modulators: enabling the FLASH effect for conformal treatments (P3RFECT)*” (F. Tommasino)
    - Protons
    - 2 years - 2 post-doc (2 yrs)

Prototype 3D RM

3D RM
prototype for spherical target
Printed with PolyJet







MICROBE-IT: MICROdosimetry-based Biological Effectiveness assessment in Ion Therapy

Research area:

Radiation biophysics / Radio Therapy / Particle Therapy

Working Packages (2 years + 1 year?):

1. WP1: **From nano- to standard and non-standard microdosimetry** (LNS)
2. WP2: **Linking microdosimetric measurements to biological effectiveness** (TIFPA, RM3)

Publications:

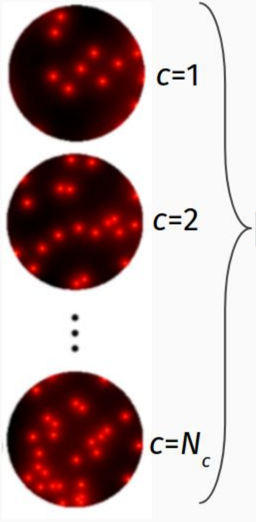
Cordoni, F., Missiaggia, M., Attili, A., Welford, S. M., Scifoni, E., & La Tessa, C. (2021). Generalized stochastic microdosimetric model: The main formulation. *Physical Review. E*, 103(1–1), 012412.

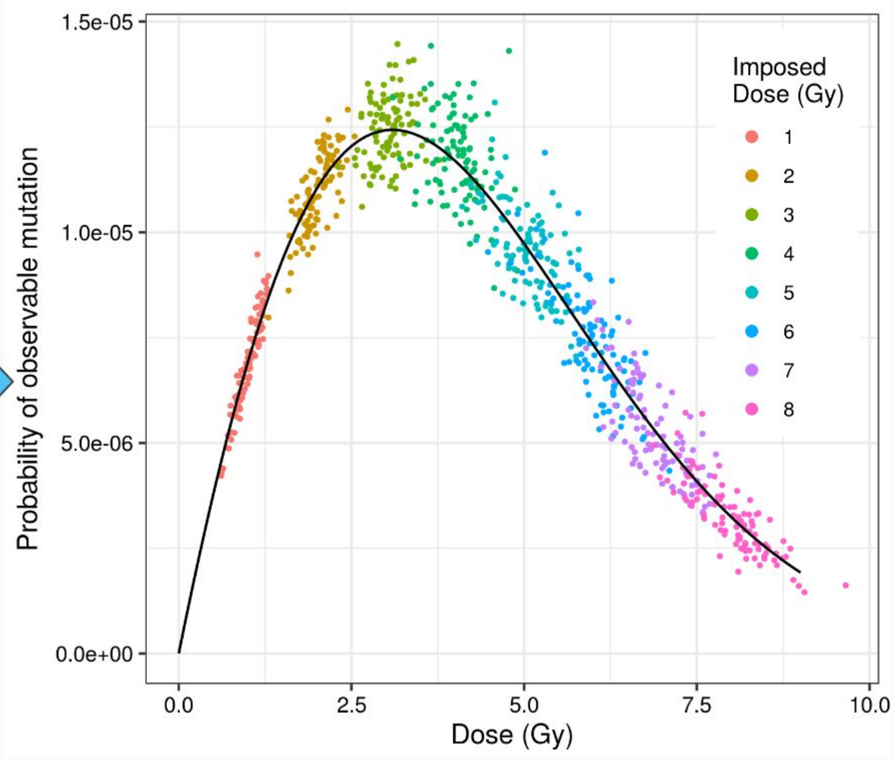
Bellinzona, V. E., Cordoni, F., Missiaggia, M., Tommasino, F., Scifoni, E., La Tessa, C., & Attili, A. (2021). Linking Microdosimetric Measurements to Biological Effectiveness in Ion Beam Therapy: A Review of Theoretical Aspects of MKM and Other Models. *Frontiers in Physics*, 8(February), 1–28.

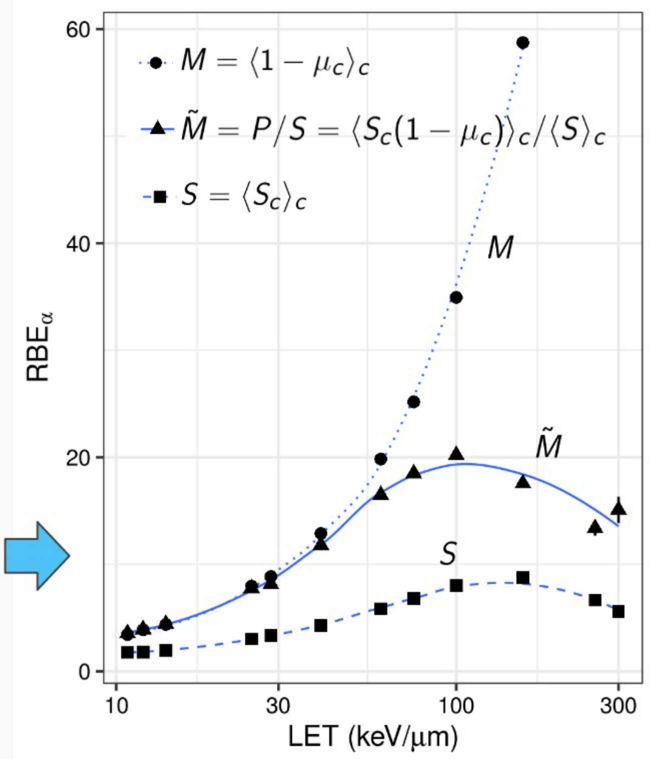
Attili, A., Scifoni, E., & Tommasino, F. (2022). Modelling the HPRT-gene mutation induction of particle beams: systematic in vitro data collection, analysis and microdosimetric kinetic model MKM implementation. *Physics in Medicine and Biology* (accepted).

Mutation induction of particle beams - MC Microdosimetric Model

Simulated Irradiated cells:







Towards Secondary Cancer Risk assessment