Treatment Planning System for hadrontherapy

OUTLINE

- Radiotherapy & Hadrontherapy
- What is a Treatment Planning System
- The tasks of the INFN-IBA TPS
- Summary & Conclusions

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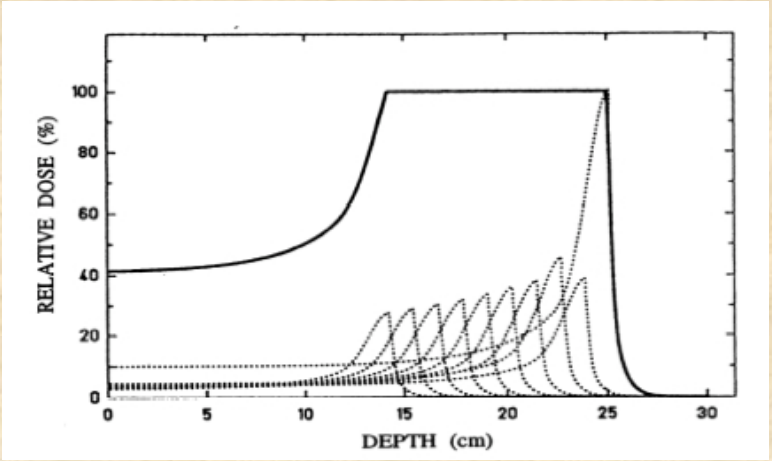
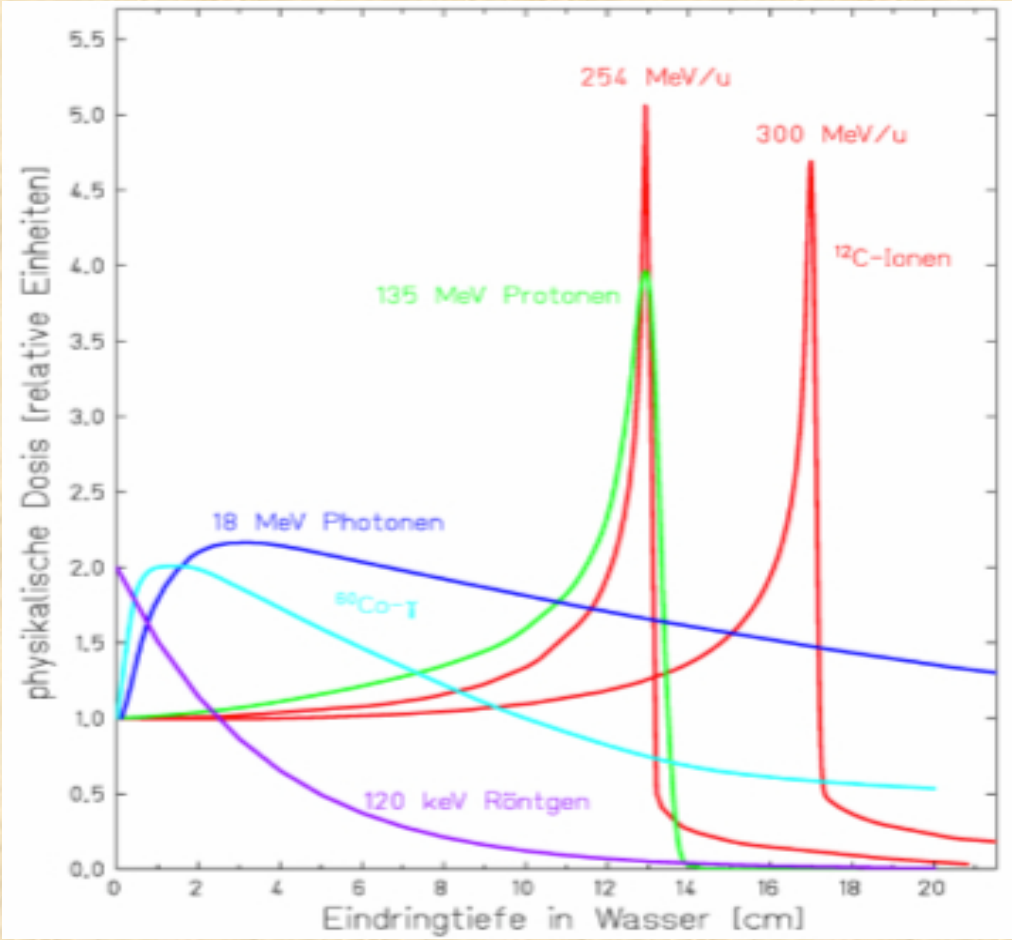
Giornate Romane su "Particelle e Fisica Applicata"

Radiotherapy: γ,e versus proton, ^{12}C

Hadrons release maximal dose at the end of the track, sparing the normal tissue

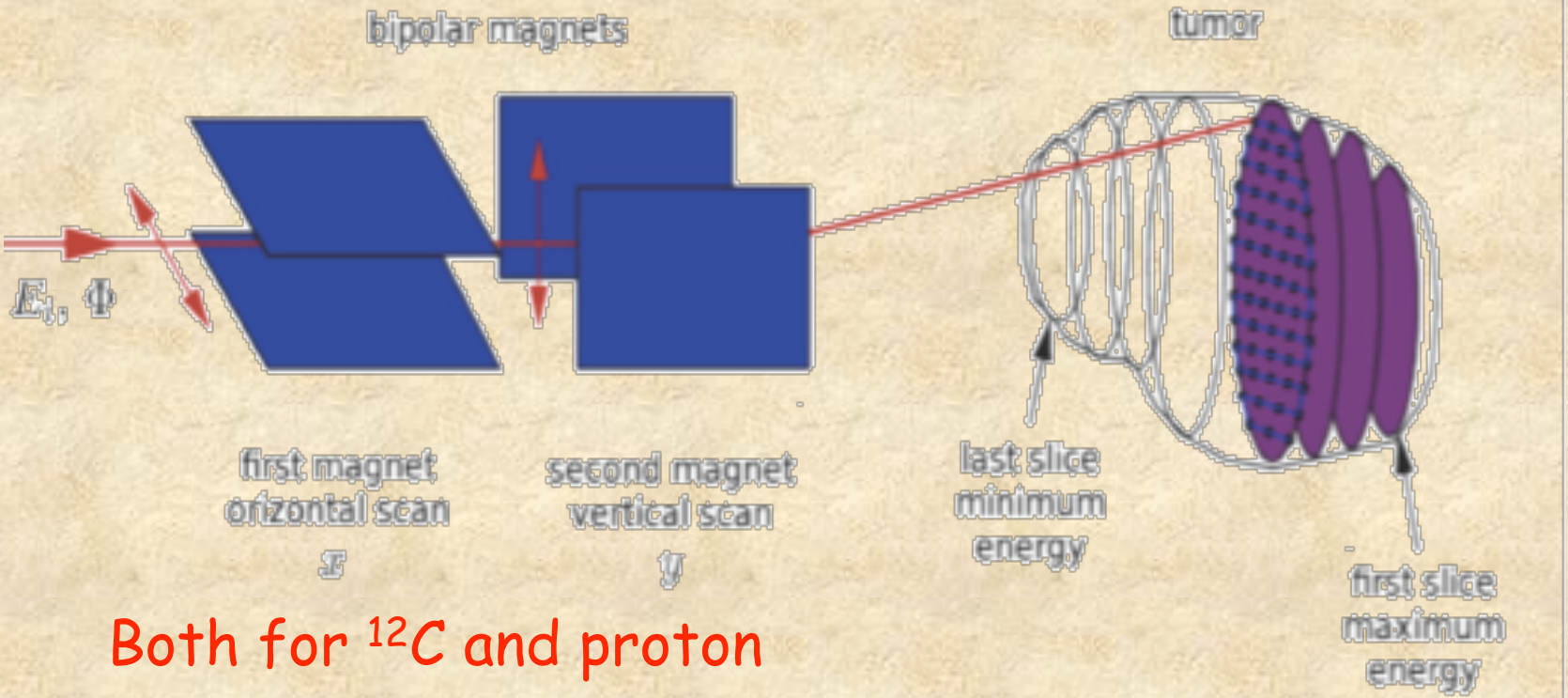
- Range function of the beam energy
- Dose decrease rapidly after the BP.
- Accurate conformal dose to tumour with Spread Out Bragg Peak





Shooting charged beams: active scanning

- Moving the proton or carbon beam like in an old TV-set and changing the energy, all the tumor region can be treated
- TPS must provide the corret set of pencil beams, with corresponding fluences, to treat the patient



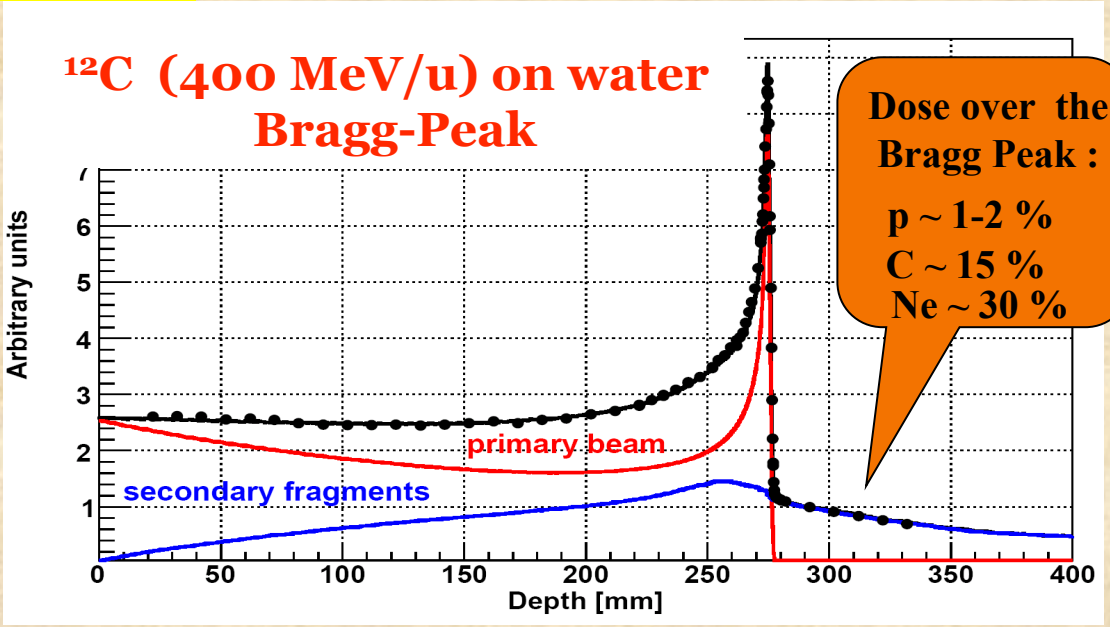
Both for ^{12}C and proton

^{12}C : fragmentation inside the patient

Dose release in healthy tissues with possible long term side effects, in particular in treatment of young patients ➔ must be carefully taken into account in the Treatment Planning System

- ✓ Production of fragments with higher range vs primary ions
- ✓ Production of fragment with different direction vs primary ions

- ✓ *Mitigation and attenuation of the primary beam*
- ✓ *Different biological effectiveness of the fragments wrt ^{12}C*



Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006
Simulation: A. Mairani PhD Thesis, 2007, Nuovo Cimento C, 31, 2008

Courtesy of Andrea Mairani

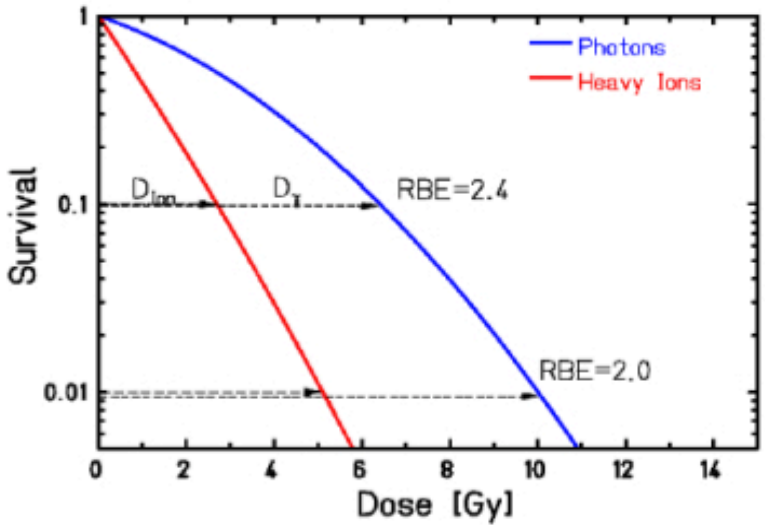
^{12}C beam and cell survival

Due to the high LET (Linear Energy Transfer ~ De/Dx), the carbon ions is much better at killing the tumour cells wuth respect to the X rays for a given dose released ➔high RBE

$$S = \frac{N_{col}}{N_{seed}} = e^{-(\alpha D + \beta D^2)}$$

Relative Biological Effectiveness

Comparison of dose values at **Isoeffect-Level!**



$$RBE = \left.\frac{D_\gamma}{D_{Ion}}\right|_{Isoeffect}$$

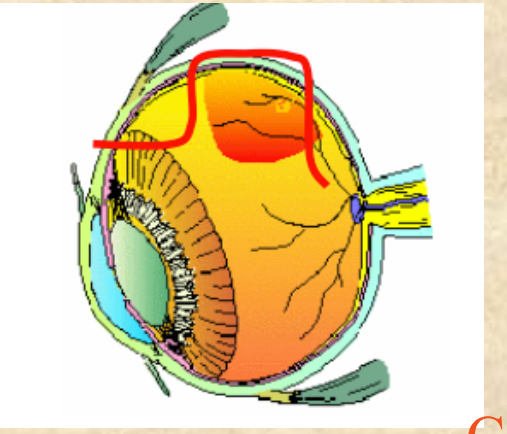
α[Gy^{-1}]: initial slope
β[Gy^{-2}]: bending of curve
α/β[Gy]: dose, at which contribution from linear term = contribution from quad. term

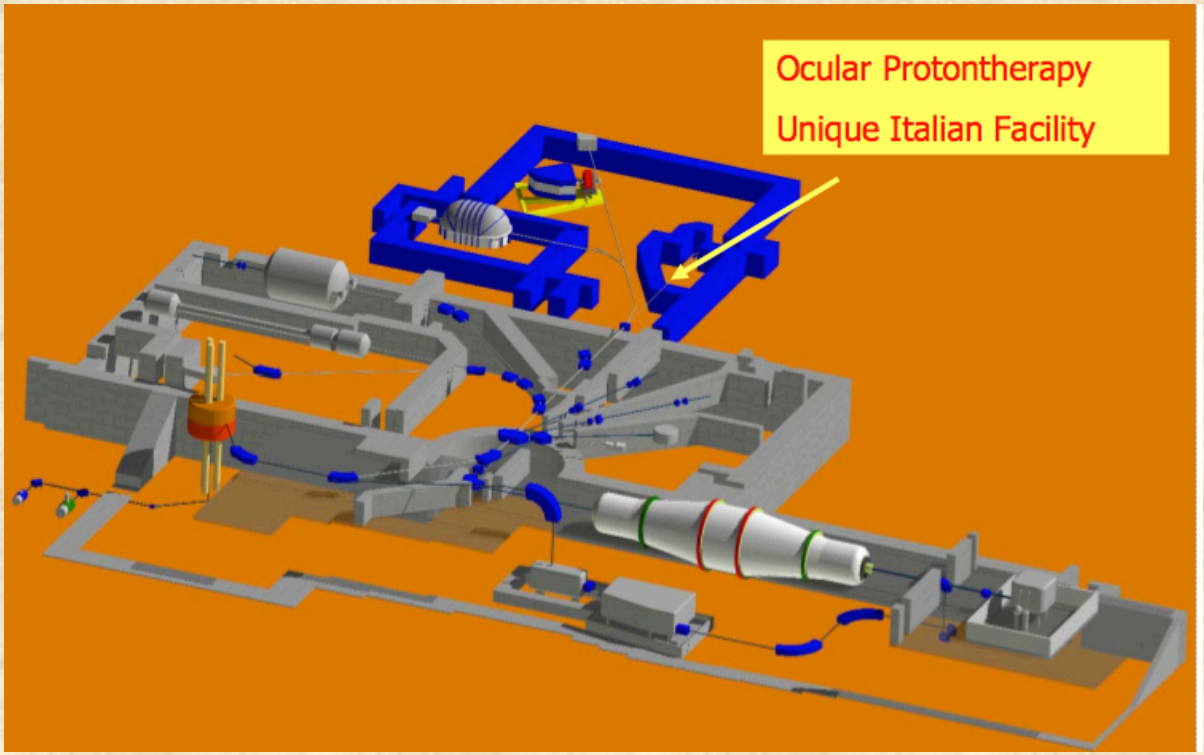
INFN & hadrontherapy CATANA @LNS

Proton 80MeV beam

Treatment of the choroidal and iris Melanoma.

In Italy about300 new cases/year

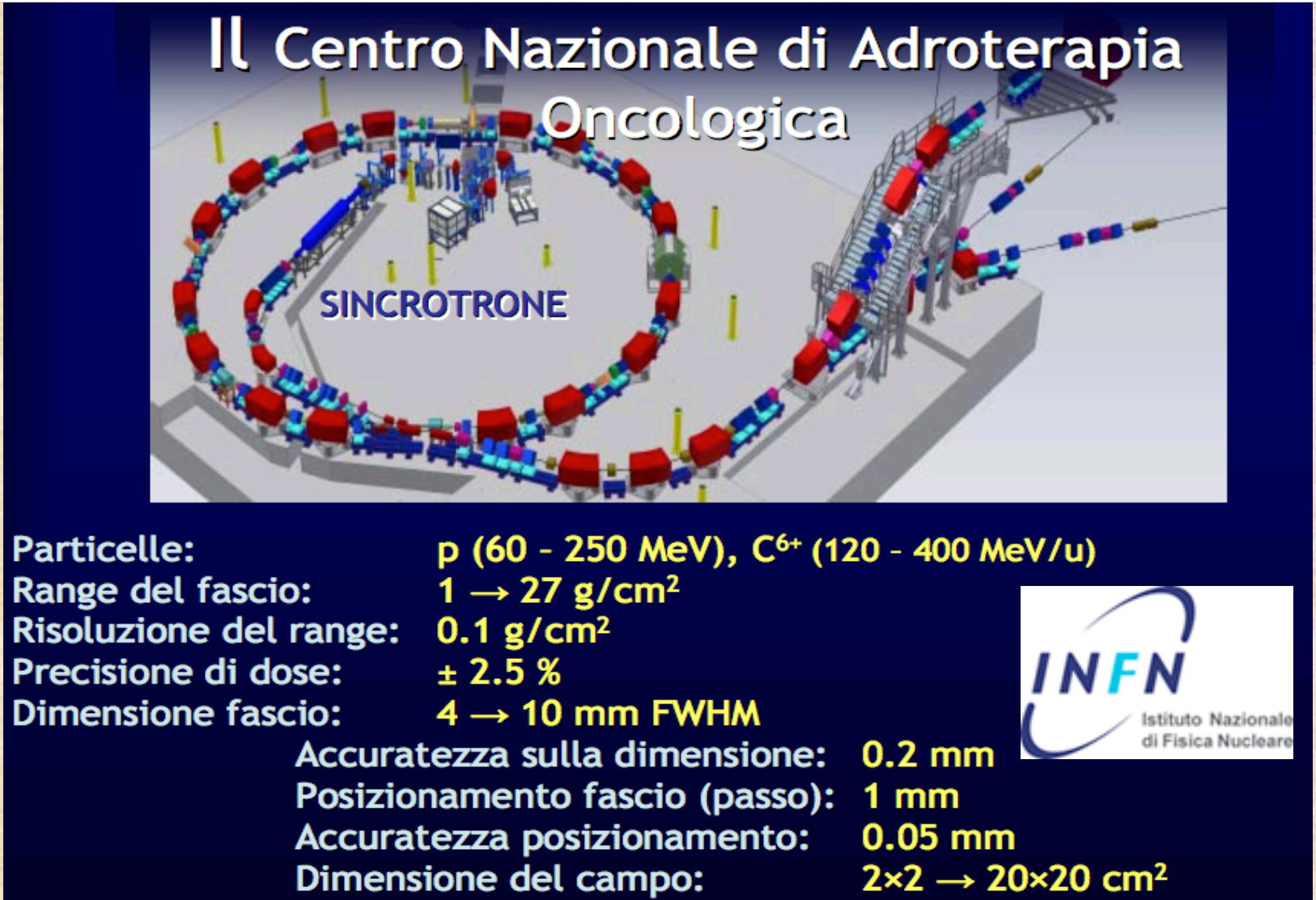




Centro di AdroTerapia ed Applicazioni Nucleari Avanzate

INFN & hadrontherapy: CNAO @Pavia

MI,TO,LNF,LNL,FE



Patient Statistics (for the facilities in operation end of 2009):

WHERE		WHAT	FIRST PATIENT	PATIENT TOTAL	DATE OF TOTAL	
Canada	Vancouver (TRIUMF)	p	1995	145	Dec-09	ocular tumors only
China	Wanjie (WPTC)	p	2004	977	Dec-09	
England	Clatterbridge	p	1989	1923	Dec-09	ocular tumors only
France	Nice (CAL)	p	1991	3935	Dec-09	ocular tumors only
France	Orsay (CPO)	p	1991	4811	Dec-09	3936 ocular tumors
Germany	Berlin (HMI)	p	1998	1437	Dec-09	
Germany	Munich (RPTC)	p	2009	78	Dec-09	
Italy	Catania (INFN-LNS)	p	2002	174	Mar-09	ocular tumors only
Japan	Chiba (HIMAC)	C ion	1994	4504	Feb-09	
Japan	Kashiwa (NCC)	p	1998	680	Dec-09	
Japan	Hyogo (HIBMC)	p	2001	2382	Nov-09	
Japan	Hyogo (HIBMC)	C ion	2002	638	Nov-09	
Japan	Tsukuba (PMRC, 2)	p	2001	1586	Dec-09	
Japan	WERC	p	2002	56	Dec-08	
Japan	Shizuoka	p	2003	852	Dec-09	
Korea	Ilsan, Korea	p	2007	519	Dec-09	
Russia	Moscow (ITEP)	p	1969	4162	Jul-09	
Russia	St. Petersburg	p	1975	1353	Dec-09	
Russia	Dubna (JINR, 2)	p	1999	595	Dec-09	
South Africa	iThemba LABS	p	1993	511	Dec-09	
Sweden	Uppsala (2)	p	1989	929	Dec-08	
Switzerland	Villigen PSI (72 MeV-Optis)	p	1984	5300	Dec-09	ocular tumors only
Switzerland	Villigen PSI (230 MeV)	p	1996	542	Dec-09	
CA., USA	UCSF - CNL	p	1994	1200	Dec-09	ocular tumors only
CA., USA	Loma Linda (LLUMC)	p	1990	14000	Oct-09	
IN., USA	Bloomington (MPRI, 2)	p	2004	890	Dec-09	
MA., USA	Boston (NPTC)	p	2001	4270	Oct-09	
TX, USA	Houston	p	2006	1700	Dec-09	
FL, USA	Jacksonville	p	2006	1847	Dec-09	
OK, USA	Oklahoma City (ProCurePTC)	p	2009	21	Dec-09	
				62017	**Total**	
			thereof	7151	C-ions	
				56854	protons	

Total for all facilities (in operation and out of operation):

2054	He
1100	pions
7151	C-ions
873	other ions
67097	protons
78275	**Grand Total**

Particle Therapy Co-Operative Group

TPS is the software between: patient anatomy and oncological prescriptions and accelerator dose delivery

Input

Informazione 3D:

- CT, MRI, PET
- PTV, OARs

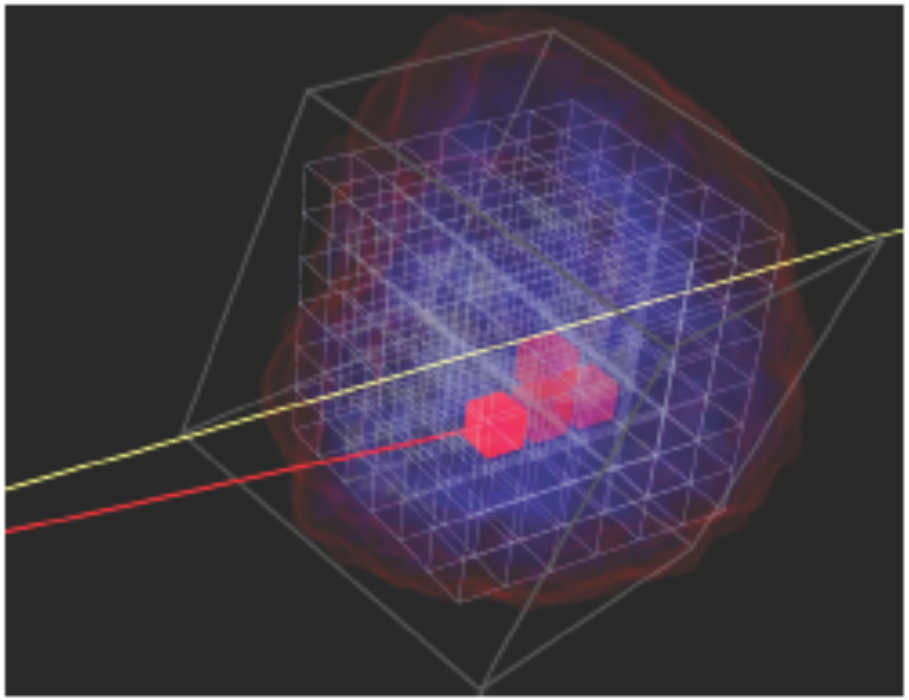
→ TPS →

Output

- $D(x, y, z)$
- $\mathrm{RBE}(x, y, z)$
- $\{\phi_i, E_{Ki}, \theta_i\}$

Voxel Scan:

$i \rightarrow$ i-th beam
$\phi_i \rightarrow$ fluence
$E_{Ki} \rightarrow$ kinetic energy
$\theta_i \rightarrow$ direction

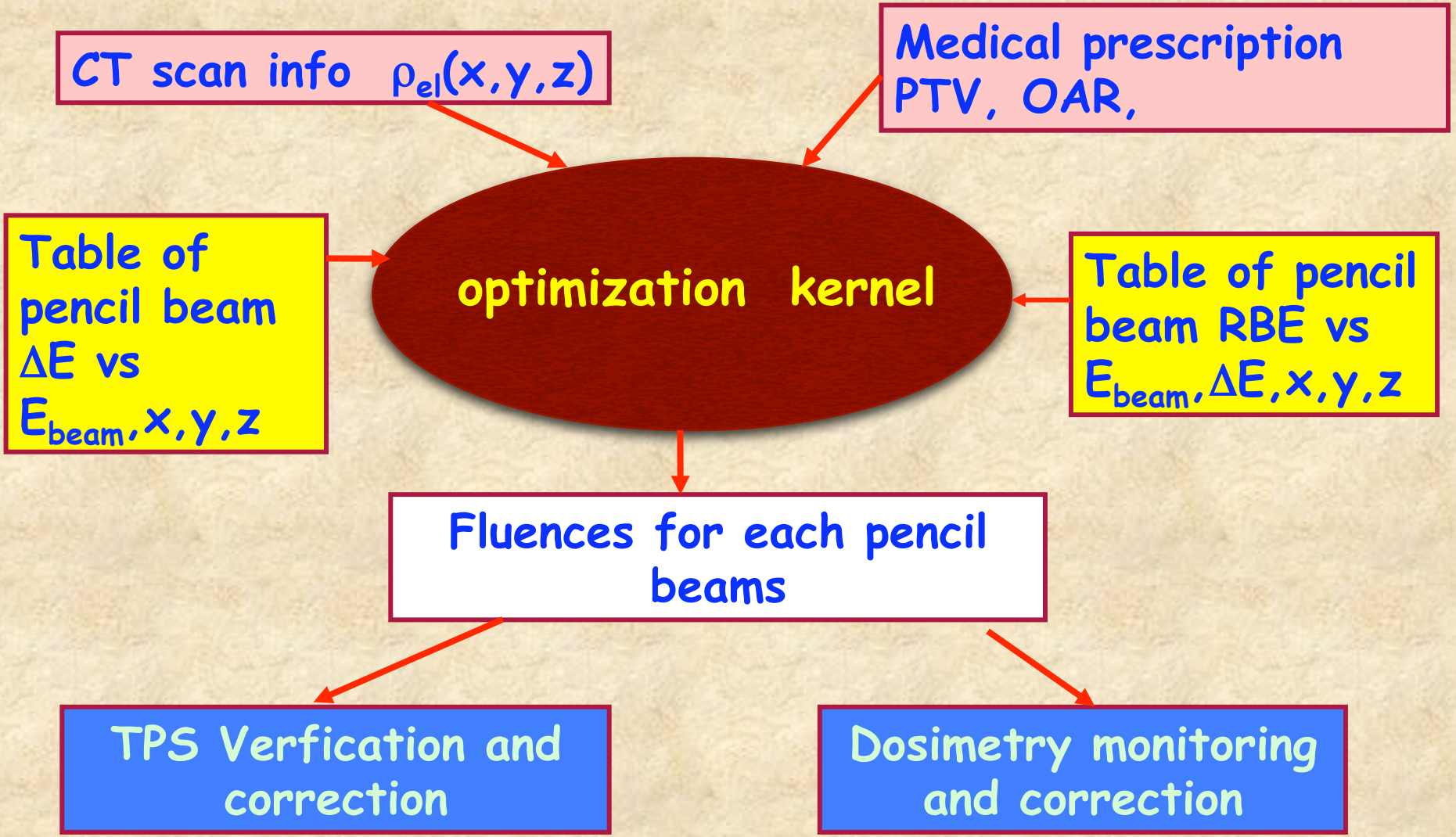


What a TPS is and what is made of

The Treatment Planning is the software which determines energy and fluence for each elementary beam in order to achieve the prescribed dose in a well defined volume

- Patient modeling. Geometry, density, composition map and related medical dose prescriptions.
- Physical dose evaluation. Evaluation of the beam energy release and its interaction in the patient.
- Biological dose evaluation. Evaluation of radiobiological efficency of the beam particles
- Optimization procedure to adapt the biological dose to medical prescription ➔ Pencil beams energy & fluence
- Validation of the TPS. MC computation of the dose actually release to the patient
- On-off line monitoring of the treatment.

A simplified scheme of a Treatment Planning System



INFN-TPS Project

- Most of the needed knowledge inside the Institute (mainly GR V)
- Cooperation agreement in 2009 between INFN and IBA (Ion Beam Application) to develop a commercial TPS for carbon and proton within 3 years (co-funded!!!)
- Collaboration with CNAO for testing and with European Institutions for radiobiology & nuclear physics

INFN-TPS Project

The Project is also a "strategic" project of Gruppo V and is split in 5 different tasks

1) Nuclear Physics: fragmentation measurement
2) MC FLUKA (G4) tailoring to hadrontherapy
3) Optimization algorithms development
4) Experimental Radiobiology
5) Monitoring "in beam" development

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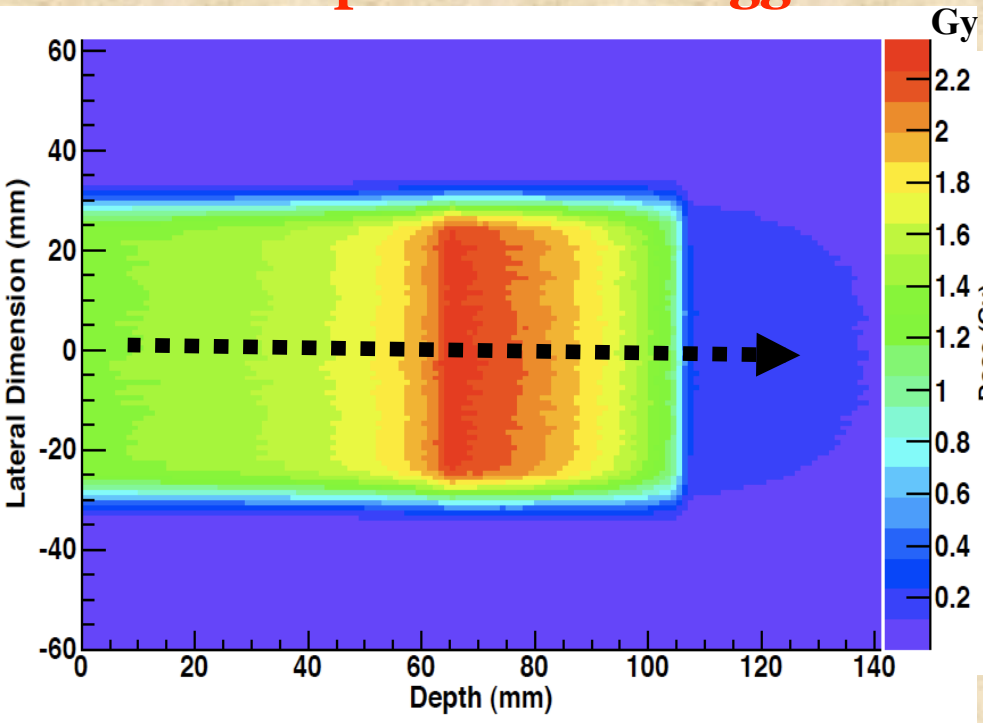
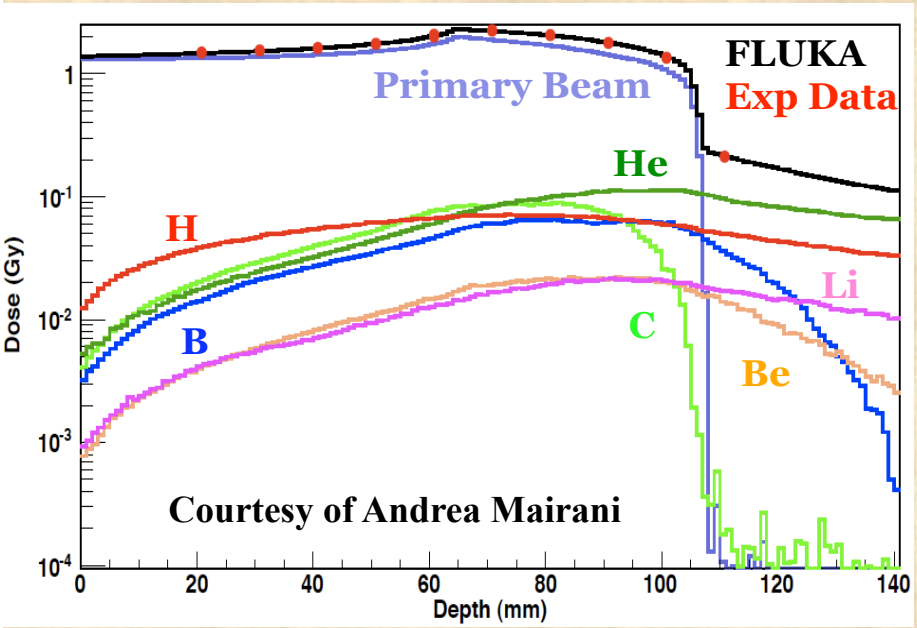
Nuclear physics task: ^{12}C fragmentation

- ✓ Production of fragments with higher range vs primary ions
- ✓ Production of fragment with different direction vs primary ions

Forward recalculation of TPS treatment plans in water @ GSI/HIT

Spread-Out Bragg Peak – Fragment Contributions



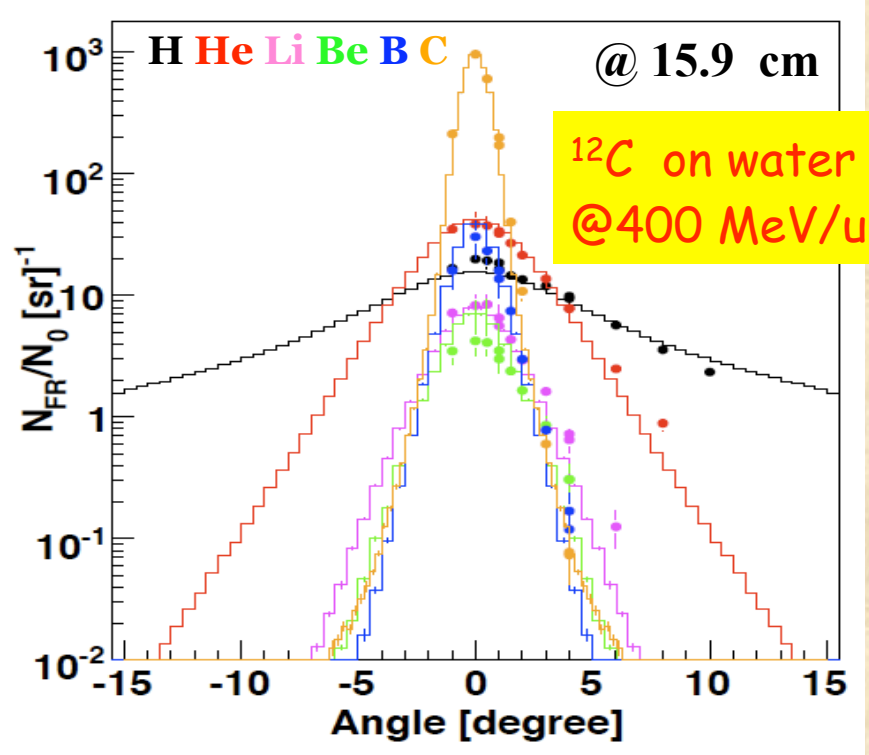


(F. Sommerer et al, EWG-MCTP Workshop, Ghent 2006, A. Mairani et al to be publ.)

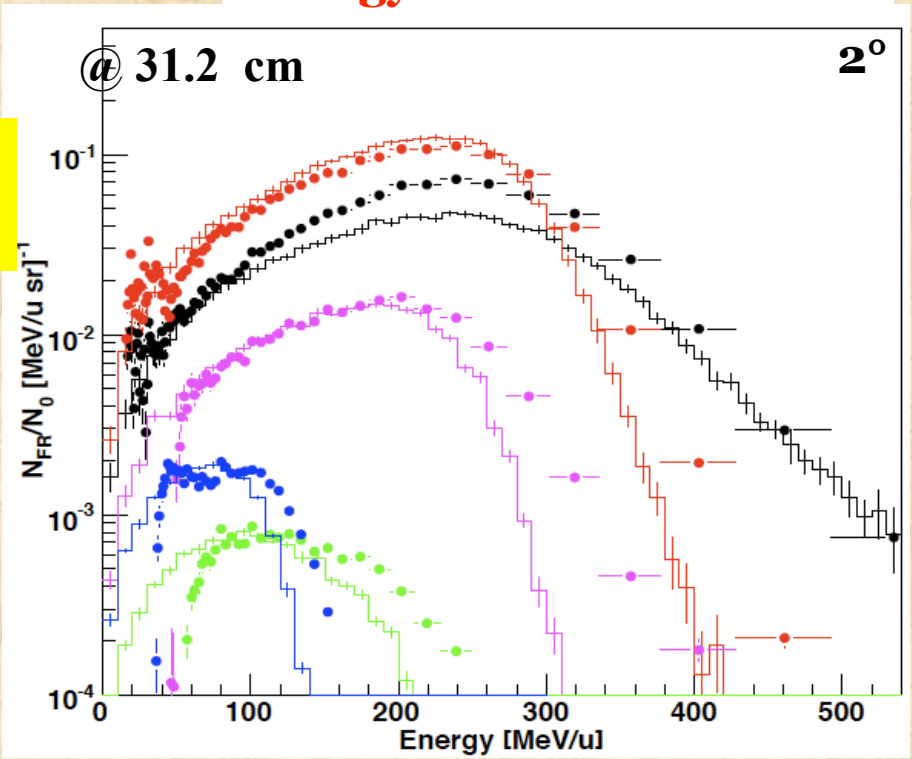
Scattered Frag.s production by ^{12}C beam

The secondary fragments broad the lateral dose profile and go beyond the tumor region.

Angular distribution



Energy distribution



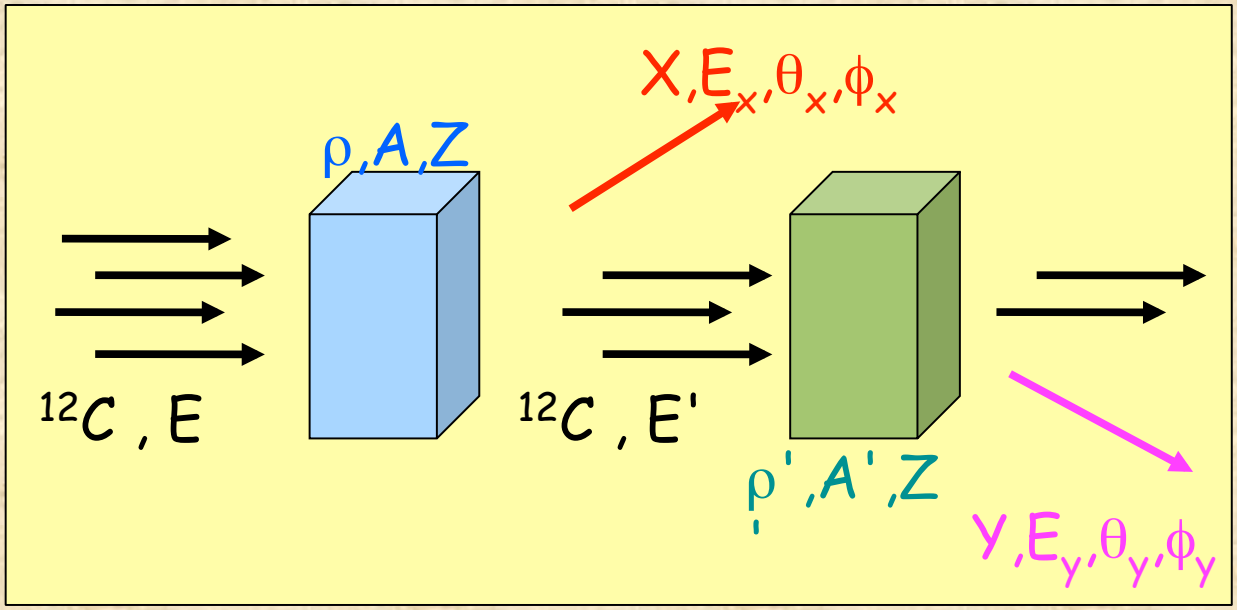
FLUKA benchmark against thick target data

Exp. Data (points) from Haettner et al, Rad. Prot. Dos. 2006
Simulation: A. Mairani PhD Thesis, 2007, PMB *to be published*

Courtesy of Andrea Mairani

What should we know about ^{12}C fragmentation?

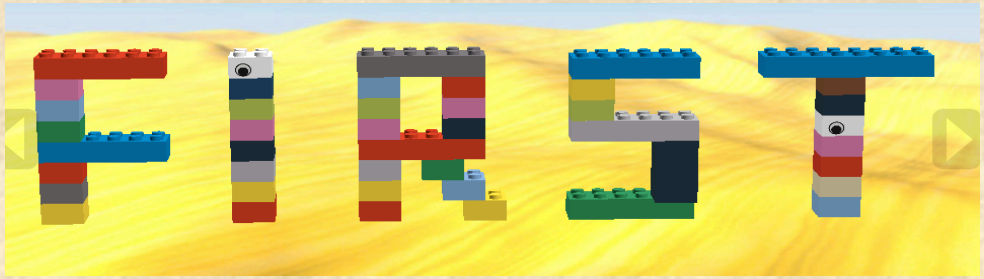
- Production yields of Z=0,1,2,3,4,5 fragments
- $d^2\sigma/d\theta dE$ with large angular acceptance
- For the ^{12}C energy range of interest (10-300 MeV/nucl)
- Measurements on thin target of all materials crossed by C beam
- Detect the correlation between emitted fragments



Not possible a complete DB of measurements

We need to improve the nuclear interaction model with the measurements!!

The FIRST collaboration



- INFN: Cagliari,LNF,LNS,Milano,Roma3,Torino: C.Agodi, G.Battistoni, M.Carpinelli, G.A.P.Cirrone, G.Cuttone , M.De Napoli, B.Golosio, Y.Hannan, E.Iarocci, F.Iazzi, R.Introzzi, A.Mairani, V.Monaco, M.C.Morone,P.Oliva, A.Paoloni, V.Patera, L.Piersanti, N.Randazzo, F.Romano, R.Sacchi, P.Sala, A.Sarti, A.Sciubba, C.Sfienti, V.Sipala, E.Spiriti
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- Univ Sevilla: J.M. Quesada, M.Alvarez, A.Bocci, Z. Abou-Haidar
- CERN: T.Bohlen

INFN Istituto Nazionale di Fisica Nucleare

FIRST stands for: Fragmentation of Ions Relevants for Space and Therapy → S371 is the GSI label

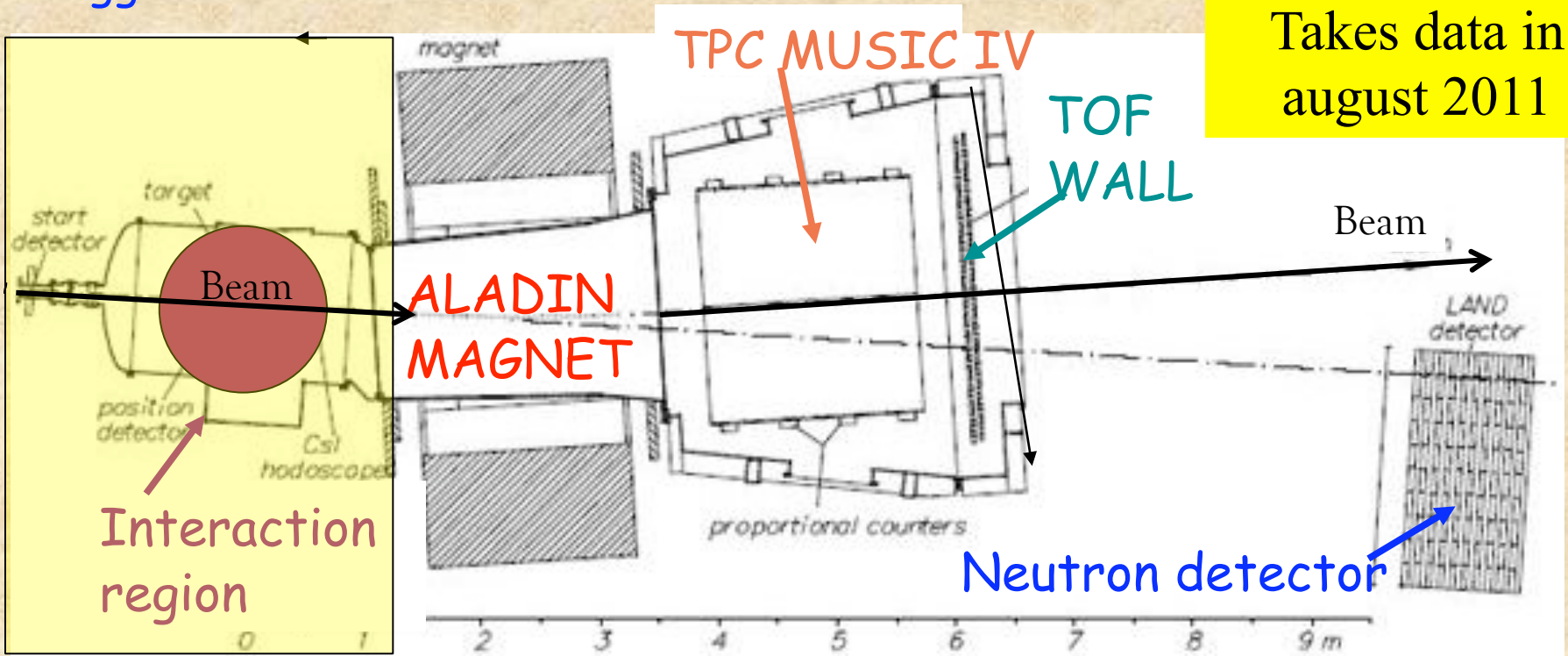
The FIRST setup @GSI

The choice of GSI had two main motivations:

- "Therapeutical" beam of ^{12}C @ 200-400 MeV/u available
- Existing setup designed for higher E and Z fragments: Dipole magnet, Large Volume TPC, TOF Wall, small-angle Neutron detector.

New detectors added to optimize the Interaction Region for this measure: Vertex tracker, Start Counter, Beam Monitor, Proton Tagger

Takes data in august 2011



Radiobiology task : I

- Characterization of therapeutic beams
- Collect experimental data for validation and development of radiobiology model

- Study the radiosensibilization of gliomas with hadrontherapy

Biological Systems

- Selected set of human normal and tumoral cell lines:
  - AG1522 cells: human normal foreskin fibroblasts,
  - CCD37Lu cells: human, normal lung fibroblasts,
  - HSG cells: human salivary gland adenocarcinoma cells,
  - T98G cells: human glioblastoma cells.
- Reference cell line:
  - V79 cells : Chinese Hamster lung fibroblasts.

Characterization of cell lines

- Growth curves; Cell doubling time.
- Cell thickness, nuclear area and nuclear radius.

Biological end-points

- Cell survival (determination of survival curve parameters α, β and α/β ratio, RBE).

Radiobiology: beams & cell lines

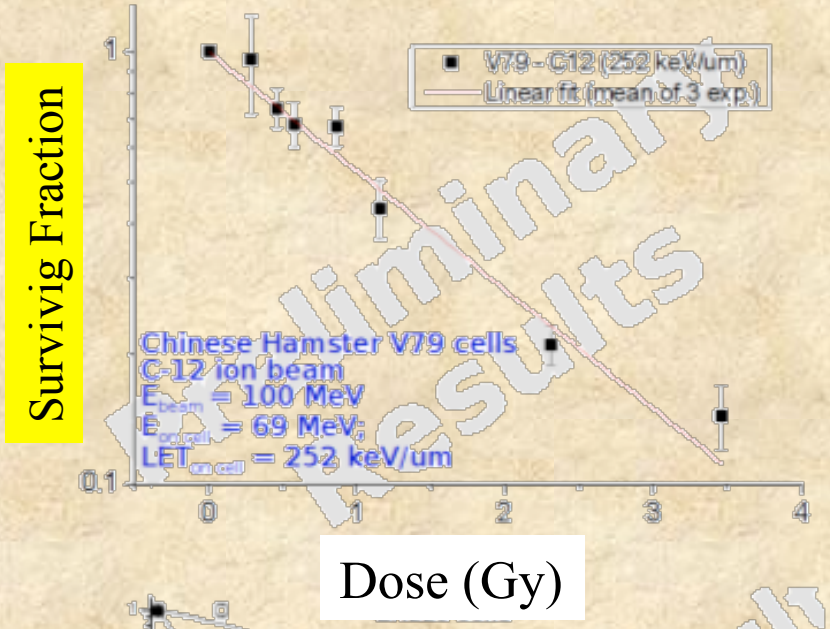
Radiations:

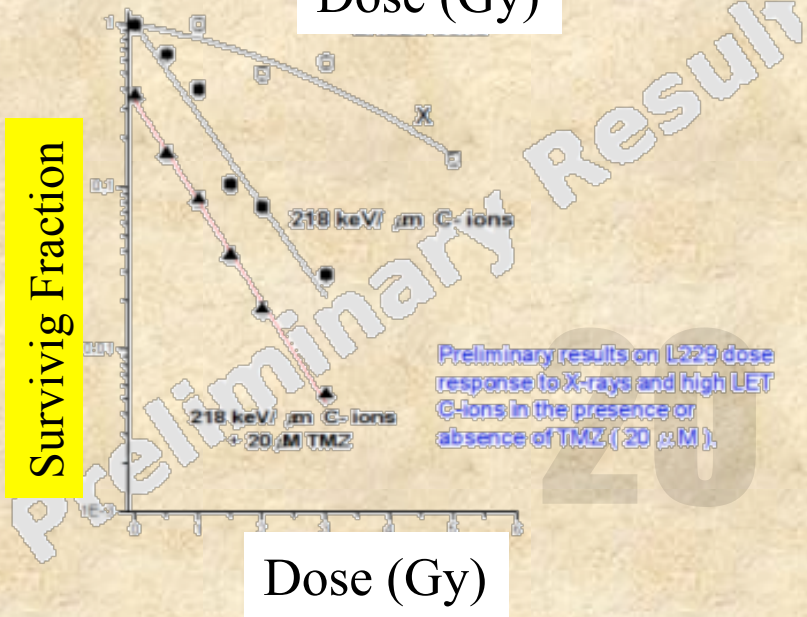
Carbon ions in the energy range: 8 to 400 MeV/n at

- INFN-LNL, Legnaro-Padova, Italy: Tandem-ALPI accelerator: 8 to 20 MeV/n.
- INFN-LNS, Catania-Italy, CS accelerator: 62 to 80 MeV/n.
- High Energy Heavy-Ion Facilities (GSI, Darmstadt-Germany/NIRS, Chiba-Japan/CNAO, Pavia-Italy): up to 400 MeV/n (*to be applied*).

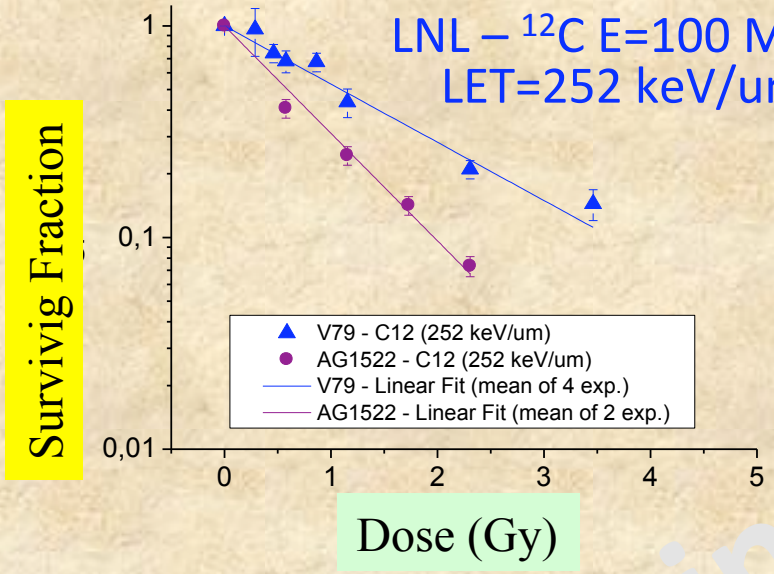
Low-energy Protons, Helium-4, Litium, Boron-ions at INFN-LNL.

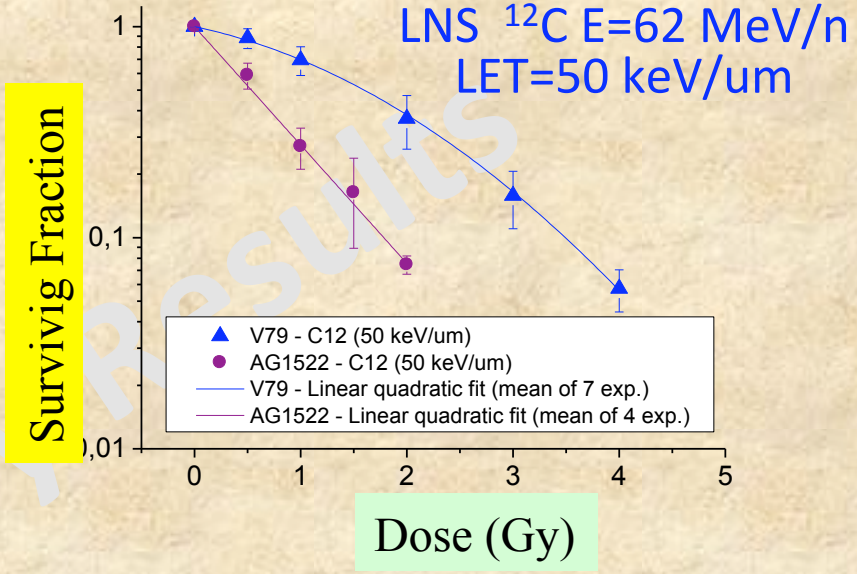
Co-60/Cs-137 gamma-ray sources; X-rays (250 kVp X-tube), *as reference radiations*.

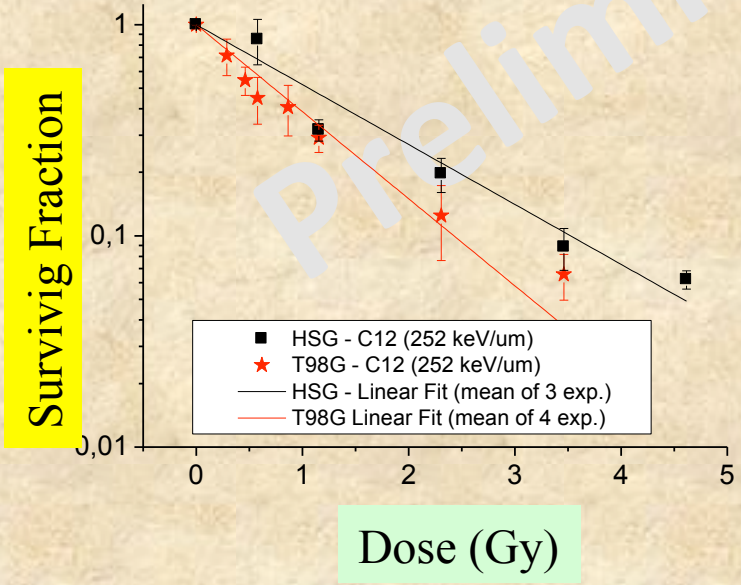


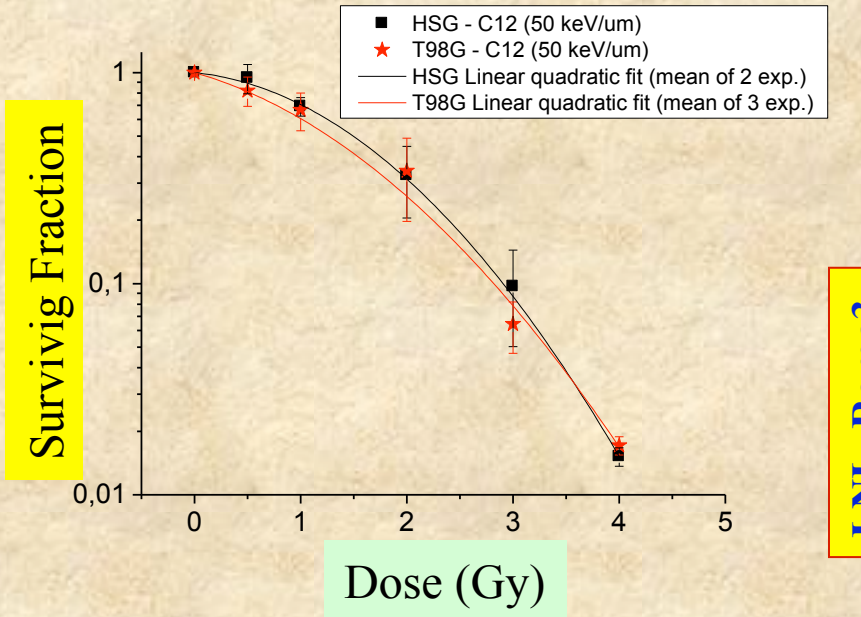


Survival curves – ^{12}C ion irradiation









LNL, Roma3

Radiobiology task : II

- Characterization of therapeutic beams
- Collect experimental data for validation and development of radiobiology model

- Study the radiosensibilization of gliomas with hadrontherapy

Biological Systems

- Selected set of human glioblastoma cell lines:
  - LN229 cells,
  - T98G cells,
  - U87 cells,
  - U373 cells.

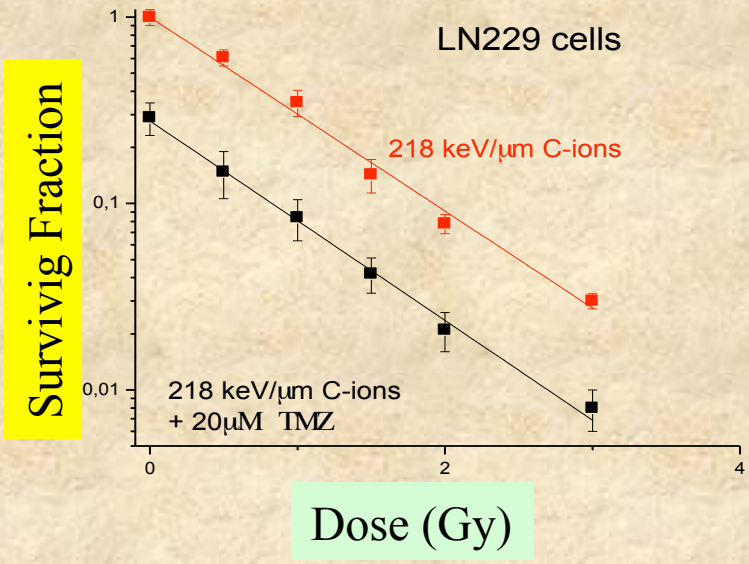
Characterization of cell lines

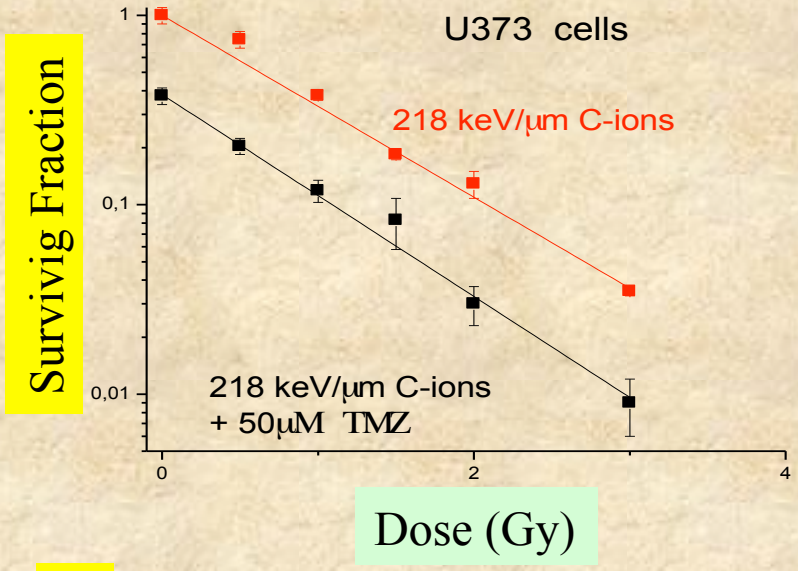
- Growth curves; Cell doubling time.
- Cell thickness, nuclear area and nuclear radius.
- TMZ cytotoxicity.

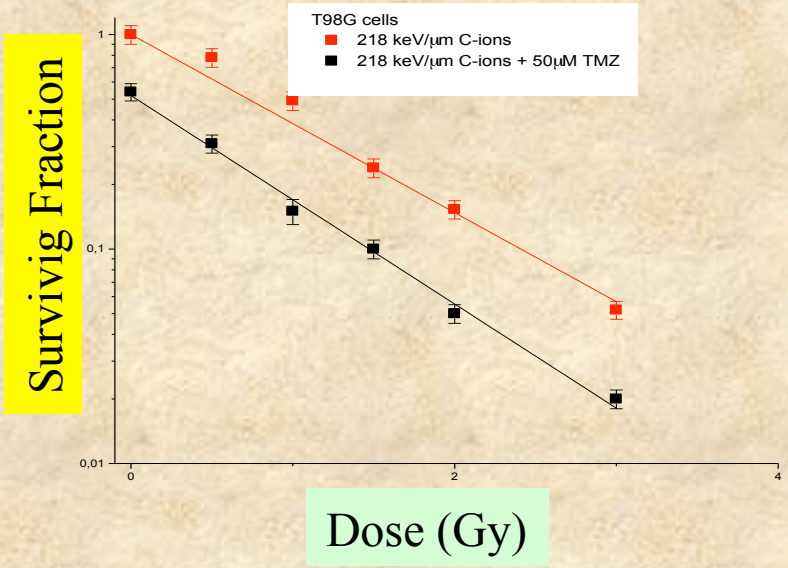
Biological end-points

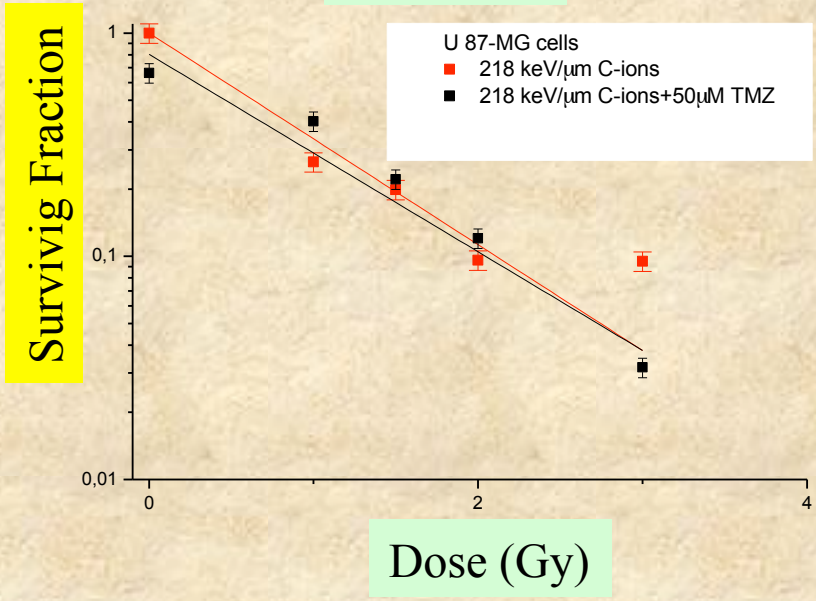
- Cell survival (determination of survival curve parameters α, β and α/β ratio, RBE).

Dose-response of LN229, U373,T98G and U87-MG to 218 keV/μm C-ions using temozolomide (TMZ)









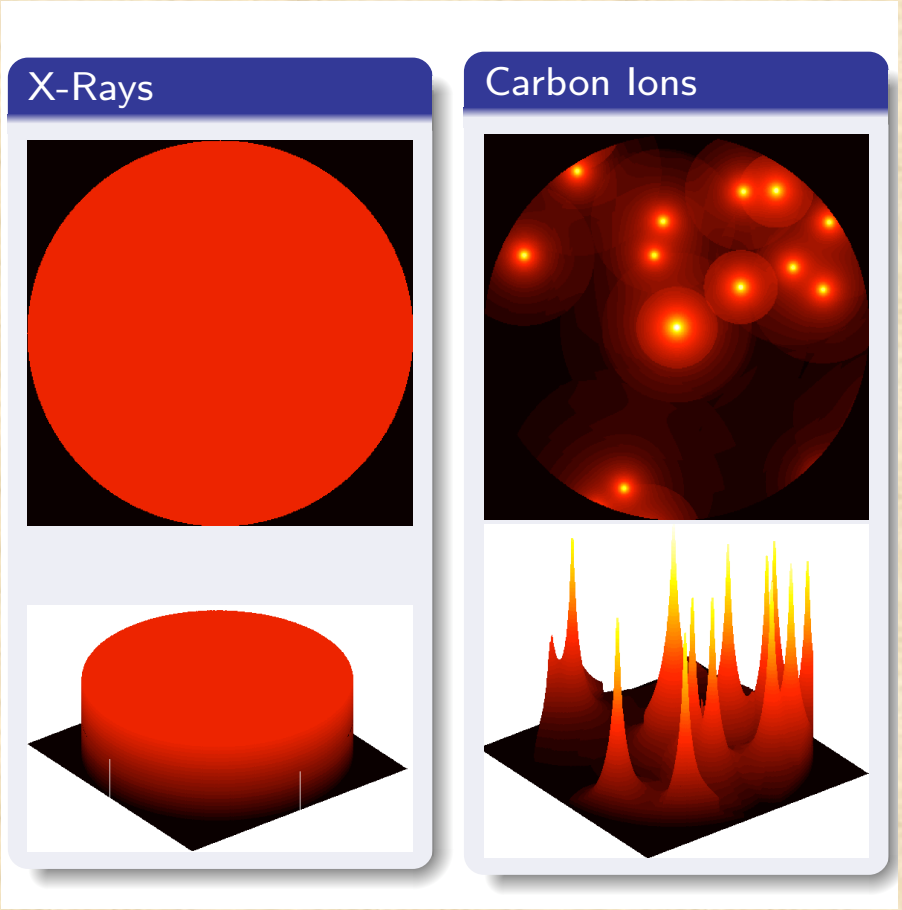
The radiobiological model

It's impossible to build a database of radiobiological measurement of RBE for all the particles, energy, cell lines. A radiobiological model is needed to interpolate.

- "Phenomenological" models can be trained with measurements and presently are used in the clinic practice with satisfactory results
- The "Local Effect Model" (LEM I,II,III) is our baseline (Scholz e Kramer, GSI). It is at the base of Siemens TPS, at presents the only carbon TPS on the market.
- As comparison, we adopetd also the Microdosimetric Kinetic Model (MKM) (R.B. Hawkins)

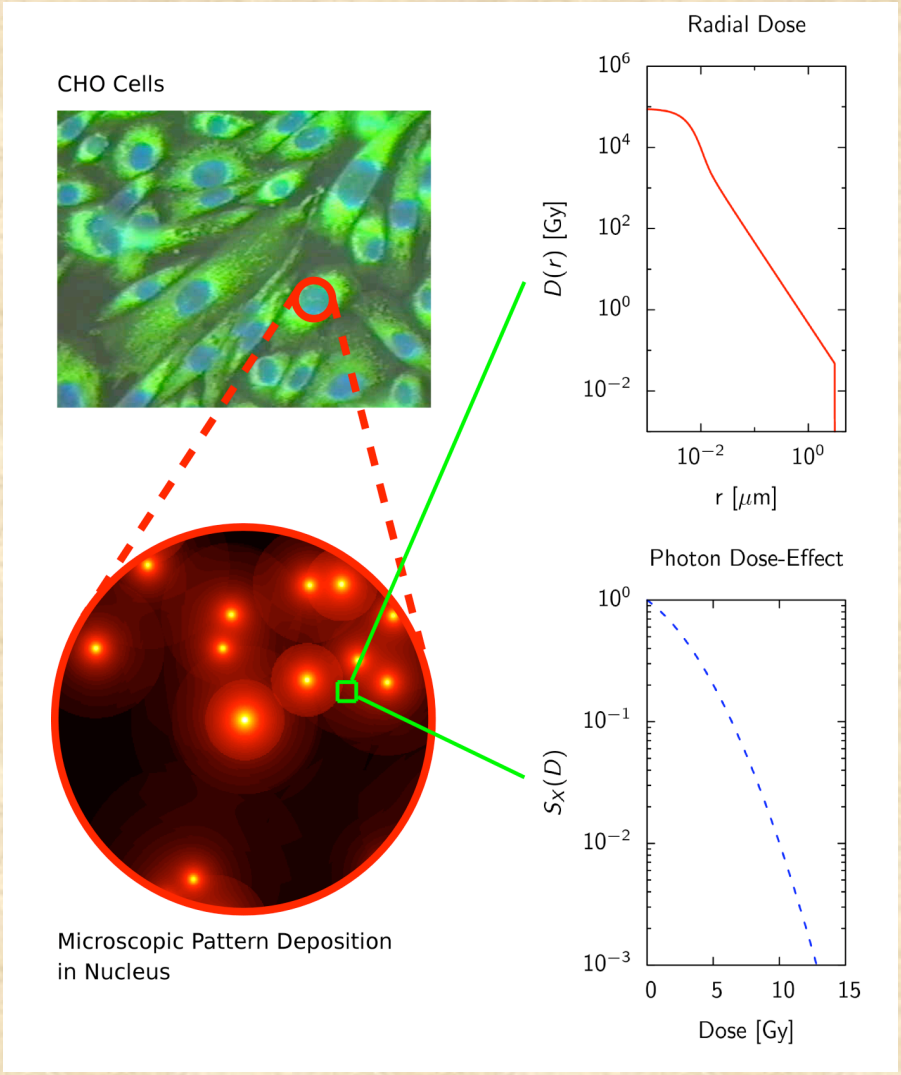
The LEM model

- Biological effect completely determined by the local distribution of dose inside the cell nucleus
- Homogeneous cell nucleus with constant density and radiosensitivity
- Locally, the effect of ions can be evaluated using the X-ray Linear Quadratic model:



$$S(D) = \begin{cases} e^{-\alpha D - \beta D^2} & D \le D_t \\ S_t \cdot e^{-s(D-D_t)} & D > D_t \end{cases}$$

LEM model: the basis



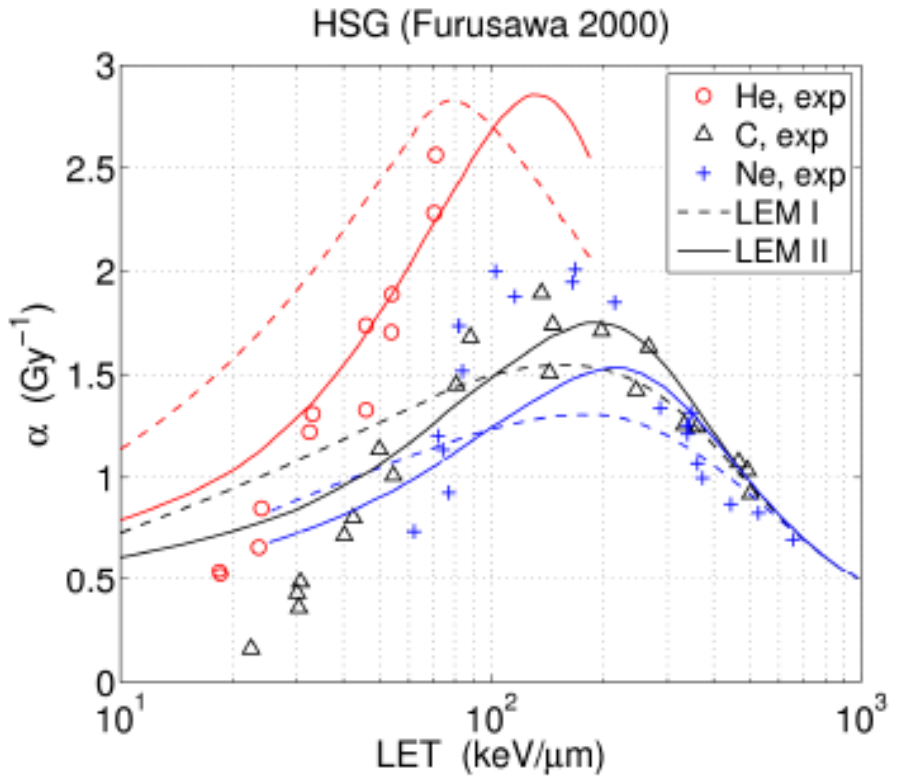
Physical parameters

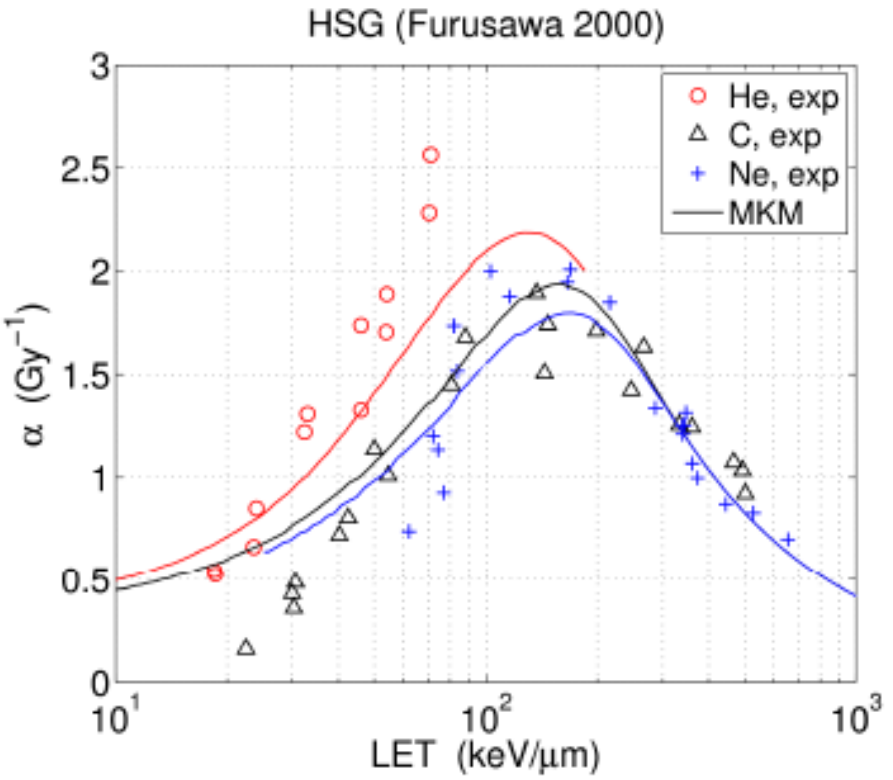
- Kinetic energy E_k
- LET
- particle type (A, Z)

Biological parameters

- LQ-L parameters α_X, β_X, D_t
- R_{Nucleus}

Comparison with experiment





LEM

$$\begin{cases} \alpha_X = 0.313\ \mathrm{Gy}^{-1} \\ \beta_X = 0.0615\ \mathrm{Gy}^{-2} \\ D_t^{\mathrm{I}} = 30\ \mathrm{Gy} \\ D_t^{\mathrm{II}} = 6\ \mathrm{Gy} \\ R_{nucl} = 5\ \mu\mathrm{m} \end{cases}$$

MKM

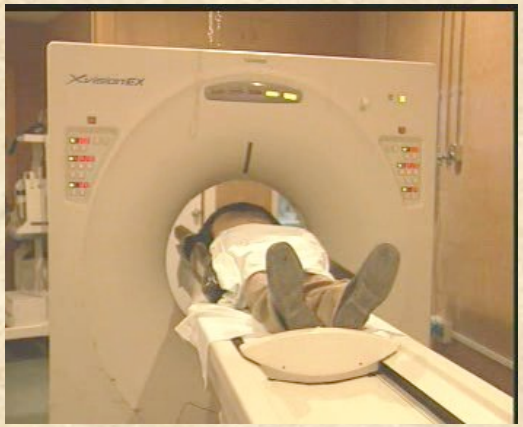
$$\begin{cases} \alpha_X = 0.313\ \mathrm{Gy}^{-1} \\ \beta_X = 0.0615\ \mathrm{Gy}^{-2} \\ R_d = 0.34\ \mu\mathrm{m} \\ \sigma = \pi\ 4.6^2\ \mu\mathrm{m}^2 \end{cases}$$

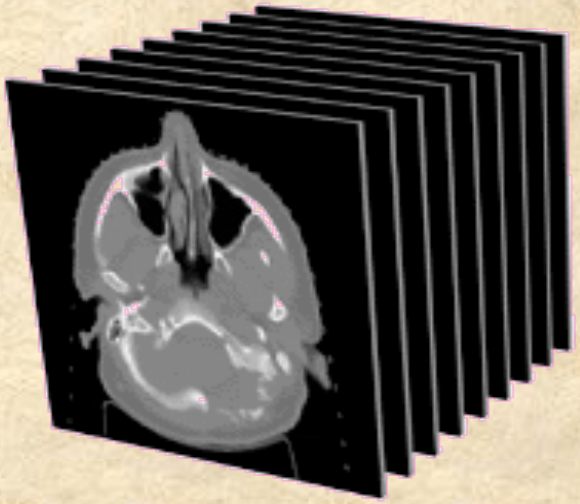
Monte Carlo Task

We use FLUKA as our baseline MC. All dose LUT are computed in water equivalent approximation

- Provides the LUT of physical dose released by the pencil beam : particle composition and energy release vs x,y,depth and beam energy
- Provides the LUT of biological dose released: coupling of the beam composition and ΔE with radiobiological model
- Verify the dose distribution predicted by the optimization process on the real patient geometry
- Predict the distribution of β+ emitters for on line PET tomography

Patient modeling: voxelization





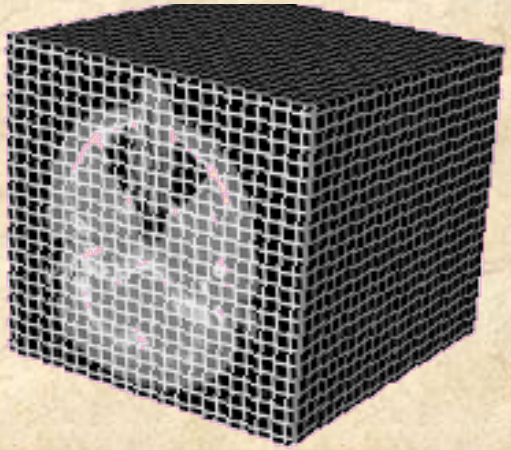
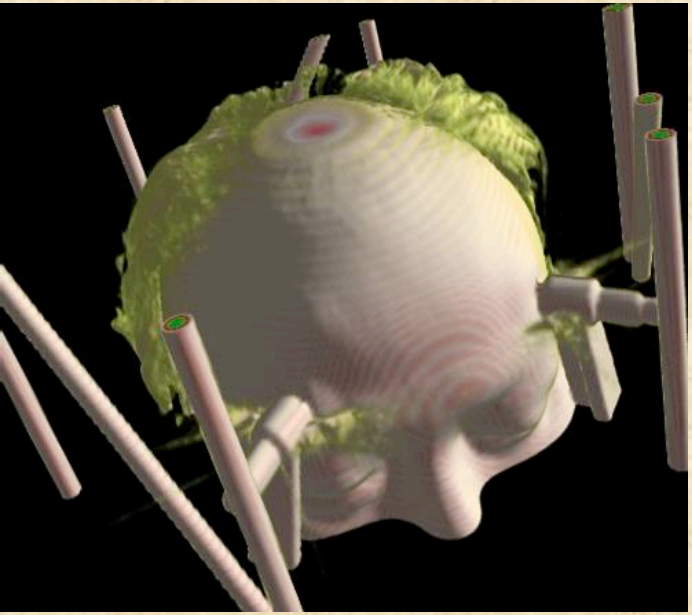


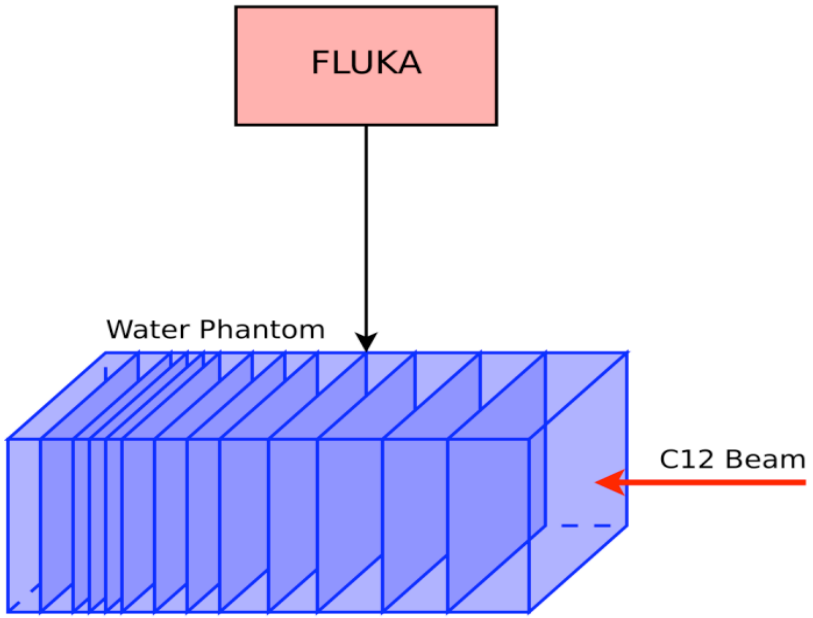
Figure 3. PEREGRINE models both the
to ensure accurate treatm

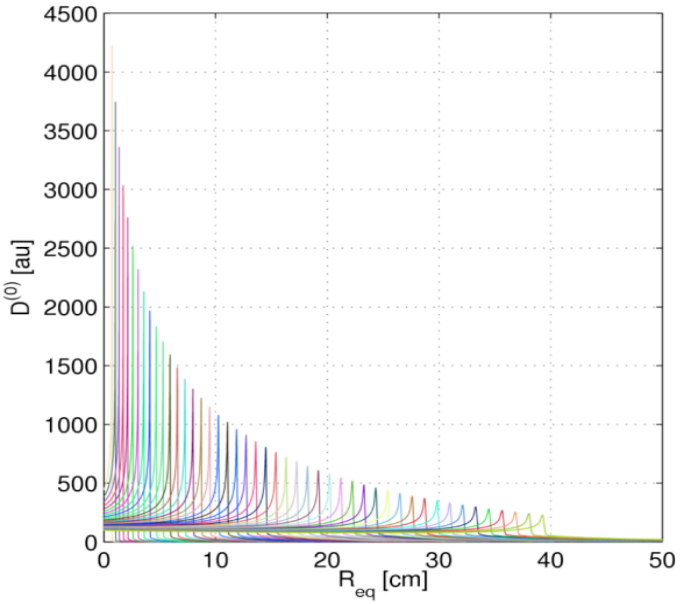


- Needed by Optimization & MC
- Reading information from CT. Frequently info from PET or NMR added. DICOM standard used
- Conversion of machine info in 3D physical info: from Hounsfield Units to electronic density (Water Equivalent approximation)
- For hadrontherapy, conversion to actual composition (A,Z,ρ) can bee needed

Physical Dose LUT production

- Water equivalent path length (WEPL) approximation is carefully simulated to gauge the impact of the discontinuity
- LUT generated in water phantom both for proton and ^{12}C in 5 MeV/amu steps



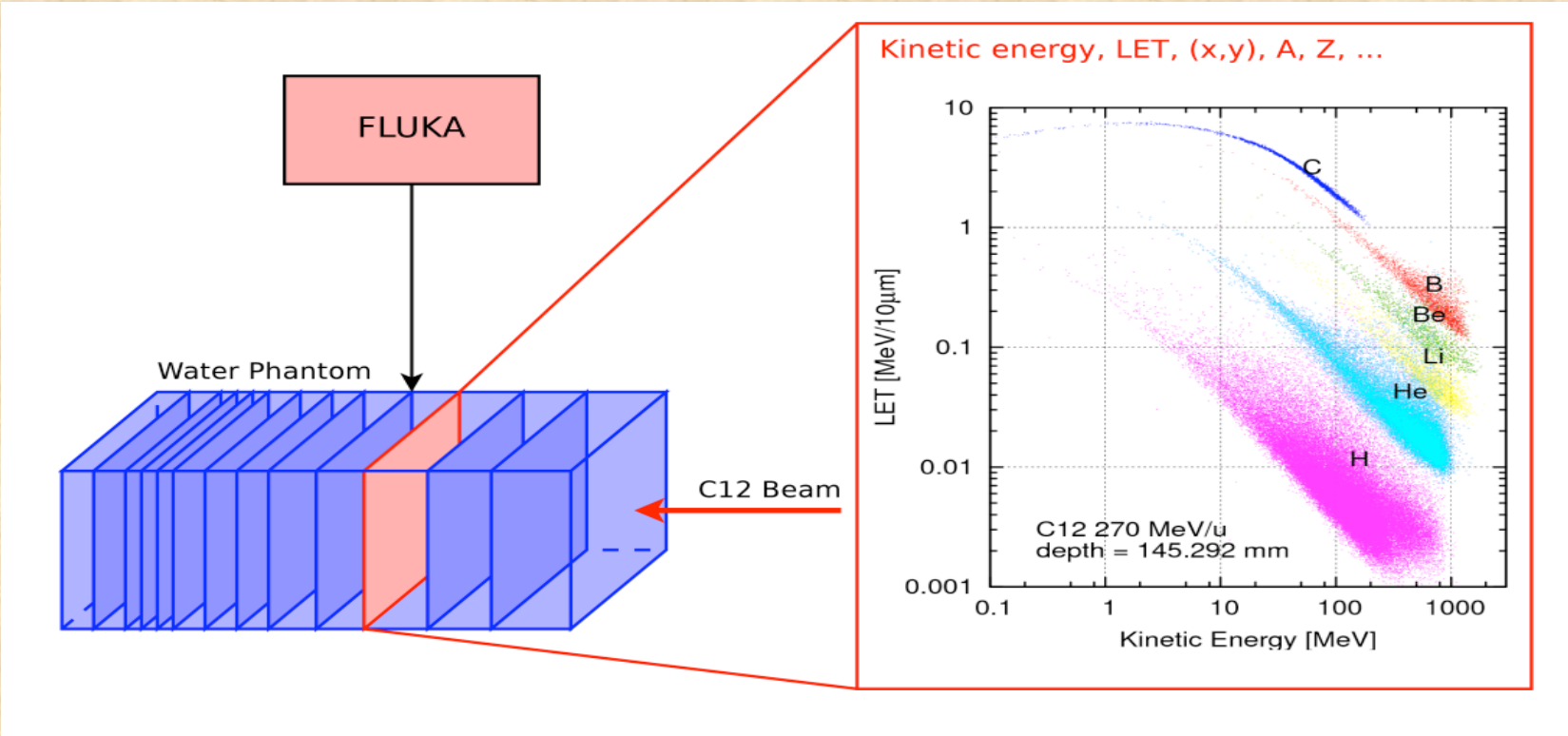


Pencil Beams:

$E = 50, \ldots, 450$ MeV/n

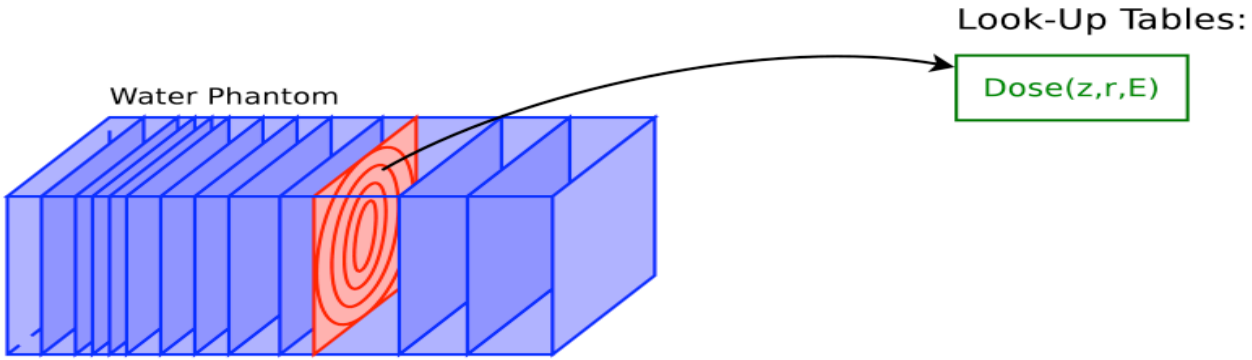
Physical Dose LUT production

- Water equivalent path length (WEPL) approximation is carefully simulated to gauge the impact of the discontinuity
- LUT generated in water phantom both for proton and ^{12}C in 5 MeV/amu steps



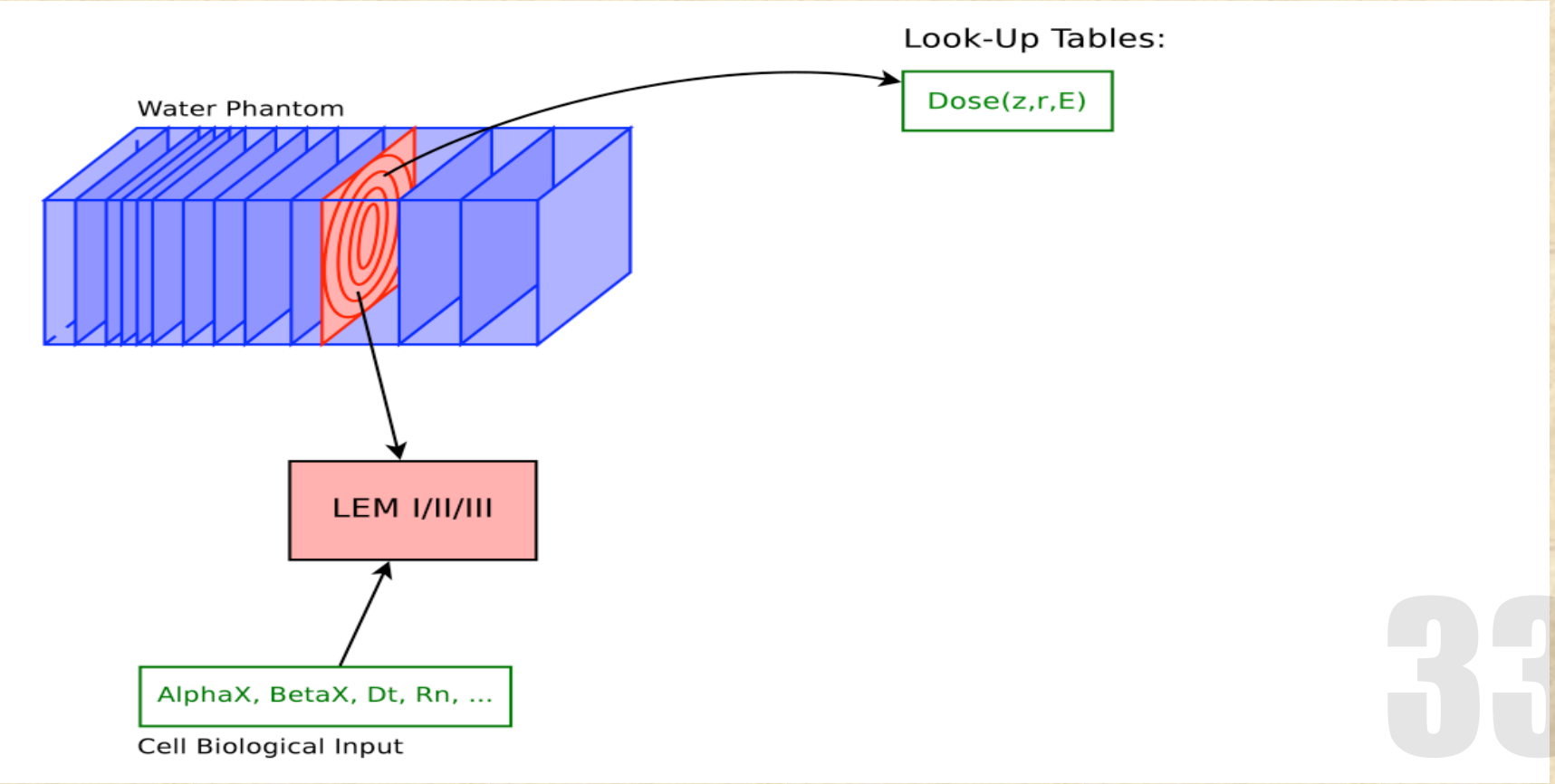
Radiobiological Dose LUT

- The Physical Dose is coupled with the rad. model table to obtain the biological dose of the pencil beam



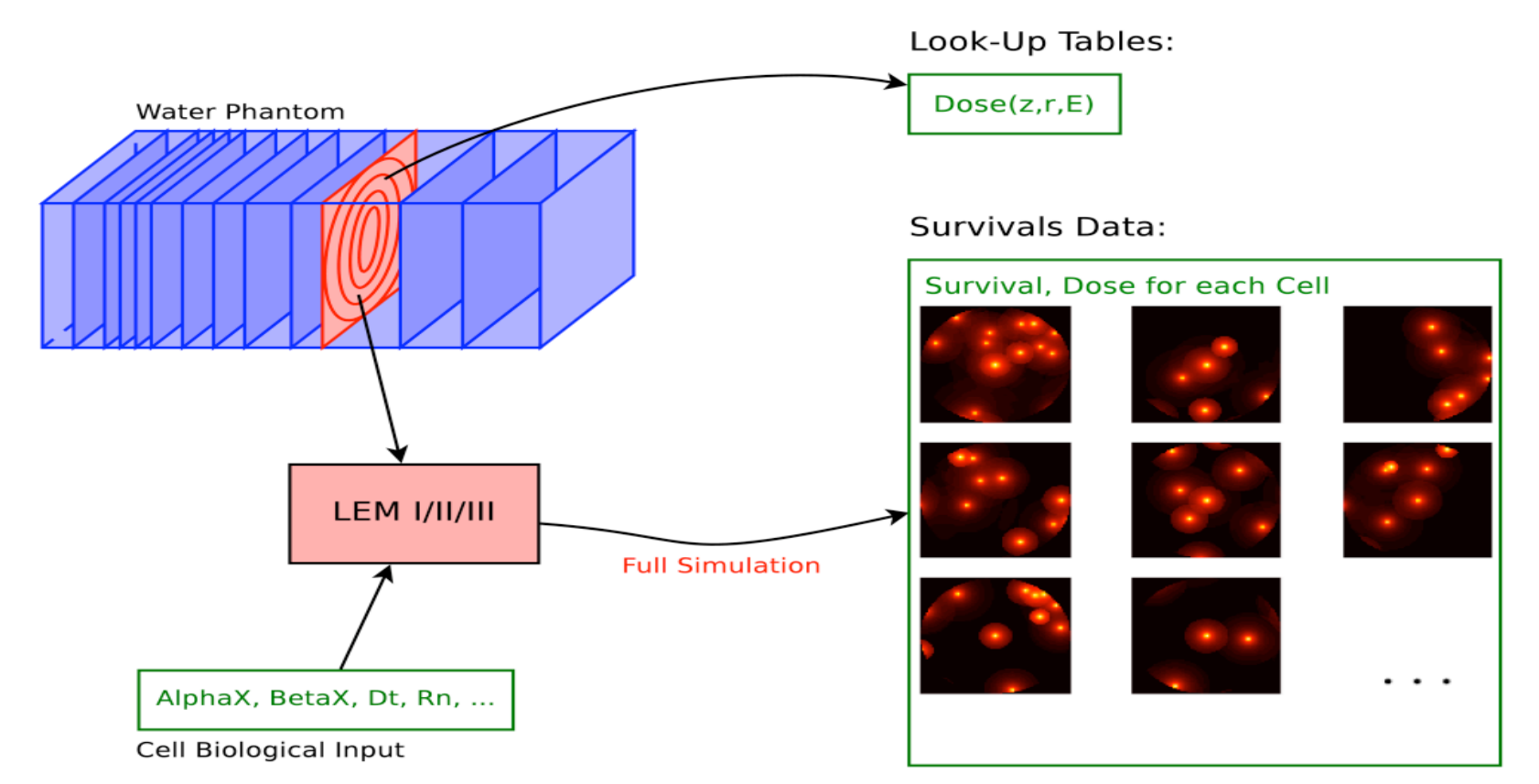
Radiobiological Dose LUT

- The Physical Dose is coupled with the rad. model table to obtain the biological dose of the pencil beam



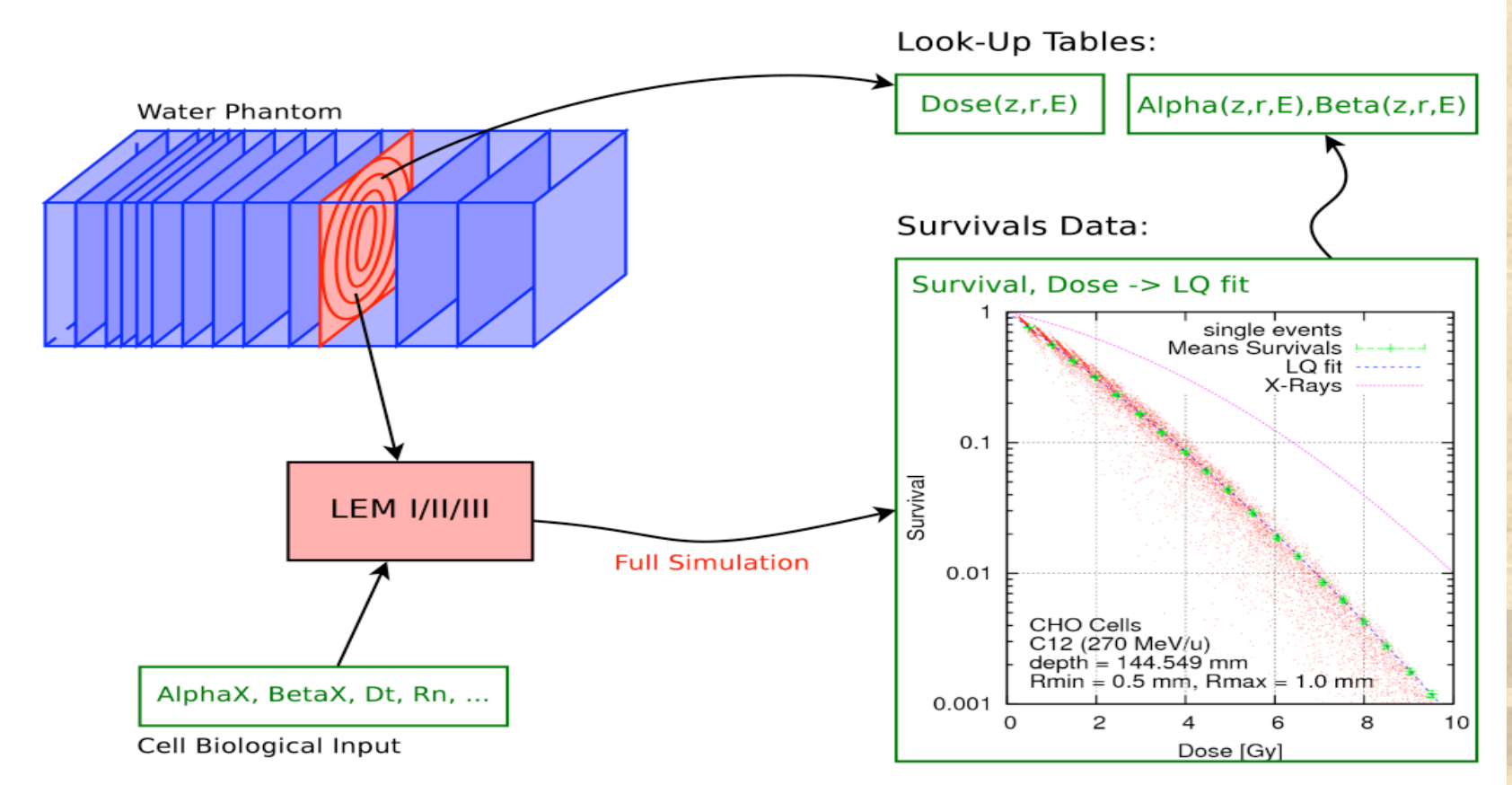
Radiobiological Dose LUT

- The Physical Dose is coupled with the rad. model table to obtain the biological dose of the pencil beam



Radiobiological Dose LUT

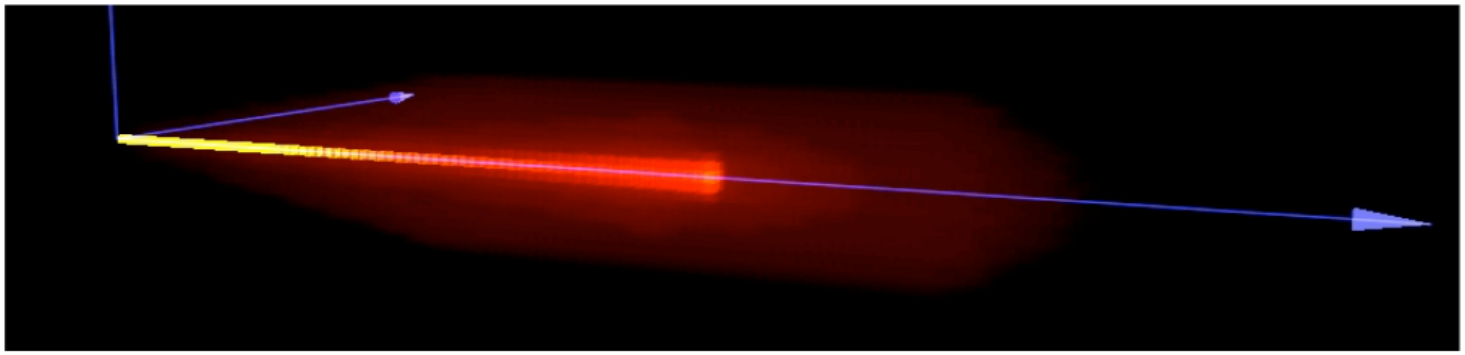
- The Physical Dose is coupled with the rad. model table to obtain the biological dose of the pencil beam



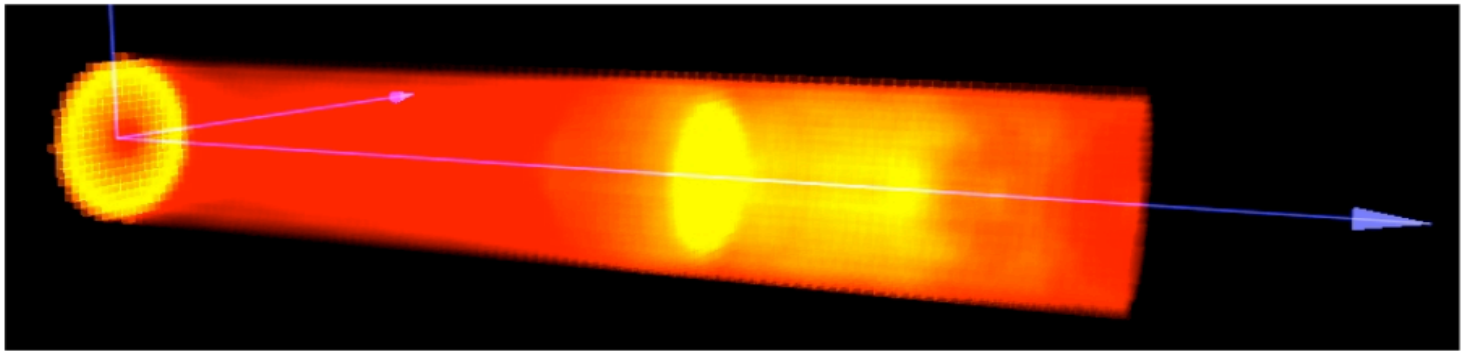
Pencil Beam Biological Dose

- The obtained biological dose of each pencil beam is the build block of the optimization procedure

Dose of 270 Mev/n C ions



Alpha of 270 Mev/n C ions



Optimization task

- Standard optimization problem (χ^2)
- More fancy approach foreseen
- External firm (CENARIO) collab.

Constraints Matrix

$$\Downarrow$$

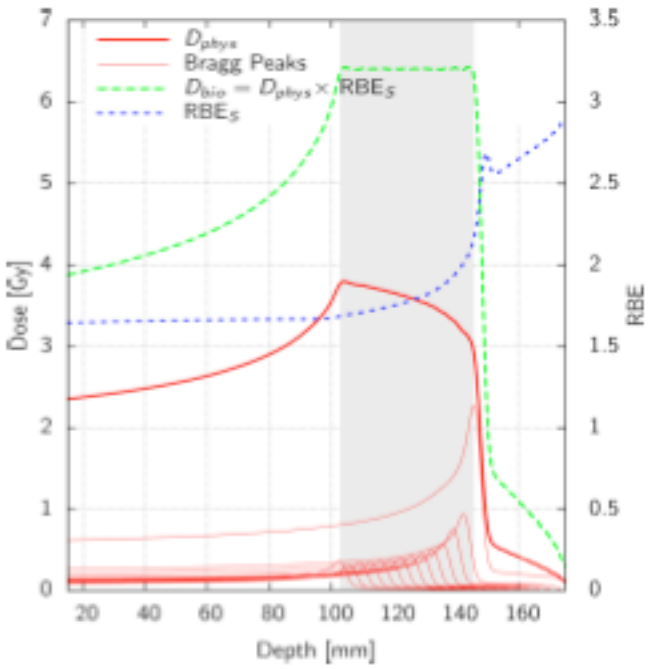
$$\chi^2(\phi) = \sum_{\lambda} \left(w_{\lambda}^{(u)} \sum_{ijk \in \mathrm{VOI}_{\lambda}(v_{\lambda}^{(u)})} \max(0, D_{ijk} - D_{\lambda}^{\max})^2 + w_{\lambda}^{(l)} \sum_{ijk \in \mathrm{VOI}_{\lambda}(v_{\lambda}^{(l)})} \max(0, D_{\lambda}^{\min} - D_{ijk})^2 \right)$$

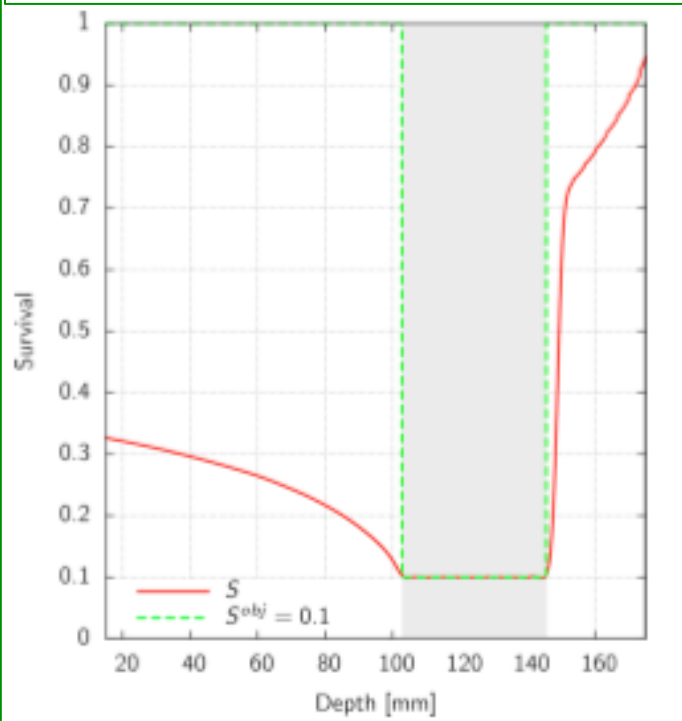
"Biological" Cost Function:

$$D_{ijk} \rightarrow D_{ijk}^{\mathrm{bio}} = D_{ijk} \times \mathrm{RBE}_{ijk}, \quad D_{ijk}^{\mathrm{bio}} = \frac{-\alpha_X + \sqrt{\alpha_X^2 + 4\beta_X N_{ijk}^{\mathrm{leth}}}}{2\beta_X}, \quad N_{ijk}^{\mathrm{leth}} = \alpha_{ijk} D_{ijk} + \beta_{ijk} D_{ijk}^2$$

$$\Downarrow$$

$$\chi^2(\phi) = \sum_{\lambda} \left(w_{\lambda}^{(u)} \sum_{ijk \in \mathrm{VOI}_{\lambda}(v_{\lambda}^{(u)})} \max(0, N_{ijk} - N_{\lambda}^{\max})^2 + w_{\lambda}^{(l)} \sum_{ijk \in \mathrm{VOI}_{\lambda}(v_{\lambda}^{(l)})} \max(0, N_{\lambda}^{\min} - N_{ijk})^2 \right)$$





baseline dose monitoring in HT : PET

Baseline for monitor in HT is PET : autoactivation by p & ^{12}C beam that creates β^+ emitters.

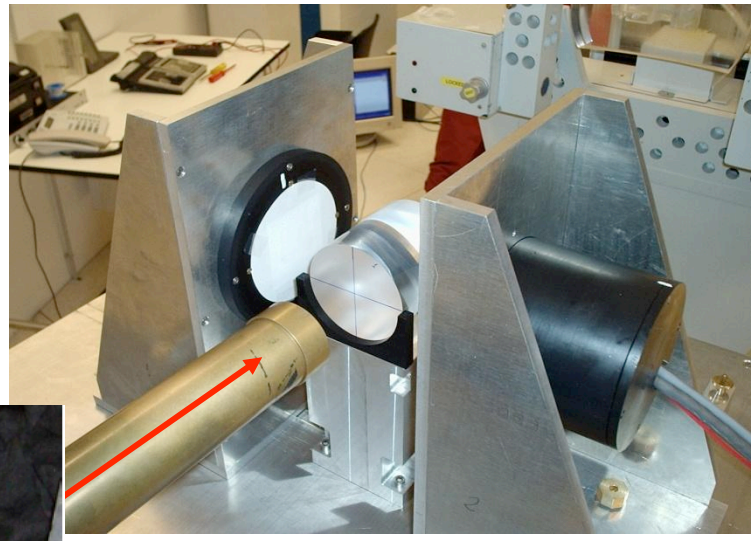
- Isotopes of short lifetime ^{11}C (20 min), ^{15}O (2 min), ^{10}C (20 s) wrt conventional PET (hours)
- Low activity in comparison to conventional PET need quite long acquisition time (few minutes)
- Metabolic wash-out, the β^+ emitters are blurred by the patient metabolism
- No direct space correlation between β^+ activity and dose release (but can be reliable computed by MC)

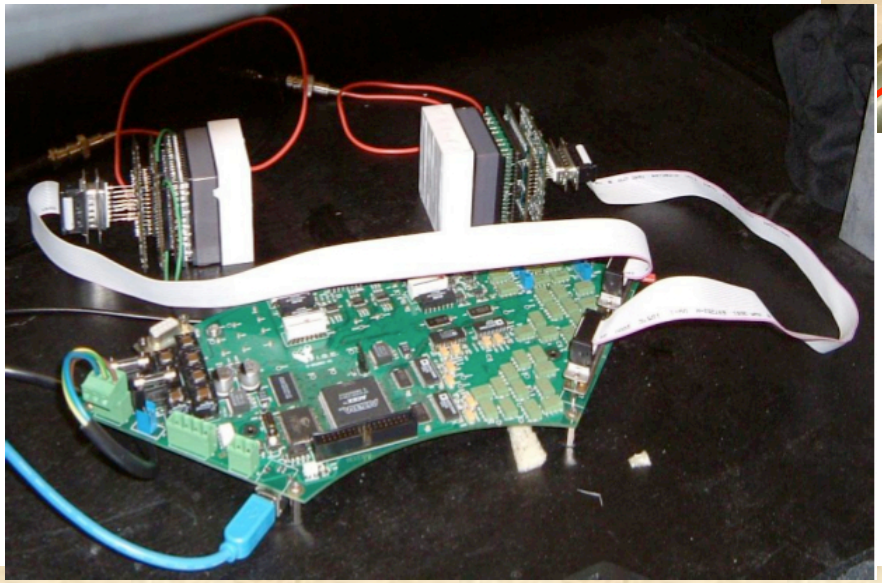
A dedicate PET: the DO-PET project

Scintillating crystals LYSO:Ce from Hilger
PS-PMT H8500 from Hamamatsu Photonics K.K.:

F.Attanasi @ IFA 2010

- Homogeneous cylindrical phantoms of PMMA at center of FoV;
- Spread-out Bragg Peak (SOBP, 10.8 mm plateau width) irradiation;
- Delivered dose: 30 Gy;
- Irradiation Time: ~60 s;

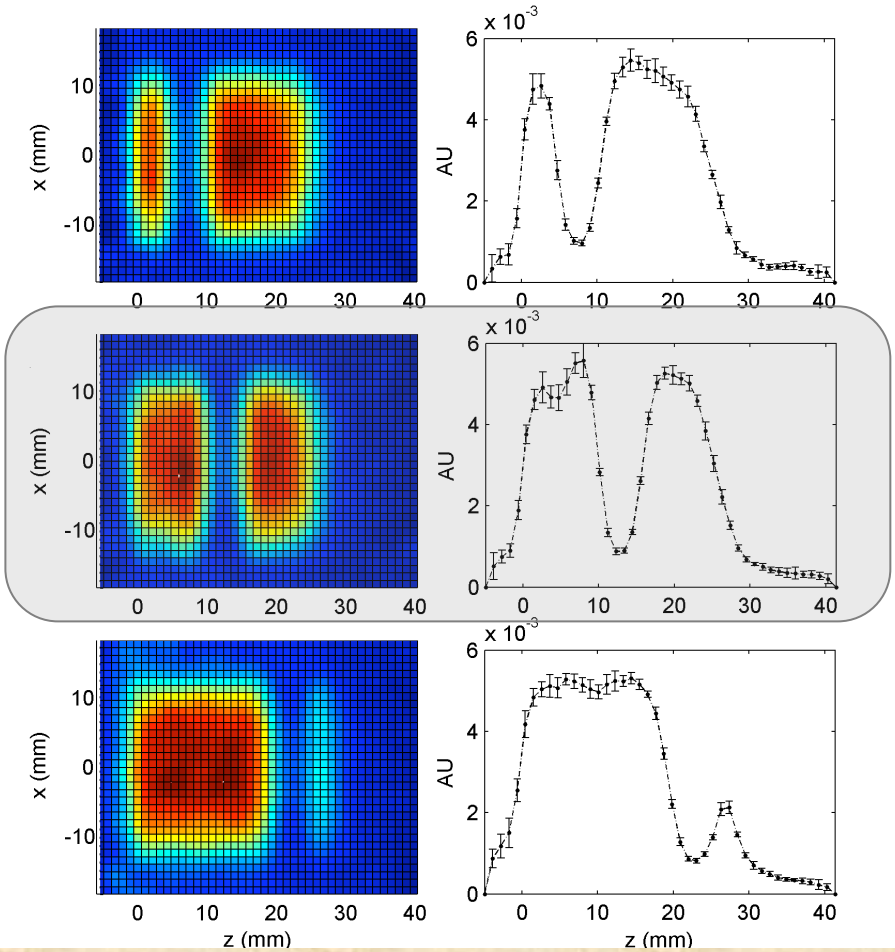




- Final collimator: 25 mm Ø;
- Distance between detectors:14 cm.
- PET acquisition time:20 min.
- FoV: 42 x 42 x 42 voxels.
- 1.076 x 1.076 x 1.076 voxel dimension.

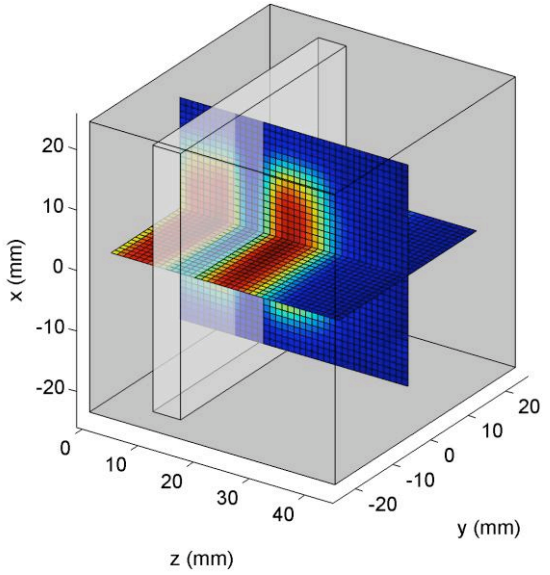
The DO-PET prototype

PMMA phantoms with 0.5 cm Air_Gap at different depth;

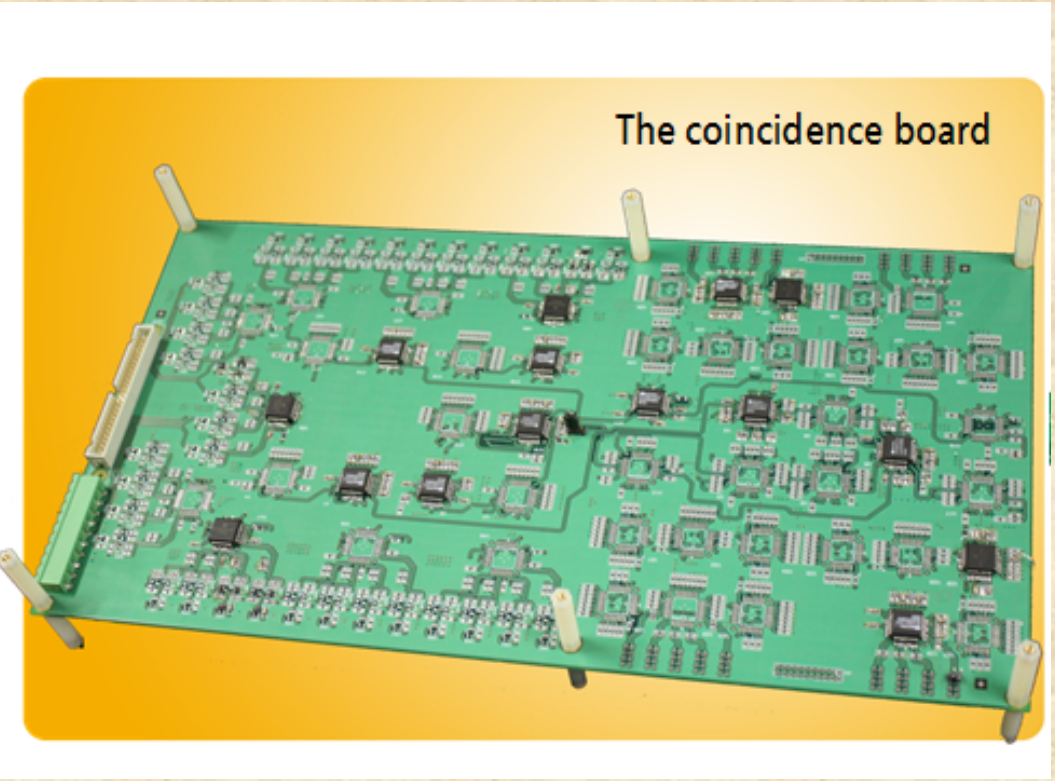


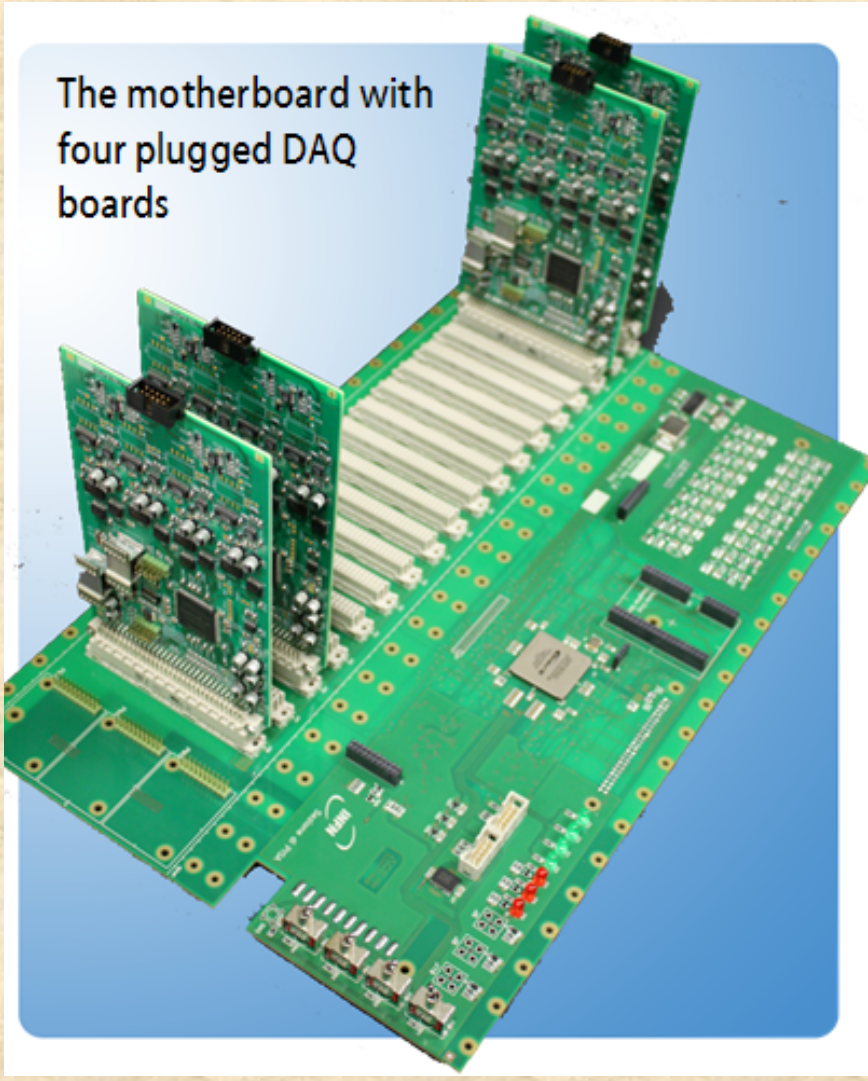
OFF beam PET : long acquisition time

- Phantom irradiations:
  - Bragg peak dose: 30 Gy
  - Irradiation time: 18 s;
- Beam cross sention: 2.5 cm Ø;
- Acquisition time: 20 min;



Final DAQ system

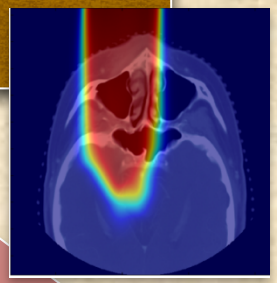




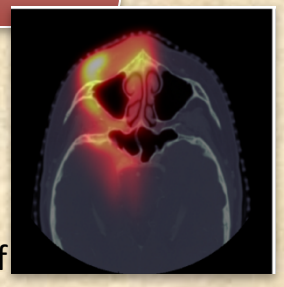
- Can handle up to 9 vs. 9 modules.
- High performance FPGA
- FPGA based fully digital coincidence logic will be implemented
- Still at the development stage

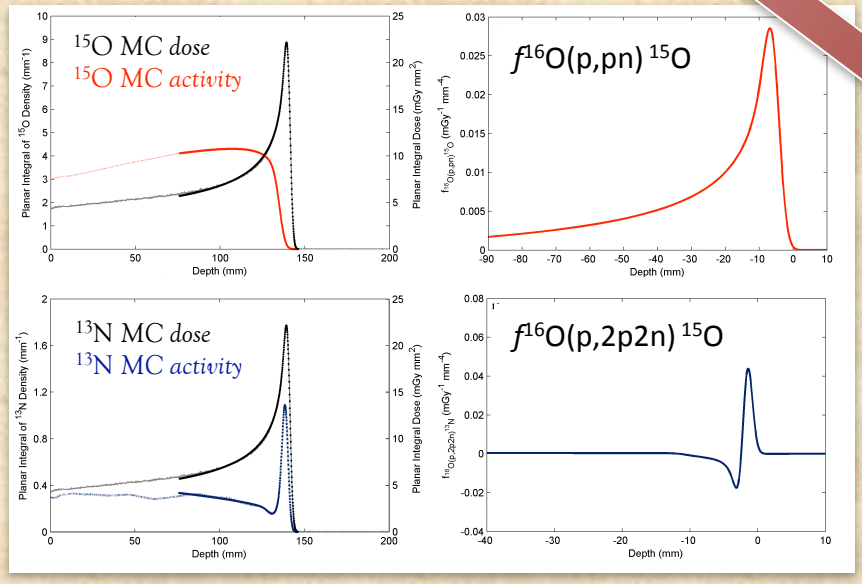
Dose-activity correlation using the a "Filtering" approach

Dose prescription → Treatment planning → Patient positioning (and imaging in-situ) → Dose delivery

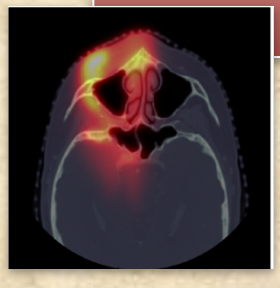


Dose delivery → Imaging PET post-treatment





Filtering



Comparison of distributions (range)

$$\sigma_{range} = \sigma_{PET}$$

F. Attanasi et al. IEEE-NSS MIC 2010

The filter is energy independent

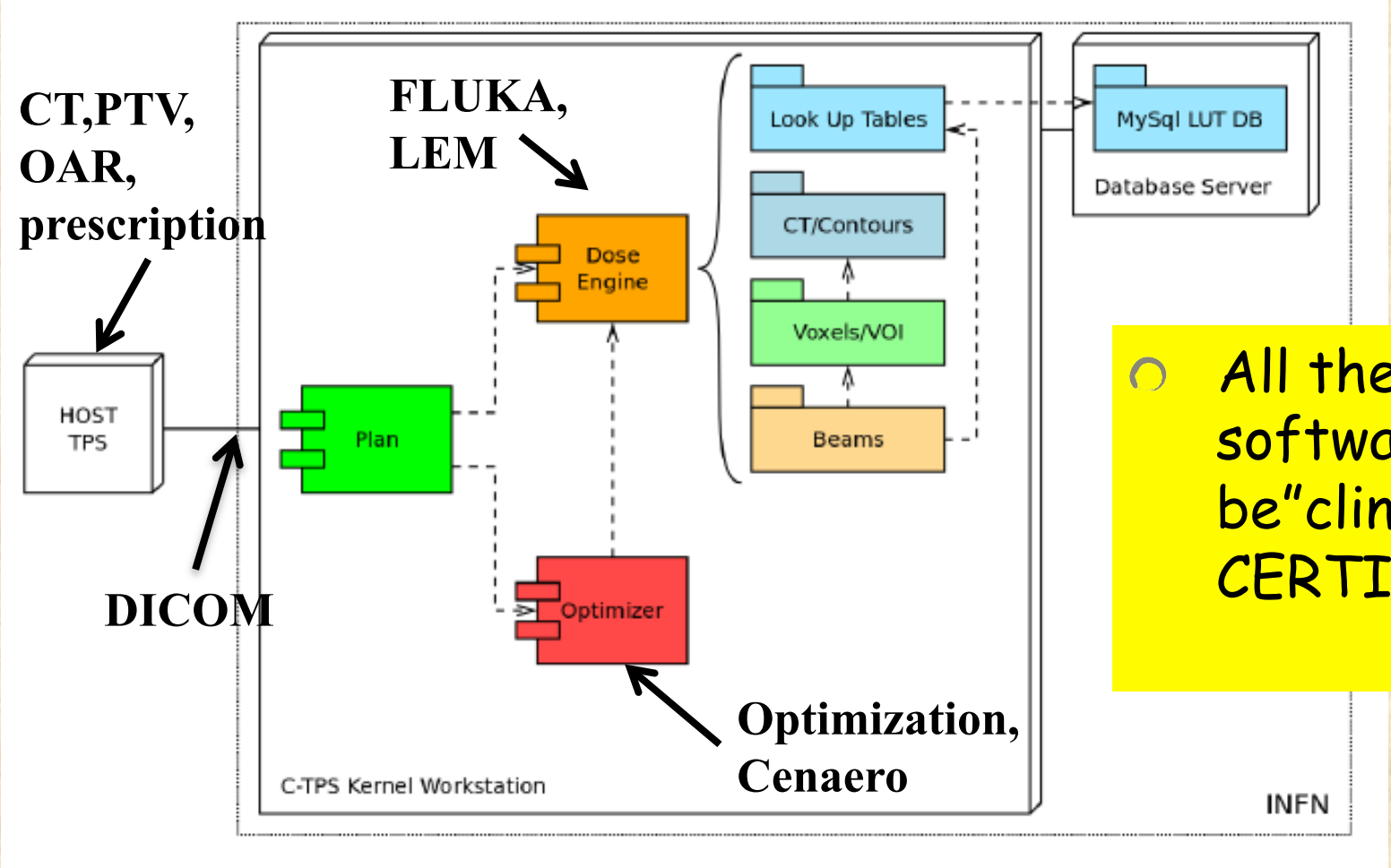
Summary & conclusions

- The TPS collaboration, in cooperation with IBA, is developing a commercial TPS for hadrontherapy active scanning
- The project context is rather broad and is focusing not only on the software but it is tackling also more general aspects as described in the different 5 tasks
- Only 1 competitor for ^{12}C (SIEMENS), few for proton
- Very "interesting" the interaction between INFN people and industrial environment (market, CE, documentation, undisclosure agreement, I.P,..)

Spares

Architecture of the TPS INFN-IBA

Platforms: Linux, Language: C++

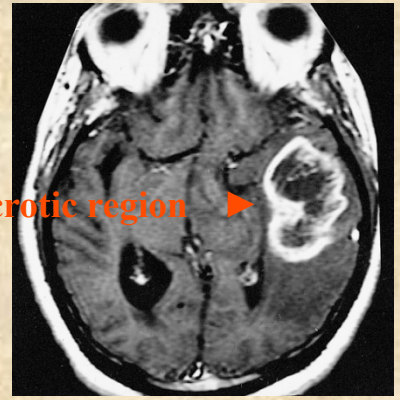


- All the software must be"clinically" CERTIFIED!!!

b) Napoli-Milano : Radiosensibilization of gliomas for hadron therapy

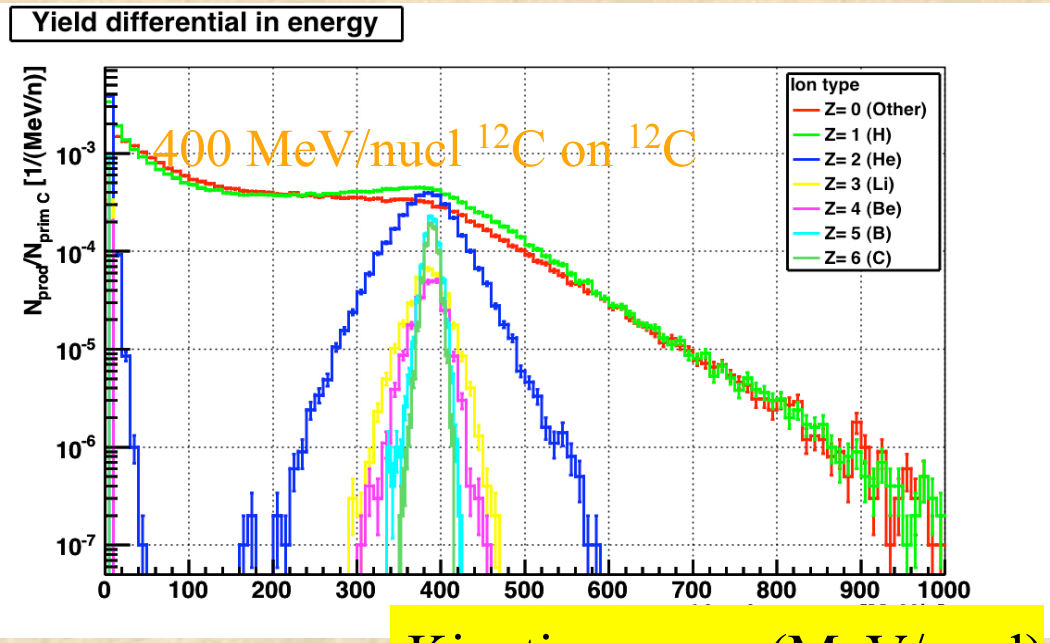
• Glioblastoma multiforme (GBM) is the most aggressive of the gliomas
• GBM is also the most common in humans
  unfavourable prognosis
  marked radioresistance
• Current approach: alkylating agent temozolomide (TMZ) in combination with conventional radiotherapy
• Alkylating agents work by different mechanisms all of which achieve the same end result : disruption of DNA function and cell death
• Suitable for hadron therapy

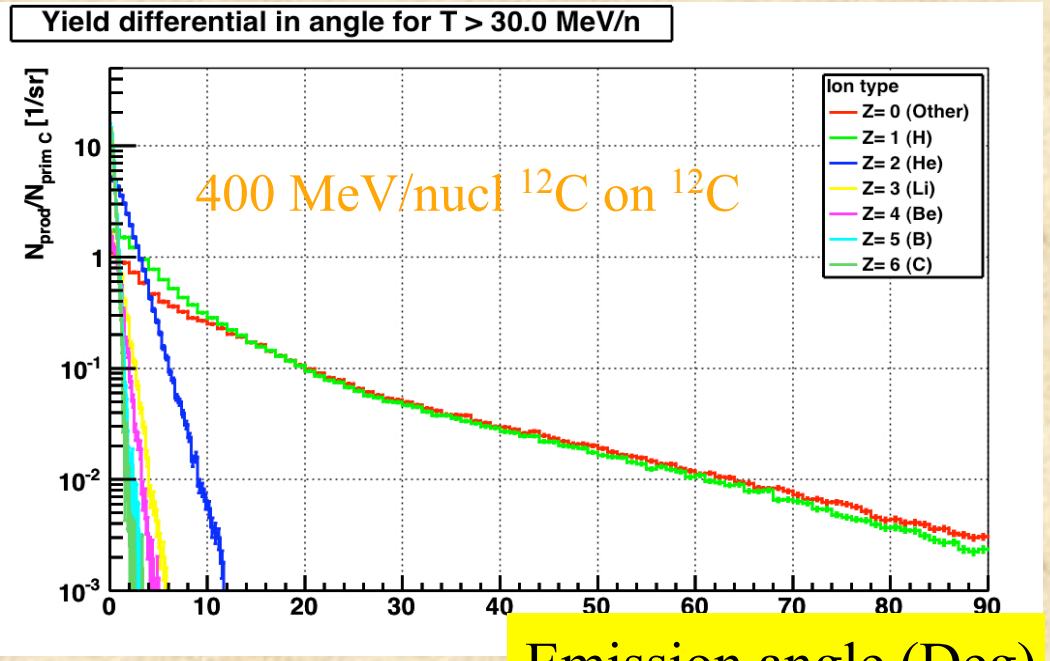
• *Possible enhancement of cell killing by TMZ as a result of high-LET irradiation*



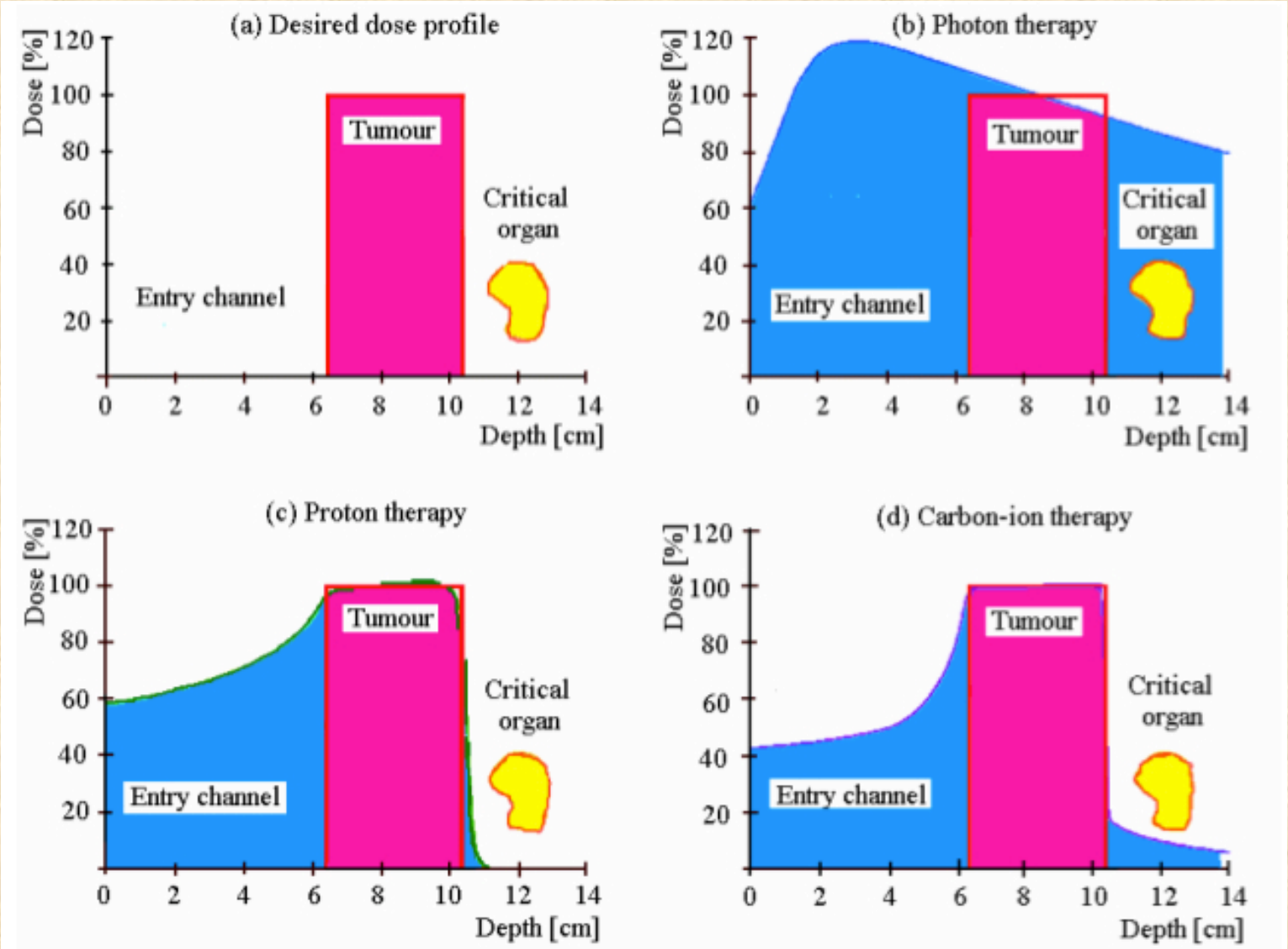
What do we expect from MC (FLUKA)?

- The Z>2 produced fragments approximately have the same velocity of the ^{12}C beam projectiles and are collimated in the forward direction
- The protons are by far the most abundant fragments with a wide β spectrum $0<\beta<0.6$ and with a wide angular distribution with long tail
- The Z=2 fragment are all emitted within 20^0 of angular aperture
- The dE/dX released by the fragment spans from ~2 to ~100 m.i.p.





Single Field Dose comparison



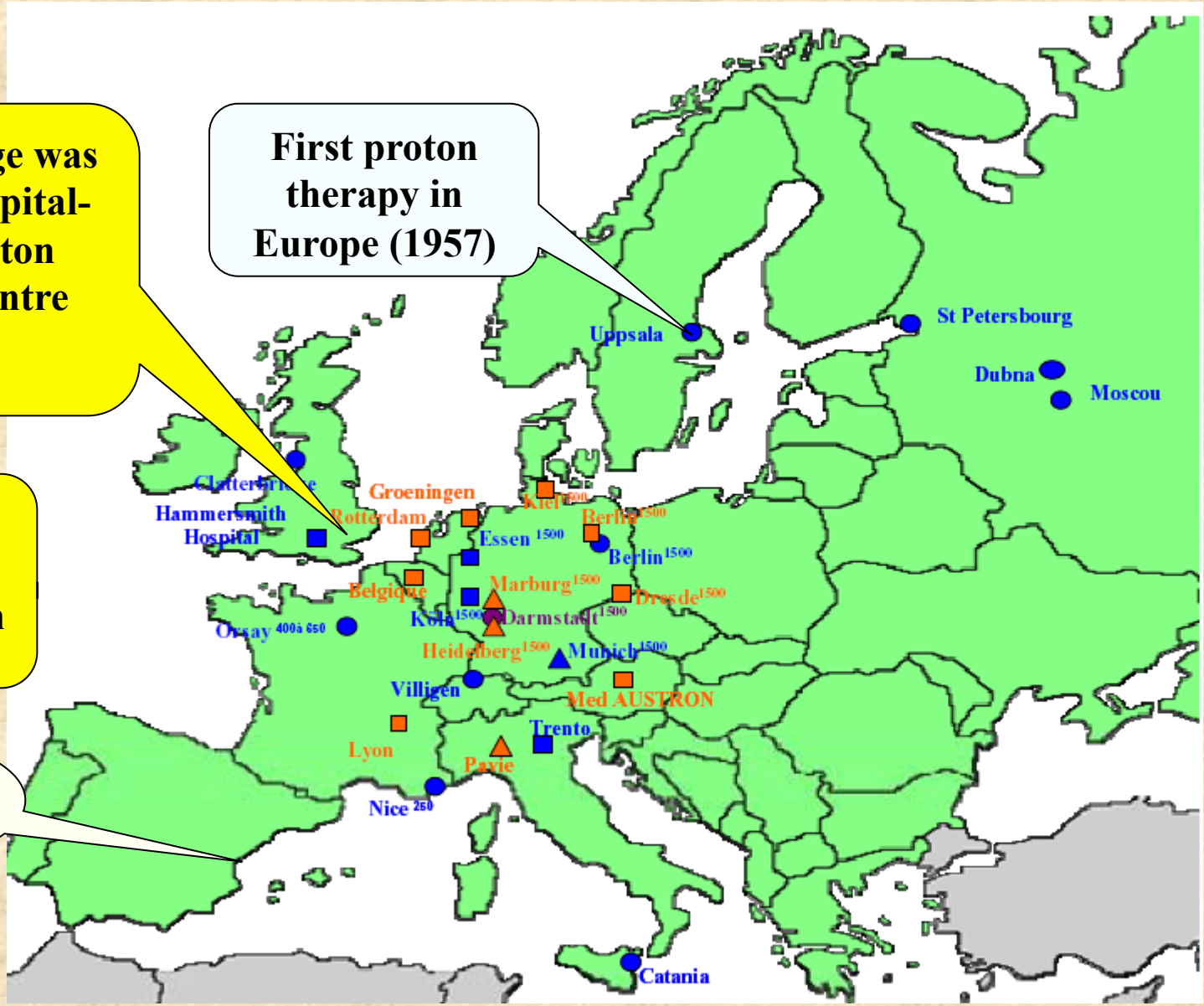
Centres in Europe (existing and planned)

Clatterbridge was the first hospital-based proton therapy centre (1989)

First proton therapy in Europe (1957)

The second UK centre MAY open in 2014!

Plans for Valencia

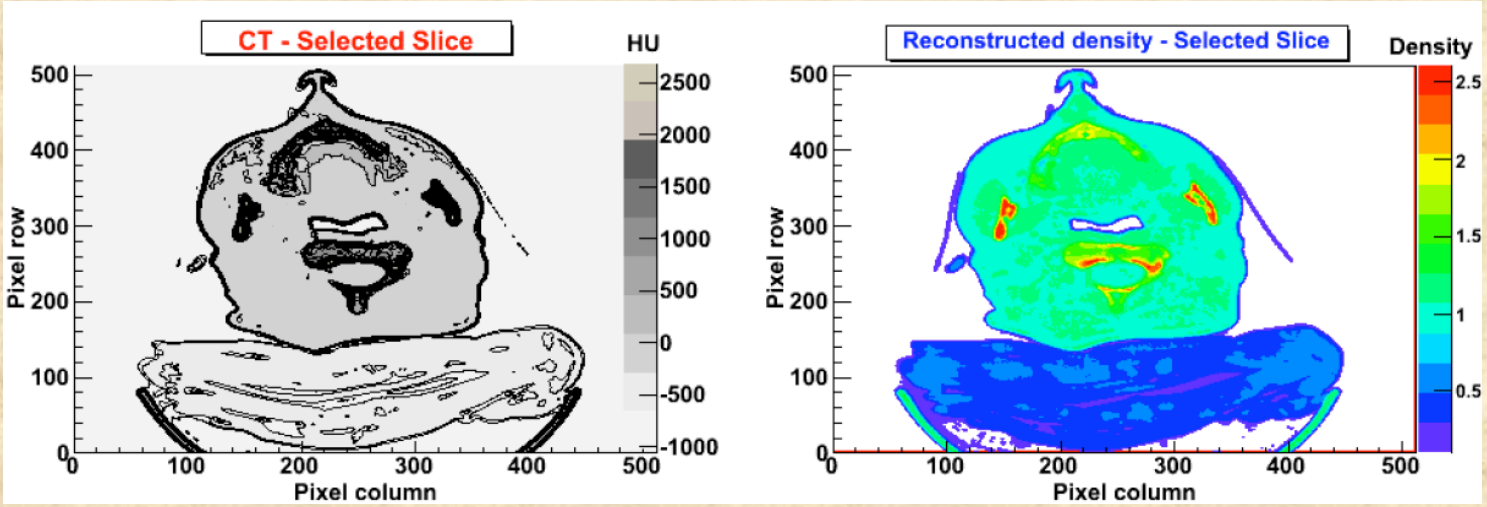


Using the information of CT in the MC & Optimization

CT = Computer Tomography expressed in H numbers

$$H = \left(\frac{\bar{\mu}}{\bar{\mu}_{H_2O}} - 1 \right) 1000$$

H (air)= -1000 and H (water) = 0

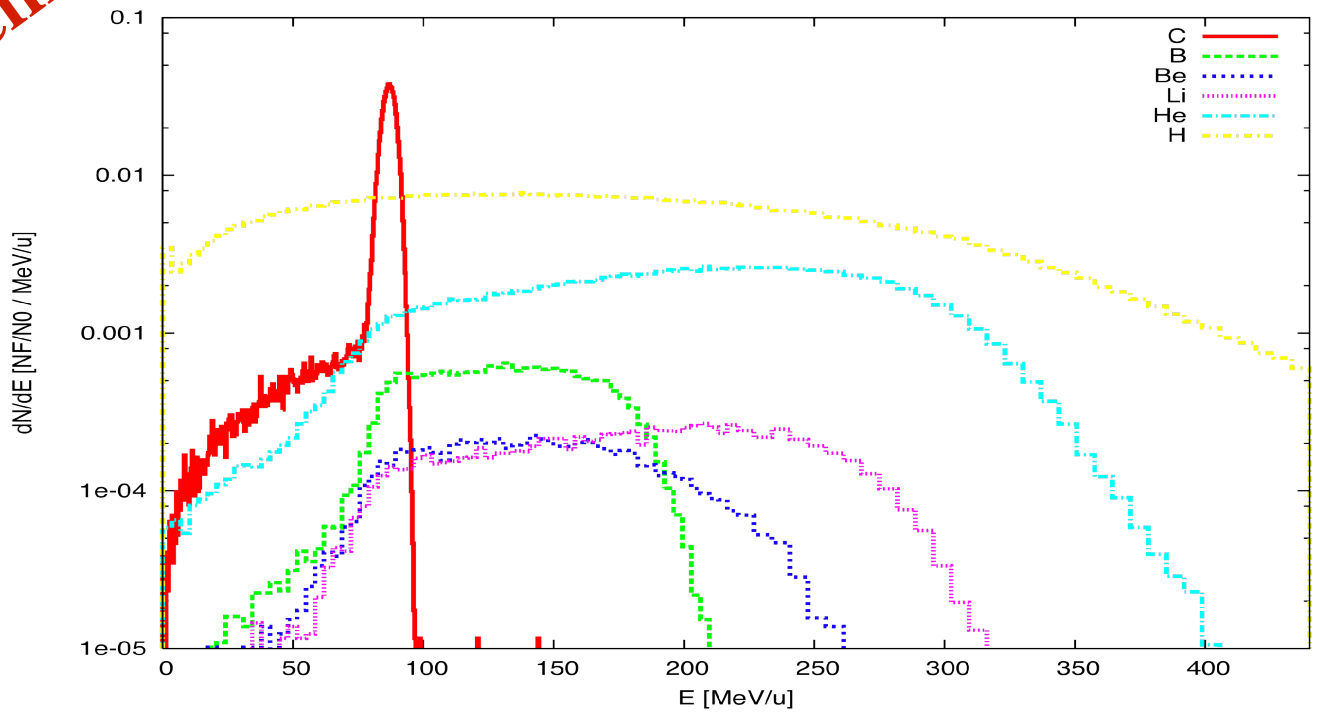


An example: FLUKA spectra database for the analytical TPS @ HIT

^{12}C ions (400 MeV/u) in Water

Fragment spectra dN(Ebeam,z,T,E)/ dE at 25.4 cm

Preliminary



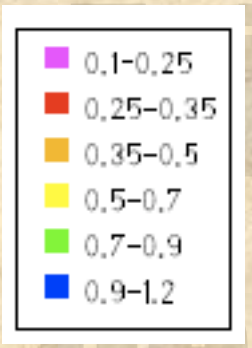
A. Mairani and K. Parodi (HIT)

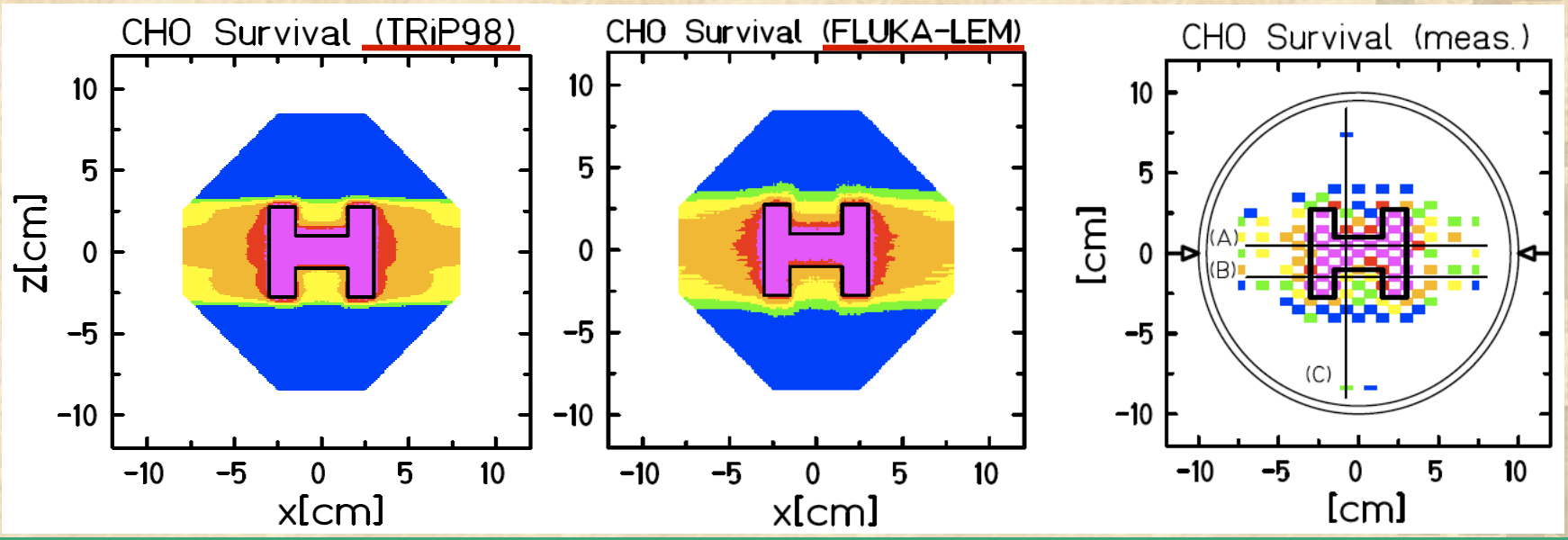
The LEM-FLUKA interface: comparison with analytical calculations and experimental data

Preliminary !!!!

Cell Survival

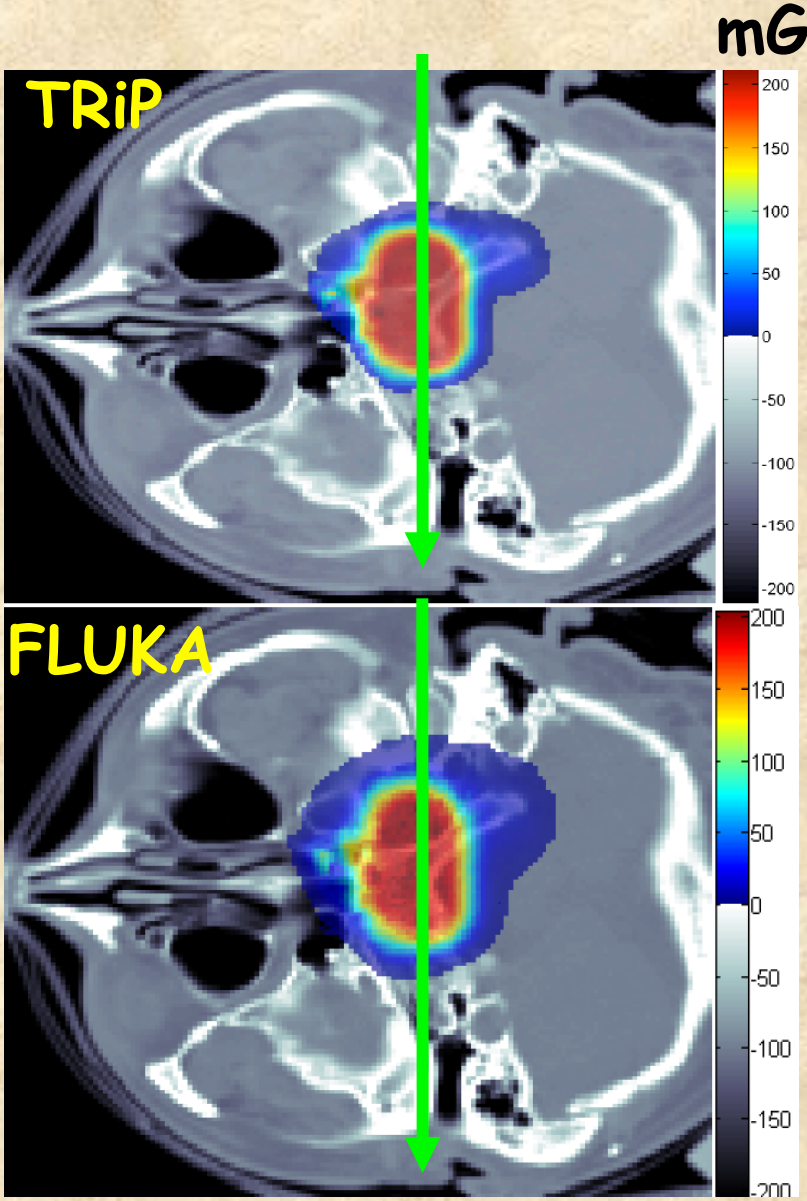
- Two opposing dose ramps with tissue sparing (as brain-stem)
- **TRiP98 Analytical calculations**: biological planning and optimization for CHO cells
- **FLUKA-LEM**: forward calculation of the optimized plan





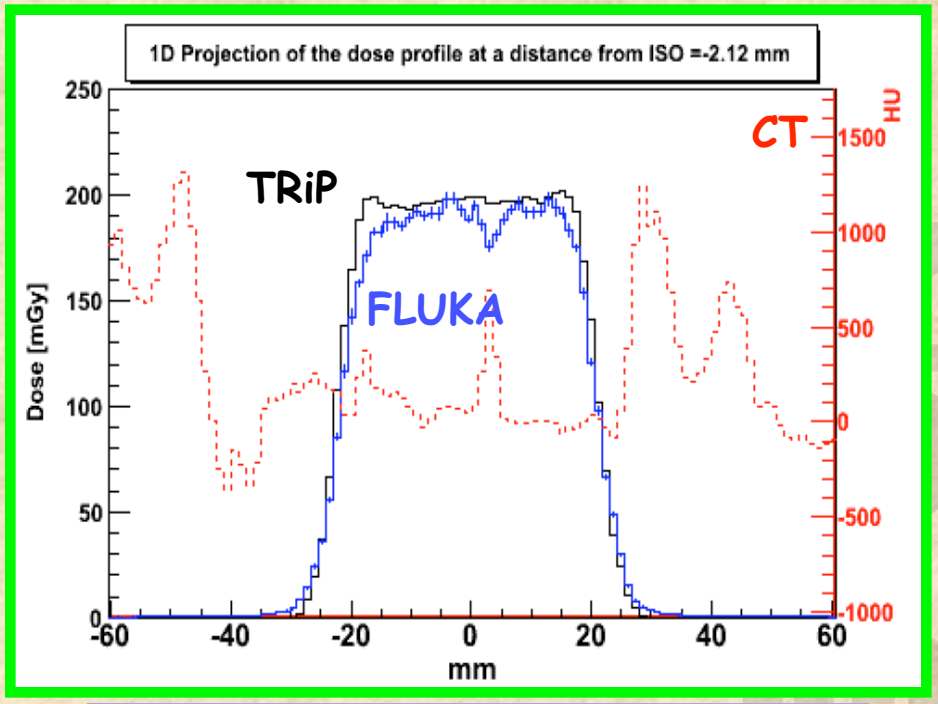
Exp. Data and analytical calculations: Krämer et al, PMB 48 (2003) 2063

Carbon therapy: MC vs TRiP for a Clivus Chordoma Patient at GSI



Absorbed dose distributions

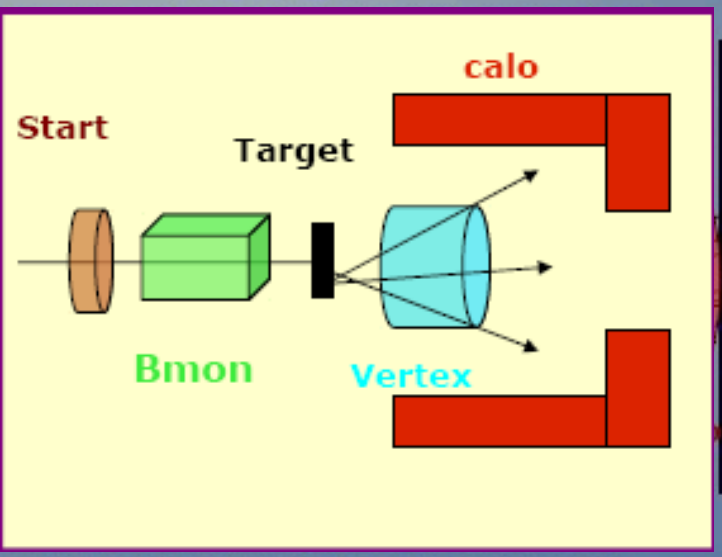
Prescribed physical dose 0.47 Gy
Comparisons performed at ~0.25 Gy

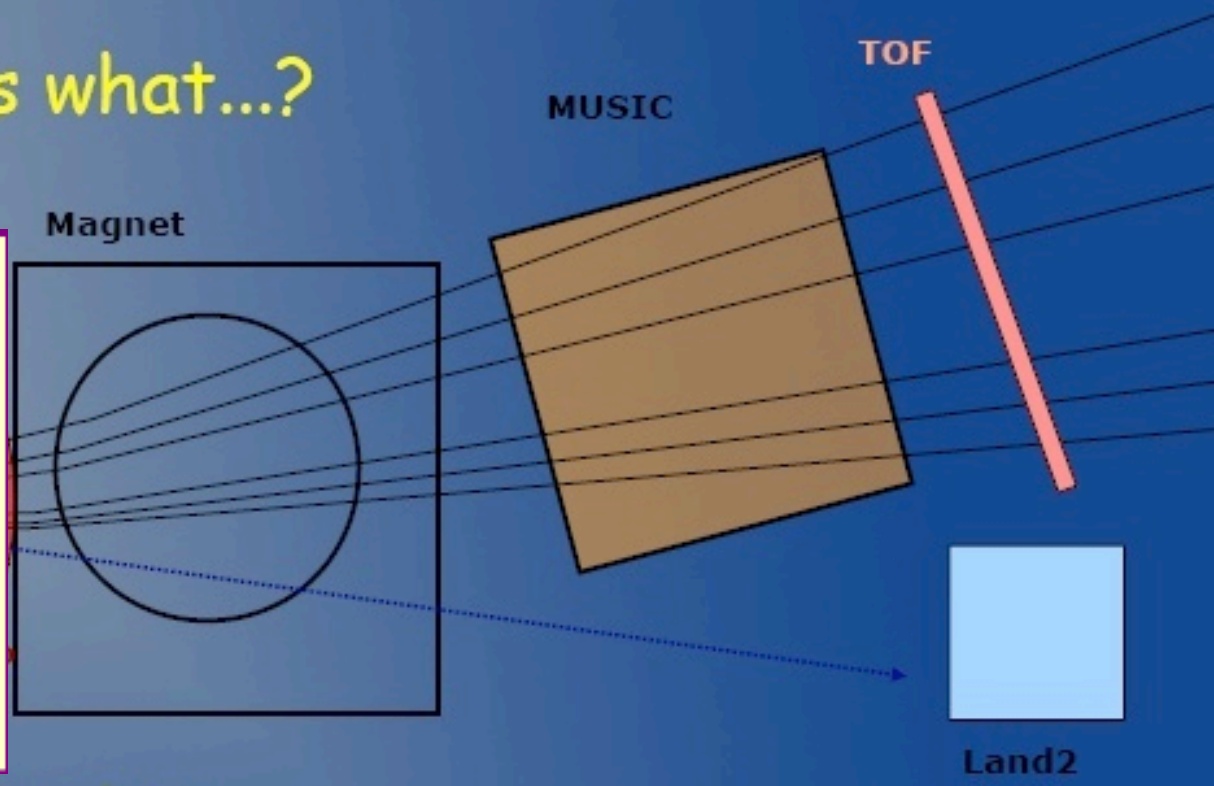


A. Mairani PhD thesis 2007, Pavia

Who measures what...?

New IT





MUSIC → Z/p , θ,φ after bending

MUSIC → Energy loss ∝ $(Z/\beta)^2$

Hodo → Large angle fragment energy, θ,φ

Vertex → Fragments emission θ,φ

Start and TOF wall → TOF= L(p,Z,θ,φ)/β

Bmon → Beam impact point

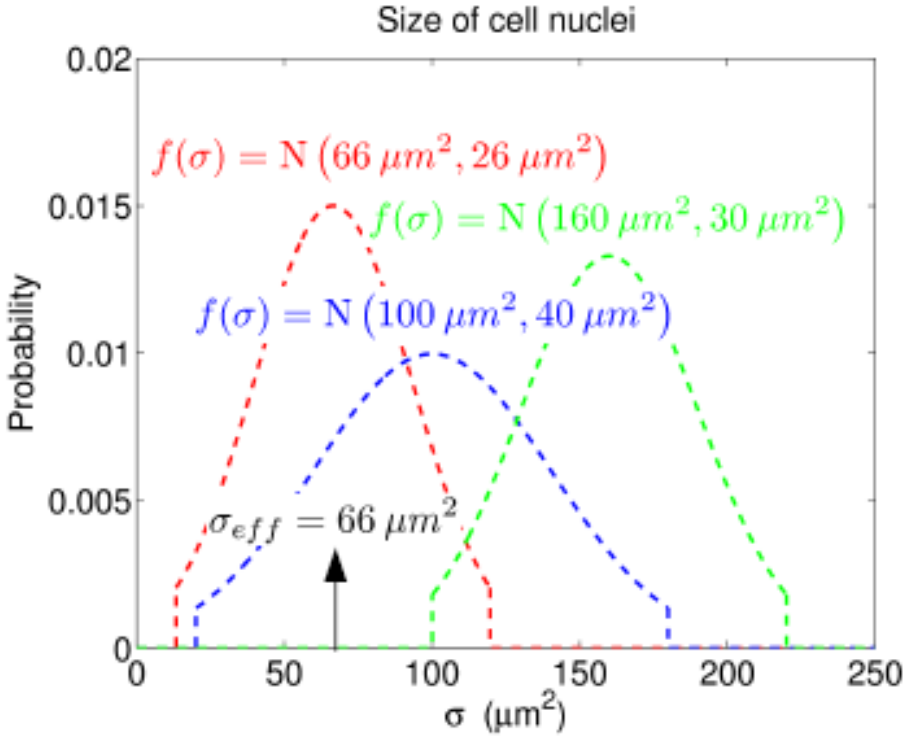
To extract Z, A, θ_{emiss}, p_{emiss} the reconstruction must exploit all the setup information

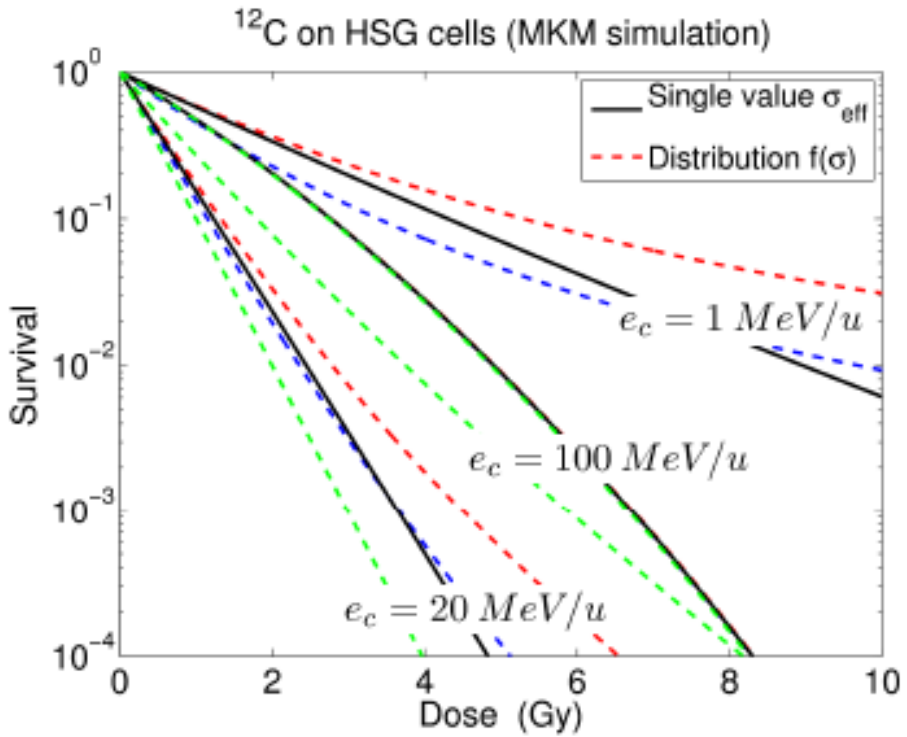
CALO → Large angle p

LAND2 → neutron flux

MKM and LEM improvements - Distribution of cell nucleus cross-sections

We allowed the cell nucleus size to vary in the LEM and MKM Monte Carlo simulations, to check the effect of a nucleus size distribution.

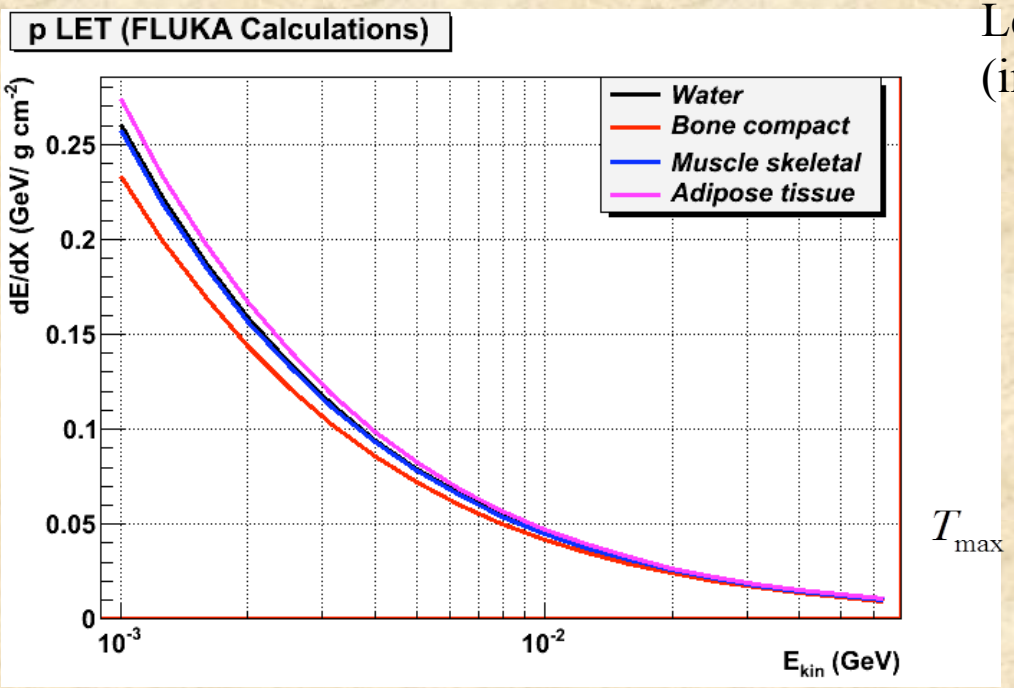




dE/dX calculation

In this energy range FLUKA is within 1/1000 of values in ICRU tables

Let us use directly ICRU tables in these plots (in g/cm^2)

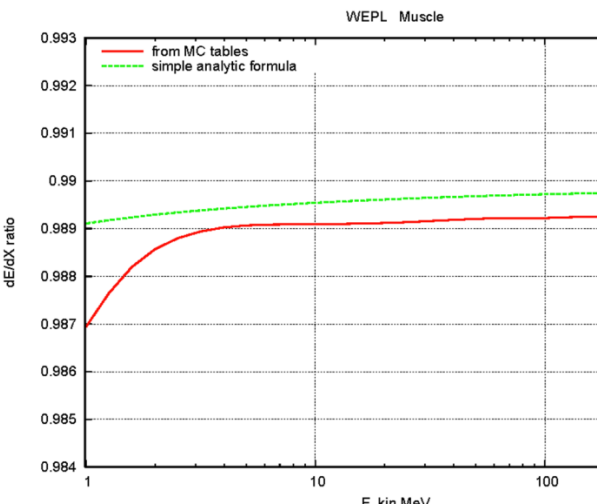


$$\frac{\left\langle \frac{Z_1}{A_1} \right\rangle \frac{1}{\beta^2}\left[\ln \frac{2m_e c^2 \beta^2 \gamma^2 T_{\max}}{I_1^2} - 2\beta^2 \right]}{\left\langle \frac{Z_2}{A_2} \right\rangle \frac{1}{\beta^2}\left[\ln \frac{2m_e c^2 \beta^2 \gamma^2 T_{\max}}{I_2^2} - 2\beta^2 \right]}$$

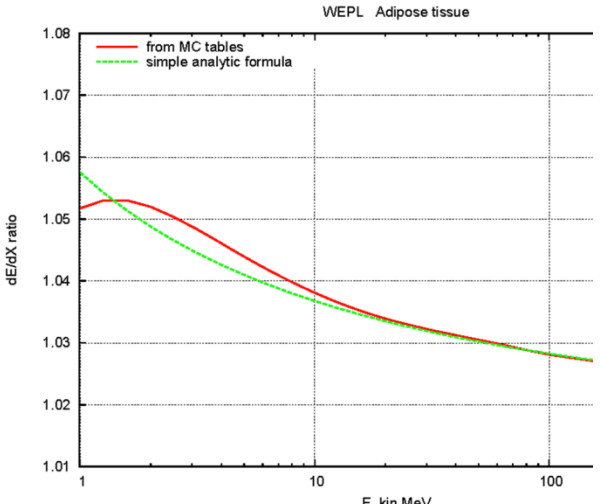
$$T_{\max} = \frac{2m_e c^2 \beta^2 \gamma^2}{1 + 2\gamma \frac{m_e}{M} + \left(\frac{m_e}{M}\right)^2}$$

$$\left\langle \frac{Z}{A} \right\rangle = \frac{1}{\rho_{tot}} \sum \rho_i \frac{Z_i}{A_i}$$

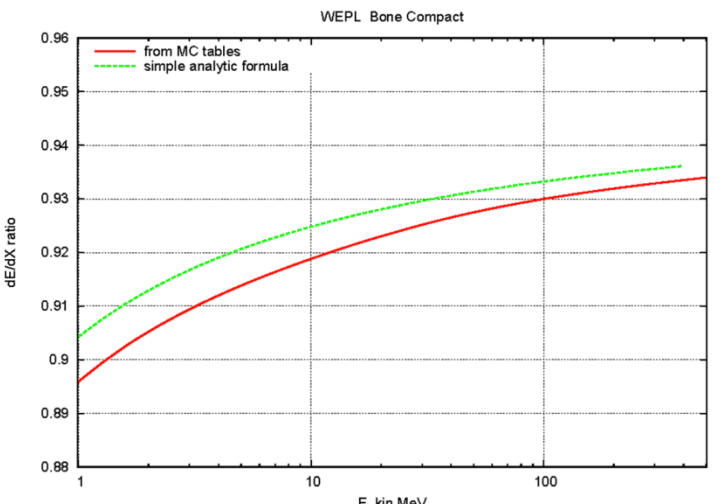
Muscle skeletal/Water



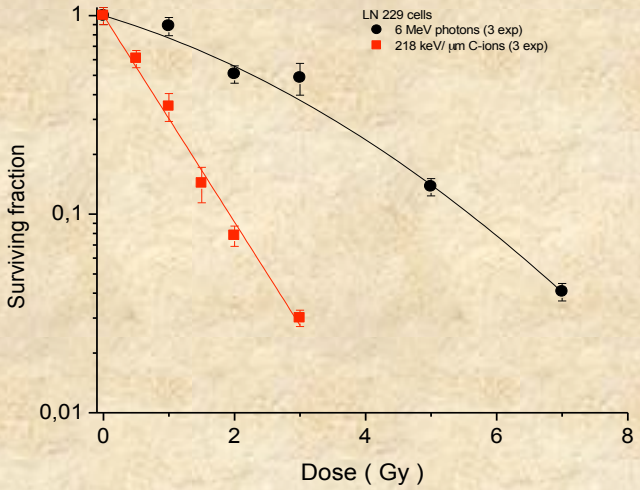
Adipose tissue/Water

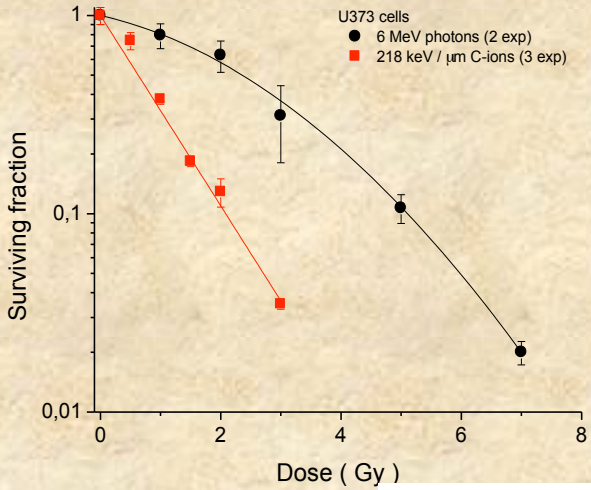


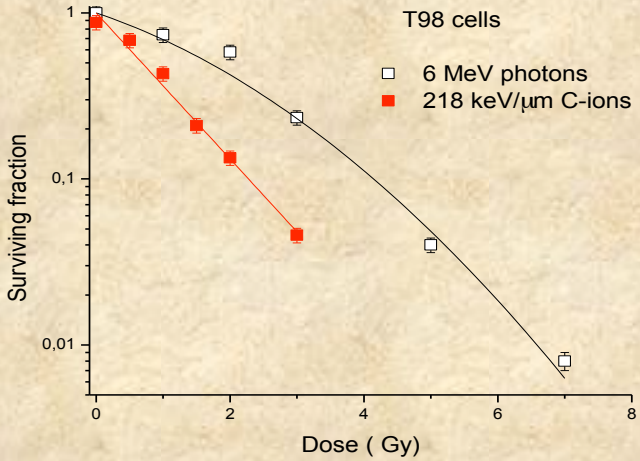
Bone Compact/water

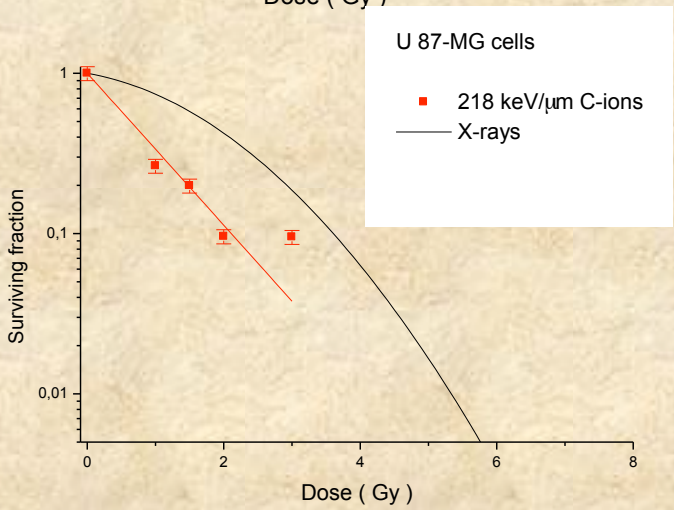


Dose-response of LN229, U373, T98G and U87-MG to 218 keV/μm C-ions and X-rays









From CT info to body materials

CT segmentation into 27 materials

Air, Lung, Adipose tissue

Soft tissue

Skeletal tissue

	w_i (pp)											
H	H	C	N	O	Na	Mg	P	S	Cl	Ar	K	Ca
−1000–−950			75.5	23.2						1.3		
−950–−120	10.3	10.5	3.1	74.9	0.2		0.2	0.3	0.3		0.2	
−120–−83	11.6	68.1	0.2	19.8	0.1			0.1	0.1			
−82–−53	11.3	56.7	0.9	30.8	0.1			0.1	0.1			
−52–−23	11.0	45.8	1.5	41.1	0.1		0.1	0.2	0.2			
−22–7	10.8	35.6	2.2	50.9			0.1	0.2	0.2			
8–18	10.6	28.4	2.6	57.8			0.1	0.2	0.2		0.1	
19–80	10.3	13.4	3.0	72.3	0.2		0.2	0.2	0.2		0.2	
80–120	9.4	20.7	6.2	62.2	0.6			0.6	0.3			
120–200	9.5	45.5	2.5	35.5	0.1		2.1	0.1	0.1		0.1	4.5
200–300	8.9	42.3	2.7	36.3	0.1		3.0	0.1	0.1		0.1	6.4
300–400	8.2	39.1	2.9	37.2	0.1		3.9	0.1	0.1		0.1	8.3
400–500	7.6	36.1	3.0	38.0	0.1	0.1	4.7	0.2	0.1			10.1
500–600	7.1	33.5	3.2	38.7	0.1	0.1	5.4	0.2				11.7
600–700	6.6	31.0	3.3	39.4	0.1	0.1	6.1	0.2				13.2
700–800	6.1	28.7	3.5	40.0	0.1	0.1	6.7	0.2				14.6
800–900	5.6	26.5	3.6	40.5	0.1	0.2	7.3	0.3				15.9
900–1000	5.2	24.6	3.7	41.1	0.1	0.2	7.8	0.3				17.0
1000–1100	4.9	22.7	3.8	41.6	0.1	0.2	8.3	0.3				18.1
1100–1200	4.5	21.0	3.9	42.0	0.1	0.2	8.8	0.3				19.2
1200–1300	4.2	19.4	4.0	42.5	0.1	0.2	9.2	0.3				20.1
1300–1400	3.9	17.9	4.1	42.9	0.1	0.2	9.6	0.3				21.0
1400–1500	3.6	16.5	4.2	43.2	0.1	0.2	10.0	0.3				21.9
1500–1600	3.4	15.5	4.2	43.5	0.1	0.2	10.3	0.3				22.5

Schneider et al PMB 45, 2000

Parodi et al, Med. Phys. 34, 2007