FLUKA FOR MEDICINE: Application to Cancer Therapy

Rationale for MC in radio- and particle-therapy

- In practice MC codes can be used for:
- startup and commissioning of new facilities
- study of detectors and accelerators
- beamline modeling and generation of TPS input data
- validate analytical TPSs in water/CT systems both for physical and <u>biological</u> aspects
- Prediction/Analysis of signals useful to check treatment (inbeam PET, gamma de-excitation, etc.)
- Biological calculations for cell survival experiments
- Additional advantage to describe complex geometries (and interfaces between rather different materials!):
- □ Accurate 3D transport
- Fully detailed description of the patient anatomy
 - → CT image converted into a MC geometry

Model challenge: interface to radiobiological model to predict "biological dose" (-actual effect) and not only physical dose

FLUKA applicazioni: IORT

First European Workshop on Monte Carlo Treatment Planning

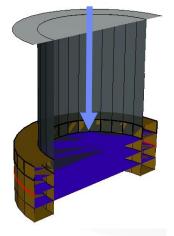
IOP Publishing

Journal of Physics: Conference Series 74 (2007) 012002

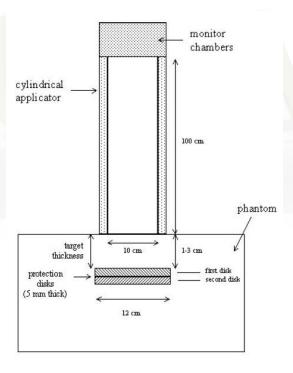
doi:10.1088/1742-6596/74/1/012002

Montecarlo simulation code in optimisation of the IntraOperative Radiation Therapy treatment with mobile dedicated accelerator

M Catalano^{1,2}, S Agosteo³, R Moretti¹, S Andreoli¹

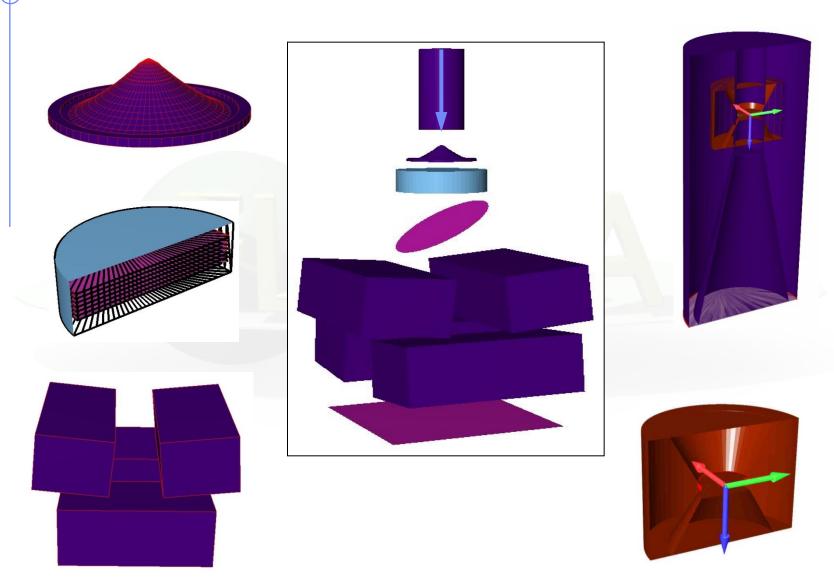




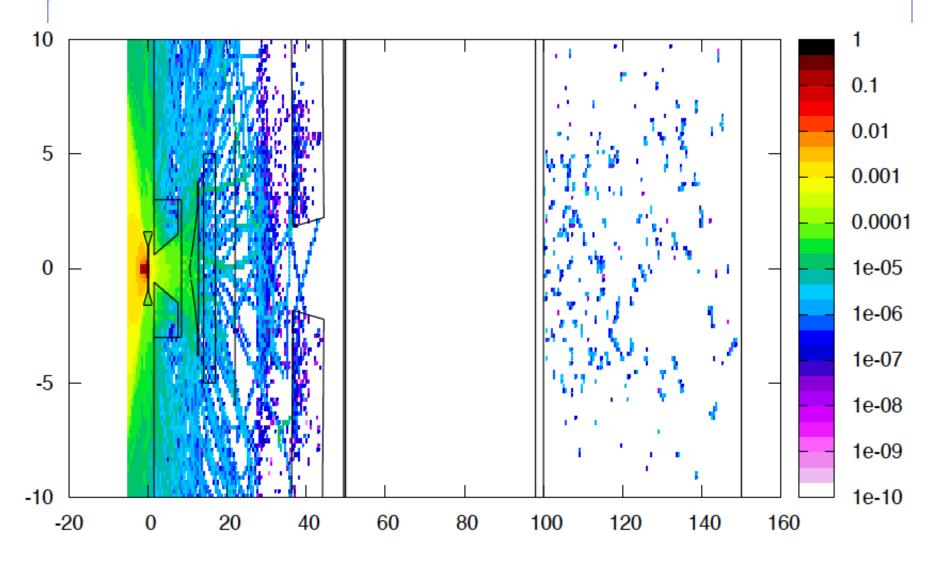




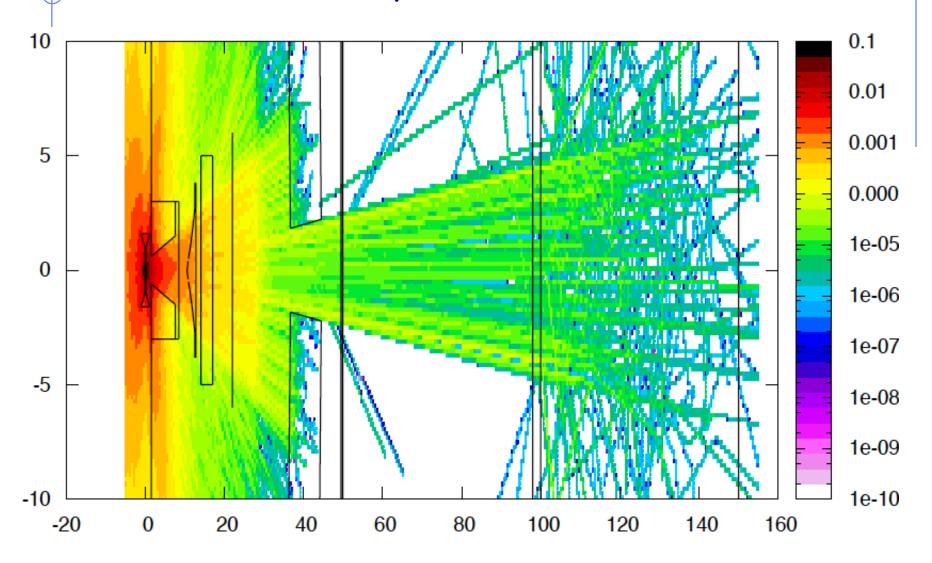
FLUKA Applications: Linac Head



6 MeV Accelerator - electron fluence distribution



6 MeV Accelerator -photon fluence distribution



6 MeV Accelerator

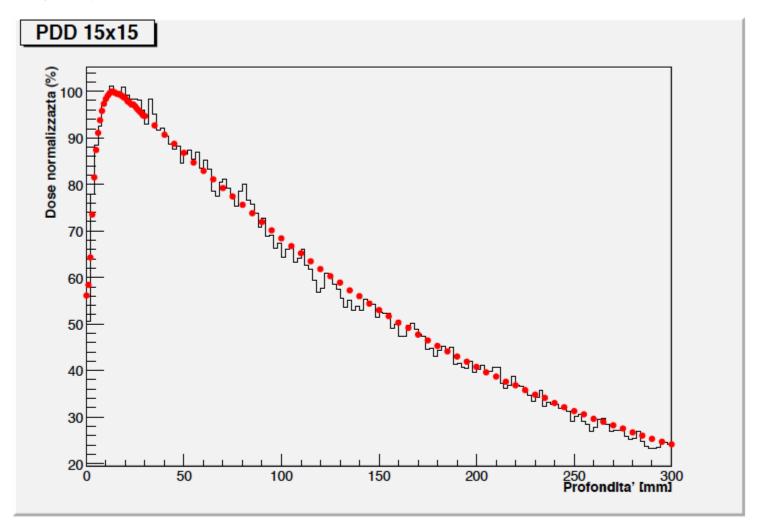


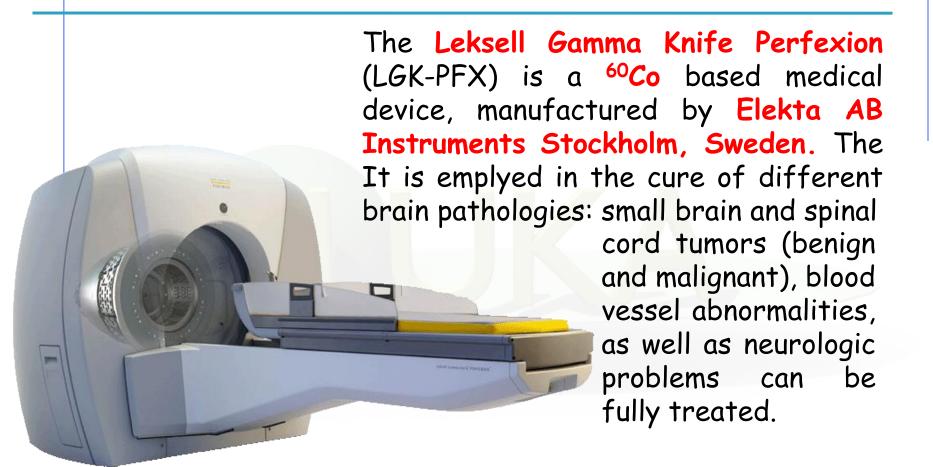
Figura 3.7: Curve di dose in profondità simulate con energia nominale pari a 6 MV; i pallini rossi sono le misure sperimentali e la linea nera rappresenta le simulazioni teoriche.





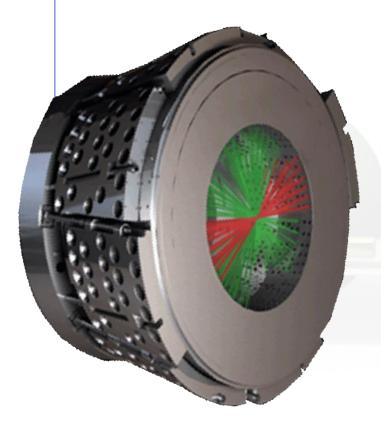
FLUKA MONTE CARLO SIMULATION FOR THE LEKSELL GAMMA KNIFE® PERFEXIONTM

The Leksell Gamma Knife Perfexion:



FLUKA Monte Carlo simulation for the Leksell Gamma Knife Perfexion System, *Homogeneous media*.

The Leksell Gamma Knife Perfexion:



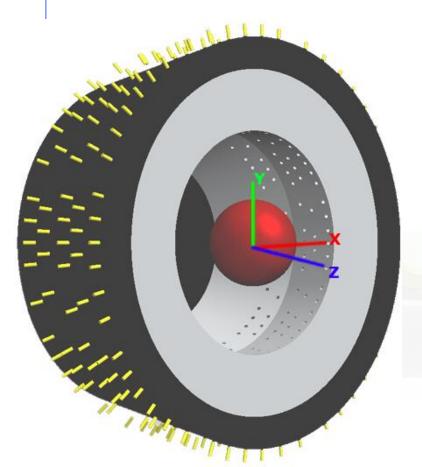
The ionizing gamma radiation is emitted from 192 60Co sources (average activity ~1TBq each).

The sources are arranged on 8 identical sectors of 24 elements.

The sectors can be placed in correspondence of three different collimation set able to focus the gamma rays on a common spot, called the isocenter of the field, having a radial dimension of about 4, 8 and 16 mm respectively.

FLUKA Monte Carlo simulation for the Leksell Gamma Knife Perfexion System, *Homogeneous media*.

FLUKA Geometry Modelization:

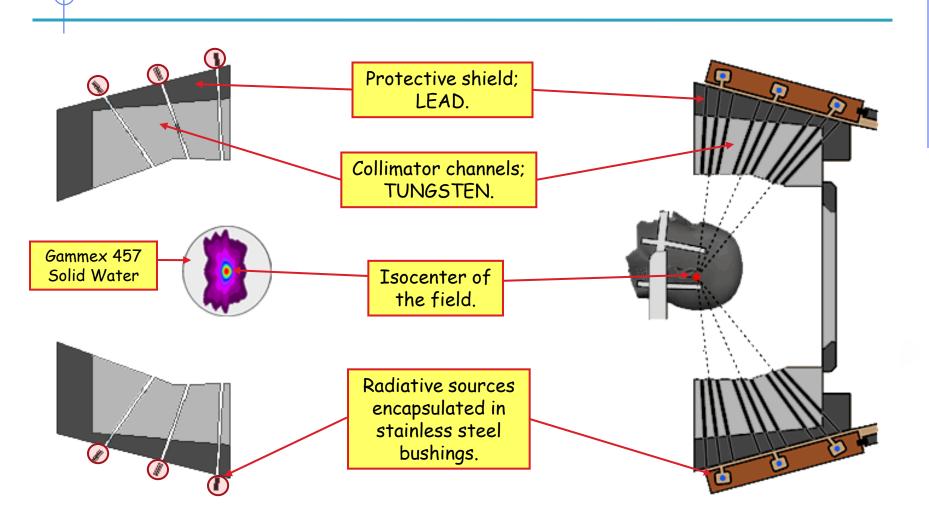


Thanks to the collaboration with ELEKTA, which provided, under a confidential agreement the detail of the geometry and all the involved material, has been possible to implement an accurate model for the radiation unit.



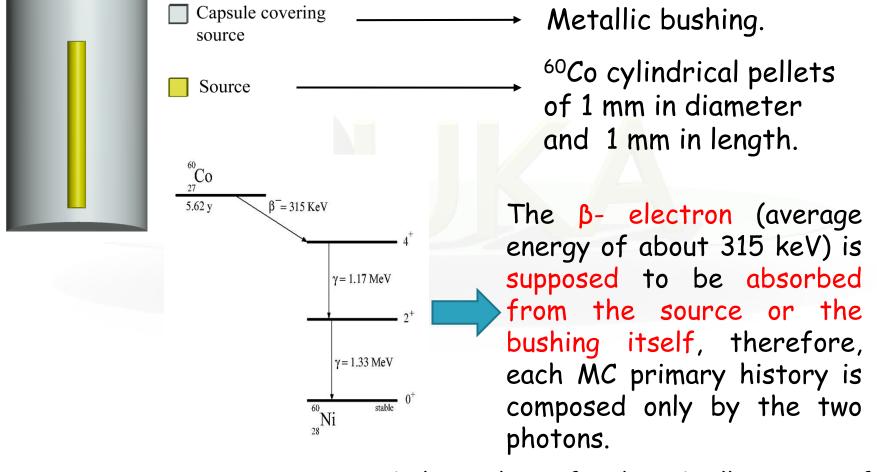
~ 1350 bodies

Geometry Modelization: Materials



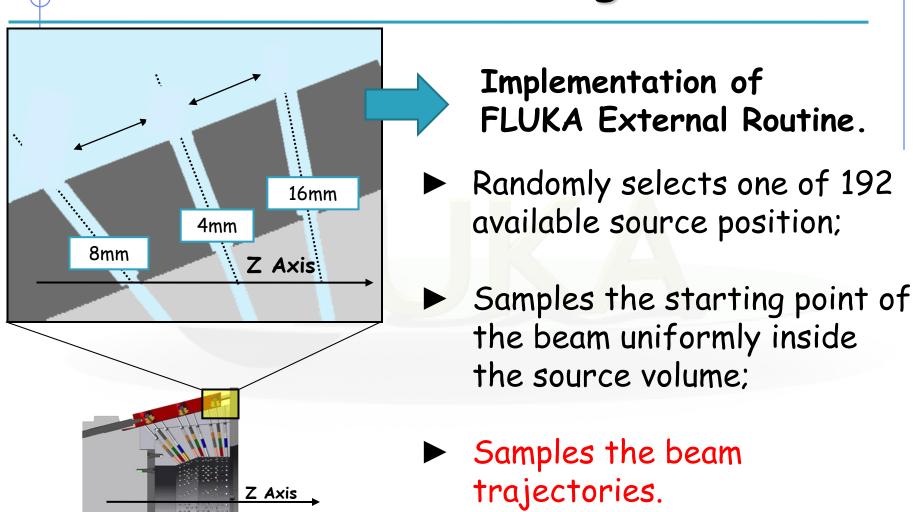
FLUKA Monte Carlo simulation for the Leksell Gamma Knife Perfexion System, *Homogeneous media*.

Source Modeling: Geometry and materials



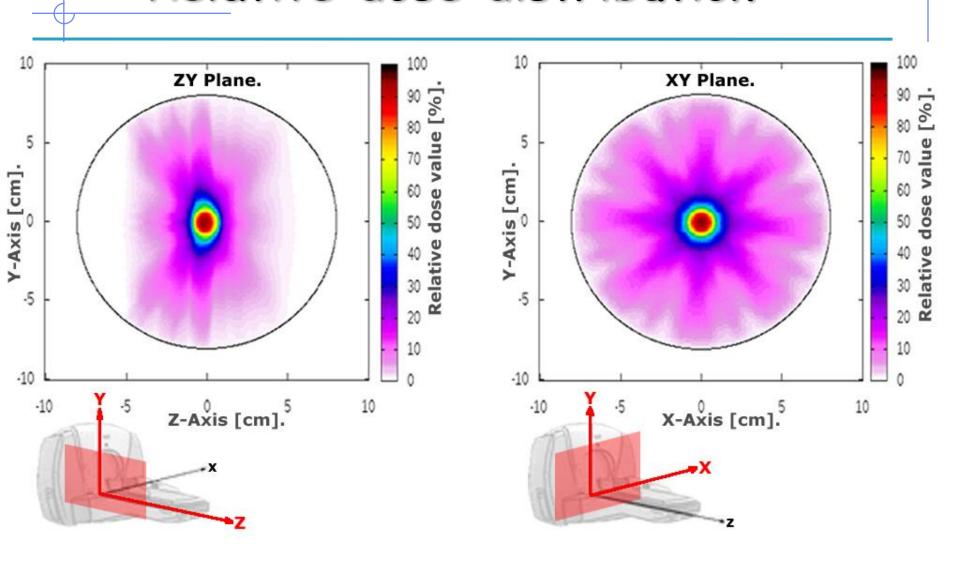
FLUKA Monte Carlo simulation for the Leksell Gamma Knife Perfexion System, *Homogeneous media*.

Source Modeling:



FLUKA Monte Carlo simulation for the Leksell Gamma Knife Perfexion System, *Homogeneous media*.

Relative dose distribution:



FLUKA Monte Carlo simulation for the Leksell Gamma Knife Perfexion System, *Homogeneous media*.

Results:

We have investigated the relative linear dose distribution along the three coordinated axes for each kind of collimator size and the Relative Output Factors (ROF).

Monte Carlo results have been compared with LGP data provided by Elekta in the same homogeneous conditions of the target.

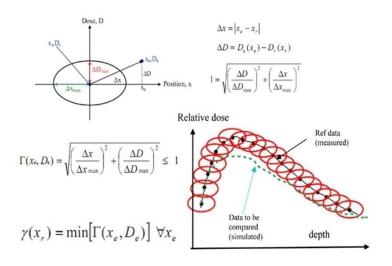
 $4 \cdot 10^9$ primary histories (total calculation time of about 20h on 26 nodes) have been performed for each simulation.

The simulations have been performed splitting the runs in a Macintosh cluster, made available by the Medical Physics department of Niguarda Ca'Granda Milan Hospital.

Relative dose profiles: quality index definition

The output data distributions of the FLUKA simulation have been smoothed by means of a linear interpolation (spline) with 2% of tolerance.

The quality index we used to perform the comparison is base on the Gamma Index (GI) method.



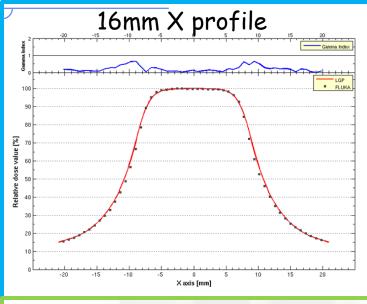
By definition, if GI>1 the test is not passed and the two distribution are not in agreement.

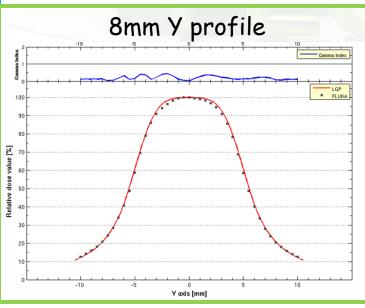
This index takes into account the relative shift both in terms of intensity and in terms of position, combining together the dose difference (DD) and the distance to agreement (DTA) methods.

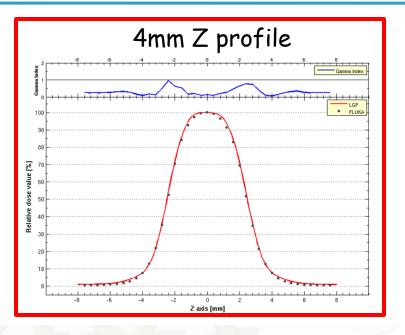
DD is the difference between the dose value in a measured data point and the dose value in a point of the calculated distribution which has the same coordinates.

DTA is the distance between a measured data point and the nearest point in the calculated dose distribution that has the same dose value.

Relative dose profile







The blue line represents the gamma index trend. It results < 1 for each simulated point, attesting the goodness of the FLUKA model.

The acceptance threshold values for DD and DTA are derived from the Report of the American Association of Physicists in Medicine for stereotactic radiosurgery, respectively as DD=3% and DTA=2.4 mm

Radioactive source decay

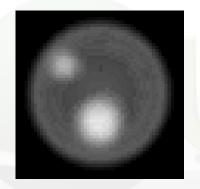
FLUKA contains data about decaying schemes of radioactive isotopes, allowing to select an isotope as radiation source. Complete databases are generated from the data collected from National Nuclear Data Center (NNDC) at Brookhaven National Laboratory. Routines are available to discriminate only a component of the emission spectrum, simulating for example only the beta emission and disregarding the gamma one.

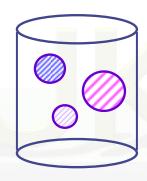
Application in nuclear medicine

Application in nuclear medicine

Calculation of absorbed dose at voxel level starting from 3D images of activity distribution (SPECT, PET images)

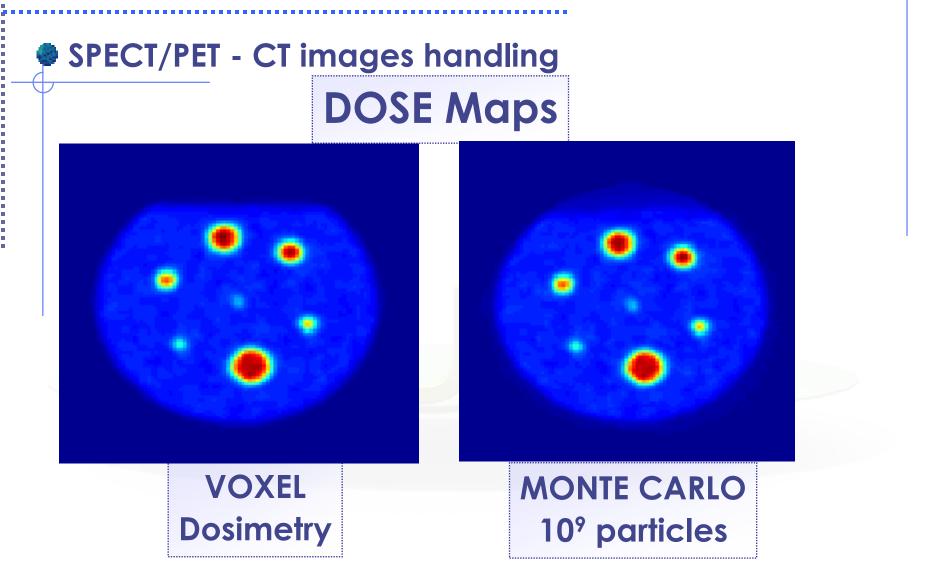
✓ Simulated ⁹⁹Tc-SPECT of water phantoms:





Collaboration INFN and IEO

✓ Dose calculation: Cylinder + spheres filled with ⁹⁰Y



With 10° particles simulated, FLUKA and VOXEL DOSIMETRY results in water agree within 5%

Rationale for MC in hadron-therapy

- Biological calculations in tumour therapy with ions depend on a precise description of the radiation field.
- In ¹²C ion irradiation, nuclear reactions cause a significant alteration of the radiation field.
- contribution of secondary fragments needs to be taken into account for accurate planning of the physical and biological dose delivery in the scheduled treatment.
- Treatment Planning Systems (TPS) for ion beam therapy essentially use analytical algorithms with input databases for the description of the ion interaction with matter.
- → Monte Carlo codes with sophisticated nuclear models are more efficient (<u>though slower</u>) computational tools to handle the mixed radiation field.

Nuclear reactions: what really matters?

- Proton therapy (p, E: 10-250 MeV):
 - > Reaction cross sections (beam attenuation) +++
 - Elastic cross sections +
 - Particle (p,n,a..) emission + (mostly for background, ++ radiobiology)
 - Positron emitter production + (data available)
- □ Therapy with ions (ions, E: 10-400 MeV/n):
 - Reaction cross sections (beam attenuation) +++
 - Fragment (a included) production +++
 - Particle emission, p +++, others +
 - ✓ Positron emitter production +++
- □ Conventional therapy (y, E: 3-30 MeV)
 - * (γ,x) (particularly (γ,n)) + (mostly for background)

Main FLUKA developments in view of medical applications (and hadron therapy in particular)

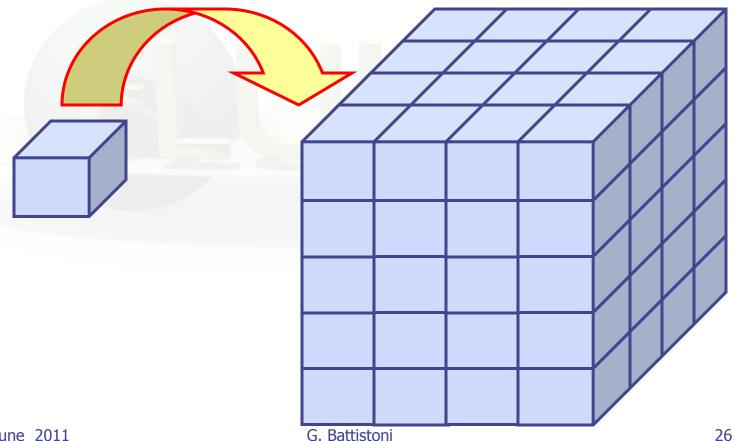
- Models for nucleus-nucleus interactions :
- Improvement of models for evaporation/fission/fragmentation used in fragment final de-excitation. Prediction of radionuclide production
- Improvement of dE/dx models (Z²+Z³ corrections, molecular effects, nuclear stopping power)
- Run time application of linear-quadratic models describing radiobiological effects
- Extensions and improvement of neutron library (thermal + ephithermal region)
- Voxel geometry
- Time-varying geometry
- Routines to import CT scans, material/density/composition assignment to CT

Main references to FLUKA in ion-therapy related matters:

- 1) F.Sommerer, K.Parodi, A.Ferrari, K.Poljanc, W.Enghardt and H.Aiginger, Investigating the accuracy of the FLUKA code for transport of therapeutic ion beams in matter, Phys. Med. Biol. 51 (2006) 4385–4398
- 2) K.Parodi, A.Ferrari, F.Sommerer and H.Paganetti, Clinical CT-based calculations of dose and positron emitter distributions in proton therapy using the FLUKA Monte Carlo code, Phys. Med. Biol. 52 (2007) 3369-3387
- 3) A. Mairani, Nucleus-Nucleus Interaction Modelling and Applications in Ion Therapy Treatment Planning, PhD Thesis, Univ. Pavia, 2007
- 4) G.B. et al. (FLUKA collaboration), The FLUKA code and its use in hadron therapy, Il Nuovo Cimento 31C, no. 1 (2008) 69.
- 5) F.Sommerer, F.Cerutti, K.Parodi, A.Ferrari, W.Enghardt and H.Aiginger, In-beam PET monitoring of mono-energetic 160 and 12C beams: experiments and FLUKA simulations for homogeneous targets, Phys. Med. Biol. 54 (2009) 3979-3996
- 6) A.Mairani, S.Brons, A.Fassò, A.Ferrari, M.Krämer, K.Parodi, M.Scholz and F. Sommerer, Monte Carlo based biological calculations in carbon ion therapy: the FLUKA code coupled with the Local Effect Model, submitted to PMB 2010

The FLUKA voxel geometry

 It is possible to describe a geometry in terms of "voxels", i.e., tiny parallelepipeds (all of equal size) forming a 3-dimensional grid



Voxel geometries: examples

The anthropomorphic GOLEM phantom



Implementation in FLUKA (radioprotection applications)

FLUKA golem section

100

80

40

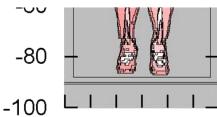
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-20

Now available the official ICRP Human Phantom
ICRP Publication 110: Adult Reference Computational Phantoms - Annals
of the ICPR Volume 39 Issue 2



Petoussi-Henss et al, 2002



G. Battistoni

The FLUKA voxel geometry

• The CT scan contains integer values "Hounsfield Unit" reflecting the X-ray attenuation coefficient μ_{x}

$$HU_x = 1000 \; (\mu_x - \mu_{H20}) \; / \; \mu_{H20} \; , \; \; typically \; -1000 \leq HU \leq 3500 \; .$$

- We will use loosely the word "organ" to indicate a group of voxels (or even more than one group) made of the same "tissue" material (same HU value or in a given HU interval)
- The code handles each organ as a CG region, possibly in addition to other conventional "non-voxel" regions defined by the user
- The voxel structure can be complemented by parts written in the standard Combinatorial geometry
- The code assumes that the voxel structure is contained in a parallelepiped. This RPP is automatically generated from the voxel information.
- To describe a voxel geometry, the user provides the CT scan or equivalent data in a format understood by FLUKA by means of an external conversion program

CT stoichiometric calibration (I)

CT segmentation into 27 materials of defined elemental composition (from analysis of 71 human CT scans)

Air, Lung,
Adipose tissue

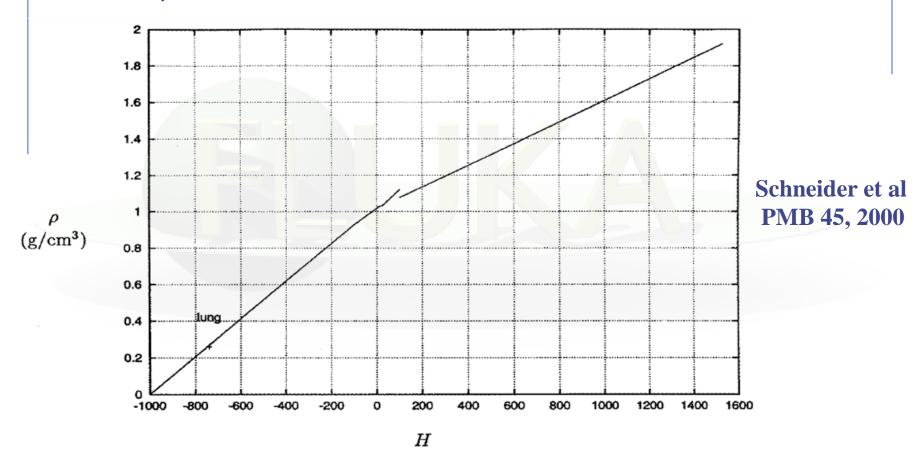
Soft tissue

Skeletal tissue

Н	$w_i(pp)$											
	Н	С	N	0	Na	Mg	P	S	C1	Ar	K	Ca
-1000950			75.5	23.2						1.3		
-950120	10.3	10.5	3.1	74.9	0.2		0.2	0.3	0.3		0.2	
-12083	11.6	68.1	0.2	19.8	0.1			0.1	0.1			
-8253	11.3	56.7	0.9	30.8	0.1			0.1	0.1			
-5223	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

CT stoichiometric calibration (II)

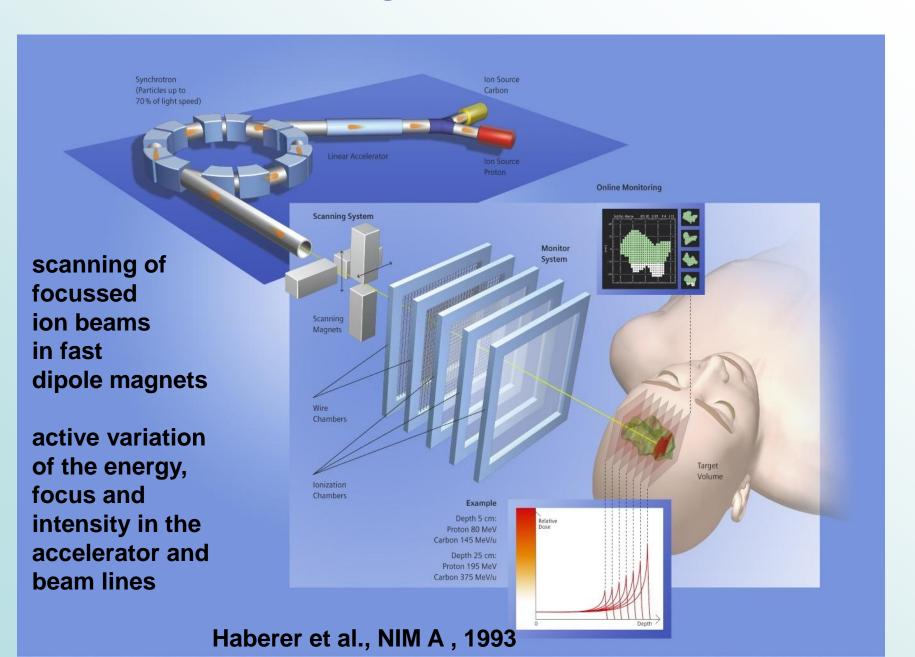
Assign to each material a "nominal mean density", e.g. using the density at the center of each HU interval (Jiang et al, MP 2004)



But "real density" (and related physical quantities)

Alghwanies a continuously with ship towalue!!!

Rasterscan Method @ GSI / HIT



MC for the Heidelberg Ion Therapy Center (HIT)

Ion species

p, ¹²C
 (later also ³He, ¹6O)

Beam delivery

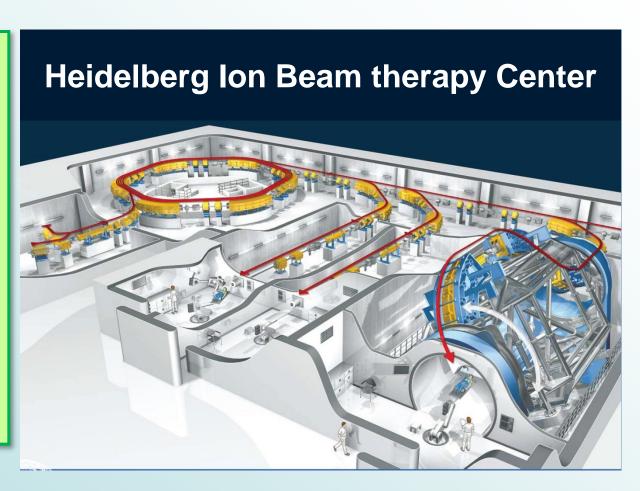
➤ Scanning with active energy variation (like @ GSI)

➤ Required parameters:

255 Energy steps

4 Foci

10 Intensities



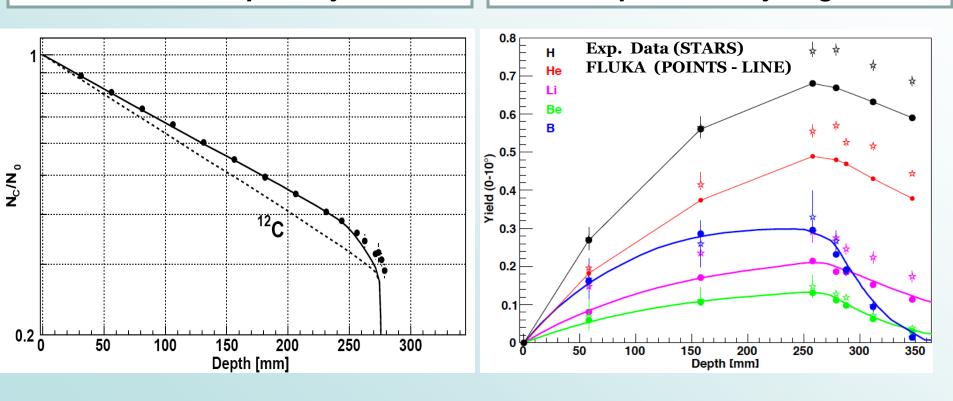
Start of clinical operation: November 2009

Mixed Radiation Field in Carbon Ion Therapy

¹²C (400 MeV/u) on water



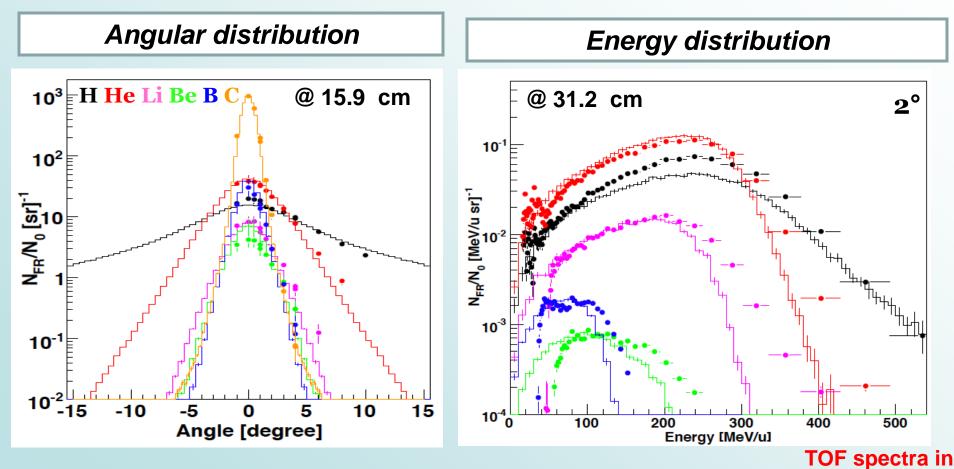
Build-up secondary fragments



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

Mixed Radiation Field in Carbon Ion Therapy

¹²C (400 MeV/u) on water



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

progress

The role of MC in ion therapy

Treatment planning systems (TPS) use analytical models

MC are increasingly used computational tools to support:

Validation of TPS absorbed and biological dose calculations: in water-equivalent system and in patient anatomy (CT)

Dedicated applications: imaging of secondary emerging radiation for treatment verification, like PET monitoring of ion therapy

MC for the Heidelberg Ion Therapy Center (HIT)

Ion species

p, ¹²C
 (later also ³He, ¹6O)

Beam delivery

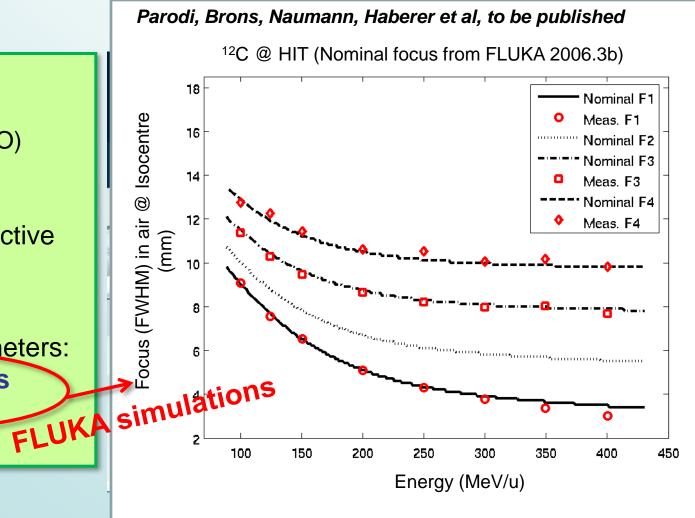
Scanning with active energy variation (like @ GSI)

> Required parameters:

255 Energy steps

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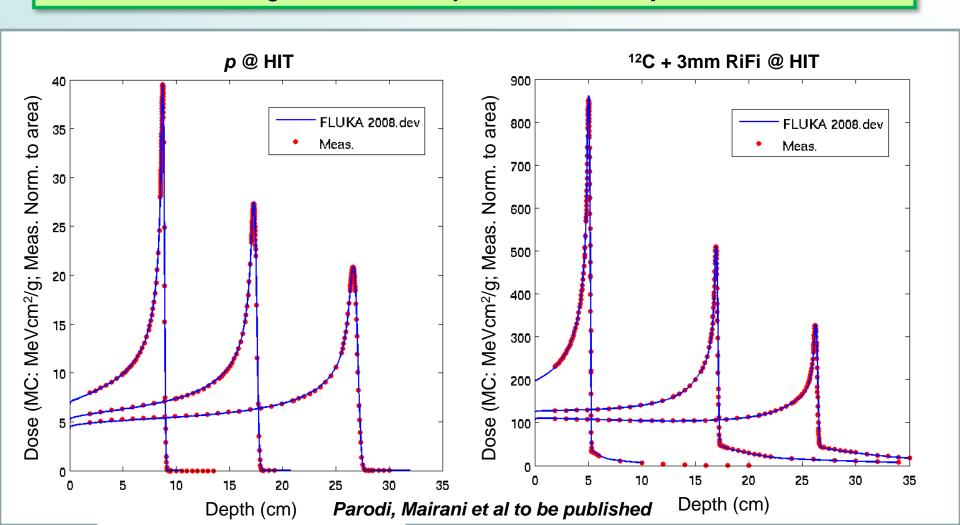
10 Intensities



...Taking into account desired 4-10 mm focus @ ISO for higher E and physical limitation from scattering in monitor system and air

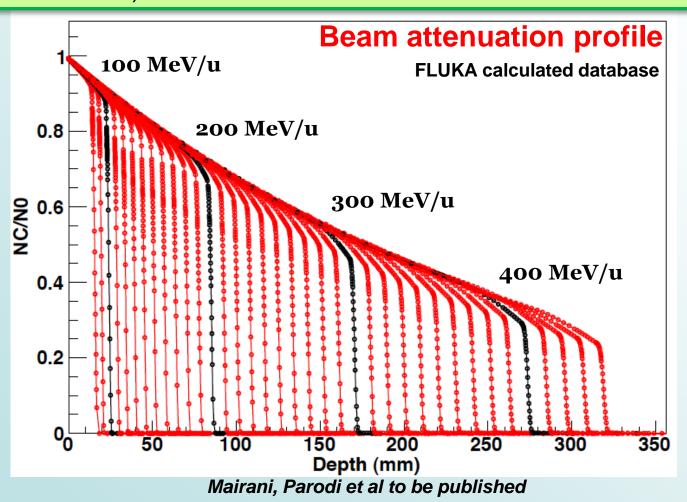
Generation of basic input data for TPS – depth dose profiles

FLUKA calculation of depth-dose profiles in water w/wo ripple filter (RiFi) for all the 255 energies delivered by accelerator for p and ¹²C



Generation of basic input data for TPS – Fragment Spectra

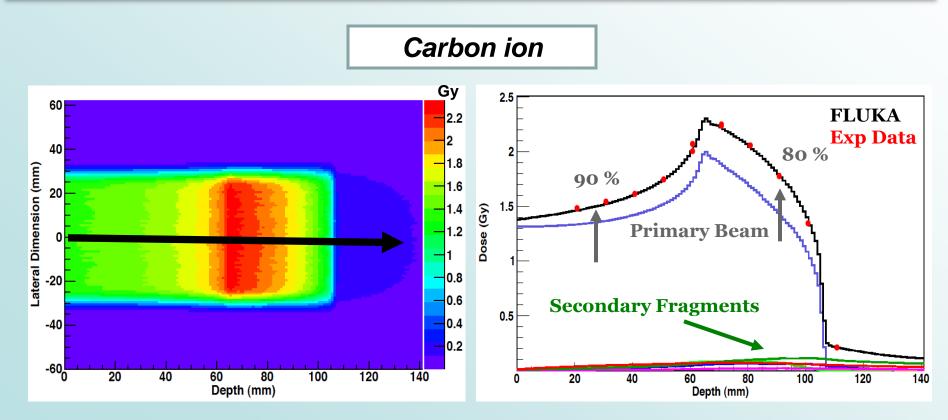
FLUKA calculation of fragment spectra in water w/wo ripple filter (RiFi) for ¹²**C** (80 – 440 MeV/u)



Forward recalculation of TPS treatment plans in water

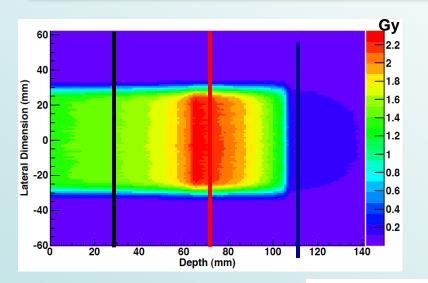
(i.e. medium where plans are experimentally verified)
FLUKA coupled with control file of raster scanning system + modeling of the beam-line

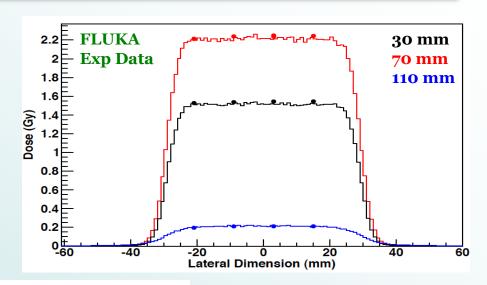
(F. Sommerer et al, EWG-MCTP Workshop, Ghent 2006, A. Mairani et al to be submitted)



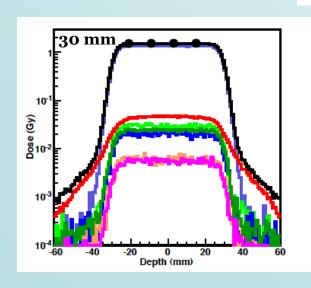
Mairani, Parodi et al to be published

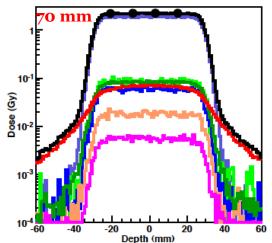
Forward recalculation of TPS treatment plans in water

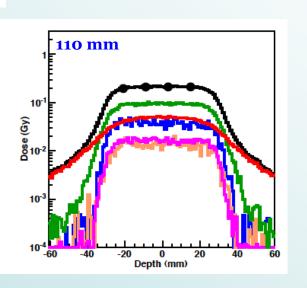




Primary Beam H He Li Be B C

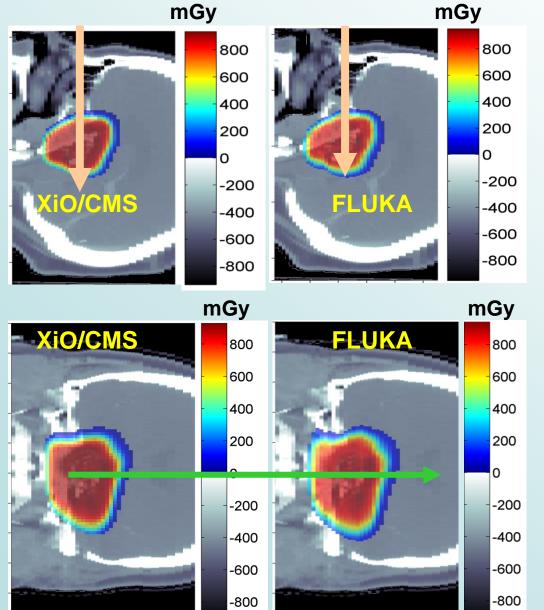


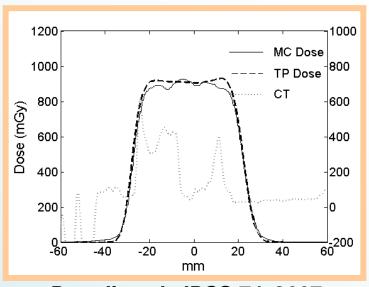




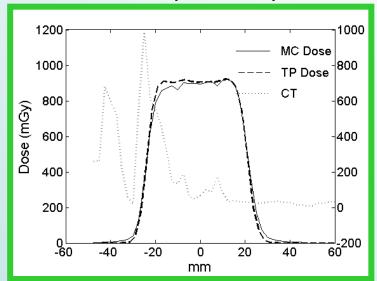
MC versus TPS for proton therapy @ MGH

Clivus Chordoma Patient



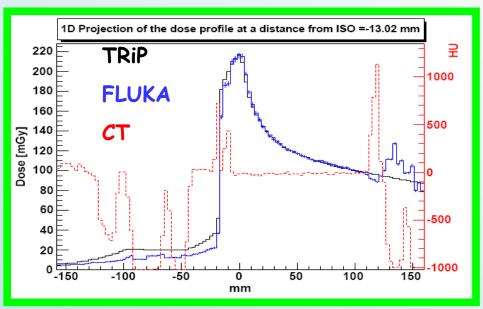


Parodi et al, JPCS 74, 2007



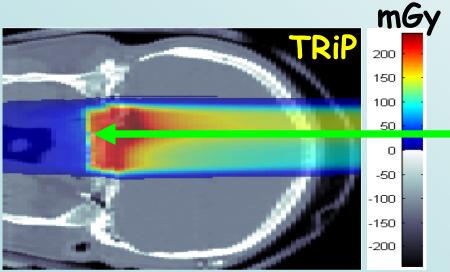
MC versus TPS for carbon ion therapy @ GSI

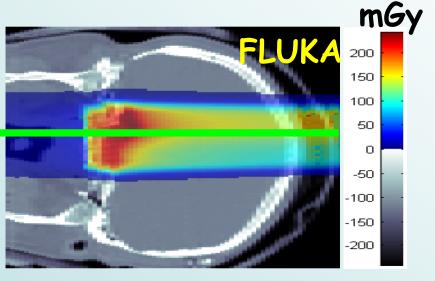
Clivus Chordoma Patient - Absorbed Dose



Absorbed Dose Spread-Out Bragg Peak in the patient

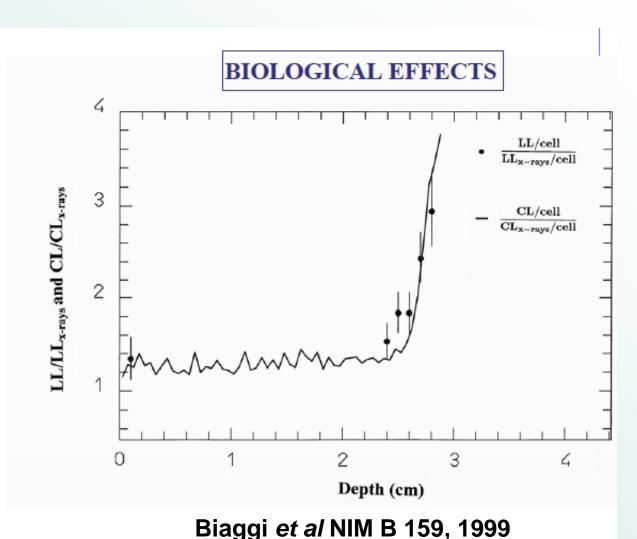
- A. Mairani PhD thesis 2007, Pavia
- A. Mairani et al IEEE 2008

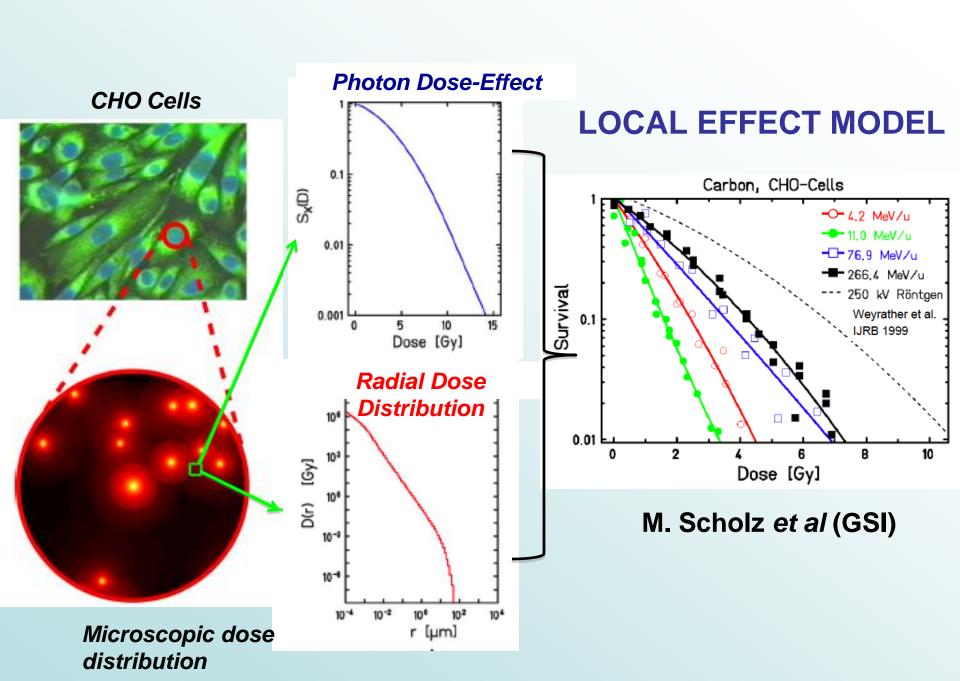




Biological MC calculations: FLUKA coupled with external bio database

- PSI therapy unit: 72 MeV proton beam
- Assumption: clustered DNA damage is an estimator of cell inactivation
- Combined physicalbiological simulation of the OPTIS beam
- No free parameter nor "a posteriori" fit to experimental data
- Results directly compared to measurements of physical dose and cell survival





Biological MC calculations: FLUKA coupled with the Local Effect Model

Starting from the intrinsic LEM coefficients, the α_D and β_D parameters are obtained in terms of macroscopic dose applying the "rapid approach" described in :

PMB 51 (2006) 1959 M. Krämer and M. Scholz

The coupling of the LEM with FLUKA has been carried out using the Theory of Dual Radiation Action (TDRA) (A. M. Kellerer and H. H. Rossi, Radiat. Res. 75 (1978) 471):

❖a biological system exposed to more than one radiation type will show synergism, implying that the total number of lesions is larger than the sum of the lesions produced by each single beam component, due to interactions between sub-lesions produced by different components.

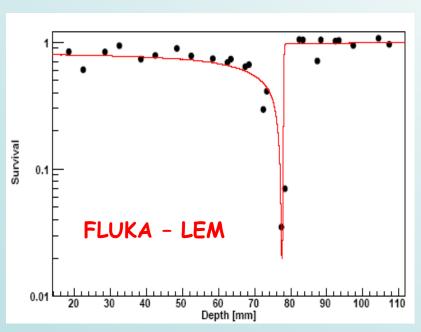
A. Mairani et al, IEEE 2008 and PMB 2010

Biological MC calculations: comparison with experimental data and analytical calculations

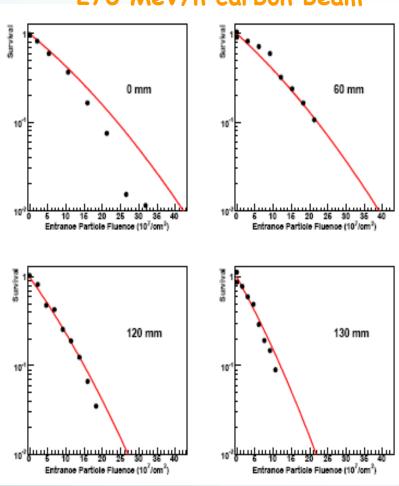
Benchmark in water (A. Mairani PhD Thesis 2007):

270 MeV/n carbon beam

187 MeV/n carbon beam



Exp. data (points) courtesy of M. Scholz (GSI) Radiat. Environ. Biophys. 36 (1997) 59



Exp. data (points) courtesy of M. Scholz (GSI) Radiat. Environ. Biophys. 36 (1997) 59

INPUT Physical Database I (CNAO)

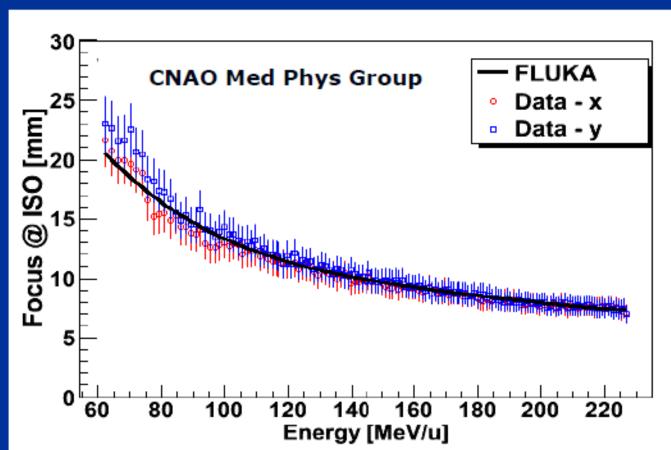
Beam delivery

Required parameters

Scanning with active energy variation

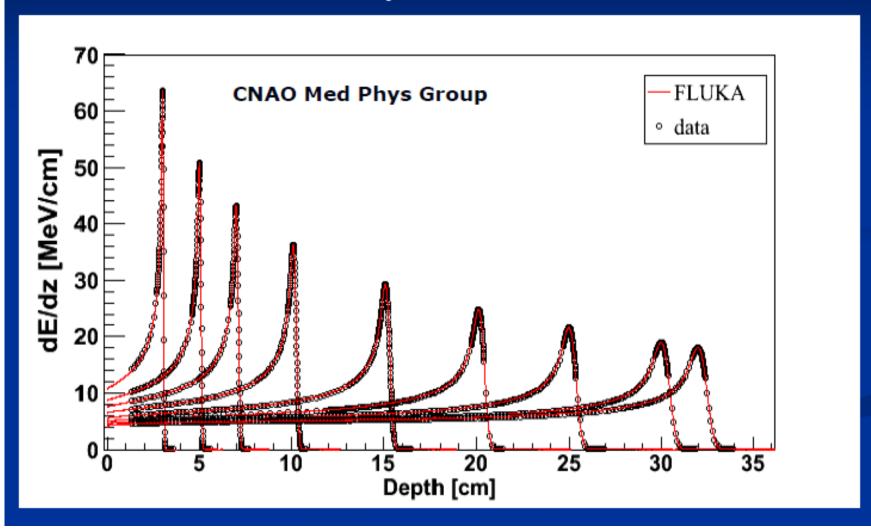
- 147 Energy steps (30-320 mm)
- 1 Focus size @ ISO

FLUKA calculated FWHM at the isocentre as function of the proton beam energy



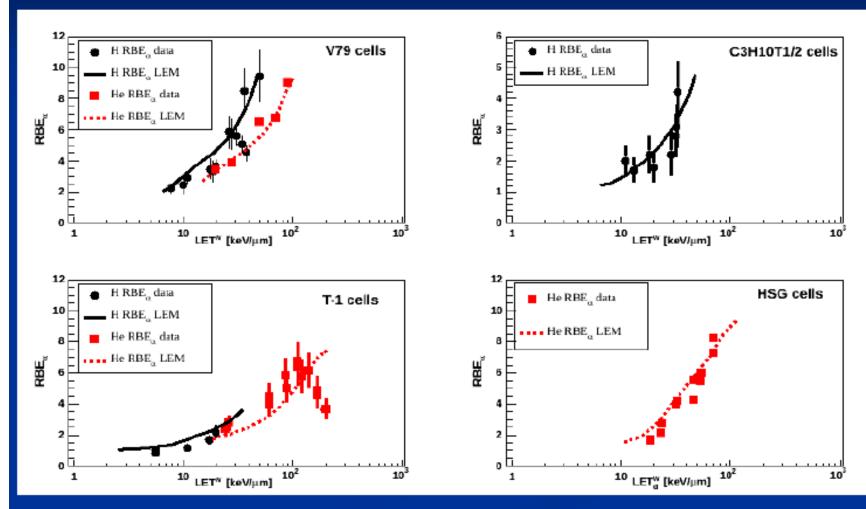
INPUT Physical Database II (CNAO)

FLUKA calculated depth-dose distribution in water



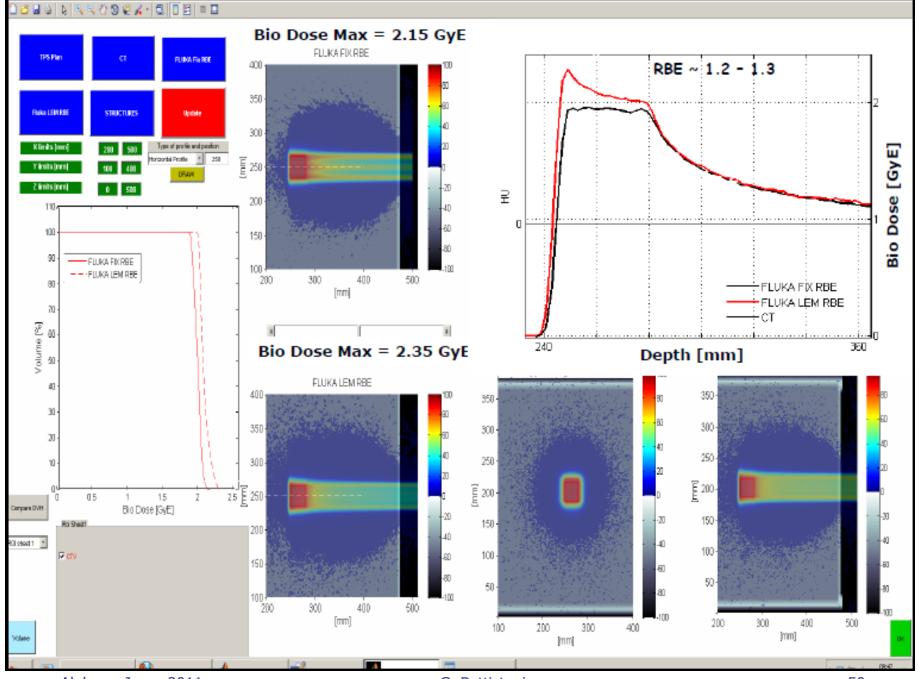
INPUT Biological Database (LEM)

LEM*** calculated initial Relative Biological Effectiveness (RBE_a)

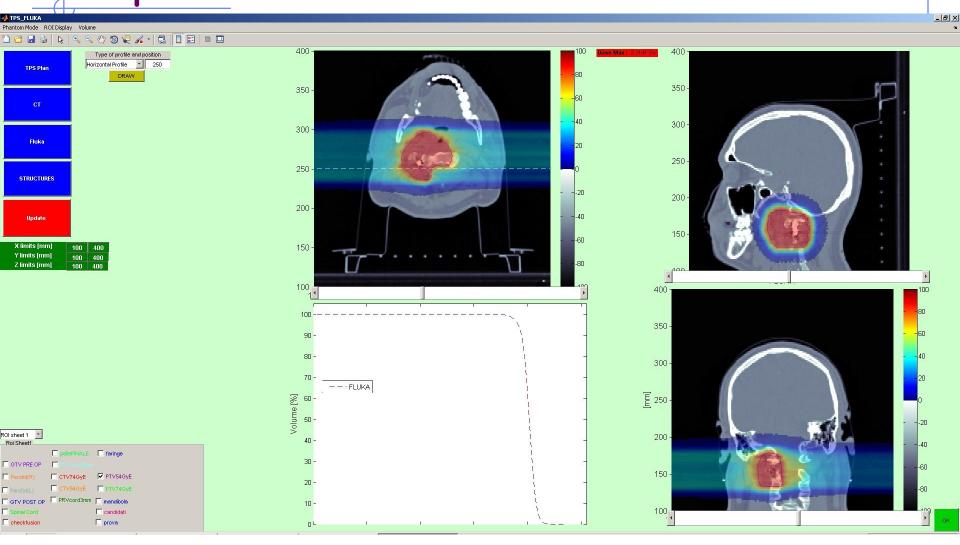


***HIT re-implementation of LEM IV version published in Elsässer et al Int. J. Rad. Oncol. Biol. Phys. 2010

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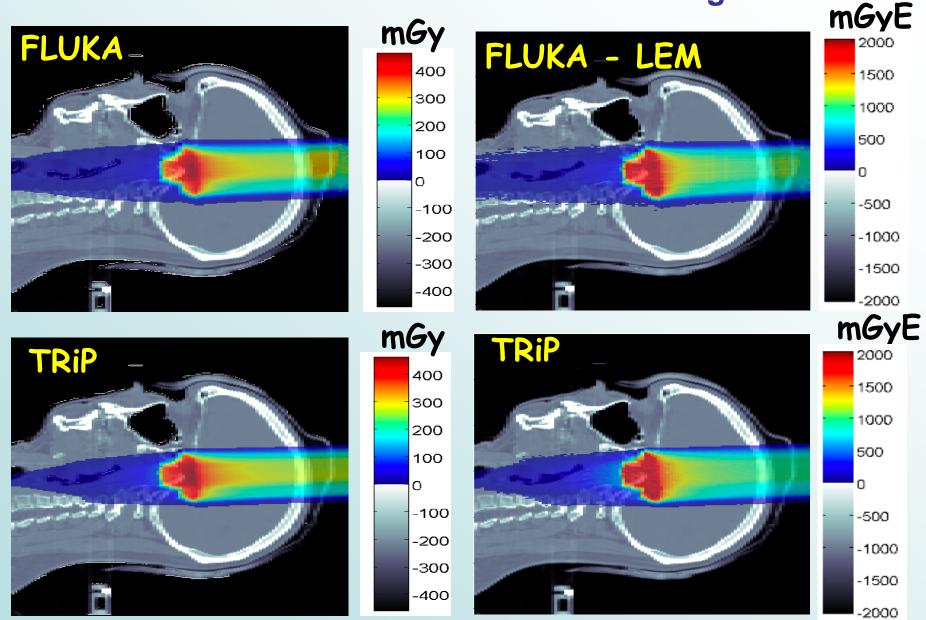


A patient case at CNAO



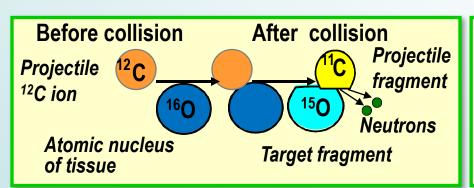
MC versus TPS for carbon ion therapy @ GSI

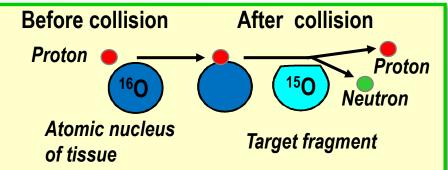
Clivus Chordoma Patient – Absorbed/Biological Dose

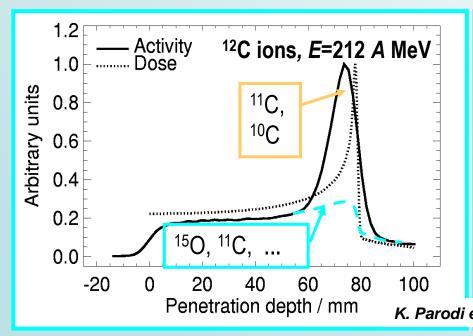


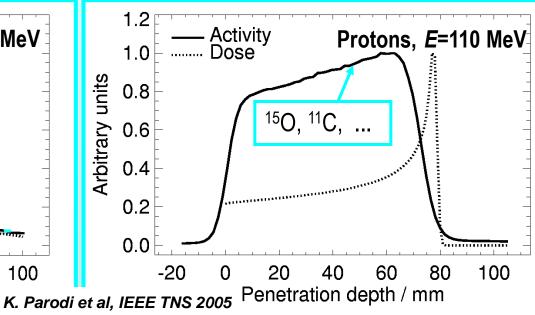
A. Mairani et al, to be published

The principle of PET verification







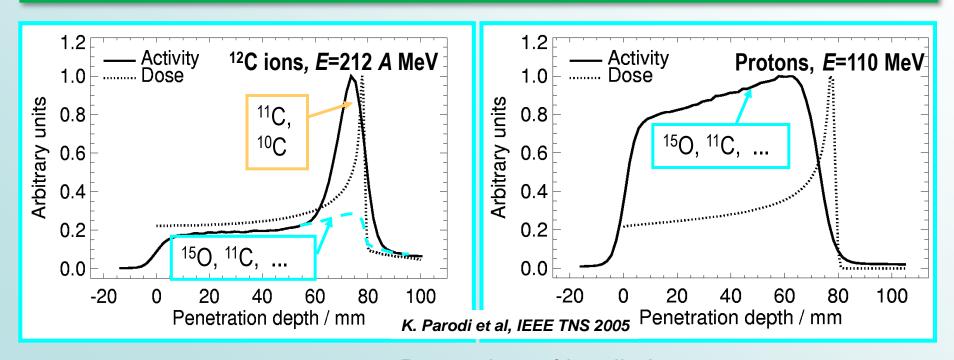


By-product of irradiation (15O, 11C, 13N...with $T_{1/2} \sim 2$, 20 and 10 min)

The principle of PET verification

$$A(r) \neq D(r)$$

→ Measured activity compared with calculation

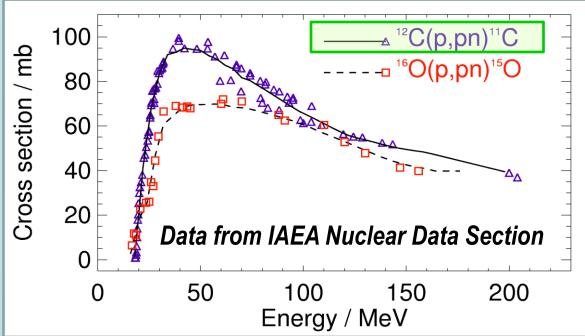


By-product of irradiation (15O, 11C, 13N...with $T_{1/2} \sim 2$, 20 and 10 min)

Calculation model of β+-activation

FLUKA Monte Carlo code using

- Field-specific beam source information from Geant4 modeling of the nozzle and beam modifiers (Paganetti et al, MP 31, 2004)
- Planning CT (segmented into 27 material) and same CT-range calibration curve as TPS (Parodi et al MP 34, 2007, PMB 52, 2007)
- Experimental cross-sections for β*-emitter production
- Semi-empirical biological modeling (Parodi et al IJROBP 2007)
- Convolution with 3D Gaussian kernel (7-7.5 mm FWHM)



...and other reaction channels on N, O, Ca yielding, e.g., ¹³N, ³⁸K, ...

(Parodi et al, PMB 45, 2002, Parodi et al, PMB 52, 2007)

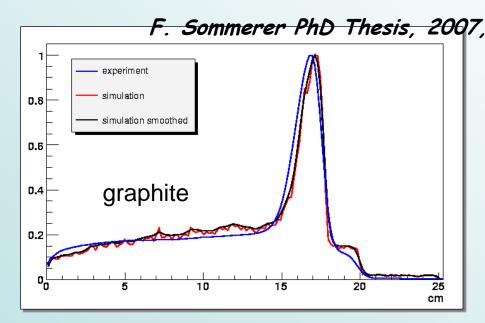
In-beam PET: ion beam fragmentation

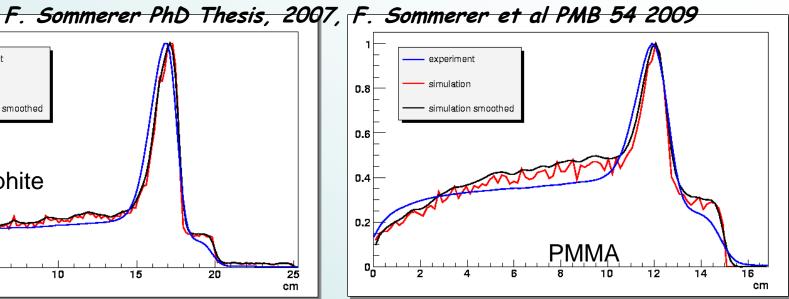
- Final goal: simulation of β⁺ emitters generated during the irradiation
- In-beam treatment plan verification with PET

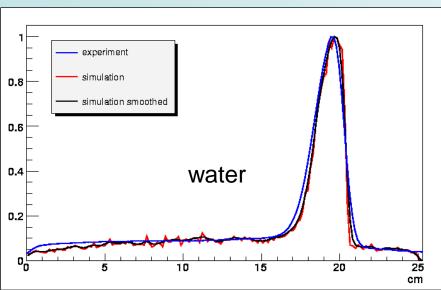
Work in progress: FLUKA validation

- Comparison with experimental data on fragment production (Schall et al.)
 - ¹²C, ¹⁴N, ¹⁶O beams, 675 MeV/A
 - Adjustable water column 0-25.5 cm
 - Z spectra of escaping fragments for Z>4
 - Cumulative yield of light fragments
 - Simulation: corrections applied for angular acceptance and for material in the beam upstream the water target
- Comparison with experimental data on β^+ -emitter production (Fiedler et. al.)

β*-Activity after Irradiation







Measured 10 - 20 min after irradiation. therefore dominated by 11C

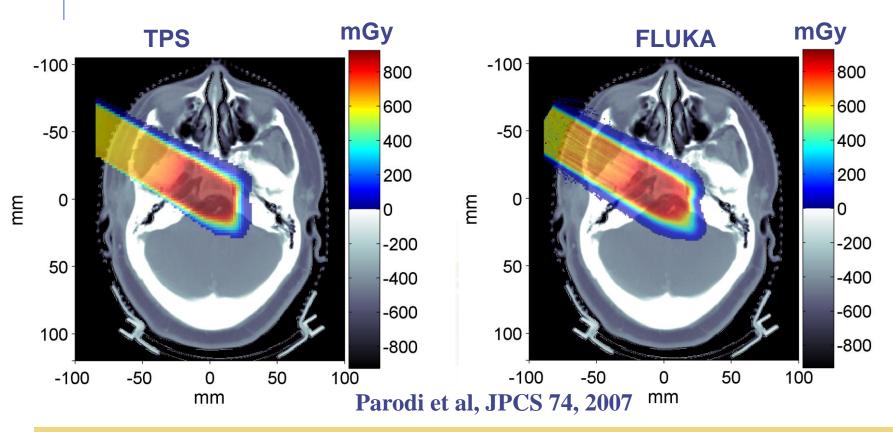
Further work:
• processing with same software than experiment
• more primaries for better statistic

Final results are expected for the end of this year

G. Battistoni

Applications of FLUKA to p therapy @ MGH

Input phase-space provided by H. Paganetti, MGH Boston



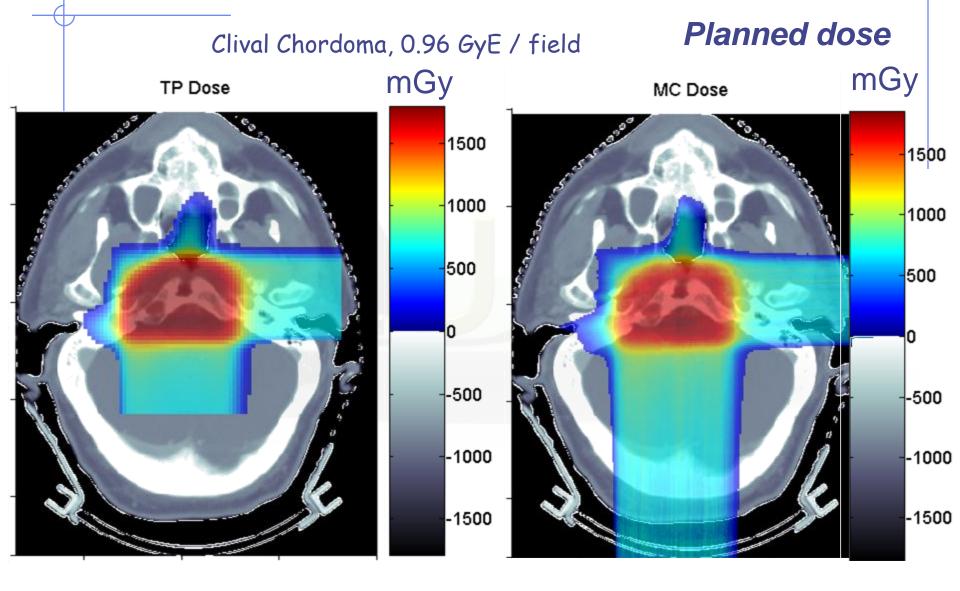
Prescribed dose: 1 GyE

 $MC: \sim 5.5 \cdot 10^6$ protons in 10 independent runs

(11h each on Linux Cluster mostly using 2.2GHz Athlon processors)

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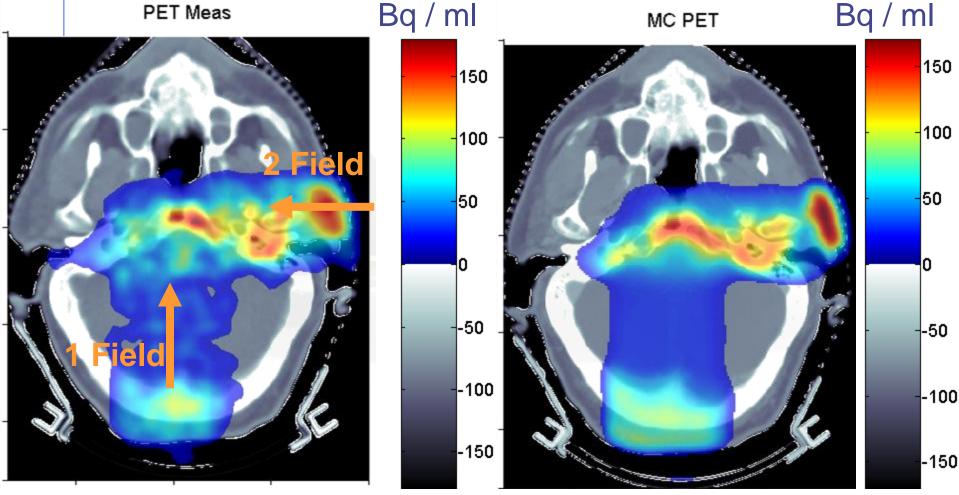
Applications of FLUKA to p therapy @ MGH



Post-radiation PET/CT @ MGH

Average Activity

Clival Chordoma, 0.96 GyE / field, $\Delta T1 \sim 26 \text{ min}$, $\Delta T2 \sim 16 \text{ min}$



K. Parodi et al, IJROBP 2007

... and FLUKA-voxel functionalities being also used at HIT ...

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Gamma De-excitation in Fluka

- At the end of evaporation : cascade of γ transitions
- At high excitation: assume continuous level density and statistical emission:

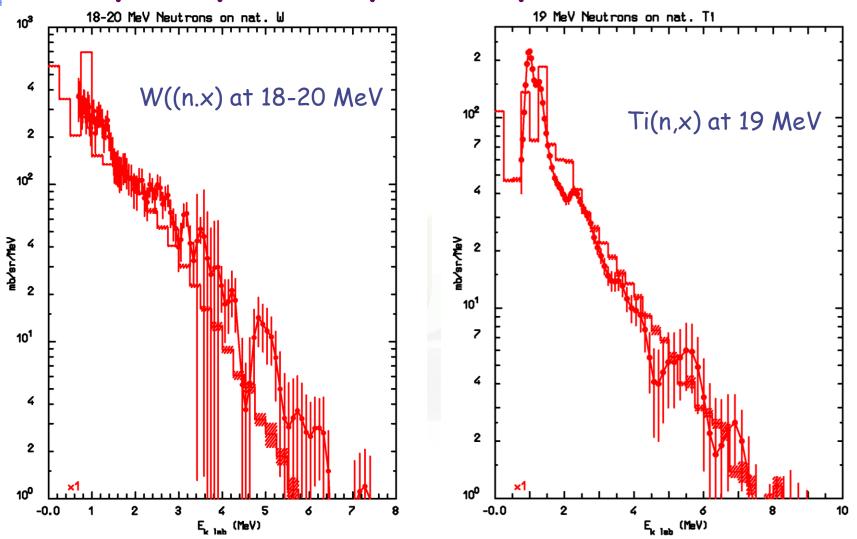
$$P(E_{\gamma})dE_{\gamma} = \frac{\rho_f(U_f)}{\rho_i(U_i)} \sum_{L} f(E_{\gamma}, L)$$
L= multipole order pelevel density at excitation energy. U

f = strength from single $f(E_{\gamma},L) = c_L F_L(A) E_{\gamma}^{(2L+1)}$ particle estimate (c)+ hindrance (F)

- At low excitation: through discrete levels
 - Tabulated experimental levels (partial coverage)
 - Rotational approximation outside tabulations

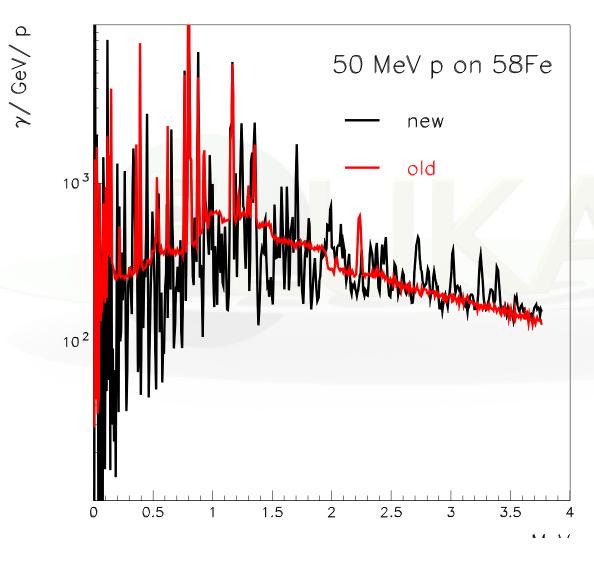
See A. Ferrari et al., Z. Phys C 71, 75 (1996)

Examples: photon spectra, pre-2011 status



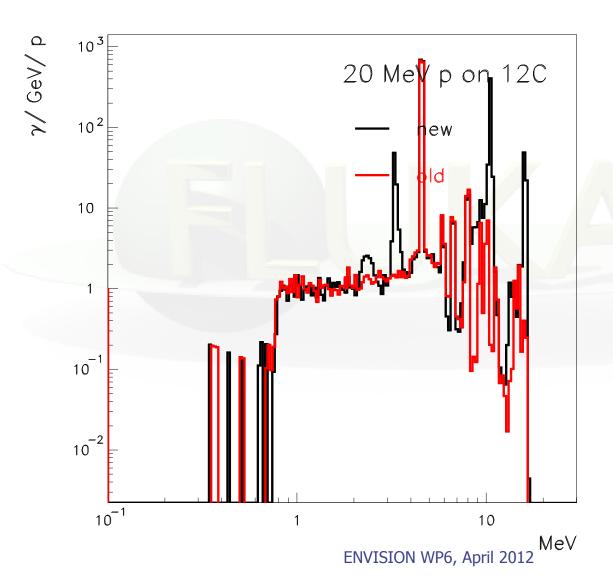
Histograms: FLUKA results with stat errors. Dots: expt data from Dickens et al. report ORNL-4847 (1973) and G.L.Morgan, report ORNL-5563 (1979) 62

Improved model: example



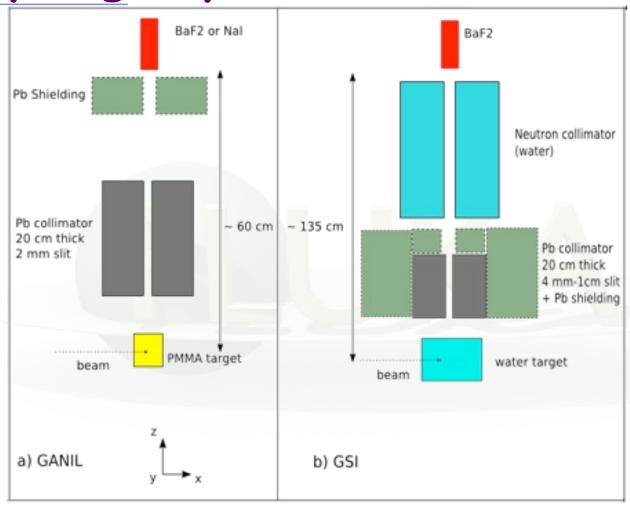
Overall shape Unchanged More details

Improved model: example 2



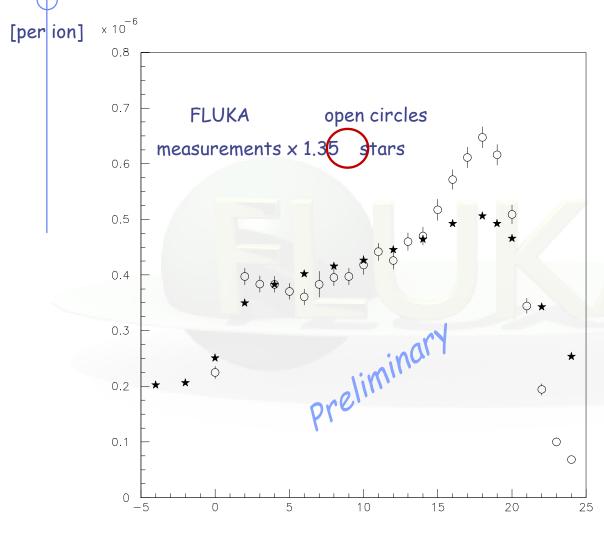
Overall shape
Unchanged
More details are evident

Lyon group: GANIL/GSI data



[figures and exp. data taken from F. Le Foulher et al IEEE TNS 57 (2009), E. Testa et al, NIMB 267 (2009) 993]

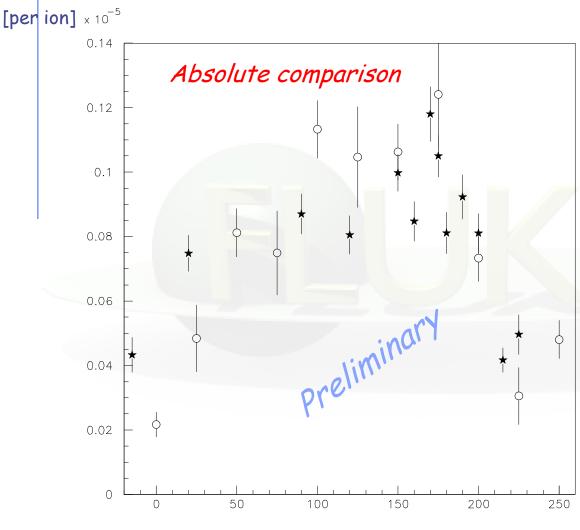
GANIL: 90 deg photon yields by 95 MeV/n 12C in PMMA



95 MeV/n ¹²C ions on a PMMA target Photons at 90 deg

Longitudinal position [mm]

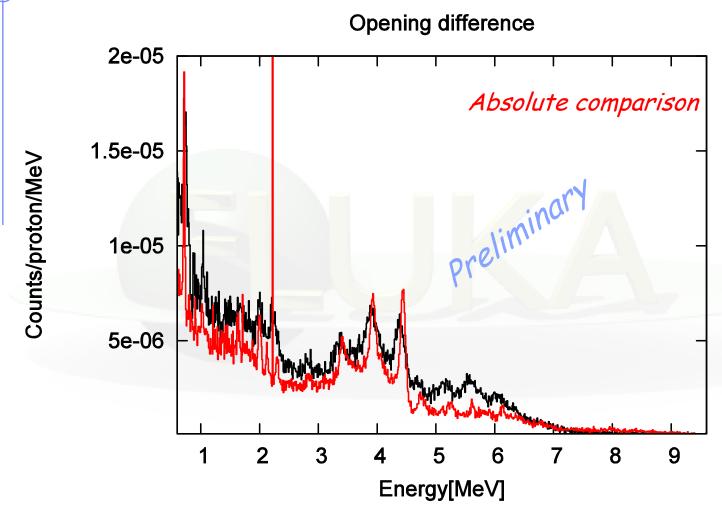
GSI: 90 deg photon yield by 310 MeV/n 12C in Water



310 MeV/n ¹²C ions on a Water target Photons at 90 deg Open circles FLUKA, stars exp.

Longitudinal position [mm]

Photon yields by 160 MeV p in PMMA



Energy spectrum of "photons" after background subtraction (collimator open - collimator closed) for 160 MeV p on PMMA. FLUKA red line, data black line (J.Smeets et al., WP3)

ENVISION WP6, April 2012

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