The INFN Treatment Planning System Project

Andrea Attili (INFN-Torino)
on behalf of the INFN-TPS collaboration

Physics for Health in Europe Workshop
CERN, 2-4 February 2010

Description of the Project

- The *Istituto Nazionale di Fisica Nucleare* (INFN) has developed for more than 15 years competences in the application of nuclear and particle physics to medicine.
- Several technologies developed by INFN for pure physics have been successfully applied to novel medical imaging and particle therapy.

Aim and features of the TPS INFN Project

- To develop an innovative Treatment Planning Systems (TPS) for therapy with ion beams.
- To produce a well defined, certified and ready-to-use deliverable in collaboration with an industrial partner → **IBA Group**, with the contribution of the TPS manufacturer **Elekta**.
- Collaboration with CNAO in Italy for testing.
- Scientific collaboration with other European Institutes for aspects concerning nuclear physics and radiobiology.

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TPS features

- The TPS is designed primarily for *carbon ions*, but with the flexibility to include other ion species and *protons*.
- It supports the *discrete active scanning* delivery mode.
- It includes the evaluation of 3D *physical dose* distributions and related 3D *RBE* distributions.
- It performs the *"biological" optimization* of the treatment.
- It accounts for *multi-tissue* heterogeneous biological response.
- It performs *multi-field* optimization.
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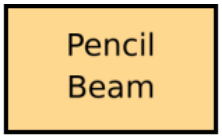
TPS *Kernel* features

- The kernel implements a fast "biological" dose evaluation engine based on a *pencil-beam* algorithm.
- The pencil beam uses pre-calculated *beam look-up tables*, organized in a *radio-biological database*, and a *WEPL* approximation.
- The look-up tables are derived from *radio-biological simulations* (to be validated through *experimental measurements*).
- The physical dose model of these simulations is based on *Fluka MC simulations*. The radio-biological model is based on an implementation of the *Local Effect Model* (LEM, versions 1,2 and 3, following the development of the GSI-Biophysics group).



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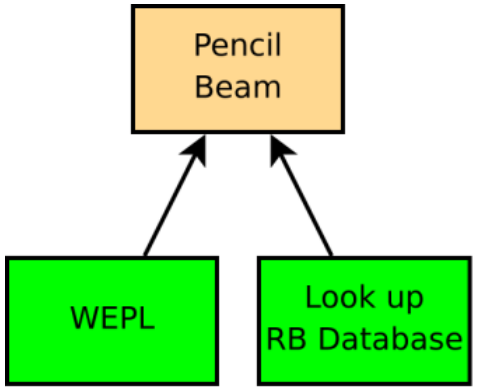

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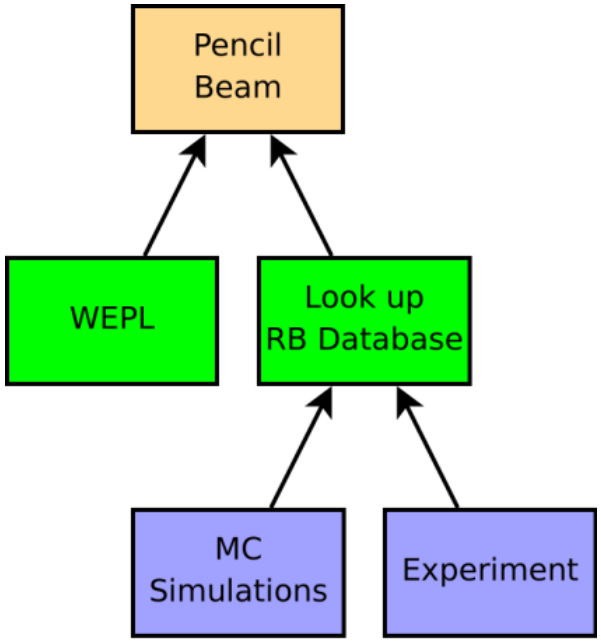

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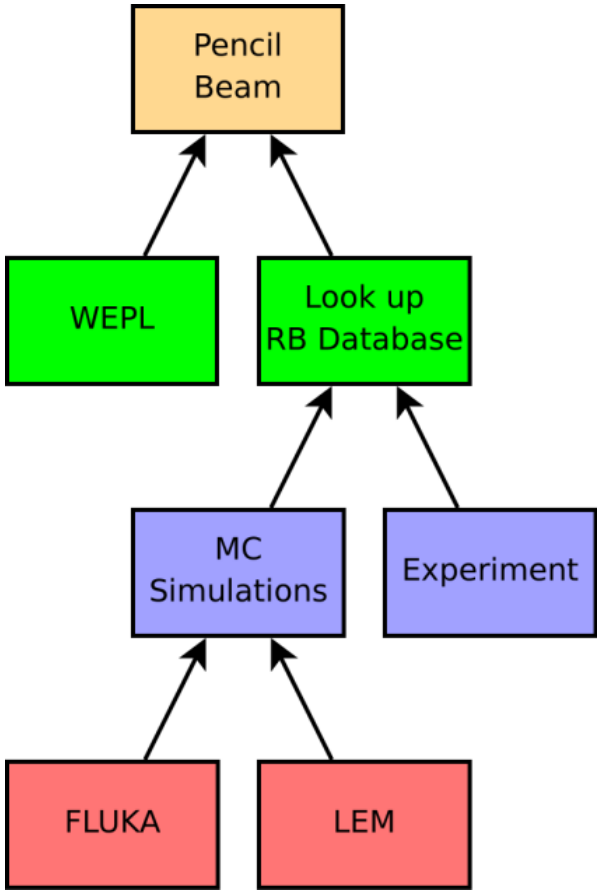

Project Data-Flow and Tasks

INFN TPS Tasks

- Nuclear Physics
- Experimental Radiobiology
- MC Simulations
- Optimization/Radiobiological Modeling
- "In beam" Monitoring

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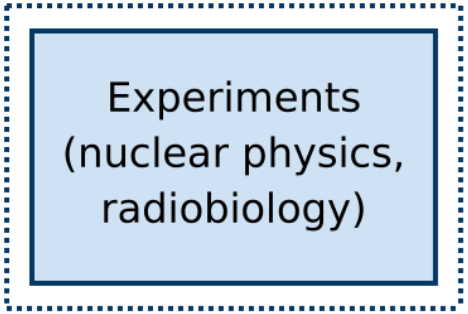

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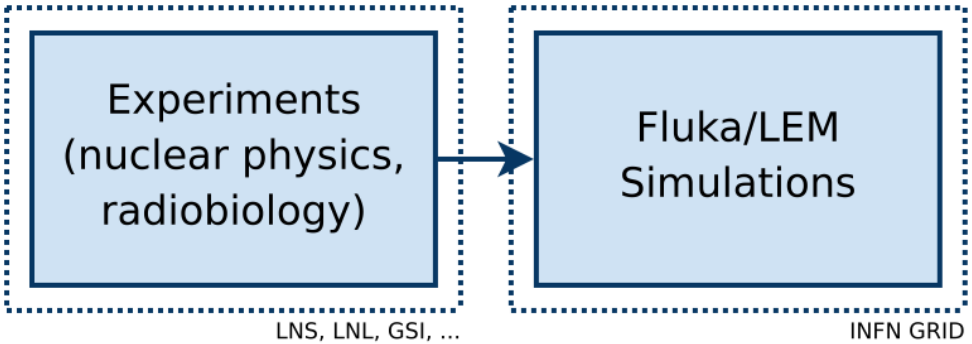

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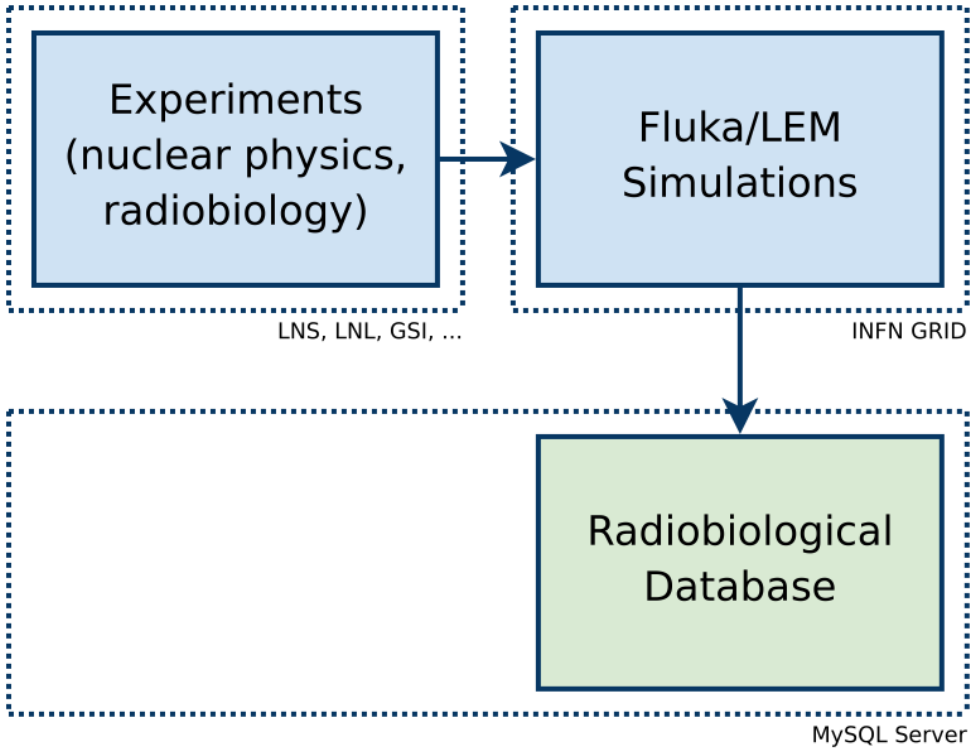

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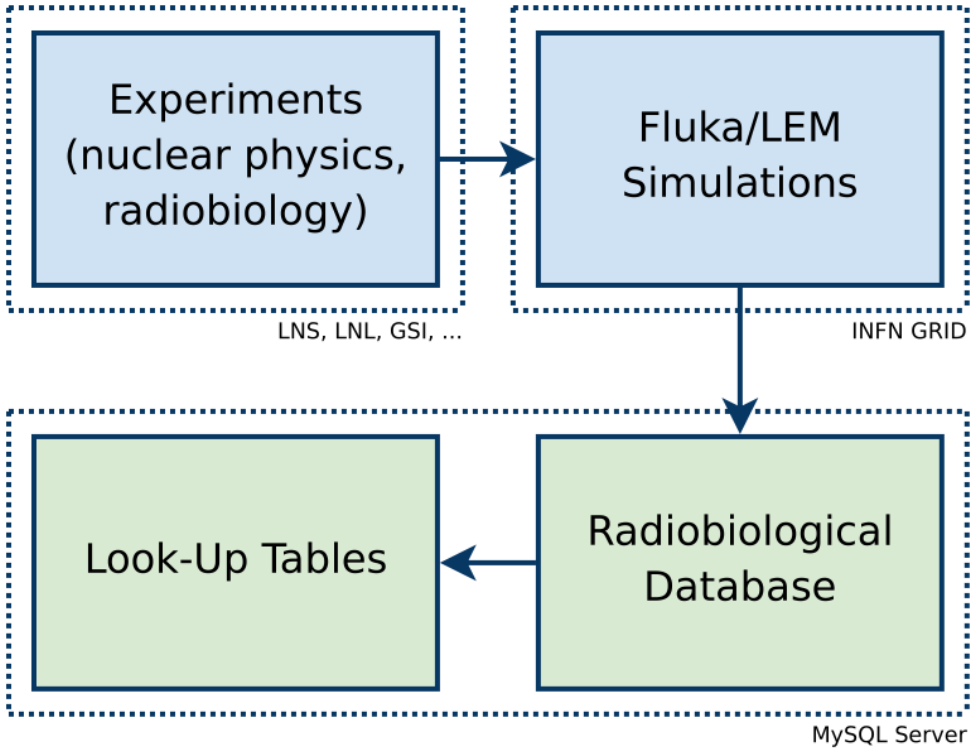

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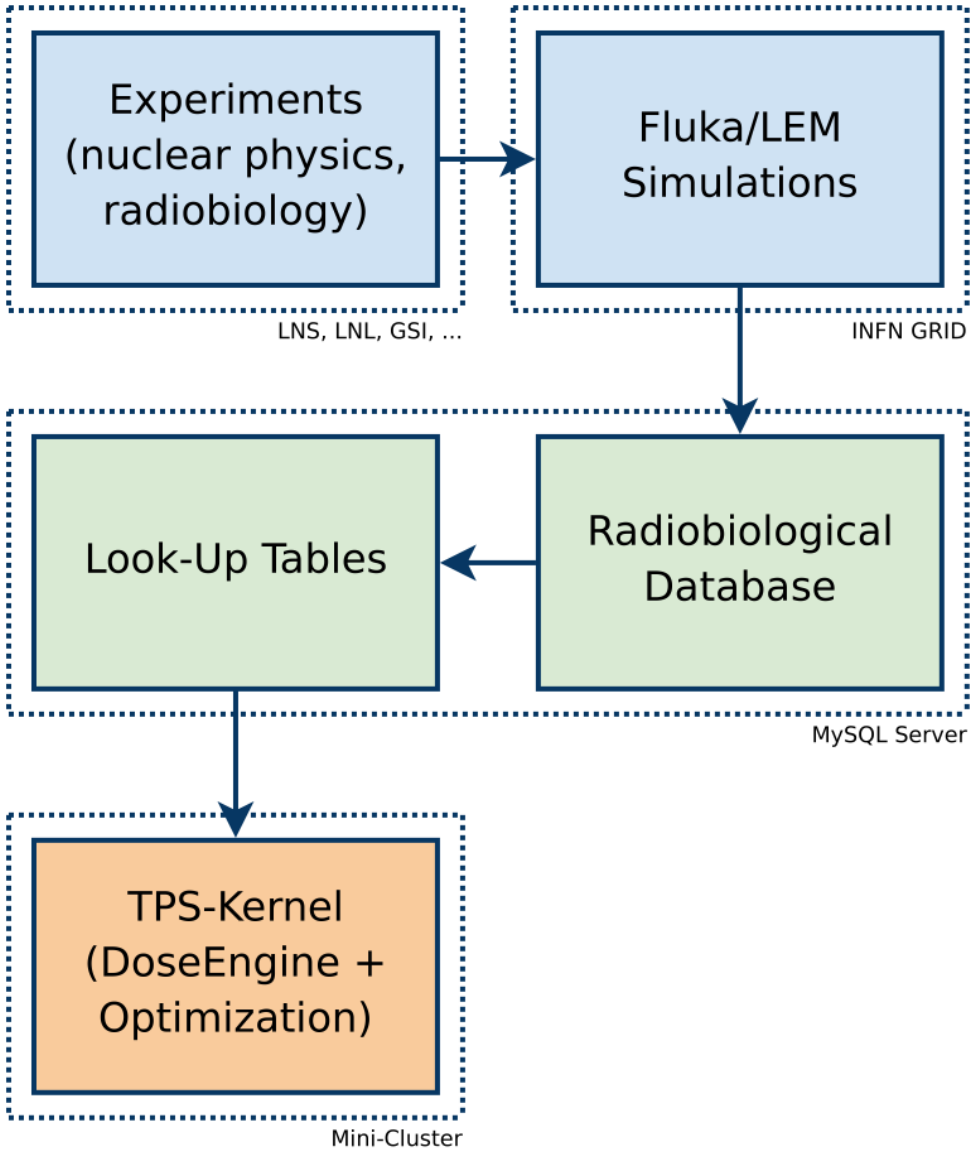

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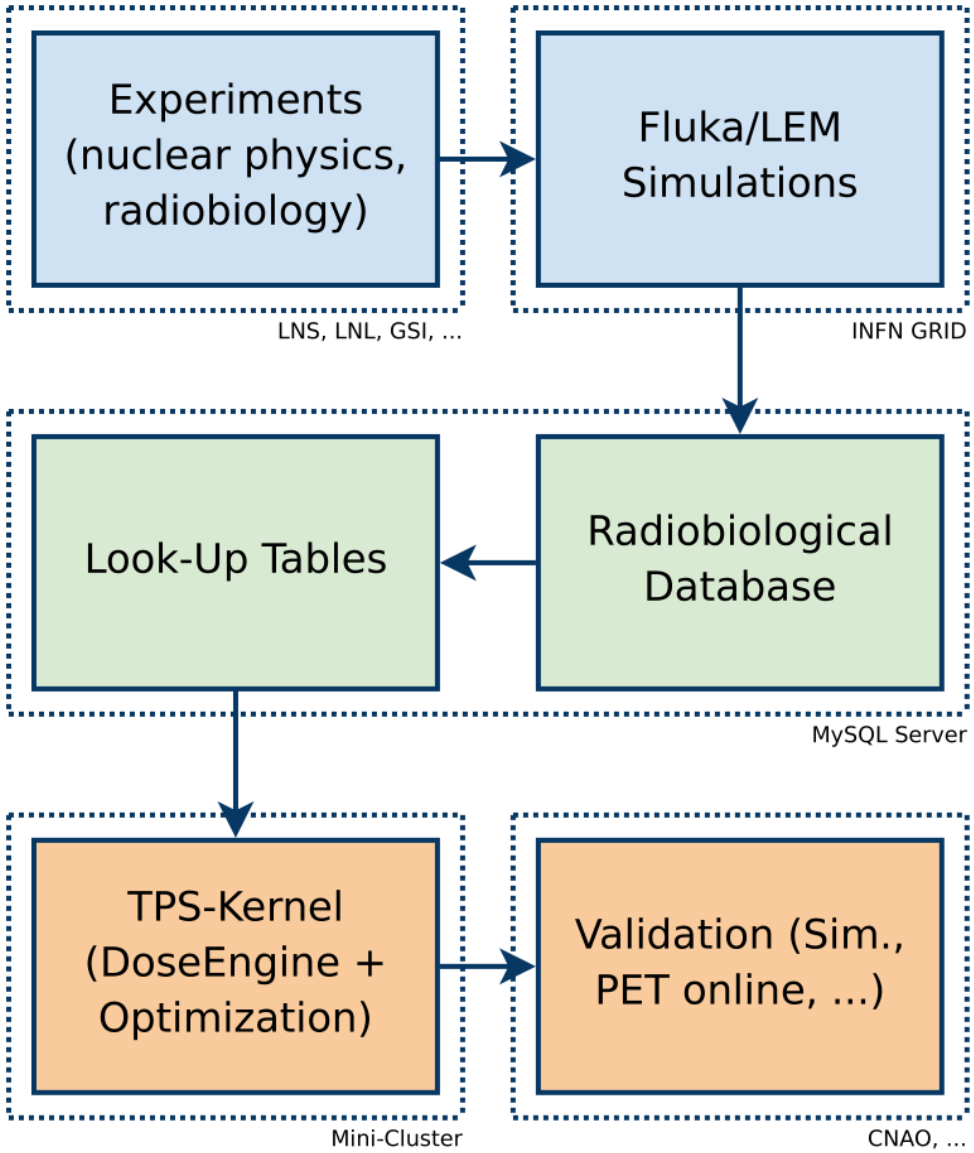

The INFN TPS Collaboration

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INFN – Sezione di Roma Tre and Università "Roma Tre", Dipartimento di Biologia, Roma

The Nuclear Physics Task

Main goals:

- Ion fragmentation experiments (mainly ^{12}C) $\rightarrow$ Up to now there is a lack of data systematic in literature of ^{12}C projectile fragmentation cross sections at energies around 20 MeV/A $\leq E/A \leq$ 400MeV/A (high interest for hadrontherapy).
- Modelling of the fragmentation processes.

Activities of the task

1. Collect new data on ion fragmentation.
2. Study of radioactive nuclei production.
3. Measurements at low energy in Italian laboratories and at higher energies in other laboratories.
4. Collaboration with MC experts to improve and validate nuclear interaction models.
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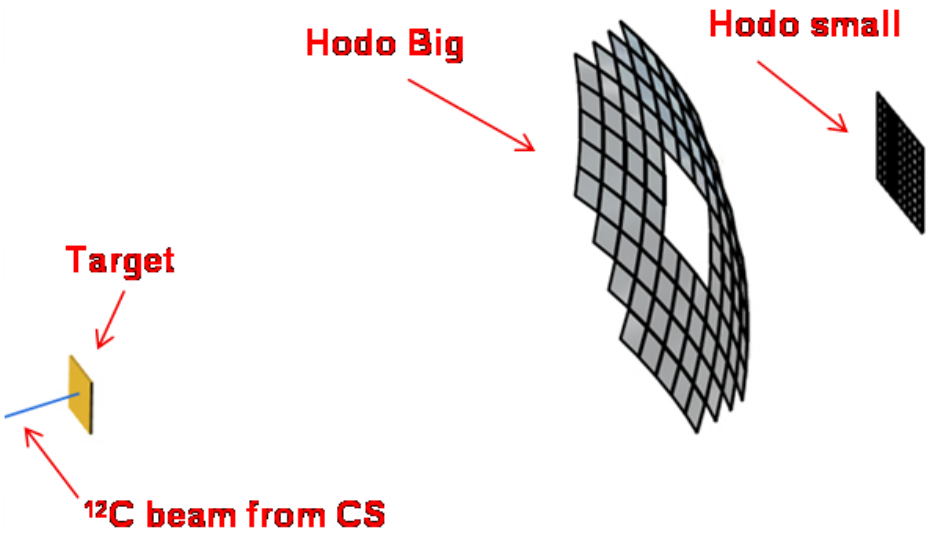
Nuclear Physics: Activities at LNS

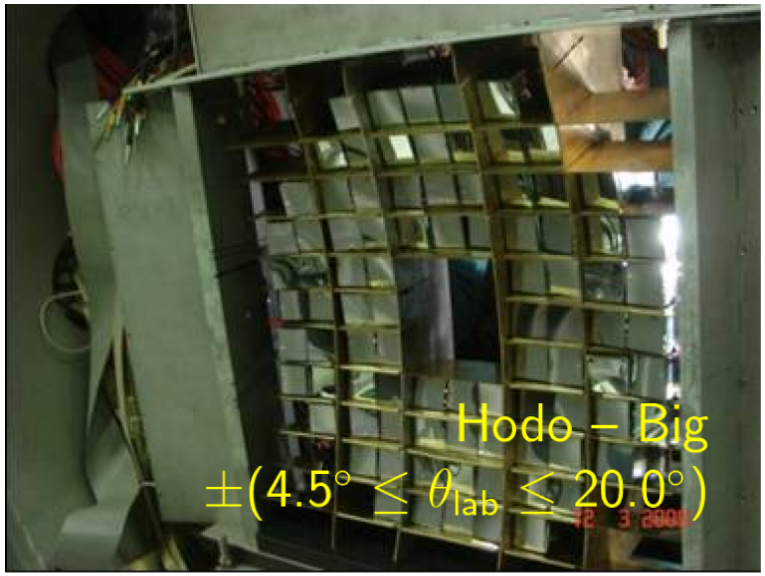
Nuclear fragmentation experiments performed using the Superconducting Cyclotron at the INFN's Laboratori Nazionali del Sud (LNS).

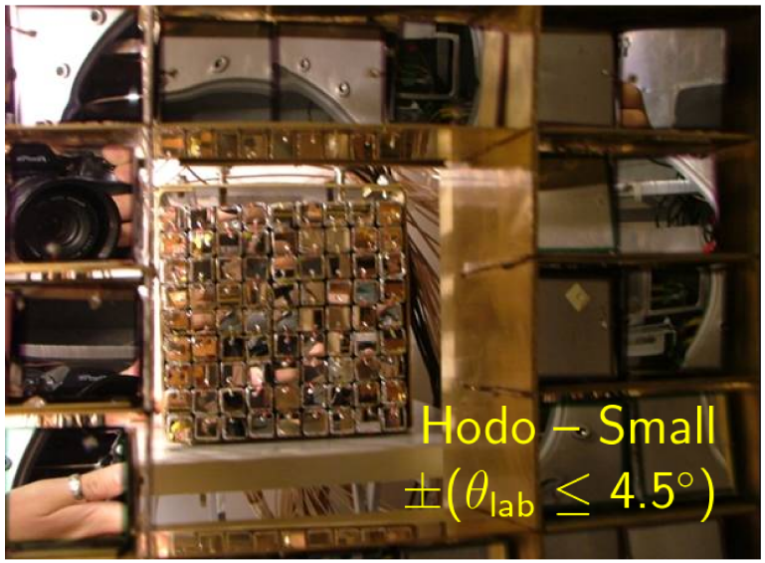
^{12}C at 32 and 64 MeV/n:

- $C + C$
- $C + CH_2$
- $C + Au$

Planned experiment for ^{12}C at 80 MeV/n.







Nuclear Physics: The FIRST Experiment

- FIRST → *Fragmentation of Ions Relevant for Space and Therapy.*
- Scientific collaboration between European Institutes: INFN, GSI, CEA and ESA.
- Experiment accepted at SIS-GSI.
- → Nuclear physics, space radiations, radiobiology, hadrontherapy.

Planned measurements (25 days)

- Total reaction cross sections (including all reaction channels).
- Double differential cross sections (angular distribution and multiplicity of fragments).
  - C + C @ 0.2, 0.4 and 1.0 GeV/u
  - C + Au @ 0.2 and 0.4 GeV/u
  - O + C @ 0.2 and 0.4 GeV/u
  - Fe + Si @ 0.5 and 1.0 GeV/u
  - Fe + C @ 1.0 GeV/u

Proposal of Experiment at SIS
Extensive study of nuclear reactions of interest for medical and space applications.

G.Cuttone, F.Marchetto, G.Raciti, E.Iarocci, V.Patera, C.Agodi, C.Sfienti, E.Rapisarda, M. De Napoli, F. Giacoppo, M.C. Morone, A. Sciubba, G.Battistoni, P.Sala, G.A.P.Cirrone, F.Romano
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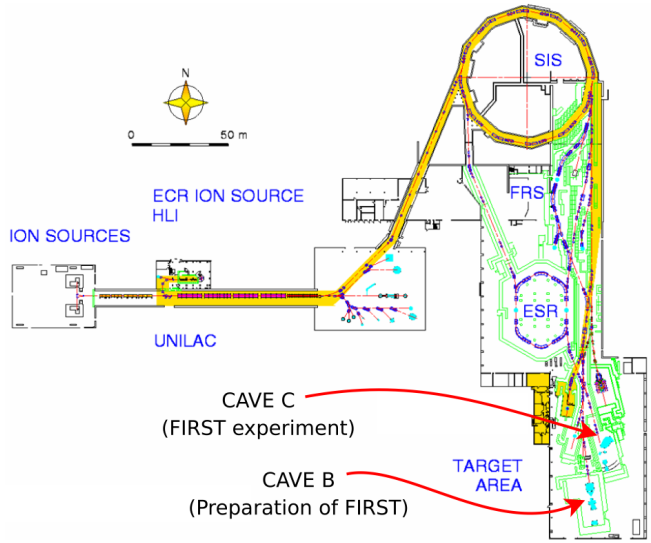
DSM/IRFU/SPhN CEA Saclay, IN2P3_Caen, Strasbourg, Lyon

M. Durante, D. Schardt, R. Pleskac, T. Aumann, C. Scheidenberger, A. Kelic, M.V.Ricciardi, K.Boretzky, M. Heil, H. Simon, M. Winkler
GSI

P. Nieminen, G. Santin
ESA

ACCEPTED



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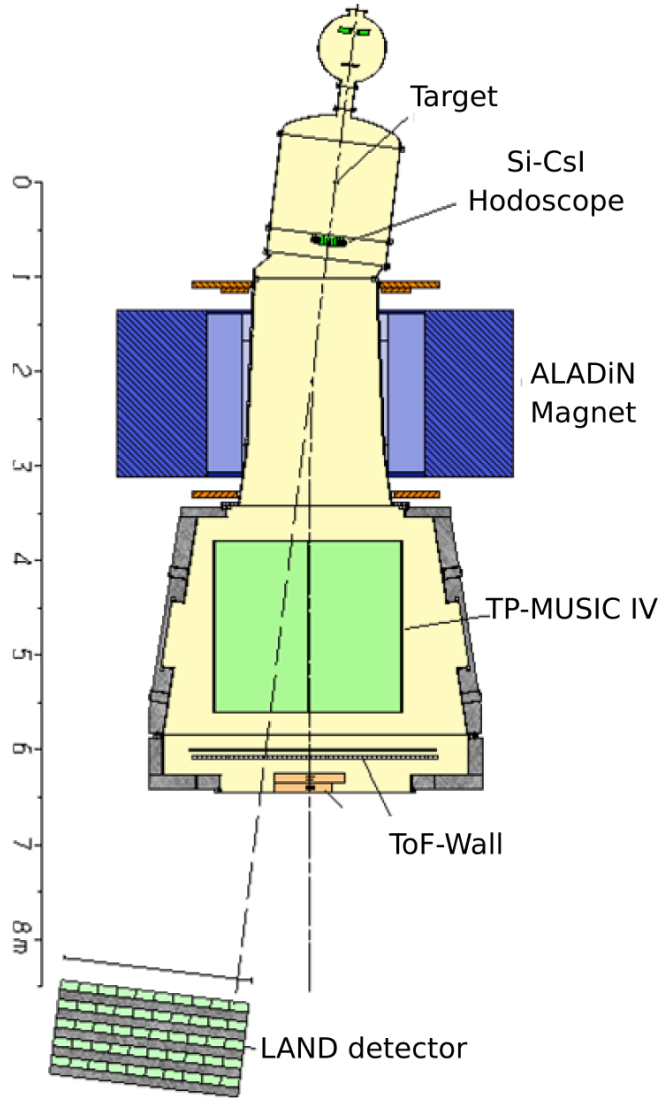

(See Poster of Till Tobias Böhlen.)

The Radiobiology Tasks

Main goals of the task:

1. Characterization of therapeutic beams.
2. Provision of reliable experimental data for the validation and further developments of the radiobiological model to be used in the TPS.
3. Study of the Radiosensibilization of gliomas for 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).

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- 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).

The Radiobiology Tasks

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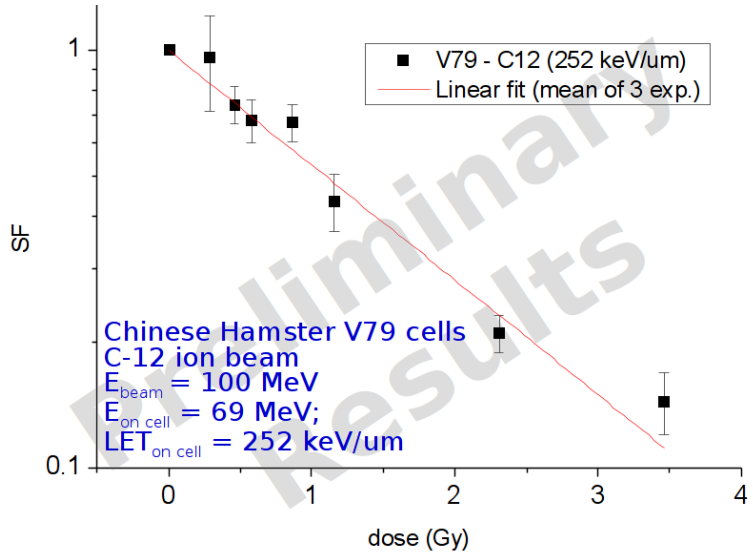
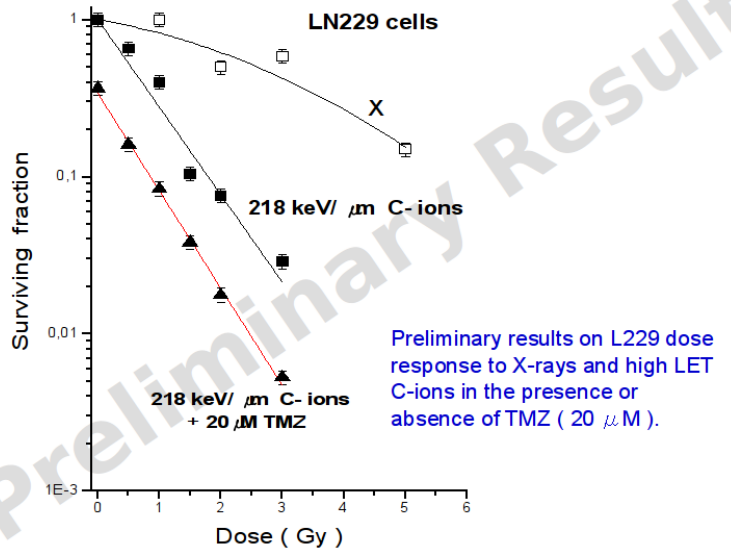
Co-60/Cs-137 gamma-ray sources; X-rays (250 kVp X-tube), *as reference radiations*.





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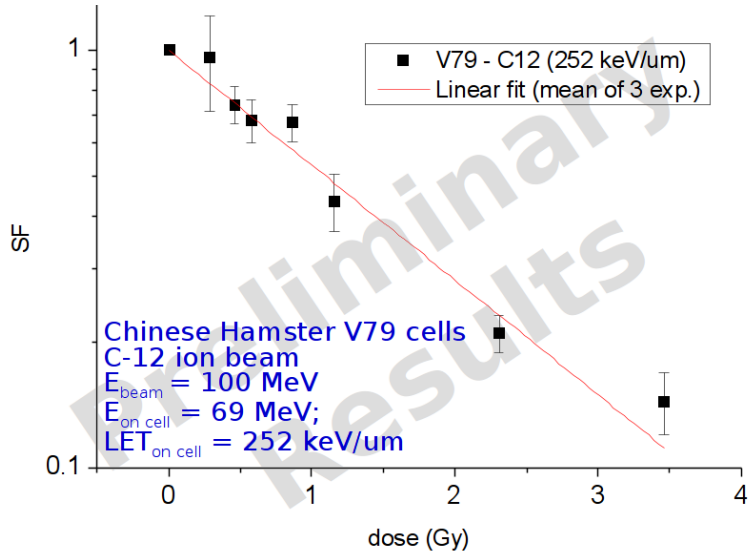

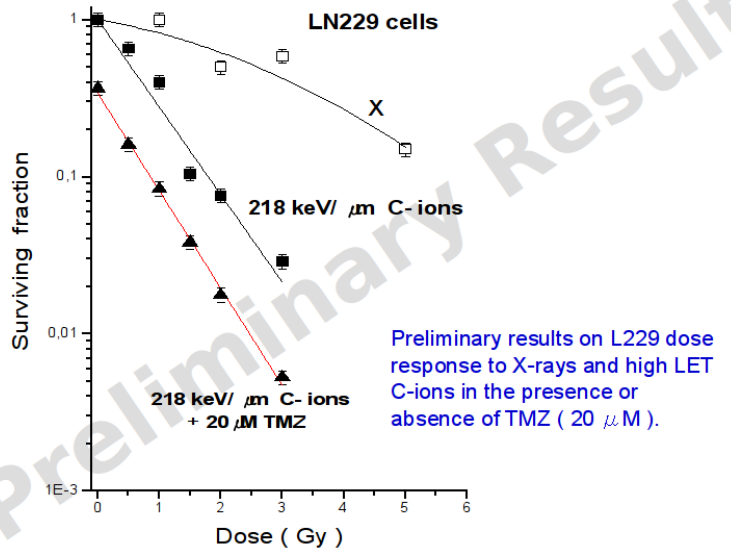

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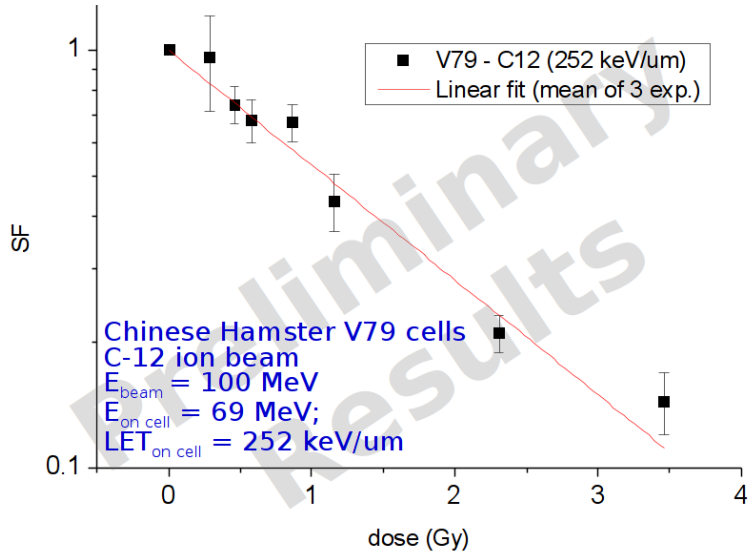

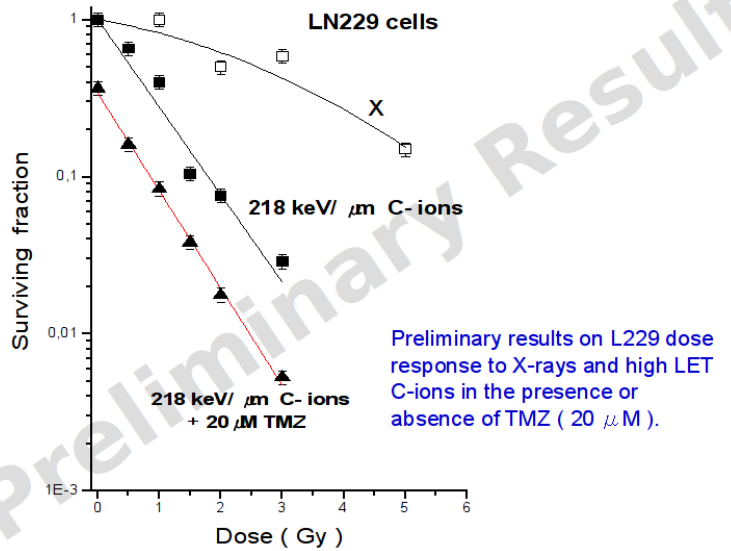

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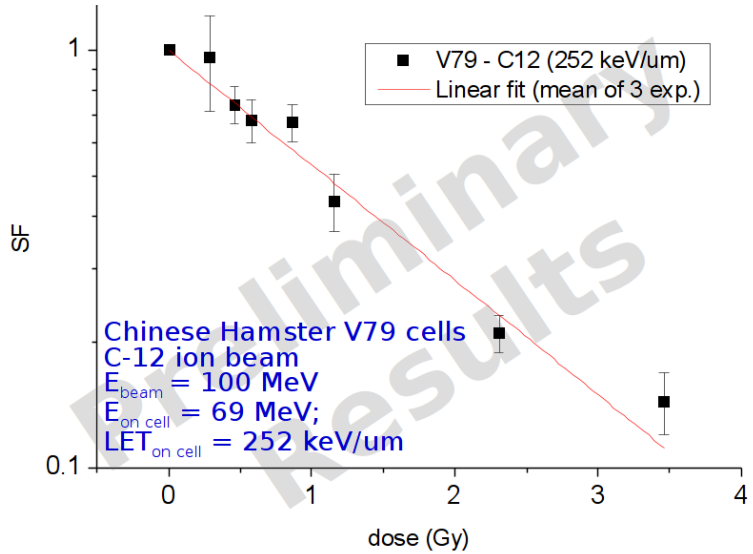
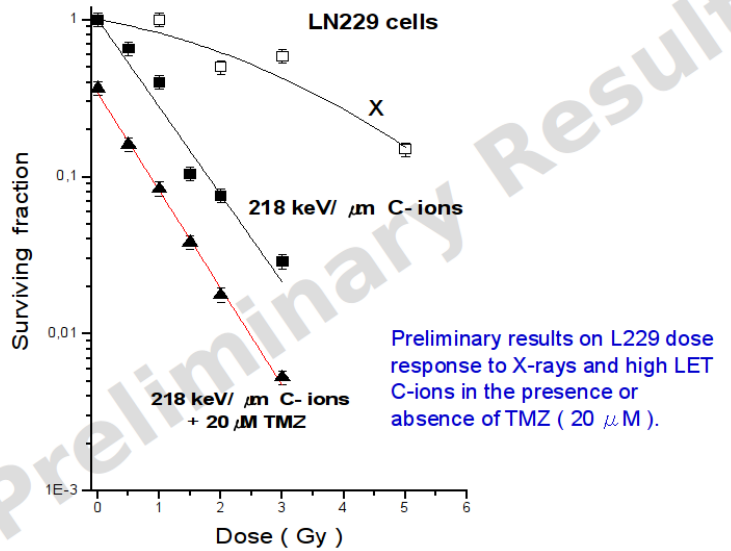




MC Simulations and Radiobiological Database

Pencil Beams:

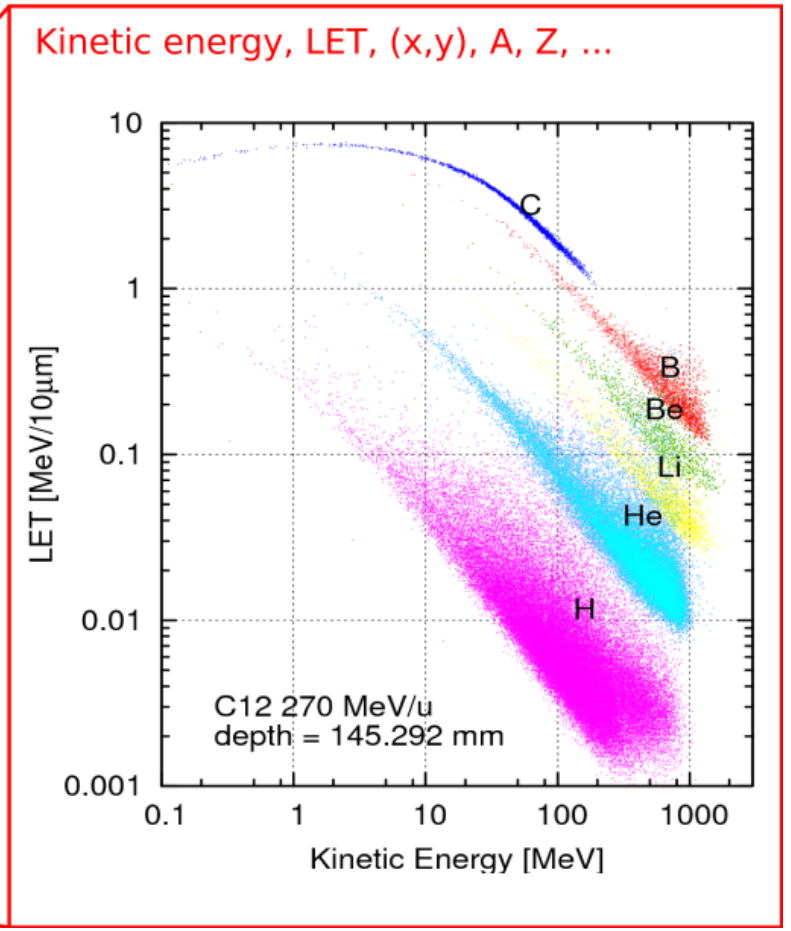
$E = 50, \ldots, 450$ MeV/n

FLUKA

Water Phantom

C12 Beam

Particles Data:



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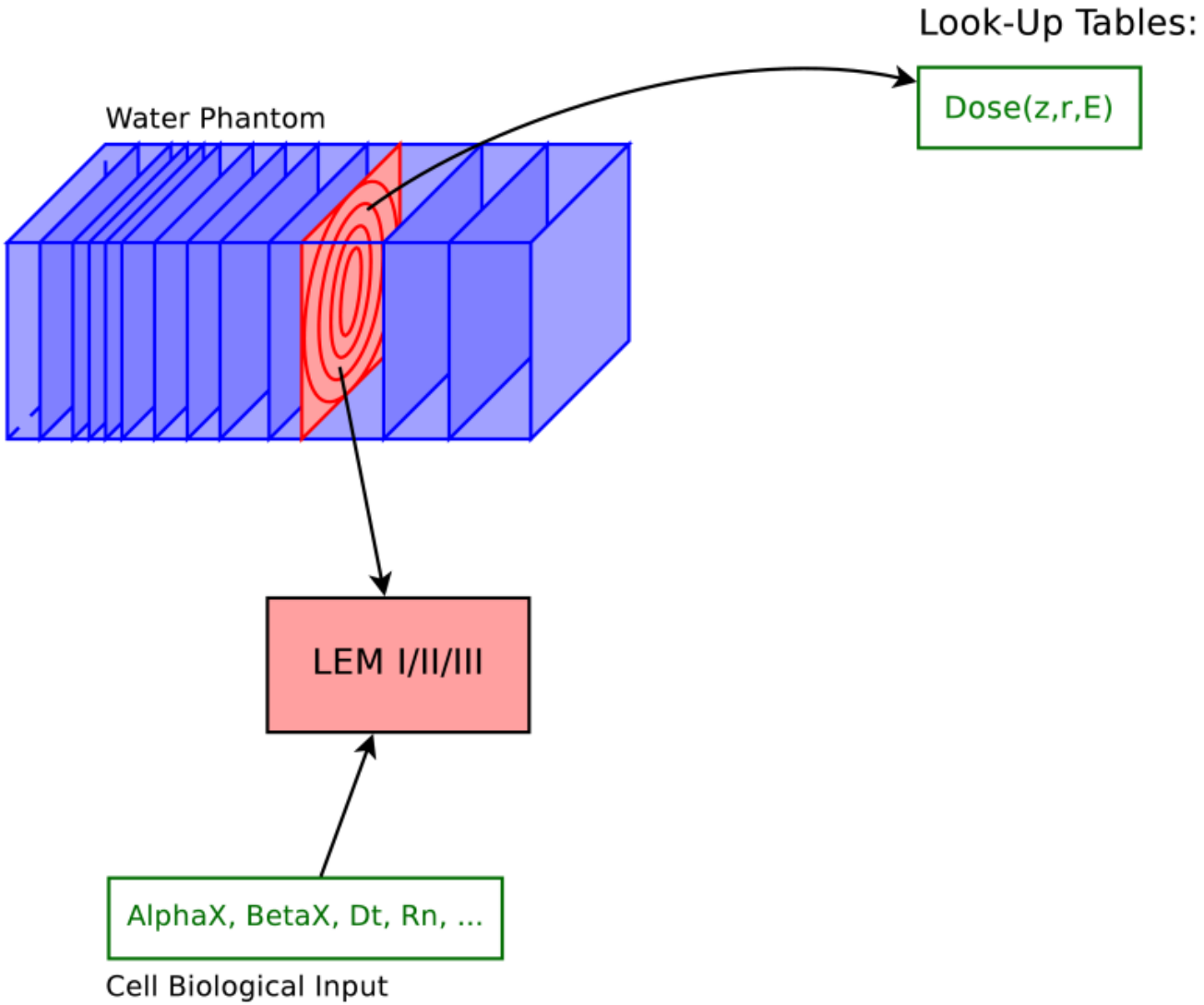


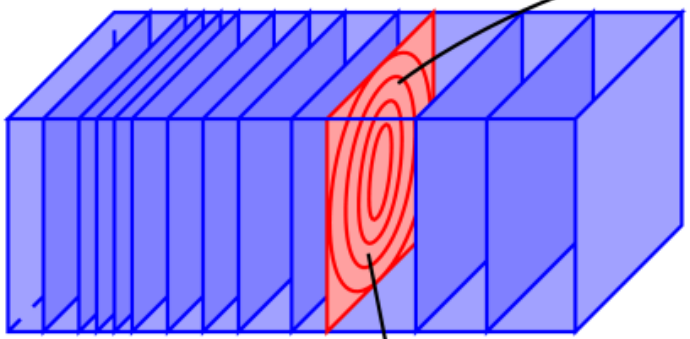
MC Simulations and Radiobiological Database

Look-Up Tables:

Dose(z,r,E)

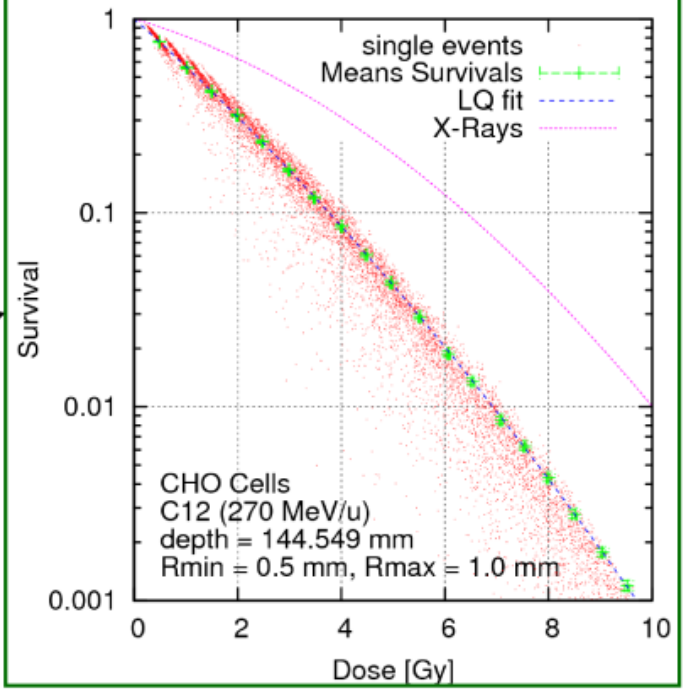
Alpha(z,r,E),Beta(z,r,E)

Water Phantom



Survivals Data:

Survival, Dose -> LQ fit



LEM I/II/III

Full Simulation

AlphaX, BetaX, Dt, Rn, ...

Cell Biological Input

MC Simulations and Radiobiological Database

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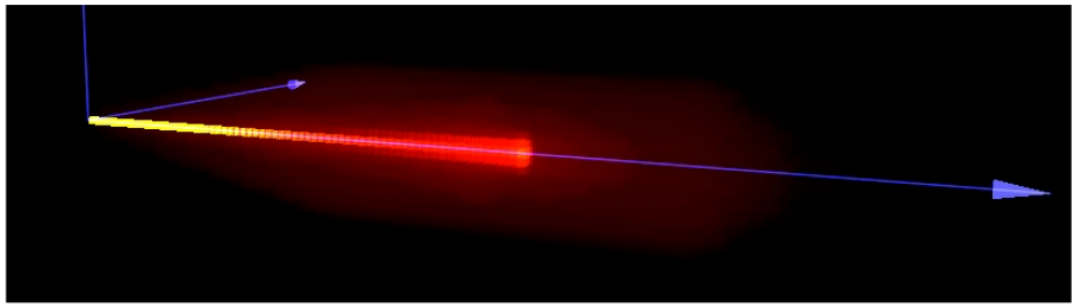
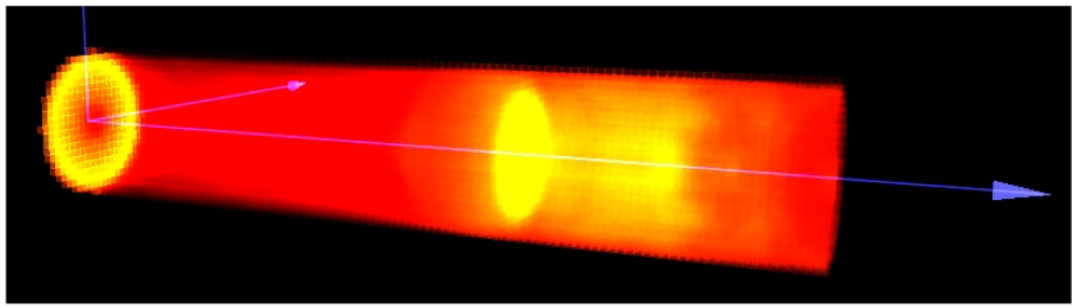


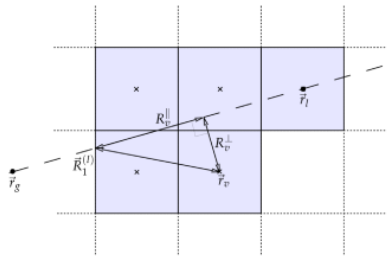
Dose of 270 Mev/n C ions



Alpha of 270 Mev/n C ions

"Biological" Beam Database

Ray-Tracing + WEPL



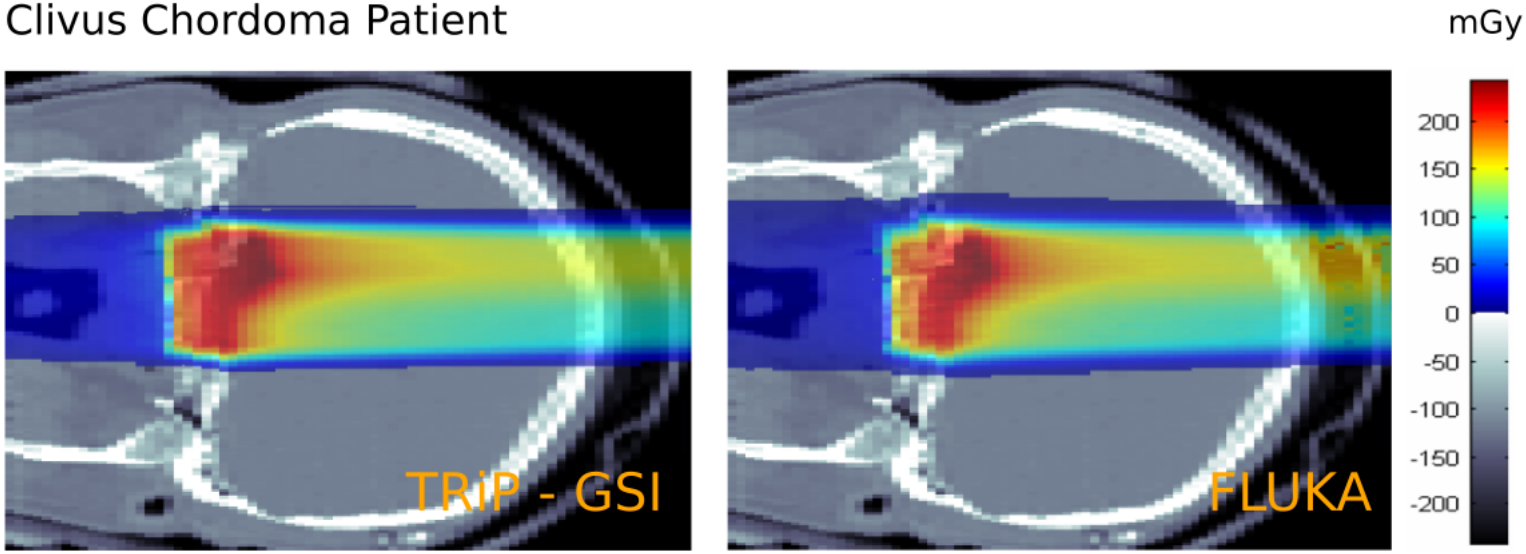
D_{ijkl}, α_{ijkl}, β_{ijkl}

TPS Kernel

Optimization

MC Simulation of Treatments

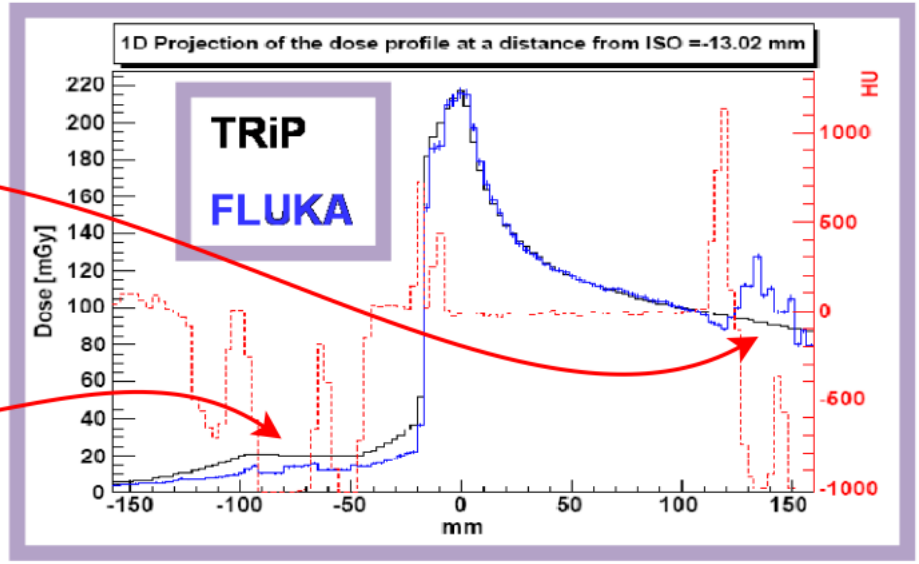
Clivus Chordoma Patient



Mairani, Ph.D Thesis; Mairani, Parodi et al, IEEE CR 2008

Prescribed Dose $\sim$ 0.25 Gy
MC $\sim 10^7$ ^{12}C in 10 runs

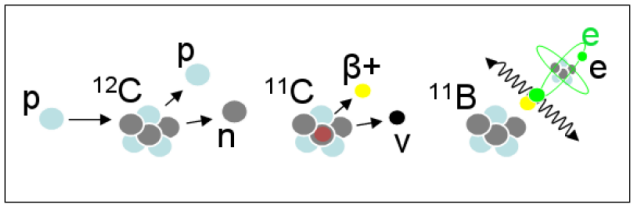
Inhomogeneities, dose-to-tissue and dose-to-water fragmentation tail

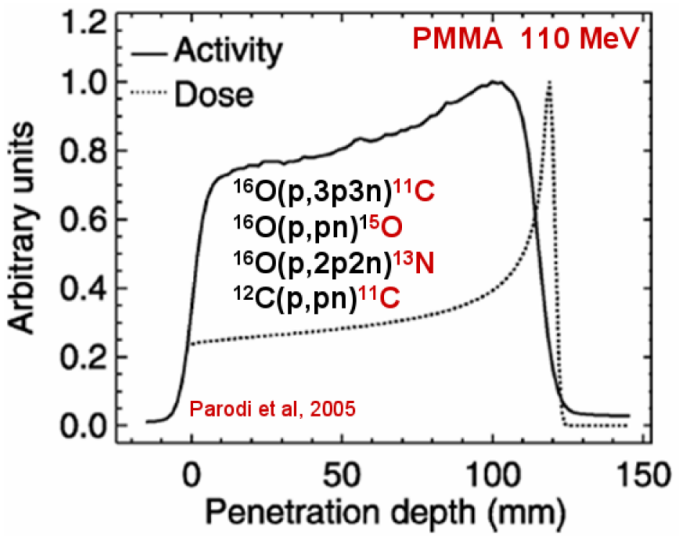


PET Online/Monitoring Tool

Exploitable benefits of ion-beams:

- Production of short-lived β^+ emitters active nuclides, by means of target nuclei fragmentation.
- Possibility of in-beam monitoring.
- Possibility of feed-back correction to Planning.





Goals of the task

1. Design, assembly and test of improved detection modules and readout for a dedicated PET System.
2. Improvement of the algorithm for the 3D reconstruction of $A(x, y, z)$
3. $A(x, y, z) \neq D(x, y, z) \rightarrow$ Realization of unfolding filters to extract the Dose.

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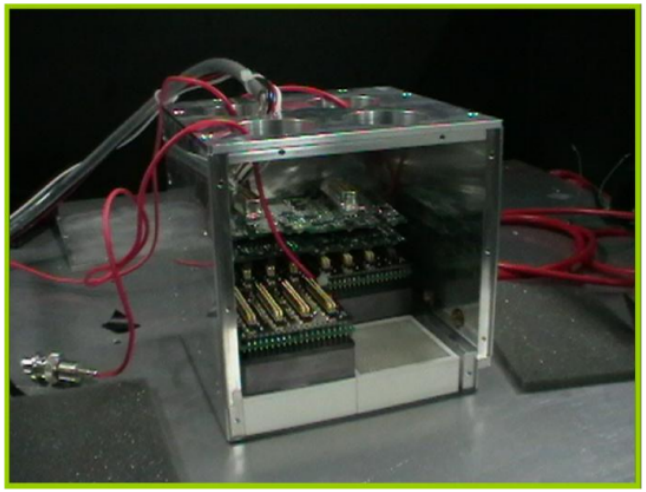
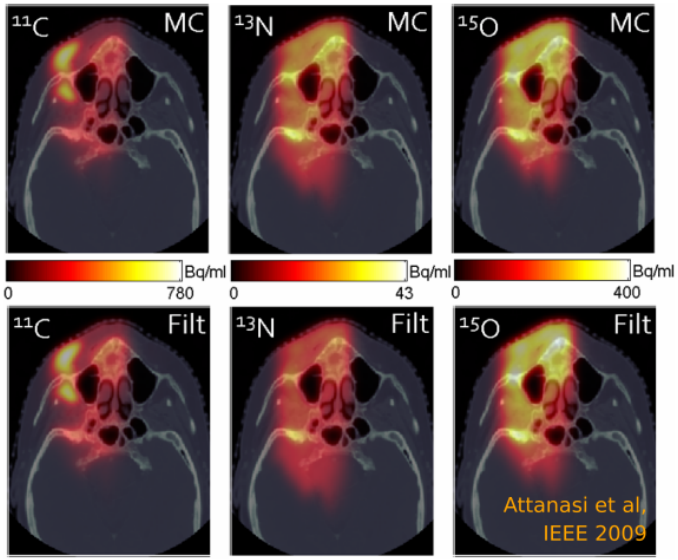


Prototype (4 vs. 4 modules of: LYSO + H8500)

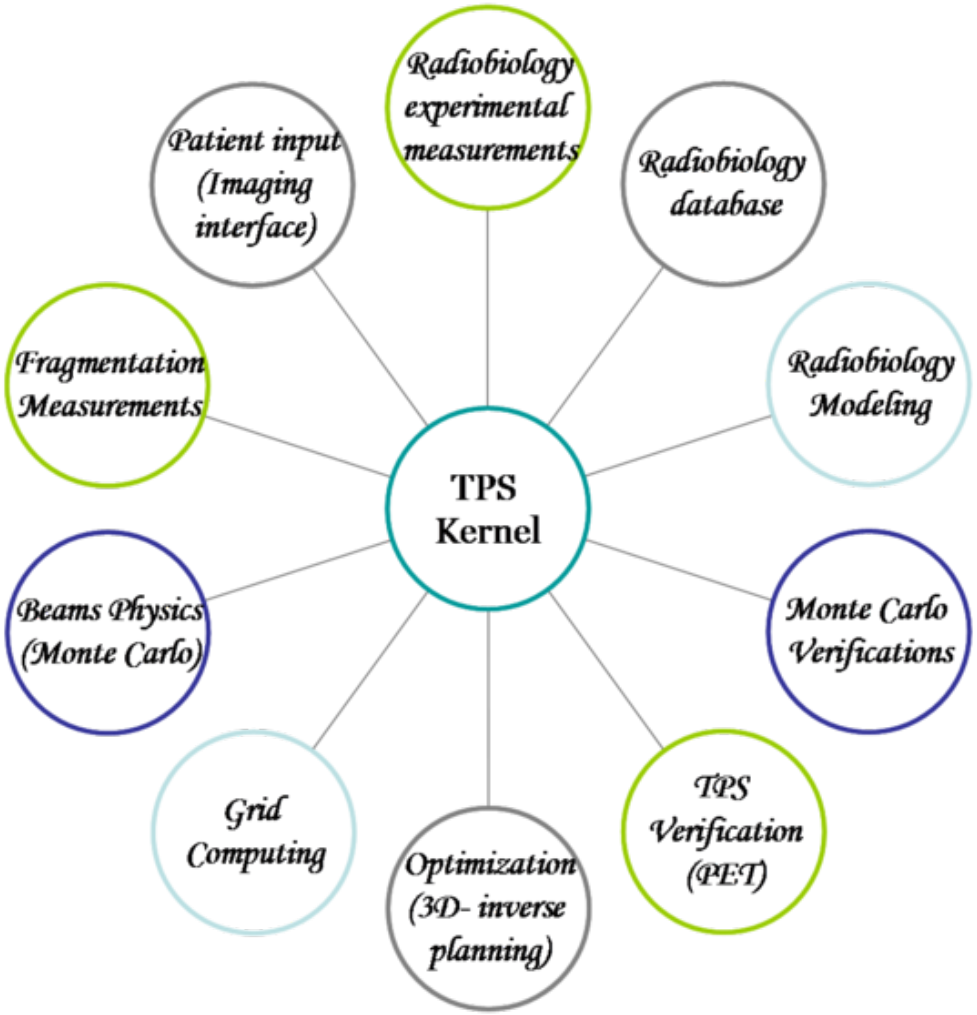


Clinical Investigation @ MGH
for head tumor with AP proton field

Conclusion: the Principal Milestones

	First year	Second year	Third year
Nuclear Physics	Measurement of ^{12}C fragmentation at 40-80 MeV	Setup of detector and measurements in the range 80-400 MeV	
Radiobiology	Measurement with ^{12}C beam up to 80 MeV (LNS)	Measurement with ^{12}C beam up to 400 MeV	
Optimization	Implementation of LEM Multifield optimization	Prod. of radiob. database for specific cless of a given clinical case Validation with full MC + LEM simulation	Data for several tumors 4D optimization Simulation tools
Monte Carlo	Interface with LEM Study of nuclear models Interface with CT	First prototype of validation tool	Production of validation tool Benchmarking activity
PET Monitoring	Start of inverse filter calculation Proc. of components for hardware developments	Assembling of new detector Data taking and inverse filter optimization	Characterization of the complete in-bema PET monitoring and integration with TPS

(3-Years Cooperation Agreement INFN-IBA)



Thank You!
(http://totlxl.to.infn.it/tpswiki)