

NEPTUNE:

*Nuclear process-driven Enhancement
of Proton Therapy UNravElled*

WP1 - Modeling

June, 19 2020

A Attili, E Scifoni, F Tommasino, G Petringa, P Cirrone, et al.



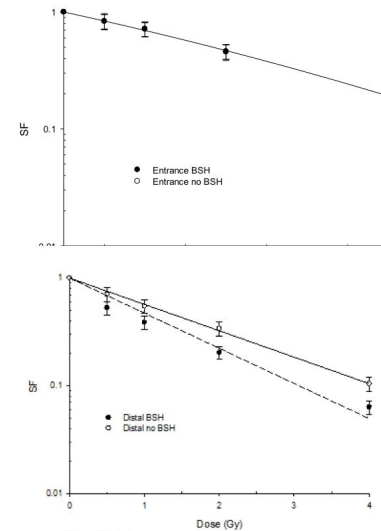
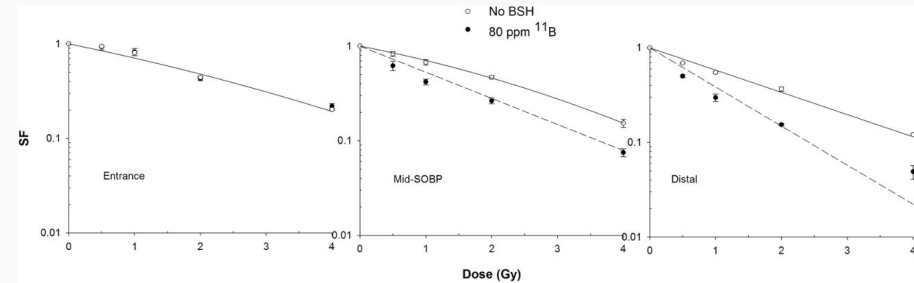
Istituto Nazionale di Fisica Nucleare

NEPTUNE WP1: milestones & deliverables

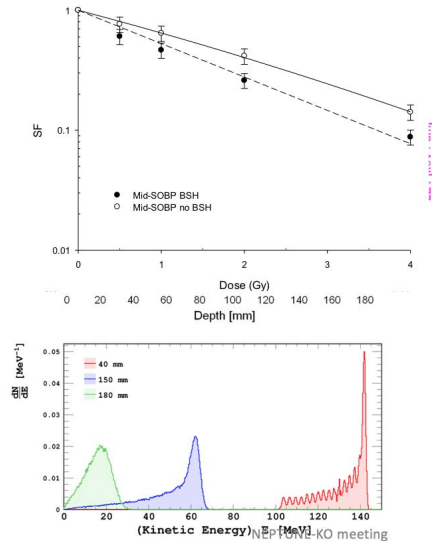
	1st year	2nd year	3rd year
D1.1: Implementation of MC simulations (Gean4) for p+11B and p+19F nuclear reaction spectra generated in the experimental setup	[Green]		
M1.1: Integration of the simulated spectra evaluated in M1.1 in the MKM	[Green]		
D1.2: Implementation of Geant4-DNA and TRAX-CHEM simulations starting from the spectra obtained in (1.a)	[Green]	[Green]	
M1.2: Inclusion of the bystander effect in the simulations developed in D1.1 and M1.1	[Green]	[Green]	
M1.3: Comparison between simulation data D1.1 and experimental data taken by WP2. Inclusion of the experimental data (cell survival) in the radiobiological simulations	[Green]	[Green]	[Green]
M1.4: Comparison between simulation data D1.1 and experimental data taken by WP2. Inclusion of the experimental data (cell survival) taken by WP4	[Green]	[Green]	[Green]
M1.5: Comparison between simulation data D1.1 and experimental data taken by WP2. Inclusion of the experimental data (ROS production) taken by WP4	[Green]	[Green]	[Green]
M1.6: Comparison between simulation data (D1.1, M1.3, D1.2 and M1.5) and experimental data taken by WP2. Inclusion of the experimental data (cell survival, DSB,CA,foci) taken by WP4	[Green]	[Green]	[Green]
M1.7: Comparison between simulation data M1.3 and experimental data taken by WP2. Inclusion of the experimental data (cell survival, DSB,CA,foci) taken by WP4	[Green]	[Green]	[Green]

NEPTUNE WP1: revised workflow

- **Goal:** finalize the analysis of the contribution of alpha particles on the radiobiological enhancement: *Is possible to reproduce the observed decrement of cell survival by using hadrontherapy models + alpha contribution only?*
- **First step:** MC simulations implementation + Radiobiological modeling (modified MKM and LEM models to account alpha short ranges) to carry on a simultaneous global fit of alpha production CS to every clonogenic assays, possibly using all available reaction channel for alpha production.

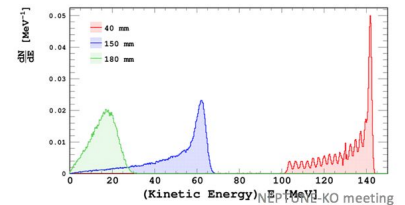
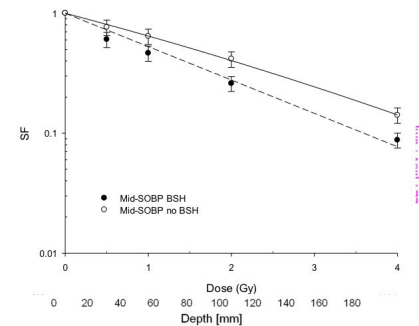
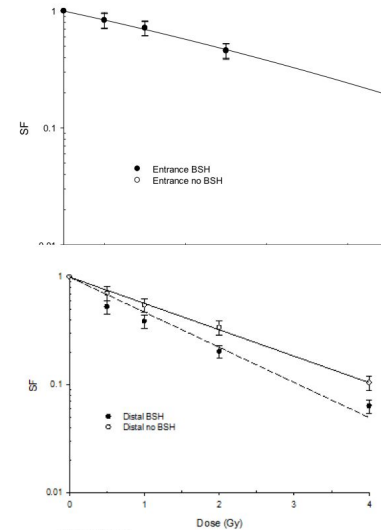
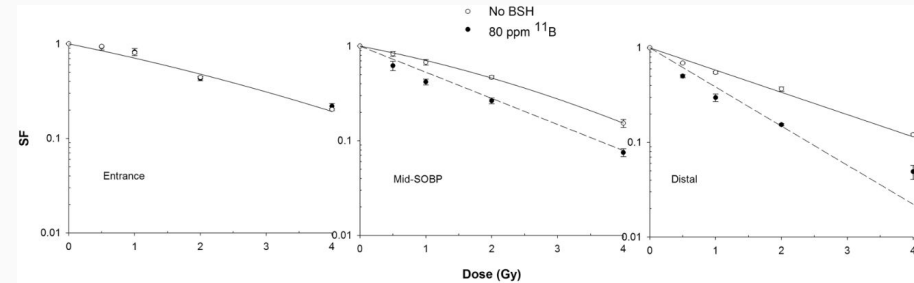


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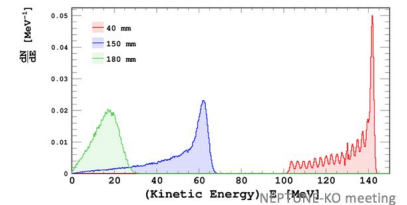
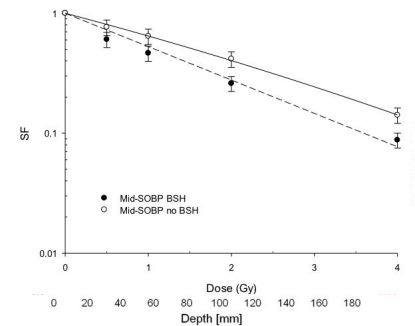
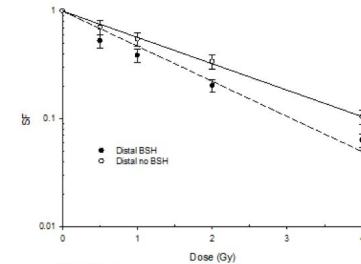
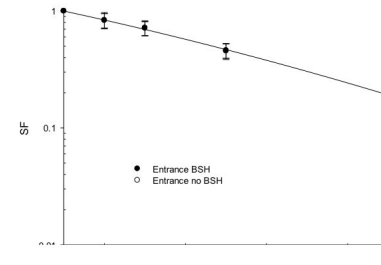
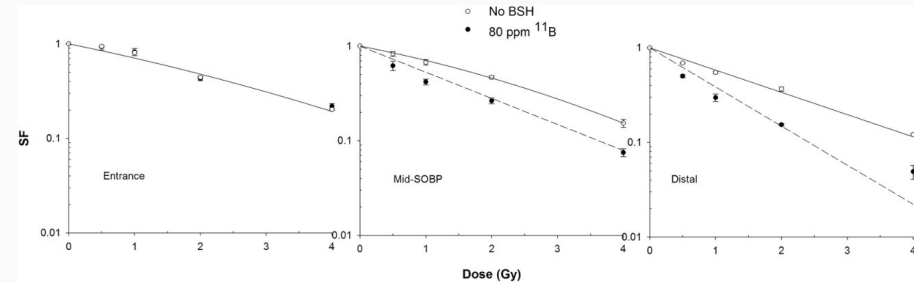
NEPTUNE WP1: revised workflow

- *Clonogenic assays* @ LNS and CNAO - DU145 and PANC-1 cells irradiated w and w/out Boron (BSH and BPA). Six positions along the SOBP in total, corresponding to different proton energy conditions.
 - **WP4:** survival raw data (including x-ray irradiation) and dose measurements with uncertainties.

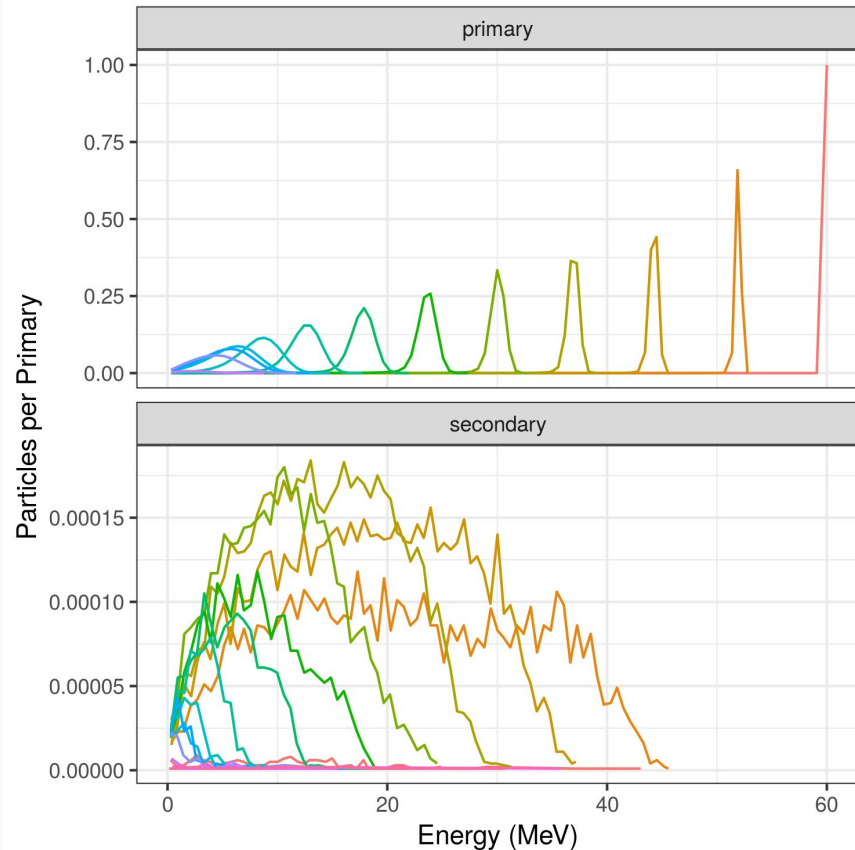
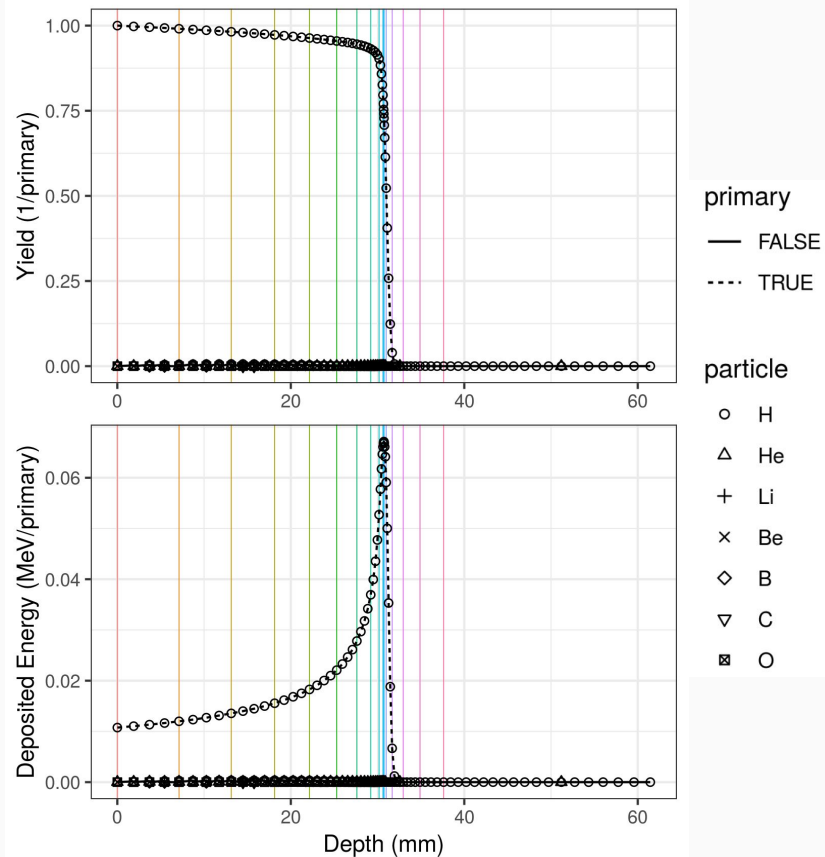


NEPTUNE WP1: revised workflow

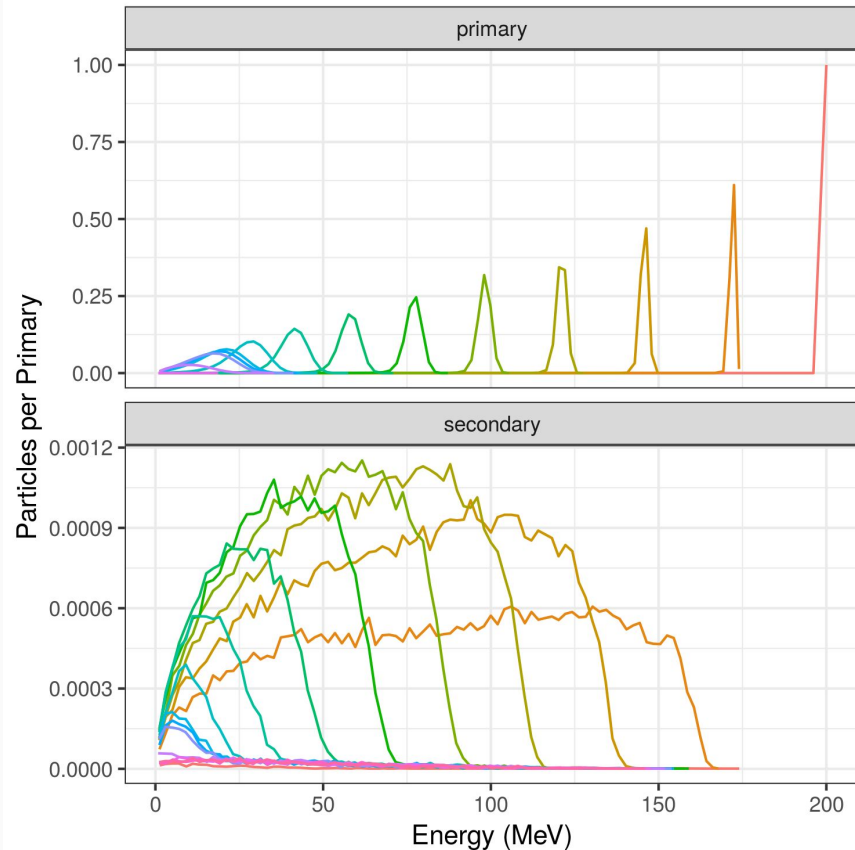
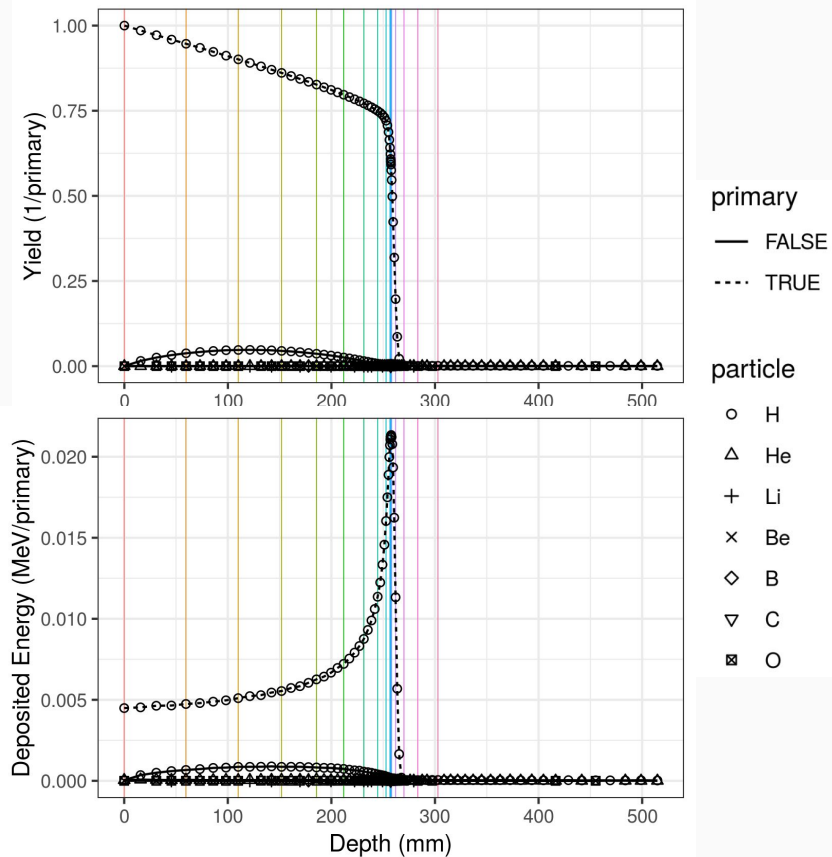
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 - **WP1:** Geant4 Simulation for LNS beamline
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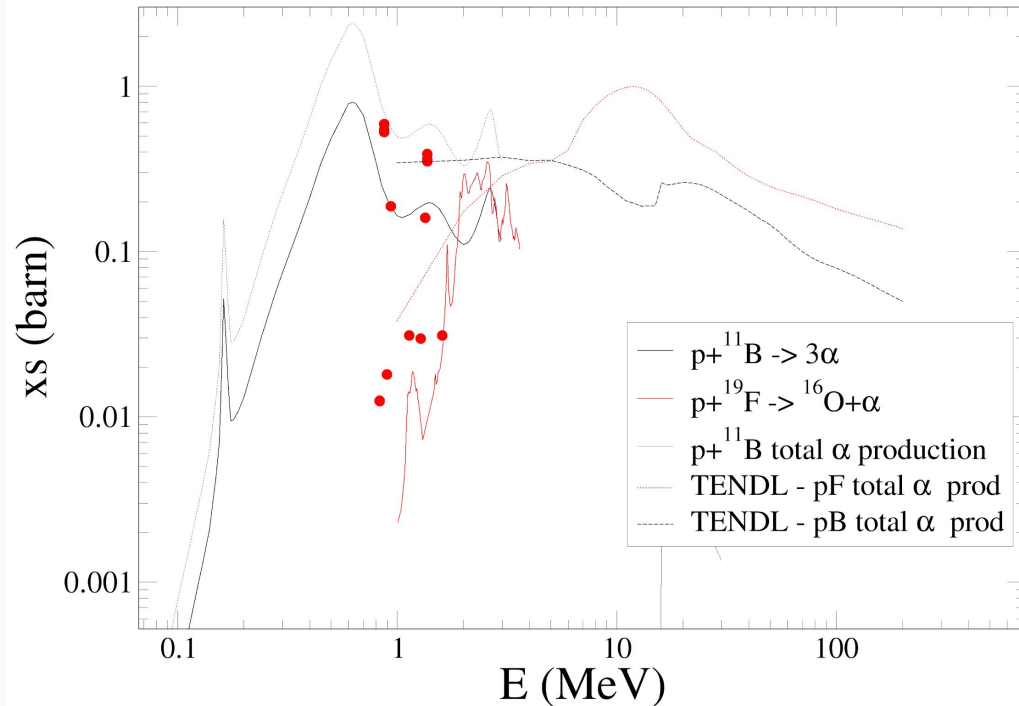
proton energy spectra for a proton beam (60 MeV) in a water phantom



proton energy spectra for a proton beam (200 MeV) in a water phantom

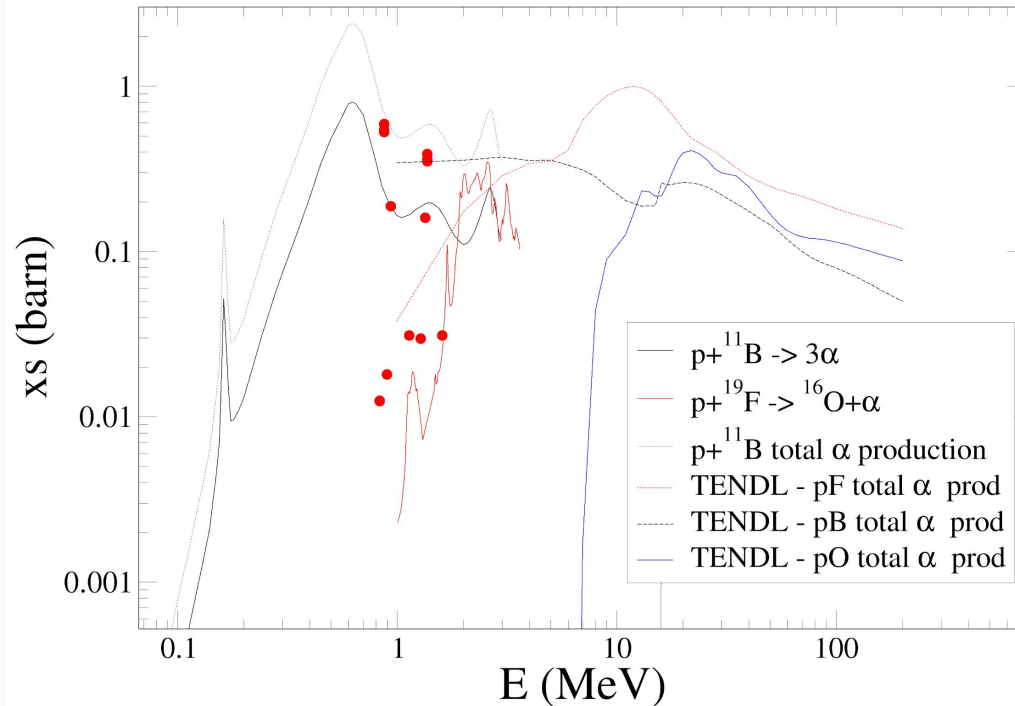


Cross sectional data for different interaction channels (TENDL + experiments)



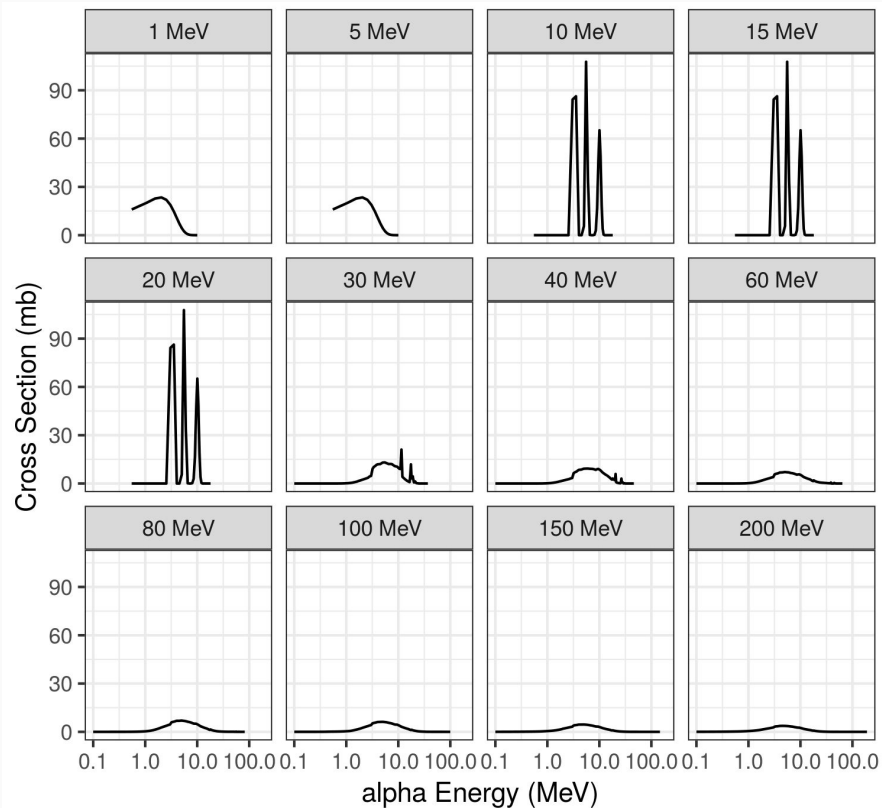
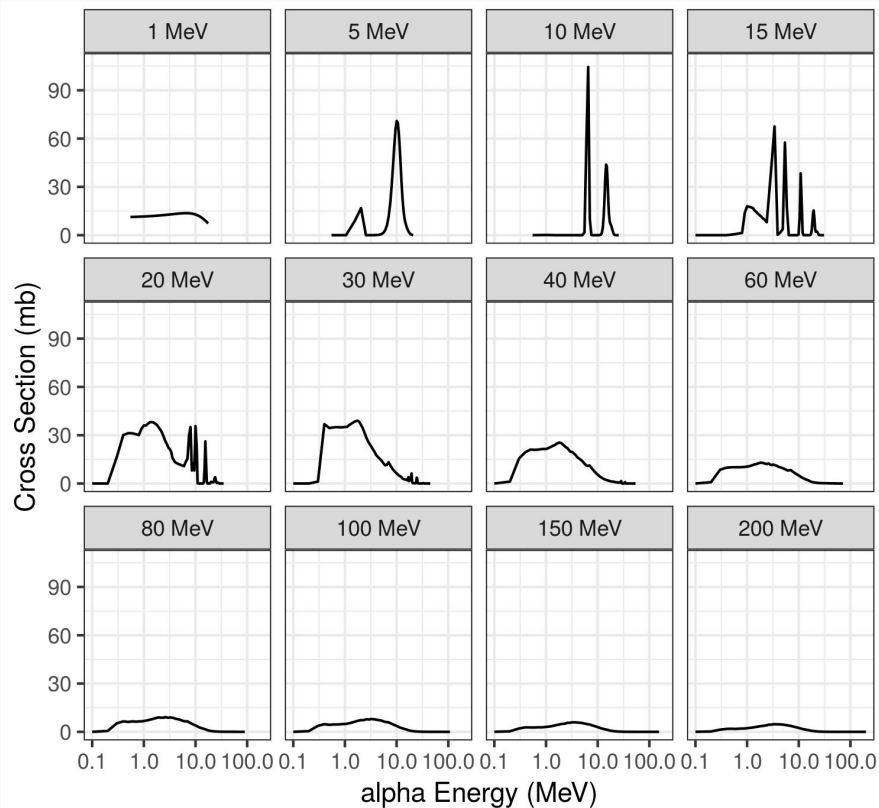
- CS data *theoretical* & *measured alpha production rate* (all available channels)
 - **WP1:**
[Geant4/EXFOR/TENDL]
 - **WP3:** (dati sperimentali normalizzati di alpha production rate)

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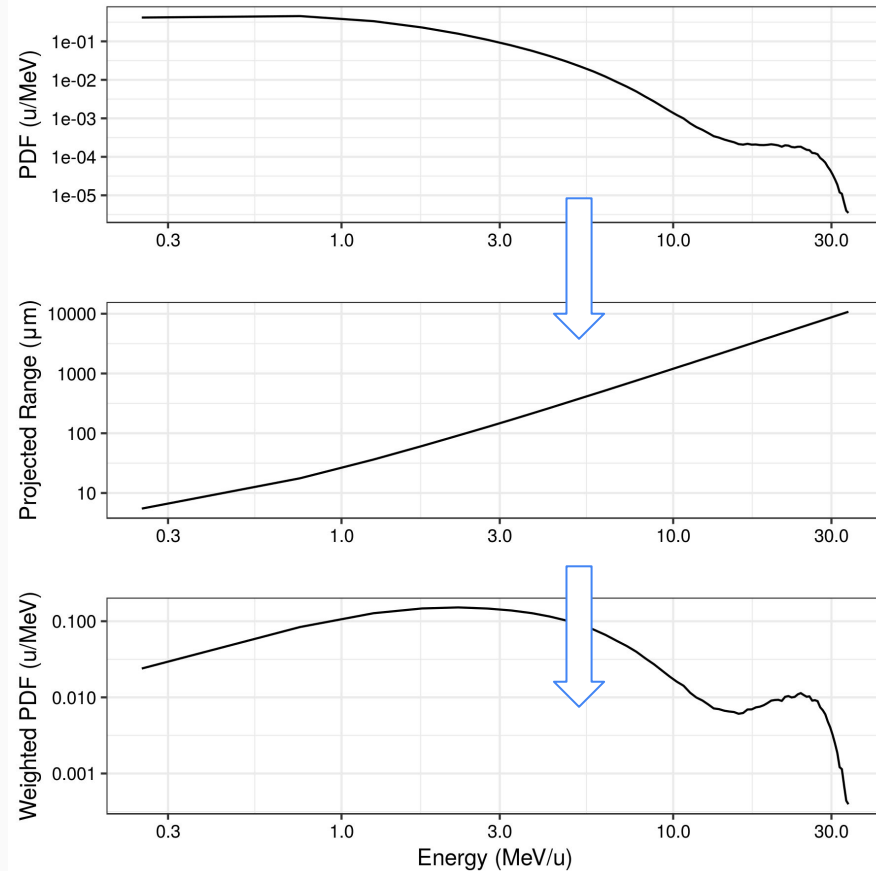
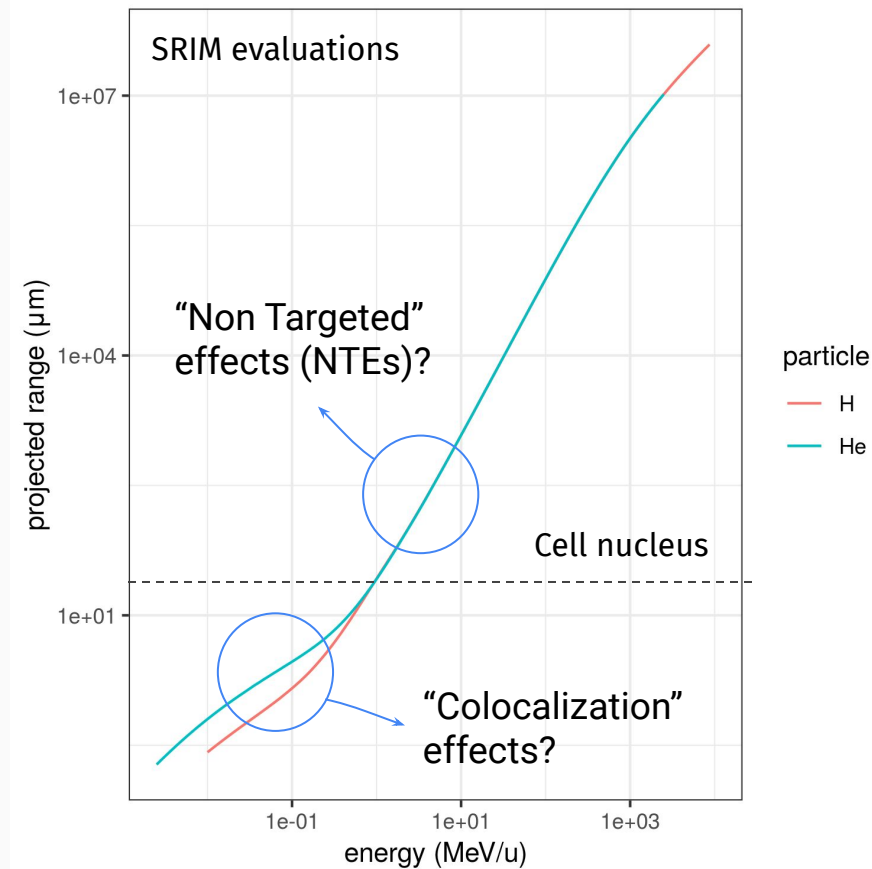


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[Geant4/EXFOR/TENDL]
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 - Link with FOOT/MOVE-IT?

differential Cross Sections σ_{pf} (TENDL)

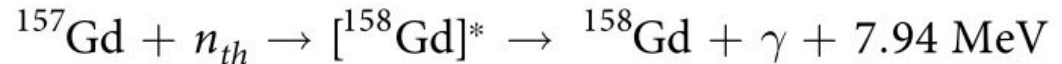
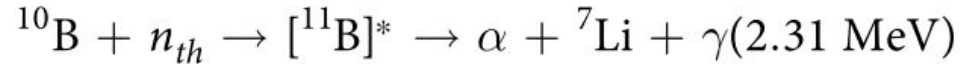


Range → Weighted spectra (with range dependent weight factor W_r)



S1: MC Simulations with Geant4 - α + Li production by Neutron mediation

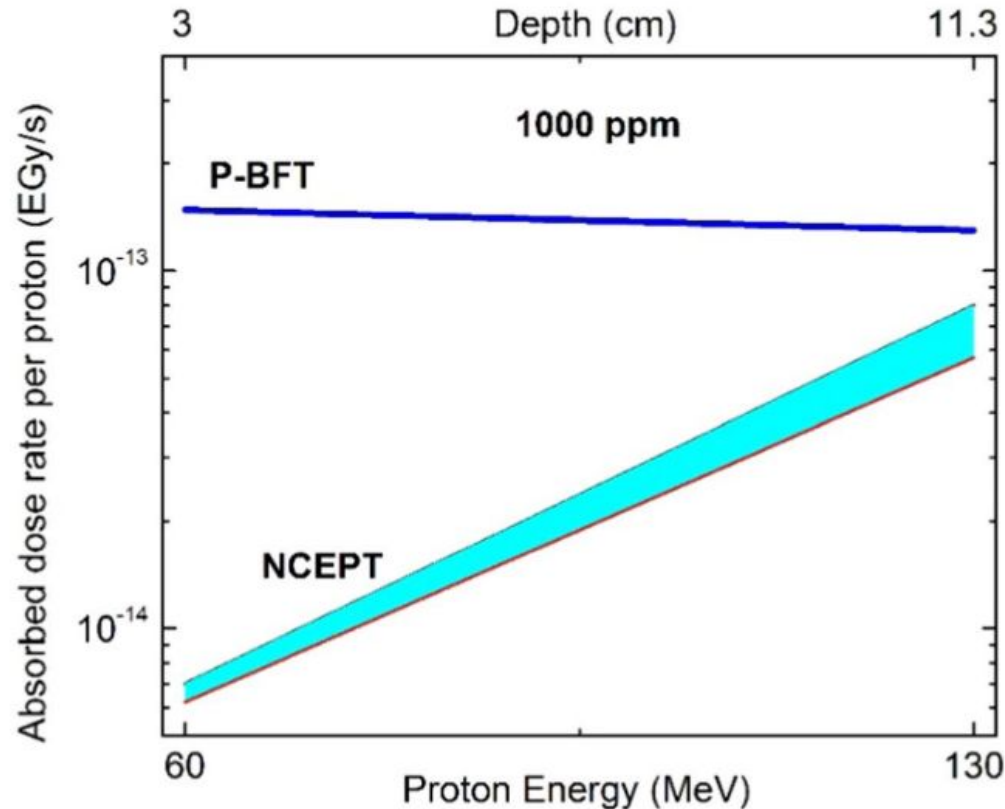
- Neutron Capture Enhanced Particle Therapy (NCEPT) : central hypothesis is that if a sufficient thermal neutron fluence is generated during proton or heavier ion therapy, it can be exploited therapeutically via the administration of a suitable non-toxic neutron capture agent containing ^{10}B or ^{157}Gd (Safavi-Naeini et al. 2018)



Target Depth (mm)	Primary Ion	Thermal neutron fluence per GyE primary dose (n/cm ² /GyE)		
		Minimum	Mean	Maximum
100–150	Proton ^{12}C	5.96×10^8	7.79×10^8	9.06×10^8
		2.86×10^8	3.34×10^8	3.60×10^8
140–190	Proton ^{12}C	6.26×10^8	8.82×10^8	1.09×10^9
		3.17×10^8	4.08×10^8	4.68×10^8

Thermal neutron fluences obtained for each target volume and treatment plan, assuming a target volume average proton or heavy ion biological dose of 1 GyE. (Safavi-Naeini et al. 2018)

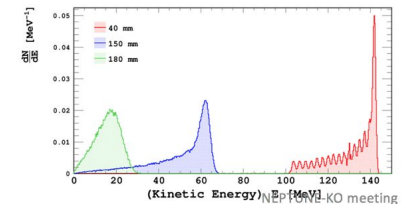
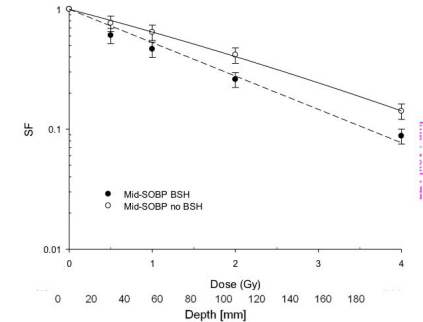
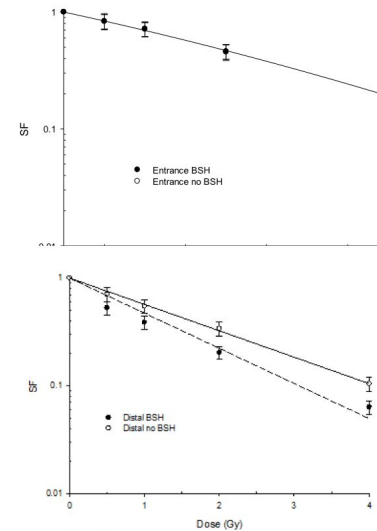
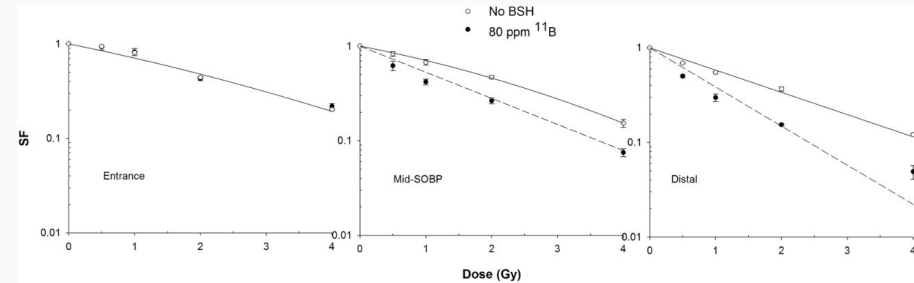
Comparing proton mediated vs neutron mediated mechanisms



Tabbakh, F., & Hosmane, N. S. (2020). Enhancement of Radiation Effectiveness in Proton Therapy: Comparison Between Fusion and Fission Methods and Further Approaches. *Scientific Reports*, 10(1), 1–12.

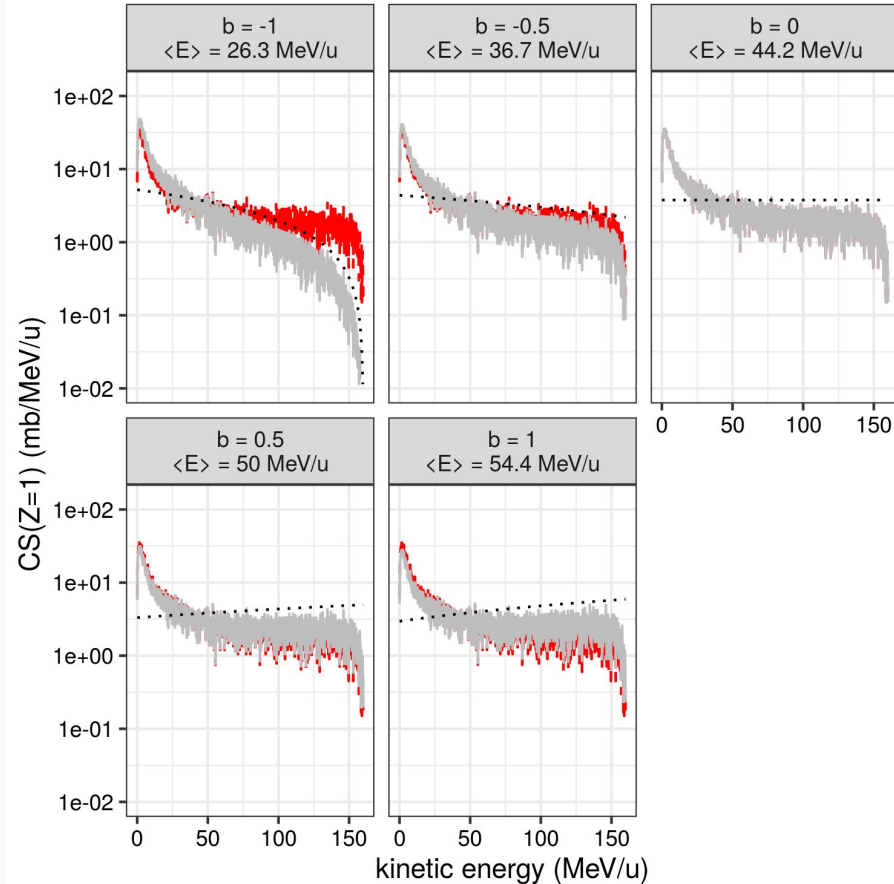
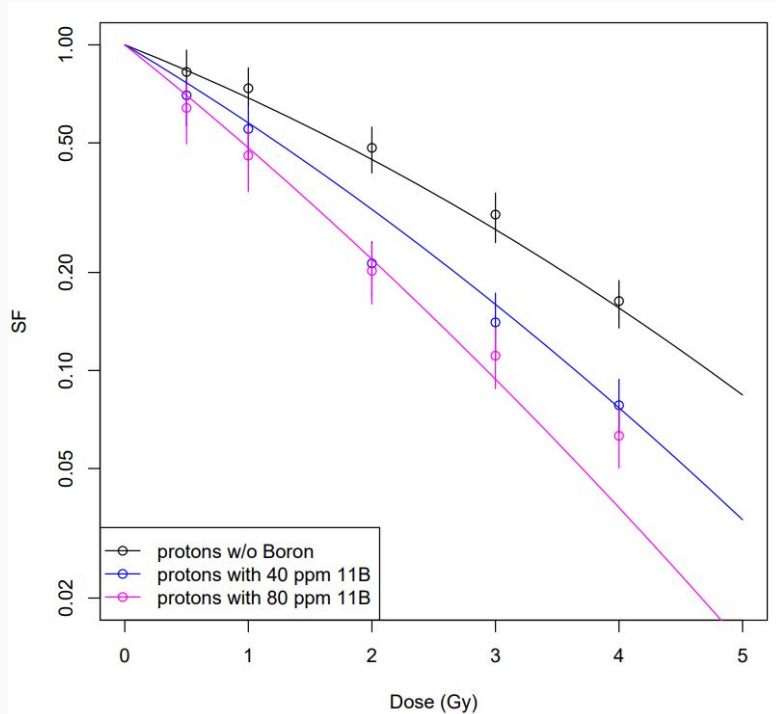
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- *Boron uptake and internalization*
 - **WP2** (, **WP4?**): [...] (misure per BSH e BPA usati negli esperimenti di sopravvivenza cellulare.)



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- **Objective:** Simultaneous global fit of total and differential CS to every clonogenic assays



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