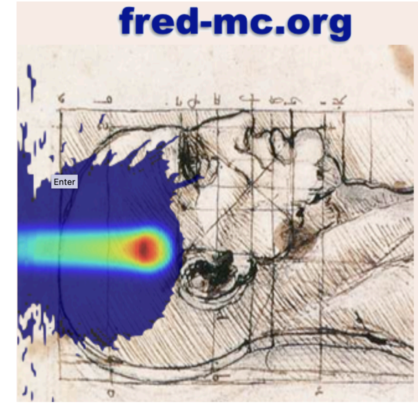

Protons and carbon ions interactions with the matter in FRED

Giacomo Traini

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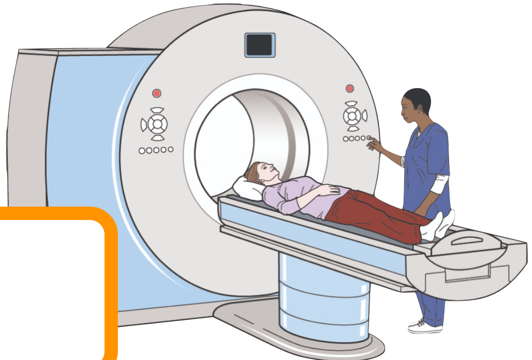
Treatment Planning System

(required) Kinetic Energy (MeV)	Stopping Power (MeV cm^2/g)			Range		
	Electronic	Nuclear	Total	CSDA (g/cm^2)	Projected (g/cm^2)	Detour Factor Projected / CSDA
1.000E-03	1.337E+02	4.315E+01	1.769E+02	6.319E-06	2.878E-06	0.4555
1.500E-03	1.638E+02	3.460E+01	1.984E+02	8.969E-06	4.400E-06	0.4906
2.000E-03	1.891E+02	2.927E+01	2.184E+02	1.137E-05	5.909E-06	0.5197
2.500E-03	2.114E+02	2.557E+01	2.370E+02	1.357E-05	7.380E-06	0.5440
3.000E-03	2.316E+02	2.281E+01	2.544E+02	1.560E-05	8.811E-06	0.5647
4.000E-03	2.675E+02	1.894E+01	2.864E+02	1.930E-05	1.155E-05	0.5986
5.000E-03	2.990E+02	1.631E+01	3.153E+02	2.262E-05	1.415E-05	0.6254
6.000E-03	3.276E+02	1.439E+01	3.420E+02	2.567E-05	1.661E-05	0.6473
7.000E-03	3.538E+02	1.292E+01	3.667E+02	2.849E-05	1.896E-05	0.6656
8.000E-03	3.782E+02	1.175E+01	3.900E+02	3.113E-05	2.121E-05	0.6813
9.000E-03	4.012E+02	1.080E+01	4.120E+02	3.363E-05	2.337E-05	0.6950
1.000E-02	4.229E+02	1.000E+01	4.329E+02	3.599E-05	2.545E-05	0.7070
1.250E-02	4.660E+02	8.485E+00	4.745E+02	4.150E-05	3.037E-05	0.7318
1.500E-02	5.036E+02	7.400E+00	5.110E+02	4.657E-05	3.499E-05	0.7514
1.750E-02						
2.000E-02						
2.250E-02						
2.500E-02						
2.750E-02						
3.000E-02						
3.500E-02						
4.000E-02						
4.500E-02						



Patient anatomic data (CT, MRI, PET)

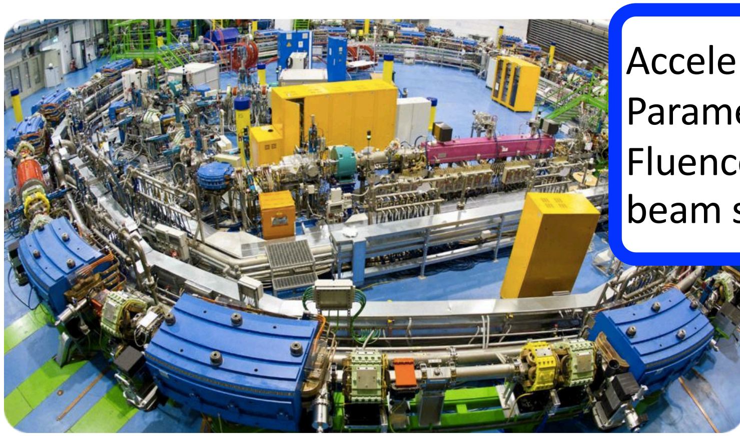
Table of:

- dE vs E_{beam}, x, y, z
- RBE vs E_{beam}, dE, x, y, z

TPS

Physician Prescription

interest	Volume	scription/tolerance dose (Gy)	Relative importance
Prostate PTV	100	74.0	1.0
Prostate PTV	5.0	72.0	1.0
Prostate PTV	10.0	76.0	1.0
Rectum	90.0	10.0	0.5
Rectum	50.0	20.0	0.5
Rectum	10.0	30.0	0.5
Bladder	90.0	10.0	0.2
Bladder	50.0	20.0	0.2
Bladder	10.0	30.0	0.2
Femoral heads	90.0	10.0	0.2
Femoral heads	50.0	20.0	0.2
Femoral heads	10.0	40.0	0.2

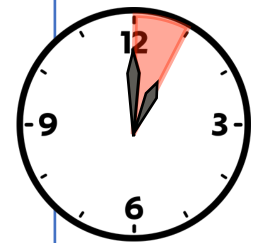


Accelerators Parameters: Fluences for each beam spot

Treatment Planning System

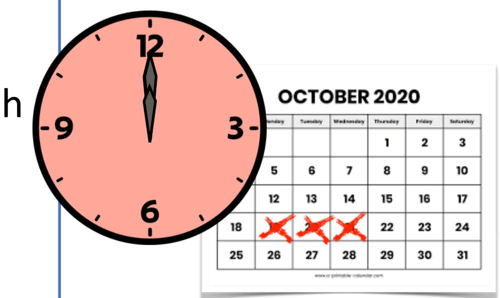
ANALITIC TPS:

- Fast (~ 1 h/core, minutes on GPU)
- Simplified beam-body interaction model using a 3D water equivalent representation of the patient morphology
- Routinely used in PT treatments



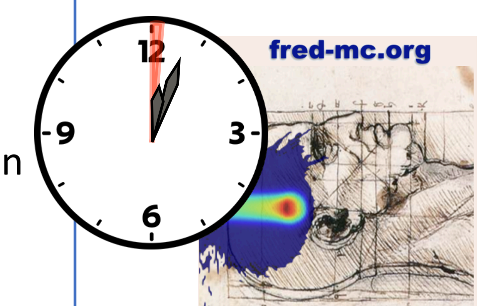
MC-TPS: (FLUKA, Geant4, TOPAS)

- Slow (~ days/core)
- Explicitly take into account the details in the interaction of particles with human tissuRoutinely used in PT treatments
- Only used to check treatment plans for a restricted number of difficult cases



FAST MC: FRED (Fast paRticle thErapy Dose evaluator

- Fast (few minutes)
- Takes into account the details in the interaction of particles with human tissues that are needed for a TPS



FRED (Fast paRticle thErapy Dose evaluator)

Protons

Proton Therapy

The most refined module, already used as Quality Assurance (to control analytics TPS) and as a research tool at several clinical and research centers in Europe.

A. Schiavi et al, PMB 62 (2017) 7482–7504

M. Senzacqua PhD Thesis

Carbon ions

Hadron Therapy

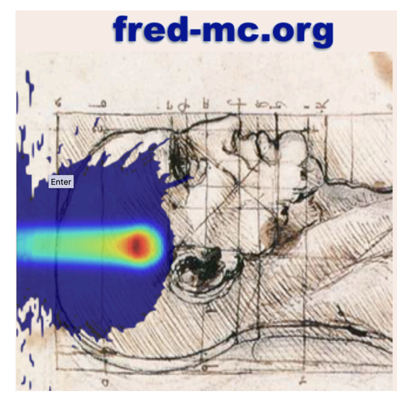
The model has been developed and now it needs to be ported on GPU and clinically validated.

M. De Simoni PhD Thesis

Electrons

Photons

IORT (IntraOperative RadioTherapy)
conventional Radiotherapy
FLASH therapy

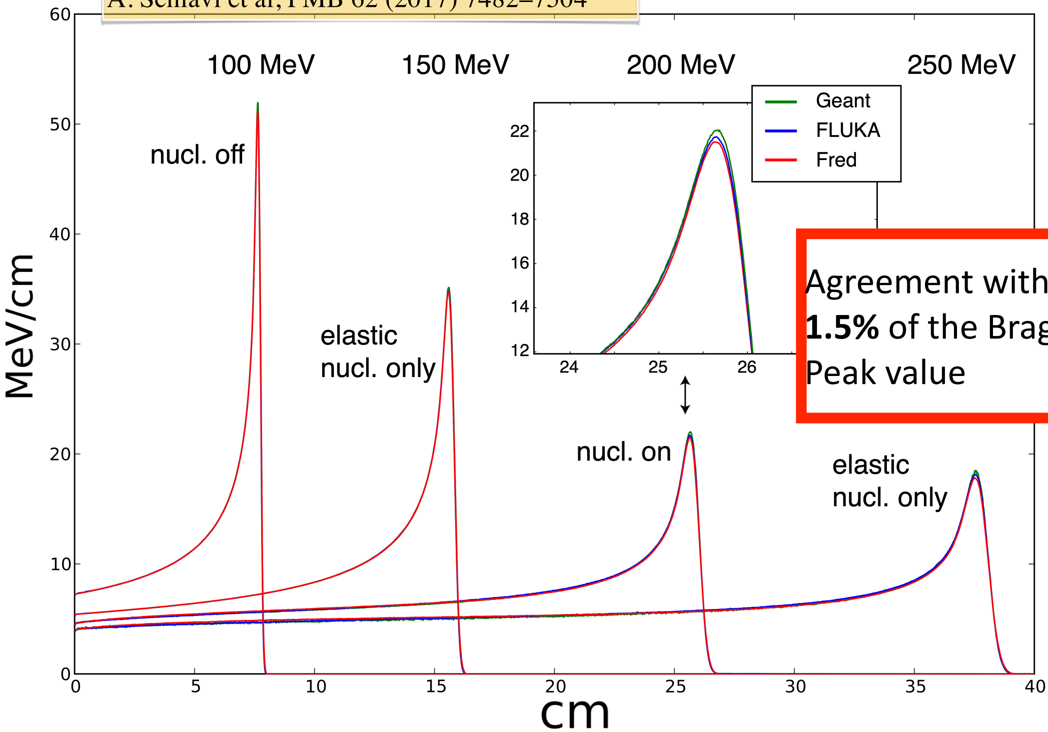


- **fred-mc.org**
- **http://arpg-serv.ing2.uniroma1.it/**

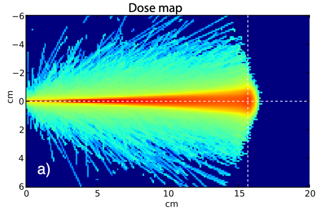
FRED for protons: current performance

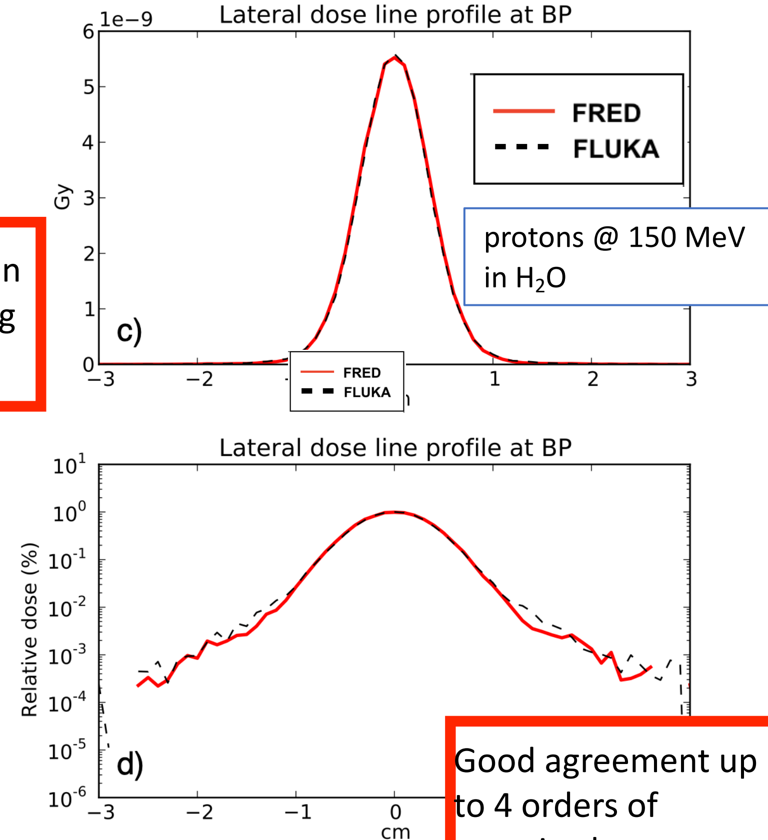
Performance tests: proton beams at different energies in a water target have been simulated with FRED, FLUKA and GEANT4 switching on and off different models.

A. Schiavi et al, PMB 62 (2017) 7482–7504



Agreement within **1.5%** of the Bragg Peak value





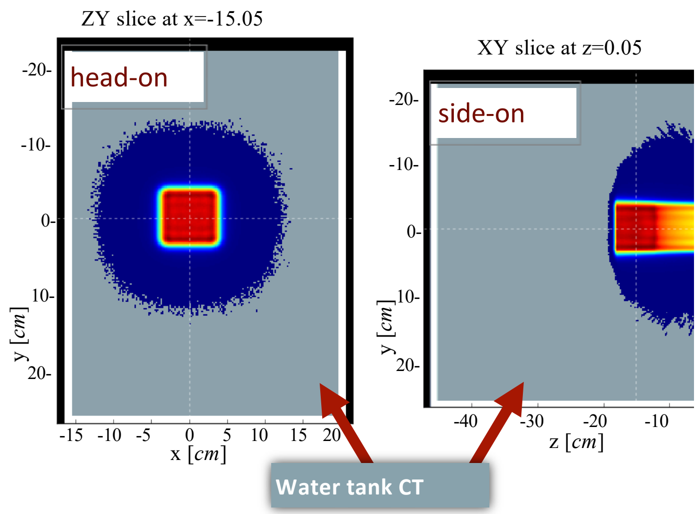
protons @ 150 MeV in H_2O

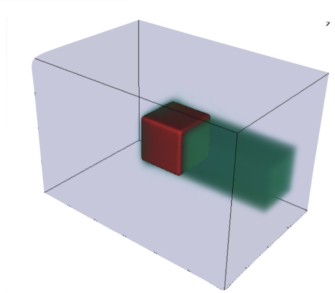
Good agreement up to 4 orders of magnitude

QA SOBP

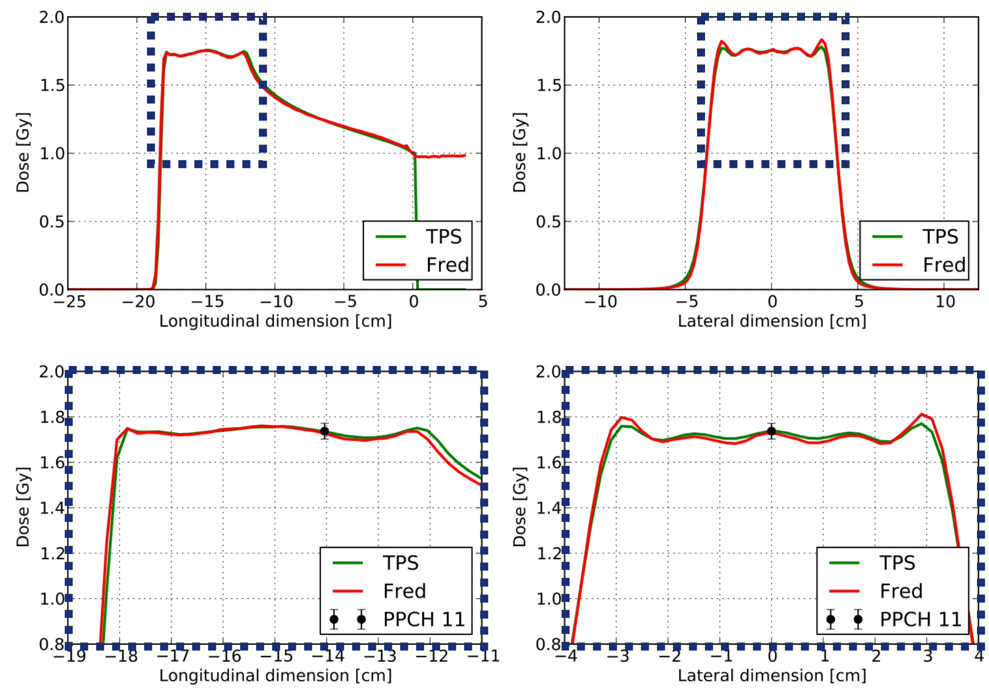
SOBP QA: set of 6 *cm*-sided cubic volumes, planned and verified in water with the same dosimetric system applied for patient-specific QA -> routine at CNAO

Irradiation geometry and dose map in the longitudinal and transverse planes for the SOBP QA cube at the depth of 15 *cm*





The SOBP QA has been calculated with TPS and then recalculated with FRED. Both have been compared with measurements (PPCH 11).

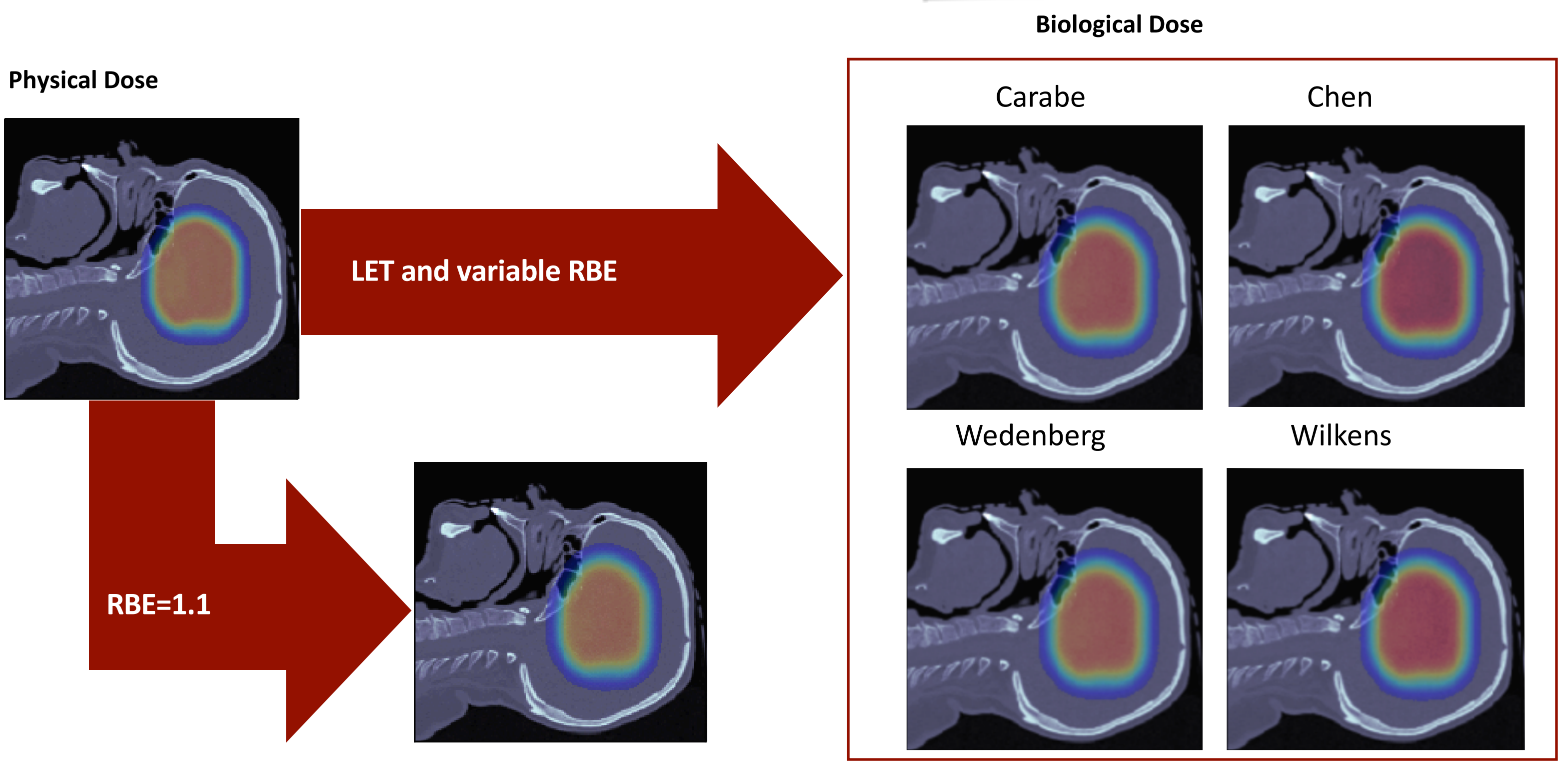


3D Gamma index (2mm/2%) passing rate for all measurements >99%

Biological dose with variable RBE

$$RBE\left(D_p, \overbrace{\frac{\alpha_p}{\alpha_x}, \frac{\beta_p}{\beta_x}}, \left(\frac{\alpha}{\beta}\right)_x\right) = \frac{D_x}{D_p} = \frac{\sqrt{\left(\frac{\alpha}{\beta}\right)_x^2 + 4\frac{\alpha_p}{\alpha_x}\left(\frac{\alpha}{\beta}\right)_x D_p + 4\frac{\beta_p}{\beta_x} D_p^2} - \left(\frac{\alpha}{\beta}\right)_x}{2D_p}$$

Variable RBE models:
Wedenberg (Wedenberg et al. 2013)
Wilkens (Wilkens and Oelfke 2004)
Chen (Chen and Ahmad 2012)
Carabe (Carabe at al. 2012)



Tracking speed capability

FRED is already used in proton therapy as a quality assurance tool in the clinical center of Maastricht and Krakow and as a research tool at several clinical and research centers in Europe (Krakow, Trento, Maastricht, Lyon and PSI)

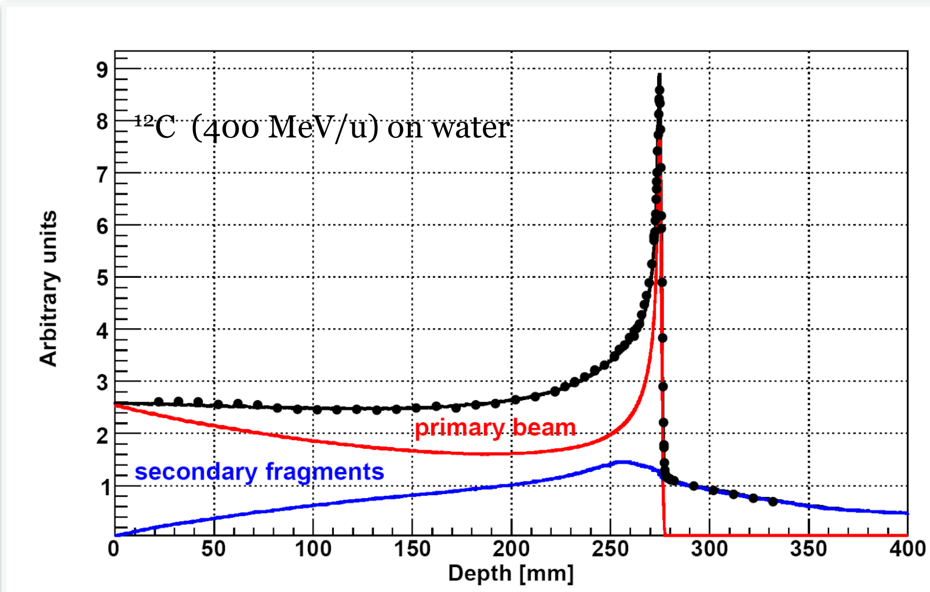
	Hardware	Primary/s	μs/primary
FLUKA/GEANT4	single CPU core	0.75 k	1340
FRED	single CPU core	15 k	68
FRED	single GPU card (NVIDIA GTX 980)	5000 k	0.2

De Simoni M. et al. Journal of Physics: Conference Series 1548 (2020)

Primary/s ∝ #GPUs

Carbon Therapy

Interest of CNAO and MedAustron for the use of FRED in carbon Therapy



- Mitigation and attenuation of the primary beam
- Different biological effectiveness of the fragments wrt the beam
- Different fragment ranges

fondazione CNAO

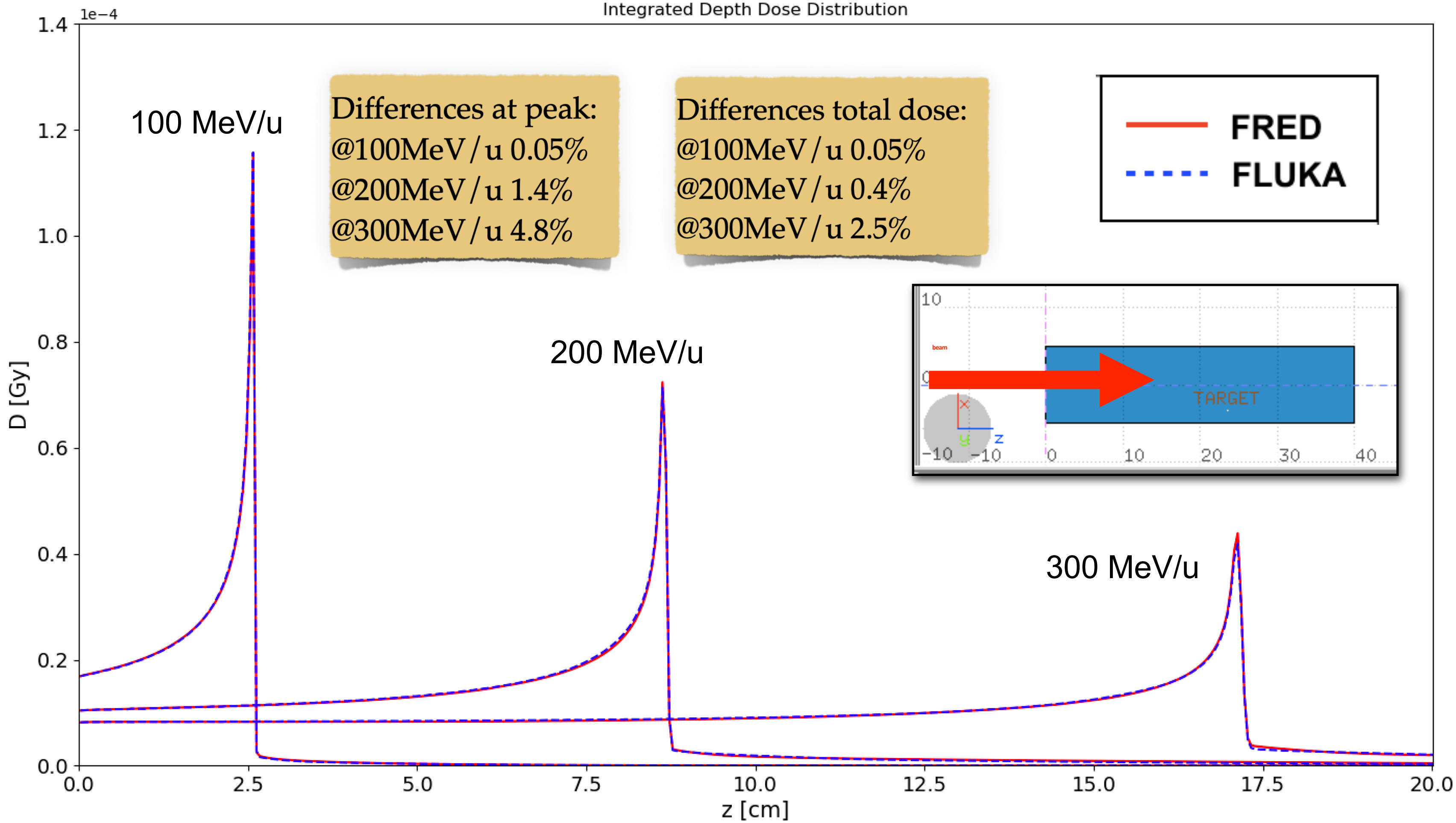
MedAustron

What we implemented:

- **Ionization energy loss** (Bethe-Bloch, Gaussian approximation, Vavilov and Landau distributions)
- **Multiple Coulomb Scattering (theory of Moliére adding a scaling factor following Fippel and Soukup approach)**
- **Nuclear Model** (phenomenologic approach based on Ganil measurement at 95 MeV/u)**:**
  - **Coefficient of mass attenuation** to decide when there is an elastic and non-elastic event. Based on data found in literature;
  - **Sampling of the fragments** and their **energy and angle distributions**. Based on double differential cross-section measurements;
- **Biological Dose and Relative Biological Effectiveness (LEM1 model)**

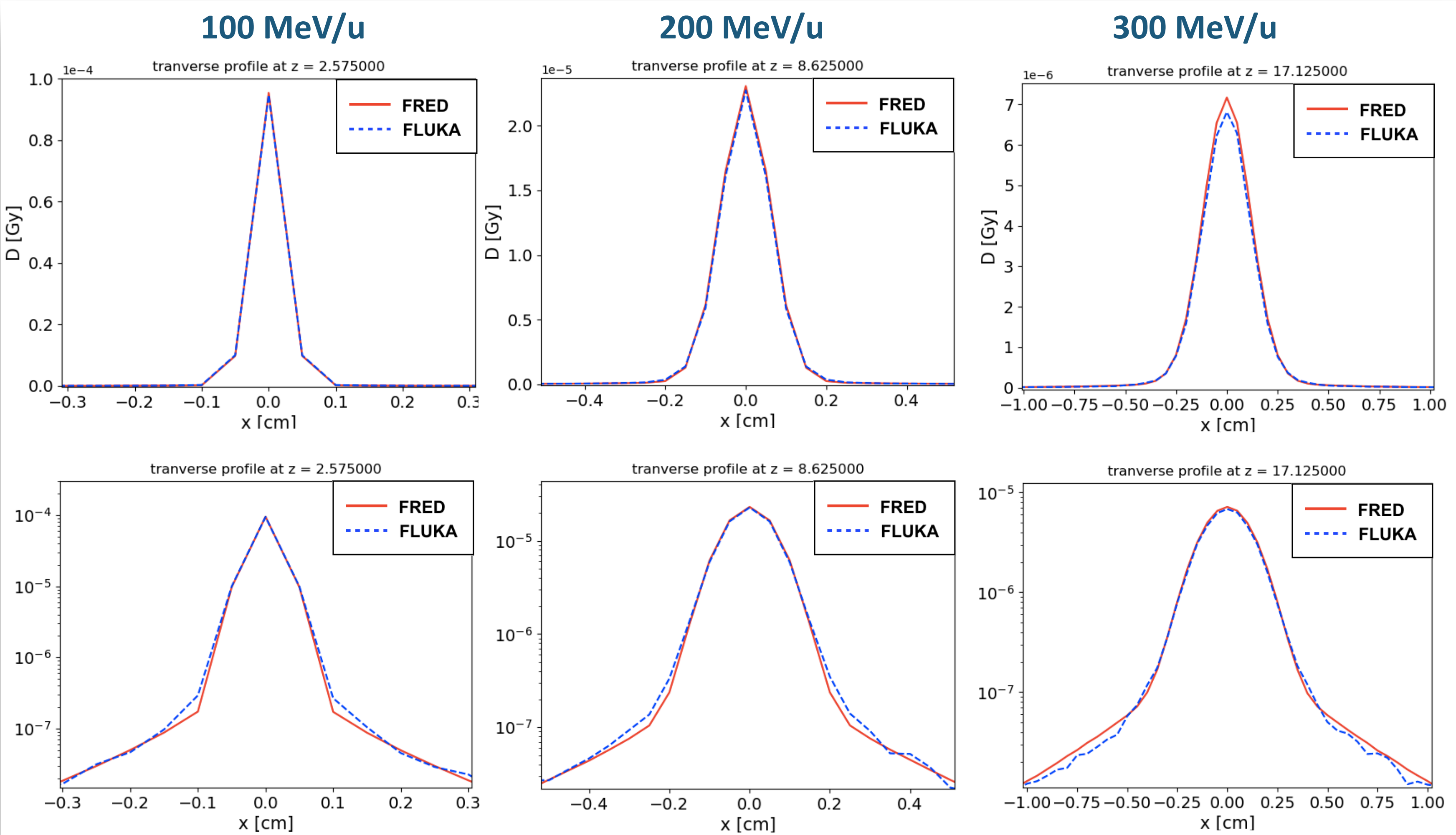
Validation of the model

Depth Dose Distribution of single pencil beam of ^{12}C in water



Validation of the model

Lateral distribution at Bragg Peak of single pencil beam of ^{12}C in water



RBE

The **LEM 1 (Local Effect Model)** has been implemented in FRED.

The principal assumption of the LEM 1 is that the total biological effect can be calculated using the scoring the local biological effect of all the particles that release dose.

For each voxel, calculation of:

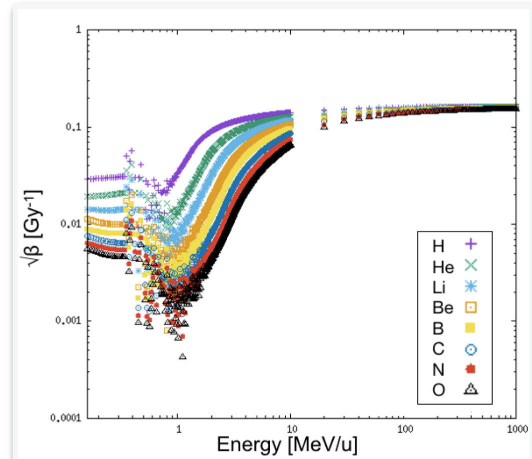
$$\bar{\alpha} = \frac{\sum_{i=1}^{n} \alpha_i D_i}{\sum_{i=1}^{n} D_i},$$

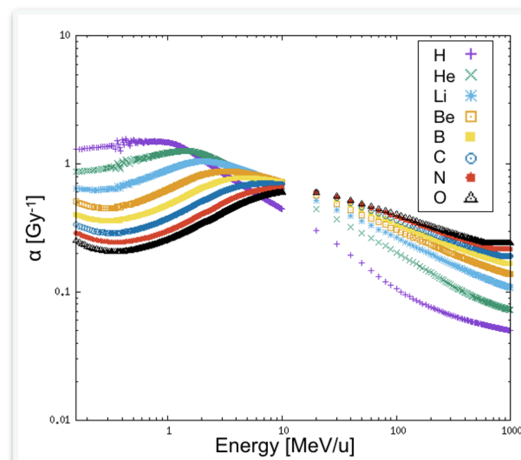
$$\bar{\beta} = \left(\frac{\sum_{i=1}^{n} \sqrt{\beta_i} D_i}{\sum_{i=1}^{n} D_i} \right)^2$$

$$-ln(S) = \begin{cases} (\bar{\beta} D_{abs} + \bar{\alpha}) D_{abs} & if\ D_{abs} \leq D_{cut} \\ (\bar{\beta} D_{cut} + \bar{\alpha}) D_{cut} + S_{max}(D_{abs} - D_{cut}) & if\ D_{cut} > D_{cut} \end{cases}$$

$$D_{RBE} = \begin{cases} \sqrt{\frac{-ln(S)}{\beta_x} + \left(\frac{\alpha_x}{2\beta_x}\right)^2} - \frac{\alpha_x}{2\beta_x} & if\ -ln(S) \leq -ln(S_{cut}) \\ \frac{-ln(S)+ln(S_{cut})}{S_{max}} + D_{cut} & if\ -ln(S) > -ln(S_{cut}) \end{cases}$$

$$RBE^i = \frac{D^i_{RBE}}{D^i}$$

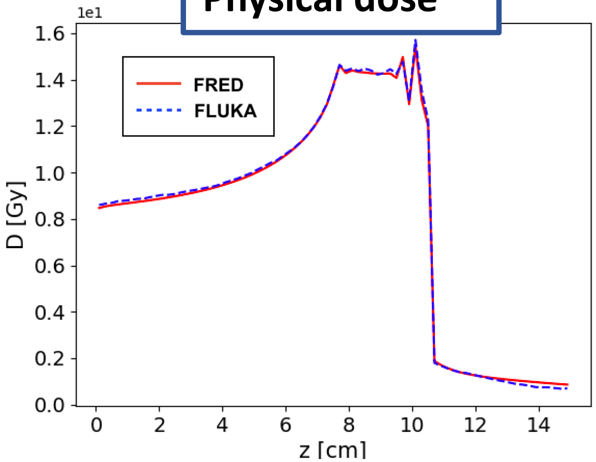




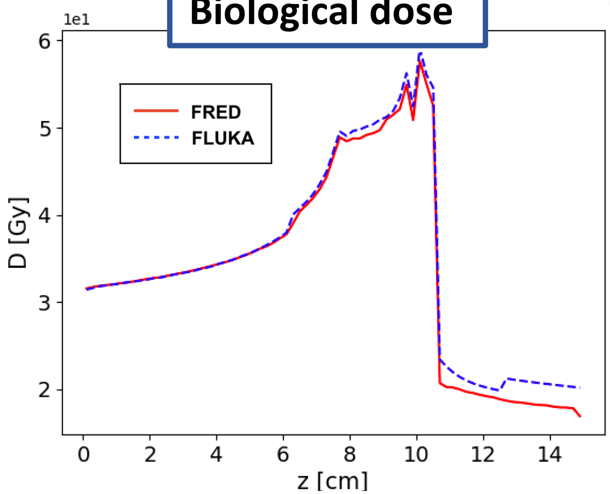
α and β from TOPAS database

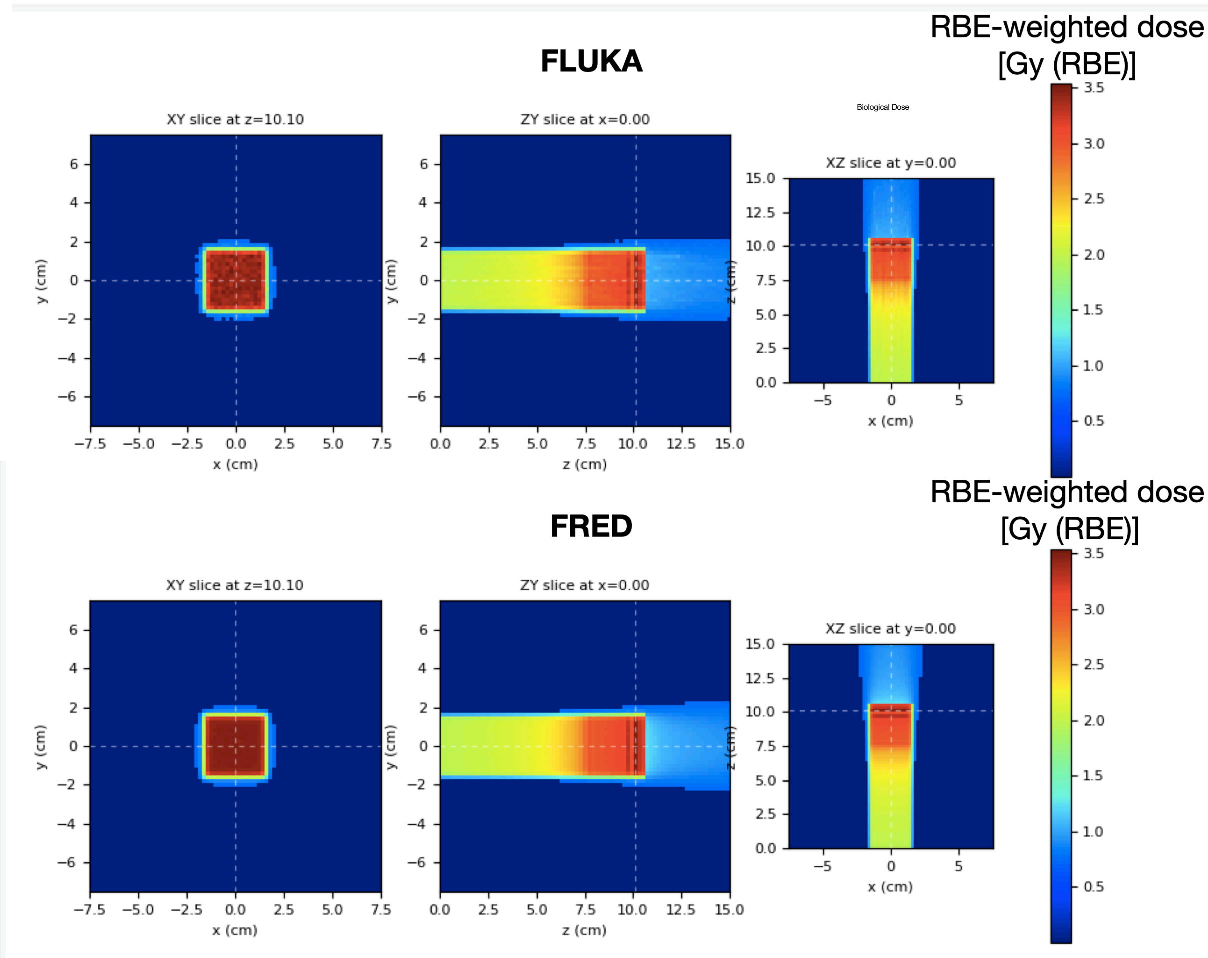
Biological Dose

Physical dose



Biological dose





Fred for e-, γ

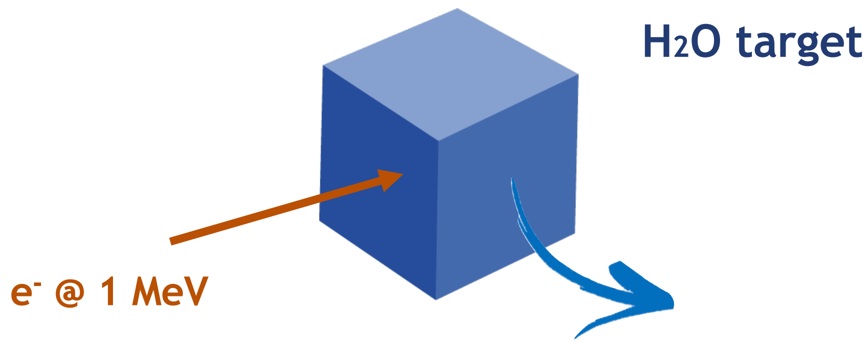
Continue processes (e^- e^+):

→dE/dx from NIST eSTAR database + straggling (GEANT4 physics manual 2019)
→Multiple scattering (A. A. Al Beteri, D.E. Raeside, Medical Physics 15, 351 (1988) doi: 10.1118/1596230).

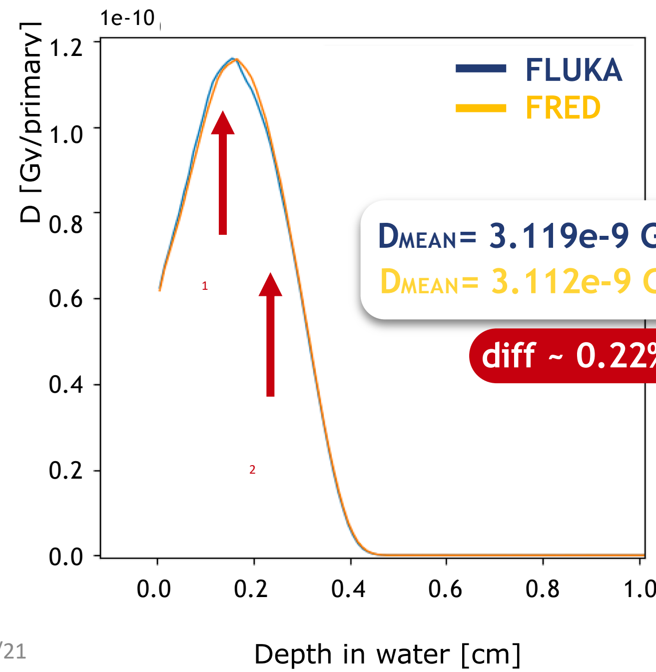
Discrete interactions (e^-, e^+, γ):

→Bremmstrahlung (dσ/dk from S.M. Seltzer, M.J. Berger, Data Nucl. Data Tables 35, 345–418 (1986). doi:10.1016/0092-640X(86)90014-8)
→ Moller/Bhabha scattering (GEANT4 physics manual 2019
→ Coherent scattering (XCOM NIST database)
→ Photoelectric (XCOM NIST database)
→ Compton (XCOM NIST database)
→ Pair production (XCOM NIST database)
→Positron annihilation at rest/ in flight (GEANT4 physics manual 2019)

Benchmark of deposited dose (e^-)



Longitudinal dose distribution

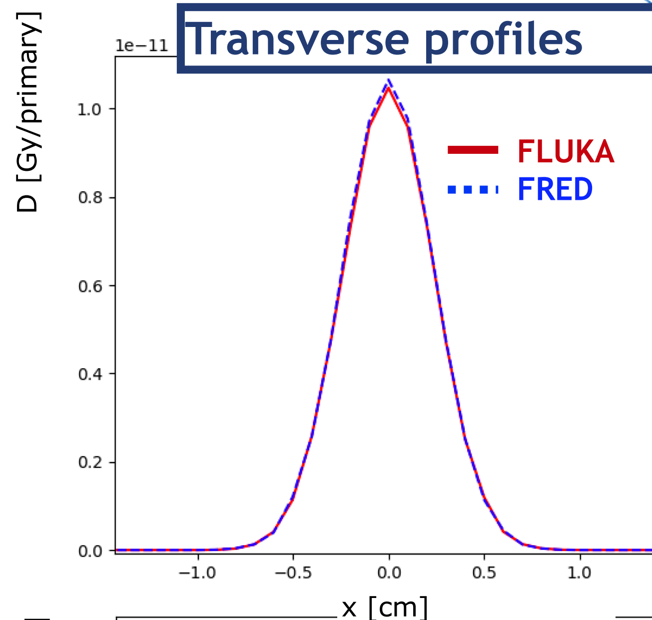


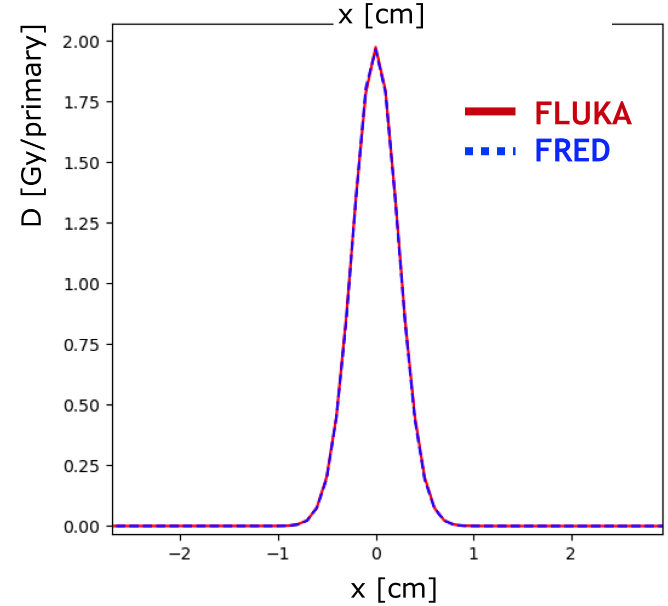
D_{MEAN}= 3.119e-9 Gy/e^-

D_{MEAN}= 3.112e-9 Gy/e^-

diff ~ 0.22%

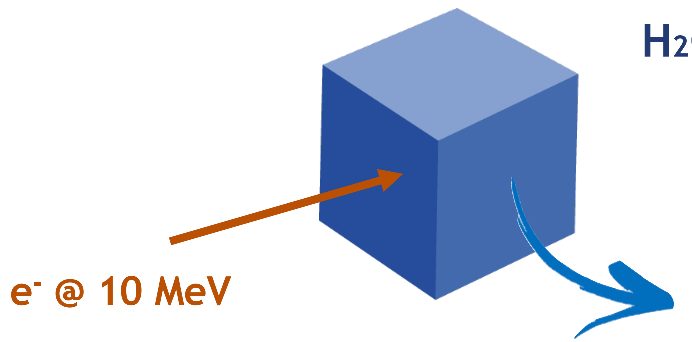
Transverse profiles



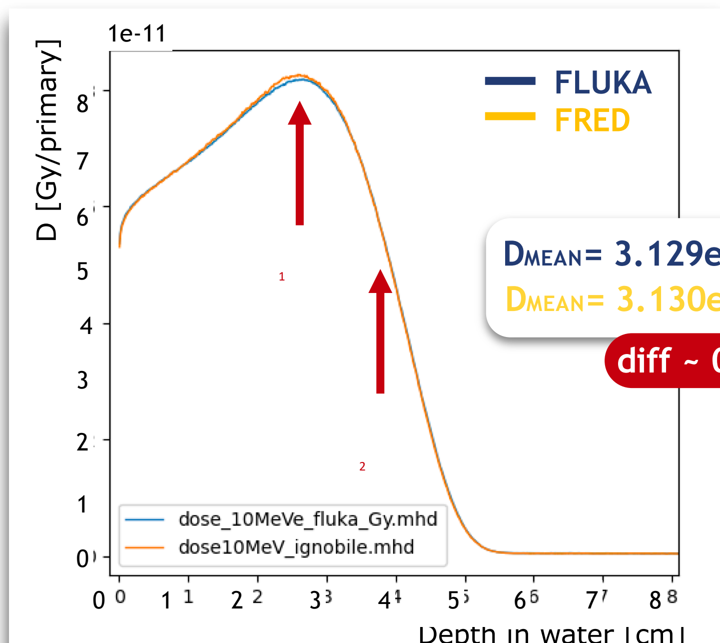


Benchmark of deposited dose (e^-)

H_2O target



Longitudinal dose distribution

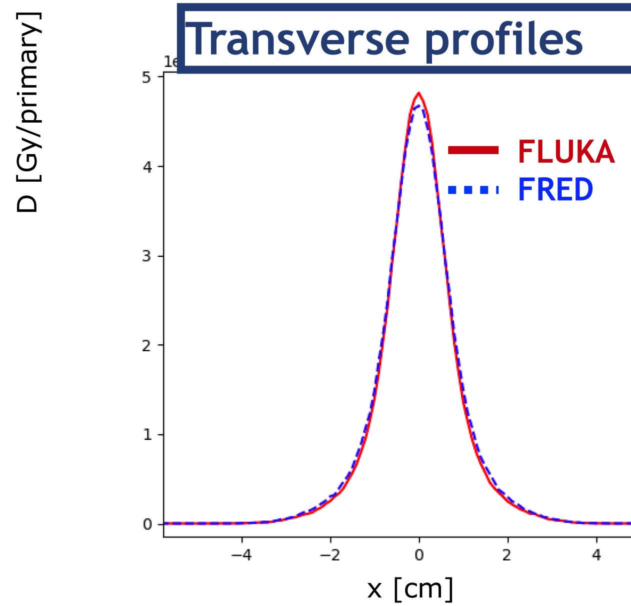


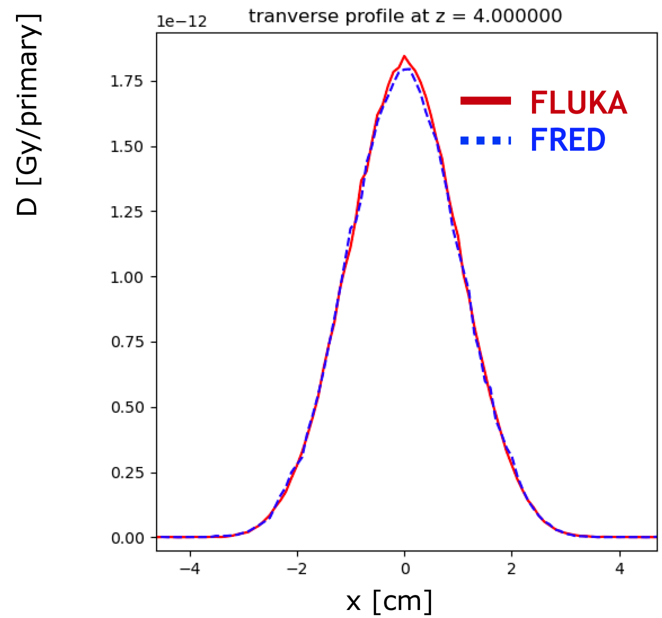
D_{MEAN} = 3.129e-8 Gy/e^-

D_{MEAN} = 3.130e-8 Gy/e^-

diff ~ 0.03%

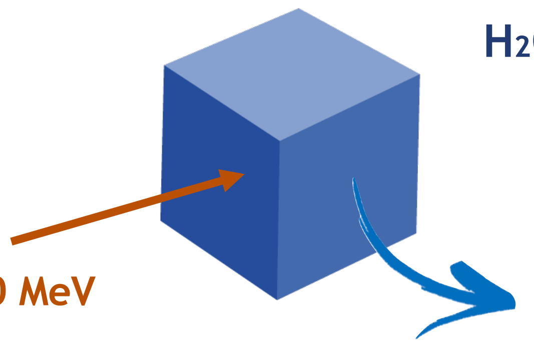
Transverse profiles





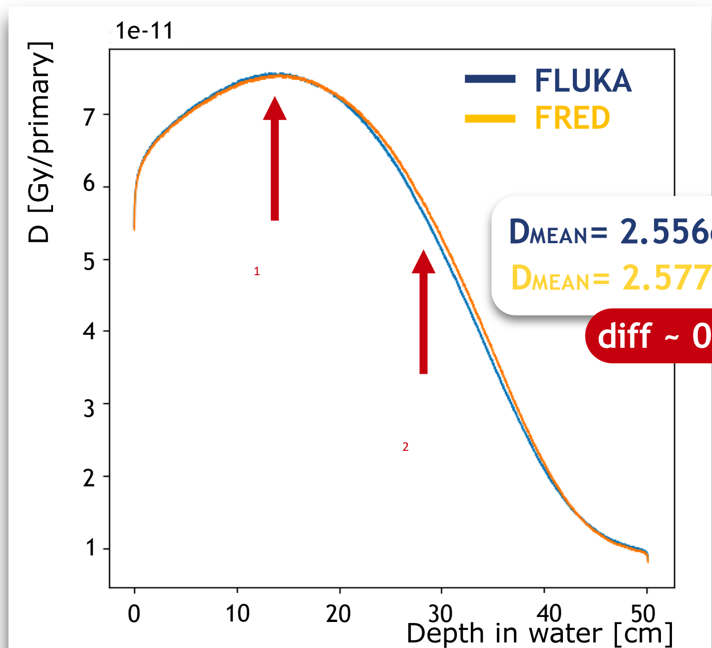
Benchmark of deposited dose (e^-)

H_2O target



e^- @ 100 MeV

Longitudinal dose distribution

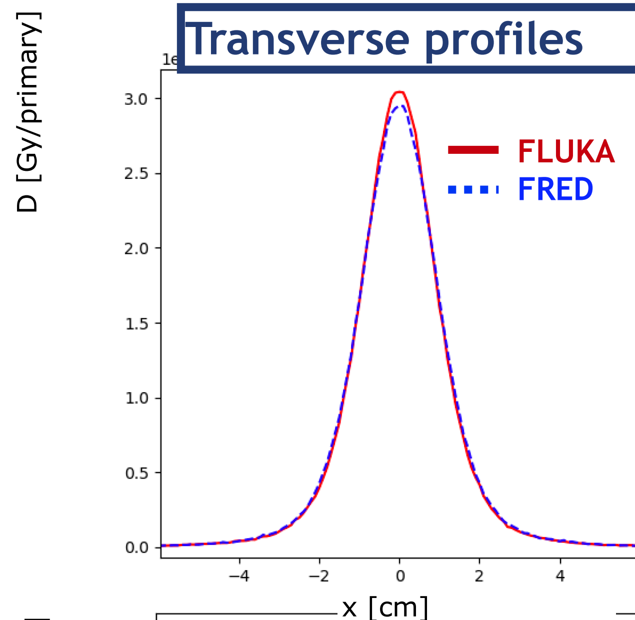


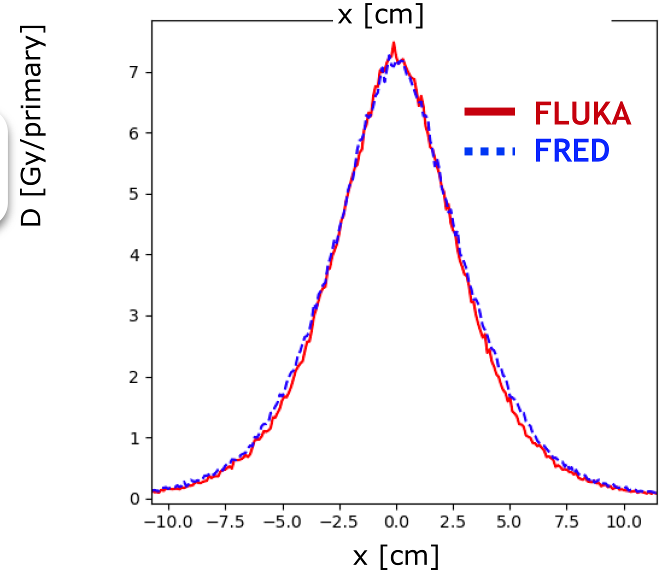
D_{MEAN}= 2.556e-7 Gy/e⁻

D_{MEAN}= 2.577e-7 Gy/e⁻

diff ~ 0.82%

Transverse profiles





The Intra-Operative Radiation Therapy (IORT)

The Intra-Operative Radiation Therapy (**IORT**) is a technique that involves precise delivery of a large dose of ionizing radiation directly to the surgery bed after the surgical tumor removal → helps to eradicate the microscopic residual tumor cells

- Uniform electrons beam with energy ranging from **5** to **10 MeV**
- The beam is passively collimated by PMMA applicator
- To screen nearly critical organs in the vicinity of the tumor, a metallic disk of high Z is inserted under the tumor bed

The main IORT **limitation** is the absence of a TPS

- dose planning not optimized to patient specific tumor
- no dose report

Since the TPS must be calculate during the surgery, where the patient is highly exposed, it is essential to **minimize the simulation time**. → **FRED-GPU**

IORT application: NOVAC 11 accelerator

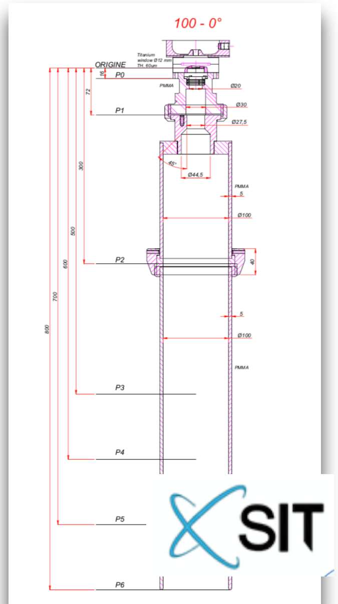
- The NOVAC 11 (by Sordina IORT Technologies SpA,Aprilia, Italy) is a linear mobile electron accelerator designed for IORT application
- Nominal energies: **4**, **6**, **8** and **10 MeV**
- Able to treat targets volume with a thickness up to **2.6 cm** inside the 90% isodose;

We used the FRED software to simulate in details the geometry of the NOVAC 11 and the coupled applicator in order to compare the experimental data of the percentage depth doses (PDDs) and off-axis profiles measured in a water phantom

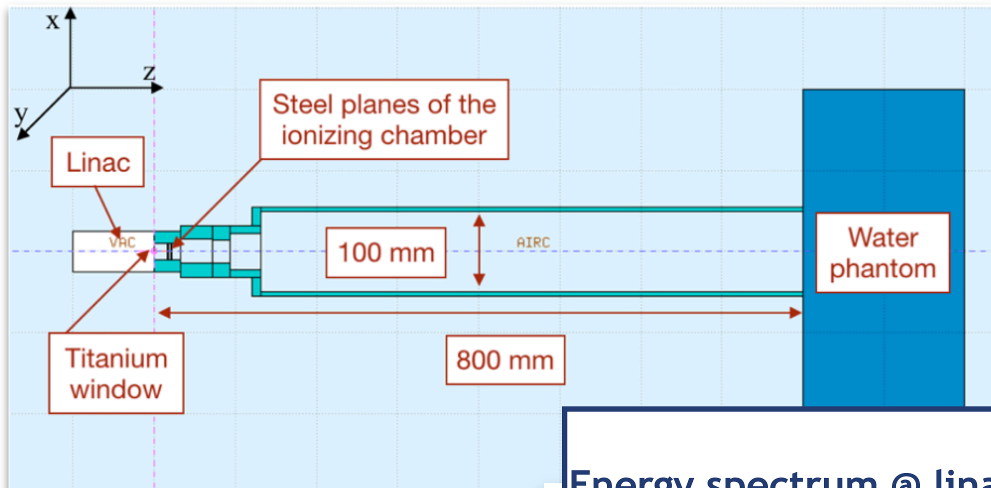
To test step-by-step the performance of the FRED simulation we compared the FRED outputs with the ones obtained using an equal **FLUKA** simulation

Simulation with FRED

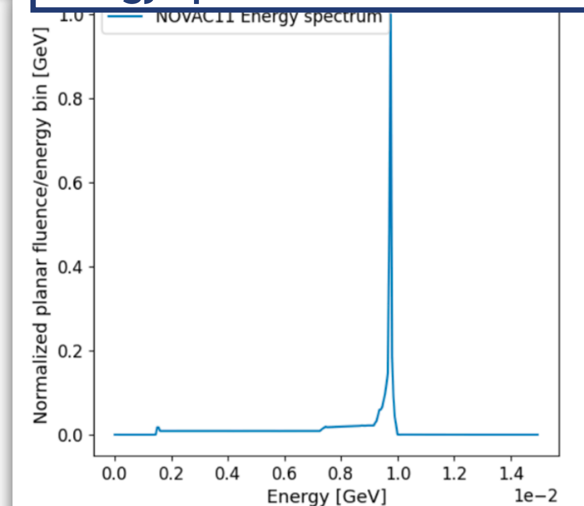
The experimental dosimetric characterization of the linear accelerator has been compared to a Monte Carlo simulation with FLUKA and FRED for a 10 MeV electrons beam.



FRED applicator geometry



Energy spectrum @ linac exit

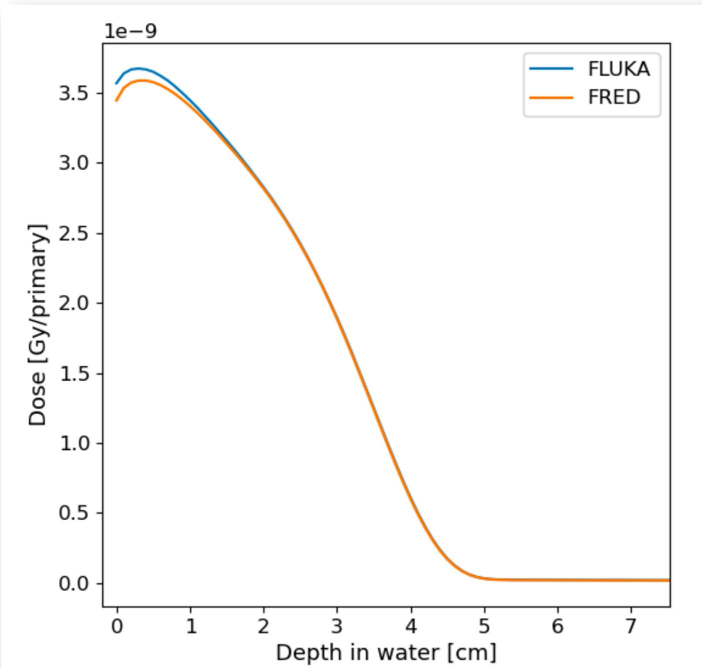


GEOMETRY:
1. PMMA cylinders with different diameters (from 20 to 100 mm)
2. Source-to-Skin Distance (SSD)=80 cm
3. Titanium window (55 μm)
4. 4 steel planes of the ionizing chamber (20 μm each)

SIMULATION PARAMETERS:
1. 10 MeV electrons beam;
2. Gauss section with FWHM=0.13 cm;
3. Transport and production energy cut = 10 keV

Benckmark (FLUKA)

Longitudinal dose distribution

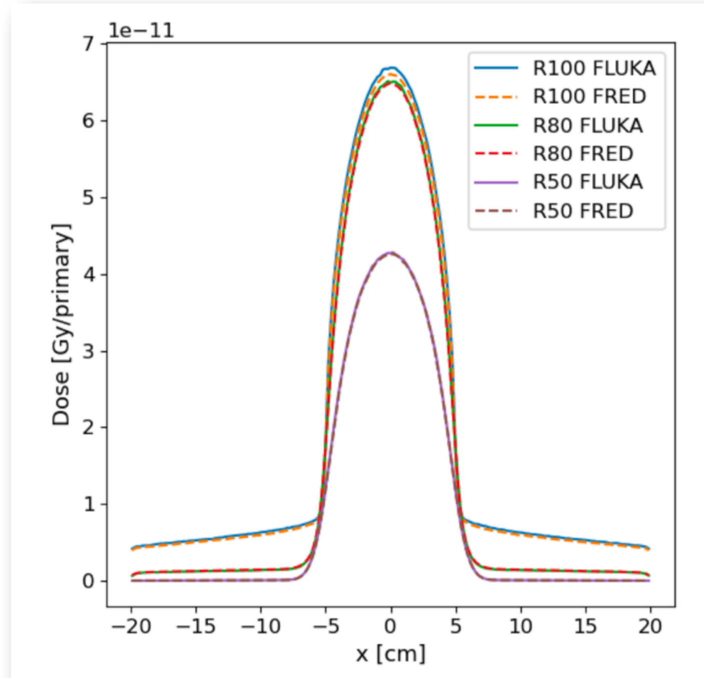


DMEAN= 1.10e-7 Gy/primary

DMEAN= 1.09e-7 Gy/primary

diff ~ 0.9%

Transverse dose distribution



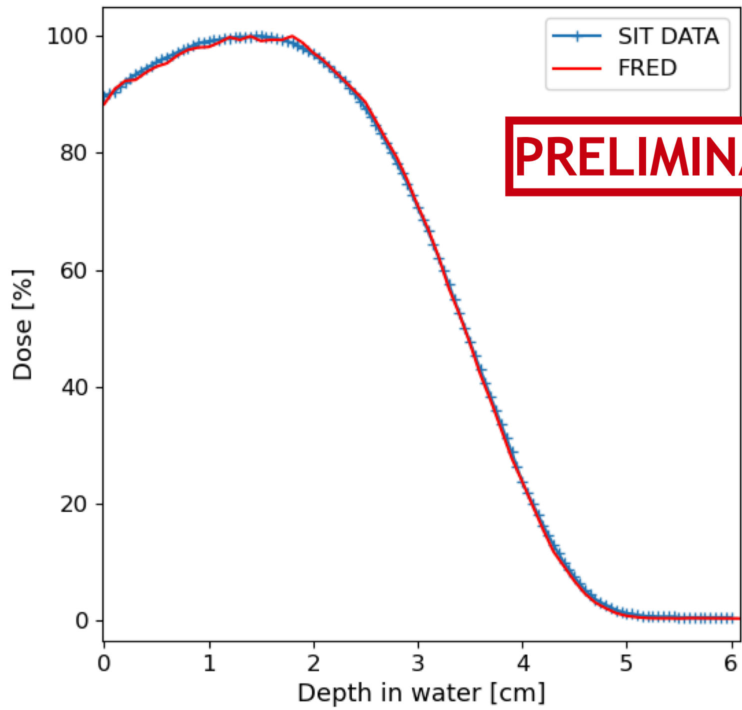
R100: 100% of the peak value ~ 0.3 cm
R80: 80% of the peak value ~ 1.9 cm
R50: 50% of the peak value ~ 3.1 cm

Benchmark (data)

The experimental setup for relative dosimetry, i.e. PDDs and off-axis profiles measurements consisted of a 3D motorized water phantom equipped with an an unshielded diode.

For the MC simulation the absorbed dose is evaluated on a water target with a transverse area of 2×2 mm^2, corresponding to the sensitive are of the adopted diode

Percentage Depth Dose



PRELIMINARY: low statistic

Gamma index 3mm/3% pass-rate 98.1%

Next steps

- Port the models on **GPU:** A scaling from the proton version allows to estimate that the tracing kernel, running on GPU hardware, can achieve order of million primary per second on a single card.
- **^{12}C ions**: Comparison of the accuracy of FRED dose recalculation with the CNAO TS for carbon therapy to achieve **clinical validation**. Improvements with FOOT data in the future.
- **Electrons**: optimisation of the code execution time also when running on CPU

Current performance with electrons

Energy	FLUKA	FRED
1 MeV	2500 e^-/s	5000 e^-/s
10 MeV	500 e^-/s	1500 e^-/s
100 MeV	130 e^-/s	400 e^-/s