NEPTUNE:

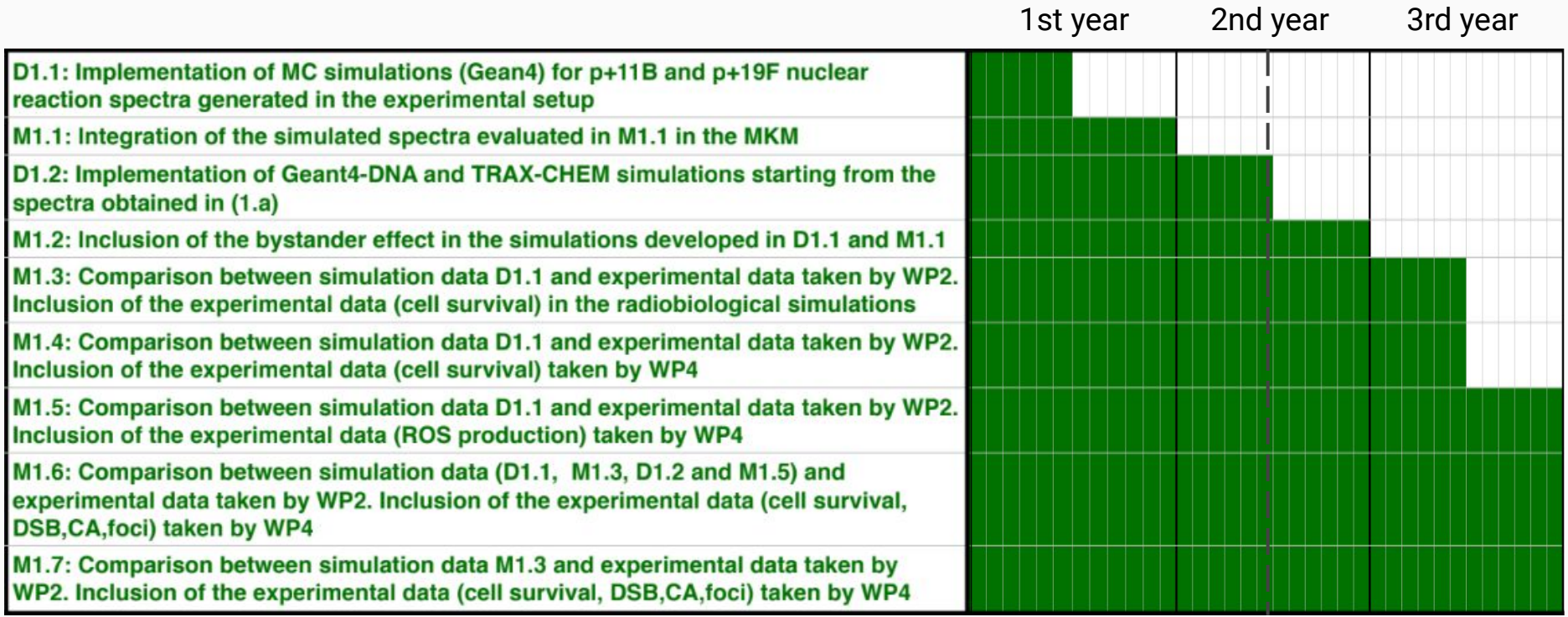
Nuclear process-driven Enhancement of Proton Therapy UNravElled

WP1 - Modeling

June, 19 2020

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

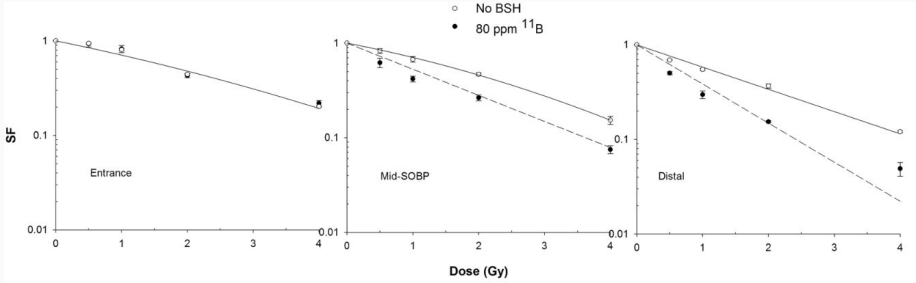
NEPTUNE WP1: milestones & deliverables

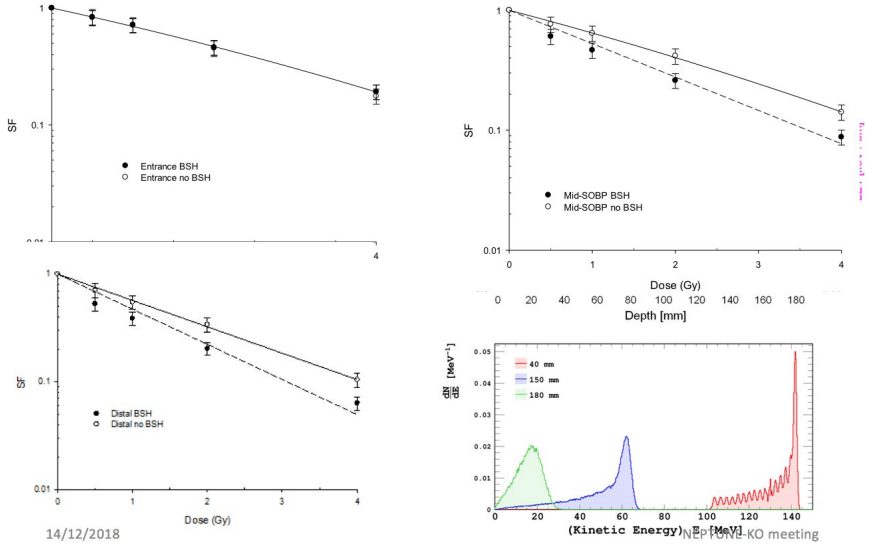


NEPTUNE WP1: revised workflow

- **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?*

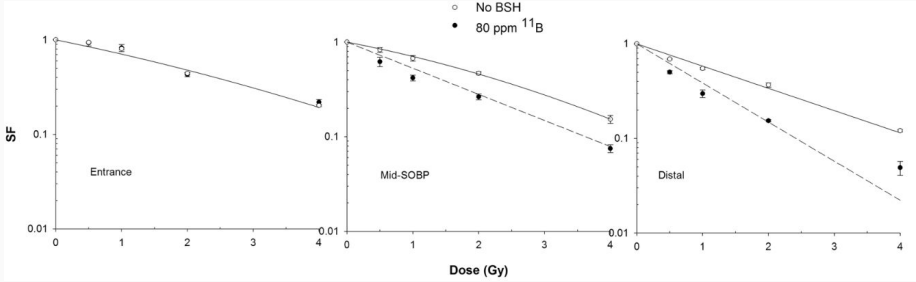
- **First step**: MC simulations implementation + Radiobiological modeling (modified MKM and LEM models to account alpha short ranges) to carry on a simultaneous global fit of alpha production CS to every clonogenic assays, possibly using all available reaction channel for alpha production.

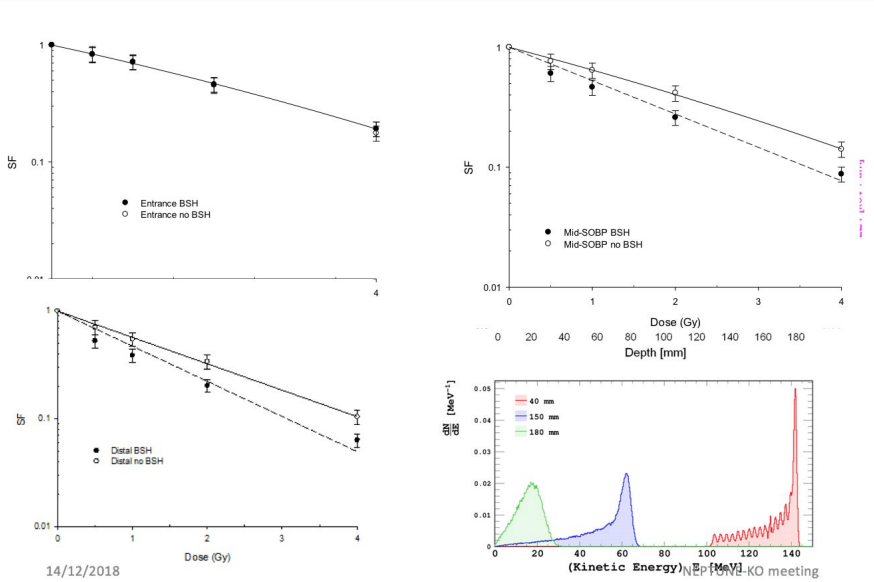




NEPTUNE WP1: revised workflow

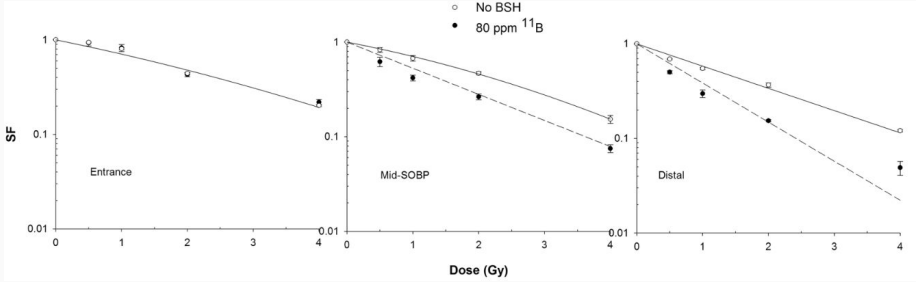
- *Clonogenic assays* @ LNS and CNAO - DU145 and PANC-1 cells irradiated w and w/out Boron (BSH and BPA). Six positions along the SOBP in total, corresponding to different proton energy conditions.
    - **WP4**: survival raw data (including x-ray irradiation) and dose measurements with uncertainties.

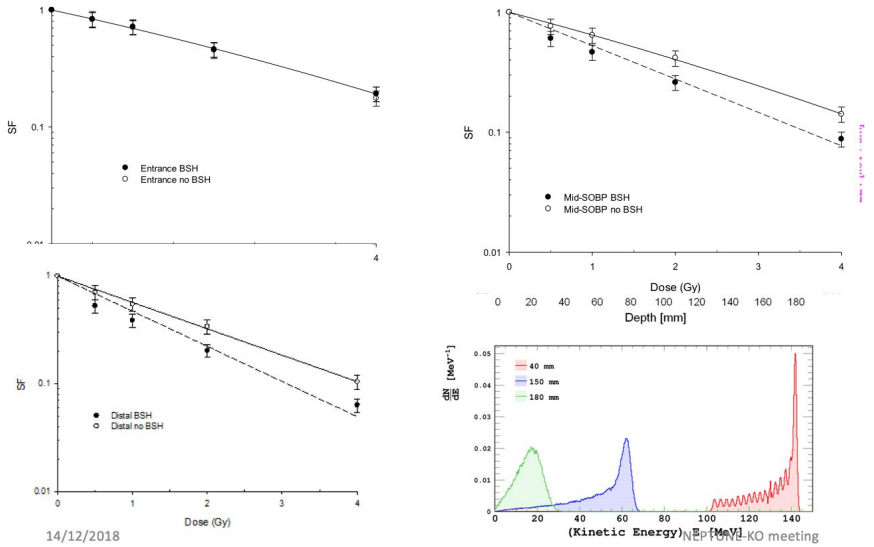




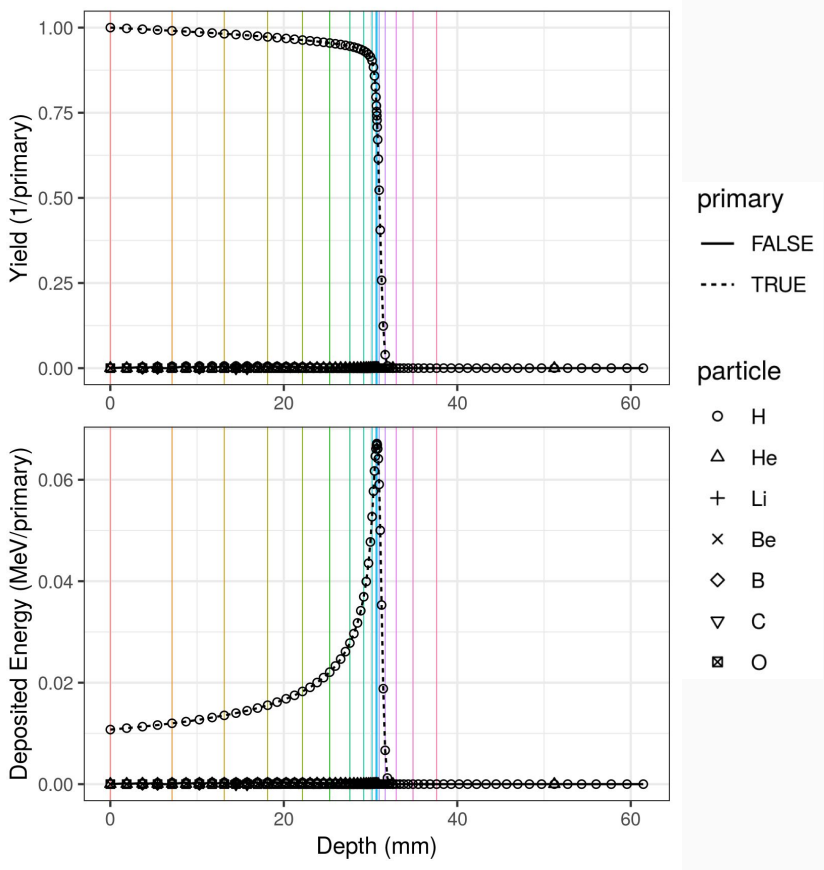
NEPTUNE WP1: revised workflow

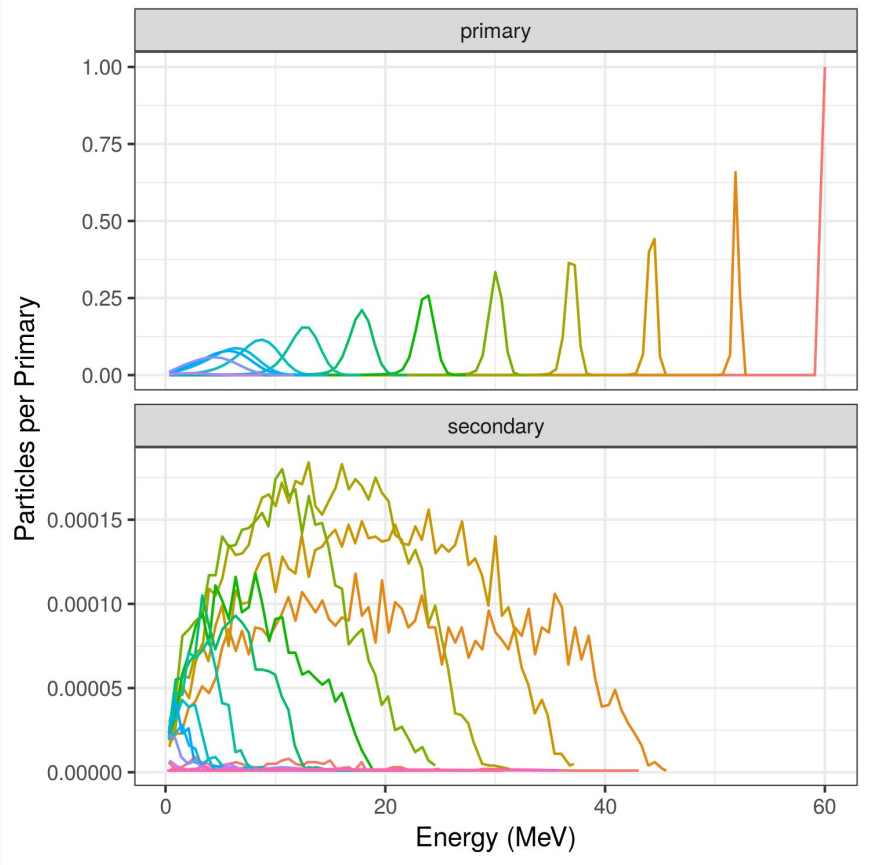
- *Clonogenic assays* @ LNS and CNAO - DU145 and PANC-1 cells irradiated w and w/out Boron (BSH and BPA). Six positions along the SOBP in total, corresponding to different proton energy conditions.
    - **WP4**: survival raw data (including x-ray irradiation) and dose measurements with uncertainties.
- *Spectra of protons* evaluated with MC @ the same cell depths along the SOBP (LNS and CNAO beamlines)
    - **WP1**: Geant4 Simualtion for LNS beamline
    - **WP3**: [...] (eventuali simulazioni già fatte per supporto alle misure microdosimentriche @ LNS)
    - **WP1**: (simulazioni di già fatte per supporto alle misure clonogeniche al CNAO)



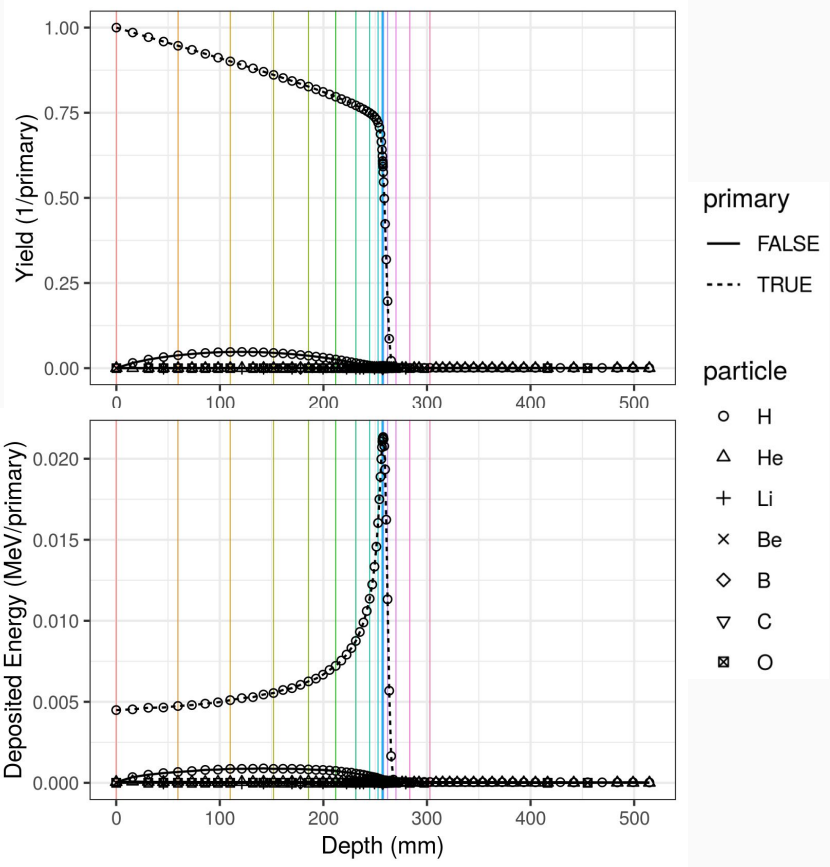


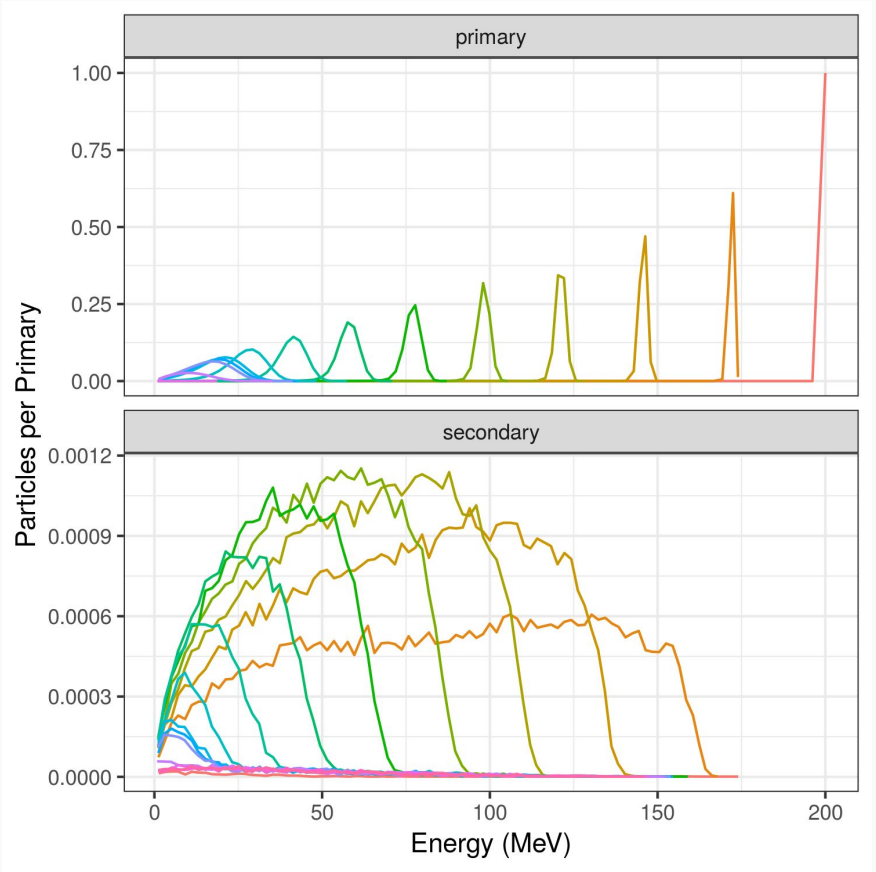
proton energy spectra for a proton beam (60 MeV) in a water phantom



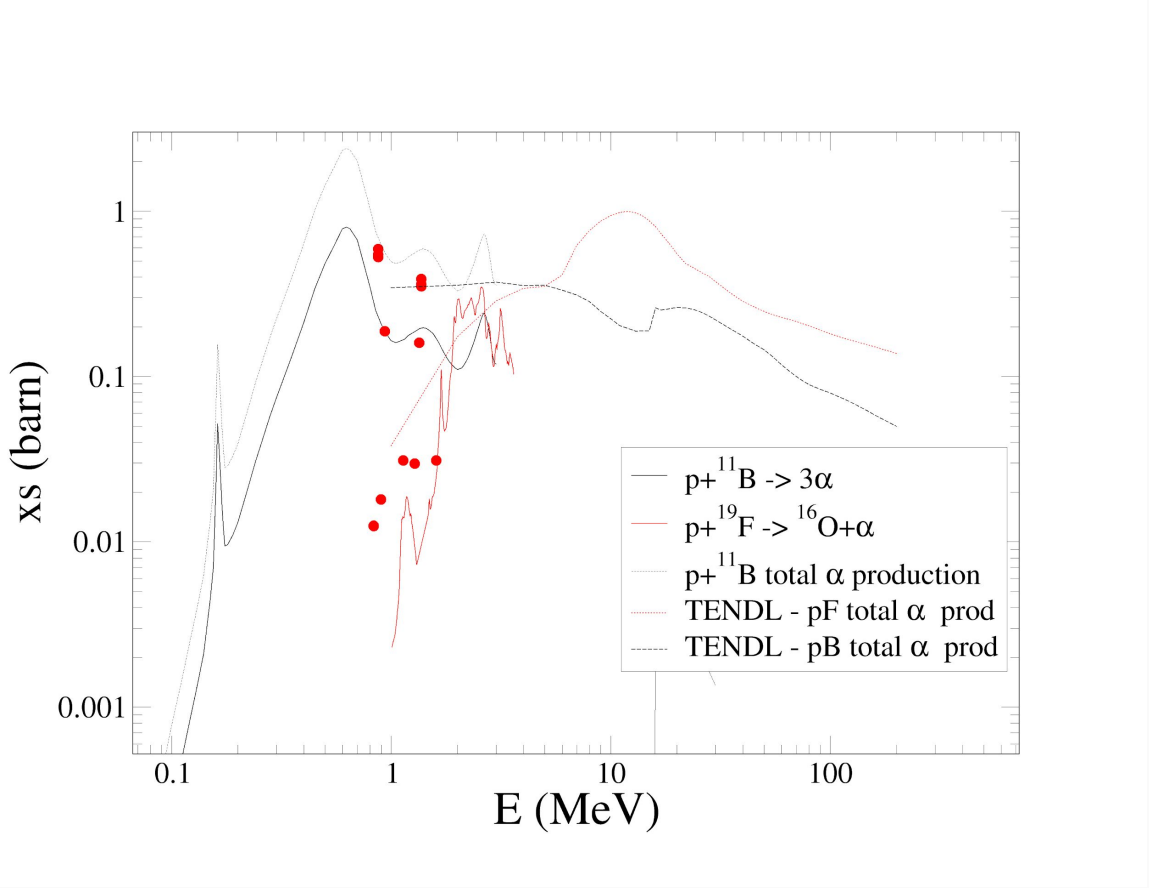


proton energy spectra for a proton beam (200 MeV) in a water phantom



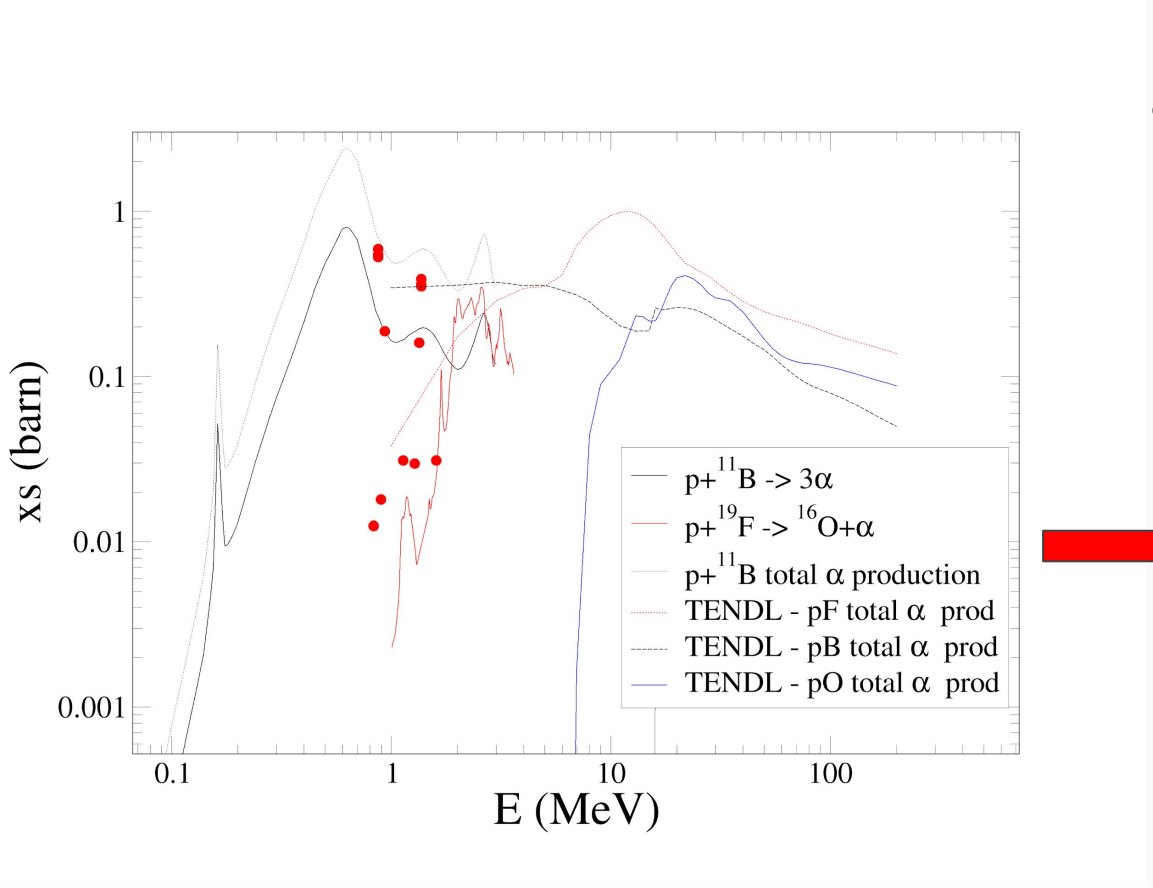


Cross sectional data for different interaction channels (TENDL + experiments)



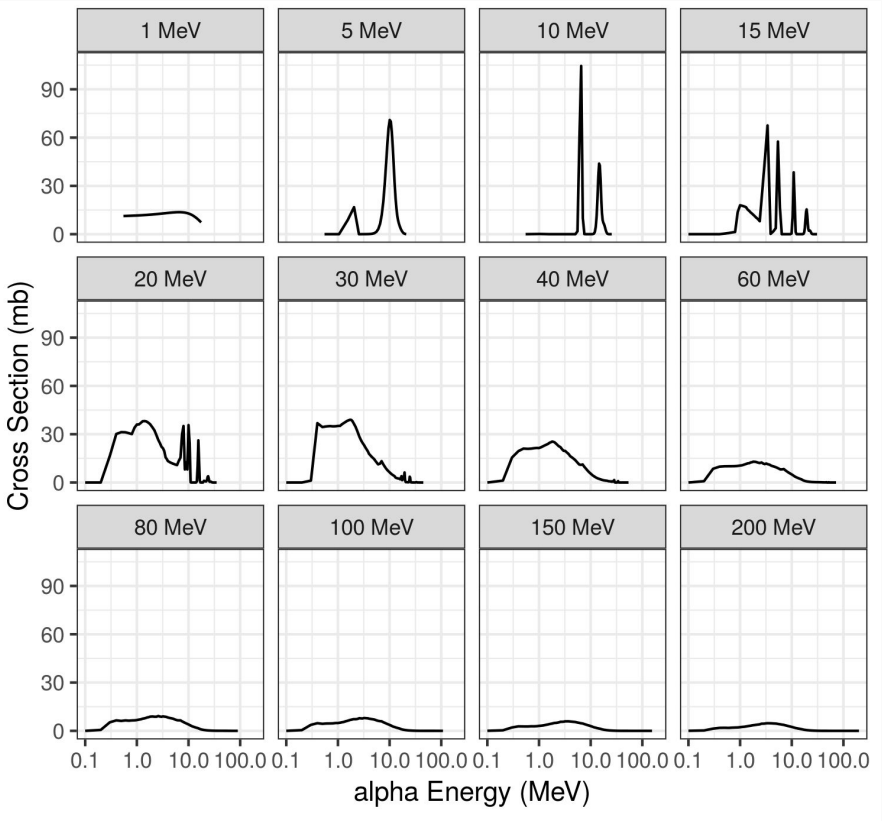
- CS data *theoretical* & *measured alpha production rate* (all available channels)
  - **WP1**: [Geant4/EXFOR/TENDL]
  - **WP3**: (dati sperimentali normalizzati di alpha production rate)

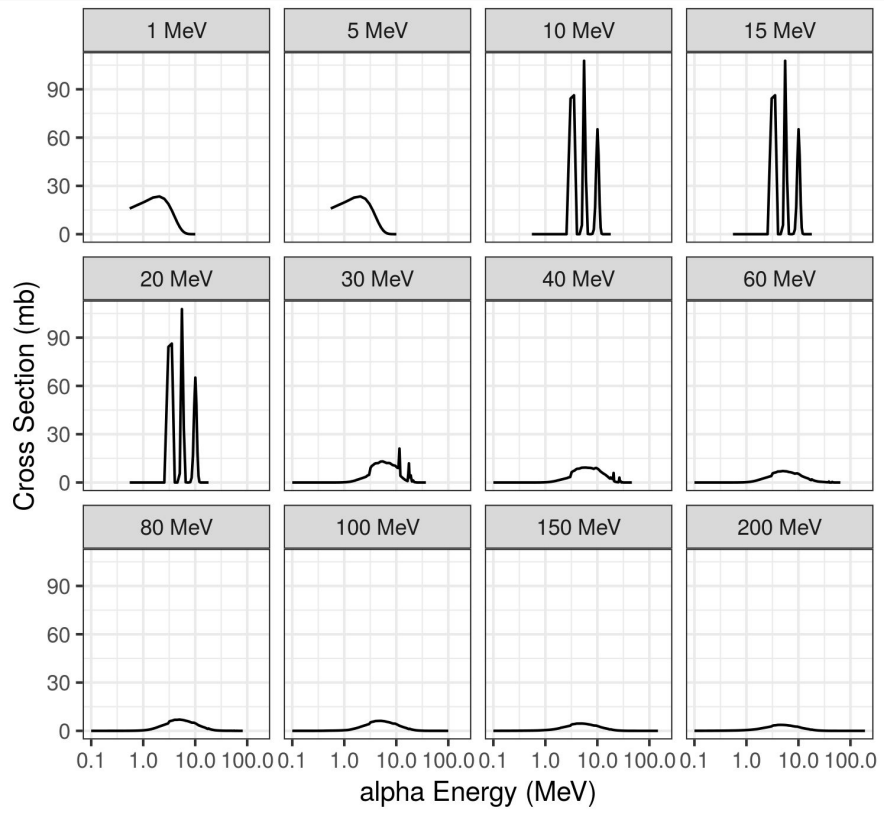
Cross sectional data for different interaction channels (TENDL + experiments)



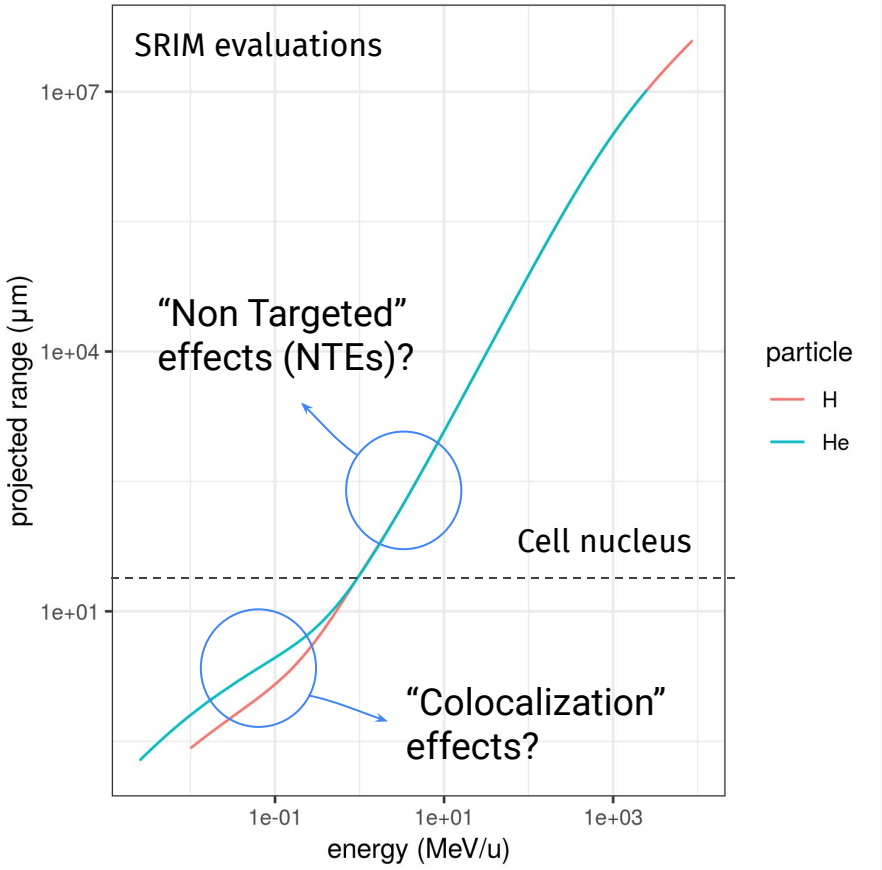
- CS data *theoretical* & *measured alpha production rate* (all available channels)
  - **WP1**: [Geant4/EXFOR/TENDL]
  - **WP3**: (dati sperimentali normalizzati di alpha production rate)
  - Link with FOOT/MOVE-IT?

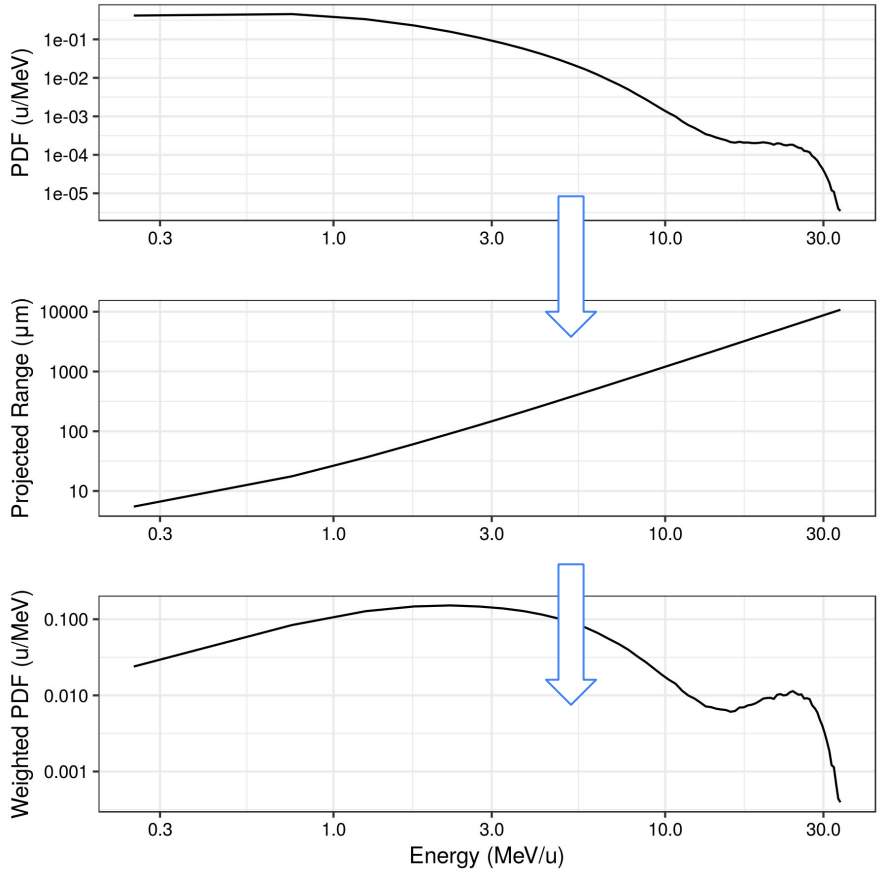
differential Cross Sections σ_{pf} (TENDL)





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





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 10B or 157Gd (Safavi-Naeini et al. 2018)

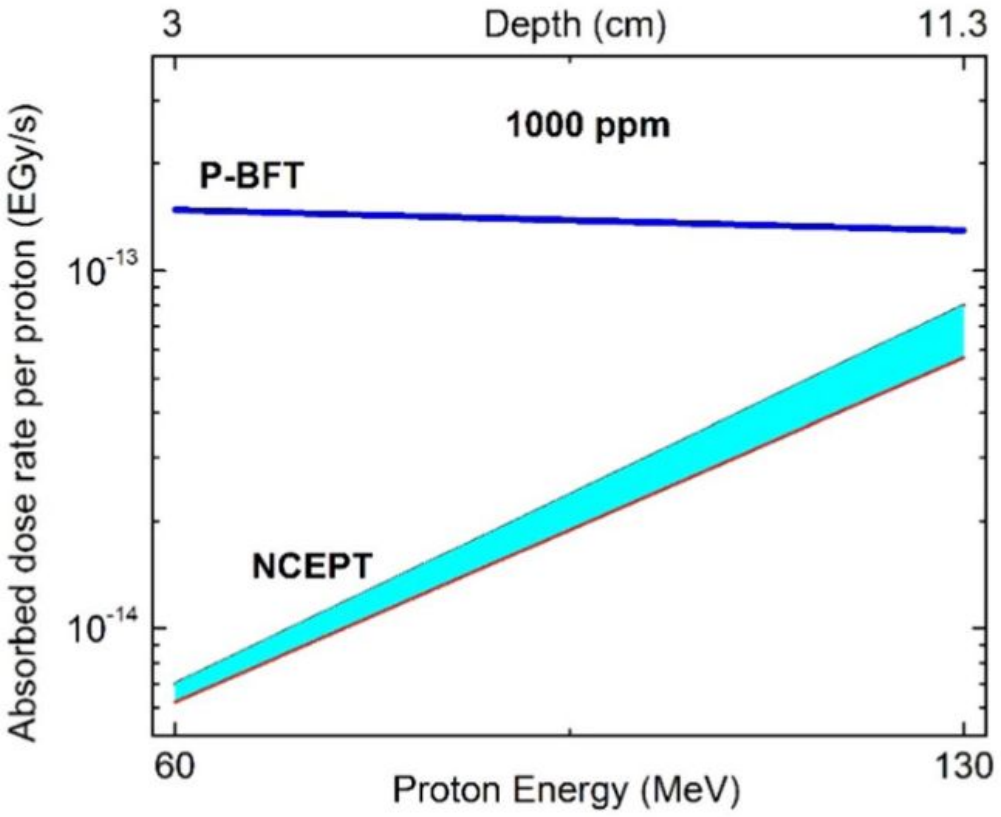
$$^{10}\mathrm{B} + n_{th} \rightarrow [^{11}\mathrm{B}]^{*} \rightarrow \alpha + {}^{7}\mathrm{Li} + \gamma(2.31\ \mathrm{MeV})$$

$$^{157}\mathrm{Gd} + n_{th} \rightarrow [^{158}\mathrm{Gd}]^{*} \rightarrow {}^{158}\mathrm{Gd} + \gamma + 7.94\ \mathrm{MeV}$$

Target Depth (mm)	Primary Ion	Thermal neutron fluence per GyE primary dose (n/cm²/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^{8}
		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)

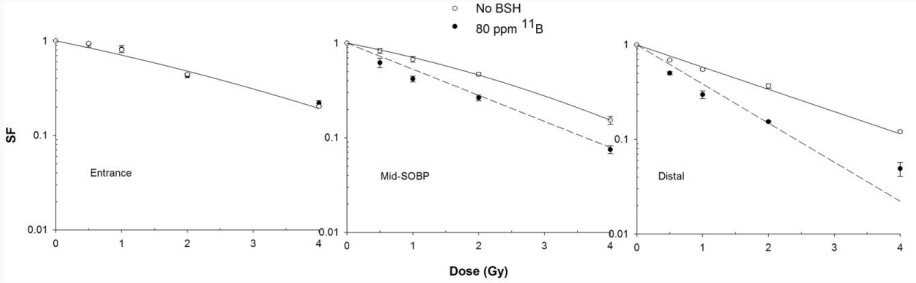
Comparing proton mediated vs neutron mediated mechanisms

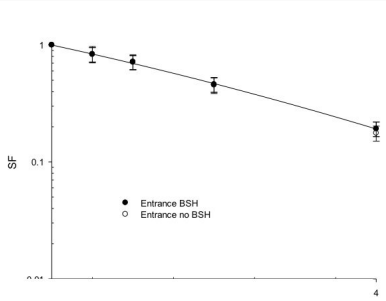


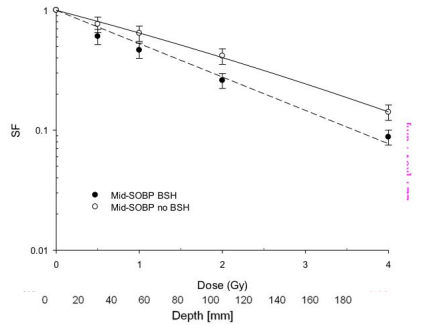
Tabbakh, F., & Hosmane, N. S. (2020). Enhancement of Radiation Effectiveness in Proton Therapy: Comparison Between Fusion and Fission Methods and Further Approaches. Scientific Reports, 10(1), 1–12.

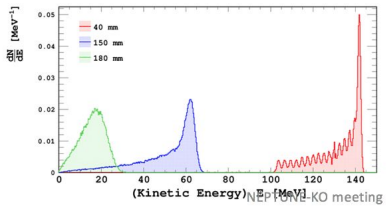
NEPTUNE WP1: revised workflow

- *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.
- *Spectra of protons* evaluated with MC @ the same cell depths along the SOBP (LNS and CNAO beamlines)
    - **WP1**: Geant4 Simulations for LNS beamline
    - **WP3**: [...] (eventuali simulazioni già fatte per supporto alle misure microdosimentriche @ LNS)
    - **WP1**: (simulazioni di già fatte per supporto alle misure clonogeniche al CNAO)
- *Boron uptake and internalization*
    - **WP2** (, **WP4?)**: [...] (misure per BSH e BPA usati negli esperimenti di sopravvivenza cellulare.)



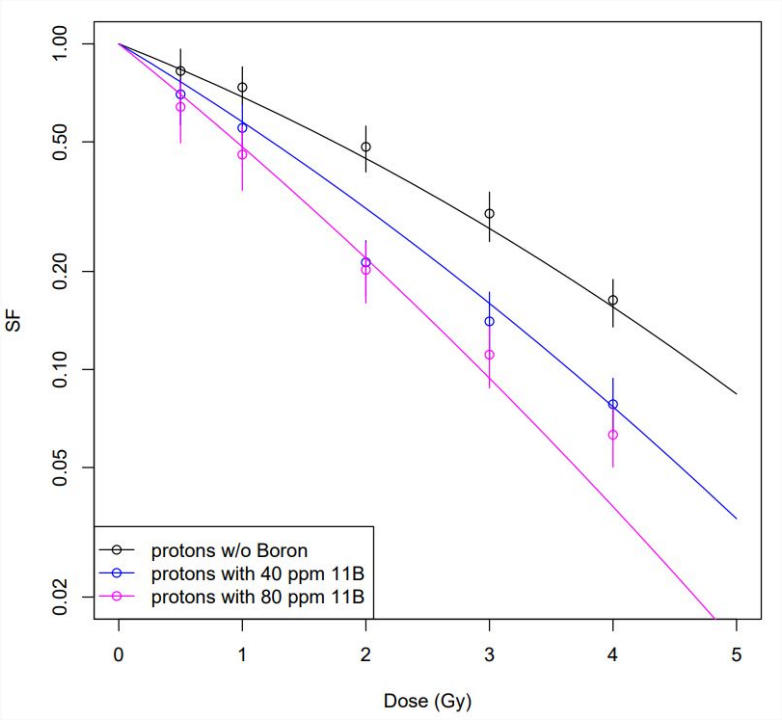


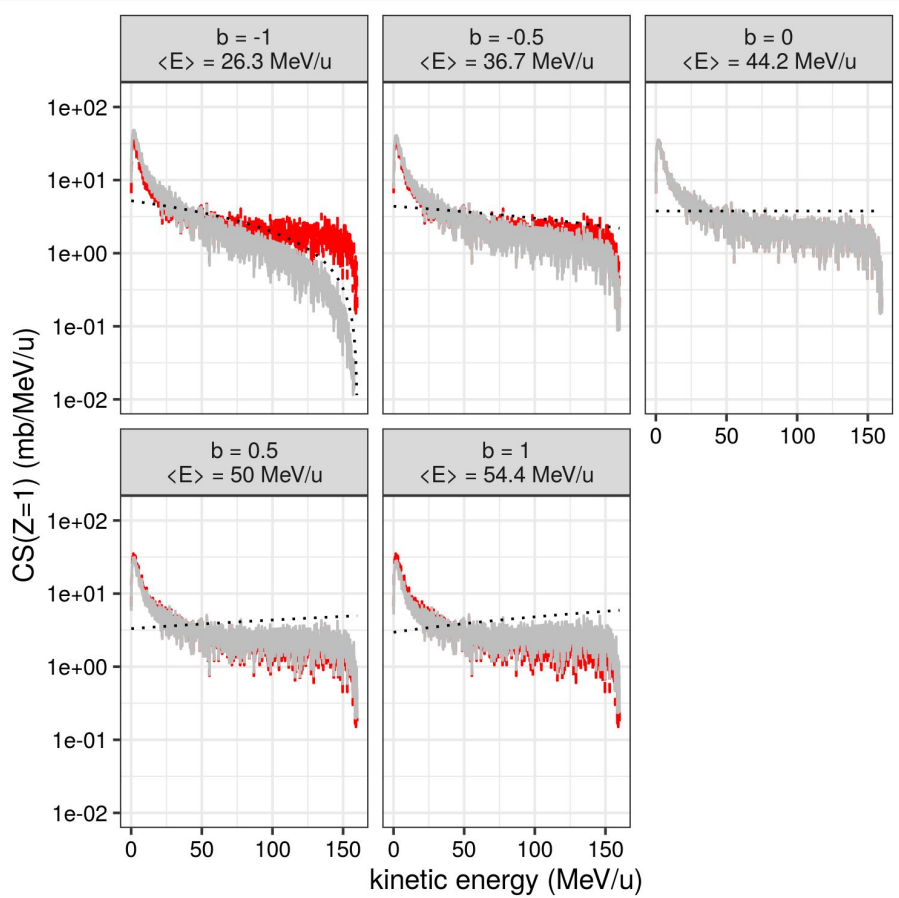


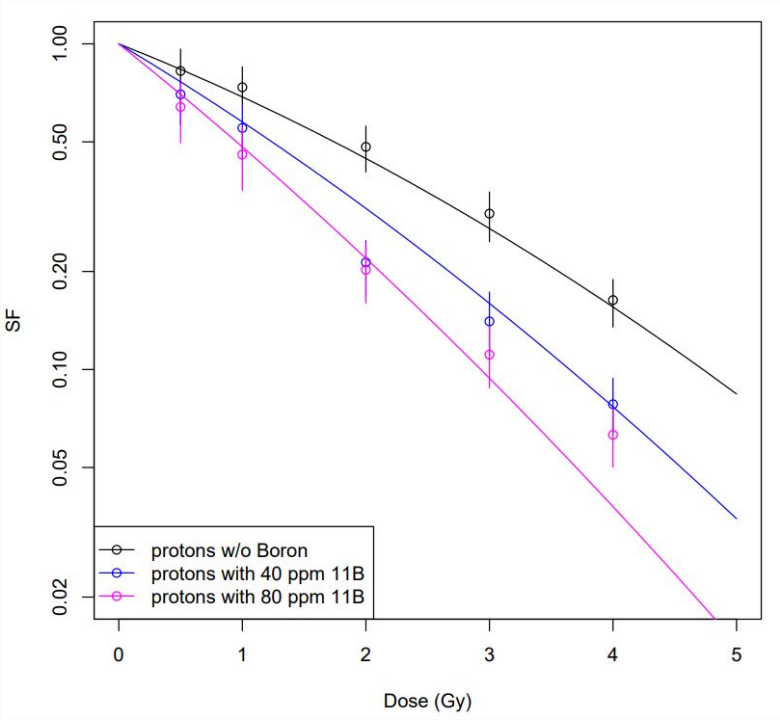
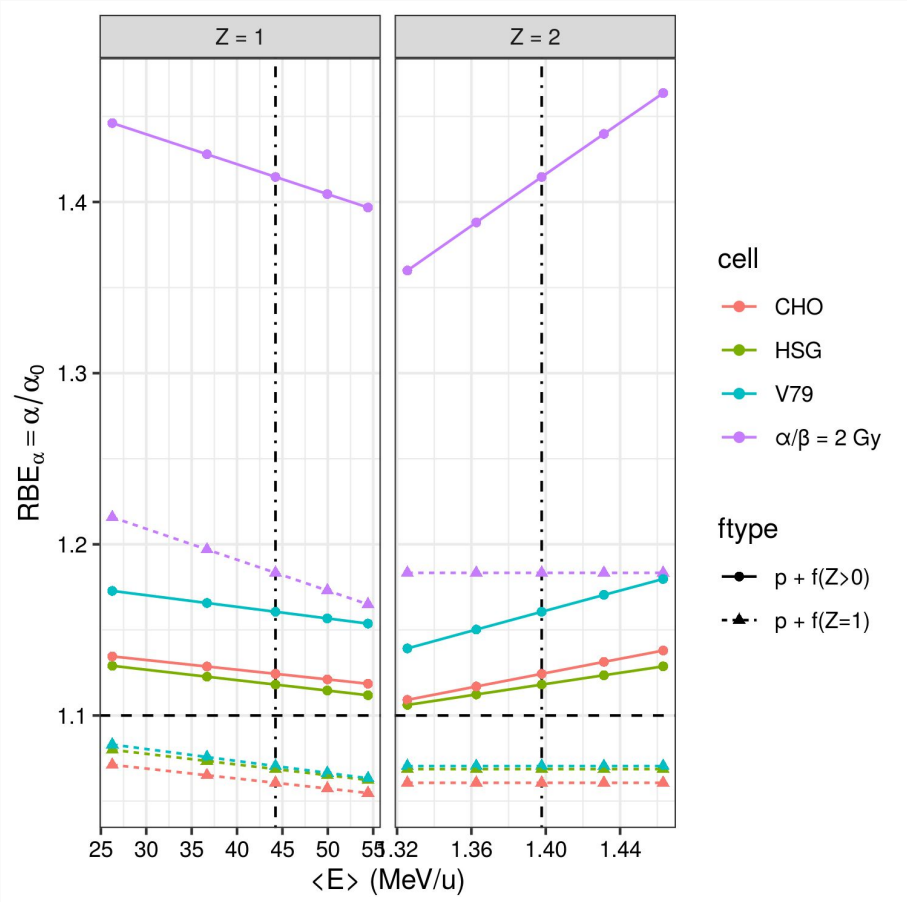


NEPTUNE WP1: revised workflow

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





NEPTUNE WP1: revised workflow

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